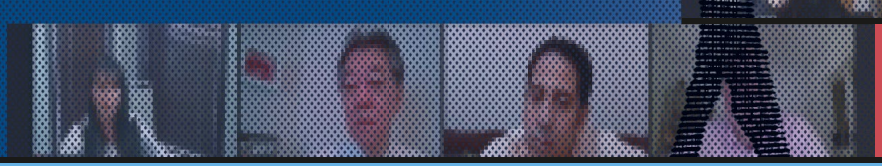
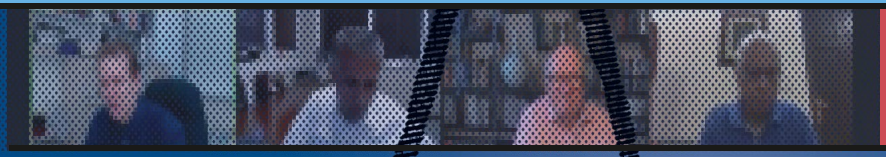
SCWD DIGITAL EXPERIENCE



11>13 December

FINAL PROGRAMME AND ABSTRACTS



2020

13TH INTERNATIONAL FULLY DIGITAL CONFERENCE ON CACHEXIA, SARCOPENIA & MUSCLE WASTING

Powered by

e-SPACE
Smart | Patient-centered | Accredited | Collaborative | Education
Global web-Conference

Follow us on www.cachexia.org

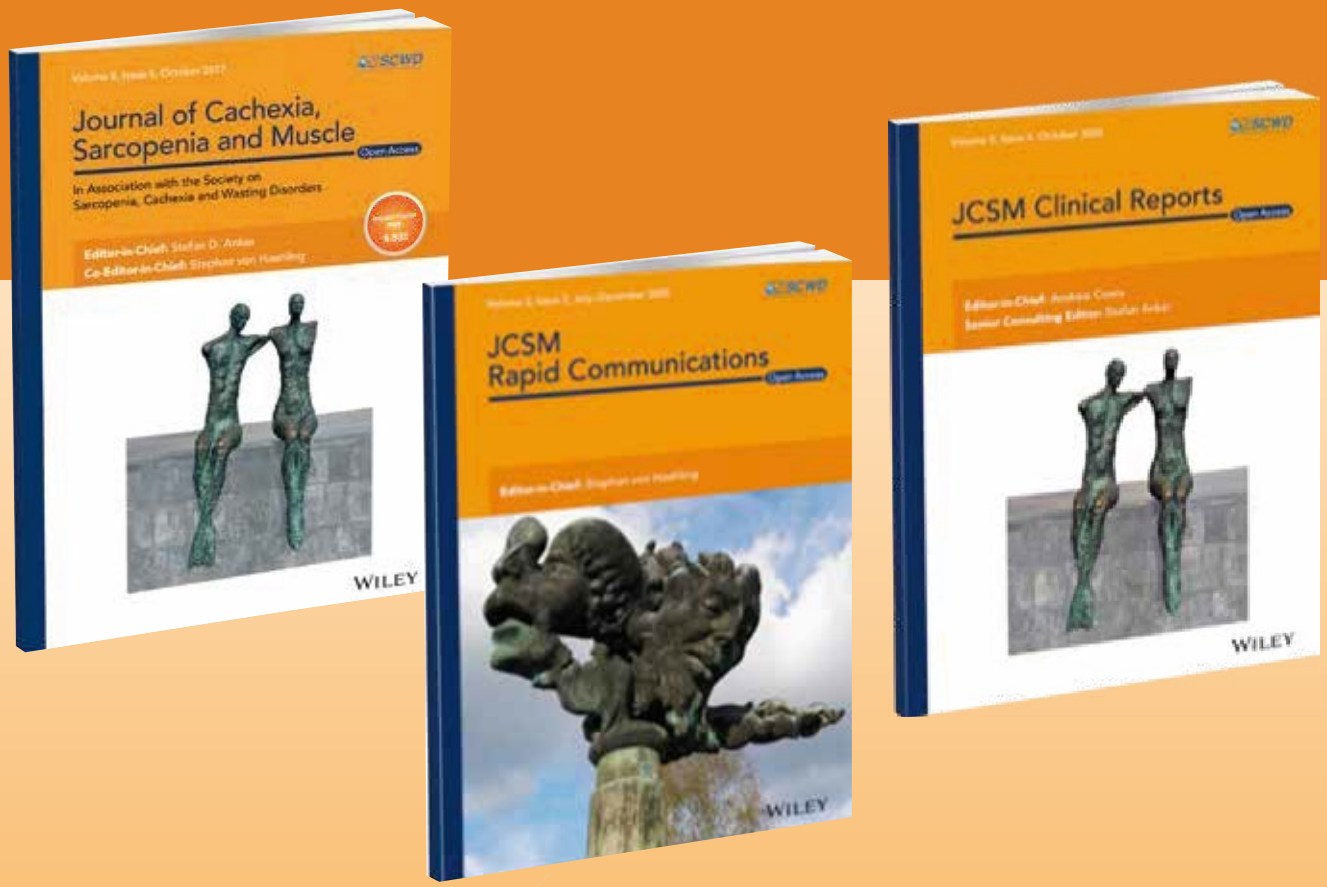
SCWD
SOCIETY ON SARCOPENIA, CACHEXIA AND WASTING DISORDERS

SCWD

SOCIETY ON SARCOPENIA, CACHEXIA AND WASTING DISORDERS

Journal of Cachexia, Sarcopenia and Muscle

Open Access



Presenting research and clinical topics on the typical aging progression and disease related changes.

Impact Factor 9.802

EDITED BY

Stefan D. Anker
& Stephan von Haehling

Submit your manuscript to JCSM: www.jcsm-journal.com

GENERAL INFORMATION 4

PROGRAM OVERVIEW 5

ABSTRACTS OF ORAL PRESENTATIONS, FRIDAY, DECEMBER 11, 2020 16

ABSTRACTS OF ORAL PRESENTATIONS, SATURDAY, DECEMBER 12, 2020 43

ABSTRACTS OF ORAL PRESENTATIONS, SUNDAY, DECEMBER 13, 2020 67

POSTER SESSIONS 84

POSTER ABSTRACTS 105

FACULTY 155

Organization

Society on Sarcopenia, Cachexia and Wasting Disorders (SCWD)
Vers-chez-les-Blanc, route du Jorat 67
c/o Intercomptas fiduciaire Sàrl,
1000 Lausanne 26
Switzerland

Congress Organizer

MedEd Global Solutions
27 rue Raffet
75016 Paris, France
Tel. +33 14 401 5181
Email: info@mededgs.com

Scientific Office:

Monika Diek
Charité - Campus Virchow-Klinikum
Augustenburger Platz 1
13353 Berlin, Germany
Tel.: +49 30 450 553 407
Email: conference2020@cachexia.info

Chairmen

Stefan D. Anker, Berlin, Germany
Andrew Coats, Norwich, UK
John E. Morley, St. Louis, MO, USA

International Scientific Committee

Stefan D. Anker, Berlin, Germany
Hidenori Arai, Obu, Japan
Josep M. Argilés, Barcelona, Spain
Vickie Baracos, Edmonton, Canada
Andrew Coats, Norwich, UK
Wolfram Doehner, Berlin, Germany
William Evans, Durham, NC, USA
Luigi Ferrucci, Baltimore, MD, USA
David J. Glass, Boston, MA, USA
Akio Inui, Kagoshima, Japan
Aminah Jatoi, Rochester, MN, USA
Kamyar Kalantar-Zadeh, Orange, CA, USA
John E. Morley, St. Louis, MO, USA
Maurizio Muscaritoli, Rome, Italy
Filippo Rossi-Fanelli, Rome, Italy
Florian Strasser, St. Gallen, Switzerland
Stephan von Haehling, Göttingen, Germany

A
13:00 – 14:10 CET

Opening session

(talk 1 and 2: 10 minutes, talk 3 and 4: 20 minutes)

Chairs: Stefan Anker, Germany
Andrew Coats, Australia
Mitja Lainscak, Slovenia

Introduction: 5 minutes

1. 13:05 – 13:15
SCWD
Stefan Anker, Germany

2. 13:15 – 13:25
JCSM and its daughter journals
Stephan von Haehling, Germany

3. 13:25 – 13:45
"Hippocrates" clinical science key note lecture
Clinical classification of cancer cachexia
Vickie Baracos, Canada

4. 13:45 – 14:05
"Prometheus" basic science key note lecture
The different shades of wasting: organ contributions to cancer cachexia
Stephan Herzig, Germany

14:05 – 14:10
Discussion

B
14:15 – 15:25 CET

Muscle wasting and cachexia in chronic illness

(each talk 12 minutes)

Chairs: Paola Costelli, Italy
Gustavo Duque, Australia
Giuseppe Rosano, UK

Introduction: 2 minutes

1. 14:17 – 14:29
Sarcopenia – Highlights 2020
John Morley, USA

2. 14:29 – 14:41
Muscle wasting and cachexia in stroke
Wolfram Doehner, Germany

3. 14.41 – 14:53
Muscle wasting and function in rheumatoid arthritis
Hidenori Arai, Japan

4. 14:53 – 15:05
Wasting of the heart causing heart failure (in cancer and beyond)
Andrew Coats, Australia

15:05 – 15:25
Discussion

15:30 – 16:25 CET

Joint Session SCWD – MASCC – EONS
Patient-centered cancer care to minimize anticancer treatment toxicity: a joint effort

Chairs: Stefan Anker, SCWD
Andreas Charalambous, EONS
Egidio Del Fabbro, MASCC

The power of nursing interventions in the comprehensive management of treatment-induced side-effects
Andreas Charalambous, Cyprus

Rehabilitation before, during, inbetween, and after anticancer treatment in curative and non-curative intent: how?!
Andrea L Cheville, USA

Cancer-disease and cancer-treatment related fatigue: multimodal evidenced-based transprofessional management
Florian Strasser, Switzerland

Evidenced-based and personalized dosing of exercise in patients with or after cancer
Joachim Wiskemann, Germany

C
16:30 – 17:40 CET

Cachexia and wasting in disorders of the skeletal muscle: from molecular mechanisms to treatment perspectives

(each talk: 12 minutes)

Chairs: Jason Doles, USA
Hanns Lochmüller, Canada
Jens Schmidt, Germany

Introduction: 2 minutes

1. 16:32 – 16:44
The metabolome and proteome of blood in patients with muscular dystrophy
Pietro Spitali, The Netherlands
2. 16:44 – 16:56
Gene therapy for muscular dystrophy: are we there yet?
Kevin M Flanigan, USA
3. 16:56 – 17:08
Motor neuron disease models
Jochen Weishaupt, Germany
4: 17:08 – 17:20
Engineering human iPS cells for muscle disease modelling and therapy development
Francesco Saverio Tedesco, UK

17:20 – 17:40
Discussion

D
16:30 – 17:40 CET

Thoracic CT imaging and other methods to assess muscle wasting in clinical and research sessions

(each talk: 12 minutes)

Chairs: Jeff Crawford, USA
Steven Heymsfield, USA
Annemie Schols, The Netherlands

Introduction: 2 minutes

1. 16:32 – 16:44
L3 and T4 landmarks predict mortality and key measures of function
Asmita Mishra, USA
2. 16:44 – 16:56
CT-based body composition measures in chronic lung disease and lung transplantation
Dmitry Rozenberg, Canada
3. 16:56 – 17:08
Use of thoracic CT imaging in clinical trials to assess muscle mass – the record so far
Vickie Baracos, Canada
4. 17:08 – 17:20
D3creatine dilution measured muscle mass in comparison to DXA lean mass for risk rediction in older men
Bill Evans, USA

17:20 – 17:40
Discussion

E
17:45 – 18:55 CET

Fat and inflammation in cachexia

(each talk: 12 minutes)

Chairs: Volker Adams, Germany
Denis Guttridge, USA
Maurilio Sampaolesi, Belgium

Introduction: 2 minutes

1. 17:47 – 17:59
Inflammation and muscle catabolism in patients with cachexia
T. Alp Ikizler, USA
2. 17:59 – 18:11
Organoid as a model to study adipose tissue remodeling in cancer cachexia
Miguel L. Batista Jr, USA
3. 18:11 – 18:23
Tumor-adipose-muscle crosstalk in cancer cachexia
Teresa Zimmers, USA
4. 18:23 – 18:35
The lipids-endotoxin interaction and inflammation in chronic illness
Stephan von Haehling, Germany

18:35 – 18:55
Discussion

F
17:45 – 18:55 CET

Cancer cachexia and muscle dysfunction

(each talk: 12 minutes)

Chairs: Andrea Bonetto, USA
Jeffrey Crawford, USA

Introduction: 2 minutes

1. 17:47 – 17:59
Mechanisms of doxorubicin toxicity in cardiac and skeletal muscle
Ashley Smuder, USA
2. 17:59 – 18:11
Advancing biomarkers in pancreatic cancer cachexia
Erin Talbert, USA
3. 18:11 – 18:23
Role of the BMP pathway in cancer cachexia
Roberta Sartori, Italy
4. 18:23 – 18:35
Mechanisms of chemotherapy-induced muscle wasting in cancer cachexia
Kate Murphy, Australia

18:35 – 18:55
Discussion

19:00 – 19:50 CET

Poster Session 1

(each presentation: 2 minutes + 2 minutes discussion)

Cachexia - mechanisms basic and animal models I
Posters 1-01 – 1-10

Chairs: Gustavo Nader, USA
Jochen Springer, Germany

19:00 – 19:50 CET

Poster Session 2

(each presentation: 2 minutes + 2 minutes discussion)

Nutrition an Appetite
Posters 6-01 – 6-10

Chairs: Nicolaas Deutz, USA
Alessandro Laviano, Italy

19:55 – 20:45 CET

Poster Session 3

(each presentation: 2 minutes + 2 minutes discussion)

Muscle wasting & Sarcopenia - mechanisms I
Posters 5-01 – 5-12

Chairs: Scott Brakenridge, USA
Jason Doles, USA

19:55 – 20:45 CET

Poster Session 4

(each presentation: 2 minutes + 2 minutes discussion)

Diagnosis of Sarcopenia I
Posters 4-01 – 4-12

Chairs: Josep Argiles, Spain
Jürgen Bauer, Germany

13:00 – 14:10 CET

Poster Session 5

(each presentation: 2 minutes + 2 minutes discussion)

Cachexia – mechanisms basic and animal models II
Posters 1-11 – 1-23

Chairs: Didier Attaix, France
Maurilio Sampaolesi, Belgium

13:00 – 14:10 CET

Poster Session 6

(each presentation: 2 minutes + 2 minutes discussion)

Cancer Cachexia
Posters 3-01 – 3-16

Chairs: Mauricio Berriel Diaz, Germany
Paola Costelli, Italy

G
14:15 – 15:25 CET

Novel research finding in muscle wasting disorders and cachexia

(each talk: 12 minutes)

Chairs: Didier Attaix, France
Xiaonan Wang, USA
David Waning, USA

Introduction: 2 minutes

1. 14:17 – 14:29
Novel players that control muscle mass in disease
Marco Sandri, Italy

2. 14:29 – 14:41
The role of glucagon in tumor-induced muscle wasting of the insects and mammals
Wei Roc Song, China

3. 14:41 – 14:53
Autophagy exacerbates muscle wasting in cancer cachexia and impairs mitochondrial function
Antonio Zorzano, Spain

4. 14:53 – 15:05
Impaired ribosome biogenesis as an underlying cause of muscle wasting
Gustavo A. Nader, USA

15:05 – 15:25
Discussion

H
14:15 – 15:25 CET

Hot topics in skeletal muscle plasticity and muscle wasting

(each talk: 12 minutes)

Chairs: Scott Brakenridge, USA
Sven Geißler, Germany
John Morley, USA

Introduction: 2 minutes

1. 14:17 – 14:29
Muscle stem cell mechanotransduction and TGF-beta signalling in muscle regeneration and fibrosis
Richard Jaspers, The Netherlands

2. 14:29 – 14:41
Is muscle fibre size constrained by oxidative capacity?
Hans Degens, UK

3. 14:41 – 14:53
Therapeutic potential of slow muscle programming for muscle diseases
Gordon Lynch, Australia

4. 14:53 – 15:05
Cell therapy strategies for skeletal muscle injury
Tobias Winkler, Germany

15:05 – 15:25
Discussion

15:30 – 16:25 CET

Industry Session

Update on clinical research on sarcopenia

Chair: Bruno Vellas, France

15:30 – 15:45
Current status of clinical research targeting Sarcopenia
Roger Fielding, USA

15:45 – 16:00

SARA program: the use of BIO101, a MAS receptor agonist, for the treatment of sarcopenia
Cendrine Tourette, France

16:00 – 16:25
Discussion
Bruno Vellas, France
Roger Fielding, USA
Waly Dioh, France
Sam Agus, USA

Sponsored by Biophytis

I
16:30 – 17:40 CET

Body weight control in humans

(each talk: 12 minutes)

Chairs: Swarnali Acharyya, USA
Josep Argiles, Spain
Aminah Jatoi, USA

Introduction: 2 minutes

1. 16:32 – 16:44
How to screen for cachexia in humans
Richard Skipworth, UK

2. 16:44 – 16:56
Cross-talk between bone and muscle in metastatic cancer
Theresa Guise, USA

3. 16:56 – 17:08
Connecting diet, metabolism, and tumor growth in human cachectic patients with cancer
Marcus Goncalves, USA

4. 17:08 – 17:20
GDF-15 is a key regulator in cancer cachexia
Bei Zhang, USA

17:20 – 17:40
Discussion

J
16:30 – 17:40 CET

Automated body composition analysis: using efficiently biomarkers and CT scans

(each talk: 12 minutes)

Chairs: Jerome Feige, Switzerland
Francesco Landi, Italy
Andrea Maier, Australia

Introduction: 2 minutes

1. 16:32 – 16:44
Biomarkers of physical frailty and sarcopenia – BIOSPHERE Study
Emanuele Marzetti, Italy

2. 16:44 – 16:56
Biomarkers to assess skeletal muscle loss and malnutrition
Adrian Slee, UK

3. 16:56 – 17:08
Clinical applications of automated CT scans
Bette Caan, USA

4. 17:08 – 17:20
Looking to the future of automated analysis
Mirza Faisal Beg, Canada

17:20 – 17:40
Discussion

K
17:45 – 18:55 CET

Pharmacological reverse of cancer cachexia

(each talk: 12 minutes)

Chairs: James Carson, USA
David Glass, USA
Teresa Zimmers, USA

Introduction: 2 minutes

1. 17:47 – 17:59
Lipocalin-2 regulates appetite and neurocognitive decline during cancer cachexia
Daniel Marks, USA

2. 17:59 – 18:11
A selective inhibitor of p38b MAPK abrogates muscle wasting and prolongs survival of tumor-bearing mice
Yi-Ping Li, USA

3. 18:11 – 18:23
GDF15 neutralization reverses cancer cachexia and restores physical performance
Zhidan Wu, USA

4. 18:23 – 18:35
Inhibition of activin-like kinase 4/5 attenuates cancer cachexia associated muscle wasting
Stef Levolger, The Netherlands

18:35 – 18:55
Discussion

L
17:45 – 18:55 CET

Sarcopenia and cachexia in renal disease

(each talk: 12 minutes)

Chairs: Luigi Ferrucci, USA
Stephan von Haehling, Germany
Hidetaka Wakabayashi, Japan

Introduction: 2 minutes

1. 17:47 – 17:59
The role of IL-1 in experimental CKD cachexia: Potential for novel therapy
Robert Mak, USA

2. 17:59 – 18:11
Kidney cachexia or protein energy wasting?
Kamyar Kalantar-Zadeh, USA

3. 18:11 – 18:23
Clinical phenotype of cachexia in kidney disease
Joanne Reid, UK

4. 18:23 – 18:35
Sarcopenia in chronic kidney disease
Cynthia Delgado, USA

18:35 – 18:55
Discussion

19:00 – 19:50 CET

Statistical Seminar

Coordinated by:
Jennifer Le-Rademacher, USA
Ruta Brazauskas, USA

19:00 – 19:30
Analysis of observational studies
Jennifer Le-Rademacher, USA
Ruta Brazauskas, USA

19:30 – 19:50
Discussion

Although clinical trials are the gold standard for evaluating experimental treatments, in settings where clinical trials may not be feasible or ethical, observational studies are the next best option. Due to the observational nature of this type of studies, there are potential selection bias or confounding factors that need to be accounted for when assessing treatment effect or comparing groups of patients. In this seminar, we will introduce various types of observational studies, common pitfalls, and common analysis approaches for observational studies. Specifically, we will focus on the pros and cons of two analysis approaches: regression modeling versus matched pairs (clusters) comparison. We will use real data examples to illustrate these methods.

19:00 – 19:50 CET

Poster Session 7

(each presentation: 2 minutes + 2 minutes discussion)

Physical activity & training
Posters 7-01 – 7-08

Chairs: Volker Adams, Germany
Fabio Penna, Italy

19:55 – 20:45 CET

Poster Session 9

(each presentation: 2 minutes + 2 minutes discussion)

Therapeutic development (clinical) + Therapeutic development (pre-clinical)I
Posters 8-01 – 8-08

Chairs: Jose Garcia, USA
Mitja Lainscak, Slovenia

19:55 – 20:45 CET

Poster Session 10

(each presentation: 2 minutes + 2 minutes discussion)

Muscle wasting & Sarcopenia - mechanisms II
Posters 5-13 – 5-24

Chairs: Srinivasan Dasarathy, USA
David Waning, USA

M
14:15 – 15:25 CET

Fat tissue and lipid metabolism

(each talk: 12 minutes)

Chairs: Roger Fielding, USA
Stephan Herzig, Germany
Jochen Springer, Germany

Introduction: 2 minutes

1. 14:17 – 14:29
Lipid metabolism in cancer cachexia
Maria Rohm, Germany

2. 14:29 – 14:41
Adipose tissue remodeling in human cancer cachexia
Marilia Seelaender, Brazil

3. 14:41 – 14:53
Fat tissues and prognosis in human chronic illness
Markus Anker, Germany

4. 14:53 – 15:05
Tumor-derived mediators of cancer cachexia
Mauricio Berriel Diaz, Germany

15:05 – 15:25
Discussion

N
14:15 – 15:25 CET

Difference in diagnostic criteria for sarcopenia and sarcopenic obesity

(each talk: 12 minutes)

Chairs: Bill Evans, USA
Marc Bonnefoy, France
Olivier Bezy, USA

Introduction: 2 minutes

1. 14:17 – 14:29
Cachexia as a global problem – data from different continents
Mitja Lainscak, Slovenia

2. 14:29 – 14:41
Obesity paradox for survival: Update 2020
Giuseppe Rosano, UK

3. 14:41 – 14:53
Diagnostic criteria for sarcopenia and sarcopenic obesity in Asia
Masaaki Konishi, Japan

4. 14:53 – 15:05
Diagnostic criteria for sarcopenia and sarcopenic obesity in Europe
Juergen Bauer, Germany

15:05 – 15:25
Discussion

15:30 – 16:25 CET

Industry Session

Neuroendocrine and autonomic dysfunction in cancer cachexia

Chairs: Stefan Anker, Germany
Andrew Coats, Australia

15:30 – 16:00
Neuroendocrine and autonomic dysfunction in cancer cachexia
Daniel Marks, USA

16:00 – 16:25
Discussion

Sponsored by Pfizer

O
16:30 – 17:40 CET

Late breaking research / trials

(each talk: 12 minutes)

Chairs: Stefan Anker, Germany
Andrew Coats Australia
Jeff Crawford, USA
Jose Garcia, USA
Aminah Jatoi, USA
Alessandro Laviano, Italy
Frank Misselwitz, Germany

Introduction: 2 minutes

1. 16:32 – 16:44
s-oxprenolol for amyotrophic lateral sclerosis (ALS)
Jochen Springer, Germany

2. 16:44 – 16:56
SARM for COPD cachexia
Bill Evans, USA

3. 16:56 – 17:08
Trial in progress: Anamorelin phase 3 studies in patients with NSCLC and cachexia
Edwin de Wit, Switzerland (Helsinn)

4. 17:08 – 17:20
MMPOWER-3 Phase 3 Clinical Trial Results: Elamipretide improved six-minute walk test in individuals with mtDNA replisome disorders
Michelangelo Mancuso, Italy

17:20 – 17:40
Discussion

P
17:45 – 18:55 CET

Skeletal muscle as a metabolic organ and the impact of exercise

(each talk: 12 minutes)

Chairs: Nicolaas Deutz, USA
Fabio Penna, Italy
Mathias Plauth, Germany

Introduction: 2 minutes

1. 17:47 – 17:59
Metabolic and molecular integration in regulation of skeletal muscle mass
Srinivasan Dasarathy, USA

2. 17:59 – 18:11
Exercise in cancer patients
Jesper Christensen, Denmark

3. 18:11 – 18:23
Nutrition and appetite stimulants: therapeutic or palliative drugs?
Maurizio Muscaritoli, Italy

4. 18:23 – 18:35
Age-related gene expression signature
David Glass, USA

18:35 – 18:55
Discussion

19:00 – 19:50 CET

Poster Session 11

(each presentation: 2 minutes + 2 minutes discussion)

Diagnosis of Sarcopenia II
Posters 4-25 – 4-36

Chairs: Marc Bonnefoy, France
Francesco Landi, Italy

19:00 – 19:50 CET

Poster Session 12

(each presentation: 2 minutes + 2 minutes discussion)

Therapeutic development (pre-clinical) II
Posters 9-01 – 9-07

Chairs: James Carson, USA
Roger Fielding, USA

19:55 – 20:45 CET

Poster Session 8

(each presentation: 2 minutes + 2 minutes discussion)

Diagnosis of Sarcopenia III
Posters 4-13 – 4-24

Chairs: Josep Argiles, Spain
Jürgen Bauer, Germany

ABSTRACTS OF ORAL PRESENTATIONS

A3

"Hippocrates" clinical science key note lecture
Clinical classification of cancer cachexia

Vickie Baracos, Canada

Knowledge of the complex underlying biology of cachexia in humans remains sparse, and this is a key limitation to the identification of therapeutic targets for this condition. New progress is being made with the collection/banking of human bio-specimens for analysis in relation to cachexia: blood is sampled for investigations of humoral mediators, metabolites, blood cell RNA profiling and DNA for gene association studies, intra-operative tissue biopsy at cancer surgery is an excellent opportunity to access skeletal muscle and adipose tissue for tissue level investigations. Tumor gene and protein expression are also being probed for molecular actors that contribute to wasting.
The focus of this presentation is to address issues related to the clinical classification of patients from whom such specimens have been derived, in a manner that enhances our capacity to develop mechanistic understanding. Generally, researchers focus on the heterogeneity of cachexia in patients with the same histological cancer type, therefore comparing patients with a history of significant weight loss (i.e. cachexic *cases*) with patients with evidence of stable weight/minimal weight loss (i.e. non-cachexic *controls*), although some additional comparator groups are sometimes included. In a recent review (PMID 31307124) it was noted that of 59 articles reporting biological characteristics of skeletal muscle specimens from patients with cancer, the majority stratified patients on a simple bivariate (low versus high weight loss(variously >5%, 10% or 15%), without application of any other cachexia criterion values. The comparison is therefore blind to the possible presence of sarcopenia, or loss of muscle mass over time, both of which have been clearly demonstrated to be common in apparently weight-stable patients with cancer; this is likely to blur the interpretability of the comparison. Likewise, the patient populations are infrequently characterized for nutritional, endocrine, inflammatory or metabolic features. I suggest an urgent need to develop a standardized approach to the clinical annotation of cachexia-related bio-specimens and an approach of purposeful sampling, with a view to improve our ability to reveal the mechanisms of cancer cachexia.

A4

"Prometheus" basic science key note lecture
The different shades of wasting: organ contributions to cancer cachexia

Stephan Herzig, Germany

Cancer cachexia is a multi-factorial condition characterized by body weight loss, which negatively affects quality of life and survival of patients with cancer, most notably pancreatic cancer. Despite the clinical relevance, there is currently no defined standard of care effectively counteracting cancer-associated progressive tissue wasting. Classically, cachexia research has been focused on skeletal muscle atrophy. However, cancer cachexia is increasingly seen as a systemic phenomenon affecting and/or influenced by various organs. In particular, cancer cachexia is associated with changes in adipose tissue and liver function that may promote the increased energy loss and mortality associated with this condition. Here, we will discuss the latest developments in molecular cachexia research that impact our understanding of the systemic dimension of this disease condition, and that go beyond the classical musculo-centric view.

References:
Energy metabolism in cachexia.
Rohm, M. ; Zeigerer, A. ; Machado, J. ; Herzig, S.
EMBO Rep. 20:e47258 (2019)

Cancer Cachexia: More Than Skeletal Muscle Wasting.
Schmidt SF, Rohm M, Herzig S, Berriel Diaz M. Trends Cancer. 2018 Dec;4(12):849-860. doi: 10.1016/j.trecan.2018.10.001. Epub 2018 Oct 24. PMID: 30470306

B1

Sarcopenia - Highlighs 2020

John Morley, USA
St Louis university, Missouri, USA

The SCWD position paper recommended rapid screening eg SARC-F, measuring grip strength or chair stand and lean mass, Treatment includes resistance exercise and a protein intake 0f 1-1,5 g/kg/day.
Over 15 papers in 2020 validated the use of SARC-F or SARC-CalF to screen for sarcopenia. Exercise reduced SARC-F score to normal over a year in the majority of subjects. The vast majority of person with sarcopenia are also frail. A mobile App is available to scree for Rapid Geriatric syndromes.
D3CrR is a better measure than appendicular lean mass to predict disability and mortality. Point of contact ultrasound can be used to diagnose sarcopenia. Exercise in hospital improves outcomes. Neuromuscular electrical stimulation and Vibration Therapy both improve function. In COPD patients HMB increases grip strength and decreases mortality. Bimagrumab is not better than habitual light exercise over 6 months in improving muscle function. Critical Illness (ICU) myopathy is now recognized as an important post ICU event. Lockdown causes sarcopenia and cOVID19 causes cachexia.
Osteosarcopenia is a geriatric syndrome which increases the risk of frailty, falls, hospitalizations, and death. Overexpression of Sestrins prevents muscle atrophy.
References:

Sarcopenia: A Time for Action. An **SCWD** Position Paper.
Bauer J, Morley JE, Schols AMWJ, Ferrucci L, Cruz-Jentoft AJ, Dent E, Baracos VE, Crawford JA, Doehner W, Heymsfield SB, Jatoi A, Kalantar-Zadeh K, Lainscak M, Landi F, Laviano A, Mancuso M, Muscaritoli M, Prado CM, Strasser F, von Haehling S, Coats AJS, Anker SD.J Cachexia Sarcopenia Muscle. 2019 Oct;10(5):956-961.

Dietary Intake, D3Cr Muscle Mass, and Appendicular Lean Mass in a Cohort of Older Men.
Rogers-Soeder TS, Peters KE, Lane NE, Shikany JM, Judd S, Langsetmo L, Hoffman AR, **Evans WJ**, Cawthon PM.J Gerontol A Biol Sci Med Sci. 2020 Jun 18;75(7):1353-1361

Muscle Atrophy and the **Sestrins**.
Martyn JAJ, Kaneki M.N Engl J Med. 2020 Sep 24;383(13):1279-1282.

B2

Muscle wasting and cachexia in stroke

Wolfram Doehner, Germany

Stroke is the leading cause of impaired physical ability in Western countries. The majority of patients remain physically disabled and limited in their daily activities. This disability is primarily attributed to the brain lesion, loss of innervation and a neuronal control failure. However beyond the neuronal control, the skeletal muscle is the main organ to effect the physical activity and failure of the muscle tissue to function properly may substantially contribute to the functional disability after stroke. Substantial alterations of muscle tissue occur after stroke that include structural changes (muscle wasting) and functional impairment (metabolic and efficacy impairment). Studies from animal models and human studies have shown that the combination of denervation, disuse, inflammation, remodelling and spasticity account for a complex pattern of muscle tissue phenotype change and atrophy. Those changes affect the muscle tissue on a global level, i.e. affect the entire body and are not limited to the paralysed limb alone. Sarcopenia is hence a common finding in patients after stroke and may contribute to slow recovery and limited rehabilitation success.
In the presentation insights of the pathophysiology of stroke specific sarcopenia and recent data from clinical trials to target muscle wasting in stroke will be discussed. Improving muscle structural and functional capacity may be a major yet undervalued target in stroke rehabilitation to improve functional outcome.

B3

Sarcopenia and rheumatoid arthritis

Hidenori Arai, Japan
National Center for Geriatrics and Gerontology

Sarcopenia is characterized by a loss of muscle strength and muscle mass, leading to falls and adverse health outcomes. Patients with rheumatoid arthritis (RA) may have a higher risk for sarcopenia due to chronic inflammation, reduced physical ability, and concomitant treatments such as corticosteroids. Although several studies have reported that RA patients have low lean mass or low muscle strength compared with the general population, few studies have been done to define sarcopenia based on the Asian Working Group for Sarcopenia (AWGS) criteria. We have conducted a cross-sectional study of 388 consecutive female patients with RA. In which sarcopenia was defined using the AWGS criteria. Associations between sarcopenia and RA disease characteristics, falls, and bone fractures were examined in univariate and multivariate logistic regression analyses. We found that the prevalence of sarcopenia in patients with RA was 37.1% (14.7%, severe sarcopenia; 22.4%, sarcopenia) and 49.0% had low muscle mass. Sarcopenic patients had a higher incidence of falls and fractures and lower bone mineral density compared to that for non-sarcopenic patients. RA duration, Steinbrocker's stage, Mini-Nutritional Assessment-short form (MNA-SF) score, and the use of biological disease modifying anti-rheumatic drugs (bDMARDs) were found to be independent factors associated with sarcopenia (1). Mochizuki, et al. also showed that the prevalence of sarcopenia was 29.6% by the AWGS criteria in Japanese patients with rheumatoid arthritis aged 65 and over (2). Because of the increase of older RA patients, more attention should be paid for the prevention and treatment of sarcopenia in the management of RA. However, pain and deformity of the joints can affect the exercise intervention. Therefore, a multidisciplinary approach should be taken in addition to the treatment by rheumatologist.

References:
1. Torii M, Hashimoto M, Hanai A, Fujii T, Furu M, Ito H, et al. Prevalence and factors associated with sarcopenia in patients with rheumatoid arthritis. Mod Rheumatol. 2019;29(4):589-95.
2. Mochizuki T, Yano K, Ikari K, Okazaki K. Sarcopenia-associated factors in Japanese patients with rheumatoid arthritis: A cross-sectional study. Geriatr Gerontol Int. 2019;19(9):907-12.

B4

Wasting of the heart causing heart failure (in cancer and beyond)

Andrew Coats, Australia

Joint Session SCWD – MASCC – EONS

The power of Nursing Interventions in the comprehensive management of treatment-induced side-effects

Andreas Charalambous, Cyprus
Cyprus University of Technology and University of Turku

Pharmacological and cellular treatment of cancer is changing dramatically with benefits for patient outcome and comfort, but also with new toxicity profiles. This comes to reinforce the complexity of cancer care. Epidemiological data demonstrate that we are faced up with a growing ageing population that has a high prevalence of comorbidities along with cancer. This leads to an increased number of symptoms and toxicities that healthcare professionals need to assess and manage in the clinical context. There is another noteworthy trend that can affect an oncology practice's strategic planning in the context of treatment-induced side-effects. The shift of cancer care from the hospital to the outpatient context, emphasizes the need that any management strategies also need to accommodate this aspect. The nursing discipline places emphasis on the human experience and hence supports the understanding of symptoms and toxicities in a multidimensional and contextual way. Drawing on the principles of the "*Theory of Unpleasant Symptoms*" a healthcare professional can find a structured and comprehensive way to understand symptoms that can facilitate in their effective management (Blakeman et al 2018). Furthermore, within the nursing discipline, the power of the nursing interventions also lies in its philosophical underpinnings that call for an approach that places the patient at the center of the care, one that acknowledges the uniqueness of the person and hence calling for an individualized approach to caring and finally, one that instigates a holistic approach that accommodates the multidimensional construct of the person. Nurse-led interventions for the comprehensive management of treatment-induced side-effects and toxicities are presented in the context of breathlessness management in lung malignancies (Molassiotis et al 2015), in minimizing radiation - induced Oral Mucositis and Xerostomia in head and neck cancer patients (Charalambous et al 2017; 2018) and in utilising Cognitive Behavioural Interventions for Symptom Clusters (Charalambous et al 2016).

References

Blakeman, JR. An integrative review of the theory of unpleasant symptoms. *J Adv Nurs*. 2019; 75: 946– 961.

Charalambous M, Raftopoulos V, Paikousis L, Katodritis N, Lambrinou E, Vomvas D, Georgiou M, Charalambous A. The effect of the use of thyme honey in minimizing radiation - induced oral mucositis in head and neck cancer patients: A randomized controlled trial. *Eur J Oncol Nurs*. 2018 Jun;34:89-97.

Charalambous A, Lambrinou E, Katodritis N, Vomvas D, Raftopoulos V, Georgiou M, Paikousis L, Charalambous M. The effectiveness of thyme honey for the management of treatment-induced xerostomia in head and neck cancer patients: A feasibility randomized control trial. *Eur J Oncol Nurs*. 2017 Apr;27:1-8.

Charalambous A, Giannakopoulou M, Bozas E, Marcou Y, Kitsios P, Paikousis L. Guided Imagery And Progressive Muscle Relaxation as a Cluster of Symptoms Management Intervention in Patients Receiving Chemotherapy: A Randomized Control Trial. PLoS One. 2016 Jun 24;11(6):e0156911

Molassiotis A, Charalambous A, Taylor P, Stamataki Z, Summers Y.
The effect of resistance inspiratory muscle training in the management of breathlessness in patients with thoracic malignancies: a feasibility randomised trial. *Support Care Cancer*. 2015 Jun;23(6):1637-45.

Joint Session SCWD – MASCC - EONS

Rehabilitation before, during, inbetween, and after anticancer treatment in curative and non-curative intent: how?!

Andrea L Cheville, USA

Joint Session SCWD – MASCC - EONS

Cancer-disease and cancer-treatment related fatigue: multimodal evidenced-based transprofessional management

Florian Strasser, Switzerland

Fatigue is a very frequent syndrome in cancer patients both treated in curative and non-curative intent. Key is to identify patients with fatigue in daily practice; therefore, screening is important using symptom assessment tools like ESAS or others. Then the multimodal characteristics of fatigue shall be assessed, for example by using the Single Item Fatigue tool, followed by an assessment of the impact of fatigue on activities of patients, for example by using the Brief Fatigue Inventory. Then it is very important to distinguish cancer treatment related fatigue (ctrf) caused by chemotherapy, immunotherapy, radiotherapy but also perioperative by anaesthesia; and in this context to assess cofactors which increase the vulnerability of patients to get ctrf, such as prior psychological distress, chronic pain syndrome, CINP or malnutrition. Cancer disease related fatigue (crf) is actually the same as cancer cachexia because cancer disease, which causes fatigue, is almost identical with the so-called pre-cachexia (international definition).

For those syndromes, multimodal management is key with protein-rich nutrition and exercise in self-management. In patients with ctrf, in addition intensified psycho-oncological treatment with use of creative therapies (music, art) is important, also MBSR-based interventions such as Yoga or Body Scan and cognitive behavioural therapy to deal with decreased energy levels. In ctrf patients endurance training is important more than strength training. In cachexia patients with so-called cancer disease related fatigue, protein-rich nutrition is important and also strength training and of course added psychological support.

Management of multi-dimensional syndromes by multimodal treatment requires the co-work of different disciplines and professions. Interprofessionality often means different professions working alongside each other; in contrast, transprofessionality means that professionals work very closely together with a passion to understand each other well and to incorporate other professionals' interventions in their own practice.

In summary, many patients are under-treated because there is lack of awareness of these very important syndromes in oncological care. Treatment of fatigue has in many situations the benefit of increased survival and also better tolerance of anti-cancer treatment.

Joint Session SCWD – MASCC - EONS

Evidenced-based and personalized dosing of exercise in patients with or after cancer

Joachim Wiskemann, Germany

In recent years, the effectiveness of exercise as beneficial and impactful supportive measure for most cancer patients has been demonstrated. Physical activity has been shown to improve physical functioning and to positively influence quality of life and mental adjustment to the disease. Moreover, adequate physical activity levels has been associated with reducing dose-limiting toxicities and improved survival rates. Based on the clinical important finding the American College of Sports Medicine, the Centers for Disease Control and Prevention as well as the American Cancer Society have developed the physical activity guidelines for cancer patients and survivors recommending at least 150 minutes of moderate-to-vigorous PA/week. However, these are general recommendations and personalization of exercise interventions is quite a challenging task due to the massive heterogeneity existing in this patient group due to the complex treatment regimes, side effects and co-morbidities. The talk will provide insides regarding evidence of exercise oncology and strategies to triage, tailor and personalize exercise

Ref

Schmitz, K.H., A.M. Campbell, M.M. Stuiver, B.M. Pinto, A.L. Schwartz, G.S. Morris, J.A. Ligibel, A. Cheville, D.A. Galvao, C.M. Alfano, A.V. Patel, T. Hue, L.H. Gerber, R. Sallis, N.J. Gusani, N.L. Stout, L. Chan, F. Flowers, C. Doyle, S. Helmrich, W. Bain, J. Sokolof, K.M. Winters-Stone, K.L. Campbell, and C.E. Matthews, Exercise is medicine in oncology: Engaging clinicians to help patients move through cancer. CA Cancer J Clin, 2019.

Campbell, K.L., K.M. Winters-Stone, J. Wiskemann, A.M. May, A.L. Schwartz, K.S. Courneya, D.S. Zucker, C.E. Matthews, J.A. Ligibel, L.H. Gerber, G.S. Morris, A.V. Patel, T.F. Hue, F.M. Perna, and K.H. Schmitz, Exercise Guidelines for Cancer Survivors: Consensus Statement from International Multidisciplinary Roundtable. Med Sci Sports Exerc, 2019. 51(11): p. 2375-2390.

C1

The metabolome and proteome of blood in patients with muscular dystrophy

Pietro Spitali, The Netherlands

Duchenne muscular dystrophy (DMD) is the most common form of muscular dystrophy. DMD is affecting boys due to mutations in the *DMD* gene located on the short arm of the X chromosome, leading to absence of the gene product called dystrophin. DMD patients experience a fast progressing condition, characterized by delayed motor development, loss of ambulation in the teens and premature death due to cardio-respiratory complications. In DMD, muscle mass is progressively lost as skeletal muscles are substituted by adipose tissue as a consequence of failed muscle regeneration. A number of therapeutic approaches ranging from dystrophin restoring therapies to modulators of the secondary pathology have proven successful in *in vitro* assays and model systems. However, drugs have mainly failed to convincingly show clear clinical benefit in clinical trials, resulting in poor access to therapies for these patients. While drug potency has been suboptimal, interventional studies have also suffered from the lack of reliable outcome measures resulting in studies with reduced power, therefore complicating the ability to show treatment related clinically meaningful changes. The availability of biomarkers able to monitor disease progression and response to therapy is therefore highly needed to facilitate drug development in the DMD field.
In this study we show how omic approaches such as proteomics and metabolomics are able to identify biomarkers in patients and animal models. Cross-sectional and longitudinal analysis of serum and plasma samples enabled to monitoring trajectories in natural history studies in patients and animal models[1]. We show how biomarker signatures can separate patients and controls, how proteins such as malate dehydrogenase 2 are associated with disease progression over time as well as with loss of ambulation[2]. We show metabolites such as the ratio between creatine and creatinine are associated with timed tests and functional scales in patients[3]. Furthermore we show how biomarkers can improve the prediction of clinically meaningful disease milestones such as loss of ambulation.
The presented data show how non-invasive biomarkers can serve as a tool to enrich the clinical trial toolbox for drug developers to support study design and analysis.

References

1. Tsonaka R, Signorelli M, Sabir E, Seyer A, Hettne K, Aartsma-Rus A *et al.* Longitudinal metabolomic analysis of plasma enables modeling disease progression in Duchenne muscular dystrophy mouse models. *Hum Mol Genet* 2020;**29**.
2. Signorelli M, Ayoglu B, Johansson C, Lochmüller H, Straub V, Muntoni F *et al.* Longitudinal serum biomarker screening identifies malate dehydrogenase 2 as candidate prognostic biomarker for Duchenne muscular dystrophy. *J Cachexia Sarcopenia Muscle* 2020;**11**:505–517.
3. Spitali P, Hettne K, Tsonaka R, Sabir E, Seyer A, Hemerik JB *et al.* Cross-sectional serum metabolomic study of multiple forms of muscular dystrophy. *J Cell Mol Med* 2018;**22**:2442–2448.

C2

Gene therapy for muscular dystrophy: are we there yet?

Kevin M Flanigan, USA
Director, Center for Gene Therapy, Nationwide Children's Hospital, Columbus, Ohio

The prospects for meaningful treatment of the muscular dystrophies are rapidly improving. Antisense oligomer therapies to alter exon splicing in order restore an open reading frame in the *DMD* mRNA transcript in boys with Duchenne muscular dystrophy (DMD) have already been approved. The focus of genetic intervention is largely shifting to gene replacement therapies utilizing adeno-associated virus (AAV) vectors, driven by the early success in *SMN* gene replacement in spinal muscular atrophy. Early results from competing trials of microdystrophin gene delivery for DMD suggest positive benefits, and trials in other muscular dystrophies are underway and planned. Challenges remain for AAV-based therapies, including bottlenecks for production; issues of immune responses and retreatment; and potential side effects, as demonstrated in trials of microdystrophin and X-linked myotubular myopathy (XL-MTM). Alternative AAV-based approaches include delivery of non-coding genes to provide long-term alteration of exon splicing, as used in a current trial to induce full-length dystrophin expression in patients with duplications of exon 2. Future approaches include genome editing using CRISP/Cas9 approaches, which have shown promise in animal models but have not yet reached clinical trials for neuromuscular diseases. Finally, lessons regarding tropism, durability of expression, and immune responses that are learned from trials in the muscular dystrophies will facilitate the use of gene modulation strategies for other disorders of muscle wasting.

C3

Cachexia and wasting in motor neuron disease models

Jochen Weishaupt, Germany

As most other neurodegenerative diseases, the most frequent motor neuron disease ALS is characterized by a loss of body weight. Many patients suffer from a profound reduction in BMI, which even precedes the onset of symptoms. Hypermetabolism is observed in both patients and genetic mouse models, although the origin of these alterations remained largely unclear. They may include but be not limited to neuodegeneration affecting also the hypothalamic-pituitary axis. Alternatively, mitochondrial damage, mitochondrial uncoupling and dysregulated energy homoeostasis in peripheral tissues may represent a systemic dimension of the neurodegenerative disease, and could be responsible for the metabolic changes observed in multiple animal models of motor neuron disease. In patients, weight loss is tightly linked to faster disease progression. Vice versa, increasing body weight by high fat diet in mouse models of ALS extends survival. Most importantly, recent clinical evidence suggests that high calory/fat diet may also exert beneficial effects in ALS patients.

C4

Engineering human iPS cells for muscle disease modelling and therapy development

Francesco Saverio Tedesco[1,2,3]*
[1]Department of Cell and Developmental Biology, University College London (UCL), UK
[2]UCL GOS Institute of Child Health & Great Ormond Street Hospital for Children, London, UK
[3]The Francis Crick Institute, London, UK

Skeletal muscle is the most abundant human tissue. It has a complex structure and some regenerative capacity, supported by a pool of muscle stem cells. Numerous, severe genetic diseases impair skeletal muscle function and regenerative capacity, with the vast majority of them still remaining incurable. Our laboratory (www.tedescolab.org) studies skeletal muscle regeneration, focusing on the development of novel therapies for incurable neuromuscular disorders of childhood. Our work pioneered the use of human artificial chromosomes and induced pluripotent stem (iPS) cells for gene and cell therapies of muscular dystrophies (Tedesco et al., 2012; Benedetti et al., 2017). Recently, we developed the first 3D artificial skeletal muscle entirely derived from patient-specific induced pluripotent stem (iPS) cells, and we showed that it can model severe forms of paediatric muscular dystrophies with high fidelity and definition (Maffioletti et al., 2018). Current projects investigate the use of small molecules to improve muscle stem cell delivery to target tissues and iPS cell-derived myogenesis for complex neuromuscular modelling and drug development. The overall goal of the Tedesco laboratory is the translation of the aforementioned regenerative strategies into novel therapies to improve outcomes for children with neuromuscular disorders.

References:
Benedetti S, Uno N, Hoshiya H, Ragazzi M, Ferrari G, Kazuki Y, Moyle LA, Tonlorenzi R, Lombardo A, Chaouch A, Mouly V, Moore M, Popplewell L, Kazuki K, Katoh M, Naldini L, Dickson G, Messina G, Oshimura M, Cossu G, **Tedesco FS**. Reversible Immortalisation Enables Genetic Correction of Human Muscle Progenitors and Engineering of Next-Generation Human Artificial Chromosomes for Duchenne Muscular Dystrophy. *EMBO Molecular Medicine,* 2017 Dec 14. doi: 10.15252/emmm.201607284.

Maffioletti SM, Sarcar S, Henderson ABH, Mannhardt I, Pinton L, Moyle LA, Steele-Stallard H, Cappellari O, Wells KE, Ferrari G, Mitchell JS, Tyzack GE, Kotiadis VN, Khedr M, Ragazzi M, Wang W, Duchen MR, Patani R, Zammit PS, Wells D, Eschenhagen T, **Tedesco FS**. Three-dimensional Human iPSC-derived Artificial Skeletal Muscles Model Muscular Dystrophies and Enable Multilineage Tissue Engineering. *Cell Reports* 2018 Apr 17;23(3):899-908. doi: 10.1016/j.celrep.2018.03.091.

Tedesco FS, Gerli M, Perani L, Benedetti S, Ungaro F, Cassano M, Antonini S, Tagliafico E, Artusi V, Tonlorenzi R, Ragazzi M, Calderazzi G, Hoshiya H, Cappellari O, Mora M, Sampaolesi M, Torrente Y, Broccoli V and Cossu G* Transplantation of Genetically Corrected Human iPSC-Derived Progenitors in Mice with Limb-Girdle Muscular Dystrophy. *Science Translational Medicine,* 2012 Jun 27;4(140):140ra89

D1

L3 and T4 landmarks predict mortality and key measures of function

Asmita Mishra, USA

Transplantation of healthy hematopoietic stem cells from an allogeneic donor (HCT) is a major treatment option for otherwise incurable hematologic cancers. Despite safer conditioning regimens and supportive care measures, the curative benefits of HCT however can be offset by treatment-related morbidity and mortality. While the impact of sarcopenia on cancer related quality of life and survival is well documented,[(1)] evaluation muscle wasting related risk in the HCT population poses unique challenges due to prolonged hospital needs, polypharmacy, drug-drug interactions, and risk of the longitudinal complication of graft-versus-host disease.

Given the higher frequency of thoracic computed tomography (CT) imaging over abdominal CT, our group aimed to evaluate the correlation of readily available thoracic imaging with functionality and survival. First, using L3 muscle index cutoffs, we have demonstrated the overall rates of sarcopenia in the HCT population unfortunately is uniformly higher than in age- and sex-matched solid tumor patients.(2) Significant but moderate correlations were found for muscle area and radiodensity, and adipose tissue quantity between L3 and T4. Furthermore, when adjusted for sex, age, and transplant specific comorbidities, both T4 muscle index and T4 muscle radiodensity were independently associated with forced expiratory volume in one second (FEV1), a parameter of pulmonary function as defined by spirometry. When considering the impact of sarcopenia on HCT survival, the median overall survival for HCT recipients without evidence of diminished muscle mass or function (i.e. no cachexia) was higher than those patients with having either sarcopenia or decreased FEV1, and substantially higher than those with both abnormalities (2,685, 782, and 104 days, respectively) In multivariate analysis, after adjusting for known covariates that are predictive of mortality after sarcopenia and reduced FEV1 was found to be a strong independent predictor of OS.

We have been able to successfully demonstrate lumbar or thoracic CT images are useful for body composition assessment in a HCT population, revealing high rates of sarcopenia, impaired functionality as denotated by FEV1, and high risk of early mortality after HCT in patients who demonstrated decreased muscle mass and function.

References:
Prado CM, Lieffers JR, McCargar LJ, Reiman T, Sawyer MB, Martin L, et al. Prevalence and clinical implications of sarcopenic obesity in patients with solid tumours of the respiratory and gastrointestinal tracts: a population-based study. The Lancet Oncology. 2008;9(7):629-35.

Mishra A, Bigam KD, Extermann M, Faramand R, Thomas K, Pidala JA, et al. Sarcopenia and low muscle radiodensity associate with impaired FEV(1) in allogeneic haematopoietic stem cell transplant recipients. Journal of cachexia, sarcopenia and muscle. 2020.

D2

Computed Tomography based Body Composition Measures in Chronic Lung Disease and Lung Transplantation

Dmitry Rozenberg, Canada

There is an increased interest in evaluating body composition in chronic lung disease and lung transplant candidates using routine clinical computed tomography (CT) scans. CT-based body composition measures (muscle and adiposity) have been shown to be associated with respiratory disease severity, physical function, and as a prognostic marker of pre- and post transplant outcomes.[1,2,3]
The aims of this presentation are to: 1) Describe the methodology of CT-based body composition measures in chronic lung disease and lung transplant candidates. 2) Highlight the association of CT-based measures of body composition with physical function, cardio-metabolic parameters, and pre- and post-transplant outcomes. 3) Discuss potential future research directions.
By the end of the presentation, the audience will have a better understanding of the variability in CT body composition measures utilized across chronic lung disease states and in lung transplant candidates. The presentation will also highlight important associations between muscle mass and adiposity measures with clinical outcomes that can be derived from a single cross-sectional area on CT scan. Future directions will highlight some principles related to standardization, consideration of three-dimensional assessments, and utilization of CT measures beyond muscle mass and adiposity.

References:
1 McDonald ML, Diaz AA, Ross JC, et al. Quantitative computed tomography measures of pectoralis muscle area and disease severity in chronic obstructive pulmonary disease. A cross-sectional study. Ann Am Thorac Soc 2014; 11:326-334

2 Moon SW, Choi JS, Lee SH, et al. Thoracic skeletal muscle quantification: low muscle mass is related with worse prognosis in idiopathic pulmonary fibrosis patients. Respir Res 2019; 20:35

3 Rozenberg D, Orsso CE, Chohan K, et al. Clinical Outcomes Associated with Computed Tomography-Based Body Composition Measures in Lung Transplantation: A Systematic Review. Transpl Int 2020

D3

Use of thoracic CT imaging in clinical trials to assess muscle mass – the record so far

Vickie Baracos, Canada

Diseases of the chest are emblematic of the enthusiasm of clinicians to exploit computed tomography images acquired during routine care[1] for the purpose of body composition assessment. Several hundred publications answering to the search terms thoracic*chest*CT*body compositions*skeletal muscle are currently available, spanning many clinical conditions including cancers (lung, esophageal, head & neck, sarcoma, and hematological malignancies including the setting of allogeneic hematopoietic stem cell transplant), interstitial lung disease, COPD, lung transplantation, patients in critical care including COVID-19, burn and trauma, and thoracic surgery including tricuspid valve surgery and thoracic endovascular aortic repair. A dominating interest of these researchers is the impact of reduced skeletal muscle mass in relation to clinical outcomes, which are notably diverse given this broad span of health conditions. The preponderance of reports are in lung cancer, esophageal cancer, lung transplantation and critical illness. In about a third of the studies, researchers used the standardized vertebral landmark that is most often used across all of the literature on CT-body composition, the 3rd lumbar vertebra. However this is possible only in those conditions where CT-abdomen is part of the standard of care, and the majority of the work is in patient populations where only thoracic studies are standard. There is a striking heterogeneity of vertebral landmarks in the diseases of the chest literature, including T4, T5, T6, T7, T8, T10, T11, T12, L1 and L3. While total muscle cross-sectional area/index is the most frequently reported parameter, many authors focused on a single muscle including specific muscles of the chest (pectoralis, diaphragm, intercostal, paraspinal) or psoas. Standardization of the approach to using thoracic imaging studies and uniform criteria of reporting are clearly needed. Nonetheless, wasting of specific muscles of the chest, notably the primary and accessory respiratory muscle groups, merit study individually in relation to their specific functions (e.g. FEV1[2]) and associated clinical outcomes (e.g. dependency on mechanical ventilation in a critical care setting)[3].

1. Mourtzakis M et al. A practical and precise approach to quantification of body composition in cancer patients using computed tomography images acquired during routine care. Appl Physiol Nutr Metab. 2008;33(5):997-1006.
2. Mishra A. et al. Sarcopenia and low muscle radiodensity associate with impaired FEV1 in allogeneic haematopoietic stem cell transplant recipients. J Cachexia Sarcopenia Muscle. 2020 Jul 29. doi: 10.1002/jcsm.12604. Epub ahead of print. PMID: 32729255.
3. Grassi A et al. Bellani G. Assisted mechanical ventilation promotes recovery of diaphragmatic thickness in critically ill patients: a prospective observational study. Crit Care. 2020;24(1):85.

D4

Muscle mass but not lean body mass or appendicular lean mass is strongly related to health-related outcomes in old men

William J Evans, USA
Department of Nutritional Sciences and Toxicology University of California and Division of Geriatrics, Duke University Medical Center

The assessment of total body skeletal muscle mass has, until recently, been problematic. Skeletal muscle is a significant but not the only component of lean body mass (LBM). In a large number of clinical trials LBM is incorrectly referred to as muscle mass and, as a result use of LBM as a surrogate for muscle mass has resulted in erroneous conclusions on the importance of skeletal muscle in development of late-life dysfunction and risk of chronic disease. The D_3-Creatine (D_3Cr) dilution method allows a direct and accurate measurement of skeletal muscle mass that is undiluted by hydration status or accumulation of intramyocellular fibrosis or lipid. The method provides a measurement of creatine pool size and, because ~98% of the body creatine pool is located in the sarcomere, muscle mass. Because the method is non-invasive and only requires a single fasting urine sample, the method is ideal to measure muscle mass in large cohort studies. The method has been incorporated into a large prospective longitudinal trial in more than 1,300 older men (MrOS corhort, > 80 yr). Results show that D_3Cr measured muscle mass but not DXA derived lean body mass or appendicular lean mass, is strongly associated with a number of important functional and health related outcomes including risk of a fall, hip fracture, disability,and mortality. In this population of elderly men, D_3Cr muscle mass has also been associated with activities of daily living and instrumental activities of daily living. These data suggest that a definition of sarcopenia must include skeletal muscle mass (1-4).

Evans WJ, Hellerstein M, Orwoll E, Cummings S, Cawthon PM. D3 -Creatine dilution and the importance of accuracy in the assessment of skeletal muscle mass. J Cachexia Sarcopenia Muscle. 2019;**10**:14-21.
Zanker J, Patel S, Blackwell T, Duchowny K, Brennan-Olsen S, Cummings SR*, et al.* Walking Speed and Muscle Mass Estimated by the D3-Creatine Dilution Method Are Important Components of Sarcopenia Associated With Incident Mobility Disability in Older Men: A Classification and Regression Tree Analysis. J Am Med Dir Assoc. 2020.
Orwoll ES, Peters KE, Hellerstein M, Cummings SR, Evans WJ, Cawthon PM. The Importance of Muscle Versus Fat Mass in Sarcopenic Obesity: A Re-evaluation Using D3-Creatine Muscle Mass Versus DXA Lean Mass Measurements. J Gerontol A Biol Sci Med Sci. 2020.
Cawthon PM, Blackwell T, Cummings SR, Orwoll ES, Duchowny KA, Kado DM*, et al.* Muscle mass assessed by D3-Creatine dilution method and incident self-reported disability and mortality in a prospective observational study of community dwelling older men. J Gerontol A Biol Sci Med Sci. 2020.

E1

Inflammation and muscle catabolism in patients with cachexia

T. Alp Ikizler, USA

Cachexia of chronic or acute diseases is a multifactorial syndrome characterized by a progressive loss of skeletal muscle mass (1). Irregularities in protein metabolism play an important role in development of nutritional derangements in patients with cachexia, where the rate of protein degradation exceeds the rate of synthesis. Patients with cachexia often display systemic inflammation and other metabolic abnormalities. Plethora of studies have shown that systemic and local inflammation is a major driver of cachexia through increase protein catabolic signaling. Pro-inflammatory cytokines such as TNF-α, IL-1, IL-6 and IL-8 are major (protein) catabolic signals that lead to reduced activity of Akt, a nexus enzyme for both protein anabolic and catabolic signaling pathways in muscle (2). Lower Akt activity reduces the inhibitory phosphorylation of the FOXO transcription factors. Proinflammatory cytokines also activate the JAK/STAT3 pathway and the CCAAT enhancer-binding proteins. When activated, these pathways synergistically produce changes in genes associated with multiple protein degradation pathways.
Recent data in the setting of kidney disease, a common condition associated with cachexia and increased systemic inflammatory response, also suggest that inflammation not only increases protein degradation in the skeletal muscle, but also suppresses protein synthesis leading to an amplified net catabolism leading to cachexia (3). Specifically, kidney disease stimulated, chromatin-modifying, nucleolar protein 66 (NO66) suppresses both ribosomal DNA transcription and muscle protein synthesis via a demethylase mechanism in mice. Notably, muscle-specific knockout of NO66 in mice improved muscle protein metabolism despite the presence of CKD. Additionally, NO66 is present in muscle biopsy specimens of patients with chronic kidney disease or those on maintenance hemodialysis. The mechanism by which NO66 suppresses protein synthesis involves inflammatory cytokines and NF-κB.
Understanding the interaction between inflammation and protein metabolism could help define new therapeutic strategies in patients with cachexia.

References

1. Peixoto da Silva S, Santos JMO, Costa ESMP, Gil da Costa RM, Medeiros R. Cancer cachexia and its pathophysiology: links with sarcopenia, anorexia and asthenia. J Cachexia Sarcopenia Muscle. 2020;11(3):619-35.
2. Price SR, Bailey JL. A New Dimension to the Mechanisms Causing Muscle Loss in CKD. Journal of the American Society of Nephrology. 2020;31(11):2495-6.
3. Zhang L, Chen Q, Chen Z, Wang Y, Gamboa JL, Ikizler TA, et al. Mechanisms Regulating Muscle Protein Synthesis in CKD. J Am Soc Nephrol. 2020;31(11):2573-87.

E2

Organoid as a model to study adipose tissue remodeling in cancer cachexia

Miguel L. Batista Jr, USA

Cancer cachexia (CC) presents itself as a syndrome with multiple manifestations, causing a marked multi-organ metabolic imbalance. Recently, cachectic wasting has been proposed to be stimulated by several inflammatory mediators, which may disrupt the integrative physiology of adipose tissues and other tissues such as the brain and muscle. In recent clinical research, the intensity of depletion of the different fat deposits has been negatively correlated with the patient's survival outcome. Studies have also shown that various metabolic disorders can alter white adipose tissue (WAT) remodeling, especially in the early stages of cachexia development. WAT dysfunction resulting from tissue remodeling is a contributor to overall cachexia, with the main modifications in WAT consisting of morpho-functional changes, increased adipocyte lipolysis, accumulation of immune cells, reduction of adipogenesis, changes in progenitor cell population, and the increase of "niches" containing beige/brite cells.

To study the various facets of cachexia-induced WAT remodeling, particularly the changes in the population of progenitor cells and beige remodeling, two-dimensional (2D) culture has been the first option for in vitro studies. However, this approach does not adequately summarize WAT complexity. Improved assays for the reconstruction of functional AT ex vivo are helpful for the comprehension of physiological interactions between the distinct cell populations. Here, this protocol describes an efficient three-dimensional (3D) printing tissue culture system based on magnetic nanoparticles. The protocol is optimized for investigating WAT remodeling induced by cachexia induced factors (tumor secretome). The results show that a 3D culture is an appropriate tool for studying WAT modeling ex vivo and may be useful for functional screens to identify bioactive molecules for individual adipose cell populations applications and aid the discovery of WAT-based cell anticachectic therapy.

References

Batista M.L. Jr et.al. Three-Dimensional Adipocyte Culture as a Model to Study Cachexia-Induced White Adipose Tissue Remodeling. Journal of Visualized Experiments. 2020 (in press).

Haisler, W. L. et al. Three-dimensional cell culturing by magnetic levitation. Nature Protocol. 8 (10), 1940-1949 (2013).

Muller, S. et al. Human adipose stromal-vascular fraction self-organizes to form vascularized adipose tissue in 3D cultures. Scientific Reports. 9 (1), 7250 (2019).

E3

Tumor-derived IL-6 and Trans-Signaling between Fat and Muscle Mediate Pancreatic Cancer Cachexia

Teresa Zimmers, USA

Joseph E. Rupert[1], Andrea Bonetto[2-4,6,7], Ashok Narasimhan[2], Yanlin Jiang[2], Jianguo Liu[2], Ernie Au[1], Libbie Silverman[2], Daenique H. A. Jengelley[1], Yunlong Liu[5-8], Leonidas G. Koniaris[2,7-9], and **Teresa A. Zimmers[1-4,6-9]**

[1]Departments of Biochemistry, [2]Surgery, [3]Otolaryngology—Head & Neck Surgery, [4]Anatomy, Cell Biology & Physiology, [5]Molecular and Medical Genetics, [6]Center for Computational Biology and Bioinformatics, Indiana University School of Medicine. [7]Indiana University Simon Comprehensive Cancer Center. [8]Indiana Center for Musculoskeletal Health. [9]Richard Roudebush Veterans Administration Medical Center, Indianapolis, IN

Most patients with pancreatic adenocarcinoma (PDAC) suffer cachexia. Interleukin-6 (IL-6) causes cachexia in mice and associates with mortality in PDAC. Here we show that tumor cell-derived IL-6 mediates crosstalk among tumor and peripheral tissues to promote cachexia. Heterogeneity in cachexia among patients with PDAC was phenocopied by orthotopic implantation of tumors in NSG mice; 6-month weight loss in patients correlated with tumor-free weight loss in recipient mice (n=8, Pearson r 0.798, p=0.0255). Muscle wasting correlated to mortality (r 0.905, p=0.005), while tumor mass did not. Xenografts that induced the greatest wasting expressed IL-6 from tumor cells. In an immunocompetent PDAC model, we show that tumor cell-derived IL-6 elicited expression of IL-6 in fat, and IL-6 and IL-6 receptor (IL6R) in muscle, raising both in blood. Evidence from mice and in vitro modeling of crosstalk using tumor cells, 3T3L1 adipocytes, and C2C12 myotubes, revealed that tumor-derived IL-6 induces adipose IL-6 and lipolysis, elevating circulating fatty acids and glycerol, which induce myosteatosis, dysmetabolism, wasting, and expression of IL-6R in muscle. Disruption of this crosstalk by depletion of tumor-derived IL-6 halved adipose wasting and abolished muscle atrophy and IL6R expression in muscle. Thus, PDAC cachexia is driven by crosstalk among tumor, adipose and muscle via a feed-forward, IL-6 signaling loop. Tumor signals to muscle and adipose through IL-6, and muscle to adipose via IL6R trans-signaling, and adipose to muscle through fatty acids and IL-6. These data reveal targetable mechanisms to disrupt cachexia in PDAC.

E4

The lipids-endotoxin interaction and inflammation in chronic illness

Stephan von Haehling, Germany

F1

Mechanisms of doxorubicin toxicity in cardiac and skeletal muscle

Ashley Smuder, USA

Anthracyclines are a class of chemotherapy agent that is greatly utilized and highly effective at reducing cancer tumor burden, with doxorubicin (DOX) among the most commonly used in clinical practice. Although DOX exhibits potent antineoplastic properties, its clinical use is limited by the prevalence of adverse effects to both cardiac and skeletal muscle. DOX-induced myotoxicity is characterized by redox imbalance and consequent impairment in cell signaling and function, which occurs due to supraphysiological reactive oxygen species (ROS) generation. Cellular proteolytic systems are partially regulated by redox status, and mitochondrial function plays a critical role in DOX-induced cardiac and skeletal muscle toxicity as a result of increased proteolytic activity. Indeed, it has been established that targeting mitochondrial ROS pharmacologically prevents DOX-induced cardiac and skeletal muscle abnormalities [1]. Muscle function is preserved when mitochondrial ROS production is attenuated, in part by inhibition of autophagy. However, autophagy itself plays a complex role in the regulation of DOX myotoxicity. Acutely, autophagy inhibition in cardiac and skeletal muscle can prevent aberrant mitochondrial ROS production and the progression of DOX myopathy, which is consistent with the idea that a regulatory cross-talk exists between these two processes [2, 3]. In contrast, our data show that prevention of autophagosome formation past the acute phase does not provide extended benefits, which potentially occurs as a result of temporal changes in autophagy signaling following DOX administration.

References:

1. Min, K., et al., *Increased mitochondrial emission of reactive oxygen species and calpain activation are required for doxorubicin-induced cardiac and skeletal muscle myopathy.* J Physiol, 2015. **593**(8): p. 2017-36.

2. Montalvo, R.N., et al., *Protection against Doxorubicin-Induced Cardiac Dysfunction Is Not Maintained Following Prolonged Autophagy Inhibition.* Int J Mol Sci, 2020. **21**(21).

3. Doerr, V., et al., *Prevention of Doxorubicin-Induced Autophagy Attenuates Oxidative Stress and Skeletal Muscle Dysfunction.* Antioxidants (Basel), 2020. **9**(3).

F2

Advancing biomarkers in pancreatic cancer cachexia

Erin Talbert, USA
Department of Health and Human Physiology and Holden Comprehensive Cancer Center, University of Iowa, Iowa City, IA, USA

Cancer patients who suffer from cachexia have worse treatment tolerance, post-surgical outcomes, survival, and quality of life than cancer patients who maintain their weight. Despite clear increased risks for patients, diagnosing cachexia still primarily relies on self-reported weight loss. A reliable biomarker to identify patients with cancer cachexia would be a valuable tool to improve clinical decision making and identification of patients at risk of adverse outcomes. Most likely to benefit from a biomarker of cancer cachexia would be patients with pancreatic ductal adenocarcinoma (PDAC), as PDAC patients have the highest incidence and greatest severity of cancer cachexia.
Our recent findings demonstrate that high circulating levels of the inflammatory cytokines might not accurately identify all patients with cancer cachexia, and in fact may be more reflective of advanced disease (1, 2). In our continued attempts to identify a cachexia biomarker useful for an earlier stage PDAC population, we recently utilized a targeted metabolomics approach to compare plasma from three cohorts: 1) control patients without cancer; 2) treatment-naïve weight-stable PDAC patients; and 3) treatment-naïve PDAC patients who reported having lost more than 5% of their pre-illness body weight, which we defined for this study as cachectic (3).
Profiling of sphingolipids and ceramides revealed that cachectic patients had decreased circulating levels of three sphingolipids compared to either non-cachectic PDAC patients or patients without cancer. Further analysis revealed that the ratio of circulating C18-ceramide to C24-ceramide (C18:C24) effectively distinguished cachectic patients from weight-stable ones (area under ROC = 0.810). Furthermore, in this population, C18:C24 outperformed a number of other previously proposed biomarkers of cachexia, including interleukin-6 (IL-6), growth differentiation factor 15 (GDF15), myostatin, activin, and monocyte chemoattractant protein 1 (MCP-1). It was notable that some biomarkers, including C18:C24, MCP-1, and GDF15, were only elevated in cachectic males. Together, our findings identify the ceramide ratio C18:C24 as a potential new biomarker of cancer cachexia, which may also be helpful in characterizing a sexual dimorphism in PDAC-induced cachexia.

References:

1. Talbert EE, Lewis HL, Farren MR, Ramsey ML, Chakedis JM, Rajasekera P, Haverick E, Sarna A, Bloomston M, Pawlik TM, Zimmers TA, Lesinski GB, Hart PA, Dillhoff ME, Schmidt CR, Guttridge DC. “Circulating MCP-1 is Associated with Cachexia in Treatment-Naïve Pancreatic Cancer Patients”. *J Cachexia Sarcopenia Muscle.* 9(2):358-368 (2018).

2. Ramsey ML, Talbert E, Ahn D, Bekaii-Saab T, Badi N, Bloomston PM, Conwell DL, Cruz-Monserrate Z, Dillhoff M, Farren MR, Hinton A, Krishna SG, Lesinski GB, Mace T, Manilchuk A, Noonan A, Pawlik TM, Rajasekera PV, Schmidt C, Guttridge D, Hart PA. “Circulating interleukin-6 is associated with disease progression, but not cachexia in pancreatic cancer.” *Pancreatology.* S1424-3903(18)30747-6 (2018).

3. Chakedis JM, Dillhoff ME, Schmidt CR, Rajasekera PV, Evans DC, Williams TM, Guttridge DC, Talbert EE. “Plasma ceramides as a sexually dimorphic biomarker of pancreatic cancer-induced cachexia.” Posted to medRxiv on June 2, 2020. DOI: https://doi.org/10.1101/2020.06.01.20111492

F3

Role of the BMP pathway in cancer cachexia

Roberta Sartori, Italy

Roberta Sartori[1,2,3†], Adam Hagg[1,4,5†], Sandra Zampieri[3,6], Andrea Armani[2,3], Camilla Pezzini[2,3], Bradley J. Turner[7], Gianpietro Zanchettin[6], Elisa S. Pierobon[6], Lucia Moletta[6], Michele Valmasoni[6], Cosimo Sperti[6], Paola Costelli[8], Stefano Merigliano[6], Fabio Penna[8], Paul Gregorevic[1,4,9,10¶], Marco Sandri [2,3,11¶]
[1]Baker Heart and Diabetes Institute, VIC, 3004 Australia; [2]Veneto Institute of Molecular Medicine, Padova, 35131 Italy; [3]Dept. of Biomedical Sciences, University of Padova, Padova, 35131 Italy; [4]Centre for Muscle Research, Dept. Physiology, The University of Melbourne, VIC, 3010 Australia; [5]Biomedicine Discovery Institute, Dept. of Physiology, Monash University, VIC, 3800, Australia; [6]Dept. of Surgery, Oncology and Gastroenterology, 3rd Surgical Clinic, University of Padova, 35128 Italy; [7]The Florey Institute of Neuroscience and Mental Health, Parkville, VIC, 3052 Australia; [8]Dept. of Clinical and Biological Sciences, University of Turin, Turin, 10125 Italy; [9]Dept. of Biochemistry and Molecular Biology, Monash University, VIC, 3800 Australia; [10]Dept. of Neurology, University of Washington School of Medicine, Seattle, WA, 98195 USA; [11]Dept. of Medicine, McGill University, Montreal, QC, H4A 3J1 Canada

† These authors contributed equally to this work.
¶ These authors contributed equally to this work.

roberta.sartori@unipd.it

Most patients with solid cancers exhibit features of cachexia, a syndrome characterized by significant loss of skeletal muscle mass and strength that ultimately accounts for 20-30% of cancer deaths. As the underlying mechanisms of this multifactorial syndrome are incompletely defined, effective therapeutics have yet to be developed. Muscle loss is the most important clinical event in cancer cachexia. Preservation of muscle mass despite unchanged tumor growth, fat loss and pro-inflammatory cytokine production improves survival in mice (*1*). The BMP (Bone and Morphogenetic Protein) axis plays a critical role in muscle mass regulation (*2, 3*). However, its role in cancer-induced muscle loss has never been investigated. We observed diminished Bone Morphogenic Protein (BMP) signaling early in the onset of skeletal muscle wasting associated with cancer cachexia in mouse model and in human cancer patients. Cancer-mediated factors trigger in muscle the expression of the BMP inhibitor Noggin, which blocks the actions of BMPs on muscle fibers and motor nerves, causing muscle wasting, neuromuscular junction (NMJ)'s disruption and denervation. Increasing BMP signaling in the muscles of tumor-bearing animals prevents muscle wasting and preserves NMJ function. We identify perturbed BMP signaling and denervation of muscle fibers as important pathogenic mechanisms of muscle wasting associated with cachexia, and present modulation of BMP-mediated signaling as an attractive approach for the development of interventions to address the loss of functional musculature in cancer patients.

References:

1. X. Zhou, J. L. Wang, J. Lu, Y. Song, K. S. Kwak, Q. Jiao, R. Rosenfeld, Q. Chen, T. Boone, W. S. Simonet, D. L. Lacey, A. L. Goldberg, H. Q. Han, Reversal of cancer cachexia and muscle wasting by ActRIIB antagonism leads to prolonged survival. *Cell* **142**, 531-543 (2010).

2. R. Sartori, E. Schirwis, B. Blaauw, S. Bortolanza, J. Zhao, E. Enzo, A. Stantzou, E. Mouisel, L. Toniolo, A. Ferry, S. Stricker, A. L. Goldberg, S. Dupont, S. Piccolo, H. Amthor, M. Sandri, BMP signaling controls muscle mass. *Nat Genet* **45**, 1309-1318 (2013).

3. C. E. Winbanks, J. L. Chen, H. Qian, Y. Liu, B. C. Bernardo, C. Beyer, K. I. Watt, R. E. Thomson, T. Connor, B. J. Turner, J. R. McMullen, L. Larsson, S. L. McGee, C. A. Harrison, P. Gregorevic, The bone morphogenetic protein axis is a positive regulator of skeletal muscle mass. *J Cell Biol* **203**, 345-357 (2013).

F4

Mechanisms of chemotherapy-induced muscle wasting in cancer cachexia

Kate Murphy, Australia

Kate T. Murphy[1], Kristy Swiderski[1], James G. Ryall[1], Jonathan R. Davey[1], Hongwei Qian[1], Séverine Lamon[2], Victoria C. Foletta[2], Jennifer Trieu[1], Annabel Chee[1], Suzannah J. Read[1], Timur Naim[1], Paul Gregorevic[1] and Gordon S. Lynch[1]
[1]Centre for Muscle Research, Department of Physiology, The University of Melbourne, Parkville Victoria 3010, Australia; [2]Institute for Physical Activity and Nutrition (IPAN), School of Exercise and Nutrition Sciences, Deakin University, Burwood Victoria 3125, Australia

Introduction: Cachexia is a debilitating complication of cancer characterized by progressive wasting and weakness of skeletal muscles that impairs quality of life and, in the worst cases, compromises survival. Anti-cancer treatments, such as chemotherapy, can also cause muscle wasting and weakness associated with an impaired response to treatment and poor prognosis. Given that many cancer patients present with cachexia at the initiation of chemotherapy, we investigated whether mice with cancer cachexia were susceptible to chemotherapy-induced muscle wasting and if so, sought to identify potential mechanisms and approaches to enhance the effectiveness of treatments in cachectic patients.
Methods: Cachectic Colon-26 (C-26) tumor-bearing mice were given 5-fluourouracil (5-FU) chemoth:rapy or vehicle (DMSO) treatment and analyzed for tumor, muscle and tissue mass, muscle fiber size and composition and whole transcriptome sequencing (RNA-Seq). Mechanisms were validated *in vitro* using C2C12 muscle cell culture and microRNA (miR) mimics and inhibitors and were confirmed *in vivo* by injecting muscles of cachectic C-26 tumor-bearing mice with recombinant adeno-associated viral (rAAV) vectors encoding a miR sponge.
Results: In cachectic C-26 tumor-bearing mice, 5-FU chemotherapy treatment reduced tumor burden ($P<0.001$) but also decreased mass of the hindlimb muscles ($P<0.05$) and the heart ($P<0.05$) compared with vehicle treated mice. The 5-FU-induced muscle wasting in mice with cancer cachexia was associated with selective atrophy and loss of large, fast muscle fibers ($P<0.05$), which RNA-sequencing and *in vitro* analyses revealed to involve miR dependent ERK2 inhibition. Intramuscular injection of rAAV vectors encoding a sponge to reduce miR expression in mice with cancer cachexia protected against 5-FU-associated ERK inhibition and increased muscle fiber size.
Conclusion: The findings demonstrate that cachectic mice remain susceptible to chemotherapy-induced wasting and identify inhibition of specific miRs as a potential adjunct therapy for attenuating chemotherapy-induced muscle wasting in patients with cancer cachexia.

Supported by project grants from the National Health and Medical Research Council (NHMRC), Victorian Cancer Agency and Cancer Council Victoria.

G1

Novel players that control muscle mass in disease

Marco Sandri[1,2,3], Italy
[1]Department of Biomedical Sciences, University of Padova, 35131 Padova, Italy. [2]Venetian Institute of Molecular Medicine, 35129 Padova, Italy.[3]Myology Center, University of Padova, 35131 Padova, Italy.

The ability to activate compensatory mechanisms in response to environmental stress is an important factor for survival and maintenance of cellular functions. The systems that are often activated both in short and prolonged stress conditions is autophagy lysosome and ubiquitin proteasome systems. Autophagy is required to clear the cell from dysfunctional organelles and altered proteins and is reported to be involved in muscle wasting during cancer growth and age-related sarcopenia. The regulation of protein breakdown as well as protein synthesis is under the control of transcription factors belonging to different signaling pathways. Here I' ll present the last findings about novel genes as well as new crass talk between signaling pathways that control protein breakdown in cancer cachexia.

G2

The role of glucagon in tumor-induced muscle wasting of the insects and mammals

Wei Roc Song, China

The role of glucagon in tumor-induced muscle wasting of the insects and mammals.
Impairment of insulin/IGF response and its associated anabolism is frequently observed in tumor-induced host wasting, including muscle wasting, lipid loss, and hyperglycemia. However, whether insulin counter-regulator hormones, like glucagon, and the associated catabolism also play important roles in the wasting development is largely unknown. Using ApcMin/+ mice as a colon-cancer model, we observed blood glucagon elevation and oral glucose intolerance at the pre-cachectic stage. We also found a similar increase of production of adipokinetic hormone (Akh, a fly glucagon) in a fly model of cancer cachexia, whereby induction of oncogene yki/YAP1 in intestinal stem cells causes rapid gut-tumor progression and, subsequently, host wasting such as muscle dysfunction, lipid loss, and hyperglycemia. Strikingly, genetic removal of Akh expression in the tumor-bearing flies potently abolishes wasting phenotypes without affecting gut-tumor growth. Finally, integrating large-scale RNAi screening and genetic validation, we excitingly revealed that gut tumors secret Pvf1, the homolog of VEGF/PDGF, to remotely target Akh-producing cells and promote its production, leading to systemic anabolism/catabolism imbalance and host wasting. We also uncovered that Pvf1/Pvr axis triggers, at least, ERK and JNK signaling pathways to orchestrate Akh production.

G3

Role of autophagy proteins in muscle wasting conditions

Antonio Zorzano, Spain
Institute for Research in Biomedicine (IRB Barcelona), Universitat de Barcelona, and CIBER de Diabetes y Enfermedades Metabólicas Asociadas (CIBERDEM), Spain

A precise balance between protein degradation and synthesis is essential to preserve skeletal muscle mass. Because of its fundamental role in human function, enabling locomotion and respiration, muscle mass loss is related to a poor quality of life and increased morbidity/ mortality. Two common but distinct conditions characterized by a loss of skeletal muscle mass are sarcopenia and cachexia.
Excessive autophagic degradation has been proposed to play a role in the onset of muscle depletion in muscle wasting conditions such as cancer cachexia or sarcopenia linked to diabetes. In this connection, the autophagy protein TP53INP2 has a direct impact on skeletal muscle mass in vivo. Muscle-specific overexpression of TP53INP2 reduces muscle mass, while deletion of TP53INP2 results in muscle hypertrophy. Furthermore, muscle-specific overexpression of TP53INP2 exhibited enhanced muscle wasting in streptozotocin-induced diabetes that was dependent on autophagy; however, TP53INP2 ablation mitigated experimental diabetes-associated muscle loss. Moreover, TP53INP2 expression was markedly repressed in muscle from patients with type 2 diabetes and in murine models of diabetes. In C26 tumor-bearing mice, autophagy inhibition promoted by Beclin-1 knockdown was unable to rescue the loss of muscle mass and worsened muscle morphology. Conversely, the stimulation of muscle autophagy by TP53INP2 overexpression exacerbated muscle atrophy in tumor-bearing mice.
Our results indicate that TP53INP2 negatively regulates skeletal muscle mass through activation of autophagy. Furthermore, we propose that an excessive autophagy results in muscle wasting under conditions such as insulinopenia or cancer.

G4

Impaired ribosome biogenesis as an underlying cause of muscle wasting

Gustavo A. Nader, USA
Dept. of Kinesiology, Huck Institutes of the Life Sciences, and Penn State Cancer Institute.
The Pennsylvania State University, State College, PA, USA

Muscle wasting in cancer is associated with deficits in protein synthesis, yet the mechanisms underlying this anabolic impairment remain poorly understood. The capacity for protein synthesis is mainly determined by the abundance of muscle ribosomes, which is in turn regulated by transcription of the ribosomal (r)RNA genes (rDNA). In this presentation, I will discuss new findings indicating that muscle wasting in a pre-clinical model of ovarian cancer is associated with a reduction in ribosomal capacity as a consequence of impaired rDNA transcription. We explored potential mechanisms involved in ribosome degradation that could also explain the diminished ribosomal capacity. Despite a marked upregulation of the ribophagy receptor NUFIP1 mRNA and loss of NUFIP1 protein, in vitro studies revealed that while inhibiting ribophagy rescued NUFIP1, it failed to prevent the loss of ribosomes. Electrophoretic analysis of rRNA fragmentation from both in vivo and in vitro models showed no evidence of endonucleolytic cleavage suggesting that rRNA degradation does not play a major role in modulating muscle ribosome levels. Our results indicate that in ovarian cancer-induced cachexia, impaired rDNA transcription reduces the muscle's ribosomal capacity and compromises its ability to synthesize proteins. Thus, impaired rDNA transcription appears to play a key role in the anabolic deficits associated with muscle wasting in cancer cachexia.

H1

Muscle stem cell mechanotransduction and TGF-beta signalling in muscle regeneration and fibrosis

Richard Jaspers, The Netherlands

H2

Is the size of skeletal muscle fibres constrained by their oxidative capacity?

Hans Degens, UK
Musculoskeletal Science & Sports Medicine Research Centre, Department of Life Sciences, Manchester Metropolitan University, Manchester, UK; Lithuanian Sports University, Institute of Sport Science and Innovations, Kaunas, Lithuania

The inverse relationship between oxidative capacity and cross-sectional area of a muscle fibre is explicable by oxygen diffusion limitations [1]. This relationship suggests a trade-off between size (or power) and oxidative capacity (or endurance) of a muscle fibre, where any increase in fibre size would be accompanied by a decrease in oxidative capacity, while any increase in oxidative capacity would be accompanied by a decrease in fibre size. We have seen, however, that in hypertrophied mouse muscles the oxidative capacity for a given fibre size is higher than in control muscles [2], and superimposition of oestrogen-related receptor gamma on a myostatin null background resulted in hypertrophic muscle with a high oxidative capacity [3]. In mice, the hypertrophic response was not attenuated by the addition of endurance training [2] and in bodybuilders superimposed endurance training resulted in an increased oxidative capacity without a reduction in size of the muscle fibres. In all these examples, the violation of the inverse relationship between fibre size and oxidative capacity was accompanied by angiogenesis and in old mice, the attenuated angiogenesis was associated with a blunted hypertrophic response [2]. These observations indicate that either 1) in normal muscles the fibre size and oxidative capacity are located below the line of the inverse relationship and/or 2) that angiogenesis is an important mechanism to break this inverse relationship.

References:

1. Van der Laarse, W.J., et al., Size principle of striated muscle cells. Neth J Zool 1998, 48, 213-223.

2. Hendrickse, P.W., et al., Regular endurance exercise of overloaded muscle of young and old male mice does not attenuate hypertrophy and improves fatigue resistance. Geroscience 2020,

3. Omairi, S., et al., Enhanced exercise and regenerative capacity in a mouse model that violates size constraints of oxidative muscle fibres. Elife 2016, 5

H3

Therapeutic potential of slow muscle programming for muscle diseases

Gordon Lynch, Australia

Justin P. Hardee[1], Karen J.B. Martins[1], Paula M. Miotto[1], James G. Ryall[1], Stefan M. Gehrig[1], Boris Reljic[2], Timur Naim[1], Dylan J. Chung[1], Jen Trieu[1], Kristy Swiderski[1], Ashleigh M. Philp[3], Andrew Philp[3], Matthew J. Watt[1], David A. Stroud[2], Rene Koopman[1], Gregory R. Steinberg[4], and Gordon S. Lynch[1]
[1]Centre for Muscle Research, Department of Physiology, The University of Melbourne, Victoria, 3010, Australia; [2]Department of Biochemistry and Molecular Biology, The Bio21 Institute, The University of Melbourne; [3]Garvan Institute of Medical Research, Sydney, New South Wales, 2010, Australia; and [6]Centre for Metabolism, Obesity and Diabetes Research, McMaster University, Hamilton, ON L8S 4L8, Canada.

In Duchenne muscular dystrophy (DMD) and in well-characterized murine models of the disease linked to the genetic loss of dystrophin, fast muscle fibres are more susceptible to contraction-mediated damage and pathological progression than slow muscle fibres, which are resistant to injury and relatively spared. Oxidative muscle fibres may be protected because they express more utrophin-A protein than glycolytic fibres, and overexpression of utrophin functionally substitutes for dystrophin in transgenic *mdx* (dystrophin null) mice and ameliorates the dystrophic pathology. Promoting an oxidative phenotype also increases utrophin-A expression, highlighting the therapeutic potential of muscle plasticity to mitigate the dystrophic pathology (Ljubicic et al. 2011). Developing strategies along these lines requires understanding the biological roles of dystrophin and utrophin in muscle adaptation and plasticity, but currently these roles are unknown.
Chronic low-frequency electrical stimulation (LFS) has improved understanding of the adaptive and metabolic plasticity of skeletal muscle and in preliminary trials, this approach has improved muscle strength in DMD patients (Lynch 2017). A mechanistic understanding of the biological roles of dystrophin and utrophin in these beneficial adaptations remains elusive, but this is essential if LFS is to be optimized for DMD and related disorders.
To understand the roles of dystrophin and utrophin in muscle adaptation and plasticity, we combined whole transcriptome RNA sequencing and mitochondrial proteomics with assessments of metabolic and contractile function, we interrogated roles for dystrophin and utrophin in fast-to-slow muscle remodeling with LFS (10 Hz, 12 h/d, 7 d/wk., 28 d) in *mdx* (dystrophin null) and *dko* (dystrophin/utrophin null) mice; two established preclinical models of DMD (Gehrig et al. 2012).
Novel biological roles of dystrophin and utrophin in adaptation and plasticity were identified through the impaired transcriptional activation of estrogen-related receptor alpha responsive genes supporting oxidative phosphorylation. Further, utrophin expression in dystrophic muscles was required for LFS-induced remodeling of mitochondrial respiratory chain complexes, enhanced fibre respiration, and conferring protection from eccentric contraction-mediated damage.
These findings reveal novel roles for dystrophin and utrophin during LFS-induced metabolic remodeling of muscle and highlight its therapeutic potential to ameliorate the dystrophic pathology with important implications for DMD and related muscle disorders.

References
Lynch, GS (2017). Therapeutic potential of skeletal muscle plasticity and slow muscle programming for muscular dystrophy and related muscle conditions. (ed) K. Sakuma – *The Plasticity of Skeletal Muscle* ISBN: 978-981-10-3291-2, Springer Nature.

Ljubicic, V, Miura, P, Burt, M, Boudreault, L, Khogali, S, Lunde, JA, Renaud, JM, Jasmin, BJ (2011). Chronic AMPK activation evokes the slow, oxidative myogenic program and triggers beneficial adaptations in mdx mouse skeletal muscle. *Hum Mol Genet* 20, 3478-3493.

Gehrig SM, van der Poel C, Sayer TA, Schertzer JD, Henstridge DC, Church JE, Lamon S, Russell AP, Davies KE, Febbraio MA, Lynch GS (2012). Hsp72 preserves muscle function and slows progression of severe muscular dystrophy. *Nature* 484, 394-398.

Supported by the National Health & Medical Research Council of Australia (GNT1124474)

H4

Cell therapy strategies for skeletal muscle injury

Tobias Winkler, Germany

Skeletal muscle injuries often cause long term disabilities in patients and cannot yet be addressed by effective therapies. We have investigated the safety and effectiveness of mesenchymal stromal cell (MSC) therapies for the treatment of muscle trauma and managed to transfer therapy from preclinical tests to the patient.

Primarily, we established a clinically relevant soleus trauma animal model and analyzed autologous and allogeneic MSC transplantation. Here, we used human placenta-derived mesenchymal like adherent stromal cells (PLX-PAD). After successful preclinical results, we translated this treatment into clinics, using iatrogenic muscle damage after total hip arthroplasty (THA) as a model system. We conducted a randomized, double blind, placebo-controlled phase I/II study with 20 patients undergoing THA via lateral approach. These patients received a transplantation of either 300x106 (300M), 150x106 (150M) PLX-PAD or placebo into the iatrogenically injured gluteus medius muscles (GM).
Our animal data showed improved muscle function after MSC therapy versus placebo. We further explored mechanistic paths and found that MSCs had an impact on CD4+/CD8+ ratios in the healing muscles, which correlated to our data from bone and tendon healing.
The phase I/II study showed no relevant AEs over 2 year FU. Change of GM strength after 6 months, showed a significant increase in the 150M group ($p=0.0067$) compared to placebo, and an increase in volume ($p = 0.004$). The 300M group showed a similar pattern as in the 150M group but no statistical significance. Histology indicated faster healing after PLX-PAD therapy and biomarker studies showed a reduction of the postoperative immunological stress reaction.
Based on these results we designed a phase III study - HIPGEN - treating patients undergoing hip fracture arthroplasty (N=240). These patients receive an intramuscular injection of 150M PLX cells to adressing muscle healing, mobility and mortality. We coordinate the HIPGEN consortium funded by the European Union Horizon 2020 program (Grant No 779293) and are currently enrolling patients in 20 sites in Germany, England, Denmark, Israel and the US. The patients are followed for function, biomechanics, quality of life, muscle volume and biomarkers. We further look into the mechanism of action in in vitro experiments on the effect of PLX cells on muscle and immune cells.
In conclusion, we could demonstrate a possible new way for skeletal muscle regeneration. Phase III data is expected soon and if successful, would pave the path for a cell therapy approach not only for the analyzed trauma but also for other skeletal muscle injuries.

I1

How to screen for cachexia in humans

Richard Skipworth, UK

The recently published GLIM (Global Leadership in Malnutrition) consensus for the diagnosis and grading of malnutrition has advocated the use of any validated malnutrition screening tool during the initial screening of at-risk populations[1]. Furthermore, the GLIM diagnostic scheme recommends inflammatory status and disease burden (2 core components of cancer cachexia) as etiologic criteria to consider during the assessment of malnutrition, thus highlighting that such an approach should be valid for cancer patients. In comparison, the 2011 consensus definition of cancer cachexia recommends weight loss, BMI or direct measures of muscularity as tools to screen for cachexia[2]. The ESPEN guidelines on nutrition in cancer patients also supports the use BMI and weight loss, plus an index of food intake, but accepts that some of these values may be obtained through validated screening questionnaires[3].

More than 70 nutritional screening tools for use in hospitals have been developed to facilitate easy screening or assessment of a patient's nutritional status or to predict poor clinical outcome related to unintentional weight loss. However, to date, only one, the CASCO tool, has been described specifically for screening patients at risk of cancer cachexia. Despite increasing research, there appears to be a continued lack of a practical and implementable screening tool, integrated into routine clinical practice, to support the specific diagnosis of cachexia, or to distinguish from malnutrition and sarcopenia[4].

In this talk, we will consider the role of screening in the diagnosis and management of cachexia, and consider various potential ways in which this may be achieved, including anthropometry/nutritional status, body composition analysis/cross-sectional imaging, and biochemistry.

References:

1. Cederholm T et al. GLIM criteria for the diagnosis of malnutrition - A consensus report from the global clinical nutrition community. J Cachexia Sarcopenia Muscle. 2019 Feb;10(1):207-217.

2. Fearon K et al. Definition and classification of cancer cachexia: an international consensus. Lancet Oncol 2011;12(5):489-95.

3. Arends J et al. ESPEN guidelines on nutrition in cancer patients. Clin Nutr 2017 Feb;36(1):11-48.

4. Miller J et al. Validated screening tools for the assessment of cachexia, sarcopenia, and malnutrition: a systematic review. Am J Clin Nutr 2018;108(6):1196-1208.

I2

Cross-talk between bone and muscle in metastatic cancer

Theresa Guise, USA

Cancer cells hijack the normal bone cells to disrupt normal bone remodeling and increase morbidity and mortality in affected patients. The effects and consequences of cancer on bone are well-known, yet little is understood about why it increases the risk of death. The lecture will present evidence that the tumor-bone microenvironment extends beyond bone to elicit systemic effects which impact morbidity and mortality in ways we never imaged. This extreme example of pathological bone remodeling in cancer to impact muscle function, metabolism and more provides the rationale to study systemic effects of abnormal bone remodeling due to any cause.

Waning DL, Mohammad KS, Reiken S, Xie W, Andersson DC, John S, Chiechi A, Wright LE, Umanskaya A, Niewolna M, Trivedi T, Charkhzarrin S, Khatiwada P, Wronska A, Haynes A, Benassi MS, Witzmann FA, Roodman GD, Marks AR, Guise TA. Excess TGFβ mediates muscle weakness associated with bone metastases in mice. Nature Medicine 2015 Nov;21(11):1262-1271. doi: 10.1038/nm.3961.Epub 2015 Oct 12. PubMed PMID: 26457758; PubMed Central PMCID: PMC4636436.

Santulli G, Pagano G, Sardu C, Xie W, Reiken S, Luca D'Ascia S, Cannone M, Marziliano N, Trimarco B, Guise TA, Lacampagne A, Marks AR Ryanodine receptor/calcium release channel regulates insulin release and glucose homeostasis. J Clin Invest, 2015 Apr 6. pii: 79273. doi: 10.1172/JCI79273. PMID:25844899

Wright LE, Harhash AA, Kozlow WM, Waning DL, Regan JN, She Y, John SK, Murthy S, Niewolna M, Marks AR, Mohammad KS, Guise TA. Aromatase inhibitor-induced bone loss increases the progression of estrogen receptor-negative breast cancer in bone and exacerbates muscle weakness in vivo. Oncotarget. 2016 Dec 25. doi:10.18632/oncotarget.14139. PubMed PMID: 28039445.

I3

Connecting diet, metabolism, and tumor growth in human cachectic patients with cancer

Marcus Goncalves, USA

Cachexia is an umbrella term used to describe a heterogenous population experiencing weight loss due to chronic illness. In subjects with cancer, a variety of factors contributes to weight loss including substances released by tumors, inflammatory cytokines, side effects from therapeutic interventions, mood disorders, immobility, and endocrine/metabolic dysfunction. This plethora of abnormalities ultimately results in skeletal muscle and adipose tissue atrophy, which reduces mobility, increases morbidity, and worsens mortality. In general, prospective intervention trials targeting cachexia have been disappointing. Typically, the enrollment criteria for these studies have been overly broad and not evidence-based. There is an urgent need for better methods of categorizing/phenotyping patients with cachexia using clinical criteria and biomarkers. This presentation will describe our experience managing cachexia in clinical practice. I will describe the extreme heterogeneity in subjects referred for cachexia management and review my diagnostic and therapeutic approach. This methodology is based on the assessment and treatment of 5 “pillars” of weight loss: 1) Secondary causes, 2) Appetite and Absorption, 3) Calories and Protein, 4) Muscle Strength and Resistance Training, and 5) Systemic Inflammation. I will present retrospective data and review anecdotal cases that highlight the usefulness of this approach and benefits to using approved medications off-label.

References:

Del Fabbro E. Combination therapy in cachexia. Ann Palliat Med. 2019 Jan;8(1):59-66. doi: 10.21037/apm.2018.08.05

I4

Growth differentiation factor 15 (GDF-15) is a key regulator of cancer cachexia

Bei Zhang, USA
Worldwide Research, Development and Medical, Pfizer

Cachexia is a metabolic disease characterized by unintentional weight loss with depletion of skeletal muscle and adipose tissue, where anorexia, nutritional imbalance, metabolic changes, and inflammation are key drivers. Paradoxically, chemotherapy also induces cachexia and nausea/emesis independent of cancer and although anti-emetic agents have beneficial effects, it remains a major challenge in cancer therapy. Therefore, treatments that target multiple aspects of cachexia are expected to be more effective in improving the debilitating conditions. GDF-15 is a cytokine well established to cause anorexia, aversion/emesis and weight loss in preclinical models and is associated with cancer cachexia and poor survival in patients. GDF-15 is also associated with platinum-based chemotherapy-induced adverse effects, however, a causal role for GDF-15 in mediating the emetic response has not been established. Furthermore, whether GDF-15 neutralization can reverse these effects and improve survival in cancer cachexia models combined with platinum chemotherapy remains to be evaluated, which is critical for providing confidence in GDF-15-based therapeutics for cachexia.

In this presentation, using mouse and/or nonhuman primate models, we provide evidence that GDF-15 inhibition via a potent and selective monoclonal antibody (mAB1) prevents platinum chemotherapy-induced emesis, anorexia, weight loss, with increased survival. Furthermore, expanding on the anti-emetic potential, we establish an association between increased emetic score status and circulating GDF-15 beyond the platinum-based chemotherapy family. The preclinical findings are supported by patient data where we demonstrate an association between elevated circulating GDF-15 levels and platinum-based chemotherapy use. These findings support that GDF-15 inhibition with mAB1 holds the potential as an effective therapeutic approach in combination with chemotherapy to alleviate GDF-15 mediated emesis and cachexia and enable optimal cancer treatment to improve patient quality of life and potentially survival.

J1

Biomarkers of physical frailty and sarcopenia – BIOSPHERE Study

Emanuele Marzetti, Italy
Fondazione Policlinico Universitario “Agostino Gemelli” IRCCS, Università Cattolica del Sacro Cuore, Rome, Italy

Although the theoretical construct of sarcopenia is widely acknowledged, its practical implementation is hampered by the existence of multiple and only partially overlapping operational definitions. The matter is further complicated by the superimposition of other age-related conditions and the heterogeneity of clinical phenotypes. The definitional ambiguities and the clinical complexity of sarcopenia have also hindered the identification of meaningful biomarkers for the conditions. To overcome existing limitations in the field, the "BIOmarkers associated with Sarcopenia and Physical frailty in ElderRly pErsons" (BIOSPHERE) study was designed to identify and validate a panel of biomarkers for the newly operationalised physical frailty & sarcopenia (PF&S) syndrome, which was framed in the context of the SPRINTT project. PF&S has a multifaceted pathophysiology that recapitulates all major hallmarks of aging, therefore representing a prototypical geroscience condition. As such, a single biomarker will hardly be able to capture its intrinsic complexity. In BIOSPHERE, we therefore developed innovative approaches for the identification and validation of PF&S biomarker, moving from the “one fits all” paradigm to multivariate methodologies. Our analytical strategy allowed identification of PF&S-specific patterns of circulating inflammatory biomolecules, amino acids and derivatives, and mitochondrial-derived vesicle cargo molecules, as well as a gut microbial fingerprint [1-3],
The innovative approach adopted in the BIOSPHERE enabled the determination of a comprehensive panel of biomarkers that could serve for (a) integrating specific biochemical measurements into the clinical assessment of PF&S, (b) providing hints to the biological pathways leading to functional impairment in old age, (c) identifying novel targets for interventions, and (d) determining surrogate endpoints to be used in clinical and research settings.

References

1. Picca A, Ponziani FR, Calvani R, Marini F, Biancolillo A, Coelho-Junior HJ, Gervasoni J, Primiano A, Putignani L, Del Chierico F, Reddel S, Gasbarrini A, Landi F, Bernabei R, Marzetti E. Gut microbial, inflammatory and metabolic signatures in older people with physical frailty and sarcopenia: results from the BIOSPHERE study. Nutrients 2019;12:65.

2. Calvani R, Picca A, Marini F, Biancolillo A, Gervasoni J, Persichilli S, Primiano A, Coelho-Junior HJ, Cesari M, Bossola M, Urbani A, Onder G, Landi F, Bernabei R, Marzetti E. Identification of biomarkers for physical frailty and sarcopenia through a new multi-marker approach: results from the BIOSPHERE study. Geroscience 2020 [Online ahead of print]. doi: 10.1007/s11357-020-00197-x.

3. Marzetti E, Guerra F, Calvani R, Marini F, Biancolillo A, Gervasoni J, Primiano A, Coelho-Júnior HJ, Landi F, Bernabei R, Bucci C, Picca A. Circulating mitochondrial-derived vesicles, inflammatory biomarkers and amino acids in older adults with physical frailty and sarcopenia: a preliminary BIOSPHERE multi-marker study using sequential and orthogonalized covariance selection - linear discriminant analysis. Front Cell Dev Biol 2020;8:564417.

J2

Biomarkers to assess skeletal muscle loss and malnutrition

Adrian Slee, UK
Division of Medicine, University College London (UCL), London, UK

Skeletal muscle loss is a key component of sarcopenia, cachexia and malnutrition (1,2). It is associated with poor clinical outcomes. Skeletal muscle loss and malnutrition are overlapping conditions and practical screening has been suggested using a range of methods such as anthropometry, scanning techniques and functional tests (1,2). There are several issues however, including accuracy of techniques and specific diagnostic cut-off points. Potential biomarkers have been suggested as early markers of dysfunction or progression and in determining trajectory of disease.
Creatinine (blood and urine) is a recognized and well-researched biomarker for estimating muscle mass. The D3 creatine dilution method has shown high accuracy compared to MRI measurements. Markers of muscle protein degradation such as 3-methylhistidine have been studied alongside markers of collagen turnover and extra cellular matrix regulation. Presence of Titin fragment in urine has also been recently identified as a novel marker of muscle damage.
Muscle loss can have complex pathophysiology (1). Therefore, a range of markers have been suggested such as hormones (e.g. androgens, IGF-1), markers of neuromuscular degeneration (e.g. c-terminal agrin), inflammation (e.g. CRP, cytokines) and myokines (e.g. myostatin, follistatin). Other novel biomarkers of muscle wasting include non-coding miRNA.
Potential biomarkers for malnutrition include visceral proteins, cholesterol, immune markers and micronutrients. A recent systematic review and meta-analysis in 111 studies with 52,911 older adults showed that in malnourished patients, albumin, transthyretin, cholesterol and total protein were significantly lower (2). Albumin and transthyretin are components of different nutritional and prognostic risk scores. Transthyretin has also been suggested as a suitable biomarker for lean body mass. The current GLIM criteria for malnutrition diagnosis suggest use of inflammatory markers as etiological criteria (1). Therefore, CRP, CRP/albumin ratio and inflammatory cytokines may also be useful in assessing risk development. Other possible biomarkers for malnutrition include IGF-1, leptin and appetite hormones.
More research is necessary to develop suitable biomarker screening panels for skeletal muscle loss and malnutrition.

References:
1. Biolo et al., Muscle contractile and metabolic dysfunction is a common feature of sarcopenia of ageing and chronic disease: from sarcopenic obesity to cachexia. *Clinical Nutrition* 2014; 33: 737-748.
2. J ensen et al,. GLIM criteria for the assessment of malnutrition: a consensus report from the global community. *JPEN.* 2019; 43(1):32-40.
3. Zhang et al,. Evaluation of blood biomarkers associated with risk of malnutrition in older adults: a systematic review and meta-analysis. *Nutrients*. 2017; 9, 829.

J3

Clinical applications of automated CT scans

Bette Caan, USA
Division of Research Kaiser Permanente Medical Program of Northern California, Oakland, California Kaiser

Important advances have been made in the automation of assessing body composition from computed tomography (CT) scans to make this process accurate, quick and cost-efficient. Since CT scans are used routinely in diagnosis and surveillance of cancer patients, these advances will allow clinicians the possibility to incorporate measures of body composition, especially the identification of patients with low muscle or sarcopenia, into clinical practice. Additionally, large reference populations of body composition derived from CT scans from patients without cancer that are age, sex and race specific, would complement the body composition data available from cancer patients. It would enable clinicians to better understand the degree of muscle loss due to aging versus cancer, and better evaluate the anabolic potential of their patients. Body composition data can also risk stratify patients for specific treatments and interventions. Patients with low muscle mass across different chemotherapy regimens are at increased risk for dose-limiting toxicities[1] and those with low muscle radiodensity, are at higher risk of cardiovascular events after a breast cancer diagnosis[2]. Additionally, there is evidence that patients with low muscle will benefit from physical activity interventions after treatment, while those with adequate muscle may not[3]. These examples illustrate how these data could be incorporated into clinical care to modify treatments to these high-risk groups, or target interventions to those patients who are most likely to benefit. Body composition can also be incorporated into predictive analytics. A recently funded study incorporates an informatics approach among surgical patients by combining automated body composition combined with frailty metrics to predict post-surgical complications and identify high risk surgical candidates. Similar approaches could be used with other cancer outcomes. Lastly, CT scans can be used for early detection of cancer. Studies have demonstrated that biomarkers such as branch chain amino acids (BCAAs) may be elevated for a significant period before a pancreatic cancer diagnosis, indicating that tumors are sequestering muscle for their own growth[4]. We are currently investigating whether this muscle loss is evidenced on CT scans in the year before pancreatic cancer is diagnosed and results are promising. As the automation of body composition metrics from CT becomes increasingly integrated into our health care systems, it is highly likely that this information will be become part of the routine set of data in a patient's medical record, and available to every clinician. The task will then be to teach clinicians how to interpret these data and how best to use them to optimize clinical care.

References

1. Prado CM, Cushen SJ, Orsso CE, Ryan AM. Sarcopenia and cachexia in the era of obesity: clinical and nutritional impact. *Proc Nutr Soc.* 2016;75(2):188-198.

2. Cespedes Feliciano EM, Chen WY, Bradshaw PT, et al. Adipose Tissue Distribution and Cardiovascular Disease Risk Among Breast Cancer Survivors. *J Clin Oncol.* 2019;37(28):2528-2536.

3. Buffart LM, Sweegers MG, May AM, et al. Targeting Exercise Interventions to Patients With Cancer in Need: An Individual Patient Data Meta-Analysis. *J Natl Cancer Inst.* 2018;110(11):1190-1200.

4. Mayers JR, Wu C, Clish CB, et al. Elevation of circulating branched-chain amino acids is an early event in human pancreatic adenocarcinoma development. *Nat Med.* 2014;20(10):1193-1198.

J4

Looking to the future of automated analysis

Mirza Faisal Beg, Canada

K1

Lipocalin-2 regulates appetite and neurocognitive decline during cancer cachexia

Daniel Marks, USA

Brennan Olson[1,4*], Christian Huisman[1,2*], Daniel L. Marks[1,2,3]
1 Papé Family Pediatric Research Institute, Oregon Health & Science University, Portland, United States.
2 Knight Cancer Institute, Oregon Health & Science University, Portland, United States.
3 Brenden-Colson Center for Pancreatic Care, Oregon Health and & Science University Portland, Portland, United States.
4 Medical Scientist Training Program, Oregon Health & Science University, Portland, United States.
*Equal Author Contributions

The behavioral and metabolic disturbances found in cancer cachexia are, at least in part, centrally regulated by the brain as a physiological reaction to tumor derived factors. For example, anorexia is extremely common in cancer patients, and is a primary determinant of both their quality of life (QoL) and overall resilience. We, along with others, demonstrated that signaling between tumor and the CNS is critical for the metabolic, behavioral, and neurocognitive complications during tumor growth. We determined that the mediobasal hypothalamus (MBH) is uniquely equipped as both a sensor and amplifier of peripheral inflammatory signaling. This region has an attenuated, dynamic blood brain barrier and contains specialized cells that transform peripheral inflammatory signals into a unique central inflammatory response, thereby altering the activity of key metabolic neurocircuitry located in this region. To investigate the involvement of this region in cancer cachexia in more detail, we performed single cell RNA-seq of the MBH in a mouse model of cancer cachexia. We found many cell-type specific changes, dominated by those occurring in endothelial cells, microglia and oligodendrocytes, and displaying signs of stress, inflammation and/or loss of membrane integrity. We established cell type-specific networks of differentially expressed genes to visualize the affected pathways, giving precise insight into the underlying molecular mechanisms of cachexia. Treatment with Lcn2, the protein product of the gene with the highest degree of induction in this region, was sufficient to induce transcription of an array of genes upregulated in cachexia in microglia and oligodendrocytes, but had no effect on genes in the cellular stress pathways. LCN2KO mice resist cancer-induced anorexia, and LCN2 treatment leads to anorexia, CNS inflammation, and neurocognitive deficits in mouse models. Taken together, our single cell transcriptome analysis of the MBH uncovers the underlying gene networks activated during cancer cachexia. The cell type-specific responses revealed here provide mechanistic insight into many of the clinical features of cachexia and will be useful for future therapeutic development.

References:

Microglia in the hypothalamus respond to tumor-derived factors and are protective against cachexia during pancreatic cancer.
Burfeind KG, Zhu X, Norgard MA, Levasseur PR, Huisman C, Michaelis KA, Olson B, **Marks DL.**Glia. 2020 Jul;68(7):1479-1494. doi: 10.1002/glia.23796. Epub 2020 Feb 10.

Pretreatment Cancer-Related Cognitive Impairment-Mechanisms and Outlook.
Olson B, **Marks DL.**Cancers (Basel). 2019 May 16;11(5):687. doi: 10.3390/cancers11050687.

K2

A selective inhibitor of p38β MAPK abrogates muscle wasting and prolongs survival of tumor-bearing mice

Yi-Ping Li, USA

Thomas K. Sin[1], Guohua Zhang[1], Zicheng Zhang[1], James Z. Zhu[1], Zuo Yan[1], Jeffrey A. Frost[1], Min Li [1, 2,3,4], and Yi-Ping Li[1]*

[1] Department of Integrative Biology and Pharmacology, The University of Texas Health Science Center at Houston, 6431 Fannin Street, Houston, TX 77030, USA. [2] The Vivian L. Smith Department of Neurosurgery, The University of Texas Health Science Center at Houston, Houston, TX 77030, USA. [3] Department of Medicine, The University of Oklahoma Health Sciences Center, Oklahoma City, OK 73104, USA. [4] Department of Surgery, The University of Oklahoma Health Sciences Center, Oklahoma City, OK 73104, USA

Cancer-associated cachexia, characterized by muscle wasting, is a lethal metabolic syndrome without defined etiology or established treatment. We previously found that p300 mediates cancer-induced muscle wasting by activating C/EBPβ through acetylating its Lys-39 residue, which then upregulates key catabolic genes. However, the signaling mechanism that activates p300 in response to cancer is unknown. Here, we show that upon cancer-induced activation of Toll-like receptor 4 (TLR4) in skeletal muscle, p38β MAPK phosphorylates Ser-12 of p300 to stimulate C/EBPβ acetylation, which is necessary and sufficient to cause muscle wasting. Thus, p38β MAPK is a central mediator and therapeutic target of cancer-induced muscle wasting. In addition, we found that nilotinib, an FDA-approved kinase inhibitor that preferentially binds p38β MAPK, inhibits p300 and C/EBPβ activation 20-fold more potently than the p38α/β MAPK inhibitor SB202190 in C2C12 myotubes, abrogating cancer cell conditioned media-induced muscle protein loss without suppressing p38α MAPK-dependent myogenesis. Systemic administration of nilotinib at a low dose (0.5 mg/kg/day, IP) in tumor-bearing mice not only alleviates muscle mass loss but also protects muscle function. Finally, nilotinib prolongs survival of tumor-bearing mice. Therefore, nilotinib appears to be a promising treatment for human cancer cachexia due to its selective inhibition of p38β MAPK.

References:

1. Liu Z, Sin KWT, Ding H, Doan HA, Gao S, Miao H, Wei Y, Wang Y, Zhang G, and **Li Y-P**. p38β MAPK Mediates ULK1-Dependent Induction of Autophagy in Skeletal Muscle of Tumor-Bearing Mice. *Cell Stress* 2(11): 311-324, 2018. Epub 10/10/2018. DOI: 10.15698/cst2018.11.163.

2. Sin TK, Zhu JZ, Zhang G, and **Li Y-P**. p300 Mediates Muscle Wasting in Lewis Lung Carcinoma. *Cancer Res.* 79(7):1331-1342, 2019. DOI: 10.1158/0008-5472.CAN-18-1653

3. Sin TK, Zhang G, Zhang Z, Gao S, Li M and **Li Y-P**. Cancer Takes a Toll on Skeletal Muscle by Releasing Heat Shock Proteins—An Emerging Mechanism of Cancer-Induced Cachexia. *Cancers* 30;11(9):1272, 2019. doi:10.3390/cancers11091272.

This study was supported by a grant from National Institute of Arthritis and Musculoskeletal and Skin Diseases to Y.-P.L. (R01 AR067319) and a grant from National Cancer Institute to Y.-P.L. and M.L. (R01 CA203108).

K3

GDF15 neutralization reverses cancer cachexia and restores physical performance

Zhidan Wu, USA
Internal Medicine Research Unit, Pfizer, Cambridge, MA, USA

Cancer cachexia is a metabolic disease characterized by unintentional weight loss, anorexia, fatigue, muscle wasting and chronic inflammation, all of which being contributing factors to poor quality of life and survival in patients. GDF-15 is a cytokine reported to cause anorexia, aversion/emesis and weight loss in preclinical models and is associated with cancer cachexia and poor survival in patients. GDF-15 inhibition was effective to reverse weight loss, muscle and fat loss in mouse tumor models. Interestingly, it remains unclear whether increased skeletal muscle mass by GDF-15 inhibition results in restoration of muscle strength and physical performance. We investigated these questions in two mouse tumor models, TOV21G (human ovarian tumor) and RENCA (murine renal tumor) using a potent and selective monoclonal antibody (mAB2) that neutralizes circulating GDF-15. Treatment with mAb2 completely reversed tumor-induced cachexia including weight loss, lean and fat mass loss in these tumor bearing mice. In addition, mAb2 increased muscle strength and exercise performance in TOV21G mice. Our findings indicate GDF-15 is a key regulator of cancer cachexia and GDF-15 inhibition holds the potential as an effective therapeutic approach to alleviate GDF-15 mediated cachexia and declined physical function in cancer cachexia patients.

References:

Borner, T., et al. (2020b). GDF15 Induces an Aversive Visceral Malaise State that Drives Anorexia and Weight Loss. Cell Rep *31*, 107543.

Lerner, L., et al. (2016). MAP3K11/GDF15 axis is a critical driver of cancer cachexia. J Cachexia Sarcopenia Muscle *7*, 467-482.

Tsai, V.WW, et al. (2018). The MIC-1/GDF15-GFRAL pathway in energy homeostasis: Implications for obesity, cachexia, and other associated diseases. Cell Metab 28, 353-368.

K4

Inhibition of activin-like kinase 4/5 attenuates cancer cachexia associated muscle wasting

Stef Levolger, The Netherlands

Cancer mediated activation of the ActRIIB-ALK4/5 heterodimer by myostatin is strongly associated with muscle wasting. We investigated in vitro and in vivo the efficacy of ALK4/5 receptor blockers SB431542 and GW788388 in preventing muscle wasting. In vitro, C2C12 skeletal muscle cells were treated with vehicle, SB431542 and GW788388. A C26-CD2F1 cachexia model was used to induce cachexia in vivo. Mice were allocated as non-tumor bearing (NTB) or C26 tumor-bearing (C26 TB) vehicle control, treated with SB431542, or GW788388 (intraperitoneally or orally). In vitro, differentiation index and mean nuclei count increased using SB431542, GW788388. In vivo, GW788388 was superior to SB431542 in limiting loss of bodyweight, grip-strength and gastrocnemius weight. And downregulated Atrogin-1 expression comparable to NTB mice. In conclusion, treatment with GW788388 prevented cancer cachexia, and downregulated associated ubiquitin ligase Atrogin-1.

Reference / publication:

Levolger, S., Wiemer, E.A.C., van Vugt, J.L.A. et al. Inhibition of activin-like kinase 4/5 attenuates cancer cachexia associated muscle wasting. Sci Rep 9, 9826 (2019). https://doi.org/10.1038/s41598-019-46178-9

L1

The role of IL-1 in experimental CKD cachexia: Potential for novel therapy

Robert Mak, USA
University of California San Diego

Inflammatory cytokine signaling has been implicated in the etiology of cachexia and muscle wasting.[1] Recent evidence in preclinical models suggests that blockade of IL-1 signaling may be a logical therapeutic target for chronic disease associated muscle wasting. IL-1β activates NF-κβ signaling and induces expression of IL-6 and atrogin-1 in myocytes. Intracerebroventricular injection of IL-1β induces cachexia and muscle wasting in mice. Anakinra is an IL-1 receptor blocker for both IL-1α and IL-1β. Anakinra is FDA-approved and is a safe and an effective therapeutic option in a variety of diseases including diseases involving muscle. Serum IL-1β is elevated in patients with chronic kidney disease(CKD) on chronic hemodialysis and a 4-week treatment with anakinra was shown to be safe in these patients while significantly reducing markers of systemic inflammation such as CRP and IL-6.[3]
We investigated evaluated the efficacy of anakinra treatment in mice with CKD, with particular focus on adipose tissue browning and muscle wasting. CKD was induced in 6-week old mice by 5/6 nephectomy. CKD mice and sham-operated controls were treated with anakinra (2.5 mg.kg.day, IP) or saline for 6 weeks. Serum chemistry and parameters of energy homeostasis (food intake and weight gain, 24-hour metabolic rate and fat and lean mass content) were measured in mice. We also studied expression of molecules regulating energy homeostasis, muscle mass metabolism and adipose tissue browning in CKD mice.
Anakinra normalized food intake and weight gain, fat and lean mass content, metabolic rate and grip strength as well as attenuated perturbations of energy homeostasis in muscle and adipose tissue in CKD mice. Anakinra attenuated upregulated signaling pathways (Akt, ERK1/2, JNK, p38 MAPK and NF-κB) that have been implicated in muscle wasting in CKD mice. Concomitantly, anakinra improved muscle regeneration and myogenesis by increasing muscle mRNA expression of pro-myogenic factors (IGF-1, Pax7 and MyoD) while decreasing mRNA expression of negative regulators of skeletal muscle mass (MuRF-1, Atrogin-1 and myostatin) in CKD mice. Moreover, anakinra attenuated elevated expression of beige adipose cell biomarkers (UCP-1, CD137, Tmem26 and Tbx1) and aberrant expression of molecules implicated in adipocyte tissue browning (Cox2/Pgf2α and NF-κB pathway) in inguinal white adipose tissue in CKD mice. Anakinra represents a viable therapeutic strategy for cachexia in CKD.

References

1. Cheung W, Yu PX, Little BM, Cone RD, Marks DL, Mak RH: Robert H. Role of leptin and melanocortin signaling in uremia-associated cachexia. J Clin Invest 115: 1659–1665,2005
2. Braun TP, Zhu X, Szumowski M, Scott GD, Grossberg AJ, Levasseur PR, et al.: Central nervous system inflammation induces muscle atrophy via activation of the hypothalamic–pituitary–adrenal axis. J Exp Med 208:2449-2463, 2011
3. Deger SM, Hung AM, Gamboa JL, Siew ED, Ellis CD, Booker C, et al.: Systemic inflammation is associated with exaggerated skeletal muscle protein catabolism in maintenance hemodialysis patients. JCI Insight 2. pii: 95185, 2017

L2

Kidney cachexia or protein energy wasting?

Kamyar Kalantar-Zadeh, USA

Weight loss and homeostatic disturbances of both energy and protein balances are characteristics of several illnesses including cancer, heart failure, and chronic kidney disease (CKD). Different definitions have been used to describe this deleterious process. The term protein-energy wasting (PEW) has been proposed for CKD patients by the International Society of Renal Nutrition and Metabolism. Since its inception, the term PEW has been exceptionally successful, highlighted by 327 original publications referenced in PubMed over 10 years. Using this classification, several studies have confirmed that PEW is among the strongest predictors of mortality in CKD patients [hazard ratio of 3.03; confidence interval of 1.69–5.26 in 1068 haemodialysis patients and 1.40 (1.04–1.89) in 1487 non-dialysed patients across PEW stages 0 to 4]. Based on this classification, prevalence of PEW is 28% to 54% among 16 434 adults undergoing maintenance dialysis. PEW prevalence increases when renal function declines, that is, from <2% in CKD stages 1–2 to 11–54% in CKD stages 3–5. A more general definition of cachexia for all chronic diseases proposed by the Society on Sarcopenia, Cachexia and Wasting Disorders was also published concurrently. In the CKD area, we found 180 publications using 'cachexia' underlining that some confusion or overlap may exist. The definitions of PEW and cachexia are somewhat similar, and the main difference is that a loss of body weight >5% is a mandatory criterion for cachexia but supportive for PEW. The recent understanding of cachexia physiopathology during CKD progression suggests that PEW and cachexia are closely related and that PEW corresponds the initial state of a continuous process that leads to cachexia, implicating the same metabolic pathways as in other chronic diseases. Despite the success of the definition of PEW, using a more uniform term such as 'kidney disease cachexia' could be more helpful to design future research through collaborative groups of researchers with focus on cachexia.

References:[1-3]

1. Kalantar-Zadeh K and Moore LW. Improving Muscle Strength and Preventing Sarcopenia and Cachexia in Chronic Kidney Disease and Transplanted Patients by Physical Activity and Exercise. ***J Ren Nutr***. 2019;29(6):465-466. doi: 10.1053/j.jrn.2019.09.005. PubMed PMID: 31676147. URL: https://www.ncbi.nlm.nih.gov/pubmed/31676147.
2. Reid J, Noble HR, Adamson G, Davenport A, Farrington K, Fouque D, Kalantar-Zadeh K, Mallett J, McKeaveney C, Porter S, Seres DS, Shields J, Slee A, Witham MD and Maxwell AP. Establishing a clinical phenotype for cachexia in end stage kidney disease - study protocol. ***BMC Nephrol***. 2018;19(1):38. doi: 10.1186/s12882-018-0819-3. PubMed PMID: 29439674; PMCID: PMC5812213. URL: https://www.ncbi.nlm.nih.gov/pubmed/29439674.
3. Kalantar-Zadeh K, Rhee C, Sim JJ, Stenvinkel P, Anker SD and Kovesdy CP. Why cachexia kills: examining the causality of poor outcomes in wasting conditions. ***J Cachexia Sarcopenia Muscle***. 2013;4(2):89-94. doi: 10.1007/s13539-013-0111-0. PubMed PMID: 23749718; PMCID: PMC3684705. URL: http://www.ncbi.nlm.nih.gov/pubmed/23749718.

L3

Clinical phenotype of cachexia in kidney disease

Joanne Reid, UK

Background
Cachexia is common among citizens with chronic illnesses and is associated with increased morbidity and mortality. However, there continues to be an absence of a uniformed disease-specific definition for cachexia in chronic kidney disease. The primary objective of this study was to identify cachexia in patients receiving haemodialysis using a generic definition[1], and then follow these patients for twelve months.

Methods
Longitudinal study of 106 adult chronic haemodialysis patients attending two hospital haemodialysis units in the United Kingdom. Multiple measures relevant to cachexia including body mass, muscle mass - mid-upper arm muscle circumference, handgrip strength, fatigue - Functional Assessment of Chronic Illness Therapy, appetite - Functional Assessment of Anorexia/Cachexia Therapy and biomarkers- C-reactive protein; serum albumin; haemoglobin and erythropoietin resistance index were recorded. Baseline analysis included group differences analysed using independent *t*-test, dichotomized values using the *X*2 test and prevalence were reported using Statistical Package for the Social Sciences 24. Longitudinal analysis was conducted using repeated measures analysis.

Results
One hundred and six patients (30 females and 76 males) were recruited. Mean age was 67.2 years and dialysis vintage 4.92 years. At baseline, 17 patients were identified as having cachexia, having had reported weight loss (e.g., >5% for >6 months) or BMI (<20 kg/m2) and three or more clinical characteristics of cachexia [1]. Seventy patients were available for analysis at 12 months (*n* = 11 cachectic versus *n* = 59 not cachectic). Functional Assessment of Anorexia/Cachexia Therapy and urea reduction ratio statistically distinguished cachectic patients (P =0.001). Measures of weight, body mass index, mid-upper arm muscle circumference, handgrip strength, CRP, erythropoietin resistance index, and functional assessment of chronic illness therapy tended to be worse in cachectic patients.

Conclusion
Cachexia is a complex, frequently under-recognized problem. This is the first study to apply the defined characteristics of cachexia to a representative sample of patients receiving haemodialysis. Additional research in this area is warranted.

Funding
Public Health Agency Northern Ireland STL/5179/15 and Northern Ireland Kidney Research Fund.

References

1. Evans W J, Morley J E, Argilés J *et al*. Cachexia: A new definition. *Clinical Nutrition* 2008; 27: 793–799 10.1016/j.clnu.2008.06.013

L4

Sarcopenia in chronic kidney disease

Cynthia Delgado, USA

Muscle wasting and poor functional status are common among patients with chronic kidney disease (CKD)1-3. Many of the functional deficits observed among patients with chronic kidney disease overlap with both the European working group (EWGSOP) on Sarcopenia in Older Peoples definition of sarcopenia and the Fried criteria for frailty.4,5 Thus the high prevalence of sarcopenia and frailty in patients with chronic kidney disease is not surprising. Interestingly, observed deficits in muscle mass, function and physical function is not limited to patients with advanced chronic kidney disease.6-8 Even among patient with early kidney disease deficits in mobility and reduced gait speed have been observed.8 Such deficits leads to disability, decreased community interaction and unemployment.9,10 In addition. mortality risk is high among individuals with early to moderate kidney disease by both EWGSOP sarcopenia and Fried Frailty definition.6,7 Despite these observations, very few interventions have targeted individuals with non-dialysis dependent kidney disease.

1. Johansen KL, Shubert T, Doyle J, Soher B, Sakkas GK, Kent-Braun JA. Muscle atrophy in patients receiving hemodialysis: effects on muscle strength, muscle quality, and physical function. Kidney Int 2003;63:291-7.
2. Foley RN, Wang C, Ishani A, Collins AJ, Murray AM. Kidney function and sarcopenia in the United States general population: NHANES III. Am J Nephrol 2007;27:279-86.
3. Kim J-K, Choi SR, Choi MJ, et al. Prevalence of and factors associated with sarcopenia in elderly patients with end-stage renal disease. Clinical nutrition 2014;33:64-8.
4. Cruz-Jentoft AJ, Bahat G, Bauer J, et al. Sarcopenia: revised European consensus on definition and diagnosis. Age and Ageing 2018;48:16-31.
5. Fried LP, Tangen CM, Walston J, et al. Frailty in older adults: evidence for a phenotype. J Gerontol A Biol Sci Med Sci 2001;56:M146-56.
6. Delgado C, Grimes BA, Glidden DV, Shlipak M, Sarnak MJ, Johansen KL. Association of Frailty based on self-reported physical function with directly measured kidney function and mortality. BMC Nephrol 2015;16:203.
7. Roshanravan B, Robinson-Cohen C, Patel KV, et al. Association between physical performance and all-cause mortality in CKD. Journal of the American Society of Nephrology 2013:ASN. 2012070702.
8. Liu CK, Lyass A, Massaro JM, D'Agostino RB, Sr., Fox CS, Murabito JM. Chronic kidney disease defined by cystatin C predicts mobility disability and changes in gait speed: the Framingham Offspring Study. J Gerontol A Biol Sci Med Sci 2014;69:301-7.
9. Bowling CB, Muntner P, Sawyer P, et al. Community mobility among older adults with reduced kidney function: a study of life-space. Am J Kidney Dis 2014;63:429-36.
10. Plantinga LC, Johansen K, Crews DC, et al. Association of CKD With Disability in the United States. American Journal of Kidney Diseases 2011;57:212-27.

M1

Lipid metabolism in cancer cachexia

Maria Rohm, Germany

Cancer cachexia is a multifactorial energy-wasting syndrome reducing the efficiency of anti-cancer therapies, quality of life, and survival of cancer patients. In the past years, most studies focused on the identification of tumour and host-derived proteins contributing to cachexia. However, there is still a lack of studies addressing the changes in bioactive lipids, despite ample evidence of altered lipid metabolism in metabolic organs such as adipose tissue [1, 2]. Circulating bioactive lipids have been identified as important endocrine mediators regulating inflammation, metabolism, and energy expenditure, thereby playing central parts in metabolic disease. Their role in cachexia is still unknown. This underlines the importance of identifying specific lipid species as a hallmark of cachexia, and exploring their use as biomarkers or drivers of disease progression.
Using a lipidomics platform, we have recently measured the lipid profile in plasma of multiple different mouse models of cancer cachexia as well as of weight stable or weight-losing cancer patients. We identified 13 lipid classes and more than 1100 lipid species, including sphingolipids, neutral and polar glycerolipids. A decrease in several lysophosphatidylcholine (LPC) species and an increase in numerous sphingolipids including sphingomyelins, ceramides (CERs), hexosyl-ceramides (HCERs) and lactosyl-ceramides (LCERs), were mutual features of cachexia in both mice and cancer patients. Sphingolipid levels gradually increased during cachexia development, supporting their potential as early biomarkers for cachexia. Altered lipid metabolism in the liver is likely key to altered sphingolipid levels, as enzymes involved in ceramide synthesis were elevated in liver but not in adipose, muscle, or tumour tissues. Total levels of specific ceramide and LPC species correlated significantly with the severity of body weight loss in both mice and humans [3].
With the identification of specific signalling lipids in cachexia and the underlying mechanism of altered sphingolipid metabolism in the liver, we have come closer to understanding the complexity of multi-organ dysfunction in metabolic wasting. Circulating lipid species may be explored as early cachexia biomarkers in the future.

References:

[1] **Rohm M**[*], Schäfer M[*], Laurent V, Üstünel BE, Niopek K, Algire C, Hautzinger O, Sijmonsma TP, Zota A, Medrikova D, Pellegata NS, Ryden M, Kulyte A, Dahlman I, Arner P, Petrovic N, Cannon B, Amri EZ, Kemp BE, Steinberg GR, Janovska P, Kopecky J, Wolfrum C, Blüher M, Berriel Diaz M, Herzig S. An AMP-activated protein kinase-stabilizing peptide ameliorates adipose tissue wasting in cancer cachexia in mice. Nat Med. 2016 Oct;22(10):1120-1130.

[2] **Rohm M**, Zeigerer A, Machado J, Herzig S. Energy metabolism in cachexia. EMBO Rep. 2019 Apr;20(4).

[3] Morigny P[*], Zuber J[*], Haid M, Kaltenecker D, Riols F, Lima JDC, Simoes E, Otoch JP, Schmidt SF, Herzig S, Adamski J, Seelaender M, Berriel Diaz M[*], **Rohm M**[*]. High levels of modified ceramides are a defining feature of murine and human cancer cachexia. J Cachexia Sarcopenia Muscle. 2020 Oct 8.

M2

Adipose tissue remodeling in human cancer cachexia

Marilia Seelaender, Brazil
Cancer Metabolism Research Group, University of Sao Paulo, Brazil

White adipose tissue (WAT) has long been considered a non-fundamental part of cachexia onset and progression, despite suffering wasting in both cancer patients and in cachexia animal models. Indeed, even the current definition of cachexia envisages WAT wasting as of minor relevance, compared with muscle loss, one of the hallmarks of the syndrome. Additionally, the common view of WAT as an expendable organ has prevented the recognition of its potential role in cachexia-associated metabolic and inflammatory responses. More recently, owing to studies unveiling the occurrence of “browning” of WAT in rodent models of cachexia, more attention was directed to WAT. Nonetheless, the inconsistent results on browning in human cachexia (1) have clearly shown that mechanisms in patients may differ from those of rodents. We have examined the role of WAT as a major contributor to the syndrome in cancer patients and reported early and progressive morpho-functional changes in adipose depots that potentially contribute to chronic systemic inflammation, impacting the outcome of disease. We shall discuss, based on our studies (2,3) comparing weight stable and cachectic colorectal cancer patients, WAT remodelling, which is associated with inflammatory infiltration, WAT lipid shedding, WAT production and secretion of inflammatory markers, marked fibrosis; and the respective involved mechanisms (increased activity of TGFβ pathway, hypoxia, augmented lipolytic activity, dysregulated triacylglycerol storage, changes in pre-adipocyte proliferation capacity). Furthermore, the heterogenous response of the different anatomical fat depots will be considered (4). The consequences of altered WAT morphology and function include augmented inflammatory organ crosstalk, and lipid accumulation in various compartments, including the skeletal muscle (disrupting fibre metabolism). Therefore, in opposition to the formerly assumed, WAT plays a most relevant role in human cachexia and understanding the mechanisms involved will allow the proposal of novel diagnosis/therapeutic strategies.

References:

(1) doi: 10.1371/journal.pone.0239990.
(2) doi: 10.1186/s12944-017-0547-x
(3) doi: 10.1186/s12885-017-3178-8
(4) doi: 10.1002/jcsm.12626

M3

Fat tissues and prognosis in human chronic illness

Markus Anker, Germany

In many chronic diseases an obesity paradox has been decribed, where patients with a higher body mass index (BMI) show a better survival. (1,2) Similar results have also been found for patients with chorinc diseases and a higher relative fat mass in the body (3). Therefore, therapies increasing BMI and relative fat mass in patients with chronic diseases might be beneficial.

1 - Kalantar-Zadeh K et al. Am J Clin Nutr 2005;81:543-554
2 - Kenchaiah S et al. Circulation. 2007;116:627–636
3 - Lavie et al. American Journal of Medicine. 2009

M4

Association of circulating PLA2G7 levels with cancer cachexia and assessment of darapladib as a therapy

Mauricio Berriel Diaz, Germany

Pauline Morigny*, Doris Kaltenecker*, Julia Zuber*, Juliano Machado*, Lisa Mehr*, Hanna Kuzi, Chris D. Hermann, Michael Voelkl, German Monogarov, Christoph Springfeld, Victor Laurent, Bernd Engelmann, Helmut Friess, Inka Zörnig, Achim Krüger, Jeroen Krijgsveld, Olga Prokopchuk, Søren Fisker Schmidt*, Maria Rohm*, Stephan Herzig*, Mauricio Berriel Diaz*
*Institute for Diabetes and Cancer, Helmholtz Center Munich, 85764 Neuherberg, Germany

Cancer-cachexia (CCx) is characterized by involuntary loss of body weight that affects many cancer patients and implies a poor prognosis, reducing both tolerance to and efficiency of anti-cancer therapies. Actual challenges in management of CCx remain in the identification of tumor- and host-derived mediators involved in systemic inflammation and organ wasting, and in the discovery of biomarkers that would allow for an earlier and personalized care of cancer patients.
We performed a quantitative secretome analysis to identify specific factors more abundantly secreted by cachexia-inducing cancer cell lines as compared to cell lines, which do not induce wasting upon implantation into mice. We identified high expression and secretion of the phospholipase PLA2G7 as hallmarks of cachexia-inducing cancer cell lines. Indeed, circulating PLA2G7 activity was increased in different mouse models of CCx with various tumor entities, and was associated with the severity of body wasting. Notably, circulating PLA2G7 levels gradually rose during cachexia development. Genetic PLA2G7 knock down in C26 tumors only partially reduced plasma PLA2G7 levels, suggesting that the host is also an important contributor. Chronic treatment with darapladib, a specific inhibitor of PLA2G7, was not sufficient to counteract inflammation and organ wasting despite a strong inhibition of the circulating PLA2G7 activity. Importantly, increased PLA2G7 levels were also a marker of CCx in independent cohorts from two medical centers consisting of colorectal and pancreatic cancer patients.
Overall, our data show that despite no immediate pathogenic role, at least when targeted as a single entity, PLA2G7 is a robust marker of CCx in both mice and humans. The early increase in circulating PLA2G7 levels in pre-cachectic mice supports future prospective studies to assess its potential as biomarker for cancer patients.

N1

Cachexia as a global problem – data from different continents

Mitja Lainscak, Slovenia

N2

Obesity paradox for survival: Update 2020

Giuseppe Rosano, UK

N3

Diagnostic criteria for sarcopenia and sarcopenic obesity in Asia

Masaaki Konishi, Japan

In 2019, The Asian Working Group for Sarcopenia (AWGS) revised the diagnostic algorithm for sarcopenia (AWGS2019 (1)). In this algorithm, sarcopenia is defined by low musle mass AND each of low muscle strength OR low physical performance. Cutoffs for height-adjusted muscle mass are: dual-energy X-ray absorptiometry, <7.0 kg/m^2 in men and <5.4 kg/m^2 in women; and bioimpedance, <7.0 kg/m^2 in men and <5.7 kg/m^2 in women. Low muscle strength is defined as handgrip strength <28 kg for men and <18 kg for women. Criteria for low physical performance are 6-m walk <1.0 m/s, Short Physical Performance Battery score ≤9, or 5-time chair stand test ≥12 seconds. AWGS 2019 does not recommend specific diagnostic criteria for sarcopenic obesity. Using the body mass index cut-offs defined for Western populations, the prevalence of obesity (≥30) is only 2–4% in East Asia, in contrast to 10–20% in Europe and the USA.(2) Furthermore, if obesity was diagnosed with body mass index ≥25 kg/m^2,(3) the prevalence of sarcopenia may be extremely low in people with obesity. Asian populations have different associations between body mass index, % body fat, and health risk than European populations.(4) Epidemiologic evidence derived from AWGS 2019 is still insufficient so far, here we discuss the prevalence and prognostic implication of sarcopenia incorporating the previous definition (AWGS 2014 version). Regarding sarcopenic obesity, although consensus on its definition and diagnostic criteria remains insufficient also in Asia, there has been evidences from several observational/intervention study.

1. Asian Working Group for Sarcopenia: 2019 Consensus Update on Sarcopenia Diagnosis and Treatment, JAMDA 2020 Volume21 Issue 3: 300-307
2. Obesity and Overweight in Asian People, Circ J. 2016 Nov 25;80(12):2425-2426.
3. World Health Organization IOTF. The Asian-Pacific perspective: Redefining obesity and its treatment. Geneva: WHO Western Pacific Region, 2000
4. Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies, Lancet 2004 Volume 363 Issue 9403: 157-163

N4

Diagnostic criteria for sarcopenia and sarcopenic obesity in Europe

Juergen M Bauer, Germany
Center for Geriatric Medicine and Network Aging Research, Heidelberg University, Germany

In 2010 the first two European consensus papers on the definition and diagnosis of sarcopenia were published by an ESPEN[1] expert group and the EWGSOP[2]. Both initiatives introduced the measurement of strength and functional parameters, e.g. handgrip strength and/or gait speed, for the diagnosis of sarcopenia, while keeping the measurement of muscle mass as an essential diagnostic criterion. In the revised 2018 version of the EWGSOP[3] strength testing (e.g. handgrip, chair stand) was further upgraded, as the diagnosis of probable sarcopenia could now be made based solely on the criterion of low strength. The measurement of muscle mass was still recommended for the confirmation of the sarcopenia diagnosis. According to the EWGSOP consensus functional tests (e.g. gait speed, TUG, SPPB) would be applied to diagnose severe sarcopenia, if present. The EWGSOP also recommended case-finding based on sarcopenia-associated symptoms and screening with the help of the SARC-F questionnaire. With regard to the pathogenesis of sarcopenia the EWGSOP differentiated primary and secondary sarcopenia. The latter is caused by a wide range of etiologic factors, while malnutrition, comorbidity and inactivity may be regarded as the most relevant ones.
In a systematic review[4] that was published by a joined expert group of ESPEN and EASO the authors stated that the current evidence does not allow definite conclusions on the definition and diagnosis of sarcopenic obesity. Therefore, they called for a consensus proposal for diagnostic criteria, both at the level of potential gold-standards as well as for surrogates that may allow wide clinical applicability. A consensus initiative following a delphi-protocol is currently on the way, whose results will be published in 2021.

References

[1]Muscaritoli M, Anker SD, Argilés J, Aversa Z, Bauer JM, Biolo G, Boirie Y, Bosaeus I, Cederholm T, Costelli P, Fearon KC, Laviano A, Maggio M, Rossi Fanelli F, Schneider SM, Schols A, Sieber CC. Consensus definition of sarcopenia, cachexia and pre-cachexia: joint document elaborated by Special Interest Groups (SIG) "cachexia-anorexia in chronic wasting diseases" and "nutrition in geriatrics". Clin Nutr. 2010 Apr;29(2):154-9.

[2]Cruz-Jentoft AJ, Baeyens JP, Bauer JM, Boirie Y, Cederholm T, Landi F, Martin FC, Michel JP, Rolland Y, Schneider SM, Topinková E, Vandewoude M, Zamboni M; European Working Group on Sarcopenia in Older People. Sarcopenia: European consensus on definition and diagnosis: Report of the European Working Group on Sarcopenia in Older People. Age Ageing. 2010 Jul;39(4):412-23.

[3]Cruz-Jentoft AJ, Bahat G, Bauer J, Boirie Y, Bruyère O, Cederholm T, Cooper C, Landi F, Rolland Y, Sayer AA, Schneider SM, Sieber CC, Topinkova E, Vandewoude M, Visser M, Zamboni M; Writing Group for the European Working Group on Sarcopenia in Older People 2 (EWGSOP2), and the Extended Group for EWGSOP2. Sarcopenia: revised European consensus on definition and diagnosis. Age Ageing. 2019 Jan 1;48(1):16-31.

[4]Donini LM, Busetto L, Bauer JM, Bischoff S, Boirie Y, Cederholm T, Cruz-Jentoft AJ, Dicker D, Frühbeck G, Giustina A, Gonzalez MC, Han HS, Heymsfield SB, Higashiguchi T, Laviano A, Lenzi A, Parrinello E, Poggiogalle E, Prado CM, Rodriguez JS, Rolland Y, Santini F, Siervo M, Tecilazich F, Vettor R, Yu J, Zamboni M, Barazzoni R. Critical appraisal of definitions and diagnostic criteria for sarcopenic obesity based on a systematic review. Clin Nutr. 2020 Aug;39(8):2368-2388.

O1

s-oxprenolol for amyotrophic lateral sclerosis (ALS)

Jochen Springer, Germany

BIH Center for Regenerative Therapies, Charitè Universitätsmedizin Berlin

Degeneration of upper and lower motorneurons in spinal cord, brainstem and motor cortex result in progressive neurodegenerative paralysis and death in amyotrophic lateral sclerosis (ALS), which also causes a form of cachexia. Close to half of the patients show a hypermetabolism, i.e. cachexia, which results in s significantly shorter survival time. Currently, only riluzole and edaravone are approved for the treatment of ALS. Here, we tested novel therapeutic options (beta blockers vs riluzole or placebo) in an internationally standardized and established model using male and female transgenic G93A ALS mice. Survival after birth was significantly improved by treatment (table1).

	Max. survival	Median survival	Hazard Ratio	95%CI	p-value
Placebo	144	129.6±2.1			
30 Rilutek	145	127.9±2.1	1.05	0.63-1.75	0.85
10 Propoanolol	145	131.4±1.6	1.10	0.63-1.91	0.74
20 Oxprenolol	149	128.1±3.3	1.09	0.64-1.85	0.76
10 R-Oxprenolol	148	133.1±2.1	0.68	0.40-1.14	0.14
20 R-Oxprenolol	146	133.7±1.8	1.01	0.46-1.27	0.29
10 S-Oxprenolol	157	138.1±1.5** ### $	0.42	0.26-0.69	0.005
20 S-Oxprenolol	166	139.0±2.0** ### §	0.53	0.31-0.91	0.020

Table 1: Hazard Ratio, 95%CI and p-value vs. placebo. **: p<0.01 vs placebo, ###: p<0.001 vs rilutek, $: p<0.05 vs respective doses of r-oxprenolol.

In a second set of experiments, effects of compounds were tested on body weight, biochemical parameter, myocyte diameter and motorneuron number 41 days after first symptoms of ALS (Table2).

	Placebo	30 Rilutek	20 R-Oxpren	10 S-Oxpren	20 S-Oxpren
Weight loss g	-1.96±0.23	-1.34±0.23	-1.56±0.36	-0.91±0.38*	-1.13±0.36*
loss LBM g	-1.74±0.30	-0.99±0.37	-1.54±0.42	-0.50±0.41*	-0.61±0.38*
Mstn 25 kDa AU	1.13±0.09	0.99±0.11	0.84±0.08	0.74±0.07*	0.76±0.11*
Mstn 52 kDa AU	0.54±0.06	0.54±0.08	0.40±0.07	0.38±0.05	0.32±0.03*
chymo	1633±138	1527±206	1891±167	1307±174	1330107
PGPH	1096±146	1127±140	1177±103	860±126	973±61
tryp	1400±166	1101±117	1381±122	924±140*	973±83*
myofiber µm	35.24±1.09	34.74±1.80	38.19±2.11	39.61±2.14	41.55±1.76**
cortex	336±43	482±27*	465±25*	525±32**	483±25*
Spinal cord	327±30	474±48*	497±45**	475±43*	656±46**

Table 2: LBM: Lean body mass, Mstn: Myostatin aktive (25 kDa) and pro-form (52 kDa), Chymo: chymotrypsin-like, PGPH: PGPH-like, und Tryp: trypsin-like proteasome activity in nmol/mg Protein/ min, myofiber: myofiber diameter (M. tibialis). *: p<0.05, **: p<0.01 vs Placebo.

In summary, *S*-oxprenolol improves survival by protecting mononeurons, reducing loss of body weigt and lean mass via downregulation of wasting related signaling.

O2

SARM for COPD cachexia

Bill Evans, USA

O3

Phase 3 SCALA program: evaluating the ghrelin receptor agonist anamorelin for the treatment of malignancy associated weight loss and anorexia in adult patients with non-small cell lung cancer (NSCLC) and cachexia

Edwin de Wit[1], Salvatore Chessari[1], Pierre Nicolas[1], Elena Palmesino[1]
[1]Helsinn Healthcare SA, Lugano, Switzerland

Background: Anorexia and weight loss are cardinal manifestations of cancer cachexia, a multifactorial and debilitating condition that occurs in more than 80% of patients, particularly in those with NSCLC. Patients with low body mass index (BMI) who experience severe symptoms of anorexia[1] represent a population in high need of intervention. Anorexia symptoms are specifically assessed through the patient-reported 5-item Anorexia Symptom Scale (5-IASS), a subscale of the Functional Assessment Anorexia Cachexia Therapy (FAACT) scale[2]. Anamorelin (ANAM) is an investigational orally active selective ghrelin receptor agonist. The aim of the phase 3 SCALA program in progress is to assess the effect of ANAM on anorexia symptoms and body weight.
Methods: The SCALA studies are two 24-week double-blind randomized placebo-controlled global trials with identical study design (NCT03743051 and NCT03743064). Approximately 316 patients are planned to be enrolled in each study involving the following Countries: AUS, BEL, BGR, DEU, HRV, HUN, ITA, POL, ROU, RUS, SRB, UKR, USA. ANAM 100 mg or placebo is administered orally once daily for 24 weeks to adult patients with stage III/IV NSCLC, cachexia (defined as weight loss >2% in previous 6 months and BMI <20kg/m^2) and anorexia (defined as score ≤17 points on the 5-IASS scale and ≤37 points on the 12-item FAACT-A/CS scale). The primary study objective is to demonstrate superiority of anamorelin versus placebo on the gain in body weight and improvement in anorexia symptoms as assessed by the 5-IASS symptom scores. Exploratory endpoints include analysis every 3 weeks up to week 24 in body weight, 5-IASS, 4-item Anorexia concerns scale[1], FAACT total score, and changes in Fatigue scores. Safety is also assessed, including adverse events monitoring, overall survival and tumor assessment using computed tomography. Randomization is stratified by line and type of anticancer therapy, and baseline 5-IASS score (≤10 vs >10). As of November 2020, 251 patients were enrolled.

1. Kaasa S et al, Ann Oncol 2020; 31 Supp 4 (S1053)
2. Gelhorn HL et al, Qual Life Res. 2019 Jun;28(6)

Disclosures
EdW, SC, PN, EP: Employee at Helsinn Healthcare SA

O4

MMPOWER-3 Phase 3 Clinical Trial Results: Elamipretide improved six-minute walk test in individuals with mtDNA replisome disorders

Michelangelo Mancuso, Italy

Michelangelo Mancuso[1], Bruce Cohen[2], Marni J. Falk[3], Amy Goldstein[3], Mary Kay Koenig[4], Michio Hirano[5], John Vissing[6], Amel Karaa[7]
[1]Azienda Ospedaliero Universitario Pisana, Pisa, Italy; [2]Akron Children's Hospital, Akron, OH, USA; [3]Children's Hospital of Philadelphia, Philadelphia, PA, USA; [4]University of Texas Health Science Center, Houston TX, USA; [5]Columbia University Medical Center, New York, NY, USA; [6]University of Copenhagen, Copenhagen, Denmark; [7]Massachusetts General Hospital, Boston, MA, USA

There are several clinical trials designed to identify novel treatments for primary mitochondrial myopathy that are either complete or in progress. Most recently,MMPOWER-3, a Phase 3, randomized, double-blind, placebo-controlled clinical trial, evaluated the effect of treatment with elamipretide, a mitochondria-targeting peptide, in patients (N=2018) with primary mitochondrial myopathy. Those enrolled patients possessed a variety of myopathy-causing pathogenic variants in either nuclear (nDNA) or mitochondrial DNA (mtDNA) genes. Although the trial did not meet the primary endpoints in the highly heterogeneous study cohort, we evaluated data from a genetic subgroup of MMPOWER-3 per protocol population in persons who successfully completed the full trial duration in a post-hoc, subgroup analysis. Specifically, we examined the effects of elamipretide on the change from baseline in the six-minute walk test (6MWT) as a function of gene variants. Of the entire patient population, 74% of individuals had primary mtDNA pathogenic variants or single deletions. Those patients with mtDNA variants receiving elamipretide showed no significant effects on their 6MWT results when compared to placebo. Further, 6MWT in the mtDNA cohort was confounded by a 'placebo effect', disproportionally driven by patients with *MT-TL1* mutations. Patients with *MT-TL1* pathogenic variants, of which m.3243A>G was the most common, represented over one-third of the mtDNA cohort but had relatively lower mtDNA heteroplasmy levels in blood (34%), and 6MWT increased 41±14 meters in the placebo group at study week 24. In contrast, we did not observe a placebo effect in the pathogenic nDNA gene cohort. Following 24 weeks of treatment with elamipretide, patients with nDNA gene mutations walked significantly farther than their placebo counterparts (31±10 versus 3±7 meters, respectively; $p<0.05$). Furthermore, analyses showed that this nDNA cohort was almost entirely comprised of patients with pathogenic variants required for mtDNA maintenance, including *POLG* (47%) and *TWNK* (15%). The results of the 6MWT at week 24 showed a change of 32±19 for POLG patients versus -0.5 ±11 meters in those who received placebo (n=12-13 per group). A relationship among the loci of *POLG* variant(s) and elamipretide response was not identified which suggests that that 6MWT improvements were not limited to specific pathogenic cluster(s) along the POLG enzyme. In addition, pharmacokinetic analyses in the nDNA cohort showed a positive correlation between plasma elamipretide concentrations and improvements on the and 6MWT results. Overall, these findings highlight the challenge of developing therapies for the broadly heterogeneous class of mitochondrial disease, and directly highlight the importance of focusing on genetic subgroups when developing treatments for individuals with primary mitochondrial myopathy. The exploration of the efficacy of elamipretide in patients with mtDNA maintenance-related disorders is the focus of future studies.

P1

Metabolic and molecular integration in regulation of skeletal muscle mass

Srinivasan Dasarathy, USA

Secondary sarcopenia is frequent in a number of chronic diseases that result in perturbed ammonia metabolism and consequent hyperammonemia. Ammonia is a cytotoxic molecule that is generated during cellular functions including amino acid catabolism, purine breakdown and from gut microbial metabolism. Hepatic ureagenesis is the physiological mechanism for ammonia disposal but during hyperammonemia, skeletal muscle uptake of ammonia is increased via an ammonia transporter, RhBG, dependent mechanism. Skeletal muscle hyperammonemia results in metabolic and molecular perturbations tha result in dysregulated proteostasis. We identified novel perturbations on the molecular landscape of the skeletal muscle during hyperammonemia using integrated multiomic analyses. Chromosomal conformation changes determined by ATAC sequencing, transcriptomics and proteomics showed decreased mitochondrial components, intermediary metabolite regulatory proteins and altered protein synthesis responses. We have noted that hyperammonemia causes cataplerosis of α-ketoglutarate, a critical tricarboxylic acid (TCA) cycle intermediate that results in mitochondrial oxidative dysfunction, decreased ATP synthesis and oxidative stress. Adaptive anaplerotic response is mediated via increased branched chain amino acid (L-leucine and L-isoleucine) uptake in the skeletal muscle via an SLC7A5 dependent mechanism. During hyperammonemia, amino acid sensor, general control non-derepressible-2 (GCN2) an eukaryotic initiation factor 2α (eIF2α) kinase is phosphorylated and its kinase function is activated with phosphorylation of eIF2α that results in impaired mTORC1 signaling. Ammonia also causes p65NFKB dependent transcriptional upregulation of myostatin, a TGFβ superfamily member that inhibits mTORC1 signaling via an AMPK dependent mechanism. These observations suggest that hyperammonemia during exercise may result in suboptimal beneficial responses in chronic disease.

P2

Exercise in cancer patients

Jesper Christensen, Denmark

Exercise training has been extensively studied as a supportive-care and/or rehabilitation strategy in the oncology setting demonstrating the capacity of exercise training to counter treatment induced symptoms and side-effects, typically by maintaining/improving physiological and/or patient-reported outcome measures during and after primary treatment [1]. Accordingly, a range of national and international societies and agencies have published cancer-specific exercise guidelines, mirroring – to a large extend – physical activity guidelines in healthy individuals, and standard care rehabilitation programs now often includes structured exercise training. In recent years, experimental data from preclinical studies [2] and explorative reports from clinical trials [3] have further suggested that exercise training can lead to physiological adaptations which may impact 'hard' cancer specific outcomes including overall and disease-free survival. Conceptually, this potential anti-cancer effect may be driven by exercise-mediated improvements in anti-cancer treatment efficacy through additive or synergistic anti-carcinogenic effects, and/or by improving treatment tolerability through the lowering of the rate/risk of treatment compromising toxicities and complications. Within this framework, the capacity to maintain or improve both quantitative and qualitive features of cancer patients' skeletal muscle mass provides a novel and intriguing physiological rational for integrating exercise training in the cancer trajectory specifically targeting muscle dysfunction as a clinically important intermediate endpoint [4]. Future research and clinical initiatives in this space may fundamentally change the perception of exercise training in the oncology setting from a complementary "add-in" option within patient-centered rehabilitation strategies, towards a targeted therapeutic intervention prescribed, administered and evaluated on par with conventional treatments.

References

1. Christensen JF, Simonsen C, Hojman P. Exercise Training in Cancer Control and Treatment. Compr Physiol 2018; 9: 165-205.
2. Betof AS, Lascola CD, Weitzel D et al. Modulation of murine breast tumor vascularity, hypoxia and chemotherapeutic response by exercise. J.Natl.Cancer Inst. 2015; 107.
3. Hayes SC, Steele ML, Spence RR et al. Exercise following breast cancer: exploratory survival analyses of two randomised, controlled trials. Breast Cancer Res Treat 2018; 167: 505-514.
4. Christensen JF, Jones LW, Andersen JL et al. Muscle dysfunction in cancer patients. Ann.Oncol. 2014; 25: 947-958.

P3

Nutrition and appetite stimulants: therapeutic or palliative drugs?

Maurizio Muscaritoli, Italy

Department of Translational and Precision Medicine – Sapienza University of Rome, Italy

Hypophagia and insufficient nutrient intake are being progressively recognized as major drivers of cancer-related malnutrition and cachexia, contributing to the changes of body composition which in turn negatively impact on patients' outcome[1]. The negative energy and protein balance secondary to insufficient nutrient intake may occur in any phase of the cancer journey, from disease onset, to the phase of active treatments to the palliative care phase for advanced patients[2,3]. The pathophysiology of reduced food intake is multifactorial and includes cancer anorexia, mechanical obstruction, dysphagia, chemotherapy-induced nausea, vomiting and diarrhea, intestinal obstruction and implies that the therapeutic approach is multimodal, including appetite stimulants, oral nutritional supplements and enteral or parenteral nutrition. Consistently, aims of increased nutrient intake/delivery vary according to the phase of the disease. In cancer patients on oncologic therapy, interventions are more supportive than palliative, the main aim being maintenance of nutritional status, prevention of cachexia and the improvement of the compliance with chemotherapy and radiotherapy. Conversely, in advanced patients, who are frequently severely hypophagic, the main aim of nutritional therapy is to delay an premature death due to starvation, dehydration and progressive malnutrition[4]. Hence, in the palliative phase, the indication for a nutritional support, in most cases home parenteral nutrition, relies on a multidimensional evaluation of different domains, including oncology, nutritional status, habits, religious beliefs, QoL and patients' and family expectations. In conclusion, pharmacological and nutritional treatments to improve nutrient intake in cancer patients may be considered both therapeutic and palliative, depending on the phase of the disease in which they are implemented.

References
Martin L, Kubrak C. How much does reduced food intake contribute to cancer-associated weight loss? Curr Opin Support Palliat Care 2018;12:410–9
Muscaritoli M, Lucia S, Farcomeni A, Lorusso V, Saracino V, Barone C, et al. Prevalence of malnutrition in patients at first medical oncology visit: the PreMiO study. Oncotarget 2017;8:79884–96
Baracos VE, Martin L, Korc M, Guttridge DC, Fearon KCH. Cancer-associated cachexia. Nat Rev Dis Primers 2018;4:17105
Bozzetti F. Is there a place for nutrition in palliative care? Supportive Care in Cancer 2020. 28:4069–4075

P4

Age-related signaling and expression changes that may contribute to sarcopenia

David Glass, USA

We produced a multi-timepoint Age-related Gene Expression Signature (AGES) from liver, kidney, skeletal muscle and hippocampus of rats, comparing 6, 9, 12, 18, 21, 24 and 27-month old animals. The data was filtered for the genes that changed in only one direction throughout the lifespan of the animals – for example, those changing either early in life (early logistic changes); at mid-age (mid-logistic); late in life (late-logistic); or linearly, throughout the lifespan. The pathways that were perturbed as a result of chronological age illustrate organ-specific and more wide-spread effects of aging, and point to mechanisms that might be counter-regulated pharmacologically in order to treat age-associated diseases. A small number of genes were regulated by aging in the same manner in every tissue, suggesting they may be more universal markers of aging. As for muscle in particular, there is a lack of pharmacological interventions available for sarcopenia, a progressive age-associated loss of muscle mass, leading to a decline in mobility and quality of life. We found mTORC1 (mammalian target of rapamycin complex 1), a well-established positive modulator of muscle mass, to be surprisingly hyperactivated in sarcopenic muscle. When we inhibited the mTORC1 pathway, this resulted an increase in muscle mass and fiber type cross sectional area in select muscle groups, which was quite surprising because mTORC1 signaling has been shown to be required for skeletal muscle mass gains in some models of hypertrophy. Furthermore, genes related to senescence were downregulated, and indicators of neuromuscular junction denervation were diminished using a low dose of a rapalog. Thus, partial mTORC1 inhibition may delay the progression of sarcopenia, by directly and indirectly counter-regulating multiple age-associated pathways, implicating mTORC1 as a therapeutic target to treat sarcopenia.
More recently, we've explored Covid-19 as an age-related disorder linked to cachexia, due to the induction of a cytokine storm. Some potential mechanisms linked to both cachexia and the more severe effects of Covid-19 will be discussed.

POSTER SESSIONS

Poster session 1 **Cachexia – mechanisms basic and animal models I** (posters 1-01 to 1-10)
Chairs: Gustavo Nader, USA; Jochen Springer, Germany

1-01

Rehabilitating cachexia - development and functional characterization of a novel longitudinal and translational model of cancer-associated cachexia

Ishan Roy[1,2], Ben Binder-Markey[1,2], Danielle Sychowski[1], Donna McAllister[3], Dominic D'Andrea[1], Colin Franz[1,2], Michael B. Dwinell[3], Richard L. Lieber[1,2]

[1]Shirley Ryan AbilityLab (formerly known as Rehabilitation Institute of Chicago), Chicago, Illinois, USA; [2]Department of Physical Medicine and Rehabilitation, Northwestern University, Chicago, Illinois, USA; [3]Department of Microbiology & Immunology, Medical College of Wisconsin, Milwaukee, Wisconsin, USA

1-02

Alterations in Mitochondrial Turnover during the Development of Cancer Cachexia in Tumor-Bearing Female Mice

Seongkyun Lim[1], Megan E. Rosa-Caldwell[1], Wesley S. Haynie[1], Lisa T. Jansen[1], Kirsten R. Dunlap[1], Francielly Morena da Silva[1], J. William Deaver[1], Michael Wiggs[2], Tyrone A. Washington1[1], Nicholas P. Greene[1]

[1]Health, Human Performance, and Recreation, University of Arkansas, Fayetteville, AR; [2]Health, Human Performance, and Recreation, Baylor University, Waco, Texas, TX

1-03

Alterations in Extracellular Matrix Remodeling During Early Stages of Cancer Cachexia in Tumor-bearing Female Mice

Francielly Morena da Silva[1], Seongkyun Lim[1], Megan E. Rosa-Caldwell[1], Wesley S. Haynie[1,] Lisa T. Jansen[1], Kristen R. Dunlap[1], J. William Deaver[1], Michael Wiggs[2], Tyrone A. Washington1[1], Nicholas P. Greene[1]

[1]Health, Human Performance, and Recreation, University of Arkansas, Fayetteville, AR; [2]Health, Human Performance, and Recreation, Baylor University, Waco, Texas, TX

1-04

Quercetin administration attenuates cancer-related cachexia and increases cancer-related survival and in C57BL/6 mice bearing syngeneic Cutaneous melanoma model

Magda Mendes Vieira[1], Amanda Mota Lacerda[1], Valéria Couto Quintão[1], Amanda Rodrigues Santos[1]; Andréia de Souza Brito[1], Otavio Cardoso Filho[1,2], Vinícius Rodrigues Dias[1,3], Ludmila Regina de Souza[1], Alfredo Maurício Batista de Paula[1,4*]

[1]Nucleus of Epidemiologic and Molecular Research Catrumano (NUPEMOC). Health Research Laboratory. Post-graduate Programme in Health Sciences. Universidade Estadual de Montes Claros (UNIMONTES), 39401-001, Montes Claros, Minas Gerais, Brazil; [2]Department of Chemical Engineering. Instituto Federal do Norte de Minas Gerais (IFNMG), Minas Gerais, Brazil; [3]Department of Physical Education. Universidade Estadual de Montes Claros (UNIMONTES), 39401-001, Montes Claros, Minas Gerais, Brazil; [4]Department of Dentistry. Universidade Estadual de Montes Claros (UNIMONTES), 39401-001, Montes Claros, Minas Gerais, Brazil

1-05

Molecular and physiologic characterization of a novel murine model of metastatic head and neck cancer cachexia

Brennan Olson[1,2], Mason A Norgard[1], Peter Levasseur[1], Xinxia Zhu, and *Daniel L Marks[1,3,4]

[1]Papé Family Pediatric Research Institute, Oregon Health & Science University, Portland, OR USA; [2]Medical Scientist Training Program, Oregon Health & Science University, Portland, OR USA; [3]Brenden-Colson Center for Pancreatic Care, Oregon Health and & Science University Portland, OR USA; [4]Knight Cancer Institute, Oregon Health & Science University, Portland, OR USA

1-06

Characterizing biological mechanisms of muscle wasting in a clinically relevant model of colorectal cancer and sequential chemotherapy treatment

Gauhar Ali[1], Vera Mazurak[2], Bhumi Bhatt[3], Sambasivarao Damaraju[3], Vickie E. Baracos[1]

[1]Department of Oncology, Faculty of Medicine and Dentistry, [2]Division of Human Nutrition, [3]Department of Laboratory Medicine and Pathology, University of Alberta, Edmonton, AB

1-07
The role of adipose tissue breakdown in the acute phase of sepsis: a comparison of interorgan fluxes of amino acids and glycerol in a *Pseudomonas aeruginosa* induced septic pig model
***Ryan Morse*[1], *Gabriella A.M. ten Have*[1], *John J. Thaden*[1],, *Marielle P. Engelen*[1], *Martin Hagve*[2], *Nicolaas E.P. Deutz*[1]**
[1]Center for Translational Research in Aging & Longevity, Department of Health & Kinesiology, Texas A&M University, College Station, TX, USA; [2]University Hospital North-Norway, Department of Gastrointestinal Surgery, Tromso, Norway.

1-08
Chronic cachexia is dependent on sustained IL-1R signaling during parasite infection
***Stephanie J. Melchor*[1], *Daniel Abebayehu*[1], *Sheryl Coutermarsh-Ott*[2], *Thomas Barker*[1], *Sarah E. Ewald*[1]**
[1]University of Virginia, Charlottesville, USA; [2]Virginia Polytechnic Institute, USA

1-09
GDF15 neutralization does not impact anorexia or survival in the lipopolysaccharide (LPS) acute inflammation mouse model
***Zhidan Wu*[1], *Olivier Bezy*[1], *Srinath Jagarlapudi*[1], *Anita Patel*[2], *Chang Zou*[1], *Donald Bennett*[1], *Laura Lin*[1], *Randy J. Seeley*[2], *Bei B. Zhang*[1], *Danna M. Breen*[1]**
[1]Pfizer Inc, Cambridge, USA; [2]University of Michigan, Ann Arbor, USA.

1-10
Metabolomic biomarker candidates for skeletal muscle loss in the collagen-induced arthritis (CIA) model
***Marianne S Oliveira*[1,2], *Jordana MS Silva*[1], *Rafaela CE Santo*[1,2], *Paulo VG Alabarse*[3], *Ricardo M Xavier*[1,2]**
[1]Laboratório de Doenças Autoimunes, Serviço de Reumatologia, Hospital de Clínicas de Porto Alegre, Porto Alegre, Brazil; [2]Faculdade de Medicina, Universidade Federal do Rio Grande do Sul, Porto Alegre, Brazil; [3]VA San Diego Healthcare System, San Diego, CA, USA

Poster session 2 **Nutrition an Appetite** (posters 6-01 to 6-10)
Chairs: Nicolaas Deutz, USA; Alessandro Laviano, Italy

6-01
Nutrition status and sarcopenia in discharged hospital patients in Iceland.
Alfons Ramel
Faculty of Food Science and Nutrition, University of Iceland, Iceland

6-02
Weight loss, malnutrition and physical function in community dwelling old adults in Iceland.
***Alfons Ramel*[1]**
Faculty of Food Science and Nutrition, University of Iceland, Iceland

6-03
Nutritional signature and body composition adaptations at high-altitude: Western trekkers vs Eastern porters
***Danilo Bondi*[1], *Vittore Verratti*[2], *Anna Maria Aloisi*[3], *Raffaela Piccinelli*[4], *Tereza Jandova*[5], *Stefano Pieretti*[6], *Cinzia Le Donne*[4], *Mattia Taraborrelli*[7], *Carmen Santangelo*[7], *Tiziana Pietrangelo*[1]**
[1] Department of Neuroscience, Imaging and Clinical Sciences, University "G. d'Annunzio" of Chieti – Pescara, Italy; [2] Department of Psychological, Health and Territorial Sciences, University "G. d'Annunzio" of Chieti – Pescara, Italy; [3] Department of Medicine, Surgery and Neuroscience, University of Siena, Italy; [4] Council for Agricultural Research and Economics, Research Centre for Food and Nutrition, Rome, Italy; [5] Faculty of Physical Education and Sport, Charles University, Prague, Czech Republic; [6] National Center for Drug Research and Evaluation, Istituto Superiore di Sanità, Rome, Italy; [7] Department of Medical, Oral and Biotechnological Sciences, University "G. d'Annunzio" of Chieti – Pescara, Italy

6-04

Association between changes in nutrients intake and changes in muscle strength and physical performance in the SarcoPhAge cohort

Laetitia Lengelé[1], Pauline Moehlinger[3], Olivier Bruyère[1], Médéa Locquet[1], Jean-Yves Reginster[1, 2], and Charlotte Beaudart[1]

[1]WHO Collaborating Centre for Public Health Aspects of Musculoskeletal Health and Aging, Division of Public Health, Epidemiology and Health Economics, University of Liège, CHU—Sart Tilman, Quartier Hôpital, Avenue Hippocrate 13 (Bât. B23), 4000 Liège, Belgium; [2]Chair for Biomarkers of Chronic Diseases, Biochemistry Department, College of Science, King Saud. University, Riyadh 11451, Saudi Arabia; [3]Paris Institute of technology for life, food and environmental sciences, Engineering and health field: people, bioproducts, environment. 16 Claude Bernard street, F-75231 Paris Cedex 05.

6-05

Resting Energy Expenditure changes after 2 weeks of Very Low-Calorie Diet are associated with baseline production rates of specific amino acids

Raven A. Wierzchowska-McNew*, Marielle P.K.J. Engelen, Sunday S. Simbo, Nicolaas E.P. Deutz

Health and Kinesiology, Texas A&M University, College Station, United States

6-06

Impairments in small intestinal function are associated with reduced muscle quality in a group of Congestive Heart Failure and healthy participants

Sarah K. Kirschner, Nicolaas E. P. Deutz, Clayton L. Cruthirds, Marielle P. K. J. Engelen

Center for Translational Research in Aging & Longevity, Department of Health & Kinesiology, Texas A&M University, College Station, TX, USA

6-07

Elevated meal-induced anabolic response after four weeks of ω3 fatty acid supplementation in Chronic Obstructive Pulmonary Disease (COPD)

Mariëlle PKJ Engelen, Renate Jonker, Rajesh Harrykissoon[2], Anthony J Zachria[2], Nicolaas EP Deutz

Center for Translational Research in Aging & Longevity.[1] Dept. Health and Kinesiology, Texas A&M University, [2]Pulmonary and Critical Care, Scott & White Medical Center, College Station, TX

6-09

Presence of cachexia and impaired appetite in hospitalized elderly cancer patients

Rayne de Almeida Marques[1], Thamirys de Souza Chaves Ribeiro[2], Vanusa Felício de Souza[2], Maria Claudia Bernardes Spexoto[3], Taisa Sabrina Silva Pereira[4], José Luiz Marques Rocha[1,2], Valdete Regina Guandalini[1,2]

[1]Graduate program in Nutrition and Health. Federal University of Espirito Santo, Vitoria, Espırito Santo, Brazil; [2]Department of Integrated Education. Nutrition Course. Federal University of Espirito Santo, Vitoria, Espırito Santo, Brazil; [3]Faculty of Pharmaceutical Sciences. Nutrition Course. Federal University of Grande Dourados. Dourados, Mato Grosso do Sul, Brazil; [4]Universidad de las Américas Puebla, Cholula, Puebla, México, Ex Hacienda Sta. Catarina Mártir S/N, San Andrés Cholula, Puebla, México

6-10

Hospitalized cancer patients with high neutrophil to lymphocytes ratio had lower calf circumference and increased risk of malnutrition

Jéssika M Siqueira[1], Jéssika D P Soares, Thaís C Borges[1], Tatyanne L N Gomes[1], Claude Pichard[2], Alessandro Laviano[3], Gustavo D Pimentel[1]

[1]Laboratory of Research in Clinical Nutrition and Sports (Labince), Faculty of Nutrition, Federal University of Goiás, Goiânia, Brazil; [2]Clinical Nutrition, Geneva University Hospital, Geneva, Switzerland; [3]Department of Translational and Precision Medicine, Sapienza University of Rome, Rome, Italy

Poster session 3 **Muscle wasting & Sarcopenia - mechanisms I** (posters 5-01 to 5-12)
Chairs: Scott Brakenridge, USA; Jason Doles, USA

5-01
Muscle Mass as a Potential Marker for Chronic Maltreatment in the Pediatric Non-Accidental Trauma Patient
Gregory Metzger[1]; Yuri V. Sebastião[1]; Carley Lutz[1]: Katherine J. Deans[1,2]; Peter C. Minneci[1,2]
[1]Center for Surgical Outcomes Research, Abigail Wexner Research Institute, Nationwide Children's Hospital, Columbus, OH; [2]Department of Pediatric Surgery, Nationwide Children's Hospital, Columbus, OH

5-02
Evaluation of the nutrients intake in a group of Jordanian elderly people with sarcopenia syndrome in Amman.
Sarah Z. Majali, Hadeel A. Ghazzawi
The University of Jordan, Amman, Jordan

5-03
Association of muscle mass reduction and hand grip strength reduction with health-related quality of life of patients with colorectal cancer
Mariana Vieira Barbosa[1], Mylena Pinto dos Santos[2], Jocilene Alves Leite[3], Viviane Dias Rodrigues[3], Renata Brum Martucci[3,4]
[1]Post-graduate Program in Medical Science, Medical Science Faculty, State University of Rio de Janeiro, Rio de Janeiro, RJ, Brazil; [2]Post-graduate Program in Food, Nutrition and Health, Nutrition Institute, State University of Rio de Janeiro, Rio de Janeiro, RJ, Brazil; [3]Nutrition and Dietetic Service, Cancer Hospital Unit I, National Cancer Institute José Alencar Gomes da Silva, Rio de Janeiro, RJ, Brazil; [4]Department of Applied Nutrition, Nutrition Institute, State University of Rio de Janeiro, Rio de Janeiro, RJ, Brazil

5-04
Ovarian cancer ascites induces skeletal muscle wasting in vitro
Jorne Ubachs[1,2,3,4], Wouter van de Worp[4,5], Rianne Vaes[3,4], Kenneth Pasmans[4,8], Ramon Langen[4,5], Ruth Meex[4,8], Sandrina Lambrechts[1,2], Toon Van Gorp[6], Roy Kruitwagen[1,2], Steven W.M. Olde Damink[3,4,7], Sander S. Rensen[3,4]
[1]Department of Obstetrics and Gynecology, Maastricht University Medical Centre, P.O. box 5800, 6202 AZ, Maastricht, the Netherlands; [2]GROW - School for Oncology and Developmental Biology, Maastricht University, P.O. box 616, 6200 MD, Maastricht, the Netherlands; [3]Department of Surgery, Maastricht University Medical Centre, P.O. box 6202 AZ Maastricht, the Netherlands; [4]NUTRIM, school of Nutrition and Translational Research in Metabolism, Maastricht University, P.O. box 616, 6200 MD, Maastricht, the Netherlands; [5]Department of Pulmonology, Maastricht University, P.O. box 616, 6200 MD, Maastricht, the Netherlands; [6] Department of Obstetrics and Gynecology, Division of Gynecological Oncology, University Hospitals Leuven, Leuven Cancer Institute, Herestraat 49, 3000 Leuven, Belgium; [7] Department of General, Visceral- and Transplantation Surgery, RWTH Aachen University, Germany; [8]Department of Human Biology, Maastricht University P.O. Box 616, 6200 MD Maastricht, The Netherlands

5-05
Postoperative loss of skeletal muscle mass is prognostic of poor survival after gastric cancer surgery
Shanjun Tan[1], Feng Zhou[2], Zhige Zhang[1], Junjie Wang[1], Jiahao Xu[1], Qiulin Zhuang[1], Qiulei Xi[1], Qingyang Meng[1], Yi Jiang[1] & Guohao Wu[1*]
[1]Department of General Surgery/Shanghai Clinical Nutrition Research Center, Zhongshan Hospital, Fudan University, Shanghai, China, [2]Department of General, Visceral and Transplant Surgery, University Hospital Heidelberg, Heidelberg, Germany

5-06
Respiratory function in subjects recovered from COVID-19 with sarcopenia
Carlos Sánchez-Moreno, Dulce González-Islas, Arturo Orea-Tejeda, Susana Galicia-Amor, Carlos Aboitiz-Rivera, Esperanza Trejo-Mellado, Juan carlos Garcia-Hernández, Lucero Flores-Diaz, Elisabeth Juárez-Silva, Patricia Martel-Palomo
Instituto Nacional de Enfermedades Respiratorias "Ismael Cosío Villegas", Mexico City, Mexico

5-07

Impact of prolonged sepsis on biomechanical and structural myofibrillar properties

Chloë Goossens[1], Sarah Derde[1], Dominik Schneidereit[2], Michael Haug[2], Barbara Reischl[2], Oliver Friedrich[2], Greet Van den Berghe[1], Lies Langouche[1*]

[1]Clinical Division and Laboratory of Intensive Care Medicine, Department of Cellular and Molecular Medicine, KU Leuven, Leuven, Belgium; [2] Institute of Medical Biotechnology, Friedrich-Alexander-University Erlangen-Nürnberg, Erlangen, Germany

5-08

Synergistic short-term and long-term effects of TGF-β1 and 3 on collagen production in differentiating myoblasts

Andi Shi[1,3,4], Michèle Hillege[1], Wüst, R[1], Gang Wu[2], Richard T Jaspers[1]

[1]Laboratory for Myology, Department of Human Movement Sciences, Faculty of Behavioural and Movement Sciences, Vrije Universiteit Amsterdam (VU), Amsterdam Movement Sciences (AMS), Amsterdam, The Netherlands; [2]Department of Oral Implantology and Prosthetic Dentistry, Academic Centre for Dentistry Amsterdam (ACTA), University of Amsterdam (UvA) and Vrije Universiteit Amsterdam (VU), The Netherlands; [3]Department of Oral and Maxillofacial Surgery/Pathology, Amsterdam UMC and Academic Center for Dentistry Amsterdam (ACTA), Vrije Universiteit Amsterdam (VU), Amsterdam Movement Science (AMS), Amsterdam, the Netherlands; [4]Key Laboratory of Oral Medicine, Guangzhou Institute of Oral Disease, Affiliated Stomatology Hospital of Guangzhou Medical University, Guangzhou Medical University, Guangzhou, China

5-09

Lack of TGF-β type I receptors *Tgfbr1* and *Acvr1b* synergistically stimulate myofibre hypertrophy and accelerates early muscle regeneration

Andi D. Shi [1, 2, 3], Michèle .G. Hillege [1], Ricardo Andrés Galli Caro [1], Gang Wu [4], Willem M.H. Hoogaars [5], Richard T. Jaspers [1]

[1]Laboratory for Myology, Department of Human Movement Sciences, Faculty of Behavioural and Movement Sciences, Vrije Universiteit Amsterdam (VU), Amsterdam Movement Sciences (AMS), Amsterdam, The Netherlands; [2]Department of Oral and Maxillofacial Surgery/Pathology, Amsterdam UMC and Academic Center for Dentistry Amsterdam (ACTA), Vrije Universiteit Amsterdam (VU), Amsterdam Movement Science (AMS), Amsterdam, the Netherlands; [3]Key Laboratory of Oral Medicine, Guangzhou Institute of Oral Disease, Affiliated Stomatology Hospital of Guangzhou Medical University, Guangzhou Medical University, Guangzhou, China; [4]Department of Oral Implantology and Prosthetic Dentistry, Academic Centre for Dentistry Amsterdam (ACTA), University of Amsterdam (UvA) and Vrije Universiteit Amsterdam (VU), The Netherlands; [5]European Research Institute for the Biology of Ageing (ERIBA);, University Medical Center Groningen (UMCG), University of Groningen, Antonius Deusinglaan 1, 9715RA, Groningen, The Netherlands

5-10

Gender differences in muscle-ageing: a cross-sectional study

Jelle de Jong[1,2], Brecht Attema[1], Arie G Nieuwenhuizen[1], Lars Verschuren[3], Martien PM Caspers[3], Robert Kleemann[2], Anita M van den Hoek[2] , Jaap Keijer[1]

[1]Human and Animal Physiology, Wageningen University, Wageningen, the Netherlands; [2]Department of Metabolic Health Research, The Netherlands Organization for Applied Scientific Research (TNO), Leiden, The Netherlands; [3]Department of Microbiology and Systems Biology, The Netherlands Organization for Applied Scientific Research (TNO), Zeist, The Netherlands

5-12

Quorum Sensing Molecules: potential theranostics in muscle wasting

Anton De Spiegeleer[1], Evelien Wynendaele[1], Nathan Debunne[1], Julie Coudenys[1], Yorick Janssens[1], Liesbeth Crombez[1], Amélie Descamps[1], Ralf Hoffmann[2], Vincent Mouly[3], Caroline Vlaeminck[1], Bart P. Braeckman[1], Dries Duchi[1], Vanessa Andries[1], Marjan De Mey[1], Tom Van de Wiele[1], Lars Vereecke[1], Nele Van Den Noortgate[1], Dirk Elewaut[1,*] and Bart De Spiegeleer[1,*]

[1]Ghent University, Ghent, Belgium; [2]University of Leipzig, Leipzig, Germany; [3]Sorbonne University, Paris, France

Poster session 4 **Diagnosis of sarcopenia I** (posters 4-02 to 4-12)
Chairs: Josep Argiles, Spain; Jürgen Bauer, Germany

4-02

The validity of SARC-F on screening sarcopenia defined by AWGS 2019 in hospitalized older adults

***Keisuke Maeda*[1,2], *Yuria Ishida*[3], *Tomoyuki Nonogaki*[4], *Akio Shimizu*[5], *Yosuke Yamanaka*[6], *Remi Matsuyama*[6], *Ryoko Kato*[4], *Junko Ueshima*[7], *Kenta Murotani*[8] *and Naoharu Mori*[2]**

[1]Department of Geriatric Medicine, National Center for Geriatrics and Gerontology; [2]Department of Palliative and Supportive Medicine, Graduate School of Medicine, Aichi Medical University; [3]Department of Nutrition, Aichi Medical University Hospital; [4]Department of Pharmacy, Aichi Medical University Hospital; [5]Department of Nutrition, Hamamatsu City Rehabilitation Hospital; [6]Department of Oral and Maxillofacial Surgery, Graduate School of Medicine, Aichi Medical University; [7]Department of Clinical Nutrition and Food Service, NTT Medical Center Tokyo; [8]Biostatistics Center, Kurume University

4-03

Comparison of diagnostic performance of SARC-F and its two modified versions (SARC-CalF and SARC-F+EBM) in community-dwelling older adults from Poland using two sets of diagnostic criteria of sarcopenia developed by The European Working Group on Sarcopenia in Older People (EWGSOP1 and EWGSOP2)

***Roma Krzymińska-Siemaszko*[1], *Ewa Deskur-Śmielecka*[1], *Aleksandra Kaluźniak-Szymanowska*[1], *Marta Lewandowicz*[1], *Katarzyna Wieczorowska-Tobis*[1]**

[1]Laboratory of Geriatric Medicine, Department of Palliative Medicine, Poznan University of Medical Sciences

4-04

Clinimetric properties of the newly developed short form Sarcopenia Quality of Life (SF-SarQoL®) questionnaire.

***Anton Geerinck*[1], *Charlotte Beaudart*[1], *Jean-Yves Reginster*[1,2], *Médéa Locquet*[1], *Christian Monseur*[3], *Sophie Gillain*[4], *Olivier Bruyère*[1]**

[1]Division of Public Health, Epidemiology and Health Economics, World Health Organization Collaborating Center for Public Health aspects of musculoskeletal health and ageing, University of Liège, Belgium; [2]Chair for Biomarkers of Chronic Diseases, Biochemistry Department, College of Science, King Saud University, Riyadh, KSA, Saudi Arabia; [3]Department of Education Sciences, University of Liège, Liège, Belgium; [4]Geriatrics Department, University Hospital of Liège, Liège, Belgium

4-05

Consequence of SARC-CalF on SARC-F's screening sensitivity and specificity among community-dwelling older adults: a systematic review

***Rômulo Roosevelt da Silva Filho*[1], *Aline de Bastos Ferreira*[1], *Erika Aparecida Silveira*[1]**

[1] Medicine Faculty, Post-Graduation Program in Health Sciences, Universidade Federal de Goiás.

4-06

Establishing a hierarchy of importance for different aspects of quality of life in sarcopenia from a patient perspective, a best-worst scaling survey.

***Anton Geerinck*[1], *Médéa Locquet*[1], *Mickael Hilligsmann*[2], *Jean-Yves Reginster*[1,3], *Olivier Bruyère*[1], *Charlotte Beaudart*[1]**

[1]Division of Public Health, Epidemiology and Health Economics, World Health Organization Collaborating Center for Public Health aspects of musculoskeletal health and ageing, University of Liège, Belgium; [2]Department of Health Services Research, University of Maastricht, The Netherlands; [3]Chair for Biomarkers of Chronic Diseases, Biochemistry Department, College of Science, King Saud University, Riyadh, KSA, Saudi Arabia.

4-07

Screening for the risk of sarcopenia in hospitalized individuals

Mara Rubia Areco Cristaldo[1], Valdete Regina Guandalini[2], Sheilla de Oliveira Faria[3], Maria Claudia Bernardes Spexoto[4]

[1]Nutrition Student, Federal University of Grande Dourados, Dourados, Mato Grosso do Sul, Brazil; [2]Adjunct Professor, Federal University of Espírito Santo, Vitória, Espírito Santo, Brazil; [3]Nutritionist, Department of Preventive Medicine, Faculty of Medicine FMUSP, University of São Paulo, São Paulo, Brazil; [4]Adjunct Professor, Faculty of Health Sciences, Federal University of Grande Dourados, Dourados, Mato Grosso do Sul, Brazil

4-09

The joint association of frailty and sarcopenia with incidence health outcomes: Findings from the UK Biobank prospective cohort study

Fanny Petermann-Rocha[1,2*] Stuart R Gray[2], Jill P Pell[1], Frederick K Ho[1], Carlos Celis-Morales[1,2]

[1]Institute of Health and Wellbeing, University of Glasgow, Glasgow, UK; [2]British Heart Foundation Glasgow Cardiovascular Research Centre, Institute of Cardiovascular and Medical Sciences, University of Glasgow, Glasgow, UK

4-10

GripBMI – a fast and simple sarcopenia screening tool in post acute inpatient rehabilitation

Irina Churilov[1], Leonid Churilov[1], Kim Brock[2], David Murphy[2], Richard J MacIsaac[2], Elif I Ekinci[3]

[1]St Vincent's Hospital Melbourne; The University of Melbourne, Fitzroy, Australia; [2]St Vincent's Hospital Melbourne; [3]The University of Melbourne; Austin Health

4-11

Development of appendicular muscle mass estimating formulas for older adults considering paralysis

Junko Ueshima[1], Keisuke Maeda[2], Kenta Murotani[3]; Akio Shimizu[4], Ayano Nagano[5], Keisuke Sato[6], Yuria Ishida[7], Naoharu Mori[8] and Masaki Suenaga[6]

[1]Department of Clinical Nutrition and Food Service, NTT Medical Center Tokyo; [2]Department of Geriatric Medicine, National Center for Geriatrics and Gerontology; [3]Biostatistics Center, Kurume University; [4]Department of Nutrition, Hamamatsu City Rehabilitation Hospital; [5]Department of Nursing, Nishinomiya Kyoritsu Neurosurgical Hospital; [6]Okinawa Chuzan Clinical Research Center, Chuzan Hospital; [7]Department of Nutrition, Aichi Medical University Hospital; [8]Department of Palliative and Supportive Medicine, Graduate School of Medicine, Aichi Medical University

4-12

Body composition of long-living patients with coronary artery disease

S.V. Topolyanskaya, L.I Dvoretski

First Moscow State Medical University (Sechenov University), Department of hospital therapy N2, Moscow, Russia

Poster session 5 **Cachexia - mechanisms basic and animal models II** (posters 1-11 to 1-23)
Chairs: Didier Attaix, France; Maurilio Sampaolesi, Belgium

1-11

Expression and role of microRNAs associated with inflammation in cancer cachexia

***Joana M.O. Santos*[1,2], *Sara Peixoto da Silva [1,2], Margarida M.S.M. Bastos [3], Paula A. Oliveira [4], Rui M. Gil da Costa*[1,3,4,5], *Rui Medeiros*[1,2,6,7,8]**

[1]Molecular Oncology and Viral Pathology Group, IPO Porto Research Center (CI-IPOP), Portuguese Oncology Institute of Porto (IPO Porto), 4200-072 Porto, Portugal; [2]Faculty of Medicine of the University of Porto (FMUP), 4200-319 Porto, Portugal; [3]Laboratory for Process Engineering, Environment, Biotechnology and Energy (LEPABE), Faculty of Engineering of the University of Porto (FEUP), 4200-465 Porto, Portugal; [4]Center for the Research and Technology of Agro-Environmental and Biological Sciences (CITAB), University of Trás-os-Montes and Alto Douro (UTAD), 5001-911 Vila Real, Portugal; [5]Postgraduate Programme in Adult Health (PPGSAD), Tumour and DNA Biobank (BTMA), Federal University of Maranhão (UFMA), 65080-805 São Luís, Brazil; [6]Research Department of the Portuguese League Against Cancer – Regional Nucleus of the North (Liga Portuguesa Contra o Cancro – Núcleo Regional do Norte), 4200-177 Porto, Portugal; [7]Virology Service, Portuguese Oncology Institute of Porto (IPO Porto), 4200-072 Porto, Portugal; [8]Biomedical Research Center (CEBIMED), Faculty of Health Sciences of the Fernando Pessoa University, 4249-004 Porto, Portugal

1-12

Distinct tissue-specific gene regulation and potential inter-organ communication in a mouse model of cancer cachexia

Ji-Won Heo, Sung-Eun Kim

Department of Food and Nutrition, Sookmyung Women's University, Seoul, Korea

1-13

Multi-compartment metabolomics and metagenomics reveal new metabolic targets in cancer cachexia.

***Sarah A. Pötgens*[1], *Morgane M. Thibaut*[1], *Nicolas Joudiou*[2], *Martina Sboarina*[1], *Audrey M. Neyrinck*[1], *Patrice D. Cani*[1,3], *Sandrine P. Claus*[4], *Nathalie M. Delzenne*[1], *Laure B. Bindels*[1#]**

[1]Metabolism and Nutrition Research Group, Louvain Drug Research Institute, UCLouvain, Université catholique de Louvain, Brussels, Belgium; [2]Nuclear and Electron Spin Technologies Platform (NEST), Louvain Drug Research Institute, UCLouvain, Université catholique de Louvain, Brussels, Belgium ; [3]Walloon Excellence in Life Sciences and BIOtechnology (WELBIO), Louvain Drug Research Institute, Université catholique de Louvain, Brussels, Belgium; [4]University of Reading, School of Chemistry, Food and Pharmacy, Department of Nutritional Sciences, Reading RG6 6AP, United Kingdom.

1-14

Characterization of a novel, mouse orthotopic lung cancer model to study lung cancer cachexia

Wouter R. P. H. van de Worp[1], Jan Theys[2], Alba Sanz González[1], Brent van der Heyden[3], Frank Verhaegen[3], Annemie M. W. J. Schols[1], Ardy van Helvoort[1,4] and Ramon C. J. Langen[1].

[1]Department of Respiratory Medicine, NUTRIM –School of Nutrition and Translational Research in Metabolism, Maastricht University Medical Center+, Maastricht, the Netherlands; [2]Department of Precision Medicine, GROW –School for Oncology and Developmental Biology, Maastricht University Medical Center+, Maastricht, the Netherlands; [3]Department of Radiation Oncology (MAASTRO), GROW – School for Oncology and Developmental Biology, Maastricht University Medical Centre+, Maastricht, the Netherlands; [4]Danone Nutricia Research, Utrecht, the Netherlands

1-15

Nutraceutical role of leucine in the protein imbalance of the cachectic heart

Gabriela de Matuoka e Chiocchetti, Luana Carolina Souza Lima, Maria Cristina Cintra Gomes-Marcondes

Laboratory of Nutrition and Cancer, Department of Structural and Functional Biology, Biology Institute, University of Campinas (UNICAMP), Brazil

1-16

Relationship between leucine and cancer in the process of sarcopenia and cachexia in ageing Walker 256 tumour-bearing rats

Leisa Lopes-Aguiar*, Gabriela de Matuoka e Chiocchetti, Rogério Willians dos Santos, Maria Cristina Cintra Gomes-Marcondes*

Laboratory of Nutrition and Cancer, Department of Structural and Functional Biology, Biology Institute, University of Campinas, Campinas, São Paulo, Brazil

1-17

A nutritional supplementation with leucine improved walking, behaviour and strength tests of cachectic Walker 256 tumour-bearing Wistar rats

Laís Rosa Viana[1], Gabriela de Matuoka e Chiocchetti[1], Willians Fernando Vieira[2], Carla de Moraes Salgado[1], Alexandre Leite Rodrigues de Oliveira[2], André Schwambach Vieira[3], Maria Cristina Cintra Gomes-Marcondes[1*]

[1]Laboratory of Nutrition and Cancer, Department of Structural and Functional Biology, Biology Institute, University of Campinas (UNICAMP), Brazil; [2]Laboratory of Nerve Regeneration, Department of Structural and Functional Biology, Institute of Biology, State University of Campinas (UNICAMP), Campinas, Sao Paulo, Brazil; [3]Laboratory of Electrophysiology, Neurobiology and Behaviour – LENC, Department of Structural and Functional Biology, Biology Institute, University of Campinas (UNICAMP), Brazil

1-18

Changes in browning of white adipose tissue in cancer cachexia

Alessio Molfino[1], Giovanni Imbimbo[1], Raffaella Carletti[1], Roberta Belli[1], Maria Ida Amabile[1], Cesarina Ramaccini[1], Giuseppe Nigri[2], Maurizio Muscaritoli[1]

[1]Department of Translational and Precision Medicine, Sapienza University of Rome, Italy
[2]Department of Medical and Surgical Sciences and Translational Medicine, St Andrea University Hospital, Sapienza University of Rome, Italy

1-20

Resolvin E1 attenuates endotoxin induced muscle atrophy in human derived muscle cells

Luke Baker[1], Neil Martin[2], Emma Watson[1], Mark Lewis[2], Martin Lindley[2]

[1]University of Leicester, Leicester UK; [2]Loughborough University, Loughborough, UK

1-21

C2C12 incubated with cancer conditioned medium as a model for functional mitochondrial measurements

Miranda van der Ende[1,2], Mieke Poland[1], Klaske van Norren[1], Sander Grefte[2]

[1]Division Human Nutrition, Wageningen University & Research, Wageningen, The Netherlands; [2]Human and Animal Physiology, Wageningen University & Research, Wageningen, The Netherlands.

1-22

Phosphorylation of dystrophin S3059 protects against C2C12 myotube atrophy

Kristy Swiderski, Christopher J. Brock, Jennifer Trieu, Annabel Chee, Savant S Thakur, Dale M. Baum, Paul Gregorevic, Kate T. Murphy, Gordon S. Lynch

Centre for Muscle Research, Department of Physiology, The University of Melbourne, VIC 3010, Australia

1-23

The role of 11β-HSD1 in glucocorticoid signalling and muscle atrophy in a model of acute exacerbation of COPD

Justine Michelle Webster[2,4,5], Wouter van de Worp[5], Sara Lambrichts[5], Gareth Lavery[2], Annemie MWJ Schols[5], Rowan S Hardy[1,2,3,6], Ramon Langen[5]

[1]Institute of Inflammation and Ageing, University of Birmingham, Birmingham, UK. [2]Institute of Metabolism and Systems Research, University of Birmingham, Birmingham, UK. [3]MRC Arthritis Research UK Centre for Musculoskeletal Ageing Research, University of Birmingham, Birmingham, UK. [4]Centre for Endocrinology, Diabetes and Metabolism, Birmingham Health Partners, Birmingham, UK. [5]Department of Respiratory Medicine, NUTRIM School of Nutrition and Translational Research in Metabolism, Faculty of Health, Medicine and Life Sciences, Maastricht University, Maastricht, Netherlands. [6]Institute of Clinical Sciences, University of Birmingham, Birmingham, UK.

Poster session 6 **Cancer Cachexia** (posters 3-01 to 3-16)
Chairs: Mauricio Berriel Diaz, Germany; Paola Costelli, Italy

---

3-01
Low cholinesterase levels at diagnosis of pancreatic cancer are associated with cachexia and pancreatic cancer prognosis
Seiko Miura
Department of General and Digestive Surgery, School of Medicine, Kanazawa Medical University, Uchinada, Ishikawa, Japan

3-02
Metabolic reprogramming drives pancreatic cancer-associated wasting
Katherine R. Pelz[1], Heike Mendez[1], Brennan Olsen[2], Xinxia Zhu[2], Daniel L. Mark[1,2], Aaron J. Grossberg[1,3,4]
[1]Brenden Colson Center for Pancreatic Care; [2]Department of Pediatrics; [3]Department of Radiation Medicine; [4]Cancer Early Detection Advanced Research Center, Oregon Health & Science University, Portland, OR, United States

3-03
The human pancreatic tumor organoid secretome suppresses macrophage mitochondrial respiration without affecting macrophage function
Min Deng, Rianne Vaes, Steven Olde Damink, Sander Rensen
Department of Surgery and NUTRIM School of Nutrition and Translational Research in Metabolism, Maastricht University, Maastricht, The Netherlands

3-04
Prevalence and severity of cancer cachexia by BMI-Weight Loss (WL) Grades in advanced stage gastrointestinal and lung cancers: a population–based study
Lisa Martin, Sean Kazemi, Hailey Fedoruk, Quincy Chu, Michael Sawyer, Vickie Baracos
University of Alberta, Edmonton, Canada

3-05
Inflammation-induced cholestasis in cancer cachexia
Morgane M. Thibaut[1], Martina Sboarina[1], Martin Roumain[2], Sarah A. Pötgens[1], Audrey M. Neyrinck[1], Florence Destrée[1], Justine Gillard[1,3], Isabelle A. Leclercq[3], Guillaume Dachy[4], Jean-Baptiste Demoulin[4], Anne Tailleux[5], Sophie Lestavel[5], Marialetizia Rastelli[1,6], Amandine Everard[1,6], Patrice D. Cani[1,6], Paolo Porporato[7], Audrey Loumaye[8], Jean-Paul Thissen[8], Giulio G. Muccioli[2], Nathalie M. Delzenne[1], Laure B. Bindels[1#]
[1]Metabolism and Nutrition Research Group, Louvain Drug Research Institute, UCLouvain, Université catholique de Louvain, Brussels, Belgium; [2]Bioanalysis and Pharmacology of Bioactive Lipids Research Group, Louvain Drug Research Institute, UCLouvain, Université catholique de Louvain, Brussels, Belgium; [3]Laboratory of Hepato-Gastroenterology, Institut de Recherche Expérimentale et Clinique, UCLouvain, Université catholique de Louvain, Brussels, Belgium; [4]Experimental Medicine Unit, de Duve Institute, UCLouvain, Université catholique de Louvain, Brussels, Belgium; [5]European Genomic Institute for Diabetes (EGID), Univ. Lille, Inserm, CHU Lille, Institut Pasteur de Lille, U1011- EGID, F-59000 Lille, France; [6]Walloon Excellence in Life Sciences and BIOtechnology (WELBIO), Louvain Drug Research Institute, UCLouvain, Université catholique de Louvain, Brussels, Belgium.
[7]Department of Molecular Biotechnology and Health Science, Molecular Biotechnology Center, University of Torino, Torino, Italy; [8]Endocrinology, Diabetology and Nutrition Department, Institut de Recherches Expérimentales et Cliniques, UCLouvain, Université Catholique de Louvain, Cliniques Universitaires Saint-Luc, Brussels, Belgium

3-06

Gray and white matter morphology in cachectic colorectal cancer patients: A voxel-based morphometry MRI study.

***Estefanía Simoes*[1], *Joanna Correia-Lima*[1], *Amanda S Santos*[1], *Larissa Santana*[1], *Naomi Antunes*[6], *Fang Bin*[2], *José Pinhata*[1,3,4], *Paulo Sergio Martins de Alcantara*[3], *Ricardo Uchida*[2], *Alessandro Laviano*[7], *Fabio Duran*[6], *Geraldo Busatto*[5,6], *Marília Seelaender*[1,4,5]**

[1]Cancer Metabolism Research Group, University of São Paulo, São Paulo, Brazil; [2]*Santa Casa* de Misericórdia de São Paulo, São Paulo, Brazil; [3]Department of Clinical Surgery, University Hospital, University of São Paulo, São Paulo, Brazil; [4]LIM 26, Hospital das Clínicas of the University of São Paulo, São Paulo, Brazil; [5]*Faculdade de Medicina*, University of São Paulo, São Paulo, Brazil; [6]Neuroimaging Laboratory (LIM-21) - Institute Psychiatry University of São Paulo, São Paulo, Brazil; [7]Department of Clinical Medicine, Sapienza University of Rome, Rome, Italy.

3-07

The Impact of Circulating Tumor Cells on Cancer Cachexia in Small-Cell Lung Cancer

Tateaki Naito, Haruyasu Murakami, Hirotsugu Kenmotsu, Toshiaki TakahashiD

Division of Thoracic Oncology, Shizuoka Cancer Center, Japan

3-08

SARC-F Questionnaire score is Associated with Mortality of Cancer Patients Receiving Palliative Care

***Naoharu Mori*[1,2], *Keisuke Maeda*[1,3], *Yuria Ishida*[1,2], *Tomoyuki Nonogaki*[1,4], *Akio Shimizu*[1,5], *Yosuke Yamanaka*[6], *Remi Matsuyama*[6], *Ryoko Kato*[1,4], *Junko Ueshima*[1,7]**

[1]Department of Palliative and Supportive Medicine, Graduate School of Medicine, Aichi Medical University; [2]Department of Nutrition, Aichi Medical University Hospital; [3]Department of Geriatric Medicine, National Center for Geriatrics and Gerontology; [4]Department of Pharmacy, Aichi Medical University Hospital; [5]Department of Nutrition, Hamamatsu City Rehabilitation Hospital; [6]Department of Oral and Maxillofacial Surgery, Graduate School of Medicine, Aichi Medical University; [7]Department of Clinical Nutrition and Food Service, NTT Medical Center Tokyo

3-09

Growth differentiation factor 11 (GDF11) is not a key regulator of cancer cachexia

Brianna LaCarubba, Susie Collins, Aaron D Antona, Joe Palandra, Greg Weber, Zhidan Wu, Bei Zhang, Ja Young Kim-Muller, Danna Breen

Pfizer, Amesbury, USA

3-10

Oxytocin, the neurohypophyseal hormone has an anticachectic potential

***Alexandra Benoni*[1,2]; *Medhi Hassani*[1,2]; *Viviana Moresi*[1]; *Zhenlin Li*[2]; *Onnik Agbulut*[2]; *Dario Coletti*[1,2]; *Zhigang Xue*[2]; *Sergio Adamo*[1]**

[1]DAHFMO Unit of Histology and Medical Embryology, and Interuniversity Institute of Myology, Sapienza University of Rome, Italy; [2]Dept. Of Biological Adaptation and Ageing B2A (CNRS UMR 8256 - INSERM ERL U1164 - UPMC P6), Sorbonne University, France

3-11

Role of miR-223-3p in cancer cachexia

***Lorena Garcia-Castillo*[1], *Marc Beltrà*[1], *Fabrizio Pin*[1], *Giovanni Birolo*[2,3], *Barbara Pardini*[2,3], *Giuseppe Matullo*[2,3], *Fabio Penna*[1] *and Paola Costelli*[1]**

[1]Department of Clinical and Biological Sciences, University of Turin, Italy; [2]Italian Institute for Genomic Medicine, IIGM (formerly Human Genetics Foundation, HuGeF), Turin, Italy; [3]Department of Medical Sciences, University of Turin, Turin, Italy.

3-12

RNA Bio-profiling Studies from Human Skeletal Muscle Biopsies in Cancer Cachexia Research: an update

***Bhumi Bhatt*[1], *Sunita Ghosh*[2], *Vera Mazurak*[3], *Vickie E. Baracos*[2] *and Sambasivarao Damaraju*[1]**

[1]Department of Laboratory Medicine and Pathology, [2]Department of Oncology, [3]Division of Human Nutrition, University of Alberta, Edmonton, Alberta

3-13
C-reactive protein and its relationship with pain in advanced cancer cachexia
Koji Amano
Department of Palliative Medicine, National Cancer Center Hospital, Chuo-ku, Tokyo 104-0045, Japan

3-14
Assessment of Nutritional Status on hospital admission, a Portuguese oncology center study
Carolina Trabulo[1,2], Joana Lopes[1], David Dias[2,3], Joao Gramaça[1]; Idilia Pina[1], Paula Ravasco[2,4]
[1]Hospital Center Barreiro-Montijo, Lisbon, Portugal; [2]Center for Interdisciplinar Research in Health, Universidade Católica Portuguesa; [3]Hospital Universitário Algarve, Portugal; [4]Hospital Universitário de Santa Maria, CHULN & Universidade de Lisboa, Portugal

3-15
Tumor-derived PTHrP in patients with cachexia
Tanja Krauss[1], Simone Heisz[1], Claudine Seeliger[1], Olga Prokopchuk[2], Klaus-Peter Janssen[2], Marc E. Martignoni[2], Melina Claussnitzer[3], and Hans Hauner[1]
[1]Else Kroener-Fresenius-Center of Nutritional Medicine, School of Life Sciences, Technical University of Munich, 85354 Freising, Germany; [2]Department of Surgery, Klinikum rechts der Isar, Technical University of Munich, Munich, Germany; [3]Broad Institute of MIT and Harvard, Cambrige, MA 02142, USA

3-16
Circulating lipids are defining features of murine and human cancer cachexia
J Zuber[1,2,3*], P Morigny[1,2,3*], M Haid[4], M Seelaender[5], M Berriel Diaz[1,2,3*], M Rohm[1,2,3*]
[1]Institute for Diabetes and Cancer, Helmholtz Center Munich, Neuherberg, Germany, [2]Joint Heidelberg-IDC Translational Diabetes Program, Inner Medicine 1, Heidelberg University Hospital, Heidelberg, Germany, [3]German Center for Diabetes Research (DZD), Neuherberg, Germany, [4]Research Unit Molecular Endocrinology and Metabolism, Helmholtz Center Munich, German Research Center for Environmental Health, Neuherberg, Germany, [5]Cancer Metabolism Research Group, LIM 26 HC, Medical School, University of São Paulo, São Paulo, Brazil

Poster session 7 **Physical activity & training** (posters 7-01 to 7-08)
Chairs: Volker Adams, Germany; Fabio Penna, Italy

7-01
Country- and gender-specific cut points for low allometrically adjusted grip strength from 13,235 older adults of low- and middle-income countries.
Pedro Pugliesi Abdalla[1], Lucimere Bohn[2], André Pereira dos Santos[1], Marcio Fernando Tasinafo Junior[1], Leonardo Santos Lopes da Silva[3], José Augusto Gonçalves Marini[1], Ana Claudia Rossini Venturini, Anderson dos Santos Carvalho[3], Gustavo André Borges[4], Dalmo Roberto Lopes Machado[1]
[1]University of São Paulo, Ribeirão Preto, Brazil; [2]University of Porto, Porto, Portugal; [3]Paulista University, [4]State University of Western Paraná

7-02
Influence of a movement program on mobility in very elderly individuals – quasi experimental study
Ana Gonçalves[1], Luísa Veiga[2], Maria Teresa Tomás[2]
[1]Centro de Bem-Estar Social Lar Padre Tobias, Samora Correia, Portugal; [2]Escola Superior de Tecnologia da Saúde de Lisboa (ESTeSL) – IPL, Portuga

7-03
Integrating a preventive care path into daily life of older adults with mobility disability risk: introducing a predictive model to the exercise response
Leo Delaire[1], Aymeric Courtay[1], Joannes Humblot[1], Mathieu Fauvernier[2, 3], Marc Bonnefoy[1]
[1] Service de médecine du vieillissement – Hôpital Lyon Sud – Hospices Civils de Lyon ; [2]UMR CNRS 5558, Université Lyon 1; [3]Service de Biostatistique – Bioinformatique, Hospices Civils de Lyon

7-04
Does the presence of abdominal obesity impact physical-functional parameters in community-dwelling elderly women?
***Patricia Parreira Batista*[1], *Jéssica Rodrigues de Almeida*[1], *Stephanie Aguiar*[1], *Cláudia Venturini*[1], *Juleimar Soares Coelho de Amorim*[2], *Leani de Souza Máximo Pereira*[1]**
[1]Postgraduate Program in Rehabilitation Sciences - Department of Physiotherapy - Universidade Federal de Minas Gerais, Belo Horizonte, Minas Gerais, Brazil; [2]Federal Institute of Education, Science and Tecnhonology of Rio de Janeiro, Physical Therapy Course- IFRJ, Rio de Janeiro, RJ, Brazil

7-05
Muscle architectural changes in Response to Eight-Week Neuromuscular Electrical Stimulation Training in Healthy Older People
***Danilo Bondi*[1], *Tereza Jandova*[1], *Marco Narici*[2], *Michal Steffl*[3], *Michele D'Attilio*[4], *Moreno D'Amico*[1], *Dagmar Pavlu*[3], *Vittore Verratti*[5], *Stefania Fulle*[1], *Tiziana Pietrangelo*[1]**
[1] Department of Neuroscience, Imaging and Clinical Sciences, University "G. d'Annunzio" of Chieti – Pescara, Italy; [2] Department of Biomedical Sciences, University of Padova, Italy; [3] Faculty of Physical Education and Sport, Charles University, Prague, Czech Republic; [4] Department of Medical and Oral Sciences and Biotechnologies, University "G. d'Annunzio" of Chieti - Pescara, Italy; [5] Department of Psychological, Health and Territorial Sciences, University "G. d'Annunzio" of Chieti – Pescara, Italy

7-06
Six minute walk test performance in Chronic Obstructive Pulmonary Disease is related to oxygen use, muscle strength, and the production of specific muscle related amino acids
***Clayton L Cruthirds*[1], *Jaekwon K. Park*[1], *Nicolaas E.P. Deutz*[1], *Marielle P.K.J. Engelen*[1]**
[1]Center for Translational Research in Aging & Longevity, Dept. Health and Kinesiology, Texas A&M University, College Station, TX

7-07
Assessing the impact of inpatient rehabilitation on functional recovery from cachexia/muscle wasting in cancer – a combinatorial approach
Ishan Roy, Kevin Huang, Akash Bhakta, Emily Marquez, Jacqueline Spangenberg, Prakash Jayabalan
Shirley Ryan AbilityLab (SRAlab, formerly known as Rehabilitation Institute of Chicago); Department of Physical Medicine and Rehabilitation, Northwestern University, Chicago, Illinois, USA

7-08
Interest and faisability of intra-dialytic resistance work sessions in the fight against dynapenia in elderly, high comorbidity patients.
***Damien Paris*[1,2], *Bruno Beaune*[1,2], *Giorgina B. Piccoli*[2], *Antoine Chatrenêt*[1,2]**
[1]Laboratory "Movement, Interactions, Performance" (EA 4334), Le Mans University, Le Mans, France; [2]Nephrology, Le Mans Hospital, Le Mans, France

Poster session 9 **Therapeutic development (clinical) + Therapeutic development (pre-clinical) I** (posters 8-01 to 8-08)
Chairs: Jose Garcia, USA; Mitja Lainscak, Slovenia

8-01
SARA-OBS study: natural progression of sarcopenia and sarcopenic obesity in older adults.
***Waly Dioh*[1], *Cendrine Tourette*[1], *Anait Azbekyan*[1], *Rene Lafont*[1,2], *Pierre Dilda*[1], *Jean Mariani*[2], *Stanislas Veillet*[1], *Sam Agus*[1]**
Biophytis, Paris, France; Sorbonne Université, CNRS, France

8-02
Changes in Plasma and Urinary Metabolites After Elamipretide in Barth Syndrome Patients: Analyses from the TAZPOWER study
***David A. Brown*[1], *Hilary J. Vernon*[2]**
[1]Stealth BioTherapeutics, Newton, MA, USA; [2]Johns Hopkins University, Baltimore, MD, USA

8-03
Investigating a multimodal nutrition and exercise intervention for the treatment of cachexia in patients with Lung and GI cancers: a randomized clinical trial in Progress.
Richard F. Dunne[1], Elizabeth Cej[1], Michelle C. Janelsins[1], Luke J. Peppone[1], Aram F. Hezel[1], Aminah Jatoi[2], Mozhgan Dorkhan[3], David C. Linehan[1], Supriya G. Mohile[1], Karen M. Mustian[1]
[1]University of Rochester Medical Center, Rochester, USA; [2]The Mayo Clinic, Rochester, USA; [3]Lund University, Lund, Sweden

8-04
Serum creatinine to Cystatin C ratio as a potential muscle mass surrogate unfolds racial differences in kidney function assessments and outcomes among Black and non-Black US Veterans
John G. Rizk[1], Susan T Crowley[2], Cachet Wenziger[3,4], Kamyar Kalantar-Zadeh[3,4], and Elani Streja[3,4]
[1]Edson College, Arizona State University, Phoenix, AZ; [2]West Haven VA Med. Center, West Haven, CT; [3]Division of Nephrology, Hypertension and Kidney Transplantation, Univ. California, Irvine, School of Medicine, Irvine, CA, USA;[4]Long Beach VA Med. Center, Long Beach, CA, USA

8-05
Modulation of AMPK activity and protein turnover signaling in disused rat soleus muscle
Timur Mirzoev, Natalia Vilchinskaya, Inna Paramonova, Svetlana Belova, Ekaterina Mochalova, Boris Shenkman
Institute of Biomedical Problems of the Russian Academy of Sciences, Moscow, Russia

8-06
Metformin administration mitigates disuse-induced rat soleus muscle wasting
Timur Mirzoev, Inna Paramonova, Sergey Rozhkov, Svetlana Belova, Natalia Vilchinskaya, Boris Shenkman
Institute of Biomedical Problems of the Russian Academy of Sciences, Moscow, Russia

8-07
Ageing-related Neuromuscular Junction Degeneration in Sarcopenia is Attenuated by Vibration Treatment
Zhengyuan Bao[1], Can Cui[1], Simon Kwoon-ho Chow[1], Ling Qin[1], Wing-hoi Cheung[1]
[1]Department of Orthopaedics & Traumatology, Faculty of Medicine, The Chinese University of Hong Kong, Shatin, N.T., Hong Kong

8-08
Voluntary wheel running with and without follistatin overexpression improves neuromuscular junction transmission but not motor unit loss in aging C57BL/6J mice
Deepti Chugh[1], Chitra C. Iyer[1], Prameela Bobbili[1], Anton J. Blatnik III[1], Brian K. Kaspar[2], Kathrin Meyer[2], Arthur HM Burghes[1], Brian C. Clark[3], W. David Arnold[1]
[1]The Ohio State University, Columbus, USA; [2]Nationwide Children's Hospital, Columbus, USA; [3]Ohio Musculoskeletal and Neurological Institute, USA

Poster session 10 **Muscle wasting & Sarcopenia - mechanisms II** (posters 5-13 to 5-24)
Chairs: Srinivasan Dasarathy, USA; David Waning, USA

5-13
Circulating levels of FGF-21 and muscle-related miRNA in cancer patients
Alessio Molfino[1], Roberta Belli[1], Giovanni Imbimbo[1], Maria Ida Amabile[1], Elisabetta Ferraro[2], Serena De Lucia[3], Giuseppe Matullo[4], Paola Costelli[3], Giuseppe Nigri[5], Maurizio Muscaritoli[1]
[1]Department of Translational and Precision Medicine, Sapienza University of Rome, Italy; [2]Department of Biology- Unit of Cell and Developmental Biology, University of Pisa, Italy; [3]Department of Clinical and Biological Science, University of Turin, Italy; [4]Department of Medical Science, University of Turin, Italy; [5]Department of Medical and Surgical Sciences and Translational Medicine, St Andrea Hospital, Sapienza University of Rome, Italy

5-14

Extracellular vesicle-derived microRNAs enhance stem cell-based regeneration of skeletal muscle in muscle wasting conditions

Laura Yedigaryan[1], Giorgia Giacomazzi[1], Ester Sarrà[1], Nefele Giarratana[1], Enrico Pozzo[1], Natacha Breuls[1], Maurilio Sampaolesi[1,2]

[1]Translational Cardiomyology Laboratory, Stem Cell Biology and Embryology, Department of Development and Regeneration, KU Leuven, Leuven, Belgium; [2]Human Anatomy Unit, Department of Public Health, Experimental and Forensic Medicine, University of Pavia, Italy

5-15

Regulation of TGF-β signaling by SPSB1 plays a role in inflammation-induced muscle atrophy

Yi Li[1], Jens Fielitz[1,2,3]

[1]Experimental and Clinical Research Center, Charité-Universitätsmedizin Berlin, Max Delbrück Center for Molecular Medicine in the Helmholtz Association, Berlin, Germany. [2]Department of Internal Medicine B, Cardiology, University Medicine Greifswald, Germany. [3]DZHK (German Center for Cardiovascular Research), partner site Greifswald, Greifswald, Germany

5-16

Skeletal muscle fibre-type and oxygen transport limitations in obese-HFpEF

Ever Espino-Gonzalez[1], Peter G Tickle[1], Alan P Benson[1], Stuart Egginton[1], T Scott Bowen[1]

[1]School of Biomedical Sciences, Faculty of Biological Sciences, University of Leeds, Leeds

5-18

Early Differential Responses by Sex to Hindlimb-Unloading Induced Muscle Atrophy

J. William Deaver[1], Megan E. Rosa-Caldwell[1], Wesley A. Haynie[1], Seongkyun Lim[1], Francielly Morena Da Silva[1], Kirsten R. Dunlap[1], Lisa T. Jansen[1], Michael P. Wiggs[2], Tyrone A. Washington[1], Nicholas P. Greene[1]

[1]Health, Human Performance, and Recreation, University of Arkansas, Fayetteville, AR; [2]Health, Human Performance, and Recreation, Baylor University, Waco, Texas, TX

5-19

Acetyltransferases p300 and CBP are not required for normal skeletal muscle regeneration after injury

Alexandra Stanley, Elizabeth Orozco, Simon Schenk

Department of Orthopaedic Surgery, School of Medicine, University of California, San Diego

5-20

Transcriptomic analysis of the obesity effects in aged-sarcopenic mice

Landen W. Saling[1], Wesley S. Haynie[1], Lemuel A. Brown[1], Seongkyun Lim[2], Francielly Morena da Silva[2], Nicholas P. Greene[2], Tyrone A. Washington[1]

[1]Exercise Muscle Biology Laboratory, University of Arkansas, Fayetteville, AR; [2]Cachexia Research Laboratory, University of Arkansas, Fayetteville, AR

5-21

Optimized Grip Testing and Comparison with In Vivo Muscle Contractility in Dynapenic Aged Mice

Greg Owendoff, Alissa Ray, Prameela Bobbili, W. David Arnold

Ohio State University Department of Neurology; Columbus, Ohio, USA

5-22

Electrical impedance myography correlates with muscle mass and neuromuscular deficits during aging: a potential instrument for sarcopenia?

Carlos J. Padilla[1], Markus Harrigan[1], Hallie Harris[1], Seward B. Rutkove[2], Brian C. Clark[3], and W. David Arnold[1]

[1]Department of Neurology, The Ohio State University, Wexner Medical Center, Columbus, Ohio; [2]Department of Neurology, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, Massachusetts, United States of America; [3]Ohio Musculoskeletal and Neurological Institute and the Department of Biomedical Sciences, 250 Irvine Hall, Athens, Ohio 45701, USA

5-23

Co-application of Oral Magnesium Supplementation and Low-Magnitude, High-Frequency Vibration Treatment Attenuates Sarcopenia via PI3k/Akt/mTOR Pathway

***Can Cui*[1], *Zhengyuan Bao*[1], *Yuning Chim*[1], *Ling Qin*[1], *Simon Kwoon-ho Chow*[1], *Wing-hoi Cheung*[1]**

[1]Department of Orthopaedics & Traumatology, Faculty of Medicine, The Chinese University of Hong Kong, Shatin, N.T., Hong Kong

5-24

Follistatin-induced Muscle Hypertrophy in Aged mice Improves Neuromuscular Junction Form and Function

Chitra C. Iyer[1], Deepti Chugh[1], Prameela J. Bobbili[1], Anton J. Blatnik III[1], Alexander E. Crum[1], Allen F. Yi[1], Brian K. Kaspar[2], Kathrin C. Meyer[2], Arthur H.M. Burghes[1], W. David Arnold[1]

[1]The Ohio State University, Columbus, USA; [2]Nationwide Children's Hospital, Columbus, USA

Poster session 11 **Diagnosis of Sarcopenia II** (posters 4-25 to 4-36)
Chairs: Marc Bonnefoy, France; Francesco Landi, Italy

4-25
Sarcopenia and health-related quality of life in colorectal cancer
Mariana Vieira Barbosa[1], Mylena Pinto dos Santos[2], Jocilene Alves Leite[3], Viviane Dias Rodrigues[3], Renata Brum Martucci[3,4]
[1]Post-graduate Program in Medical Science, Medical Science Faculty, State University of Rio de Janeiro, Rio de Janeiro, RJ, Brazil; [2]Post-graduate Program in Food, Nutrition and Health, Nutrition Institute, State University of Rio de Janeiro, Rio de Janeiro, RJ, Brazil; [3]Nutrition and Dietetic Service, Cancer Hospital Unit I, National Cancer Institute José Alencar Gomes da Silva, Rio de Janeiro, RJ, Brazil; [5]Department of Applied Nutrition, Nutrition Institute, State University of Rio de Janeiro, Rio de Janeiro, RJ, Brazil

4-26
Sarcopenia in cancer palliative care: results of a prospective study.
Dubu Jonas, Le Du Katell
Institut Inter régionaL de Cancérologie, Centre Jean Bernard Clinique Victor Hugo, 72 000 Le Mans, France

4-27
Adipose tissue radiodensity: characteristics and relation to survival in a population-based cancer cohort and literature review
Md Monirujjaman[1], Lisa Martin[1], Cynthia Stretch[2], Vickie E Baracos[3], Vera C Mazurak[*1]
[1]Department of Food Agriculture and Nutritional Sciences, University of Alberta; [2]Department of Oncology, University of Calgary, Calgary, Canada; [3]Department of Oncology, University of Alberta

4-28
Differences in the prevalence of low muscle mass in cancer patients based on different cut-off values
Jona Van den Broeck[1], Martine J Sealy[2], Carola Brussaard[3], Harriet Jager-Wittenaar[2], Aldo Scafoglieri[1]
[1]Vrije Universiteit Brussel, Jette (Brussels) Belgium; [2]Hanze University Applied Sciences Groningen, The Netherlands; [3]Universitair Ziekenhuis Brussel, Belgium

4-29
Sarcopenia predicts dose-limiting toxicity in pancreatic cancer treated with nab-paclitaxel and gemcitabine
Susie Youn[1,2], Angela Chen[3], Vincent Ha[3], Michael McCall[1], Dean Eurich[2], Carole Chambers[3], Michael Sawyer[2]
[1]Department of Surgery, University of Alberta, Edmonton, AB, Canada; [2]School of Public Health, University of Alberta, Edmonton, AB, Canada; [3]Cross Cancer Institute, University of Alberta, Edmonton, AB, Canada

4-30
Predicting chemotherapy toxicity in older patients with cancer based on variables related to sarcopenia. ONCOSARCO Project.
MJ Molina-Garrido
Head of the Cancer in the Elderly Consultation. Medical Oncology Department. Hospital General Virgen de la Luz in Cuenca, Cuenca, Spain

4-31
Who is most at risk of severe chemotherapy toxicity, sarcopenic or frail elderly patients?. The ONCOSARCO Project
MJ Molina-Garrido
Cancer in the Elderly Consultation, Medical Oncology Department, Hospital General Virgen de la Luz in Cuenca, Cuenca, Spain

4-32
Could aortic calcification reveal the body composition inflammatory changes?
***Ioanna Drami*[1], *Katarina Knight*[2], *Ross Dolan*[2], *Laura E Gould*[1], *Edward T Pring*[1], *John T Jenkins*[1]**
[1]St Mark's Hospital and Academic Institute, Imperial College London, London, UK; [2]Academic Unit of Colorectal Surgery University of Glasgow, Glasgow, UK;

4-33
Bioelectrical impedance analysis-derived phase angle as a marker of Computerized Tomography-muscle mass abnormalities and muscle function in patients with cancer
***Nilian Carla Souza*[1,2], *Carla Maria Avesani*[3,4], *Carla M. Prado*[5], *Renata Brum Martucci*[1,3], *Viviane Dias Rodrigues*[1], *Nivaldo Barroso de Pinho*[6], *Steven B. Heymsfield*[7], *Maria Cristina Gonzalez*[8]**
[1]Nutrition and Dietetic Service, Cancer Hospital Unit I, National Cancer Institute José Alencar Gomes da Silva, Rio de Janeiro, Brazil; [2] Graduation Program in Nutrition, Food and Health, Nutrition Institute, Rio de Janeiro State University, Rio de Janeiro, Brazil; [3] Department of Applied Nutrition, Nutrition Institute, Rio de Janeiro State University, Rio de Janeiro, Brazil; [4] Clinical Science, Intervention and Technology, Karolinska Institutet, Stockholm, Sweden; [5] Human Nutrition Research Unit, Department of Agricultural, Food and Nutritional Science, University of Alberta, Edmonton, Alberta, Canada; [6] Brazilian Society of Oncology Nutrition, Rio de Janeiro, Brazil; [7] Pennington Biomedical Research Center, Louisiana State University, Baton Rouge, Louisiana, USA; [8] Post-graduate Program in Health and Behavior, Catholic University of Pelotas, Pelotas, Rio Grande do Sul, Brazil

4-34
Does sarcopenia equate to frailty: comparing subjects EWGSOP sarcopenic status and their Clinical Frailty Scale?
***Angela G Juby*[1], *Christpoher MJ Davis*[2], *Suglo Minimaana*[1], *Diana R Mager*[3]**
[1]Division of Geriatrics, Department of Medicine, Faculty of Medicine and Dentistry; [2]Faculty of Physical Education; [3]Faculty of Agriculture, Food and Nutrition Sciences; University of Alberta, Edmonton, Canada

4-35
Older men with sarcopenia have rapid progression of abdominal aortic calcification – the prospective MINOS study
Pawel Szulc, Roland Chapurlat
INSERM UMR1033, University of Lyon, Hôpital Edouard Herriot, Lyon, France

4-36
Sirtuin1 function is critical for preventing skeletal muscle wasting in cerebral ischemic stroke
Junaith S Mohamed, Peter J Ferrandi, Stephen E Alway
Department of Diagnostic and Health Sciences, College of Health Professions, The University of Tennessee Health Science Center, Memphis, TN, USA

Poster session 12 **Therapeutic development (pre-clinical) II** (posters 9-01 to 9-07)
Chairs: James Carson, USA; Roger Fielding, USA

9-01
Growth differentiation factor 15 (GDF-15) blockade restores muscle function and physical performance in a mouse model of cancer-induced cachexia.
***Brianna LaCarubba*[1], *Xiangping Li*[1], *Anthony Rinaldi*[1], *Stephanie Joaquim*[1], *Abdul Sheikh*[1], *John Stansfield*[2], *Donald Bennett*[2], *Danna Breen*[1], *Bei Zhang*[1], *Zhidan Wu*[1], *Ja Young Kim-Muller*[1]**
[1]Internal Medicine Research Unit, Pfizer Inc., Cambridge, MA, USA, [2]Biostatistics, Early Clinical Development, Pfizer Inc., Cambridge, MA, USA

9-02
Growth differentiation factor 15 (GDF-15) inhibition attenuates platinum-based chemotherapy-induced emesis, anorexia and weight loss and increases survival
Danna M. Breen, Kevin Beaumont, Donald Bennett, Julia Brosnan, Roberto Calle, Jeffrey R. Chabot, Susie Collins, Teresa Cunio, Ryan M. Esquejo, Stephanie Joaquim, Alison Joyce, Hanna Kim, Laura Lin, Betty Pettersen, Shuxi Qiao, Michelle Rossulek, Brendan Tierney, Karen M. Walters, Gregory Weber, Zhidan Wu, Bei B. Zhang, Morris J. Birnbaum
Pfizer Worldwide Research, Development & Medical, Cambridge, USA

9-03
Folfox Chemotherapy induces Chronic Metabolic Dysfunction and Fatigue in Mice
Brittany R. Counts, Jessica L. Halle, and James A. Carson
Integrative Muscle Biology Laboratory, Division of Rehabilitation Sciences, College of Health Professions, University of Tennessee Health Science Center, Memphis TN, USA

9-04
Dietary EPA and DHA restore altered lipid metabolism pathways associated with chemotherapy-induced myosteatosis in a preclinical model of colorectal cancer: a skeletal muscle transcriptomic analysis
Peter Isesele[1], Alaa Almasud[1], Bhumi Bhatt[2], Sambasivarao Damaraju[2], Vickie Baracos[3,] Vera C Mazurak[1]
[1]Department of Agricultural Food and Nutritional Science, University of Alberta, Edmonton, Alberta, Canada. T6G 2P5; [2]Department of Laboratory Medicine and Pathology, Faculty of Medicine and Dentistry, University of Alberta, Edmonton, AB T6G 2R3; [3]Division of palliative Care Medicine, Department of Oncology, University of Alberta, Edmonton, AB, Canada

9-05
Protection Against Doxorubicin-Induced Cardiac Dysfunction is Not Maintained Following Prolonged Autophagy Inhibition
Ryan N. Montalvo[1], Vivian Doerr[1], Oh Sung Kwon[2], Erin E. Talbert[3], Jeung-Ki Yoo[1], Moon-Hyon Hwang[1], Branden L. Nguyen[1], Demetra D. Christou[1], Andreas N. Kavazis[4], and Ashley J. Smuder[1]
[1]University of Florida, Department of Applied Physiology and Kinesiology; Gainesville, FL, USA; [2]University of Connecticut, Department of Kinesiology, Storrs, CT, USA; [3]University of Iowa, Department of Health and Human Physiology, Iowa City, IA, USA; [4]Auburn University, School of Kinesiology, Auburn, AL, USA

9-06
Alterations in hepatic fatty acids in chemotherapy-associated steatohepatitis (CASH) reveal depletion of total polyunsaturated fatty acids following irinotecan plus 5-fluorouracil treatment in an animal model of colorectal cancer
Md Monirujjaman[1], Asha Pant[1], Karen Kelly[1], Randy Nelson[1], Oliver Bathe[2], Rene Jacobs[1], Vickie Baracos[3], Vera C Mazurak[1]
[1]Alberta Institute for Human Nutrition, Department of Agricultural Food and Nutritional Science, 4-126 Li Ka Shing Centre for Health Research Innovation, University of Alberta, Edmonton, Alberta, Canada. T6G 2P5; [2]Department of Surgical Oncology, University of Calgary; [3]Department of Oncology, Cross Cancer Institute, University of Alberta

9-07
Atenolol improves skeletal muscle architecture and inhibits immobilization-induced muscle atrophy
Sapana Kushwaha[1]*, Deepak Rawat[1] and Anand Kumar[1]
[1]Department of Pharmaceutical Sciences, School of Biomedical and Pharmaceutical Sciences Babasaheb Bhimrao Ambedkar University (A Central University), Vidya Vihar, Lucknow, India

Poster session 8 **Diagnosis of Sarcopenia III** (posters 4-13 to 4-24)
Chairs: Josep Argiles, Spain; Jürgen Bauer, Germany

4-13
Sarcopenia detection using a handheld dynamometer in fracture Neck of Femur patients presenting to a District General Hospital

Sanjay Suman, Faisal Jamil, William Ogburn
Medway NHS Foundation Trust, Gillingham, UK

4-14
Longitudinal association of severe sarcopenia and mild cognitive impairment among older Mexican adults
Manrique-Espinoza B, Salinas-Rodríguez A, Palazuelos-González R
Center for Evaluation Research and Surveys, National Institute of Public Health, Cuernavaca, Morelos, Mexico

4-15
Sarcopenia and circulating leptin levels in community-dwelling older Chileans
Cecilia Albala, Carlos Marquez, Lydia Lera, Barbara Angel, Hugo Sánchez
INTA, Universidad de Chile, Santiago, Chile

4-16
Investigation into the relationship between markers of nutritional status, sarcopenia and frailty, and clinical outcomes in older hospital patients
Adriana Salame[1], Dr David Smithard[2] and Dr Adrian Slee[1]*
[1]Division of Medicine, University College London, London, UK, [2]Queen Elizabeth Hospital, Woolwich, London, UK

4-17
Associations between sarcopenia, osteoporosis and frailty in community dwelling older adults: findings from the Hertfordshire Cohort Study (HCS)
Faidra Laskou, Karen Jameson, Cyrus Cooper, Harnish P Patel, Elaine Dennison
MRC Unit Southampton, Southampton, UK

4-18
Sarcopenia is associated with mortality in adults: A systematic review and meta-analysis
Andrea B. Maier[1], Jane Xu[2], Ching S. Wan[2], Kiriakos Ktoris[1], Esmee M Reijnierse[2]
[1]Vrije Universiteit, @AgeAmsterdam, Amsterdam, The Netherlands; [2]University of Melbourne, @AgeMelbourne

4-19
Muscle Assessment by Echografy in a Cohort of Older Adults and its Utility in Sarcopenia Diagnosis
Marta Neira Alvarez[1], Miguel A Vazquez Ronda[2], Llanos Soler Rangel[2], Patricia Martinez Martin[2], Isabel Rabago Lorite[2], Gonzalo Serralta San Martin[2]
[1]Department of Geriatrics, Infanta Sofía University Hospital. Infanta Sofía and Henares HospitalS Foundation for Biomedical Research and Innovation (FIIB HUIS HHEN), Madrid (Spain). European University; [2]Department of Internal Medicine, Infanta Sofía University Hospital. Infanta Sofía and Henares Hospitals Foundation for Biomedical Research and Innovation (FIIB HUIS HHEN), Madrid (Spain). European University

4-20
Cut-points for adverse muscle composition predicts all-cause mortality
Jennifer Linge[1,2], Mickael Peterson[1], Olof Dahlqvist Leinhard[1,2,3]
[1]AMRA Medical, Linköping, Sweden; [2]Department of Health, Medicine and Caring Sciences, Linköping University, Sweden; [3]Center for Medical Image Science and Visualization (CMIV), Linköping University, Sweden

4-21
Sarcopenia and Cardiovascular Risk in Patients with Chronic Kidney Disease on Peritoneal Dialysis
Sheila Borges, Renata Costa Fortes
School of Health Sciences, Brasília, Distrito Federal, Brazil

4-22
Sarcopenia and Cardiovascular Risk in Patients with Chronic Kidney Disease on Hemodialysis: a Cross-Sectional Study
Sheila Borges; Renata Costa Fortes
[1]School of Health Sciences, Brasília, Distrito Federal, Brazil

4-23
Sarcopenia, chronic kidney disease and the risk of mortality and end stage renal disease: findings from 428,331 individuals in the UK Biobank
Thomas J Wilkinson[1], Joanne Miksza[2], Luke A. Baker[1], Courtney J Lightfoot[1], Emma L. Watson[1], Thomas Yates[3], Alice C. Smith[1]
[1]Leicester Kidney Lifestyle Team, University of Leicester; [2]Leicester Real World Evidence Centre, University of Leicester; [3]Leicester Biomedical Research Centre, Leicester

4-24
Sarcopenia in patients with bladder or kidney cancer
Patrícia Fonseca dos Reis[1,2], Renata Brum Martucci [1,2], Jocilene Leite Alves[2]
[1]Medical Science Post-Graduation, Rio de Janeiro State University, Rio de Janeiro, Brazil; [2]Nutrition and Dietetic Service, National Cancer Institute, Rio de Janeiro, Brazil

POSTER ABSTRACTS

1-01

Rehabilitating cachexia - development and functional characterization of a novel longitudinal and translational model of cancer-associated cachexia

Ishan Roy[1,2], Ben Binder-Markey[1,2], Danielle Sychowski[1], Donna McAllister[3], Dominic D'Andrea[1], Colin Franz[1,2], Michael B. Dwinell[3], Richard L. Lieber[1,2]
[1]Shirley Ryan AbilityLab (formerly known as Rehabilitation Institute of Chicago), Chicago, Illinois, USA; [2]Department of Physical Medicine and Rehabilitation, Northwestern University, Chicago, Illinois, USA; [3]Department of Microbiology & Immunology, Medical College of Wisconsin, Milwaukee, Wisconsin, USA

Introduction: The physiologic mechanisms that drive functional changes due to cachexia are poorly understood. Existing cachexia models limit our ability to address these mechanisms because they either express a rare tumor type or cause rapid death. Such models are not amenable to multi-domain functional analysis of rehabilitation protocols, which typically require 6-8 weeks. The goal of this study was to develop and functionally characterize a longitudinal model of cancer-associated cachexia.
Methods: The "KPC orthotopic injection" pancreatic cancer mouse model was selected for optimization. We tested multiple cell clones, cell doses, and vehicle types in order to maximize survival. *Ex vivo* analysis included skeletal and cardiac muscle mass. Functional characterization included: hind-limb grip strength for muscle function; open-field arena for ambulation and anxiety; Y-maze for spatial memory; and Morris Water Maze and Rotarod for endurance.
Results: Serial dilution of multiple KPC clones yielded optimal conditions for extending median survival, from 3 weeks up to 8.5 weeks post-injection using the KPC orthotopic model ($p<0.0001$). In weekly *ex vivo* analysis, the optimized model resulted in progressive skeletal and cardiac muscle mass loss at 5 weeks post-injection and continued through 9 weeks ($p<0.01$). Starting 5 weeks post-injection, animals had 8% decline in grip strength ($p<0.01$) and a sustained decrease in distance ambulated and gait speed of 30-50% ($p<0.05$). Animal subjects retained spatial memory similar to controls, indicating that functional deficits were not confounded by behavioral change. There was also a trend towards decreased motor endurance ($p=0.07$) at five weeks and increased open-field anxiety ($p=0.06$) at eight weeks.
Conclusion: This optimized model of cancer-associated cachexia demonstrates progressive loss of muscle and function in multiple domains while accounting for potential confounding factors of cognition and behavior. The model is tailored for longitudinal studies and sets the stage for mechanistic and translational studies of cachexia rehabilitation.

1-02

Alterations in Mitochondrial Turnover during the Development of Cancer Cachexia in Tumor-Bearing Female Mice

Seongkyun Lim[1], Megan E. Rosa-Caldwell[1], Wesley S. Haynie[1], Lisa T. Jansen[1], Kirsten R. Dunlap[1], Francielly Morena da Silva[1], J. William Deaver[1], Michael Wiggs[2], Tyrone A. Washington1[1], Nicholas P. Greene[1]
[1]Health, Human Performance, and Recreation, University of Arkansas, Fayetteville, AR; [2]Health, Human Performance, and Recreation, Baylor University, Waco, Texas, TX

Introduction: Cachexia is prevalent in ~80% of cancer patients and responsible for ~20% of cancer-related deaths. While the exact mechanisms leading to the onset of cancer cachexia (CC) are unknown, it has been reported previously that mitochondrial degeneration could be a culprit, as its appearance precedes skeletal muscle atrophy. We have recently reported that mitochondrial degeneration occurs during the early stages of CC in tumor-bearing male mice. However, alterations to mitochondrial health during CC in female animals are not fully elucidated. Therefore, the purpose of this study is to characterize alterations in mitochondrial health during the development of CC in female mice.
Methods: 50 female C57BL6/J mice were injected with Lewis Lung Carcinoma cells at 8-wks age. The tumors were allowed to develop for 1, 2, 3, and 4wks, and PBS-injected control group (n=10) were age-matched with the 4wks. The 3 and 4wks were combined and reclassified by low tumor (LT) weight (≤1.2g) and high tumor (HT) weight (≥2g). Gastrocnemius tissue was collected for analysis of mitochondrial turnover via immunoblotting, RT-qPCR, and histological assessment of MitoTimer (Redox sensitive reporter gene).
Results: Both body and muscle weights were reduced in HT compared to other groups ($p<0.05$). Both mRNA and protein content of Bnip3 (mitophagy) were ~53% ($p<0.05$) and ~147% ($p<0.001$) higher in HT compared to other groups, respectively. MitoTimer pure red puncta (completely degenerated mitochondria) was ~107% higher in HT compared to PBS and 1wk ($p<0.01$). MitoTimer red:green ratio (oxidative stress) was ~40% higher in HT compared to 1wk and 2wk ($p<0.01$). mRNA abundance of PGC-1α (mitochondrial biogenesis) was ~45% lower in HT compared to PBS and 1wk ($p<0.001$) although protein content of COX-IV (mitochondrial content) remained unchanged.
Conclusions: Our data suggest alterations in mitochondrial turnover occurred in HT suggesting muscle mitochondrial degeneration is associated with tumor burden in female mice.

Acknowledgements: This study was funded by the National Institutes of Health, Award number: R15 AR069913/AR/NIAMS.

1-03

Alterations in Extracellular Matrix Remodeling During Early Stages of Cancer Cachexia in Tumor-bearing Female Mice

Francielly Morena da Silva[1], Seongkyun Lim[1], Megan E. Rosa-Caldwell[1], Wesley S. Haynie[1], Lisa T. Jansen[1], Kristen R. Dunlap[1], J. William Deaver[1], Michael Wiggs[2], Tyrone A. Washington1[1], Nicholas P. Greene[1]
[1]Health, Human Performance, and Recreation, University of Arkansas, Fayetteville, AR; [2]Health, Human Performance, and Recreation, Baylor University, Waco, Texas, TX

Introduction: Cancer Cachexia (CC) is responsible for up to 30-40% of cancer-associated deaths. Defined by muscle atrophy, CC if further characterized by reduced muscular strength, increased collagen deposition and ECM dysregulation. The ECM is critical for proper force transmission and is also a reservoir for growth factors and other signaling molecules. Matrix metalloproteinases (MMPs) are a family of enzymes capable of degrading ECM components such as non-contractile proteins, and are elevated during CC development, along with enhanced collagen deposition in cachectic muscle. Further investigation of ECM remodeling during CC progression is needed.
Purpose: To investigate how ECM dynamics change during CC development. METHODS: 50 8-wks old female C57BL6/J mice were injected with Lewis Lung Carcinoma cells into their hind-flank. The tumor was allowed to grow for 1, 2, 3 and 4-wks, with a 4-wk age-matched PBS control group (n=10/group). The 3 and 4wks were combined and reclassified by low (tumor weight-TW ≤1.2g; LT) and high (TW≥2g; HT) tumor mass. Gastrocnemius tissue was collected and prepared for mRNA abundance analysis using RT-qPCR.
Results: Collagen-1 and Collagen-3 mRNA abundances were ~2-fold ($p<0.0001$) and ~1-fold ($p<0.0001$) higher in 1wk compared to the other groups, respectively. The ratio of Collagen 3:1 mRNA abundance was decreased ~37% from 1wk compared to control, LT, and HT ($p<0.008$), but not

different compared to 2wks. MMP-2 mRNA abundance was ~50% higher at 1wk compared to LT and HT ($p<0.01$) but was not different from control and 2wks. However, MMP-9 mRNA abundance was ~3-fold greater in HT compared to all the other conditions ($p<0.0001$).
Conclusions: Altered Collagen-3:1 ratio and increased MMP-2 in early stages of tumor growth precede CC and are followed by elevated MMP-9 in CC suggests changes in ECM remodeling during early stages of CC. This could hinder muscle contractile function in cancer patients.

Acknowledgements: This study was funded by the National Institutes of Health, Award number: R15 AR069913/AR/NIAMS.

1-04
Quercetin administration attenuates cancer-related cachexia and increases cancer-related survival and in C57BL/6 mice bearing syngeneic Cutaneous melanoma model

Magda Mendes Vieira[1], Amanda Mota Lacerda[1], Valéria Couto Quintão[1], Amanda Rodrigues Santos[1]; Andréia de Souza Brito[1], Otavio Cardoso Filho[1,2], Vinícius Rodrigues Dias[1,3], Ludmila Regina de Souza[1], Alfredo Maurício Batista de Paula[1,4*]
[1]Nucleus of Epidemiologic and Molecular Research Catrumano (NUPEMOC). Health Research Laboratory. Post-graduate Programme in Health Sciences. Universidade Estadual de Montes Claros (UNIMONTES), 39401-001, Montes Claros, Minas Gerais, Brazil; [2]Department of Chemical Engineering. Instituto Federal do Norte de Minas Gerais (IFNMG), Minas Gerais, Brazil; [3]Department of Physical Education. Universidade Estadual de Montes Claros (UNIMONTES), 39401-001, Montes Claros, Minas Gerais, Brazil; [4]Department of Dentistry. Universidade Estadual de Montes Claros (UNIMONTES), 39401-001, Montes Claros, Minas Gerais, Brazil

Introduction: During late stages of the tumor progression, it might occur cancer-related cachexia (CRC), a paraneoplastic syndrome characterized as a progressive, systemic, physical consumption state in an individual with cancer. Quercetin (Querc) is a flavanol that exhibits a wide range of modulatory effects on disturbed molecular pathways related to cancer progression, including those related to CRC.
Aim: We investigated the effects of Querc on tumor volume, CRC diagnosis time, skeletal muscle volume and strength, count of skeletal muscle fibers and white adipocytes, and cancer-related survival (CRS) of the C57BL/6 mice bearing a syngeneic, Cutaneous melanoma model (SCMM).
Methods: B16F10 cells were injected into flank of the sixty-nine female C57BL/6 mice to establish the SCMM. After the clinical appearance of the tumor, the animals were divided into four groups: i. mice no-tumor induced, oral gavage with placebo (PBS, control-non-tumor) ii. tumor-bearing mice and administration of placebo (control-tumor); iii. tumor-bearing mice treated with Querc 20 mg/Kg body weight (Querc20); and iv. tumor-bearing mice treated with Querc 50 mg/Kg (Querc50). Animals received placebo or Querc 20 and 50 mg/Kg body weight using oral gavage for 12 days. For CRS analysis, animals were divided in three groups: v. tumor-bearing mice and administration of placebo; vi. tumor-bearing mice treated with Querc20, and vii. tumor-bearing mice treated with Querc50. Groups were monitored for 18 days. Diagnosis of CRC was established when body weight loss ≥ 5%. Serum levels of albumin and C-reactive protein (CRP) were measured by enzyme immunoassays. Forelimb skeletal muscle volume and strength were assessed using a high-frequency power Doppler ultrasound and dynamometer devices, respectively. Skeletal muscle tissue (SMT) samples were collected and subjected to gene expression analysis using qPCR. The present study was analyzed and approved by an ethics committee on research and animal welfare (CEEBEA/UNIMONTES: protocol number: 102/2016).
Results: Control mice with tumor exhibited a significant increase of tumor volume compared to mice treated with Querc20 and Querc50. Mice treated with Querc50 significantly exhibited inhibition of body weight loss, higher time for CRC occurrence, and showed a better overall CRS. Querc20 administration significantly reduced CRP serum expression in mice bearing cutaneous with TMSMCM. SMT from mice treated with Querc50 exhibited a significant increase of myokine gene expression of *TRIM55* but significant downregulation of *TRIM63*.
Conclusions: Querc exhibited anti-tumor and anti-cachectic effects and improved the overall CRS of mice bearing SCMM. Further animal and human studies are needed to validate the use of Querc as a phytonutrient as a neoadjuvant agent during cancer treatment.

1-05
Molecular and physiologic characterization of a novel murine model of metastatic head and neck cancer cachexia

Brennan Olson[1,2], Mason A Norgard[1], Peter Levasseur[1], Xinxia Zhu, and *Daniel L Marks[1,3,4]
[1]Papé Family Pediatric Research Institute, Oregon Health & Science University, Portland, OR USA; [2]Medical Scientist Training Program, Oregon Health & Science University, Portland, OR USA; [3]Brenden-Colson Center for Pancreatic Care, Oregon Health and & Science University Portland, OR USA; [4]Knight Cancer Institute, Oregon Health & Science University, Portland, OR USA

Introduction: Effective therapies for cachexia are lacking, potentially owing to the mismatch in clinically relevant models of cachexia. Cachexia observed in a clinical setting is commonly associated with advanced or late-stage cancers that are metastatic. With nearly half of all patients with head and neck cancer (HNC) experiencing cachexia at diagnosis, and with an even larger proportion of patients developing cachexia after metastatic progression, establishing a robust model of metastatic HNC cachexia may provide a valuable translational tool to the field. To this end, we sought to establish and characterize a metastatic model of human papilloma virus (HPV) positive head and neck squamous cell carcinoma that recapitulates the cardinal clinical and molecular features of cachexia.
Methods: Male and female C57BL/6 mice were implanted subcutaneously with an oropharyngeal squamous cell carcinoma cells stably transformed with HPV16 E6 and E7 together with hRas and luciferase (mEERL) that metastasizes to the lungs (MLM)[1]. We then robustly characterize the physiologic, behavioral, and molecular signatures during cachexia development.
Results: MLM-implanted mice rapidly developed primary tumors and eventual metastatic lesions to the lungs. Behaviorally, mice progressively lost lean and fat mass, displayed decreased locomotor activities, and mild appetite suppression during tumor development. Canonical muscle catabolism programs associated with cachexia, including E3 ubiquitin ligase and autophagy pathways, along with browning of adipose tissue, are observed and correlate closely with metastatic development. Finally, we observe both neuroendocrine and autonomic aberrations during MLM-cachexia, including activation of the hypothalamic-pituitary adrenal axis and sympathetic nervous system.
Conclusions: This syngeneic MLM allograft model of cancer cachexia is reliable, consistent, and readily recapitulates the key clinical and molecular features of cachexia. Since few metastatic or HNC models of cachexia exist, we believe this model is well suited for future mechanistic studies and preclinical therapy development of metastatic disease-associated cachexia.

References
1. Vermeer DW, Coppock JD, Zeng E, et al. Metastatic model of HPV+ oropharyngeal squamous cell carcinoma

demonstrates heterogeneity in tumor metastasis. *Oncotarget.* 2016;7(17):24194-24207.

1-06

Characterizing biological mechanisms of muscle wasting in a clinically relevant model of colorectal cancer and sequential chemotherapy treatment

Gauhar Ali[1], Vera Mazurak[2], Bhumi Bhatt[3], Sambasivarao Damaraju[3], Vickie E. Baracos[1]
[1]Department of Oncology, Faculty of Medicine and Dentistry, [2]Division of Human Nutrition, [3]Department of Laboratory Medicine and Pathology, University of Alberta, Edmonton, AB

Introduction: Cancer patients experience muscle wasting that may be attributable to their tumor or chemotherapy, the effect of which occur simultaneously in the clinical setting. These are often studied separately, so their possible synergistic effects in the development and progression of muscle wasting and effect on dynamic changes in gene expression in muscle over time, have not been investigated. We address this question in a pre-clinical model with sequential chemotherapy treatments, as experienced clinically.
Methods: Chemotherapy (irinotecan plus 5-fluorouracil) was initiated 2 weeks after Ward colorectal carcinoma implantation in Female Fischer 344 rats. mRNA profiling and expression was determined in gastrocnemius muscle by RNA sequencing. Differential gene expression (DE) analysis was performed (fold-change cut-off ≥1.5 and p-value<0.05) and Ingenuity Pathway Analysis (IPA) was used for functional annotation of the identified DE mRNAs.
Results: Of the 230 total significant (p<0.05) canonical pathways identified in IPA analysis, 16 were attributed to tumor alone; the most significant being *Transcriptional Regulatory Network in Embryonic Stem Cells*(p=2.45E-05), *DNA Methylation and Transcriptional Repression Signaling*(p=7.59E-05) and *NER Pathway*(p=4.17E04). 90 additional pathways were prominent by one cycle of chemotherapy; *Type II Diabetes Mellitus Signaling*(p=4.79E-06), *Small Cell Lung Cancer Signaling*(p=9.33E-05) and *FAT10 Cancer Signaling Pathway*(p=1.78E-04) were most significant. A 2nd second cycle of chemotherapy identified 124 additional pathways, exclusive of those earlier induced by the tumor and 1st cycle of chemotherapy; *Protein Ubiquitination Pathway*(p=1.62E-07), *Estrogen Receptor Signaling*(p=4.57E-06) and *Integrin Signaling*(p=5.37E-06) were amongst the significant pathways identified.
Conclusion: The tumor and sequential cycles of chemotherapy treatments resulted in a succession of changes in skeletal muscle transcriptome. This study contributes to an understanding of muscle biology at the level of gene expression changes along the treatment trajectory and supports the model of dynamic gene expression networks contributing to possible outcomes and negates the assumptions of a steady-state model.

1-07

The role of adipose tissue breakdown in the acute phase of sepsis: a comparison of interorgan fluxes of amino acids and glycerol in a *Pseudomonas aeruginosa* induced septic pig model

Ryan Morse[1], Gabriella A.M. ten Have[1], John J. Thaden[1],, Marielle P. Engelen[1], Martin Hagve[2], Nicolaas E.P. Deutz[1]
[1]Center for Translational Research in Aging & Longevity, Department of Health & Kinesiology, Texas A&M University, College Station, TX, USA; [2]University Hospital North-Norway, Department of Gastrointestinal Surgery, Tromso, Norway.

Rationale: Sepsis leads to an acute breakdown of muscle to support increased caloric and amino acid requirements. Little is known about the role of adipose tissue breakdown in glucose substrate supply during the acute phase of sepsis. Therefore, in a translational porcine model of sepsis, we explored uptake and release of total amino acids(AA), glycerol, and glucose across gut, liver and muscle.
Methods: Acute sepsis was induced in 13 pigs (±25 kg) by iv infusion of *Pseudomonas aeruginosa* for 18 hours *and* 8 controls (C). Plasma samples were obtained across Hindquarter (HQ), Portal Drained Viscera (PDV), and liver. Concentrations of glucose, glycerol, and AA were measured by mass spectrometry. Net organ balances were calculated using (Arterial-Venous difference) * plasma flow. Data are expressed as mean[95%CI]. Statistics: Release and uptake:Wilcoxon; Comparison between groups: ANOVA. Significance: p<0.05.
Results: Arterial concentrations: In sepsis(S) plasma glucose decreased (C:4.4[4.0,4.8] vs S:3.1[2.7,3.5]mM, p<0.0001), and there was a trend toward increased AA (p=0.0563), with no difference in glycerol. HQ: We observed AA release(p<0.001), with unchanged release of glycerol or uptake of glucose. PDV: We found a decrease in glycerol(p=0.0072) and glucose(p=0.0027) uptake. Liver: Increased AA uptake(p=0.0068) and a trend towards decreased glucose release(p=0.0803), but unchanged glycerol uptake.
Conclusions: In the acute phase of sepsis, the expected increase in muscle glycerol production through lipolysis to provide substrate for gluconeogenesis is not observed. We hypothesize that the increased demand for glucogenic substrate by the liver is not supplied by lipolysis, but instead by the breakdown of muscle tissue.

Sponsor: NIH R01GM084447, S10RR027047

1-08

Chronic cachexia is dependent on sustained IL-1R signaling during parasite infection

Stephanie J. Melchor[1], Daniel Abebayehu[1], Sheryl Coutermarsh-Ott[2], Thomas Barker[1], Sarah E. Ewald[1]
[1]University of Virginia, Charlottesville, USA; [2]Virginia Polytechnic Institute, USA

Cachexia is an immune-metabolic disease of progressive muscle wasting that impairs patient
survival and quality of life across a range of chronic diseases. *T. gondii* is a protozoan parasite that
causes lifelong infection in many warm-blooded organisms, including humans and mice. Here we
show that mice infected with *T. gondii* develop robust, sustained cachexia that lasts for at least 18
weeks. Consistent with an emerging role for the IL-1 axis in disease tolerance, we show that mice
deficient in the Type 1 IL-1 receptor (IL-1R) have more severe acute muscle wasting, adipocyte and
hepatocyte necrosis, independent of parasite burden. Unexpectedly, IL-1R-/- mice rapidly recover from acute disease, despite sustained parasite infection, and are protected from chronic cachexia as well as perivascular liver and muscle fibrosis. These data are consistent with a model where IL-1R signaling benefits cell survival and tissue integrity over short periods of inflammation, but sustained reliance on IL-1 mediated tolerance programs come at the cost of fibrosis and cachexia.

1-09
GDF15 neutralization does not impact anorexia or survival in the lipopolysaccharide (LPS) acute inflammation mouse model

Zhidan Wu[1], Olivier Bezy[1], Srinath Jagarlapudi[1], Anita Patel[2], Chang Zou[1], Donald Bennett[1], Laura Lin[1], Randy J. Seeley[2], Bei B. Zhang[1], Danna M. Breen[1]
[1]Pfizer Inc, Cambridge, USA; [2]University of Michigan, Ann Arbor, USA.

Growth differentiation factor 15 (GDF-15) causes anorexia and weight loss in animal models. Higher circulating levels are associated with cachexia and increased mortality in cancer and other chronic diseases such as sepsis. In preclinical tumor models, GDF-15 inhibition reverses cachexia and improves survival, however the role of infection- and sepsis-induced GDF-15 in mouse models is controversial based on published reports. In order to investigate the role of sepsis-induced GDF-15, we examined whether GDF-15 neutralization via a validated, highly potent monoclonal antibody (mAB2) modulates lipopolysaccharide (LPS)-induced anorexia, weight loss, and mortality in rodents. mAB2 efficacy was confirmed by reversing AAV-GDF-15-induced weight loss in wildtype mice. LPS (sub-lethal dose, 5 mg/kg) injection transiently increased circulating GDF-15 in wildtype mice, reaching concentrations like those reported in septic patients within 90 minutes and remaining elevated after 48 hours (~1 ng/mL). LPS decreased food intake and body weight, and increased illness behavior and mortality. GDF-15 neutralization with mAB2 did not prevent or exacerbate any of the effects of LPS. Similarly, in GDF-15 knockout mice, the LPS effect on food intake and survival was comparable to that observed in wildtype controls. Therefore, effective inhibition of circulating active GDF-15 via antibody or gene knockout demonstrated that survival was independent of GDF-15 in the LPS acute inflammation model.

1-10
Metabolomic biomarker candidates for skeletal muscle loss in the collagen-induced arthritis (CIA) model

Marianne S Oliveira[1,2], Jordana MS Silva[1], Rafaela CE Santo[1,2], Paulo VG Alabarse[3], Ricardo M Xavier[1,2]
[1]Laboratório de Doenças Autoimunes, Serviço de Reumatologia, Hospital de Clínicas de Porto Alegre, Porto Alegre, Brazil; [2]Faculdade de Medicina, Universidade Federal do Rio Grande do Sul, Porto Alegre, Brazil; [3]VA San Diego Healthcare System, San Diego, CA, USA

Background: Rheumatoid arthritis (RA) is an autoimmune disease characterized by synovial joint degradation and extra-articular manifestations, such as loss of muscle mass. Currently, there is no consensus for the diagnosis or treatment of the debilitating RA muscle loss. Metabolomics analysis may provide a systematic overview of metabolic changes during the development of the disease. The aim of this study was to investigate metabolites in urine of mice submitted to collagen-induced arthritis model as possible biomarkers of disease-related muscle loss.
Methods: DBA1/J male mice were divided in two groups: collagen-induced arthritis (CIA; n=13) and healthy controls (CO; n=11). During the experimental period, urine samples were collected at days 0, 18, 35, 45, 55, and 65 days after disease induction. Subsequently, urine samples were subjected to metabolomics analysis using nuclear magnetic resonance spectroscopy (NMR). Metabolites were identified using the Chenomx and the Birmingham Metabolite libraries. Statistical model was performed using Principal Component Analysis (PCA), Partial Least-Squares Discriminant Analysis (PLSDA) and Partial least-squares regression analysis (PLSR), followed by metabolic pathway analysis. The final list of metabolites was filtered to identify muscle metabolism related pathways.
Results: Almost 400 metabolites were identified in the whole set of urine samples, and there were statistically significant differences between CIA vs CO, and time-dependent differences as the disease developed. Twenty-eight metabolites were associated with pathways related to muscle tissues, including muscle catabolic and anabolic processes. The following list of metabolites is suggested as potential biomarkers of muscle loss in arthritis: 3-methylhistidine, 4-aminobutyric acid, acetylcholine, arginine, aspartate, carnosine, creatine, creatinine, glutamine, histamine, histidine, isoleucine, leucine, l-methionine, lysine, myo-inositol, n,n-dimethylglycine, n-acetyl alanine, n-acetylmethionine, pantothenate, phenylalanine, phosphocholine, phosphocreatine, pyridoxine, sarcosine, succinyl acetone, thiamine and urocanate.
Conclusions: Several metabolites related to muscle metabolism were found in urine of CIA mice, with significant differences in comparison with CO mice. Also, altered metabolites were identified relatively to the stage of disease development. These data suggest that most metabolic alterations occurring in muscle tissues may be detected in the urine of arthritic mice, enabling further validation in the urine of RA patients, targeting prognosis, diagnosis, and monitoring of muscle loss mediated by the disease.

1-11
Expression and role of microRNAs associated with inflammation in cancer cachexia

Joana M.O. Santos[1,2], Sara Peixoto da Silva [1,2], Margarida M.S.M. Bastos [3], Paula A. Oliveira [4], Rui M. Gil da Costa[1,3,4,5], Rui Medeiros[1,2,6,7,8]
[1]Molecular Oncology and Viral Pathology Group, IPO Porto Research Center (CI-IPOP), Portuguese Oncology Institute of Porto (IPO Porto), 4200-072 Porto, Portugal; [2]Faculty of Medicine of the University of Porto (FMUP), 4200-319 Porto, Portugal; [3]Laboratory for Process Engineering, Environment, Biotechnology and Energy (LEPABE), Faculty of Engineering of the University of Porto (FEUP), 4200-465 Porto, Portugal; [4]Center for the Research and Technology of Agro-Environmental and Biological Sciences (CITAB), University of Trás-os-Montes and Alto Douro (UTAD), 5001-911 Vila Real, Portugal; [5]Postgraduate Programme in Adult Health (PPGSAD), Tumour and DNA Biobank (BTMA), Federal University of Maranhão (UFMA), 65080-805 São Luís, Brazil; [6]Research Department of the Portuguese League Against Cancer – Regional Nucleus of the North (Liga Portuguesa Contra o Cancro – Núcleo Regional do Norte), 4200-177 Porto, Portugal; [7]Virology Service, Portuguese Oncology Institute of Porto (IPO Porto), 4200-072 Porto, Portugal; [8]Biomedical Research Center (CEBIMED), Faculty of Health Sciences of the Fernando Pessoa University, 4249-004 Porto, Portugal

Introduction: Systemic inflammation is one of the main drivers of cachexia which is a wasting syndrome present in some cancer patients. This syndrome has an high impact on the quality of life and survival of cancer patients. MicroRNAs have been emerging as important players on cancer cachexia and it is well known that there is reciprocal regulation of microRNAs and pro-inflammatory signalling pathways. K14-HPV16 mice have been recently reported by our group as a model of cancer cachexia, presenting lesions ranging from hyperplasia to invasive carcinoma in several anatomic locations, systemic inflammation and muscle wasting.
Methods: Thus, the aim of this work is to study the expression of inflammation-related microRNAs in gastrocnemius of K14-HPV16 mice and to explore their role on muscle wasting using bioinformatic tools.
Results: Our results showed that miR-223-3p (p=0.004), let-7b-5p (p=0.034), miR-21a-5p (p=0.034), miR-150-5p (p=0.027) and miR-155-5p (p=0.011) were overexpressed in gastrocnemius samples from cachectic K14-HPV16 mice compared to the control group. Our bioinformatic analysis, showed that these microRNAs' targets participate in several

process related to muscle wasting, such as muscle structure development, response to growth factor, regulation of cell differentiation, muscle cell proliferation and regulation of MAPK signaling. In fact, references to MAPK signaling were constantly present in all of our analysis. When analysing protein-protein interaction-network, two major functional modules were obtained. Among the top 10 hub proteins there are Kras, Igf1r and Nras that participate in MAPK pathway.
Conclusions: Thus, we can conclude that inflammation-related microRNAs miR-223-3p, let-7b-5p, miR-21a-5p, miR-150-5p and miR-155-5p, play a role on muscle wasting in K14-HPV16 transgenic mice. To the best of our knowledge, this study is the first to report an association between let-7b-5p, miR-150 and miR-155 with muscle wasting caused by cancer. Bioinformatic data indicate that these microRNAs converge in regulating the MAPK signaling pathway, an important player in muscle biology.
Funding sources: This study was funded by the Portuguese League Against Cancer—Regional Nucleus of the North (Liga Portuguesa Contra o Cancro—Núcleo Regional do Norte), by the Research Center of the Portuguese Oncology Institute of Porto (project no. PI86-CI-IPOP-66-2017 and PI127-CI-IPOP-118-2019), by Base Funding—UIDB/00511/2020 of the Laboratory for Process Engineering, Environment, Biotechnology and Energy—LEPABE—funded by national funds through the FCT/MCTES (PIDDAC), by European Investment Funds from FEDER/COMPETE/POCI—Operational Competitiveness and Internationalization Program, and by National Funds from FCT—Portuguese Foundation for Science and Technology, under the project UID/AGR/04033/2019. Joana M.O. Santos is supported by a PhD fellowship (SFRH/BD/135871/2018) from FCT—Fundação para a Ciência e a Tecnologia.

1-12
Distinct tissue-specific gene regulation and potential inter-organ communication in a mouse model of cancer cachexia

Ji-Won Heo, Sung-Eun Kim
Department of Food and Nutrition, Sookmyung Women's University, Seoul, Korea

Introduction: Cancer cachexia is a multifactorial syndrome characterized by body weight loss, which negatively affects chemotherapy efficiency and quality of life of cancer patients. Accumulating evidence reveals that cancer cachexia is a systemic disorder influencing and/or affected by various organs including skeletal muscle, adipose tissue, and liver. In the present study, we performed bioinformatics analysis of gene expression profiles in skeletal muscle, white adipose tissue, and liver of cachetic mice in order to understand inter-organ crosstalk in cancer cachexia.
Methods: Genome-wide expression changes in skeletal muscle, adipose tissue, and liver of CT26-tumor bearing mice were analyzed by SurePrint G3 Mouse Gene Expression 8x60K v2 (Agilent, Inc.) Bioinformatics analysis was performed using Gene Set Enrichment Analysis, Database for Annotation, Visualization and Integrated Discovery, and Ingenuity Pathway Analysis (QIAGEN) to explore communications between different organs. Gene expression results of selected genes were validated by qRT-PCR.
Results: We identified 299, 508, and 1311 genes differentially regulated in skeletal muscle, adipose tissue, and liver, respectively. Seventy-eight genes, including 77 up-regulated and 1 down-regulated, involved in response to stimulus and immune system process were differentially regulated in all organs. The top networks matched by the genes commonly differentially regulated in all organs were (1) cellular function and maintenance, hematological system development and function, immunological disease, (2) cardiovascular disease, cell death and survival, cell-to-cell signaling and interaction, and (3) antimicrobial response, infectious diseases, inflammatory response. These top networks included *Bcl3, Csf2rb, Fcgr2a, Lilrb3, Cebpd, Cxcl14, Osmr, Serpina3,* and *Socs3*, which interacted strongly with surrounding genes associated with inflammation and energy metabolism induced by cancer cachexia.
Conclusions: This study provided evidence that several genes up-regulated in skeletal muscle, adipose tissue, and liver might be candidate early biomarkers for early detection and prevention of cancer cachexia.
(This research was supported by the Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Education (NRF-2016R1A6A3A11934151 to S-EK).)

1-13
Multi-compartment metabolomics and metagenomics reveal new metabolic targets in cancer cachexia.

Sarah A. Pötgens[1], Morgane M. Thibaut[1], Nicolas Joudiou[2], Martina Sboarina[1], Audrey M. Neyrinck[1], Patrice D. Cani[1,3], Sandrine P. Claus[4], Nathalie M. Delzenne[1], Laure B. Bindels[1#]
[1]Metabolism and Nutrition Research Group, Louvain Drug Research Institute, UCLouvain, Université catholique de Louvain, Brussels, Belgium; [2]Nuclear and Electron Spin Technologies Platform (NEST), Louvain Drug Research Institute, UCLouvain, Université catholique de Louvain, Brussels, Belgium ;
[3]Walloon Excellence in Life Sciences and BIOtechnology (WELBIO), Louvain Drug Research Institute, Université catholique de Louvain, Brussels, Belgium; [4]University of Reading, School of Chemistry, Food and Pharmacy, Department of Nutritional Sciences, Reading RG6 6AP, United Kingdom.

Introduction: Cancer cachexia is a multifactorial syndrome characterised by multiple metabolic dysfunctions. Besides the muscle, other organs such as the liver and the gut microbiota may also contribute to this syndrome and deserve further investigation.
Methods: We combined proton Nuclear Magnetic Resonance (^{1}H-NMR) metabolomics in multiple compartments with 16S rDNA sequencing. These analyses were complemented by molecular and biochemical analyses, as well as hepatic transcriptomics.
Results: ^{1}H-NMR revealed major changes between control and cachectic (C26) mice in the four analysed compartments (*i.e.* cecal content, portal vein, liver and vena cava). More specifically, glucose metabolism pathways in the C26 model were altered with a reduction in glycolysis and gluconeogenesis and an activation of the hexosamine pathway, arguing against the existence of a Cori cycle in this model. In parallel, amino acid uptake by the liver, with an up to 4-fold accumulation of nine amino acids, was mainly used for acute phase response protein synthesis rather than to fuel the tricarboxylic acid cycle and gluconeogenesis. We also identified a 35% reduction in hepatic carnitine levels and a lower activation of the phosphatidylcholine pathway as potential contributors to the hepatic steatosis present in this model. Our work also reveals a reduction of different beneficial intestinal bacterial activities in cancer cachexia with decreased levels of acetate, butyrate and aromatic amino acid metabolites, which may contribute to the altered intestinal homeostasis in these mice. Finally, we report a 2-fold intestinal transit acceleration as a key factor shaping the gut microbiota composition and activity in cancer cachexia, which together lead to a fecal loss of proteins and amino acids.
Conclusions: Our work highlight new metabolic pathways potentially involved in cancer cachexia and further supports the interest of exploring the gut microbiota composition and activity, as well as intestinal transit, in cancer patients with and without cachexia.

1-14

Characterization of a novel, mouse orthotopic lung cancer model to study lung cancer cachexia

Wouter R. P. H. van de Worp[1], Jan Theys[2], Alba Sanz González[1], Brent van der Heyden[3], Frank Verhaegen[3], Annemie M. W. J. Schols[1], Ardy van Helvoort[1,4] and Ramon C. J. Langen[1].

[1]Department of Respiratory Medicine, NUTRIM –School of Nutrition and Translational Research in Metabolism, Maastricht University Medical Center+, Maastricht, the Netherlands; [2]Department of Precision Medicine, GROW – School for Oncology and Developmental Biology, Maastricht University Medical Center+, Maastricht, the Netherlands; [3]Department of Radiation Oncology (MAASTRO), GROW – School for Oncology and Developmental Biology, Maastricht University Medical Centre+, Maastricht, the Netherlands; [4]Danone Nutricia Research, Utrecht, the Netherlands

Introduction: Although various lung tumor-bearing animal models have been used to explore underlying mechanisms of cancer cachexia, these models do not recapitulate anatomical and immunological features key to lung cancer and associated muscle wasting. As these shortcomings may hamper translating experimental findings into the clinic, we characterized a syngeneic, orthotopic lung cancer mouse model to study the etiology of lung cancer-induced muscle wasting.
Methods: Immune competent, male 129S2/Sv mice, 11 weeks old, were randomly allocated to either (1) sham control group or (2) tumor-bearing group. Syngeneic lung epithelium-derived adenocarcinoma cells (K-ras^{G12D}; p53$^{R172H\Delta G}$) were inoculated intrapulmonary into the left lung lobe of the mice. Body weight and food intake were measured daily. At baseline and weekly after surgery, grip strength was measured and tumor growth and muscle volume were assessed using micro cone beam CT imaging. At the end of the study, animals were euthanized and skeletal muscles of the lower hind limbs were collected.
Results: Approximately 60% of the tumor-bearing mice developed cachexia. The cachectic mice showed reduced final body weight (13.7 ± 5.7%) and CT-based muscle mass (13.8 ± 8.1%) compared to sham controls and had a median survival time of 33.5 days post-surgery until humane endpoint. In cachectic mice, markers for proteolysis, both ubiquitin proteasome system (Atrogin-1 and MuRF-1) and autophagy-lysosomal pathway (GABARAPL and Bnip3), were significantly upregulated, whereas markers for protein synthesis (e.g. p-4E-BP1) were significantly decreased. Furthermore, cachectic mice showed increased glucocorticoid signaling indicated by increased expression of direct targets of the glucocorticoid receptor (KLF15 and Glul) compared to sham controls.
Conclusions: We developed an orthotopic model of lung cancer cachexia in immune competent mice. This model will contribute to understanding the underlying mechanisms of lung cancer or treatment-induced cachexia, and can be deployed to test the efficacy of intervention strategies.

1-15

Nutraceutical role of leucine in the protein imbalance of the cachectic heart

Gabriela de Matuoka e Chiocchetti, Luana Carolina Souza Lima, Maria Cristina Cintra Gomes-Marcondes
Laboratory of Nutrition and Cancer, Department of Structural and Functional Biology, Biology Institute, University of Campinas (UNICAMP), Brazil

Background: The relationship between cancer cachexia and heart disease implies in a decreased size of the heart, managed by the relative rates of protein synthesis and degradation. However, there is a lack of studies directly measuring these rates in the heart of experimental models of cancer cachexia. On the other hand, recent studies have elucidated that leucine diet has beneficial effects on skeletal muscle in tumour-bearing animals, specially by reversing the protein imbalance caused by cancer cachexia. Nevertheless, there is no sufficient knowledge about the nutraceutical effect of leucine in the cachectic heart. Therefore, we evaluated the rates of protein synthesis and degradation in the heart of cachectic rats supplemented with leucine, in other to correlate them with heart size and cachexia index.
Materials and methods: Wistar adult rats were distributed into 4 groups: control (C) and Walker 256 tumour-bearing (W), both groups fed a control diet (18% protein), and leucine (L) and leucine tumour-bearing (LW) groups fed a leucine-rich diet (18% protein + 3% leucine). After 21 days or pre-agonistic period, the rats were euthanised and morphometric parameters were assessed. The was dissected and incubated with cycloheximide for protein degradation assay. Tyrosine released in incubation buffer were assayed. The statistical analysis was performed by one-way ANOVA, followed by post-hoc Bonferroni's test. The correlation of Pearson was also calculated.
Results and conclusion: The heart weight was significant lower in W group in comparison to C group (P=0.0092) and negatively correlated with cachexia index (r =-0,6222), indicating that cancer cachexia was affecting the heart size in our experimental model. Regarding the protein degradation, the tyrosine release was curiously lower in the W group in comparison with C group (P=0.0162), and positively correlated with the heart size (r=0,4688), suggesting a protection of the heart tissue, in comparison with the skeletal muscle. No effect of leucine supplementation was observed. Pathways analysis are needed to better understand if the leucine has an positive effect minimising the protein imbalance in the cachectic heart.

Funding: This research was funded by FAPESP (#2017/02739-4; #2019/14803-4).

1-16

Relationship between leucine and cancer in the process of sarcopenia and cachexia in ageing Walker 256 tumour-bearing rats

Leisa Lopes-Aguiar*, Gabriela de Matuoka e Chiocchetti, Rogério Willians dos Santos, Maria Cristina Cintra Gomes-Marcondes*
Laboratory of Nutrition and Cancer, Department of Structural and Functional Biology, Biology Institute, University of Campinas, Campinas, São Paulo, Brazil

Introduction: The elucidation of sarcopenia and cachexia mechanisms is important to prevent the process of skeletal muscle atrophy. Current evidence has shown that nutritional supplementation with leucine can preserve the muscle mass in cancer cachexia. However, the role of leucine in the process of sarcopenia and cancer cachexia is not yet totally known. Therefore, we evaluated the relationship between leucine and cancer in ageing Walker 256 tumour-bearing rats.
Methods: 22 ageing Wistar rats were distributed into the following different experimental groups: control (C) and Walker 256 tumour-bearing (W) both subjected to a normoproteic diet (18% protein); leucine (L) and Walker 256 tumour-bearing (WL) both subjected to leucine-rich diet (18% protein plus 3% L-leucine). The tumour implant was performed by subcutaneous inoculation of viable neoplastic cells from Walker 256 tumour. After 21 days or pre-agonistic period, all animals were euthanised and the morphometric and metabolic parameters were assessed. The statistical analysis were performed by one-way ANOVA, followed by post-hoc Tukey's test.
Results: The body weight was significantly decreased in both tumour-bearing groups, with deeply reduction in W (110%, *P*=0.006), but little lighter in WL (71%, *P*=0.024) in comparison to C and L groups, respectively. The normalised gastrocnemius and tibialis anterior muscles showed the same pattern of muscle mass reduction in W (gastrocnemius: 29%,

P=0.003; tibialis: 24%, *P*=0.004), since it was a lighter reduction in WL (gastrocnemius: 14%, *P*=0.010; tibialis: 15%, *P*=0.036) when compared to C and L groups, respectively. In addition, the metabolic rate was also lower in W (151%, *P*=0.024) and WL (185%, *P*=0.007) groups in comparison to L group.
Conclusions: Our preliminary results suggest that the process of sarcopenia and cancer cachexia led to reduced morphometric and metabolic parameters. However, additional studies are needed to assess the relationship between leucine and cancer in ageing Walker 256 tumour-bearing rats.

Funding: This research was funded by FAPESP (#2017/02739-4; #2019/20558-2).

1-17
A nutritional supplementation with leucine improved walking, behaviour and strength tests of cachectic Walker 256 tumour-bearing Wistar rats

Laís Rosa Viana[1], Gabriela de Matuoka e Chiocchetti[1], Willians Fernando Vieira[2], Carla de Moraes Salgado[1], Alexandre Leite Rodrigues de Oliveira[2], André Schwambach Vieira[3], Maria Cristina Cintra Gomes-Marcondes[1*]
[1]Laboratory of Nutrition and Cancer, Department of Structural and Functional Biology, Biology Institute, University of Campinas (UNICAMP), Brazil; [2]Laboratory of Nerve Regeneration, Department of Structural and Functional Biology, Institute of Biology, State University of Campinas (UNICAMP), Campinas, Sao Paulo, Brazil; [3]Laboratory of Electrophysiology, Neurobiology and Behaviour – LENC, Department of Structural and Functional Biology, Biology Institute, University of Campinas (UNICAMP), Brazil

Background: Muscle loss associated with cancer cachexia jeopardises the quality of life, reducing muscle function. Branched-chain amino acid leucine has a high interest mainly for maintaining lean body mass in experimental model of cancer cachexia. We aimed to evaluate the effects of a leucine-rich diet on muscular functional activity, through CatWalk (walking test), *EthoVisionXT12* (behaviour test) and Grip strength (strength test) in tumour-bearing cachectic rats.
Methods: Wistar adult rats were distributed into 4 groups: control (C) and Walker 256 tumour-bearing (W), both groups fed a control diet (18% protein), and leucine (L) and leucine tumour-bearing (LW) groups fed a leucine-rich diet (18% protein + 3% leucine). Their functional activity tests were assessed a week before tumour inoculation and at the endpoint moment.
Results: The Catwalk test revealed that the walking pattern was significant altered at the endpoint moment in both W and LW group. Despite not having completely preventing the functional decline, leucine-rich diet minimised this decay in some of the analysed parameters. The maximum contact area, and the print area of forelimb paws were just decreased in W group. Despite having a decreased on the maximum intensity mean of the footprint in both W and LW groups, the decline was lighter in LW (4.38% (P<0.01) and 3.26% (P<0.05), fore and hindlimb paws respectively) in comparison to W group (5.79% (P<0.001) and 6.79% (P<0.001), respectively). In a similar way, the behavior analysis has shown that Walker 256 tumour evolution led to a negative impact on the mobility of tumour-bearing rats. In W group, the distance moved, velocity and time moving were significantly reduced, as well as the muscle strength. On the other hand, the distance moved and the velocity remained unchanged in LW group. Although the time moving was also diminished, in LW was lighter (35.71% (P<0.01)) than in W group (50.04% (P<0.001)). Additionally, the LW group not only maintained the muscle strength but was also similar to both control groups, C and L.
Conclusion: Walker 256 tumour-bearing rats fed a leucine-rich diet had better functional activity (faster, more mobile and resilient), tended to be protected against impaired gait pattern and were protected against muscle strength loss. (Financial support: #2015/21890-0; #2017/02739-4)

1-18
Changes in browning of white adipose tissue in cancer cachexia

Alessio Molfino[1], Giovanni Imbimbo[1], Raffaella Carletti[1], Roberta Belli[1], Maria Ida Amabile[1], Cesarina Ramaccini[1], Giuseppe Nigri[2], Maurizio Muscaritoli[1]
[1]Department of Translational and Precision Medicine, Sapienza University of Rome, Italy
[2]Department of Medical and Surgical Sciences and Translational Medicine, St Andrea University Hospital, Sapienza University of Rome, Italy

Introduction: Browning of white adipose tissue (WAT) contributes to the progression of cachexia involving several pathways including uncoupling protein 1 (UCP1). Our study aimed at assessing molecular phenotype of browning in cancer patients with or without cachexia compared to healthy controls.
Methods: We enrolled gastrointestinal cancer patients and controls undergoing surgery for gastrointestinal tumors and for non-malignant diseases. We diagnosed anorexia by FAACT score and pre-cachexia and cachexia according to international criteria. During surgery, we collected subcutaneous adipose tissue samples. By RT-PCR, we analyzed markers of browning including CIDEA, UCP1, TMEM26, PGC-1α mRNA levels and we conducted histomorphological analysis of adipose tissue cells (cross sectional area-CSA).
Results: We studied 25 gastrointestinal cancer patients and 15 controls. In cancer patients, cachexia and anorexia accounted for 56% and 76%, respectively. UCP1 levels resulted lower in cancer patients compared to controls (P=0.003), in patients with cachexia + pre-cachexia group vs controls (P=0.009) and in non-cachectic vs controls (P=0.01). Moreover, CIDEA mRNA levels were increased in cancer patients compared to controls, in particular in pre-cachexia + cachexia group vs controls (P=0.003), whereas no differences were observed between non-cachectic and controls. TMEM26 levels were increased in cachectic patients vs non-cachectic (p=0.027) and vs controls (P=0.046), and PGC-1α levels were slightly up-regulated in cancer cachexia compared to controls (P=0.048). The CSA of adipose cells was decreased in cancer patients with respect to controls (P<0.01), but we did not observe differences among cancer patients with and without cachexia.
Conclusion: Our study showed perturbation in browning process in WAT of cancer patients with and without cachexia compared to controls. Interestingly, we showed a downregulation of UCP1 mRNA levels in WAT of cancer patients, indicating changes in thermogenic pathways during the disease.

1-20
Resolvin E1 attenuates endotoxin induced muscle atrophy in human derived muscle cells

Luke Baker[1], Neil Martin[2], Emma Watson[1], Mark Lewis[2], Martin Lindley[2]
[1]University of Leicester, Leicester UK; [2]Loughborough University, Loughborough, UK

Loss in skeletal muscle size and function is a common debilitating co-morbidity in an array of chronic disease states as well as during the ageing process. This can lead to a loss of physical activity and ability to perform everyday tasks, leading those affected into a downward spiral of muscle loss and inactivity which has been strongly linked to increased rates of morbidity and mortality. Many factors have been linked to induce such processes, one of which is inflammation,

with therapeutic research looking for ways to resolve chronic inflammation to subsequently alleviate related muscle atrophy. Resolvin E1 (RvE1) is a specialised pro-resolving lipid mediator, derived from the metabolism of the omega-3 fatty acid EPA, which has shown to have beneficial pro-resolving properties in an array of cell types, including our previous work in immortalised skeletal muscle cell lines. Our work is the first to show beneficial pro-resolving properties of RvE1 in human skeletal muscle cells. RvE1 was seen to attenuate lipopolysaccharide (LPS) induced inflammatory related gene expression of both IL-6 (LPS 7.82 ± 0.52 vs. RvE1 3.93 ± 0.32, p = 0.015) and MCP-1 (LPS 21.45 ± 0.92 vs. RvE1 17.31 ± 0.52, p = 0.023) leading to an alleviation in downstream endotoxin induced myotube atrophy (µm) (LPS 20.29 ± 1.36 vs. RvE1 28.76 ± 1.13, p = 0.003). Further to this preliminary evidence suggests that RvE1 may induce its effects through the inhibition of classical canonical inflammatory signalling. Our novel findings provide initial rational for further investigation of RvE1 as a naturally occurring nutritional therapeutic in chronic conditions characterised with a degree of inflammatory induced skeletal muscle atrophy.

1-21
C2C12 incubated with cancer conditioned medium as a model for functional mitochondrial measurements

Miranda van der Ende[1,2], Mieke Poland[1], Klaske van Norren[1], Sander Grefte[2]
[1]Division Human Nutrition, Wageningen University & Research, Wageningen, The Netherlands; [2]Human and

decreased (P < 0.05 on day 5 and 7) after incubation with 4662 and KPC conditioned medium. It could be suggested that mitochondrial activity is influenced by the treatment. Next,

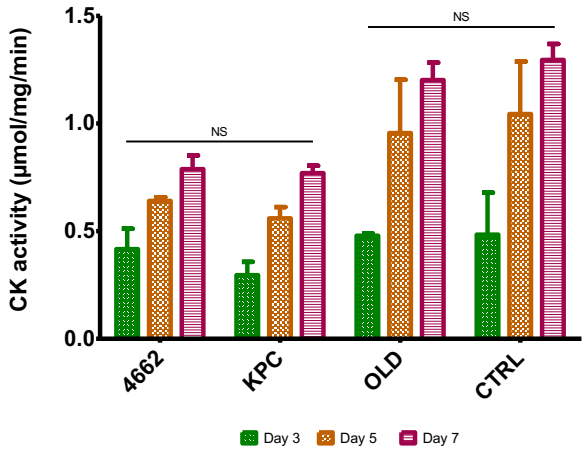


Figure 1: CK activity (B) of 7 day differentiated C2C12 myotubes incubated with 33% conditioned medium of KPC cells, 4662 cells, old differentiation medium (OLD) or fresh differentiation medium (CTRL). Samples measured on day 3, 5 and 7 of differentiation. N=3 experiments in triplo, depicted as mean ±SD.

References

1. van der Ende, M, et al. (2018) Mitochondrial dynamics in cancer-induced cachexia. Biochim Biophys Acta 1870(2):137-150.
2. Burckart K, Beca S, Urban RJ, Sheffield-Moore M. (2010) Pathogenesis of muscle wasting in cancer cachexia: targeted anabolic and anticatabolic therapies. Curr Opin Clin Nutr Metab Care. 13(4):410-6.
3. Bessman SP, Geiger PJ (1981) Transport of energy in muscle: The phosphorylcreatine shuttle. Science 211(4481):448-452.

Animal Physiology, Wageningen University & Research, Wageningen, The Netherlands.

Cancer cachexia is a complex metabolic syndrome characterized by clinically relevant loss of muscle mass with or without loss of fat mass. From extensive literature research we know that gene and protein expression of muscle mitochondrial dynamics are altered during cancer cachexia in animal models [1]. Additionally, we know that the regeneration of muscle is hampered [2]. To study the changes in mitochondrial dynamics in relation to muscle regeneration a cell model is being developed. Here, we show the first results of this model. C2C12 myoblast were incubated with conditioned medium of genetically similar pancreatic tumour cell lines that differ in cachexia-inducing capacity *in vivo* (kind gift of Elizabeth Jaffee and Daniel Marks). Additionally, a new, and probably more realistic, control was added. This control is 33% of used (old) differentiation medium to correct for the usage of nutrients by the cells while making conditioned medium. The C2C12 cells were exposed to 33% conditioned tumour medium during a 7-day differentiation period after which creatine kinase (CK) activity was measured. CK transports ATP from the mitochondrial membrane to the parts of the cell that need the energy [3, 4]. It has been shown that myotubes have a bigger energy expenditure than myoblasts and thus need more CK activity [5]. Therefore, CK activity can be used as an indirect measure for differentiated C2C12 myotubes and mitochondrial activity. Results are shown in figure 1 (n=3 experiments in triplo) and suggests that compared to control (both fresh and old medium) the CK activity is significantly

we want to do RNAseq and further study the mitochondrial dynamics by functional assays, such as sea horse.

4. Delaporte C, Dautreaux B, Fardeau M (1984) Human myotube differentiation in vitro in different culture conditions. Biol Cell. 57(1):17-22.
5. Veliça P, Bunce C (2011) A quick, simple and unbiased method to quantify C2C12 myogenic differentiation. Muscle Nerve 44:366-370.

1-22
Phosphorylation of dystrophin S3059 protects against C2C12 myotube atrophy

Kristy Swiderski, Christopher J. Brock, Jennifer Trieu, Annabel Chee, Savant S Thakur, Dale M. Baum, Paul Gregorevic, Kate T. Murphy, Gordon S. Lynch
Centre for Muscle Research, Department of Physiology, The University of Melbourne, VIC 3010, Australia

Introduction: The dystrophin-glycoprotein complex (DGC) is a multi-protein structure required to maintain muscle fibre membrane integrity, transmit force, and maintain muscle proteostasis. Dystrophin membrane localisation is perturbed in muscles wasting as a consequence of cancer cachexia, tenotomy and advanced ageing, which are all associated with inflammation. Through proteomics and mutagenesis studies, we identified novel phosphorylated residues within endogenous dystrophin, and showed that phosphorylation at serine 3059 (S3059) enhanced interaction between dystrophin and β-dystroglycan. We hypothesised that dystrophin S3059 phosphorylation is fundamental to the aetiology of muscle wasting and investigated the role of S3059 phosphorylation on DGC protein interactions and muscle cell size.
Methods: Phospho-null (mutation to alanine) and phosphomimetic (mutation to glutamine) mutations were made in dystrophin constructs which were transfected into C2C12 muscle cells or AAV-293 cells in the presence or absence of various kinase inhibitors to assess effects on myotube diameter and protein function.
Results: Over-expression of a dystrophin construct unable to be phosphorylated at S3059 (SA) reduced myotube size in

C2C12 cells. Furthermore, over-expression of a dystrophin construct with a phosphomimetic mutation at S3059 (SE) attenuated myotube atrophy in the presence of C-26 cells. Addition of inhibitors of extracellular regulated kinase 2 (ERK2) and cyclin-dependent kinase 1 (Cdk1) or the ERK activator phorbol myristate acetate (PMA), indicated that ERK2 and/or Cdk1 may phosphorylate the dystrophin protein to increase the association between dystrophin and β-dystroglycan.
Conclusions: These findings demonstrate a link between loss of dystrophin S3059 phosphorylation and destabilisation of the DGC which may be mediated by ERK2 and/or Cdk1. Determining the mechanisms underlying post-translational modification of S3059 will identify novel targets to restore DGC interactions to preserve and protect muscles and improve clinical outcomes for patients whose muscles are wasting and seemingly unresponsive to other treatments.
Supported by the National Health & Medical Research Council (GNT1144772)

1-23
The role of 11β-HSD1 in glucocorticoid signalling and muscle atrophy in a model of acute exacerbation of COPD

Justine Michelle Webster[2,4,5], Wouter van de Worp[5], Sara Lambrichts[5], Gareth Lavery[2], Annemie MWJ Schols[5], Rowan S Hardy[1,2,3,6], Ramon Langen[5]
[1]Institute of Inflammation and Ageing, University of Birmingham, Birmingham, UK. [2]Institute of Metabolism and Systems Research, University of Birmingham, Birmingham, UK. [3]MRC Arthritis Research UK Centre for Musculoskeletal Ageing Research, University of Birmingham, Birmingham, UK. [4]Centre for Endocrinology, Diabetes and Metabolism, Birmingham Health Partners, Birmingham, UK. [5]Department of Respiratory Medicine, NUTRIM School of Nutrition and Translational Research in Metabolism, Faculty of Health, Medicine and Life Sciences, Maastricht University, Maastricht, Netherlands. [6]Institute of Clinical Sciences, University of Birmingham, Birmingham, UK.

Background and objective: Chronic obstructive pulmonary disease (COPD) is associated with skeletal muscle atrophy. Disease progression is accelerated by episodes of acute exacerbation (AE), with increased inflammation levels of glucocorticoids (GCs) as potential triggers for muscle atrophy. 11 beta-hydroxysteroid dehydrogenase 1 (11β-HSD1) activates GCs within muscle and is induced by inflammation. Using animals with a global knock out (KO) of 11β-HSD1, we aimed to delineate the contribution of GC activation by 11β-HSD1 to skeletal muscle atrophy in a model of COPD-AE and assess its potential as a therapeutic target.
Methods: Emphysema was induced by two intra-tracheal (IT) instillations of elastase in WT and global 11β-HSD1 KO animals, followed with a single bolus of IT-LPS or vehicle control (AE). CT scans were obtained to confirm elastase-induced emphysema, and to determine muscle mass changes following LPS. After 48 hours, animals were sacrificed and muscles, serum and lungs collected. Muscle (gastrocnemius) and lung tissue were assessed for anabolic, catabolic (muscle only), inflammatory, and GC-sensitive mRNA and protein expression using RT-qPCR and western blot. ELISA was used to assess IL-6 levels in serum.
Results & conclusion: Muscle wasting was evident in both WT and 11β-HSD1/KO relative to vehicle treated controls in response to LPS. This was characterised by increased expression of atrophy markers FoxO1, Atrogin-1 and Mstn and upregulation of the inflammatory markers CXCL1 and IL-1β in muscle of both groups. Serum IL-6 was significantly increased in LPS treated mice, though no changes were seen in IL-6 expression in muscle.
Severity of muscle wasting was exacerbated in 11β-HSD1/KO animals in response to AE, where muscle weights and CT-derived muscle volumes were significantly lower relative to WT counterparts. This was accompanied by increased expression of MuRF1 in 11β-HSD1/KO relative to WTs in response to LPS.
These findings suggest muscle atrophy in response to pulmonary inflammation is increased in emphysematous 11β-HSD1/KO mice compared to WT controls, highlighting the important role of 11β-HSD1 and GC signalling in skeletal muscle wasting during COPD-AE.

3-01
Low cholinesterase levels at diagnosis of pancreatic cancer are associated with cachexia and pancreatic cancer prognosis

Seiko Miura
Department of General and Digestive Surgery, School of Medicine, Kanazawa Medical University, Uchinada, Ishikawa, Japan

Introduction: The relationship between cachexia and prognosis of pancreatic cancer patients has been unclear. In this study, we aimed to discover new prognostic factors and the effect of cachexia on the survival rates of pancreatic cancer patients. We look into cholinesterase has a half-life of about 10 days, which is the enzyme produced in hepatocytes and rapidly secreted into the blood without being stored and is measured as an index of hepatic protein synthesis.
Methods: A total of 106 pancreatic cancer patients were enrolled. Patients who did not show symptoms of cachexia (77 non-cachexia) at the time of cancer diagnosis had overall longer survival than those who were cachexic (29 cachexia). We selected 30 possible prognostic variables including history, nutritional status, treatment modalities, and clinicopathologic characteristics.
Results: Twelve variables showed statistically significant association with patient survival (univariate analysis) and seemed to be the important prognostic factors. Potentially confounding factors of cachexia were selected by checking the relationship to cachexia, mutual relationships among variables. Ten variables were finally studied by Cox model (multivariate analysis); i.e. albumin, cholinesterase (ChE), C-reactive protein (CRP), total lymphocyte count (TLC), Resection, BSA, clinical stage, gender, age and cachexia. Four prognostically significant variables were found: clinical stage (1.031), TLC (1.787) and ChE (2.764) and Gender (1.833).
Conclusions: Although cachexia was no longer significant after adjusting confounding factors, cachexia alone effects the prognosis of pancreatic cancer patients. TLC and ChE were found to be robust markers for prognostic factors of pancreatic cancer patients. These findings suggest that at the time of diagnosis of pancreatic cancer patients, the presence of cachexia is considered to be a useful prognostic measure. Since ChE is hardly affected by biliary atresia that can occur in pancreatic cancer, it is considered to be useful as an index of nutritional status.

3-02
Metabolic reprogramming drives pancreatic cancer-associated wasting

Katherine R. Pelz[1], Heike Mendez[1], Brennan Olsen[2], Xinxia Zhu[2], Daniel L. Mark[1,2], Aaron J. Grossberg[1,3,4]
[1]Brenden Colson Center for Pancreatic Care; [2]Department of Pediatrics; [3]Department of Radiation Medicine; [4]Cancer Early Detection Advanced Research Center, Oregon Health & Science University, Portland, OR, United States

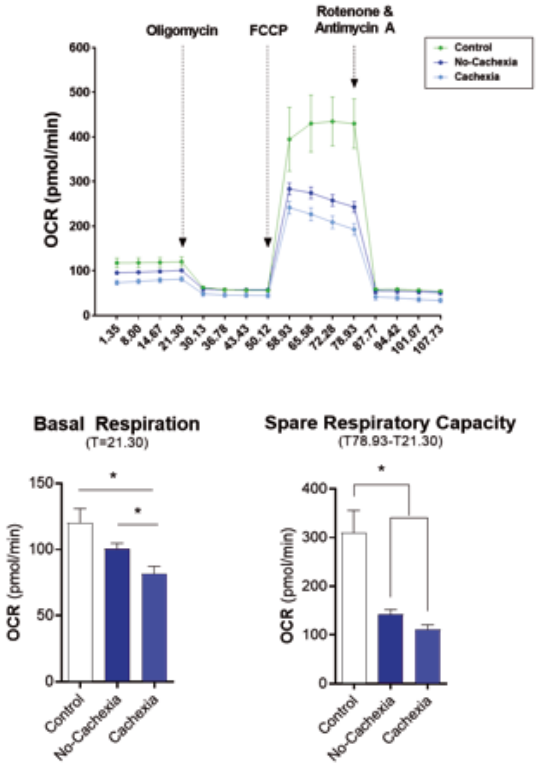
Introduction: Cachexia, defined by muscle and adipose tissue wasting, affects between 50-80% of patients with pancreatic adenocarcinoma (PDAC) and corresponds with decreased quality of life, survival, and ability to tolerate therapeutic interventions. The loss of adipose tissue has been attributed to altered pancreatic exocrine function, suggesting that malabsorption drives cachexia. However, nutritional

interventions cannot fully reverse cachexia and enzyme replacement paradoxically leads to worsened survival in preclinical models. By modifying nutritional challenges at different stages of cachexia development, we sought to understand the relative contributions of undernutrition and metabolic reprogramming to adipose and skeletal muscle wasting.
Methods: Adult C57BL/6J mice received orthotopic PDAC tumor or sham injections. We nutritionally challenged mice using 50% food restriction (FR) or overnight fasting using 2x2 factorial designs. Gonadal adipose and gastrocnemius muscle mass were quantified. Blood glucose and ketones were measured using a point-of-care glucometer and ketometer, respectively. Ketogenic and gluconeogenic potential were evaluated by fasting mice overnight, followed by octanoate (0.2 g/kg) or alanine challenge (2 g/kg), respectively. Liver metabolic gene expression was measured using qPCR. Exocrine pancreatic function was estimated by quantifying fecal protein, fat, and protease activity. Statistical comparisons were performed using *t*-tests and one-way, 2-way, and repeated measures ANOVAs, as appropriate.
Results: Food restricted PDAC mice exhibited no difference in fat mass compared to their sham counterparts, but lost significantly more muscle mass. Fecal lipid, protease, and protein analyses at this timepoint show no evidence of malabsorption. Both our pre-cachectic and cachectic mice show decreased fasting blood glucose and ketones compared to sham, as well as impaired gluconeogenic and ketogenic potential. Expression of genes involved in ketogenesis and gluconeogenesis was decreased in livers of PDAC mice compared to sham.
Conclusions: PDAC increases susceptibility to undernutrition by impairing gluconeogenic and ketogenic capacity, supporting a paraneoplastic etiology for PDAC cachexia.

3-03
The human pancreatic tumor organoid secretome suppresses macrophage mitochondrial respiration without affecting macrophage function

Min Deng, Rianne Vaes, Steven Olde Damink, Sander Rensen
Department of Surgery and NUTRIM School of Nutrition and Translational Research in Metabolism, Maastricht University, Maastricht, The Netherlands

Background: Systemic inflammation induced by tumor-derived factors is considered to play a key role in the pathogenesis of cancer cachexia. Pro-inflammatory immune responses are generally characterized by a metabolic shift from oxidative phosphorylation to aerobic glycolysis, but nothing is known about the potential impact of tumor factors on immunometabolism in the context of cancer cachexia. We hypothesized that tumor factors from cachectic pancreatic cancer patients reduce oxidative phosphorylation in macrophages.
Methods: Pancreatic tumor organoids from cachectic (n=3) and non-cachectic patients (n=3) were incubated with RPMI for 24 hours to generate conditioned medium (CM). Human monocytes were isolated from peripheral blood mononuclear cells by positive selection using magnetic CD14 microbeads and differentiated to macrophages. The macrophages were incubated with RPMI or CM (50% v/v) for 24 hours. We then analyzed mitochondrial respiration using the Agilent Seahorse XF96 extracellular flux analyzer (Seahorse Bioscience). Furthermore, we conducted functional assays, focusing on macrophage apoptosis, lipid uptake, and phagocytosis.
Results: Macrophages exposed to CM from pancreatic tumor organoids showed a reduced commitment to oxidative phosphorylation, as evident from their strongly suppressed basal oxygen consumption rate (91.6±26.9 pmol/min vs. 120.2±21.6 pmol/min for macrophages incubated with control medium, p=0.017). This reduction was comparable to that seen after LPS stimulation (85.8±32.0 pmol/min). In line with this, we observed significantly decreased levels of ATP production in macrophages exposed to organoid CM. Interestingly, the basal oxygen consumption rate of macrophages exposed to CM from organoids established from cachectic vs non-cachectic patients also differed significantly (81.7±29.0 vs. 100.8±21.4 pmol/min). Similar observations were made for the spare respiratory capacity of the macrophages (control: 309.6±92.1 vs. non-cachectic: 142.0±53.7 vs. cachectic: 111.0±51.5 pmol/min) as well as the maximal respiratory capacity. However, initial analyses of the functionality of macrophages that were exposed to CM from cachectic vs. non-cachectic organoids revealed no significant differences.
Conclusion: Factors released by pancreatic tumor organoids from cachectic patients suppress macrophage respiration, but this does not appear to majorly affect key macrophage functions.



Human monocyte-derived macrophages respond to conditioned medium generated from pancreatic tumo organoids of cachectic pancreatic cancer patients as detected by the mitochondria stress test.

3-04
Prevalence and severity of cancer cachexia by BMI-Weight Loss (WL) Grades in advanced stage gastrointestinal and lung cancers: a population–based study

Lisa Martin, Sean Kazemi, Hailey Fedoruk, Quincy Chu, Michael Sawyer, Vickie Baracos
University of Alberta, Edmonton, Canada

Background: Prevalence and severity of cachexia in contemporary cancer patient populations is not known. Our aim was to report real-world population-based BMI and WL data from patients receiving cancer care in Alberta, Canada (population ~4 million).
Method: Population-based data was acquired from provincial electronic medical records and the Alberta Cancer Registry (ACR), certified by the North American Association for Central Cancer Registries. ACR Search criteria included: individuals starting 1st-line palliative chemotherapy for cancers of pancreas, biliary tract, or lung (non-small cell (NSCLC) or small cell (SCLC)) of advanced stage, between 1/1/2013 and

12/31/2017. Data collected: age, sex, diagnosis, stage, height, weight, and BMI (kg/m2). Weight change was calculated from start of systemic therapy. Mortality-based BMI-WL Grades (0-4; Martin et al. J Clin Oncol 2015; 33:90) were applied.
Results: The search identified n=208, n=313, n=534, n=236 consecutive patients with biliary tract, pancreas, NSCLC and SCLC, respectively. A total of 18,067 records (~14/patient) of weight/BMI were evaluated. Overall, BMI at start of systemic therapy was variable (13-50 kg/m2) with a prominent right skew: 3.8% were underweight (BMI<18.5), while 15.1%, 5.9% and 3.8% were obese Class I, II and III, respectively, with little variation by tumor site (P>0.1). Body weight over time showed intra-individual variability. Some patients remined within BMI-WL Grade 0: biliary tract (13.9%ab), pancreas (9.6%a), NSCLC (8.8%a) and SCLC (16.7%b; P=0.003), respectively. By contrast, the proportion (P=0.0004) and median days (P<0.01) to attain BMI-WL Grade 4 differed by tumor site: biliary tract (25.5%b, 182 days [95% CI 96-267]), pancreas (41.2%c; 104 [62-145]), NSCLC (27.5%b; 244 [180-307]) and SCLC (17.2%a, 161 [67-255]), respectively.
Conclusions: Population-based data provide evidence of cachexia prevalence and severity, and this is tumor site specific, with severe and rapidly evolving cachexia in pancreatic cancer, followed by NSCLC, biliary tract cancer and SCLC.

3-05
Inflammation-induced cholestasis in cancer cachexia

Morgane M. Thibaut[1], Martina Sboarina[1], Martin Roumain[2], Sarah A. Pötgens[1], Audrey M. Neyrinck[1], Florence Destrée[1], Justine Gillard[1,3], Isabelle A. Leclercq[3], Guillaume Dachy[4], Jean-Baptiste Demoulin[4], Anne Tailleux[5], Sophie Lestavel[5], Marialetizia Rastelli[1,6], Amandine Everard[1,6], Patrice D. Cani[1,6], Paolo Porporato[7], Audrey Loumaye[8], Jean-Paul Thissen[8], Giulio G. Muccioli[2], Nathalie M. Delzenne[1], Laure B. Bindels[1#]
[1]Metabolism and Nutrition Research Group, Louvain Drug Research Institute, UCLouvain, Université catholique de Louvain, Brussels, Belgium; [2]Bioanalysis and Pharmacology of Bioactive Lipids Research Group, Louvain Drug Research Institute, UCLouvain, Université catholique de Louvain, Brussels, Belgium; [3]Laboratory of Hepato-Gastroenterology, Institut de Recherche Expérimentale et Clinique, UCLouvain, Université catholique de Louvain, Brussels, Belgium; [4]Experimental Medicine Unit, de Duve Institute, UCLouvain, Université catholique de Louvain, Brussels, Belgium; [5]European Genomic Institute for Diabetes (EGID), Univ. Lille, Inserm, CHU Lille, Institut Pasteur de Lille, U1011- EGID, F-59000 Lille, France; [6]Walloon Excellence in Life Sciences and BIOtechnology (WELBIO), Louvain Drug Research Institute, UCLouvain, Université catholique de Louvain, Brussels, Belgium.
[7]Department of Molecular Biotechnology and Health Science, Molecular Biotechnology Center, University of Torino, Torino, Italy; [8]Endocrinology, Diabetology and Nutrition Department, Institut de Recherches Expérimentales et Cliniques, UCLouvain, Université Catholique de Louvain, Cliniques Universitaires Saint-Luc, Brussels, Belgium

Introduction: Cancer cachexia is a debilitating metabolic syndrome contributing to cancer death. Organs other than the muscle may contribute to the pathogenesis of cancer cachexia. This work explores new mechanisms underlying hepatic alterations in cancer cachexia.
Methods: We used transcriptomics to reveal the hepatic gene expression profile in the C26 cachectic mouse model. We performed bile acid, tissue mRNA, histological, biochemical and western blot analyses. Two interventional studies were performed using a neutralizing IL-6 antibody and a bile acid sequestrant, cholestyramine. Our findings were evaluated in a cohort of 94 colorectal cancer patients with or without cachexia (43/51).
Results: In C26 cachectic mice, we discovered alterations in five inflammatory pathways as well as in other pathways, including bile acid, fatty acid and xenobiotic metabolism. The hepatobiliary transport system was deeply impaired in cachectic mice, leading to increased systemic and hepatic bile acid levels, increased hepatic inflammatory cytokines and neutrophil recruitment to the liver of cachectic mice. Adaptive mechanisms were set up to counteract this bile acid accumulation by repressing bile acid synthesis and by enhancing alternative routes of basolateral bile acid efflux. Targeting bile acids using cholestyramine reduced hepatic inflammation, without affecting the hepatobiliary transporters. Reducing IL-6 levels counteracted the change in expression of genes involved in the hepatobiliary transport, bile acid synthesis and inflammation. Serum bile acid levels were increased in cachectic versus non-cachectic cancer patients and were strongly correlated to systemic inflammation.
Conclusion: We show alterations in bile acid metabolism and hepatobiliary secretion in cancer cachexia. In this context, we demonstrate the contribution of systemic inflammation to the impairment of the hepatobiliary transport system, and the role played by bile acids in the hepatic inflammation. This work paves the way to a better understanding of the role of the liver in cancer cachexia.

3-06
Gray and white matter morphology in cachectic colorectal cancer patients: A voxel-based morphometry MRI study.

Estefanía Simoes[1], Joanna Correia-Lima[1], Amanda S Santos[1], Larissa Santana[1], Naomi Antunes[6], Fang Bin[2], José Pinhata[1,3,4], Paulo Sergio Martins de Alcantara[3], Ricardo Uchida[2], Alessandro Laviano[7], Fabio Duran[6], Geraldo Busatto[5,6], Marília Seelaender[1,4,5]
[1]Cancer Metabolism Research Group, University of São Paulo, São Paulo, Brazil; [2]*Santa Casa* de Misericórdia de São Paulo, São Paulo, Brazil; [3]Department of Clinical Surgery, University Hospital, University of São Paulo, São Paulo, Brazil; [4]LIM 26, Hospital das Clínicas of the University of São Paulo, São Paulo, Brazil; [5]*Faculdade de Medicina*, University of São Paulo, São Paulo, Brazil; [6]Neuroimaging Laboratory (LIM-21) - Institute Psychiatry University of São Paulo, São Paulo, Brazil; [7]Department of Clinical Medicine, Sapienza University of Rome, Rome, Italy.

Background: Cancer cachexia is a clinically challenging multifactorial and multiorgan syndrome, characterized by loss of appetite and weight loss, ultimately leading to poor outcome of the disease. Systemic inflammation which characterizes the syndrome leads to central nervous system (CNS) dysregulation and neuroinflammation, with impact on neural circuits controlling feeding behavior and body composition. However, how precisely cachexia affects the morphology and function of the human central nervous system is unknown.
Aim: To evaluate possible alterations of gray and white matter in the CNS (central nervous system) of cachectic patient's comparing with weight-stable counterparts. **Methods**– Patients with colorectal cancer were divided into Weight-Stable Cancer (**WSC**, n=12), and Cachectic Cancer (**CC**, n=10) groups. Structural magnetic resonance imaging (Philips Achieva Scanner 3 Tesla) was performed after signature of the informed consent form. Voxel-based morphometry analyses were carried out with Statistical Parametric Mapping Package (SPM12).
Results: Gray matter (GM) of CC presented significant structural differences when compared with WSC (pFWE: p-value corrected using small volume correction). Cachectic patients showed increased GM in areas related to food intake, satiety and behavior: caudate nucleus (right pFWE=0.048; left pFWE=0.0402), putamen (left pFWE=0.011) and orbitofrontal cortex (right pFWE=0.001; left pFWE=0.005). Also, decreased GM in CC was found in Insula (right pFWE=0.025) and in the temporal gyrus (left pFWE=0.001). Considering

white matter volumes, no significant differences were found between CC and WSC.
Conclusions: The results indicate that cachexia compromises CNS morphology mostly causing changes in GM of cachectic patients, not affecting WM. Cachexia leads to alterations in regional volume patterns, that reflect neuroinflammation and neuronal damage. The described changes in the neuroanatomy may contribute to loss of homeostatic functions and deficient information processing, as well as metabolic and behavioral derangements in human cachexia.

3-07
The Impact of Circulating Tumor Cells on Cancer Cachexia in Small-Cell Lung Cancer

Tateaki Naito, Haruyasu Murakami, Hirotsugu Kenmotsu, Toshiaki TakahashiD
Division of Thoracic Oncology, Shizuoka Cancer Center, Japan

Introduction: The severity of cancer cachexia may associate with the aggressiveness of cancer itself. Enumeration of circulating tumor cells (CTCs) reflects the tumor burden and metastatic potential of small-cell lung cancer (SCLC). This study aimed to explore the relationship between cancer cachexia and CTCs in SCLC.
Methods: In total, 51 patients with newly diagnosed SCLC, starting chemotherapy or chemoradiotherapy, were prospectively enrolled (Trial No. UMIN000003333). CTCs were isolated from the baseline blood samples using the CellSearch System (Veridex LLC). In this post-hoc analysis, we evaluated the presence of cancer cachexia (Fearon K, 2011) and the weight-loss grading system (Martin L, 2013).
Results: Among 29 evaluable patients, 19 (65.5%) had cancer cachexia with a median of cancer cachexia grade 3 (range, 0 to 4). Median CTCs was 4 (range, 0 to 1683) per 7.5ml of blood. The extensive disease showed more CTCs than the limited disease (9 vs. 2, $p<0.05$). There is no difference in CTCs between cachectic and non-cachectic patients (5 vs. 3, $p=0.75$). CTCs did not correlate to weight-loss grade (Spearman rho=0.04, $p=0.86$).
Conclusions: CTCs has no impacts on either presence or severity of cancer cachexia. The metastatic potential of SCLC may not be the determinant of cancer cachexia.

3-08
SARC-F Questionnaire score is Associated with Mortality of Cancer Patients Receiving Palliative Care

Naoharu Mori[1,2], Keisuke Maeda[1,3], Yuria Ishida[1,2], Tomoyuki Nonogaki[1,4], Akio Shimizu[1,5], Yosuke Yamanaka[6], Remi Matsuyama[6], Ryoko Kato[1,4], Junko Ueshima[1,7]
[1]Department of Palliative and Supportive Medicine, Graduate School of Medicine, Aichi Medical University; [2]Department of Nutrition, Aichi Medical University Hospital; [3]Department of Geriatric Medicine, National Center for Geriatrics and Gerontology; [4]Department of Pharmacy, Aichi Medical University Hospital; [5]Department of Nutrition, Hamamatsu City Rehabilitation Hospital; [6]Department of Oral and Maxillofacial Surgery, Graduate School of Medicine, Aichi Medical University; [7]Department of Clinical Nutrition and Food Service, NTT Medical Center Tokyo

Background: Predicting life expectancy is essential for cancer patients receiving palliative care. Sarcopenia is associated with their prognosis, but the relationship between mortality and the Simple Questionnaire to Rapidly Diagnose Sarcopenia (SARC-F) score is unclear. We investigated the prognostic efficacy of SARC-F in cancer patients receiving palliative care.
Methods: The subjects comprised adult solid cancer patients receiving palliative care from May 2019 to April 2020. We retrospectively analyzed biochemical laboratory findings (serum albumin [Alb]) and C-reactive protein [CRP]), edema status, hand grip strength (HGS), leg circumference (CC), and SARC-F score, routinely recorded at admission. Cox's proportional hazards model was used to estimate the median mortality hazard ratio (HR) of each finding.
Results: Of the 304 patients (28.6% male, median age 68 yrs.), median survival was 96 (range 72-127, 95% CI) days. Univariate analysis found mortality correlated with Alb (HR 0.517, range 0.423–0.634, 95% CI, $p<0.001$), CRP (1.069 1.047–1.092, 95% CI, $p= p<0.001$) , edema (1.365 1.218–1.530, 95% CI, $p<0.001$) , HGS (0.969 0.953–0.985, 95% CI, $p<0.001$) , CC (0.964 0.933–0.997, 95% CI, $p= 0.034$) and SARC-F score (1.158 1.108–1.210, 95% CI, $p<0.001$). Multivariate analysis adjusted for age and sex found SARC-F score (HR 1.120, range 1.053– 1.191, 95% CI, $p<0.001$), CRP (1.042 1.010–1.074, 95% CI, $p=0.010$) and edema (1.427, 1.199–1.697, 95% CI, $p<0.001$), independently predicted survival duration.
Conclusions: Along with prognostic factors CRP and edema, SARC-F score was associated with mortality in patients with advanced cancer. As a minimally invasive clinical measure, SARC-F is considered a useful predictor of prognosis for cancer patients in palliative care.

3-09
Growth differentiation factor 11 (GDF11) is not a key regulator of cancer cachexia

Brianna LaCarubba, Susie Collins, Aaron D Antona, Joe Palandra, Greg Weber, Zhidan Wu, Bei Zhang, Ja Young Kim-Muller, Danna Breen
Pfizer, Amesbury, USA

Introduction: GDF11 is a member of the transforming growth factor β superfamily of cytokines and induces signaling through the activin type 2 (ActRII) receptor to regulate muscle mass. Supraphysiological levels of GDF11 have been reported to decrease food intake in preclinical models by elevating growth differentiation factor 15 (GDF15) a cytokine associated with cachexia in cancer patients. It is unknown however if GDF11 plays a role in cancer cachexia. Therefore, we examined whether circulating GDF11 and GDF15 levels were associated with weight loss in non-small-cell lung carcinoma (NSCLC) patients and in preclinical cachexia models.
Methods: GDF11 concentrations from plasma of NSCLC patients and preclinical cachexia models were measured using a novel immunoaffinity LC-MS/MS assay. GDF15 levels were measured using ELISA.
Results: In NSCLC patients, the circulating GDF11 concentration was similar between patients that lost body weight (WL) (> 5% WL (n = 125); 0-5% WL (n = 116)) and those that were weight stable and/or gained weight (WS) (n = 86) (~0.5 ng/mL in all groups) during chemotherapy treatment. GDF11 was not associated with weight loss (p = 0.45, >5% WL vs WS). In contrast, circulating GDF15 was higher in patients that experienced weight loss (> 5% WL: 3.2 ng/mL; 0-5% WL: 2.3 ng/mL; WS: 2.1 ng/mL) and was associated with weight loss (p = 0.005, >5% WL vs WS). In cachectic mouse tumor models reported to be GDF15-dependent (human fibrosarcoma (HT-1080); mouse renal cell carcinoma (RENCA)), we confirmed a weight loss phenotype and a robust elevation of plasma GDF15 (HT-1080: ~ 3 ng/mL; RENCA: ~ 5 ng/mL). GDF11 was unchanged in both models (non-tumor-bearing: ~0.5 ng/mL; tumor-bearing: ~0.4 ng/mL).
Conclusions: These data suggest that GDF11 is not a key regulator of cancer cachexia and add to the growing body of evidence supporting an important role of GDF15.

3-10
Oxytocin, the neurohypophyseal hormone has an anticachectic potential

Alexandra Benoni[1,2]; Medhi Hassani[1,2]; Viviana Moresi[1]; Zhenlin Li[2]; Onnik Agbulut[2]; Dario Coletti[1,2]; Zhigang Xue[2]; Sergio Adamo[1]
[1]DAHFMO Unit of Histology and Medical Embryology, and Interuniversity Institute of Myology, Sapienza University of Rome, Italy; [2]Dept. Of Biological Adaptation and Ageing B2A (CNRS UMR 8256 - INSERM ERL U1164 - UPMC P6), Sorbonne University, France

Introduction: Oxytocin (OT) affects the CNS, the uterus and the mammary gland; only lately, OT was also shown to promote myogenic differentiation, thus affecting skeletal muscle cells. OT levels decrease with aging and its exogenous administration counteracts sarcopenia in aged mice. Several pharmacological and hormonal treatments are currently proposed against cancer cachexia, with, for instance, Anamorelin currently in phase III-clinical trial. However, to date, the cachexia syndrome remains incurable.
Methods: We exploited an *in vitro* model, based on L6 myoblast cell cultures exposed to C26 tumor-conditioned medium (C26-CM). *In vivo*, a fragment of C26 tumor was grafted to 8 weeks of age male BALB/C mice. A regeneration assay was performed by freeze injury on the *Tibialis anterioris* in mice, followed by treatments with either OT, TNF or both by intramuscular injection. Gastrocnemius muscle and myogenic cells were analyzed by morphometric/morphologic and molecular analyses.
Results: We observed an inhibition of differentiation by the C26-CM, reversed by the addition of OT. We observed *in vivo,* in C26-tumor-bearing mice, that daily OT injections counteract the C26-dependent skeletal muscle wasting in skeletal muscle. We observed a rescue of skeletal mass, muscle fiber cross-sectional area and markers of protein catabolism, resulting in a recovery of the body weight of the animals. OT accelerated muscle regeneration following focal injury, a process that was inhibited by the pro-inflammatory cytokine TNF, used to mimic the pro-cachectic environment.
Conclusions: Since hampered muscle regeneration and satellite cell function are important phenomena contributing to muscle wasting in cachexia, our data indicate that OT treatment positively affects myogenic cultures as well as muscle homeostasis in tumor bearing mice, fully reverting muscle atrophy. Since OT is authorized for clinical use, these results could readily be translated into effective clinical practice to prevent and/or treat cachexia in cancer patients.

3-11
Role of miR-223-3p in cancer cachexia

Lorena Garcia-Castillo[1], Marc Beltrà[1], Fabrizio Pin[1], Giovanni Birolo[2,3], Barbara Pardini[2,3], Giuseppe Matullo[2,3], Fabio Penna[1] and Paola Costelli[1]
[1]Department of Clinical and Biological Sciences, University of Turin, Italy; [2]Italian Institute for Genomic Medicine, IIGM (formerly Human Genetics Foundation, HuGeF), Turin, Italy; [3]Department of Medical Sciences, University of Turin, Turin, Italy

Cancer cachexia is a multifactorial syndrome characterized by anorexia and body weight loss, mainly due to muscle and fat wasting. MicroRNAs (miRNAs) are a class of non-coding post-transcriptional regulators that play, among other functions, a central role in myogenic progenitor commitment, proliferation and differentiation by inhibiting the translation of specific genes. There is strong evidence that miRNAs would function as an effective system that regulates muscle protein degradation system but their role in cachexia remains unclear. The aim of the present study was to perform a miRNA profiling in the skeletal muscle of mice bearing the C26 tumor, characterized by progressive skeletal muscle wasting. sRNA-Seq data revealed that miRNA expression is dysregulated in the skeletal muscle of C26-bearing animals. Some miRNAs were statistically upregulated in the tumor-bearing mice (miR-21a-5p, miR-29a-3p, miR-29c-3p, miR-223-3p). Gene ontology analysis highlighted miR-223-3p as a central regulator of muscle homeostasis since it targets genes involved in both muscle development and muscle wasting, including Mef2c and Foxo3. MiR223-3p is upregulated in early stages of muscle regeneration after injury but its role in cancer cachexia is still unknown. To clarify this point, miR-223-3p was overexpressed in the skeletal muscle of healthy and C26-bearing animals. Briefly, a plasmid coding for miR-223-3p was locally transfected by means of *in vivo* electroporation in the *tibialis anterior* (TA) muscle. The contralateral TA was transfected with a plasmid encoding for a scrambled sequence and used as control. Plasmid transfection was successful as GFP+ myofibers were observed throughout the muscle. The overexpression of miR-223-3p plasmid did not rescue *tibialis anterior* weight loss in tumor-bearing mice.
Further analysis must be performed to better understand the local effect of miR-223-3p overexpression, such as GFP+ myofiber cross-sectional area (CSA) assessment and gene expression of some pathways related to proteolytic systems and muscle regeneration.

3-12
RNA Bio-profiling Studies from Human Skeletal Muscle Biopsies in Cancer Cachexia Research: an update

Bhumi Bhatt[1], Sunita Ghosh[2], Vera Mazurak[3], Vickie E. Baracos[2] and Sambasivarao Damaraju[1]
[1]Department of Laboratory Medicine and Pathology, [2]Department of Oncology, [3]Division of Human Nutrition, University of Alberta, Edmonton, Alberta

Background: Cancer-associated muscle wasting is associated with poor clinical outcomes. Bio-profiling studies using human skeletal muscle (HSM) biopsies are limited and a comprehensive review of literature in this area may potentially identify the gaps and help design studies towards an understanding of the molecular mechanisms of cancer cachexia (CC).
Methods: A Scopus web search was conducted from 1976-2020 using cachexia, sarcopenia (defined by low Skeletal Muscle Index), myosteatosis (low Skeletal Muscle Radiodensity), and related search terms. 5582 research articles were retrieved and excluded for non-cancer related, and non-HSM biopsy studies leaving 74 original articles of interest.
Results and conclusions: 35 of 74 studies were on bio-profiling (transcriptomic, proteomics, metabolomics) and morphology of skeletal muscle in cachexic cancer patients compared with either non-cachexic cancer patients or healthy controls. Variations in CC classifications e.g., weight loss, sarcopenia, myosteatosis, and/or international consensus diagnostic criteria were identified. Low sample size, heterogeneous cancer types, stratifications on weight loss alone, or comparisons with reference to healthy controls were evident. 10 of 35 were whole transcriptome or proteomic profiles (hypothesis generating studies) and the remaining (n=25) utilized candidate gene or protein biomarker approaches (hypothesis testing studies) to validate the biomarkers identified in rodent models. However, these approaches may not capture the complex interplay of biomolecules in CC. Only two studies were on miRNAs, and none addressed other small non-coding or long non-coding (lnc) RNAs. Expression analysis was based on aggregated samples and sex-related differences were not accounted.
Future directions: Integrative analysis of mRNA/splice variants, miRNAs, snoRNAs, tRNAs, piRNAs, and lncRNAs (RNAome) may identify complex regulatory networks, pathways and post-transcriptional mechanisms underlying the pathophysiology of CC. Establishing a common pipeline for analysis of sequencing datasets and analysis accounting for clinical characteristics, and body composition may offer

comprehensive insights into the molecular mechanisms of CC.

3-13
C-reactive protein and its relationship with pain in advanced cancer cachexia

Koji Amano
Department of Palliative Medicine, National Cancer Center Hospital, Chuo-ku, Tokyo 104-0045, Japan

Introduction: To investigate relationships between serum levels of C-reactive protein (CRP) and subtypes of pain in patients with advanced cancer cachexia.
Methods: This study involved a secondary analysis of a multicenter prospective cohort study conducted in 23 palliative care units across Japan. Patients rated the severity of pain on the Numerical Rating Scale (NRS) and physicians evaluated pain on the Integrated Palliative care Outcome Scale (IPOS). Physicians assessed neuropathic pain and breakthrough pain based on their presence or absence. Patients were divided into four groups according to CRP levels: low (CRP < 1 mg/dl), moderate (1 ≤ CRP < 5 mg/dl), high (5 ≤ CRP < 10 mg/dl), and very high (10 mg/dl ≤ CRP). Comparisons were performed using the Kruskal-Wallis test or chi-squared test. To evaluate the relationship between CRP, pain NRS, pain IPOS, neuropathic pain, and breakthrough pain, adjusted odds ratios (ORs) and 95% confidence intervals (CIs) in the logistic models were calculated.
Results: A total of 1513 patients were divided into the four groups: low (n = 234), moderate (n = 513), high (n = 352), and very high (n = 414). Spearman's correlation coefficient between pain NRS and pain IPOS was 0.66 ($p < 0.001$). Spearman's correlation coefficients between CRP, pain NRS, and pain IPOS were 0.15 ($p < 0.001$) and 0.16 ($p < 0.001$), respectively. In the models of pain NRS and pain IPOS, significantly higher adjusted ORs than in the low CRP group were observed in the very high CRP group (1.81 [95% CI 1.14-2.88], P = 0.01; 1.74 [95% CI 1.18-2.57], P = 0.005, respectively). There were no relationships between CRP, neuropathic pain, and breakthrough pain.
Conclusion: This study indicated the relationships between CRP, pain NRS, and pain IPOS. However, the results did not demonstrate a causal relationship among them.

3-14
Assessment of Nutritional Status on hospital admission, a Portuguese oncology center study

Carolina Trabulo[1,2]; Joanna Lopes[1]; David Dias[2,3]; Joao Gramaça[1]; Idilia Pina[1]; Paula Ravasco[2,4]
[1]Hospital Center Barreiro-Montijo, Lisbon, Portugal; [2]Center for Interdisciplinar Research in Health, Universidade Católica Portuguesa; [3]Hospital Universitário Algarve, Portugal; [4]Hospital Universitário de Santa Maria, CHULN & Universidade de Lisboa, Portugal

Background: Malnutrition is a substantial predictor of reduced survival, as well as quality of life, increased frequency of hospital readmission and length of stay. The nutritional status of the oncology patients has a determining role in the evolution of the disease, allowing to signal those in need of nutritional intervention. The aim of the present study was to stratify the nutritional risk in an oncology unit through the application of the Patient Generated Subjective Global Assessment score (PG-SGA), designed and validated for oncology patients.
Methods: Observational study of 601 cancer patients, assessed during admission to an Oncology Unit (OU) in the period from November 2016 to February 2020. All patients were considered eligible for inclusion, except non-collaborating and/ or comatose. The nutritional status was assessed using PG-SGA.
Results: A total of 561 patients admitted to the OU where assessed, with an average age of 65 ± 13 years, 54% of whom were female. 83% had a score> 9, with a critical need for nutritional support. More than half of the sample had some degree of malnutrition: 75,8% moderate and 12,7% severe.
Conclusion: The scored PG-SGA is an easy tool used determine nutrition assessment that allows quick identification and prioritization of malnutrition in hospitalized patients with cancer.

3-15
Tumor-derived PTHrP in patients with cachexia

Tanja Krauss[1], Simone Heisz[1], Claudine Seeliger[1], Olga Prokopchuk[2], Klaus-Peter Janssen[2], Marc E. Martignoni[2], Melina Claussnitzer[3], and Hans Hauner[1]
[1]Else Kroener-Fresenius-Center of Nutritional Medicine, School of Life Sciences, Technical University of Munich, 85354 Freising, Germany; [2]Department of Surgery, Klinikum rechts der Isar, Technical University of Munich, Munich, Germany; [3]Broad Institute of MIT and Harvard, Cambrige, MA 02142, USA

Background: Cancer cachexia is characterized by an ongoing loss of skeletal muscle mass with or without loss of fat mass in patients with cancer. The metabolic alterations and inflammation contribute to adipose tissue wasting. There is evidence that white adipose tissue may undergo a browning process, resulting in lipid mobilization and energy expenditure by increased thermogenesis. Tumor-derived PTHrP seems to be a key molecule playing multiple roles in cachexia, from fat "browning" to a possible therapeutic target.
Methods: To identify potential therapeutic targets, we built a biobank (blood, liver tissue, muscle tissue and fat tissue) in cooperation with the Surgical Clinic and Polyclinic of the "Klinikum rechts der Isar". In this cancer cachexia study, plasma PTHrP, clinical parameters and routine blood values were measured by ELISA in patients with benign and malign diseases of the gastrointestinal tract.
Results: Ninety-two patients with cancerous diseases and 18 control patients were included in the study. Plasma PTHrP levels were associated with significantly higher levels of leucocytes and thrombocytes ($p < 0.05$). Additionally, patients with higher PTHrP levels exhibited a decrease in values of the liver enzymes gamma-glutamyl transferase (GGT), glutamic pyruvate transaminase (GPT) and glutamic oxaloacetic transaminase (GOT) ($p < 0.05$). There were no significant differences between patients with and without cancer or cancer cachexia.
Conclusion: This data show a negative relationship between plasma concentrations of PTHrP and liver enzymes. Plasma PTHrP levels did not predict cancer-associated weight-loss in this heterogeneous, diverse cohort. These findings suggest further investigation about the role of PTHrP in circulatory regulation and its potential therapeutic applications.

3-16

Circulating lipids are defining features of murine and human cancer cachexia

J Zuber[1,2,3*], P Morigny[1,2,3*], M Haid[4], M Seelaender[5], M Berriel Diaz[1,2,3*], M Rohm[1,2,3*]
[1]Institute for Diabetes and Cancer, Helmholtz Center Munich, Neuherberg, Germany, [2]Joint Heidelberg-IDC Translational Diabetes Program, Inner Medicine 1, Heidelberg University Hospital, Heidelberg, Germany, [3]German Center for Diabetes Research (DZD), Neuherberg, Germany, [4]Research Unit Molecular Endocrinology and Metabolism, Helmholtz Center Munich, German Research Center for Environmental Health, Neuherberg, Germany, [5]Cancer Metabolism Research Group, LIM 26 HC, Medical School, University of São Paulo, São Paulo, Brazil

Introduction: Cancer cachexia (CCx) is a multifactorial, energy-wasting syndrome reducing the efficiency of anti-cancer therapies and survival of cancer patients. To find novel therapies, previous studies focused on the identification of tumor and host-derived proteins involved in tissue wasting. However, there is still a lack of studies addressing the changes in bioactive lipids in CCx. The aim of this study was to identify specific lipid species as hallmark of CCx by performing a broad range lipid analysis of plasma from well-established CCx mouse models, and cachectic and weight stable cancer patients.
Methods: Plasma from non-cachectic, pre-cachectic and cachectic mice, and weight stable and cachectic cancer patients, was analyzed using the Lipidyzer™ platform. We quantified 13 lipid classes and over 1100 individual lipid species.
Results: We found a decrease in several lysophosphatidylcholine (LPC) species and an increase in numerous sphingolipids as mutual features of CCx in mice and cancer patients. Notably, sphingolipid levels gradually increased during cachexia development, suggesting they might be potential biomarkers. Additionally, correlations between specific lipid species and readouts of CCx were performed. LPC(16:1), LPC(20:3), SM(16:0), SM(24:1), CER(16:0), CER(24:1), HCER(16:0), and HCER(24:1) were the most consistently affected lipid species between mice and humans, and correlated negatively (LPCs) or positively (SMs, CERs and HCERs) with the severity of body weight loss. Moreover, the study describes a mechanistic insight into ceramide metabolism in cachexia, as we identified liver ceramide synthesis pathways as the likely origin of elevated circulating ceramides in wasting.
Conclusion: High levels of sphingolipids are a defining feature of murine and human CCx and may contribute to tissue wasting through the inhibition of anabolic signals. The progressive increase in sphingolipids during cachexia development supports their potential as early biomarkers. Thus, this study may pave the way for future research on lipids as biomarkers and mediators of CCx [1].

4-02
The validity of SARC-F on screening sarcopenia defined by AWGS 2019 in hospitalized older adults

Keisuke Maeda[1,2], Yuria Ishida[3], Tomoyuki Nonogaki[4], Akio Shimizu[5], Yosuke Yamanaka[6], Remi Matsuyama[6], Ryoko Kato[4], Junko Ueshima[7], Kenta Murotani[8] and Naoharu Mori[2]
[1]Department of Geriatric Medicine, National Center for Geriatrics and Gerontology; [2]Department of Palliative and Supportive Medicine, Graduate School of Medicine, Aichi Medical University; [3]Department of Nutrition, Aichi Medical University Hospital; [4]Department of Pharmacy, Aichi Medical University Hospital; [5]Department of Nutrition, Hamamatsu City Rehabilitation Hospital; [6]Department of Oral and Maxillofacial Surgery, Graduate School of Medicine, Aichi Medical University; [7]Department of Clinical Nutrition and Food Service, NTT Medical Center Tokyo; [8]Biostatistics Center, Kurume University

Introduction: The importance of early detection of sarcopenia in older adults has been proposed. However, the validity of the SARC-F screening tool for sarcopenia detection in older adult in-patients has not been investigated. In this study, we aimed to examine the accuracy of the SARC-F≥4 for detecting sarcopenia when administered at hospital admission.
Methods: This cross-sectional, retrospective study enrolled hospitalized older adults (age ≥65 years) who underwent a nutritional assessment by the nutrition support team during their hospitalization. The SARC-F was recorded at the time of admission. The criteria proposed by the Asia Working Group for Sarcopenia in 2019 were applied to diagnose sarcopenia and possible sarcopenia. Appendicular muscle mass was estimated using validated equations and three different models for sarcopenia diagnosis. Sensitivity, specificity, and positive/negative likelihood ratios were calculated to determine the accuracy of the SARC-F≥4 for sarcopenia detection. Receiver-operating characteristic analyses were performed to calculate the area under the curve (AUC).
Results: We enrolled 1,689 patients (mean age: 77.2±7.3 years; male: 54.4%) in this study, of which, 636 (37.7%) exhibited SARC-F≥4. Patients with SARC-F≥4 had a significantly higher prevalence of sarcopenia than those with SARC-F <4 (65.4–78.9% vs. 40.9–45.2%, p<0.001). Sensitivity, specificity, and positive/negative likelihood ratios of SARC-F≥4 for sarcopenia were 49.1–51.3%, 73.9–81.2%, and 1.88–2.72/0.60–0.69 and those for possible sarcopenia were 48.0%, 84.5%, and 3.11/0.62, respectively. The AUC for sarcopenia and possible sarcopenia was 0.644–0.695 and 0.708, respectively. The AUC of SARC-F for possible sarcopenia was equivalent to or larger than that for sarcopenia (DeLong test p=0.438, 0.088, and <0.001 vs. the three models)
Conclusions: SARC-F≥4 is a suitable screening tool for sarcopenia in hospitalized older adults. SARC-F assessment could facilitate the detection and exclusion of sarcopenia at hospitalization and may lead to early adoption of a therapeutic and preventive approach.

4-03
Comparison of diagnostic performance of SARC-F and its two modified versions (SARC-CalF and SARC-F+EBM) in community-dwelling older adults from Poland using two sets of diagnostic criteria of sarcopenia developed by The European Working Group on Sarcopenia in Older People (EWGSOP1 and EWGSOP2)

Roma Krzymińska-Siemaszko[1], Ewa Deskur-Śmielecka[1], Aleksandra Kaluźniak-Szymanowska[1], Marta Lewandowicz[1], Katarzyna Wieczorowska-Tobis[1]
[1]Laboratory of Geriatric Medicine, Department of Palliative Medicine, Poznan University of Medical Sciences

Introduction: The most popular screening tool for sarcopenia diagnosis is the SARC-F questionnaire. As its sensitivity is unsatisfactory, two modified versions of the questionnaire have been published: SARC-CalF (including calf circumference as an additional item) and SARC-F+EBM (assessing additionally age and Body Mass Index). The aim of the analysis was to compare the performance of SARC-F, SARC-CalF, and SARC-F+EBM questionnaires against two reference standards of sarcopenia diagnosis -EWGSOP1 and EWGSOP2 criteria.
Methods: We performed the sensitivity/specificity analysis and compared the overall diagnostic accuracy of SARC-F, SARC-CalF(33/34cm)[cut-off points: 33cm for women (W) and 34cm for men (M)], and SARC-F+EBM in 160 community-dwelling volunteers aged ≥60 yrs from Poland (W:55.6%). According to the EWGSOP1 criteria, sarcopenia was defined as low muscle mass (LMM) [ALM index and Polish cut off points: ≤7.4kg/m^2(M) and ≤5.6kg/m^2(W)] combined with low muscle strength (LMS) [handgrip strength (HGS)<30 kg(M) and <20 kg(W)] or low physical performance (LPP) (gait speed ≤0.8m/s). According to the EWGSOP2 criteria, sarcopenia was defined as LMS [HGS<27kg(M) and <16kg(W), and/or chair stand test (CST)>15s] combined with LMM [ALM index ≤7.0kg/m^2(M) and ≤5.5 kg/m^2(W)].
Results: Depending on the version of the SARC-F questionnaire used, from 18.8% (SARC-F) to 29.4% (SARC-F+EBM) subjects were identified as having a risk of sarcopenia. Sarcopenia was identified in 20.6% by the EWGSOP1 criteria and in 11.3% by the EWGSOP2 criteria. With respect to the two reference standards used, the sensitivity of SARC-F, SARC-CalF(33/34cm), and SARC-F+EBM ranged 33.3–50.0%, 60.6–72.2%, 57.6-72.2%, respectively. The specificity ranged 85.0–85.2%, 86.6–90.6%, 76.1–78.0%, respectively. The AUC of SARC-F, SARC-CalF(33/34cm) and SARC-F+EBM ranged 0.652–0.711, 0.796–0.829, 0.771–0.803, respectively.

Conclusions: The modified versions of SARC-F have better diagnostic performance as compared to the original questionnaire. The SARC-CalF(33/34cm) seems to be the best screening tool for sarcopenia in community-dwelling older adults.

4-04

Clinimetric properties of the newly developed short form Sarcopenia Quality of Life (SF-SarQoL®) questionnaire

Anton Geerinck[1], Charlotte Beaudart[1], Jean-Yves Reginster[1,2], Médéa Locquet[1], Christian Monseur[3], Sophie Gillain[4], Olivier Bruyère[1]

[1]Division of Public Health, Epidemiology and Health Economics, World Health Organization Collaborating Center for Public Health aspects of musculoskeletal health and ageing, University of Liège, Belgium; [2]Chair for Biomarkers of Chronic Diseases, Biochemistry Department, College of Science, King Saud University, Riyadh, KSA, Saudi Arabia; [3]Department of Education Sciences, University of Liège, Liège, Belgium; [4]Geriatrics Department, University Hospital of Liège, Liège, Belgium

Introduction: A short version of the Sarcopenia Quality of Life (SarQoL®) questionnaire has recently been developed, reducing the number of items from 55 to 14, significantly easing response burden. To support the evaluation of quality of life in sarcopenia and the use of the SF-SarQoL® in clinical studies, we investigated its clinimetric properties

Methods: The SF-SarQoL®, EQ-5D and the original SarQoL® questionnaire were administered via a postal-based survey to a sample of older, community-dwelling people who had previously participated in the SarcoPhAge study, a Belgian cohort. Two weeks later, they completed the SF-SarQoL® a second time. Sarcopenia was diagnosed in a clinical setting according to the EWGSOP2 criteria. We investigated the discriminative power, internal consistency, criterion and construct validity, test-retest reliability and factor structure.

Results: A total of 214 people, with a median age of 76 (73-81) years old and mostly female (63.1%), participated. Excellent discriminative power was found between people with low (n=70) and normal grip strength (n=143) [33.33 (20.25-41.35) vs. 47.44 (29.49-69.44); p<0.001] and between sarcopenic (n=21) and non-sarcopenic individuals (n=193) [34.62 (16.03-42.95) vs. 41.03 (27.78-62.82); p=0.043]. Internal consistency was high (α=0.915 and ω=0.917) indicating that the SF-SarQoL® is homogeneous. A very strong correlation between the short and long versions of the SarQoL®, at ICC=0.837 (0.791-0.873), confirmed criterion validity. We also found strong correlations with the EQ-5D index score (r=0.664; p<0.001) and the EQ-VAS (r=0.699; p<0.001), reinforcing the construct validity claim. Test-retest reliability, calculated among 133 participants, was high with an ICC of 0.910 (0.842-0.944). A confirmatory factor analysis confirmed a one-dimensional model (CFI = 1.000; TLI = 1.008; RMSEA < 0.001; SRMR = 0.050).

Conclusions: The 14-item short form of the SarQoL® questionnaire is a valid and reliable tool, and could be used to measure quality of life in sarcopenia in epidemiological studies and clinical trials.

4-05

Consequence of SARC-CalF on SARC-F's screening sensitivity and specificity among community-dwelling older adults: a systematic review

Rômulo Roosevelt da Silva Filho[1], Aline de Bastos Ferreira[1], Erika Aparecida Silveira[1]

[1]Medicine Faculty, Post-Graduation Program in Health Sciences, Universidade Federal de Goiás.

Introduction: Recent studies suggest SARC-F+calf circumference (SARC-CalF) could enhance sarcopenia screening accuracy, compared to solely SARC-F. We aimed to analyze the scientific evidence assessing the effect of SARC-CalF on SARC-F's sensitivity and specificity in community-dwelling elders.

Methods: Systematic review of cross-sectional studies, conducted according to PRISMA guidelines. PubMed and Scielo databases were consulted. Sensitivity and specificity of SARC-F and SARC-CalF were established towards sarcopenia diagnosis according to the revised European Consensus (EWGSOP2). The search strategy applied was: SARC-F AND (SARC-CalF OR "calf circumference" OR calf) AND (diagnosis OR screening OR risk OR sensitivity OR specificity) AND (community-dwelling OR non-institutionalized OR community OR dwelling) AND (EWGSOP2 OR "revised European Consensus"). Inclusion criteria: cross-sectional studies; SARC-F and SARC-CalF screening; EWGSOP2 diagnosis of sarcopenia; adults ≥ 60 years. Exclusion criteria: nursing home residents; hospitalized.

Results: We found three studies. Two of them were conducted with Polish elderly of both sexes, ≥ 65 years. One study was conducted with Brazilian female-only subjects ≥ 60 years. Low calf circumference and SARC-F risk score were determined either by standardized or validated cut-offs. Analyzing those three studies, the prevalence of overall sarcopenia ranged from 13.9% to 17.0%; from 2,1% to 15,2% in women and from 14.7% to 23.8% in men. Sensitivity of SARC-F ranged from 0.0 to 41.2 and specificity ranged from 85.9 to 95.4. For SARC-CalF, sensitivity ranged from 37.5 to 83.3 and specificity ranged from 79.0 to 93.9. SARC-CalF didn't significantly alter sensitivity and specificity of SARC-F in two studies. In the female-only study, SARC-CalF enhanced sensitivity (0.0 to 83.3 [95%CI: 53.5-100.0]), but decreased specificity (95.4 [95%CI: 92.9-97.8] to 79.0 [95%CI: 74.3-83.8]). **Conclusion:** Based on EWGSOP2 criteria, SARC-CalF does not enhance SARC-F's sensitivity or specificity. However, there is evidence suggesting SARC-CalF could enhance sensibility and decrease specificity among aged women.

4-06

Establishing a hierarchy of importance for different aspects of quality of life in sarcopenia from a patient perspective, a best-worst scaling survey.

Anton Geerinck[1], Médéa Locquet[1], Mickael Hilligsmann[2], Jean-Yves Reginster[1,3], Olivier Bruyère[1], Charlotte Beaudart[1]

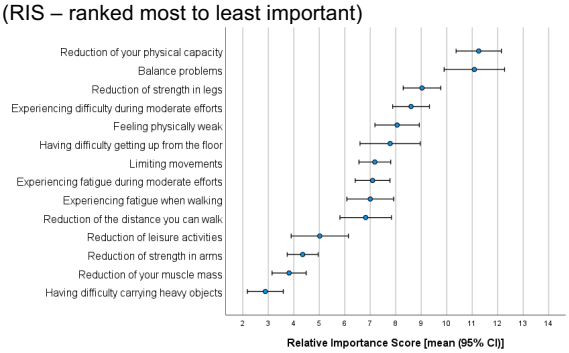
[1]Division of Public Health, Epidemiology and Health Economics, World Health Organization Collaborating Center for Public Health aspects of musculoskeletal health and ageing, University of Liège, Belgium; [2]Department of Health Services Research, University of Maastricht, The Netherlands; [3]Chair for Biomarkers of Chronic Diseases, Biochemistry Department, College of Science, King Saud University, Riyadh, KSA, Saudi Arabia.

Introduction: Information on the quality of life (QOL) of sarcopenic individuals is slowly accumulating. However, our understanding of what patients find the most and least important with regards to QOL in sarcopenia is still in its infancy. We therefore sought to establish an importance hierarchy among 14 aspects of QOL in sarcopenia using a best-worst scaling (BWS) approach, facilitating a more nuanced, item-based, interpretation of future results.

Methods: The 14 items in the short form Sarcopenia Quality of Life (SF-SarQoL®) questionnaire were used to design 24 choice tasks of 4 items each. Participants indicated the most and least important item for a set of 12 choice tasks. The BWS survey was distributed by post to a sample of older, community-dwelling people who had previously participated in the Belgian SarcoPhAge cohort. Relative importance scores (RIS) were estimated using the Hierarchical Bayes method, and were rescaled so that the sum of all RIS was 100.

Results: In total, 163 people were included in the analysis. Participants had a median age of 75 (73-81) years old, and

most were women (n=107 – 65.6%). The 3 most important items were: “feeling a reduction of your physical capacity” (RIS=11.26), “having problems with balance” (RIS=11.09) and “feeling a reduction of the strength in your legs” (RIS=9.03). The 3 least important items were: “feeling a reduction of the strength in your arms” (RIS=4.35), “feeling a reduction of your muscle mass” (RIS=3.82) and “having difficulty carrying heavy objects” (RIS=2.89). The complete hierarchy of importance is presented in figure 1.
Conclusion: This is the first study to report a hierarchy of importance of QOL aspects in sarcopenia, and shows that some aspects are more important than others. These results might help bypass the focus on summary scores and inform a weighted approach to changes in QoL measured with the SF-SarQoL®.
Figure 1: Hierarchy of the 14 aspects of QOL in sarcopenia (RIS – ranked most to least important)



4-07
Screening for the risk of sarcopenia in hospitalized individuals

Mara Rubia Areco Cristaldo[1], Valdete Regina Guandalini[2], Sheilla de Oliveira Faria[3], Maria Claudia Bernardes Spexoto[4]
[1]Nutrition Student, Federal University of Grande Dourados, Dourados, Mato Grosso do Sul, Brazil; [2]Adjunct Professor, Federal University of Espírito Santo, Vitória, Espírito Santo, Brazil; [3]Nutritionist, Department of Preventive Medicine, Faculty of Medicine FMUSP, University of São Paulo, São Paulo, Brazil; [4]Adjunct Professor, Faculty of Health Sciences, Federal University of Grande Dourados, Dourados, Mato Grosso do Sul, Brazil

Introduction: SARC-F is recommended by European Working Group on Sarcopenia in Older People (EWGSOP2) as a convenient tool for tracking the risk of sarcopenia in communities and clinical settings. The use of SARC-Calf (SARC-F + Calf Circumference-CC) seems to improve the screening performance of sarcopenia in clinical practice. Thus, we aimed to evaluate the risk of sarcopenia using the SARC-F and SARC-Calf instruments and estimate the association between the risk of sarcopenia and the variables of interest.
Methods: Cross-sectional study evaluating a convenience sample of individuals hospitalized between April 2019 and March 2020 at a University Hospital in Brazil. Risk of sarcopenia was assessed with SARC-F and SARC-Calf. Handgrip strength (HGS), muscle mass and physical performance were evaluated using dynamometry, CC and 4-meter gait speed (GS), respectively.
Results: A total of 90 patients were evaluated with a mean age of 65.4(SD=9.7) years. The majority of the sample were men, elderly, hospitalized for surgical procedure and without current labor activity. Most patients (61.1%) had an adequate CC. The risk of sarcopenia was 41.1% using SARC-F and 31.1% using SARC-Calf. In addition, diagnosis of sarcopenia using the SARC-F was found to be associated with sex (p=.032), HGS (p<.001) and GS (p<.001), while associations were found between SARC-Calf and the variables age group (adult/elderly) (p=.029), labor activity (p=.008), HGS (p<.001) and GS (p=.007).
Conclusion: The risk of sarcopenia was observed in about a third of the patients evaluated. As in both instruments the risk was associated with HGS and GS, they may be a satisfactory instrument to assess muscle function and strength in hospitalized individuals. We recommend that SARC-F, with or without the CC measurement, should be incorporated into daily practice in order to allow early intervention and thus reduce complications and negative clinical outcomes.

4-09
The joint association of frailty and sarcopenia with incidence health outcomes: Findings from the UK Biobank prospective cohort study

Fanny Petermann-Rocha[1,2*], Stuart R Gray[2], Jill P Pell[1], Frederick K Ho[1], Carlos Celis-Morales[1,2]
[1]Institute of Health and Wellbeing, University of Glasgow, Glasgow, UK; [2]British Heart Foundation Glasgow Cardiovascular Research Centre, Institute of Cardiovascular and Medical Sciences, University of Glasgow, Glasgow, UK

Introduction: Frailty and sarcopenia independently predict worse health-related outcomes. However, there is limited evidence regarding their joint association with incident health outcomes. This study aimed to investigate the joint association of frailty and sarcopenia with cardiovascular disease (CVD), respiratory disease and cancer incidence in middle-aged and older adults in the UK Biobank study.
Methods: 316,980 UK Biobank participants were included in this prospective study. Sarcopenia was defined according to the EWGSOP2 2019. Frailty was defined using a modified version of the Fried criteria. Combined classifications of sarcopenia and frailty were generated with the following seven subgroups derived: i) normal, ii) no-sarcopenic/pre-frail, iii) no-sarcopenic/frail, iv) pre-sarcopenic/pre-frail, v) pre-sarcopenic/frail, vi) sarcopenic/pre-frail, and vii) sarcopenic/frail. No participants had (pre)sarcopenia but not frailty. Associations between these exposures and incident health outcomes were investigated using Cox-proportional hazard models.
Results: 51.7% of the participants were not sarcopenic nor frail (normal), 41.3% were pre-frail or frail, 6.5% pre-sarcopenia and frail (including pre-frail) and 0.5% as having both sarcopenia and frailty (including pre-frailty). All combinations of frailty and sarcopenia were associated with incidence for CVD and respiratory disease. The combination sarcopenic/frail showed the strongest association with CVD (HR: 1.68 [95% CI: 1.22 to 2.30]) and respiratory disease incidence (HR: 1.77 [95% CI: 1.40 to 2.24]). No associations were identified between the combinations of sarcopenia and frailty and cancer incidence.
Conclusions: Our findings indicate that different combinations of frailty and sarcopenia were associated with incident health outcomes, highlighting the joint association between both conditions. However, those individuals with frailty and sarcopenia showed the strongest associations with CVD and respiratory disease incidence.

4-10
GripBMI – a fast and simple sarcopenia screening tool in post acute inpatient rehabilitation

Irina Churilov[1], Leonid Churilov[1], Kim Brock[2], David Murphy[2], Richard J MacIsaac[2], Elif I Ekinci[3]
[1]St Vincent's Hospital Melbourne; The University of Melbourne, Fitzroy, Australia; [2]St Vincent's Hospital Melbourne; [3]The University of Melbourne; Austin Health

Introduction: Sarcopenia is prevalent in post acute inpatient rehabilitation. An easy to administer screening test may improve identification of sarcopenia in this population, which may promote its early detection and treatment.

Aims:
a) To investigate clinical utility of SARC-F as a European Working Group on Sarcopenia in Older People2 (EWGSOP2) recommended tool for sarcopenia case finding in inpatient rehabilitation.
b) To develop an easy, pragmatic screening test for sarcopenia in healthcare settings with limited ability to measure the patients' muscle mass.

Methods: This cross-sectional study with prospective data collection recruited patients admitted to rehabilitation in a metropolitan tertiary referral hospital in Australia. Participant's true sarcopenia status was ascertained using EWGSOP2 cut offs for grip strength and muscle mass. Two SARC-F questionnaires were administered, for participants' current and premorbid status. To develop GripBMI screening tool, BMI test positivity cut off was established on training sample and validated in conjunction with the established grip strength cut off on validation sample using area under the Receiver Operating Curve (ROC) analysis.

Results: True prevalence of sarcopenia in 277 participants (median age 64 years (IQR 53-72), 52% male) was 14% (95%CI 11%-19%). Screening utility for sarcopenia of SARC-F positive status at the time of admission had ROC of 0.50, and of premorbid SARC-F positive status had ROC of 0.51.
Of 42 participants positive on the GripBMI screen, 33 had sarcopenia, and out of 235 participants negative on the GripBMI screen, 7 participants had sarcopenia, resulting in GripBMI ROC area 0.89, sensitivity 83%, specificity 96%, positive predictive value 79%, negative predictive value 97%, diagnostic OR 119 (95% CI 42-338).

Conclusions: The GripBMI screening tool uses the combination of EWGSOP2 recommended low grip strength cut offs and Body Mass Index of less than 25 as a positive screening test for sarcopenia.

Reference
Clinical Nutrition 2020; in press

4-11
Development of appendicular muscle mass estimating formulas for older adults considering paralysis

Junko Ueshima[1], Keisuke Maeda[2], Kenta Murotani[3]; Akio Shimizu[4], Ayano Nagano[5], Keisuke Sato[6], Yuria Ishida[7], Naoharu Mori[8] and Masaki Suenaga[6]
[1]Department of Clinical Nutrition and Food Service, NTT Medical Center Tokyo; [2]Department of Geriatric Medicine, National Center for Geriatrics and Gerontology; [3]Biostatistics Center, Kurume University; [4]Department of Nutrition, Hamamatsu City Rehabilitation Hospital; [5]Department of Nursing, Nishinomiya Kyoritsu Neurosurgical Hospital; [6]Okinawa Chuzan Clinical Research Center, Chuzan Hospital; [7]Department of Nutrition, Aichi Medical University Hospital; [8]Department of Palliative and Supportive Medicine, Graduate School of Medicine, Aichi Medical University

Introduction: Sarcopenia is a progressive, systemic skeletal muscle disease with poor outcomes associated with public health. This study aimed to develop appendicular skeletal muscle mass (ASM) estimating formulas using anthropometric measurements while considering paralysis to accommodate older adults with disabilities.

Methods: This retrospective study included stroke patients aged ≥65 years who were admitted to Chuzan Hospital between August 2018 and December 2019. A total of 315 patients were analyzed. We used the five-fold cross-validation method to develop six different ASM estimating formulas. These formulas included age, gender, height, weight, arm circumference, triceps skinfold, calf circumference, and presence of paralysis. The correlation between the ASM calculated from the developed equation (estimated ASM) and the ASM measured by bioelectrical impedance analysis (measured ASM) and the precision of the estimating formulas in detecting muscle mass loss was verified. Pearson's correlation coefficient (r) and intraclass correlation coefficient (ICC) were used to examine the correlation between the estimated and measured ASMs. The precision of detection of muscle mass loss calculated from the ASM estimating formula was assessed on the basis of sensitivity, specificity, accuracy, F-value, and Matthew's correlation coefficient (MCC).

Results: The mean measured ASM was 13.7 ± 4.3 kg. 241 (76.5%) patients had decreased measured ASM. The mean adjusted R^2 of the six formulas that were developed was 0.861–0.871. The r and ICC of the ASM estimated by all formulas and measured ASM were strongly correlated (r = 0.929–0.936 and ICC = 0.926–0.934). These formulas demonstrated excellent sensitivity (86.0%–88.2%), specificity (72.5%–81.1%), accuracy (0.838–0.870), F-value (0.899–0.918), and MCC (0.509–0.612) for measured ASM depletion.

Conclusion: In this study, we developed six formulas to estimate ASM using anthropometric measurements that can be measured in daily clinical practice with consideration on the presence of paralysis.

4-12
Body composition of long-living patients with coronary artery disease

Svetlana V. Topolyanskaya, Leonid I Dvoretski
First Moscow State Medical University (Sechenov University), Department of hospital therapy N2, Moscow, Russia

Introduction: Very limited data are available on body composition of long-living patients with coronary artery disease (CAD), therefore, we evaluated body composition of long-living patients with CAD.

Methods: 200 hospitalized patients with CAD (females – 69,3%, males – 30,7%) aged 90-106 years were enrolled in this cross-sectional study. Body composition was assessed by dual-energy X-ray absorptiometry.

Results: 70.3% of patients were overweight or obese. Obesity was observed in 30.2% of patients; in 93.5% of them it was 1-st degree obesity, 2-nd degree was only in 6.5%, and 3-d degree was never met. The body weight deficit was found in only one patient (0.49%). Mean body mass index was 27.6 (18.2-38.8) kg/m^2. Women had more fat then men: total fat – 39.8% vs 30.0% (p<0.0001), lower extremities fat –42.4% vs 27.4% (p<0.0001). The mean total T-score was -1.75SD. The greatest BMD was recorded in lumbar spine (1005.6±190.6 mg/cm^3), the lowest BMD – in ribs (626.2±83.9 mg/cm^3). As expected, female patients had lower BMD in all parts of the body (p<0.0001). Mean total mass of lean tissue in women was 38.4 kg, and in men - 48.8 kg (p <0.000001). The musculoskeletal index remained within the normal range in 77.2% and was below normal in 22.8%. A decrease in the musculoskeletal index was observed in 22.9% of men and 19.1% of women (p = 0.5). Significant positive correlations were found between lean tissue and BMD (p <0.000001). Muscle strength (according to dynamometry data) positively correlated with lean tissue content (r = 0.55; p <0.000001). The content of lean tissue was positively correlated with the distance covered in the 6-minute walk test (p = 0.007

Conclusion: Study results demonstrated some features of body composition in patients with CAD aged 90 years or older. Significant associations between bone, fat and lean tissue were observed in the study population.

4-13
Sarcopenia detection using a handheld dynamometer in fracture Neck of Femur patients presenting to a District General Hospital

Sanjay Suman, Faisal Jamil, William Ogburn
Medway NHS Foundation Trust, Gillingham, UK

Introduction: Frail elderly with Sarcopenia (loss of muscle strength and muscle mass) represent the highest proportion of those who fall and fracture Neck of Femur (NOF), but

Sarcopenia is often not formally diagnosed. This is despite tools and a published diagnostic algorithm being available (European Working Group on Sarcopenia in Older People, EWGSOP). Sarcopenia often co-exists with frailty, malnutrition and carries a higher burden of inpatient complications.
Methods: A prospective study was carried out (October 2019-February 2020) at Medway Maritime Hospital, recruiting patients aged ≥65 with NOF fracture. For measuring grip strength, a handheld dynamometer was used (Cut off points; <27 kg Male, <16 kg in female). Additional parameters included nutritional and frailty status ("MUST", Clinical Frailty Scale respectively), length of stay and inpatient complications.
Results: 55 (39 women, 16 men) patients were included in this study. The prevalence of sarcopenia as determined by a handheld dynamometer was 67.2 % (37/55). Mild frailty was detected in 32%, moderate frailty in 29% and severe frailty in 7%. Amongst the frail individuals (37/55), the prevalence of sarcopenia was 78% (29/37). All severely frail individuals had sarcopenia. Individuals with sarcopenia had the highest rate for inpatient complications including delirium (18/37; 48%), constipation (34/37; 92%) and hospital acquired infections (10/37; 27%). Overall Malnutrition prevalence was 40% (22/55). Amongst the Sarcopenia group, 54% (20/37) were malnourished and on average stayed 5 days longer as inpatients.
Conclusions: Sarcopenia and frailty were detected in a high proportion of fracture NOF individuals who were also at risk of malnutrition and inpatient complications, with a longer inpatient LOS. A handheld dynamometer can be used as a simple practical tool for detecting sarcopenia in this group. This allows effective strategies such as nutritional supplementation, mobilisation and individualized exercise regime to be started early, delivered as part of a multidisciplinary intervention.

4-14
Longitudinal association of severe sarcopenia and mild cognitive impairment among older Mexican adults

Manrique-Espinoza B, Salinas-Rodríguez A, Palazuelos-González R
Center for Evaluation Research and Surveys, National Institute of Public Health, Cuernavaca, Morelos, Mexico

Introduction: Recent evidence from cross-sectional and longitudinal studies supports the hypothesis that sarcopenia is associated with a worse cognitive function and mild cognitive impairment (MCI). However, primary evidence comes from high-income countries, while in low- and middle-income countries, this association has been largely unexplored. This study aimed to estimate the longitudinal association between sarcopenia and mild cognitive impairment in a sample of older Mexican adults.
Methods: Data comes from the three waves of the WHO Study on global AGEing and adult health (SAGE) in Mexico (2009, 2014, 2017). Four hundred ninety-five older adults aged 50 and over were included. Severe sarcopenia was defined according to the European Working Group's algorithm on Sarcopenia in Older People 2, considering low grip strength, low muscle quantity and low gait speed. Mild cognitive impairment (MCI) was ascertained based on the recommendations of the National Institute on Aging-Alzheimer's Association, and cognitive function was evaluated by a Composite Cognitive Score (CCS) applying five cognitive tests: immediate and delayed recall, forward and backward digit span and verbal fluency test. Three-level mixed effect models (logistic and linear) were used to estimate the longitudinal associations between severe sarcopenia and MCI & CCS.
Results: Prevalence of severe sarcopenia were 12.57%, 21.24% and 25% for waves 1, 2, and 3, respectively. Severe sarcopenia was associated with MCI (OR=1.74, CI 95%: 1.02; 2.96, p-value=0.04) and CCS (β=-0.57, CI 95%: -0.9; -0.2, p-value<0.01).
Conclusion: Longitudinal significant associations were observed between severe sarcopenia and MCI & CCS among older Mexican adults. These results provide novel information for low- and middle-income countries. Although ageing is one significant risk factor for sarcopenia, promoting muscle health with modifiable factors such as physical activity and nutrition, could help to prevent MCI and worsening cognitive function.

4-15
Sarcopenia and circulating leptin levels in community-dwelling older Chileans

Cecilia Albala, Carlos Marquez, Lydia Lera, Barbara Angel, Hugo Sánchez
INTA, Universidad de Chile, Santiago, Chile

Background: Leptin is an adipokine secreted by adipocytes, but also produced in skeletal muscle and bone cells and circulating leptin exerts anabolic effects on muscle mass. Our objective was to determine if sarcopenic subjects have lower levels of circulating leptin and lower availability of leptin, represented by the free leptin index (FLI)
Methods: A cross-sectional study in 570 subjects (70,7% women, mean age 72y±6.8) community-dwelling people participating in the ALEXANDROS cohorts, designed to study disability associated with obesity in community-dwelling people 60y and older living in Santiago/Chile. Sarcopenia was identified using the EWGSOP 2010 algorithm validated for Chile. The nutritional state was determined with the WHO BMI cut-points. The lean/fat mass ratio was calculated to adjust the associations. Blood samples for measuring leptin, soluble leptin receptor (sOB-R) were available for the analysis. Free leptin index (FLI) was calculated as the ratio of leptin over sOB-R.
Results: In the sample of 570 people, 20,7% (118) were diagnosed as sarcopenic (21.8% in women, 18.0% in men). Two-thirds of the subjects were overweight or normal, only 3 people were undernourished and 34,6% had Obesity, being higher the prevalence in women than men (38% vs 26.4%respectively) Sarcopenic obesity was identified in 7 women. Both total plasma leptin and FLI were lower in sarcopenic than non-sarcopenic people (leptin 17.3 vs.25.4 ng/ml, p<0.0001; FLI: 0.608 vs 0.957, p=0.0001). After logistic regression analysis adjusted by age, sex and lean/fat mass index the OR for sarcopenia was negatively associated with total leptin OR:0.942 (95%CI 0.907-0.979), being higher the strength of the association with FLI: OR = 0.427 (95%CI: 0 .204-0.892)
Conclusions: The results support the importance of circulating leptin as a protective factor for sarcopenia. Moreover, FLI, an indicator of leptin availability had a stronger negative association with sarcopenia.

4-16
Investigation into the relationship between markers of nutritional status, sarcopenia and frailty, and clinical outcomes in older hospital patients

Adriana Salame[1], David Smithard[2], Adrian Slee[1]*
[1]Division of Medicine, University College London, London, UK, [2]Queen Elizabeth Hospital, Woolwich, London, UK

Background: Older inpatients are at greater risk for malnutrition, sarcopenia and frailty. These three conditions are interlinked and bring about poor outcomes; thus, their early detection using valid and simple tools is critical in improving patient care and prognosis. The purpose of this study is to investigate the relationship between markers of malnutrition, sarcopenia and frailty and clinical outcomes.
Methods: This study was drawn from a clinical audit of 256 hospitalized older people with available data for Nutrition Screening Tool (NST), SARC-F and Clinical Frailty Scale

(CFS) scores, weight, height, blood markers albumin and C-reactive protein (CRP), length of stay (LOS) and mortality. The Geriatric Nutritional Risk Index (GNRI) was computed from available data, and all variables inputted into an excel database.
Results: NST, SARC-F and CFS scores, and CRP, albumin and CRP/albumin levels significantly differed between alive and deceased (P<0.05). Malnutrition risk prevalence was comparable between NST and GNRI screening, and exceeded 30% of patients, while 66% and 68% were sarcopenic and frail respectively. A significant overlap between malnutrition, as identified according to NST and GNRI, sarcopenia and frailty was found. Only GNRI and NST fairly correlated with LOS (coefficients -0.324 and 0.284 respectively). Significant mortality predictors were, in order of best performance, CFS, SARC-F, CRP/albumin and CRP (areas under the curve ~0.7).
Conclusions: This study highlights the important overlapping prevalence of malnutrition, sarcopenia and frailty in hospitalized elderly, and demonstrates that CFS, SARC-F, CRP and CRP/albumin are valuable mortality predictors, although the exact relationships were not clarified.

4-17
Associations between sarcopenia, osteoporosis and frailty in community dwelling older adults: findings from the Hertfordshire Cohort Study (HCS)

Faidra Laskou, Karen Jameson, Cyrus Cooper, Harnish P Patel, Elaine Dennison
MRC Unit Southampton, Southampton, UK

Introduction: Frailty is associated with a range of adverse health outcomes. A recent study in Japan suggested that the presence of both osteoporosis (OP) and sarcopenia (SP) increased the risk of frailty. We explored these relationships in the UK Hertfordshire Cohort Study.
Methods: Our study comprised of 216 men and 216 women. Participants were assessed at baseline and followed up 5 years later. OP was defined as BMD T- scores ≤-2.5 at the femoral neck using dual-energy X-ray absorptiometry or use of anti-osteoporosis medication. EWSGOP cut-off criteria for low grip strength and ALM index were used to define SP. Frailty was defined using the Fried criteria. Logistic regression was performed to analyse associations between OP/SP and frailty.
Results: The mean (SD) age was 75.7 (2.6) years. At baseline, the prevalence of frailty and pre-frailty was 12.2% (men, 8%, women, 16.3 %), and 57% (men, 55.7%; women, 58.2%) respectively. Individuals living with frailty were older, tended to drink less alcohol, were less physically active, had lower walking speed and grip strength (P<0.001), and were more likely to be female (P=0.007). 0.6% had co-existence of SP, OP and frailty; 0.6% had SP and frailty; 1.6% had OP and frailty and 1.6% had SP and OP. SP only was significantly associated with frailty at baseline (p<0.001). The presence of OP at baseline was a significant predictive factor for the occurrence of frailty at follow-up (odds ratio [OR], 3.04; 95% confidence interval [95% CI], 1.11,8.38; P=0.031), while the risk of developing frailty was increased in both osteoporotic and sarcopenic participants at baseline; this was not significant (OR; 10.08, 95% CI,0.55,186.08; P=0.12).
Conclusion: The presence of OP is a significant predictive factor for developing frailty and might be used as a trigger for appropriate interventions to reduce or reverse its development in older adults.

4-18
Sarcopenia is associated with mortality in adults: A systematic review and meta-analysis

Andrea B. Maier[1], Jane Xu[2], Ching S. Wan[2], Kiriakos Ktoris[1], Esmee M Reijnierse[2]
[1]Vrije Universiteit, @AgeAmsterdam, Amsterdam, The Netherlands; [2]University of Melbourne, @AgeMelbourne

Background: Sarcopenia can predispose individuals to falls, fractures, hospitalization and mortality. The prevalence of sarcopenia depends on the population studied and the definition used for the diagnosis. This systematic review and meta-analysis aimed to investigate the association between sarcopenia and mortality and if it is dependent of the population and sarcopenia definition.
Methods: A systematic search was conducted in MEDLINE, EMBASE and Cochrane from 1st January 2010 to 6th April 2020 for articles relating to sarcopenia and mortality. Articles were included if they met the following criteria: cohorts with a mean or median age ≥18 years and either of the following sarcopenia definitions: Asian Working Group for Sarcopenia (AWGS and AWGS2019), European working group on Sarcopenia in Older People (EWGSOP and EWGSOP2), Foundation for the National Institutes of Health (FNIH), International Working group for Sarcopenia (IWGS) or Sarcopenia Definition and Outcomes Consortium (SDOC). Hazard ratios (HR) and odds ratios (OR) were pooled separately in meta-analyses using a random-effects model, stratified by population (community-dwelling, outpatients, inpatients, nursing home residents). Subgroup analyses were performed for sarcopenia definition and follow-up period.
Results: Out of 3025 articles, 57 articles were included in the systematic review and 56 in the meta-analysis (42,108 participants, mean age of 49.4±11.7 to 86.6±1.0 years, 40.3% females). Overall, sarcopenia was associated with a significantly higher risk of mortality (HR: 2.00 (95% CI: 1.71, 2.34); OR: 2.35 (95% CI: 1.69, 3.28)), that was independent of population, sarcopenia definition and follow-up period in subgroup analyses.
Conclusions: Sarcopenia is associated with a significantly higher risk of mortality, independent of population and sarcopenia definition, which highlights the need for screening and early diagnosis in all populations.

4-19
Muscle Assessment by Echografy in a Cohort of Older Adults and its Utility in Sarcopenia Diagnosis

Marta Neira Alvarez[1], Miguel A Vazquez Ronda[2], Llanos Soler Rangel[2], Patricia Martinez Martin[2], Isabel Rabago Lorite[2], Gonzalo Serralta San Martin[2]
[1]Department of Geriatrics, Infanta Sofía University Hospital. Infanta Sofía and Henares HospitalS Foundation for Biomedical Research and Innovation (FIIB HUIS HHEN), Madrid (Spain). European University; [2]Department of Internal Medicine, Infanta Sofía University Hospital. Infanta Sofía and Henares Hospitals Foundation for Biomedical Research and Innovation (FIIB HUIS HHEN), Madrid (Spain). European University.

Diagnosis of sarcopenia is based on the assessment of muscle mass. All of the many approaches available are subject to drawbacks. Ultrasound is a non-invasive, low-cost, and accessible technique for assessing the morphology of skeletal muscle
The aim of this study was to evaluate the utility of muscle ultrasound in the diagnosis of sarcopenia by studying concordance between ultrasound and dual-energy x-ray absorptiometry (DXA) and its relationship with muscle function and strength.
Fifty-seven elderly patients were studied. Mean age was 78 years (SD, 74.9-81.9 years), and 33 were women (58%).

Thirty-six patients met the criteria for confirmed sarcopenia (10 with severe sarcopenia).
We found a good correlation between appendicular muscle mass measured by DXA and gastrocnemius muscle mass measured by ultrasound both in terms of muscle thickness in the transverse plane (correlation, 0.567) and in length of the fiber in the longitudinal plane (correlation, 0.627). However, we found no significant correlations for the rectus femoris. Intra-observer and interobserver correlations showed coefficients greater than 0.8 for gastrocnemius medialis thickness and length. In addition, gastrocnemius muscle measurements in both the longitudinal and the transverse planes and fiber length were significantly reduced in patients with severe sarcopenia ($p < 0.05$).
In conclusion, gastrocnemius medialis measurements obtained by ultrasound are reliable and reproducible and correlate well with DXA values and muscle function.

4-20
Cut-points for adverse muscle composition predicts all-cause mortality

Jennifer Linge[1,2], Mickael Peterson[1], Olof Dahlqvist Leinhard[1,2,3]
[1]AMRA Medical, Linköping, Sweden; [2]Department of Health, Medicine and Caring Sciences, Linköping University, Sweden; [3]Center for Medical Image Science and Visualization (CMIV), Linköping University, Sweden

Introduction: Adverse muscle composition (MC) as measured by magnetic resonance imaging (MRI) has previously been linked to poor functional performance, metabolic comorbidity and increased hospitalization[1,2]. The aim of this study was to investigate the association between Adverse MC and all-cause mortality in the UK Biobank imaging cohort.
Methods: 24,848 participants were scanned using a 6-minute MRI protocol. Images were analyzed for thigh fat-free muscle volume (FFMV) and muscle fat infiltration (MFI) using AMRA Researcher, Linköping, Sweden. For each participant, a sex- and BMI invariant FFMV z-score was calculated[1]. Participants were partitioned into four MC groups using the 25th percentile for low FFMV z-score (-0.68 SD) and the sex-specific 75th percentile (8.8/7.7 % (females/males)) for high MFI: (1) Adverse MC, (2) 'Only low FFMV z-score', (3) 'Only high MFI', (4) Normal MC[2]. Association of MC groups with all-cause mortality was investigated using cox-proportional hazard modeling with Normal MC as referent (unadjusted and adjusted for sex, age, BMI, smoking, cancer diagnosis).
Results: The cohort consisted of 52% females with mean (SD) age 63.4 (7.5) years and BMI 26.5 (4.4) kg/m^2, and were followed for 3.6 (1.2) years. 256 deaths were recorded post imaging. Adverse MC was detected in 10.3% of the participants and most strongly predicted death (**Figure 1**) with a 3.9-fold higher risk of death (HR: 3.9 (2.8-5.3), $p<0.001$) compared to Normal MC (**Figure 2**). 'Only low FFMV z-score' (HR: 1.6 (1.1-2.3), $p=0.018$) and 'Only high MFI' (HR: 2.0 (1.5-2.8), $p<0.001$) were significantly associated with higher HR. After adjustment, results for Adverse MC and 'Only high MFI' persisted whereas the association of 'Only low FFMV z-score' with death was attenuated (Figure 2).
Conclusions: Cut-points for Adverse MC identified a common phenotype associated with increased mortality risk. The results highlight that sarcopenia guidelines can be strengthened by including cut-points for muscle fat.

Figure 1 (left), Kaplan Meier survival curve for muscle composition (MC) groups.

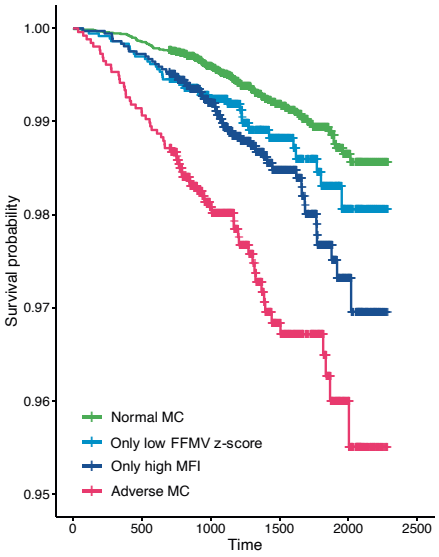
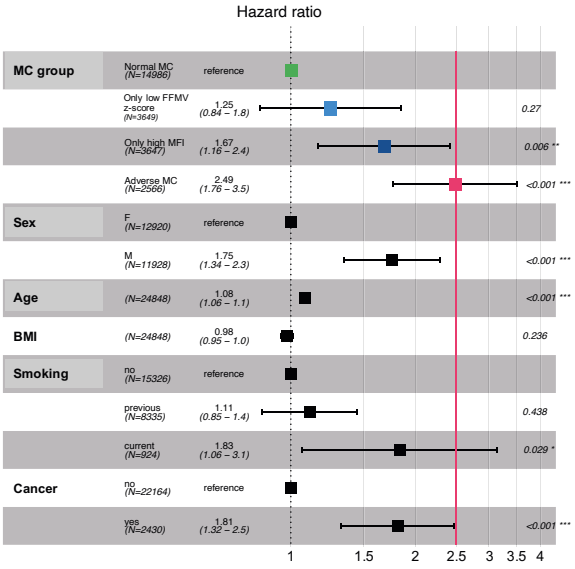


Figure 2 (right), Results from the cox-proportional hazard modelling of MC groups with all-cause mortality with Normal MC as referent adjusted for sex, age, BMI, smoking, cancer. FFMV, fat-free muscle volume; MFI, muscle fat infiltration.



References:

1. Linge J et al. On the Definition of Sarcopenia in the Presence of Aging and Obesity—Initial Results from UK Biobank. J Gerontol A Biol Sci Med Sci 2020. doi: 10.1093/gerona/glz229
2. Linge J et al. Adverse Muscle Composition is Linked to Poor Functional Performance and Metabolic Comorbidities in NAFLD. JHEP Reports 2020. In print.

4-21

Sarcopenia and Cardiovascular Risk in Patients with Chronic Kidney Disease on Peritoneal Dialysis

Sheila Borges; Renata Costa Fortes
School of Health Sciences, Brasília, Distrito Federal, Brazil

Introduction: Sarcopenia is related to mortality and, possibly, to cardiovascular events in chronic kidney disease (CKD). The aim of the present study was to evaluate the association between sarcopenia and cardiovascular risk in patients with CKD on automated peritoneal dialysis (APD). **Methods:** Cross-sectional analytical study, in patients with CKD in APD, both gender, over 18 years old, with more than three months in dialysis treatment. The variables evaluated were: dialysis time, anthropometric measurements; presence of comorbidities; serum levels of albumin, creatinine, urea, ferritin and protein and calorie intake. The used definition of sarcopenia followed the steps described by the European Working Group on Sarcopenia in Older People. Initially, the SARC-F instrument was applied to screen for sarcopenia. The evaluation of muscle mass was performed through bioimpedance by spectroscopy, in addition to the measurement of handgrip strength and physical performance. Malnutrition was determined by the 7-point subjective global assessment (7p-SGA). The cardiovascular risk was identified by the triglycerides/HDL-cholesterol ratio, considering a cutoff point ≥ 3.80. Multiple binary logistic regression analysis was performed to identify the main variables related to the presence of sarcopenia. The level of significance considered was p<0,05.
Results: The sample consisted of 52 participants, aged 53.90±14.86 years old. The prevalence of sarcopenia was 28.85% and cardiovascular risk was discovered in 48.08% of the participants. This condition was predominant in males and in hypertensive individuals and there was a statistical difference between the presence of sarcopenia in relation to 7p-ASG (p=0,043), phase angle (p=0,005) and albumin (p<0,001). **Conclusion:** The reduced levels of albumin increased the chances of sarcopenia by 22.22 times. In the present study, no casual relation was found between sarcopenia and cardiovascular risk.

4-22

Sarcopenia and Cardiovascular Risk in Patients with Chronic Kidney Disease on Hemodialysis: a Cross-Sectional Study

Sheila Borges, Renata Costa Fortes
School of Health Sciences, Brasília, Distrito Federal, Brazil

Introduction: The repercussion of sarcopenia involves adverse events such as falls, decline in functional capacity, frailty and increased cardiovascular risk, especially, in chronic kidney disease (CKD). The aim was to evaluate the association between sarcopenia and cardiovascular risk in individuals undergoing hemodialysis (HD).
Methods: Cross-sectional analytical study, with CKD patients, of both gender, above 18 years old, with more than three months on HD. The variables evaluated were: dialysis time, anthropometric measurements; presence of comorbidities; levels of albumin, creatinine, urea, ferritin, protein and calorie intake, and dialysis efficacy by Kt/V. The used definition of sarcopenia followed the steps described by the European Working Group on Sarcopenia in Older People. The evaluation of muscle mass was performed by means of bioimpedance by spectroscopy, in addition to the measurement of handgrip strength and physical performance, being the gait speed test to confirm severe sarcopenia. The presence of malnutrition was by the 7-Point Subjective Global Assessment. The cardiovascular risk was identified by the triglycerides/HDL-cholesterol ratio, considering the cutoff point ≥3,8. Multiple binary logistic regression analysis was performed to identify the main variables related to the presence of sarcopenia. The level of significance considered was p<0,05.
Results: The sample consisted of 74 participants, aged 57.1±27.6 years. Sarcopenia was found in 31.1% (n=23) and cardiovascular risk in 54.9% (n=39) participants. This condition was predominant in males and diabetics, and a statistical significance between the presence of sarcopenia and the phase angle (p=0.002) was observed. Hypertensive participants were 31.05 times more likely to have sarcopenia (OR=31.05; 95%CI 1.89-511.06; p=0.016). In every decrease of one phase angle unit, the chance of sarcopenia increased 10.64 times (OR=1/0.094; 95%CI 0.02-0.38; p=0.001).
Conclusion: No relationship was found between cardiovascular risk and sarcopenia using the TGL-HDL-cholesterol ratio. The presence of hypertension was an independent factor for sarcopenia.

4-23

Sarcopenia, chronic kidney disease and the risk of mortality and end stage renal disease: findings from 428,331 individuals in the UK Biobank

Thomas J Wilkinson[1], Joanne Miksza[2], Luke A. Baker[1], Courtney J Lightfoot[1], Emma L. Watson[1], Thomas Yates[3], Alice C. Smith[1]
[1]Leicester Kidney Lifestyle Team, University of Leicester; [2]Leicester Real World Evidence Centre, University of Leicester; [3]Leicester Biomedical Research Centre, Leicester

Introduction: Sarcopenia describes a degenerative and generalised skeletal muscle disorder involving the loss of muscle mass and function. Whilst sarcopenia has been widely studied in end-stage renal disease (ESRD) patients, there is limited evidence of its prevalence and effects in those not requiring renal replacement therapy (RRT). Using the UK Biobank, we aimed to identify the prevalence of sarcopenia in CKD and its association with mortality and risk of ESRD.
Methods: 428,331 participants were categorised into a CKD (eGFR <60ml/min/1.73m^2) and a non-CKD comparative group (no evidence of CKD). Sarcopenia was diagnosed using the EWGSOP2 criteria. Patients were followed up until death or until they reached incident ESRD. All-cause mortality was extracted from national death records. Patients were followed up for a median of 9.0 years.
Results: CKD was identified in n=8,768 individuals (age 62.7 (±5.9) years, 44% male, eGFR 52.5 (±7.7) ml/min/1.73m^2) compared to n=419,563 in the non-CKD group (age 56.1 (±8.1) years, 47% male). Probable sarcopenia was identified in 10% of individuals with CKD compared to 5% in those without CKD (P<0.001). Confirmed sarcopenia was observed in 0.3% of those with CKD (vs. 0.2% in the non-CKD group, P<0.001). In CKD, regardless of criteria, sarcopenia was associated with a increased risk of mortality: probable sarcopenia, hazard ratio (HR) 2.1 (95%CI 2.0 to 2.2), P<0.001; confirmed sarcopenia, HR 4.1 (95%CI 2.1 to 8.0), P<0.001; severe sarcopenia, HR 5.1 (95%CI 2.1 to 12.3), P<0.001. Patients with probable sarcopenia were two-fold more likely to reach ESRD (HR 2.3 (95%CI 1.7 to 3.1), P<0.001)
Conclusions: In the largest cohort of its kind, probable sarcopenia was present in 10% of individuals with CKD. Regardless of criteria, CKD patients with sarcopenia were ~2-5 times more likely to die than those without sarcopenia. Patients with probable sarcopenia were twice more likely to reach ESRD.

4-24
Sarcopenia in patients with bladder or kidney cancer

Patrícia Fonseca dos Reis[1,2], Renata Brum Martucci [1,2], Jocilene Leite Alves[2]
[1]Medical Science Post-Graduation, Rio de Janeiro State University, Rio de Janeiro, Brazil; [2]Nutrition and Dietetic Service, National Cancer Institute, Rio de Janeiro, Brazil

Introduction: Sarcopenia is characterized by low muscle strength, low muscle quantity or quality, and when severe, low physical performance. It is associated to age and diseases, such as cancer, increasing the risk of adverse events. The aim of this study was to evaluate the occurrence of sarcopenia in patients with bladder or kidney cancer.
Methods: Cross sectional study with bladder or kidney cancer patients, aged 20 years or more. Clinical and nutritional data were collected from medical records and nutritional appointment. Sarcopenia was defined according to EWGSOP2 (2018) as: (1) Probable sarcopenia- low muscle strength (Grip strength <27 kg for men and <16 kg for women); (2) Sarcopenia- low skeletal muscle index (SMI), <38.5 cm^2/m^2 for female and <52.4 cm^2/m^2 for male, assessed by CT scan of the third lumbar vertebra, and (3) Severe sarcopenia- (1) + (2) + low performance (Gait speed ≤0.8 m/s). Muscle quality was assessed by muscle radiation attenuation (MRA) from CT images.
Results: Twenty-seven patients were evaluated (37% bladder and 63% kidney cancer); median age 62 years; 66.7% male; 25.9% (n=7) with probable sarcopenia, of which 57.1% (n=4) confirmed sarcopenia and 25% (n=1) severe sarcopenia. Fourteen patients (51.8%) had low SMI, of these the median of MRA was 31.9 HU, while in the others it was 40.3 HU (p<0.05). Individuals with low muscle strength had worse MRA (29.7 HU vs 37.8 HU, p<0.05), but SMI was not different. Grip strength and gait speed was not statistically different between patients with or without low SMI. So as body mass index, type or phase of cancer treatment and cancer stage did not varied according to muscle strength, SMI or MRA.
Conclusions: A high prevalence of probable sarcopenia and sarcopenia was observed in patients with bladder and kidney cancer. Low muscle strength was associated with muscle quality.

4-25
Sarcopenia and health-related quality of life in colorectal cancer

Mariana Vieira Barbosa[1], Mylena Pinto dos Santos[2], Jocilene Alves Leite[3], Viviane Dias Rodrigues[3], Renata Brum Martucci[3,4]
[1]Post-graduate Program in Medical Science, Medical Science Faculty, State University of Rio de Janeiro, Rio de Janeiro, RJ, Brazil; [2]Post-graduate Program in Food, Nutrition and Health, Nutrition Institute, State University of Rio de Janeiro, Rio de Janeiro, RJ, Brazil; [3]Nutrition and Dietetic Service, Cancer Hospital Unit I, National Cancer Institute José Alencar Gomes da Silva, Rio de Janeiro, RJ, Brazil; [5]Department of Applied Nutrition, Nutrition Institute, State University of Rio de Janeiro, Rio de Janeiro, RJ, Brazil

Introduction: Cancer and its treatment have a significant impact on patients' body composition, functionality and health-related quality of life (HRQoL). Despite this, the association between cancer sarcopenia and HRQoL has been poorly investigated.
Purpose: We aimed to evaluate the association between sarcopenia and HRQoL of patients with colorectal cancer (CRC).
Methods: A cross-sectional study with patients with CRC, at the National Cancer Institute, in 2018. The body composition was assessed by computed tomography images and sarcopenia was defined by the European consensus review guidelines for sarcopenia, published in 2019. HRQoL was assessed using the EORTC questionnaire QLQ-C30 (European Organization for Research and Treatment of Cancer Quality of Life Questionnaire). Multivariate linear regression analysis was performed between sarcopenia and the HRQoL domains (95% CI).
Results: A total of 142 patients were included, with a mean of age of 62.7 years (±11.4), with 5.6% of patients diagnosed with probable sarcopenia, 5.6% with sarcopenia and 4.3% with severe sarcopenia. Patients with sarcopenia and patients with severe sarcopenia were grouped in the same group ("with sarcopenia"). Two linear regression models were tested to verify the association between sarcopenia and HRQoL: in the first model, the association of patients without sarcopenia versus probable sarcopenia and sarcopenia was verified; in the second model, the association of patients without sarcopenia and probable sarcopenia versus sarcopenia was verified. After adjusting for sociodemographic, clinical and nutritional variables, the analysis showed that the combined association of probable sarcopenic and sarcopenic patients influenced the worsening of HRQoL, reducing the overall health status (B=-15.0; p=0.002), the physical (B=-15.2; p=0.001) and emotional functions (B=-22.6; p=0.013), and increasing symptoms of fatigue (B=13.5; p=0.017), pain (B=18.8; p=0.020), dyspnea (B=10.8; p=0.021) and loss of appetite (B=11.9; p=0.044).
Conclusion: Sarcopenia and/or probable sarcopenia were negatively associated with HRQoL of patients with CRC.

4-26
Sarcopenia in cancer palliative care: results of a prospective study

Dubu Jonas, Le Du Katell
Institut Inter régionaL de Cancérologie, Centre Jean Bernard Clinique Victor Hugo, Le Mans, France

Introduction: Cancer is one of the leading causes of death in the world and despite a great deal of progress in disease detection and treatment, cancer incidence is steadily increasing (+ 33% in 2015) and particularly in certain locations (pancreas, lungs, brain and stomach)[1,2]. Metastatic cancer is most often incurable with the exception of germ cell tumors[3,4]. Palliative care support is then most often offered. The symptoms most often reported by patients are: pain, fatigue, decreased appetite, nausea, and are directly related to phenomena such as cachexia, loss of autonomy and deterioration of psychological state, resulting in decreased overall survival[5]. Chemotherapies and targeted therapies can provide a benefit in quality of life and survival only in the early phase[6]. Other prognostic factors can impact the quality of life and overall survival in these situations: sarcopenia and nutritional status disorders.
Methods: It's a non-interventional, prospective 3-month study. Several data like performance status, lumbar skeletal muscle index (by CT scan), albumin, CRP, or LDH, are collected from medical records in the classic balance sheet at inclusion, 3 months, and 6 months.
Results: 37 patients were included between the 06/01/2019 and the 08/31/2019 with a median age of 68 years old. 31 were evaluable for sarcopenia. 58.1% of patients with metastatic cancer were sarcopenic at the diagnosis and 61% at 6 months. At the inclusion, 87.5% of sarcopenic patients were men (p < 0.0002) and sarcopenia status was associated with lung localisation (p < 0.0332) and non-operable cancer (p <0.0069). 33% of patients had an albuminemia below 30 g/L and 66% at 6 months.
Overall survival is 7,5 months for the 31 patients without any difference between sarcopenia and non sarcopenia group. There is no correlation with PRONOPALL score and sarcopenia.
Conclusion: The majority of patients in our study were sarcopenic at the inclusion and at 6 months. However, the workforce was too small to correlate sarcopenia with survival. Further larger studies are needed to establish stronger

results. The aim of this study was to collect a database on the prevalence of sarcopenia in patients in a palliative situation. The subsequent aim of detect the sarcopenic patients should be a specialized care: nutrition and adapted physical activity.

References
(1) Fitzmaurice C, Allen C, Barber RM, Barregard L, Bhutta ZA et al. Global, regional, and national cancer incidence, mortality, years of life lost, years lived with disability, and disability-adjusted life-years for 32 cancer groups, 1990 to 2015 : a systematic analysis for the global burden of disease study. JAMA Oncol 2017 Apr 1 ; 3 (4) : 524-548.
(2) Siegel R, Naischadham D, Jemal A. Cancer statistics, 2013. CA Cancer J Clin 2013 Jan; 63(1): 11-30.
(3) Prigerson HG, Bao Y, Shah MA, Paulk ME, LeBlanc TW et al. Chemotherapy use, performance status, and quality of life at the end of life. JAMA Oncol 2015 Sep; 1(6): 778-84.
(4) Quaresma M, Coleman MP, Rachet B. 40-years trends in an index of survival for all cancers combined and survival adjusted for age and sex for each cancer in England and Wales, 1971-2011 : a population-based study. Lancet 2015 Mar 28; 385(9974): 1206-18.
(5) Trajkovic-Vidakovic M, de Graeff A, Voest EE, Teunissen SC. Symptoms tell it all : a systematic review of the value of symptom assessment to predict survival in advanced cancer patients. Crit Rev Oncol Hematol 2012 Oct; 84(1): 130-48.
(6) Hiu D, Hannon BL, Zimmermann C, Bruera E. Improving patient and caregiver outcomes in oncology : team-based, timely and targeted palliative care. CA Cancer J Clin 2018 Sep;68(5): 356-376.

4-27

Adipose tissue radiodensity: characteristics and relation to survival in a population-based cancer cohort and literature review

Md Monirujjaman[1], Lisa Martin[1], Cynthia Stretch[2], Vickie E Baracos[3], Vera C Mazurak[*1]
[1]Department of Food Agriculture and Nutritional Sciences, University of Alberta; [2]Department of Oncology, University of Calgary, Calgary, Canada; [3]Department of Oncology, University of Alberta

Introduction: The concept of adipose tissue radiodensity is emerging and its association with cancer mortality has not been explored. Most studies have evaluated adipose tissue radiodensity in cardiovascular disease and only few descriptive studies that exist in the oncology setting with small sample sizes and the region of the computed tomography (CT) image and range of HU values was variable. Present study evaluated the relationship between adipose tissue radiodensity and overall survival in a large cancer cohort, and discussed in the context of published literature.
Methods: A comprehensive review of published literature provides context around what is known about adipose tissue radiodensity and clinical outcomes in other populations. The literature reviewed highlights variability with respect to the region applied for abdominal CT scan, range and mean radiodensity values for visceral and subcutaneous adipose tissue. CT was used to quantify visceral adipose tissue (VAT; -150 to -50 HU), and subcutaneous adipose tissue (SAT; -190 to -30 HU) at L3 region in 1314 patients with gastrointestinal and respiratory cancers. Univariable and multivariable analyses were conducted using cox proportional hazard models.
Results: The study population consisted of both male (53.4%) and female (43.6%) patients with a mean age of 63.4±11.4 years and mean body mass index of 25.5±4.97 kg/m^2. The majority of patients had advanced cancer colorectal (56%) or lung (33%) cancers. Having higher VAT and SAT radiodensity was independently associated with overall survival (OS) (VAT, HR:1.29; CI:1.13-1.48, p<0.001; SAT, HR: 1.34, CI:1.16-1.54, p<0.0001) in both males and females after adjusting for age, sex, cancer type, stage, performance status, muscle radiodensity and sarcopenia.
Conclusions: VAT and SAT radiodensity independently relate to OS. Consistent reporting of region, range and mean radiodensity of abdominal CT scan in the literature will enable future studies to further evaluate the importance of this new prognostic factor.

4-28

Differences in the prevalence of low muscle mass in cancer patients based on different cut-off values

Jona Van den Broeck[1], Martine J Sealy[2], Carola Brussaard[3], Harriet Jager-Wittenaar[2], Aldo Scafoglieri[1]
[1]Vrije Universiteit Brussel, Jette (Brussels) Belgium; [2]Hanze University Applied Sciences Groningen, The Netherlands; [3]Universitair Ziekenhuis Brussel, Belgium

Introduction: Low muscle mass is an important characteristic of sarcopenia (1,2,3,4). Computed tomography (CT) is a gold standard for quantifying muscle mass (3). The prevalence of low muscle mass has been studied in cancer patients, but many cut-off values have been used (2). In this study, we aimed to evaluate differences in prevalence of low muscle mass in patients with cancer based on different cut-off values. In addition, we also investigated the reason for these differences.
Methods: In this retrospective cross-sectional study, 74 Caucasian men were included. Their characteristics are shown in Table 1. Muscle mass was quantified using the CT images performed during initial cancer diagnosis. MIM software (Version 7.0.1) was used to process the images. Muscles were contoured using a single slice of L3 vertebra level (Figure 1). After contouring, the skeletal muscle index (SMI) was calculated. Seven different cut-off values for low muscle mass in Caucasian adults were applied (van der Werf (1); Derstine (2), van Vledder (5); Martin (6); Levolger (7); Cousin (8); Mourtzakis (9)).
Results: The prevalence of low muscle mass ranged from 18% to 73%. The cut-off values based on percentiles (5), based on twice the standard deviation (2), and those associated with lower survival (5-7) resulted in lower prevalence of low muscle mass than cut-off values based on the median of the sample (8) or based on cut-off values used for dual-energy X-ray absorptiometry (DXA) (9). The prevalence rates based on the various cut-off values and characteristics of the sample in which the cut-off values were originally developed are shown in Table 2.
Conclusions: This study demonstrates large differences in prevalence of low muscle mass based on different cut-off values. Uniformity in applying cut-off values in both the research setting and clinical practice is required, to be able to compare results across populations and settings.

References
1. A. van der Werf, J. A. E. Langius, M. A. E. de van der Scheuren, S. A. Nurmohamed, K. A. M. I. van der Pant, S. Blauwhoff-Buskermolen, et al., Percentiles for skeletal muscle index, area and radiation attenuation based on computed tomography imaging in a healthy Caucasian population, *European Journal of Clinical Nutrition* (2018), 72, 288-296, DOI:10.1038/s41430-017-0034-5
2. B. A. Derstine, S. A. Holcombe, B. E. Ross, N. C. Wang, G. L. Su, and S. C. Wang, Skeletal muscle cut-off values for sarcopenia diagnosis using T10 to L5 measurements in a healthy US population, *Scientific reports* (2018), 8, 11369, DOI:10.1038/s41598-018-29825-5
3. A. J. Cruz-Jentoft, G. Bahat, J. Bauer, Y. Boirie, O. Bruyère, T. Cederholm, et al. Sarcopenia: revised European consensus on definition and diagnosis, *Age Ageing* (2019), 48(1), 16-31
4. T. Cederholm, G. L. Jensen, M. I. T. D. Correia, M. C. Gonzalez, R. Fukushima, T. Higashiguchi, et al., GLIM criteria for the diagnosis of malnutrition - A consensus report from the global clinical nutrition community, *Clin Nutr.* (2019), 38(1),1-9
5. M. G. van Vledder, S. Levolger, N. Ayez, C. Verhoef, T. C. K. Tran, and J. N. M. IJzermans, Body composition

and outcome in patients undergoing resection of colorectal liver metastases, *Britisch Journal of Surgery Society* (2012), 99, 550-557
6. L. Martin, L. Birdsell, N. MacDonald, T. Reiman, M. T. Clandinin, L. J. McGargar, et al., Cancer cachexia in the age of obesity: Skeletal muscle depletion is a powerful prognostic factor, independent of body mass index, *Journal of clinical oncology* (2013), 13, 3112-1539, DOI: 10.1200/JCO.2012.45.2722
7. S. Levolger, M. G. van Vledder, R. Muslem, M. Koek, W. J. Niessen, R. A. De Man, et al., sarcopenia impairs survival in patients with potentially curable hepatocellular carcinoma, *Journal of surgical oncology* (2015), 112, 208-213, DOI: 10.1002:jso.23976
8. S. Cousin, A. Hollebecque, S. Koscielny, O. Mir, A. Varga, V. E. Baracos, et al., Skeletal muscle mass is associated with toxicity in patients included in phase I trials, *Invest New Drugs* (2014), 32, 382-387, DOI: 10.1007/s10637-013-0053-6
9. M. Mourtzakis, C. M. M. Prado, J. R. Lieffers, T. Reiman, L. J. McCargar, and V. E. Baracos, A practical and precise approach to quantification of body composition in cancer patients using computed tomography images acquired during routine care, *Appl. Physiol. Nutr. Metab.* (2008), 33, 997-1006, DOI: 10.1139/H08-075

Tables and figures

Figure 1. Contouring of muscles on the L3 level

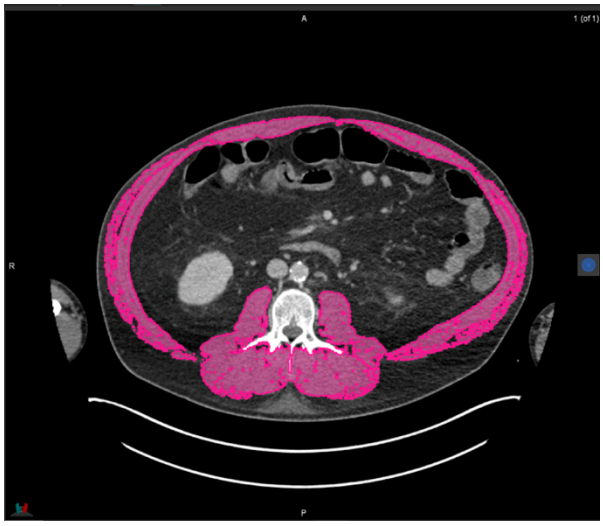


Table 1. Characteristics of the cancer patients

	Total	Melanoma	Oesophageal cancer	Head and neck cancer	P value
N	74	34	23	17	
Age (years, mean ± SD)	66.2 11.6	66.0 ±11.5	70.8 ±10.7	59.9 ±10.6	0.10
Weight (kg, mean ± SD)	79.3 ±18.2	87.5 ±18.0	75.1 ±14.2	67.4 ±15.6	<0.01
Height (m, mean ± SD)	1.73 ±0.08	1.75 ±0.09	1.72 ±0.09	1.73 ±0.07	0.30
BMI (kg/m², mean ± SD)	26.4 ±6.7	28.8 ±7.5	25.5 ±4.6	22.6 ±5.2	0.02

SD= Standard deviation

Table 2. Prevalence of low muscle mass based on the different cut-off values

Author	Cut-off value SMI (cm^2/m^2)	Total prevalence N (%)	Characteristics of the sample in which the cut-off value was originally developed			
			Age (years, mean ± SD)	BMI (km/m^2, mean ± SD)	Health condition	Determination cut-off value
van der Werf (2018)	41.6	13 (18%)	53 ±12	25.7 ±3.5	Healthy	5th Percentile
Van Vledder (2012) (5)	43.75	17 (23%)	64.5	25.2 ±3.8	Cancer (mixed)	Associated with lower survival
Derstine (2018) (2)	45.4	20 (27%)	31 ±6	27.0 ±4.8	Young and healthy	2 SD lower than mean value of SMI
Martin (2013) (6)	52	31 (42%)	54.8 ±11.4	25.6 ±5.4	Cancer (mixed)	Associated with lower survival
Levolger (2015) (7)	53	43 (58%)	62	25.2	Cancer (liver)	Associated with lower survival
Cousin (2014) (8)	54.1	51 (69%)	57	24.6 ±3.7	Cancer (mixed)	Median of SMI
Mourtzakis (2008) (9)	55	54 (73%)	63 ±10	25.7 ±5.2	Cancer (mixed)	Based on cut-offs for DXA

SMI= Skeletal muscle index, BMI= Body mass index, SD= Standard deviation, DXA= Dual energy X-ray absorptiometry

4-29

Sarcopenia predicts dose-limiting toxicity in pancreatic cancer treated with nab-paclitaxel and gemcitabine

Susie Youn[1,2], Angela Chen[3], Vincent Ha[3], Michael McCall[1], Dean Eurich[2], Carole Chambers[3], Michael Sawyer[2]

[1]Department of Surgery, University of Alberta, Edmonton, AB, Canada; [2]School of Public Health, University of Alberta, Edmonton, AB, Canada; [3]Cross Cancer Institute, University of Alberta, Edmonton, AB, Canada

Introduction: Pancreatic cancer is one of the leading causes of cancer-related deaths worldwide. Gemcitabine (GEM) plus nab-paclitaxel (nab) has been shown to improve overall survival (OS) compared to GEM monotherapy in patients with metastatic pancreatic cancer. However, GEM/nab is associated with increased toxicity. Our study evaluated whether sarcopenia increased the likelihood of chemotherapy toxicity in pancreatic cancer patients treated with GEM/nab.

Methods: A retrospective review was performed of all patients who received GEM/nab as first-line therapy for metastatic pancreatic cancer at a tertiary care center in Alberta, Canada from 2014-2017. Patients were included if a computed tomography (CT) scan of the abdomen and pelvis was performed within 60 days of starting chemotherapy. Skeletal muscle surface area was measured at the 3rd lumbar vertebrae and normalized for height to calculate skeletal muscle index (SMI). Optimal stratification was used to establish sex-specific SMI cut-offs with dose-limiting toxicity (DLT) as an outcome.

Results: One hundred and fifty-two patients were included in the study. Eighty-eight patients (57.8%) were male and median age was 66.5 years (range 34-95). SMI cut-offs were determined as <48.0 cm^2/m^2 in males and <39.55 cm^2/m^2 in females. Sarcopenia prevalence using these cut-offs was 54.6%. DLT incidence was significantly higher in sarcopenic versus non-sarcopenic patients (55.4 vs. 23.2% respectively, p<0.001). In multivariate logistic regression accounting for advanced age (≥65), sex, and performance status (PS), sarcopenia significantly increased the likelihood of DLT (OR 5.93, 95% CI 2.66-13.23, p<0.001, Table 1). Sarcopenia did not impact OS (HR 1.30, 95% CI 0.94-1.80, p=0.118) or progression-free survival (HR 0.66, 95% CI 0.42-1.03, p=0.071).

Conclusions: In pancreatic cancer treated with GEM/nab, sarcopenic patients are significantly more likely to experience DLT, independent of age, sex, and PS. These findings could have implications for reduced chemotherapy dosing in sarcopenic patients.

Table 1. Multivariate logistic regression of variables impacting likelihood of dose-limiting toxicity. OR, odds ratio; CI, confidence interval; ECOG, Eastern Cooperative Oncology Group performance status.

Variable	OR (95% CI)	p-value
Female sex	1.24 (0.61-2.51)	0.560
Age (≥65 years)	0.48 (0.23-1.01)	0.054
ECOG PS (baseline 0) 1 2	 0.56 (0.22-1.43) 0.42 (0.14-1.23)	 0.223 0.112
Sarcopenia	5.93 (2.66-13.23)	<0.001

4-30

Predicting chemotherapy toxicity in older patients with cancer based on variables related to sarcopenia. ONCOSARCO Project.

MJ Molina-Garrido
Head of the Cancer in the Elderly Consultation. Medical Oncology Department. Hospital General Virgen de la Luz in Cuenca, Cuenca, Spain

Introduction: It has been suggested that sarcopenic patients may have an increased risk of poor outcomes, including worse functional recovery, institutionalization, and higher mortality. In this abstract, we want to analyze which parameters related to sarcopenia (muscle mass, muscle strength and physical function) are associated with severe toxicity to chemotherapy in older patients with cancer.
Material and methods: We prospectively recruited 103 older patients of at least 70 years old with diagnosis of a solid malignant tumor who were evaluated in our Cancer in the Elderly Consultation of a Spanish general hospital before being treated with chemotherapy (ONCOSARCO Project). A prechemotherapy assessment that included sociodemographics, tumor/treatment variables, and variables related to sarcopenia (muscle mass: skeletal muscle mass index; muscle strength: pinch-gauge, spherical and cylindrical hand grip; physical function: gait speed, 5 sit-to-stand chair test, hip flexion strength and knee extension strength) was performed. A prechemotherapy assessment
that included sociodemographics, tumor/treatment variables, and geriatric assessment variables was performed. Association between these factors and the development. of grade 3–5 toxicity was examined by using logistic regression. Association between those factors related with sarcopenia, and the development of grade 3–5 toxicity after four months of treatment was examined by using logistic regression.
Results: Between all the analyzed variables, just the basal knee extension strength (odds ratio 0.839; 95% confidence interval 0.688-1.023; p=0.083) was associated with toxicity. This model has a specificity of 14.8% and a sensitivity of 90.2% and it properly classifies 67% of cases.
Conclusions: Older patients with cancer with low basal extension knee strength have a higher risk of severe chemotherapy toxicity. This variable should be considered when planning to initiate chemotherapy in these patients and could be considered to be included in the initial algorithm to detect sarcopenia in this subpopulation.

This project was supported by a Beca Mutua Madrileña

4-31

Who is most at risk of severe chemotherapy toxicity, sarcopenic or frail elderly patients?. The ONCOSARCO Project

MJ Molina-Garrido
Cancer in the Elderly Consultation, Medical Oncology Department, Hospital General Virgen de la Luz in Cuenca, Cuenca, Spain

Introduction: In cancer patients, sarcopenia has been shown to lead to decreased overall survival and higher levels of morbidity. Few data exist comparing the impact of sarcopenia and frailty on severe toxicity to chemotherapy in patients with cancer (just solid tumors).
To assess the association between sarcopenia, frailty and chemotherapy toxicity (grade 3-5), we conducted a prospective analysis (The ONCOSARCO Project) of consecutive patients ≥70 years treated with chemotherapy.
Material and methods: Frailty (measured by Fried's criteria and Balducci's criteria) and sarcopenia (defined as low muscle muss with alternative cutoff points and low muscle strength-, as indicated by the European Working Group on Sarcopenia in Older People (EWGSOP1) criteria) were included for analysis. Age, sex, Charlson comorbidity index, type of tumor, tumoral stage, regimen of chemotherapy (mono- or polychemotherapy) and initial doses of chemotherapy (full or reduced doses) were also included in this analysis (logistic regression).
Results: 103 patients met the criteria. Approximately 60% of patients had stage IV tumors. 50.5% of patients were treated with polychemotherapy and 56.3% received reduced doses of chemotherapy.
Thirty patients (29.1%) were sarcopenic, 6 patients (5.8%) were frail according to Balducci's criteria and 45.6% were frail according to Fried's criteria.
In the multivariable analysis, just a) prefrailty compared with frailty according to Fried's criteria (odds ratio- OR 0.329; 95% confidence interval- CI: 0.112-0.968; p=0.044), b) sex female (OR 0.289; 95% CI: 0.085-0.980; p=0.046), and c) full doses of chemotherapy (OR 4.252; 95% CI 1.400-12.909; p=0.011) were significantly associated to the risk of severe chemotherapy toxicity. However, sarcopenia (p=0.620) or frailty measured by Balducci's criteria (p=0.781) were not significantly associated to chemotherapy toxicity.
Conclusions: According to our results, sarcopenia is not a significant predictor of severe chemotherapy toxicity in older patients with cancer. However, frailty, as defined by Fried, is associated with this adverse event.

This project was supported by a Beca Mutua Madrileña

4-32

Could aortic calcification reveal the body composition inflammatory changes?

Ioanna Drami[1], Katarina Knight[2], Ross Dolan[2], Laura E Gould[1], Edward T Pring[1], John T Jenkins[1]
[1]St Mark's Hospital and Academic Institute, Imperial College London, London, UK; [2]Academic Unit of Colorectal Surgery University of Glasgow, Glasgow, UK

Introduction: The CT body composition (BC) metrics of visceral adiposity and myosteatosis relate to systemic inflammation and surgical outcomes in different cancer types. Aortic calcification (AC) is a result of a systemic inflammatory pathway. The aim of this study was to identify a correlation between these CT derived markers of inflammation and aortic calcification in a rectal cancer population.
Methods: Analysis was performed on a prospectively maintained database of 391 rectal cancer patients from March 2006 to January 2017. BC analysis was performed at their preoperative CT, by an experienced radiologist using Slice-O-Matic. AC was scored on the same CT images using a validated semi-quantitative method. Calcifications were evaluated in the axial plane, by a trained assessor, at the proximal aorta (origin of the superior mesenteric artery) and the distal aorta (level of the aortoiliac bifurcation). A score of 0 to 4 was assigned to each aortic level, according to the number of calcified quadrants visible.
Results: Median age of our cohort was 67 years old, 69% were sarcopenic, 49% had VO and 66% had myosteatosis. There was poor correlation (Spearman's test) for both proximal and distal AC in relation to VO (r_s 0.31, p= 0.78, r_s 0.142, p= 0.199 respectively). The correlation between proximal AC, distal AC and myosteatosis was weak, (r_s 0.12, p=0.914, r_s -0.27, p=0.806).
Conclusions: AC and VO and myosteatosis did not significantly correlate in our rectal cancer population. Further research is required to examine these phenomena in a population with more profound and prevalent AC to affirm these findings.

4-33

Bioelectrical impedance analysis-derived phase angle as a marker of Computerized Tomography-muscle mass abnormalities and muscle function in patients with cancer

Nilian Carla Souza[1,2], Carla Maria Avesani[3,4], Carla M. Prado [5], Renata Brum Martucci[1,3], Viviane Dias Rodrigues[1], Nivaldo Barroso de Pinho[6], Steven B. Heymsfield[7], Maria Cristina Gonzalez[8]

[1]Nutrition and Dietetic Service, Cancer Hospital Unit I, National Cancer Institute José Alencar Gomes da Silva, Rio de Janeiro, Brazil; [2]Graduation Program in Nutrition, Food and Health, Nutrition Institute, Rio de Janeiro State University, Rio de Janeiro, Brazil; [3]Department of Applied Nutrition, Nutrition Institute, Rio de Janeiro State University, Rio de Janeiro, Brazil; [4]Clinical Science, Intervention and Technology, Karolinska Institutet, Stockholm, Sweden; [5]Human Nutrition Research Unit, Department of Agricultural, Food and Nutritional Science, University of Alberta, Edmonton, Alberta, Canada; [6]Brazilian Society of Oncology Nutrition, Rio de Janeiro, Brazil; [7]Pennington Biomedical Research Center, Louisiana State University, Baton Rouge, Louisiana, USA; [8]Post-graduate Program in Health and Behavior, Catholic University of Pelotas, Pelotas, Rio Grande do Sul, Brazil

Introduction: Considering the applicability of phase angle (PA) as a marker of muscle mass and function, we aimed to investigate whether PA is a predictor of muscle mass abnormalities and functional impairment in patients with cancer.
Methods: In a sample of patients with colorectal cancer (CRC), PA was obtained from measurements of resistance and reactance from bioelectrical impedance analysis. Computerized tomography imaging at the third lumbar vertebra was used to evaluate muscle abnormalities by quantifying skeletal muscle index (SMI) and skeletal muscle density (SMD). Muscle function was assessed by handgrip strength (HGS) and gait speed (GS). Low SMI was classified as: < 45.4 cm^2/m^2 for men and < 34.4 cm^2/m^2 for women, and low HGS as: <30 kg for men and <16 kg for women.
Results: This cross-sectional study included 190 patients (age 60.5 ± 11.3 years; 57% men). PA was highly correlated with SMI (r = 0.70) and moderately correlated with HGS (r = 0.54). PA explained 48% of the SMI variability (R^2 = 0.485), 21% of the SMD variability (R^2 = 0.214), 26% of HGS (R^2 = 0.261) and 9.8% of GS (R^2 = 0.098). In the multivariate model adjusted for age, sex, body mas index, performance status, comorbidities and cancer stage, 1-degree decrease in PA was associated with low SMI (Odds Ratio (OR) = 6.56, 95% CI: 2.90-14.86) and also with low SMI and HGS combined (OR = 11.10, 95% CI: 2.61-47.25). In addition, Receiving Operating Characteristics curve analysis showed that PA had a good diagnostic accuracy for detecting low SMI and low SMI and HGS combined (AUC = 0.81, 95% CI: 0.74-0.88; AUC= 0.82, 95% CI: 0.74-0.89; respectively).
Conclusions: PA was a predictor of muscle abnormalities and functional impairment and had a good diagnostic accuracy for detecting low muscle mass and strength in patients with CRC.

4-34

Does sarcopenia equate to frailty: comparing subjects EWGSOP sarcopenic status and their Clinical Frailty Scale?

Angela G Juby[1], Christpoher MJ Davis[2], Suglo Minimaana[1], Diana R Mager[3]

[1]Division of Geriatrics, Department of Medicine, Faculty of Medicine and Dentistry; [2]Faculty of Physical Education; [3]Faculty of Agriculture, Food and Nutrition Sciences; University of Alberta, Edmonton, Canada

Introduction: The prevalence of sarcopenia increases with age. Sarcopenia is associated with an increased risk for frailty, drug side effects, worsening chronic disease, falls/fractures, and dependence. The European Working Group of Sarcopenia in Older People (EWGSOP) classifies sarcopenic status on lean muscle mass, grip strength and gait speed. The Clinical Frailty Scale (CFS) has 9 classifications. Because sarcopenia and frailty both increase with age, are they two sides of the same coin, or do we need to screen for both?
Methods: Community dwelling Seniors participating in a wellness study were evaluated for EWGSOP sarcopenic status. Blinded to this information, they were separately evaluated using CFS.
Results: There were 39 participants (6 men, 33 women), average age 75.7years (67-90). Average MMSE 29.1 (22-30), MoCA 26.4 (18-30). For sarcopenic status: 11 were normal, 11 were obese, and the remainder various stages of sarcopenia. For frailty status: 24 were CFS 3 or higher. Poor correlation was found between EWGSOP sarcopenic status and CFS (R=0.43), lean muscle mass (appendicular lean mass/height2) and CFS (R=0.21 in women), EWGSOP grip strength cut-offs and CFS (R=0.46). However, good correlation was found between CFS and 6m absolute walk time (R=0.82) and gait speed (R=-0.61). As these subjects were community dwelling, this study is limited by fewer individuals in the sarcopenic or frail spectrum.
Conclusions: This study suggests there is poor correlation in community dwelling Seniors between sarcopenic status (as defined by EWGSOP criteria), absolute muscle mass or grip strength and frailty. However, there was good correlation with gait time and speed, suggesting that functional measures of muscle are more important than absolute muscle mass in the development of frailty. Sarcopenia, as defined by EWGSOP does not equate to frailty as defined by CFS. The use of standardized definitions has important implications for research into potential therapeutic interventions.

4-35

Older men with sarcopenia have rapid progression of abdominal aortic calcification – the prospective MINOS study

Pawel Szulc, Roland Chapurlat

INSERM UMR1033, University of Lyon, Hôpital Edouard Herriot, Lyon, France

Low muscle mass and strength (sarcopenia) are associated with high cardiovascular risk. We assessed the risk of rapid progression of abdominal aortic calcification (AAC) in older men with low relative appendicular lean mass (RALM) and poor physical performance.
A cohort of 621 men aged 50-85 was followed prospectively. Body composition was assessed by DXA (HOLOGIC QDR1500). Poor physical performance was defined as incapacity to perform ≥1 of 5 clinical tests (balance, muscle strength). AAC was assessed using Kauppila's semiquantitative score (baseline, after 3 and 7.5 years). The improvement of reclassification was assessed using Harrell's test (comparison of the areas under the curve [AUC]).
Rapid AAC progression (>0.5 point/year) was found in 167 men (27%). After adjustment for potential confounders including baseline AAC, the risk of rapid AAC progression increased with lower RALM (OR=1.37/SD, 95%CI: 1.09–1.74, p<0.01) and was higher in the lowest (<7.4kg/m^2) vs. the highest (>8.6kg/m^2) quartile (OR=1.99, 95%CI: 1.06–3.74, p<0.01). Poor physical performance was associated with rapid AAC progression (OR=2.46, 95%CI: 1.16–5.21, p<0.05). Men who had both low RALM and poor physical performance had higher risk of rapid AAC progression (OR=4.98, 95%CI: 1.72–14.43, p<0.01) vs. men without these characteristics. Low RALM and poor physical performance were each associated with AAC progression mainly in men without other risk factors, e.g. 310 men aged <70 with normal testosteronemia and without diabetes or heart disease (OR=2.33/SD decrease, 95%CI: 1.27–4.28, p<0.01 and

OR=6.01, 95%CI: 1.06–33.97, p<0.05, respectively). The assessment of RALM and physical function improved the identification of men with accelerated AAC progression slightly but significantly after adjustment for the confounders including baseline severity of calcification (ΔAUC=0.026, 95%CI: 0.005–0.046, p<0.05).
Overall, low RALM and poor physical performance are associated with higher risk of rapid AAC progression and possibly represent another measure of cardiovascular risk.

4-36
Sirtuin1 function is critical for preventing skeletal muscle wasting in cerebral ischemic stroke

Junaith S Mohamed, Peter J Ferrandi, Stephen E Alway
Department of Diagnostic and Health Sciences, College of Health Professions, The University of Tennessee Health Science Center, Memphis, TN, USA

Introduction: Stroke, a sudden interruption in the blood supply to the brain, is a leading cause of mortality and long-term disability in patients worldwide. All acute stroke severely induces muscle wasting and weakness, which predominantly contributes more to the long-term functional disability in stroke patients than any other disease. No approved pharmacological drug is presently available to treat stroke-induced muscle loss due to the lack of our understanding of the molecular and/or cellular mechanisms that underlie muscle wasting in stroke. As a result, nearly two-thirds of the stroke survivors remain in a state of insufficient recovery from the physical disability that has drastically reduced their health and quality of life.
Methods: To understand the molecular origin of post-stroke muscle wasting, we performed a high-throughput RNA sequencing using a pre-clinical mouse model of cerebral ischemic stroke and validated the promising candidate using gene knock in and knockout strategies as well as a transgenic mouse model.
Results: RNA-seq data revealed that the elevated muscle wasting observed in response to stroke was primarily associated with the altered expression of genes involved in the muscle protein degradation pathways. Further analysis of RNA-seq data identified Sirtuin1 (SirT1) as a critical protein that plays a significant role in regulating post-stroke muscle mass. SirT1 rescue in skeletal muscle prevented stroke-induced muscle wasting *via* inhibiting the activation of the ubiquitin proteasomal pathway and restoring autophagy function by governing their upstream regulators.
Conclusions: While our RNA-seq identified dysregulation of many genes, SirT1 play a major role in preserving post-stroke muscle mass and that protection needs SirT1 deacetylase activity.

5-01
Muscle Mass as a Potential Marker for Chronic Maltreatment in the Pediatric Non-Accidental Trauma Patient

Gregory Metzger[1]; Yuri V. Sebastião[1]; Carley Lutz[1]: Katherine J. Deans[1,2]; Peter C. Minneci[1,2]
[1]Center for Surgical Outcomes Research, Abigail Wexner Research Institute, Nationwide Children's Hospital, Columbus, OH; [2]Department of Pediatric Surgery, Nationwide Children's Hospital, Columbus, OH

Introduction: Non-accidental trauma (NAT) is a leading cause of injury and death amongst young children. Although NAT is often recorded as a single event, children that experience NAT are at risk of suffering chronic maltreatment. Decreased muscle mass has been identified in pediatric populations with chronic diseases and it may be a useful measure to identify chronic maltreatment in children with documented NAT. The purpose of this study was to compare the muscle mass of a pediatric population with documented NAT to a population of healthy patients.
Methods: Patients aged 2 to 18 years with documented non-accidental trauma who underwent an abdominal CT scan were identified. Bilateral psoas muscle surface area was measured via CT. Quantile regression was used to determine age- and sex-specific percentiles of psoas muscle area and psoas muscle index (PMI, cm/m^2). A previously identified healthy pediatric population (n=774) was used as reference for comparison of the 25th, 50th, and 75th percentiles of psoas area and PMI. Outcomes from the NAT encounter were recorded.
Results: A total of 73 NAT patients were identified (59% male; median age: 3.5 years, IQR: 2.4-5.2). About 70% of male and 63% of female NAT patients charted below the reference 50th percentile for PMI (Figure 1). Discharge to a rehab facility was documented for 11% (8) of patients and 8% (6) experienced in-hospital mortality. Admission was required for 74% (54) and 29% (21) spent at least 1 day in the ICU. There were no significant differences between NAT patients and the reference population in age-adjusted percentiles for total psoas muscle area in either sex. However, the 50th and 75th percentiles of PMI for male NAT patients were significantly lower than the reference population.
Conclusion: PMI may represent a means to screen for chronic maltreatment in children with documented NAT.

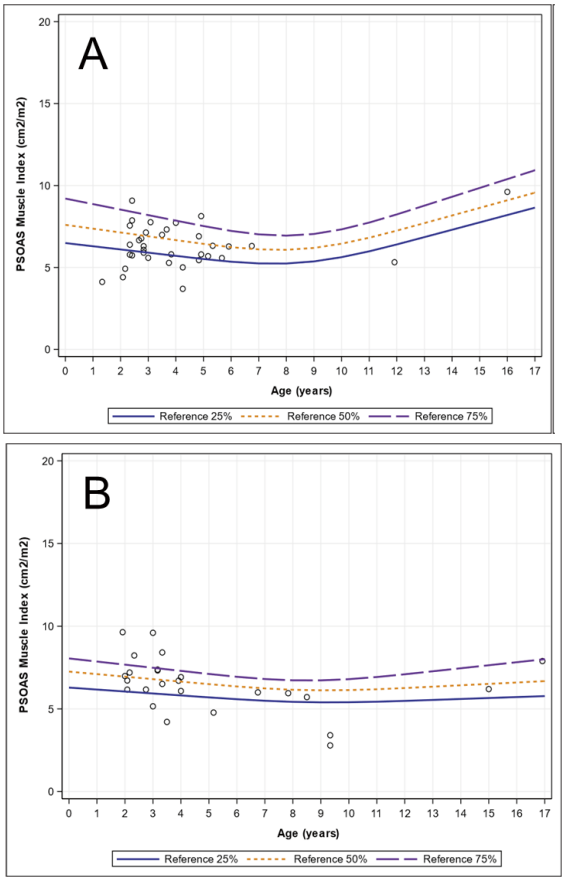


Figure 1: The Psoas Muscle Index (PMI) for individual A) male and B) female NAT patients plotted against reference curves derived from a healthy cohort. Lines show the 25%, 50%, and 75% percentiles.

5-02
Evaluation of the nutrients intake in a group of Jordanian elderly people with sarcopenia syndrome in Amman.

Sarah Z. Majali, Hadeel A. Ghazzawi
The University of Jordan, Amman, Jordan

Aim: Sarcopenia is an age-related syndrome that is characterized by a progressive loss of muscle mass, strength and function. This study was performed in order to evaluate nutrients intakes, physical activity level and to investigate the effect of sarcopenia syndrome on food intake in a group of Jordanian elderly people with sarcopenia syndrome in Amman.
Method: The study sample consisted of 25 non-sarcopenic people and 25 sarcopenic patient's aged more than 60-year old with male to female ratio of (1:1). A special questionnaire was used to collect demographic data, health data and data about syndrome characteristics, nutritional assessment and physical activity. A 24-hour recall was also used to collect food intake data. Body weight, height, skinfold thicknesses were measured.
Results: The mean age of the sarcopenic patient's was 77.5 ± 6.9 years and the mean weight was significantly lower in sarcopenic patient's than that of the non-sarcopenic people. In this study, all macronutrients and micronutrients from dietary intake information were analyzed. Vitamin intakes (water and fat soluble) as well as minerals (major and trace), amino acids and essential fatty acids were assessed. The mean intake of energy and carbohydrates, fat and dietary fiber was lower than their recommendations, while the mean intake of protein was within the range of their recommendation in sarcopenia group. The mean intake of omega 3 and omega 6 was below than their recommendations.
Conclusion: It could be concluded that sarcopenic patient's in Jordan have similar characteristics with patient's studied in worldwide regarding age of patient's, female to male ratio and main symptoms. Sarcopenic patient's in Jordan generally have inadequate dietary intake. Therefore, the diet of sarcopenic patient's needs modification and follow-up.
Keywords: Sarcopenia syndrome, Macronutrients, Micronutrients, Jordan, body fat percentage, nutritional assessment, physical activity level.

5-03
Association of muscle mass reduction and hand grip strength reduction with health-related quality of life of patients with colorectal cancer

Mariana Vieira Barbosa[1], Mylena Pinto dos Santos[2], Jocilene Alves Leite[3], Viviane Dias Rodrigues[3], Renata Brum Martucci[3,4]
[1]Post-graduate Program in Medical Science, Medical Science Faculty, State University of Rio de Janeiro, Rio de Janeiro, RJ, Brazil; [2]Post-graduate Program in Food, Nutrition and Health, Nutrition Institute, State University of Rio de Janeiro, Rio de Janeiro, RJ, Brazil; [3]Nutrition and Dietetic Service, Cancer Hospital Unit I, National Cancer Institute José Alencar Gomes da Silva, Rio de Janeiro, RJ, Brazil; [4]Department of Applied Nutrition, Nutrition Institute, State University of Rio de Janeiro, Rio de Janeiro, RJ, Brazil

Introduction: The association of parameters of body composition and functionality with health-related quality of life (HRQoL) in cancer patients is poorly investigated, even though it is impacted by the disease. Purpose: We aimed to evaluate the association of muscle mass reduction and handgrip strength (HGS) reduction with HRQoL of patients with colorectal cancer (CRC).
Methods: A cross-sectional study with patients with CRC, at the National Cancer Institute, in 2018. The muscle mass was assessed by computed tomography images and reported as skeletal muscle mass index (SMI), with the cutoff points: <38.5cm^2/m^2 (women) and <52.4cm^2/m^2 (men) (PRADO et al., 2008). The HGS was measured by the Jamar® hydraulic hand dynamometer (Sammons Preston TM, Canada), with the cutoff points: <16kg (women) and <27kg (men) (CRUZ-JENTOFT et al., 2019). HRQoL was assessed using the EORTC questionnaire QLQ-C30 (European Organization for Research and Treatment of Cancer Quality of Life Questionnaire). Multivariate linear regression analysis was performed between reduced SMI and reduced HGS and the HRQoL domains (95% CI).
Results: A total of 142 patients were included, with a mean of age of 62.7 years (±11.4). Of these, 48 patients had reduced SMI and 22 patients had reduced HGS. After adjustment for socio-demographic, clinical and nutritional variables, the reduction in SMI was not associated with the HRQoL scales. The reduction in HGS was negatively associated with HRQoL, reducing the overall health status (B=-16.4; 95% CI:-25.6/-7.3; p=0.001), the physical (B=-14,7; 95% CI:-23.6/-5.8; p=0.001) and emotional functions (B=-25.2; 95% CI:-43.0/-7.4; p=0.006), and increasing symptoms of fatigue (B=13.3; 95% CI:2.0/24.5; p=0.021), pain (B=18.4; 95% CI:2.3/34.4; p=0.025), dyspnea (B=11.3; 95% CI:2.0/20.5; p=0.017) and loss of appetite (B=12.6; 95% CI:0.6/24.6; p=0.039).
Conclusion: The reduction of HGS, a measure that evaluates strength and functional status, was negatively associated with the HRQoL of patients with CRC.

5-04
Ovarian cancer ascites induces skeletal muscle wasting in vitro

Jorne Ubachs[1,2,3,4], Wouter van de Worp[4,5], Rianne Vaes[3,4], Kenneth Pasmans[4,8], Ramon Langen[4,5], Ruth Meex[4,8], Sandrina Lambrechts[1,2], Toon Van Gorp[6], Roy Kruitwagen[1,2], Steven W.M. Olde Damink[3,4,7], Sander S. Rensen[3,4]
[1]Department of Obstetrics and Gynecology, Maastricht University Medical Centre, P.O. box 5800, 6202 AZ, Maastricht, the Netherlands; [2]GROW - School for Oncology and Developmental Biology, Maastricht University, P.O. box 616, 6200 MD, Maastricht, the Netherlands; [3]Department of Surgery, Maastricht University Medical Centre, P.O. box 6202 AZ Maastricht, the Netherlands; [4]NUTRIM, school of Nutrition and Translational Research in Metabolism, Maastricht University, P.O. box 616, 6200 MD, Maastricht, the Netherlands; [5]Department of Pulmonology, Maastricht University, P.O. box 616, 6200 MD, Maastricht, the Netherlands; [6] Department of Obstetrics and Gynecology, Division of Gynecological Oncology, University Hospitals Leuven, Leuven Cancer Institute, Herestraat 49, 3000 Leuven, Belgium; [7] Department of General, Visceral- and Transplantation Surgery, RWTH Aachen University, Germany; [8]Department of Human Biology, Maastricht University P.O. Box 616, 6200 MD Maastricht, The Netherlands

Background: Cachexia-associated skeletal muscle wasting or 'sarcopenia' is highly prevalent in ovarian cancer, and contributes to poor outcome. Drivers of cachexia-associated sarcopenia in ovarian cancer remain elusive, underscoring the need for novel and better models to identify tumor factors inducing sarcopenia. We aimed to assess whether factors present in ascites of sarcopenic versus non-sarcopenic ovarian cancer patients differentially affect protein metabolism in skeletal muscle cells, and to determine if these effects are correlated to cachexia-related patient characteristics.
Methods: Fifteen patients with an ovarian mass and ascites underwent extensive physical screening focusing on cachexia-related parameters. Patients were diagnosed with malignant (n=12) or benign disease (n=3). Based on CT-based body composition imaging, six cancer patients were classified as sarcopenic and six were not; the three patients with a benign condition served as an additional non-sarcopenic control group. Ascites was collected and used for *in vitro* exposure of C2C12 myotubes and direct measurements of protein synthesis and breakdown by

radioactive isotope tracing, qPCR-based analysis of atrophy-related gene expression, and NF-kB activity reporter assays.
Results: C2C12 protein synthesis was lower after exposure to ascites from sarcopenic patients (sarcopenia 3.1±0.1 nmol/h/mg protein vs. non-sarcopenia 5.5±0.2 nmol/h/mg protein, p<0.01), and protein breakdown rates tended to be higher (sarcopenia 31.2±5.2% vs. non-sarcopenia 20.9±1.9%, p=0.08). Ascites did not affect MuRF-1, Atrogin-1, or REDD1 expression of C2C12 myotubes, but NF-κB activity was specifically increased in cells exposed to ascites from sarcopenic patients (sarcopenia 2.2±0.4 vs. non-sarcopenia 1.2±0.2, p=0.01). Protein synthesis and breakdown correlated with NF-κB activity (r_s=-0.60, p=0.03 and r_s=0.67, p=0.01, respectively). The skeletal muscle index of the ascites donors was correlated to both *in vitro* protein synthesis (r_s=0.70, p=0.005) and protein breakdown rates (r_s=-0.57, p=0.04).
Conclusion: Ascites of sarcopenic ovarian cancer patients induces pronounced skeletal muscle protein metabolism changes in C2C12 cells that correlate with clinical muscle measures of the patient and are characteristic of cachexia. The use of ascites offers a new experimental tool to study the impact of both tumor-derived and systemic factors in various cachexia model systems, enabling identification of novel drivers of tissue wasting in ovarian cancer.

5-05
Postoperative loss of skeletal muscle mass is prognostic of poor survival after gastric cancer surgery

Shanjun Tan[1], Feng Zhou[2], Zhige Zhang[1], Junjie Wang[1], Jiahao Xu[1], Qiulin Zhuang[1], Qiulei Xi[1], Qingyang Meng[1], Yi Jiang[1], Guohao Wu[1]
[1]Department of General Surgery/Shanghai Clinical Nutrition Research Center, Zhongshan Hospital, Fudan University, Shanghai, China, [2]Department of General, Visceral and Transplant Surgery, University Hospital Heidelberg, Heidelberg, Germany

Background: Skeletal muscle mass deterioration is common in gastric cancer (GC) patients and is linked to poor prognosis, but information regarding the effect of skeletal muscle mass changes in the postoperative period is scarce. Here, we investigated the link between postoperative loss of skeletal muscle mass and survival following GC surgery.
Methods: Patients who underwent GC surgery between January 2015 and December 2016 were prospectively recruited into the study. Computed tomography at L3 vertebral level was used to examine skeletal muscle index prior to surgery and 6 months after surgery. Skeletal muscle index changes were categorized as presence or absence of ≥ 5% loss. Overall survival (OS) and disease-free survival (DFS) were analyzed, and Cox proportional hazard models used to identify their predictors.
Results: The study comprised of 318 gastric cancer patients of which 63.5% were male. The group's mean age was 58.14 years. Sixty-five patients experienced postoperative skeletal muscle index loss ≥ 5% and had poorer OS (P = 0.004) and DFS (P = 0.020). We find that postoperative skeletal muscle index loss ≥ 5% predicts OS [hazard ratio (HR): 2.769, 95% confidence interval (CI): 1.865-4.111; P < 0.001] and DFS (HR: 2.533, 95% CI: 1.753-3.659; P < 0.001).
Conclusions: Loss of skeletal muscle mass postoperatively is linked to poor survival following GC surgery. Further studies are needed to determine whether stabilizing or enhancing skeletal muscle mass improves survival.

5-06
Respiratory function in subjects recovered from COVID-19 with sarcopenia

Carlos Sánchez-Moreno, Dulce González-Islas, Arturo Orea-Tejeda, Susana Galicia-Amor, Carlos Aboitiz-Rivera, Esperanza Trejo-Mellado, Juan carlos Garcia-Hernández, Lucero Flores-Diaz, Elisabeth Juárez-Silva, Patricia Martel-Palomo
Instituto Nacional de Enfermedades Respiratorias "Ismael Cosío Villegas", Mexico City, Mexico

Introducction: Coronavirus disease 2019 (Covid-19) is an emerging disease that causes severe complications in subjects with risk factors: advanced age, diabetes, hypertension, obesity, among others. Patients with a diagnosis of COVID-19 with severe disease have prolonged hospital stays, which causes dynapenia, muscle depletion, and sarcopenia, concomitant factors that could condition a more severe evolution of the disease and poor prognosis. Besides, the subjects recovered from COVID-19 have post-recovery sequelae such as a reduction in muscle mass, respiratory function.
Objective: Describe lung function in recovered COVID-19 whith sarcopenia patients.
Methods: Cross-sectional study in 102 patients recovered from COVID-19. Patients who required hospitalization due to unfavorable clinical evolution due to COVID-19 were included. Lung function was assessed using PIMAX, PEMAX, DLCO2 spirometry. Body composition was evaluated by electrical bioimpedance. Sarcopenia was diagnosed by appendicular muscle mass index (men: <7 kg / m, women <5.5 kg) and hand strength (men <27 kg, women <16 kg).
Results: The average age of the population was 44 years ± 11.66, 58.88% were men, the subjects with sarcopenia had a higher prevalence of diabetes (26.32% vs 7.81%, p = 0.039) and hypertension (28.95% vs 12.5%, p = 0.039) compared to subjects without sarcopenia. Subjects without sarcopenia had better respiratory parameters of FEV1 (2.73 lt vs 3.19 lt, p = 0.003), FEV1 post (2.70 lt vs 3.24 lt, p = 0.0005), FVC (3.19 lt vs 3.9 lt, p < 0.001), FVC post (3.22 lt vs 3.90 lt, p < 0.001), FEV1 / FVC (84.17 vs 81.83, p = 0.040), DLCO (25.21 vs 31.83, p < 0.001), and better exercise tolerance (464.16 m vs 535.84 m, p < 0.001) compared to the subjects with sarcopenia.
Conclusion: Sarcopenic patients recovered from COVID-19 have a higher prevalence of comorbidities, worse respiratory function, and probably worse prognosis.

5-07
Impact of prolonged sepsis on biomechanical and structural myofibrillar properties

Chloë Goossens[1], Sarah Derde[1], Dominik Schneidereit[2], Michael Haug[2], Barbara Reischl[2], Oliver Friedrich[2], Greet Van den Berghe[1], Lies Langouche[1]
[1]Clinical Division and Laboratory of Intensive Care Medicine, Department of Cellular and Molecular Medicine, KU Leuven, Leuven, Belgium; [2] Institute of Medical Biotechnology, Friedrich-Alexander-University Erlangen-Nürnberg, Erlangen, Germany

Introduction: Debilitating muscle weakness frequently develops in septic patients. As ultrastructural myofiber abnormalities have been linked to impaired force output in other muscle disorders, we evaluated the effect of sepsis on biomechanical and structural myofibrillar properties.
Methods: We used a validated murine model of prolonged sepsis-induced muscle weakness (cecal-ligation-and-puncture) and pair-fed healthy control mice. After 5 days, mice were sacrificed (n=31) and EDL myofibers were mechanically isolated. The *MyoRobot* opto-biomechatronics system[1] was used to evaluate calcium sensitivity of the contractile apparatus (force production at decreasing pCa steps) and myofiber axial elasticity (passively stretching myofibers to

140% of L_0). Sarcomere organization was assessed with label-free imaging of myosin filaments by second harmonic generation microscopy and quantitative morphometry analysis.
Results: Parameters of calcium sensitivity (force-pCa curve-derived pCa_{50} values and Hill coefficients), were similar in septic mice and controls ($p \geq 0.6$). Myofibrillar myosin parallel orientation was reduced with sepsis ($p < 0.0001$), indicating sarcomere disorganization. During passive stretching, myofibers from septic mice ruptured more frequently than those from controls (73% vs. 48% rupturing; $p = 0.04$). The subgroup of septic myofibers that ruptured showed lower axial compliance and higher Young's moduli ($p < 0.0001$), pointing towards elevated myofibrillar stiffness. Additionally, myofibers that ruptured also produced less maximal force prior to the stretching protocol than those that did not rupture, but only in septic mice ($p = 0.04$), not in controls ($p = 0.3$). The subgroup of septic myofibers that could be fully stretched without rupturing showed less passive restoration force at 140% stretch and lower Young's moduli than controls ($p \leq 0.03$).
Conclusions: Prolonged sepsis altered myofibrillar properties. The largest subgroup of septic myofibers was less capable of tolerating strain, which appeared associated with reduced active myofibrillar force generation. These changes on the myofibrillar level likely affect the structural integrity and force generation of the complete muscle.

1 Haug et al. (2019). Biosens Bioelectron. 138:111284

5-08
Synergistic short-term and long-term effects of TGF-β1 and 3 on collagen production in differentiating myoblasts

Andi Shi[1,3,4], Michèle Hillege[1], Wüst, R[1], Gang Wu[2], Richard T Jaspers[1]
[1]Laboratory for Myology, Department of Human Movement Sciences, Faculty of Behavioural and Movement Sciences, Vrije Universiteit Amsterdam (VU), Amsterdam Movement Sciences (AMS), Amsterdam, The Netherlands; [2]Department of Oral Implantology and Prosthetic Dentistry, Academic Centre for Dentistry Amsterdam (ACTA), University of Amsterdam (UvA) and Vrije Universiteit Amsterdam (VU), The Netherlands; [3]Department of Oral and Maxillofacial Surgery/Pathology, Amsterdam UMC and Academic Center for Dentistry Amsterdam (ACTA), Vrije Universiteit Amsterdam (VU), Amsterdam Movement Science (AMS), Amsterdam, the Netherlands; [4]Key Laboratory of Oral Medicine, Guangzhou Institute of Oral Disease, Affiliated Stomatology Hospital of Guangzhou Medical University, Guangzhou Medical University, Guangzhou, China

Background: Skeletal muscle fibrosis and regeneration are modulated by transforming growth factor-β superfamily (TGF-β). Amongst them, TGF-β1 is highly potent pro-fibrogenic factors, while TGF-β3 has been implicated to reduce scar tissue and collagen production within in skin and vocal mucosa. However, little is known about the individual and synergistic short-term and long-term effects of TGF-β1 and 3 on collagen expression in myoblasts and myotubes.
Methods: In this study C2C12 myoblasts were incubated with TGF-β1 or/and TGF-β3 for 24 h up to 7 days. q-PCR, Sirius red staining, immunofluorescence staining (IF) and CyQUANT cell proliferation assay were performed to determine collagen accumulation, cell differentiation and proliferation.
Results: Here we show that fibrotic genes expression (*Col1A1*, *Ctgf* and *Fgf-2*) of C2C12 myoblasts, except for *Col4A1*, significantly increased by each treatment after 24 h. In addition, *Acvr1b* and *Tgfbr1* expression declined after 48 h, while *Tgf-β1* expression was upregulated by either TGF-β1 or TGF-β3. After 3 days of culture in growth medium (GM), collagen production quantified by Sirius red of C2C12 myoblasts was stimulated by TGF-β1 and/or TGF-β3. During follow up, after 7 days in GM, myoblasts were differentiated into myotubes, collagen deposition was doubled while both isoforms did not stimulate C2C12 collagen production any further. Collagen was localized within and outside myotubes. Both TGF-β1 and TGF-β3 inhibited myotube differentiation, which was antagonized by TGF-β receptor I inhibitor (TβRI). Enhanced collagen production by TGF-β1 and TGF-β3 after 3 days of culture in GM was not due to increased number of myoblasts.
Conclusions: These results indicate that both TGF-β1 and TGF-β3 individually and in combination stimulate collagen production of C2C12 differentiating myoblasts. TGF-β3 is not effective to antagonize TGF-β1 induced muscle fibrosis. Together these data suggest that elevated TGF-β isoform expression during muscle regeneration contributes to the collagen production by enhanced collagen production of differentiating myoblasts.

5-09
Lack of TGF-β type I receptors *Tgfbr1* and *Acvr1b* synergistically stimulate myofibre hypertrophy and accelerates early muscle regeneration

Andi D. Shi [1,2,3], Michèle .G. Hillege[1], Ricardo Andrés Galli Caro[1], Gang Wu[4], Willem M.H. Hoogaars[5], Richard T. Jaspers[1]
[1]Laboratory for Myology, Department of Human Movement Sciences, Faculty of Behavioural and Movement Sciences, Vrije Universiteit Amsterdam (VU), Amsterdam Movement Sciences (AMS), Amsterdam, The Netherlands; [2]Department of Oral and Maxillofacial Surgery/Pathology, Amsterdam UMC and Academic Center for Dentistry Amsterdam (ACTA), Vrije Universiteit Amsterdam (VU), Amsterdam Movement Science (AMS), Amsterdam, the Netherlands; [3]Key Laboratory of Oral Medicine, Guangzhou Institute of Oral Disease, Affiliated Stomatology Hospital of Guangzhou Medical University, Guangzhou Medical University, Guangzhou, China; [4]Department of Oral Implantology and Prosthetic Dentistry, Academic Centre for Dentistry Amsterdam (ACTA), University of Amsterdam (UvA) and Vrije Universiteit Amsterdam (VU), The Netherlands; [5]European Research Institute for the Biology of Ageing (ERIBA);, University Medical Center Groningen (UMCG), University of Groningen, Antonius Deusinglaan 1, 9715RA, Groningen, The Netherlands

Introduction: TGF-β, myostation and activin A signalling is crucial for the regulation of muscle mass and contributes to the progressive pathology of muscle wasting disorders by its role in muscle fibrosis and inhibiting muscle stem cell proliferation and differentiation. Inhibition of TGF-β signalling through knockdown of TGF-β type I receptors *Tgfbr1* and *Acvr1b* may be a promising therapeutic target.
Methods: We investigated muscle morphology and early muscle regeneration in a mouse model of myofibre specific *Tgfbr1* and *Acvr1b* knockout. Mice were sacrificed at day 0 (uninjured), 2 and 4 post cardiotoxin injection.
Results: Our study indicates that while individual knockdown of *Tgfbr1* or *Acvr1b* in adult myofibre has little effect on TA weight or myofibre size, simultaneous targeting *Tgfbr1* and *Acvr1b* more than doubled TA weight and type IIB myofibre size , without affecting the number of myonuclei per myofibre. Knockdown of both *Tgfbr1* and *Acvr1b* caused a reduction in *Murf-1* expression levels as well as an increase in phosphorylated Akt and p70S6K protein levels, indicating that the observed hypertrophy may be caused by an imbalance in protein protein synthesis and degradation. Four days post injury, individual receptor knockdout resulted in reduced regeneration index compared to control animals. Size of regenerating myofibres lacking both receptors significantly increased compared to that of myofibres lacking either *Tgfbr1* or *Acvr1b*. Concurrently, combined knockout resulted in an increased number of satellite cells as well as increased expression of growth factors and myogenic genes. ECM gene expressions (i.e. *Ctgf*, *Col3a1* and *Col1a1*) and endomysium

thickness were elevated when both *Tgfbr1* and *Acvr1b* were knocked out.
Conclusions: These results demonstrate that while individual knockout of *Tgfbr1* or *Acvr1b* within adult myofibre impairs muscle regeneration capacity, simultaneous knockout of *Tgfbr1* and *Acvr1b* results in muscle hypertrophy and accelerate early muscle regeneration after acute injury with concomitant increase in endomysium collagen expression.

5-10
Gender differences in muscle-ageing: a cross-sectional study

Jelle de Jong[1,2], Brecht Attema[1], Arie G Nieuwenhuizen[1], Lars Verschuren[3], Martien PM Caspers[3], Robert Kleemann[2], Anita M van den Hoek[2] , Jaap Keijer[1]
[1]Human and Animal Physiology, Wageningen University, Wageningen, the Netherlands; [2]Department of Metabolic Health Research, The Netherlands Organization for Applied Scientific Research (TNO), Leiden, The Netherlands; [3]Department of Microbiology and Systems Biology, The Netherlands Organization for Applied Scientific Research (TNO), Zeist, The Netherlands

Study purpose: To gain insight in the underlying processes and to assess potential gender differences in the etiology of muscle aging.
Method: RNA sequencing analysis was performed on muscle biopsies from the *vastus lateralis* muscle of young (13 males and 13 females; 23 ± 2 yrs) and old subjects (15 males and 13 females; 80.5 ± 3.5 yrs). In both groups, males and females did not differ in age. Ingenuity Pathway Analysis was performed to compare old versus young subjects, for each gender separately.
Results: 2007 unique differential expressed genes (DEGs) were found in old vs. young females, whereas only 788 unique DEGs were found in old vs. young males, indicating large gender specific effects. In males, classic ageing pathways involved in (mitochondrial) metabolism, cellular growth and oxidative stress were differently regulated. Whereas in females, pathways related to inflammation and protein ubiquitination were differently regulated, in addition to pathways related to cellular growth or apoptosis and cell-cell and extracellular matrix interactions. Well-known inflammation-related genes, such as IL10RA, ICAM1, EGF, STAT5B, ITGB2, were among the most differentially expressed genes in women, and discriminated the aged *vastus lateralis* muscle from that of men.
Conclusion: These findings demonstrate that around the age of 80 years, women exhibit more inflammation in the *vastus lateralis* (and perhaps other muscle groups) than men. Possibly, inflammation plays an equally important role in male muscle-ageing, but at an earlier or later phase. In either case, these findings should highlight the necessity for researchers to take into account gender-difference when performing research on muscle-ageing.

5-12
Quorum Sensing Molecules: potential theranostics in muscle wasting

Anton De Spiegeleer[1], Evelien Wynendaele[1], Nathan Debunne[1], Julie Coudenys[1], Yorick Janssens[1], Liesbeth Crombez[1], Amélie Descamps[1], Ralf Hoffmann[2], Vincent Mouly[3], Caroline Vlaeminck[1], Bart P. Braeckman[1], Dries Duchi[1], Vanessa Andries[1], Marjan De Mey[1], Tom Van de Wiele[1], Lars Vereecke[1], Nele Van Den Noortgate[1], Dirk Elewaut[1,*] and Bart De Spiegeleer[1,*]
[1]Ghent University, Ghent, Belgium; [2]University of Leipzig, Leipzig, Germany; [3]Sorbonne University, Paris, France.

Recent studies point towards the gut bacteria and their metabolites contributing to muscle wasting. Most gut-muscle studies are focused on short-chain fatty acids and their bacterial producers. However, other bacterial metabolites are largely unexplored. Quorum sensing molecules (QSM) are bacterial metabolites, constitutively produced by living bacteria, but showing an increased production under certain conditions. Although their traditional function is inter-bacterial communication, recently they have been shown to also affect host cells.
Our group investigated the effects of QSM on muscle, both *in vitro* as well as *in vivo*. First, we screened the effects of 75 QSM on C2C12 muscle viability, differentiation, inflammation, mitochondrial changes and protein degradation. In a further set of experiments, a number of QSM-hits were evaluated for dose response effects in murine C2C12 and human muscle cells. For the peptide QSM, alanine scans were conducted to identify the critical amino acids in muscle activity and find lead-peptides with antagonistic activity which can be used as a starting point for further development.
C. elegans and mice *in vivo* experiments confirmed the *in vitro* findings. QSM decreasing viability *in vitro* induced a muscle wasting phenotype *in vivo*. In *C. elegans*, this muscle wasting phenotype was characterised by i.a. a significant decrease in wave initiation rate, brush stroke and activity index. The muscle wasting in mice was characterised by a decrease in grip strength and muscle mass.
Moreover, we found bacterial strains not producing QSM negatively influencing aspects of muscle homeostasis, belonging to the same species as the bacteria producing these QSM. These strains are potential probiotic and live biotherapeutic products (LBP).
This novel and ongoing research, exploring a causative factor linked to the microbiome, opens new perspectives for the diagnosis and therapy of muscle wasting diseases.

5-13
Circulating levels of FGF-21 and muscle-related miRNA in cancer patients

Alessio Molfino[1], Roberta Belli[1], Giovanni Imbimbo[1], Maria Ida Amabile[1], Elisabetta Ferraro[2], Serena De Lucia[3], Giuseppe Matullo[4], Paola Costelli[3], Giuseppe Nigri[5], Maurizio Muscaritoli[1]
[1]Department of Translational and Precision Medicine, Sapienza University of Rome, Italy; [2]Department of Biology-Unit of Cell and Developmental Biology, University of Pisa, Italy; [3]Department of Clinical and Biological Science, University of Turin, Italy; [4]Department of Medical Science, University of Turin, Italy; [5]Department of Medical and Surgical Sciences and Translational Medicine, St Andrea Hospital, Sapienza University of Rome, Italy

Introduction: During cancer different cytokines and miRNAs are modulated. MyomiRs are described as striated muscle-specific or muscle-enriched miRNAs and have been recently characterized as novel biomarkers for elderly and chronic diseases, including cancer. We investigated whether Fibroblast growth factor (FGF)-21, known to be involved in metabolic derangements and myo-miRNAs, likely altered in disease-related malnutrition, were perturbed in gastro-intestinal cancer patients (CP).
Methods: We enrolled patients with gastric, pancreatic and colorectal cancer, and healthy subjects, serving as controls. FGF-21 serum levels were measured by ELISA. We performed Next Generation Sequencing (NGS) on RNA extracted from skeletal muscle and plasma from all the study subjects, for the miRNAome sequencing. RT-PCR was used to validate and assess miRNAs involved in muscle metabolism in muscle and plasma samples.
Results: 25 gastro-intestinal CP and 15 healthy controls were enrolled. FGF-21 median levels were higher in CP compared to controls (516 vs 184.08, p=0.02). By NGS, we observed a lower expression of miR15b-3p, miR16-2-3p, miR142a-5p, miR144-3p, miR200b-3p and miR203a-3p in muscle of CP compared to controls ($p<0.05$). By RT-PCR, a significant down-regulation was confirmed only for miR15b-3p and miR203a-3p. In plasma, we observed an up-regulation of

miR21-5p (p=0.02) and down-regulation of miR15b-3p (p=0.02) in CP vs controls. In colon CP we observed a down-regulation of miR15b-3p (p=0.04) and up-regulation of miR133a-3p (p=0.01) and miR206 (p=0.04) vs controls. In Male CP, we also found in plasma an up-regulation of miR133a-3p (p=0.04) and miR206 (p=0.04) compared to female. In all male participants, we showed in plasma a significant up-regulation of miR206 (p=0.03) compared to female.
Conclusion: In gastro-intestinal CP, FGF-21 was significantly increased compared to controls. Perturbation of myomiRs was documented with mechanisms, sex differences, and biological implications to be further elucidated.

5-14
Extracellular vesicle-derived microRNAs enhance stem cell-based regeneration of skeletal muscle in muscle wasting conditions

Laura Yedigaryan[1], Giorgia Giacomazzi[1], Ester Sarrà[1], Nefele Giarratana[1], Enrico Pozzo[1], Natacha Breuls[1], Maurilio Sampaolesi[1,2]
[1]Translational Cardiomyology Laboratory, Stem Cell Biology and Embryology, Department of Development and Regeneration, KU Leuven, Leuven, Belgium; [2]Human Anatomy Unit, Department of Public Health, Experimental and Forensic Medicine, University of Pavia, Italy

Introduction: In physiological and pathological conditions, skeletal muscle exudes the innate ability of growth and regeneration. Chronic muscle illnesses, caused by acquired and genetic factors, severely disrupt the balance in muscle mass plasticity that is sustained through the interplay of anabolism and catabolism. Given the potential role of paracrine factors in myogenic stem cells, extracellular vesicles (EVs) have been studied as hosts for factors such as proteins, messenger RNAs, and non-coding RNAs, including miRNAs (1). In this scenario, specific molecular signatures can be detected in circulating EV cargos that may influence skeletal muscle homeostasis (2). Therefore, we screened the content of EVs derived from hypertrophic, dystrophic, and aged mice.
Methods and Results: The cargos of EVs were analysed and signatures of hypertrophic and dystrophic remodelling were unravelled. The anticipated effects of EVs derived from hypertrophic mouse models were confirmed on C2C12 cells and human mesoangioblasts (hMABs) subjected to myogenic differentiation. The cause of this effect was resolved through the analysis of the transcriptome, protein cargo, and miRNAs of circulating EVs. We found specific EV-miRNA signatures associated with hypertrophic and dystrophic muscle remodelling. Therefore, we tested several combinations of mimics and antagomirs of relevant EV-carried miRNAs upon the myogenic differentiation of hMABs *in vitro* and *in vivo* and identified a miRNA cocktail able to improve skeletal muscle features in hMAB-transplanted aged mice.
Conclusions: Overall, we have established that EVs derived from hypertrophic mouse models enhance the myogenic potential of myogenic stem cells both *in vitro* and *in vivo*. New insights into the role of EVs in muscle regeneration may allow future therapeutic achievements, by either delivering EVs with custom-engineered cargos alone, or in combination with stem cell therapy.

References
1. Daniel C. Bittel, Jyoti K. Jaiswal Contribution of Extracellular Vesicles in Rebuilding Injured Muscles. Front Physiol. 2019; 10: 828.
2. Natacha Breuls, Nefele Giarratana, Laura Yedigaryan and Maurilio Sampaolesi, “Epigenetic Modifications in Induced Pluripotent Stem Cells to Boost Myogenic Commitment”, in Advances in Stem Cell Biology, volume Induced Pluripotent Stem Cells - Novel Concepts, Editor: Alexander Birbrair, Elsevier, In press.

5-15
Regulation of TGF-β signaling by SPSB1 plays a role in inflammation-induced muscle atrophy

Yi Li[1], Jens Fielitz[1,2,3]
[1]Experimental and Clinical Research Center, Charité-Universitätsmedizin Berlin, Max Delbrück Center for Molecular Medicine in the Helmholtz Association, Berlin, Germany. [2]Department of Internal Medicine B, Cardiology, University Medicine Greifswald, Germany. [3]DZHK (German Center for Cardiovascular Research), partner site Greifswald, Greifswald, Germany

Introduction: Critically ill intensive care unit (ICU) patients often develop a significant loss of muscle weight leading to muscle weakness (ICU acquired weakness, ICUAW). However, exact mechanisms underlying muscle atrophy in ICUAW are not well defined. Next generation sequencing revealed an up-regulation of *Spsb1* in the tibialis anterior muscle of septic mice. The SPRY domain- and SOCS box-containing protein 1 (SPSB1) was shown to inhibit transforming growth factor beta (TGF-β) signaling by targeting TGF-beta receptor type-2 (TβRII), but its relevance in muscle atrophy is unknown. We aimed to investigate downstream targets and signaling pathways regulated by SPSB1 and their roles in inflammation-induced muscle atrophy in cultivated myocytes.
Methods: The effects of *Spsb1* over-expression on undifferentiated and differentiated myocytes were studied by analyzing gene expression, protein content, protein synthesis and the atrophy phenotype. Co-immunoprecipitation assays were performed to identify downstream targets of SPSB1.
Results: Treatment of differentiated C2C12 myotubes with TGF-β and lipopolysaccharides induced *Spsb1* gene expression. Over-expression of *Spsb1* significantly impaired fusion of C2C12 myoblast and myogenic differentiation. Accordingly, the transcripts of known differentiation-related factors *Mymk*, *Mymx, Myog* and *Myh* were significantly decreased in *Spsb1* over-expressing myocytes. Decreased myogenic differentiation was accompanied by strongly impaired protein synthesis in *Spsb1*over-expressing myocytes. Using site directed mutagenesis, we uncovered the effects of *Spsb1* over-expression depend on both its SPRY- and its SOCS box- domain. Further mechanistic analyses revealed that SPSB1 directly binds to TβRII and inhibits the TGF-β-Akt signaling pathway. Co-expression of myristylated Akt and SPSB1 attenuated the defects in myogenic differentiation and fusion caused by SPSB1 over-expression.
Conclusions: The TGF-β signaling pathway is negatively regulated by SPSB1, which results in myotube atrophy and inhibition of myoblast fusion and differentiation. SPSB1 could serve as a new target to prevent inflammatory muscle failure.

5-16
Skeletal muscle fibre-type and oxygen transport limitations in obese-HFpEF

Ever Espino-Gonzalez[1], Peter G Tickle[1], Alan P Benson[1], Stuart Egginton[1], T Scott Bowen[1]
[1]School of Biomedical Sciences, Faculty of Biological Sciences, University of Leeds, Leeds

The skeletal muscle pathophysiology of heart failure with preserved ejection fraction (HFpEF) remains poorly understood, but could be influenced by distinct changes in muscle phenotype. Fibre-type specific measures of fibre atrophy, capillary rarefaction, and muscle oxygen tension (PO_2) remain poorly defined in HFpEF, with inconsistent evidence regarding the role of a perfusive *vs.* diffusive oxygen transport limitation. This study, therefore, used an animal model to further examine global *vs.* local skeletal muscle remodelling induced by HFpEF, while evaluating perfusive blood flow. Methods: Lean (n=8) and obese (n=8) diabetic Zucker fatty/spontaneously hypertensive heart failure F1 hybrid (ZSF1) rats were compared at 20 weeks, when HFpEF

is known to develop in the obese strain. Global and fibre type-specific histological properties (i.e. fibre cross-sectional area, myosin isoform, capillarity, and estimated muscle PO_2) were quantified in soleus and diaphragm muscles. Direct femoral artery blood flow measurements using perivascular probes (Transonic, NY, USA) were made at rest and during hindlimb stimulation. Results: HFpEF soleus had fibre atrophy by 24%, 17% lower capillary-to-fibre ratio (C:F), a fibre-type shift from Type I to Type IIa, lower local capillary-to-fibre ratio (LCFR) and increased local capillary density (LCD) in Type I fibres and preserved muscle PO_2 (all $P<0.05$). HFpEF rats also had impaired (73%) functional hyperaemia during stimulation ($P<0.05$). The diaphragm of HFpEF rats showed atrophy in Type IIb/IIx fibres and hypertrophy in Type I fibres, with increased global and local indices of capillarity and muscle PO_2. Conclusion: Impaired leg blood flow response to exercise alongside global and fibre-type specific alterations were found in HFpEF, indicating perfusive limitations. HFpEF demonstrated diaphragmatic alterations similar to those caused by denervation (atrophied fast/glycolytic fibres and hypertrophied slow/oxidative fibres). These findings provide new insights into HFpEF-induced peripheral alterations that may contribute to exercise intolerance, and highlight potential candidates for novel therapeutic interventions.

5-18
Early Differential Responses by Sex to Hindlimb-Unloading Induced Muscle Atrophy

J. William Deaver[1], Megan E. Rosa-Caldwell[1], Wesley A. Haynie[1], Seongkyun Lim[1], Francielly Morena Da Silva[1], Kirsten R. Dunlap[1], Lisa T. Jansen[1], Michael P. Wiggs[2], Tyrone A. Washington[1], Nicholas P. Greene[1]
[1]Health, Human Performance, and Recreation, University of Arkansas, Fayetteville, AR, USA [2]Health, Human Performance, and Recreation, Baylor University, Waco, Texas, TX, USA

Introduction: Previous investigations of disuse muscle atrophy have identified multiple cellular signaling markers indicative of skeletal muscle wasting. However, there has been little research into the early onset of the condition, especially considering differences between sexes. Therefore, this study sought to identify potential differences between sexes through time course evaluation of multiple muscles over a time course of hindlimb unloading (HU).
Methods: 100 C57BL/6 mice (50 males, 50 females) were subjected to HU for 0, 24, 48, 72, or 168-hrs, to induce disuse atrophy (n=10/group/sex). EDL, gastrocnemius, and soleus were collected for analysis of markers of protein turnover by RT-qPCR. Significance indicated when $p<0.05$.
Results: Gadd45a induction in males and females, across EDL (male @ 24-hr, 2-fold increase; female @ 48-hr, 4-fold), gastrocnemius (male @ 24-hr, 1.8-fold; female @ 48-hr, 4.6-fold), and soleus (male @ 48-hrs, 2.5-fold; female @ 24, 48, and 72-hrs, >5-fold) was observed. In males, UBC was not different in EDL but was elevated at 24-hr in gastrocnemius (1.7-fold), and 72-hr in solei (16-fold). In females UBC was elevated at 48-hr in EDL (3-fold), gastrocnemius (3.4-fold), and soleus (1.6-fold). REDD1 was induced in female EDL (@ 24-hr, 5.1-fold), with no change in male EDL at any time point. In gastrocnemius, REDD1 was induced in male (@ 24-hr, 3.2-fold) and female mice (@ 24, 72, and 168-hrs, >6-fold). In soleus, REDD1 was induced in male (@ 48 and 72-hrs, >5-fold) and female (@ 24 and 168-hrs, >3-fold). Finally, DEPTOR was significantly elevated (1.9-fold) in male solei by 72-hrs but was not different across time in female solei.
Conclusions: Markers of disuse atrophy show differential responses by sex during onset of muscle wasting. Several markers are only elevated after initial loss of muscle mass, indicating they may be reactionary responses and not mechanistic driving forces of skeletal muscle atrophy.

Acknowledgements: This study was funded by the National Institutes of Health, Award number: R15AR069913/AR/NIAMS and P20GM125503.

5-19
Acetyltransferases p300 and CBP are not required for normal skeletal muscle regeneration after injury

Alexandra Stanley, Elizabeth Orozco, Simon Schenk
Department of Orthopaedic Surgery, School of Medicine, University of California, San Diego, USA

Introduction: Lysine acetylation is a reversible post-translational modification that regulates multiple intracellular molecular pathways, including metabolism, cell cycle, and DNA damage repair. Due to its ability to regulate histone acetylation and the activity and function of various transcriptional (co)regulators, the acetyltransferase p300 (E1A binding protein p300) has been proposed to be critical to skeletal muscle differentiation and regeneration; however, the contribution of p300 or its ortholog, CBP (cAMP-response element-binding protein binding protein), to *in vivo* skeletal muscle regeneration following injury has not been studied.
Methods: Mice with skeletal muscle-specific and inducible knockout of either p300 (mPZ-CKO) or CBP (mCZ-PKO) were generated by crossing mice with a tamoxifen-inducible Cre recombinase expressed under the human α-skeletal actin promoter with mice having LoxP sites flanking exon 9 of the Ep300 or Crebbp genes. Cre-negative 'wildtype' littermates (WT) served as experimental controls, and tamoxifen dosing was initiated at 12 weeks of age. Following dosing, the tibialis anterior was injured with cardiotoxin (CTX), and gait and histological elements were analyzed at 4, 10, and 14 days post-injury (DPI). Expression of genetic markers associated with myogenic regeneration were assessed by quantitative PCR.
Results: As expected, in WT mice CTX caused extensive damage, reduced fiber cross-sectional area (CSA) and increased percent centralized nuclei (%CN) at 4DPI, which gradually resolved by 14DPI. Interestingly, these changes were comparable in mPZ-CKO and mCZ-PKO mice across all time points. All animals retained full mobility and normal gait throughout the study. Myogenic regulatory factors (MRFs) were expressed at dynamic levels throughout muscle regeneration in WT animals, as expected; these patterns were retained in mPZ-CKO and mCZ-PKO mice.
Conclusions: Overall, these findings demonstrate that loss of p300 in skeletal muscle does not compromise skeletal muscle regeneration post-injury. Moreover, just one allele of p300 or CBP is sufficient to maintain normal skeletal muscle regeneration after injury.

5-20
Transcriptomic analysis of the obesity effects in aged-sarcopenic mice

Landen W. Saling[1], Wesley S. Haynie[1], Lemuel A. Brown[1], Seongkyun Lim[2], Francielly Morena da Silva[2], Nicholas P. Greene[2], Tyrone A. Washington[1]
[1]Exercise Muscle Biology Laboratory, University of Arkansas, Fayetteville, AR; [2]Cachexia Research Laboratory, University of Arkansas, Fayetteville, AR, USA

Sarcopenic obesity is characterized as a comorbidity of excess body fat with concurrent losses in muscle mass due to aging. Sarcopenic obese individuals show greater disability due to muscle weakness and functional limitations when compared to individuals that suffer from sarcopenia or obesity alone. It is largely known that age-induced muscle wasting negatively impacts ability to perform and maintain functional independence. However, how obesity impacts cellular signaling pathways in aged-sarcopenic mice has not been fully explored. Determining specific signaling pathways dysregulated in aged-obesity is necessary for further

investigations and for the creation of future treatment strategies.
Purpose: Therefore, we performed global gene expression analysis of aged obese versus aged lean mice to further understand the altered mechanisms that occur in sarcopenic obesity.
Methods: Twenty-four aged (22-24 months old) C57/BL6J mice were randomly assigned a high-fat (HFD, 60% fat) or normal chow (NC, 5.5% fat) diet after weaning. Sarcopenic lean mice consumed normal chow and sarcopenic obese mice consumed HFD. The plantaris muscle from both groups was excised and submitted for global gene expression analysis, differentially expressed (DE) genes were defined as Log2FC ≥0.6 and p≤0.05. IPA Analysis software was used to analyze altered signaling pathways and genes.
Results: Plantaris weight relative to tibia length was ~7% lower in sarcopenic obese mice compared to sarcopenic lean mice ($p<0.05$). 160 DE genes, with 100 upregulated and 60 downregulated were identified. Among these we observed upregulated RAB15 (2.24 Log2FC) and downregulated SMOX (-1.25 Log2FC). Prominent alterations in signaling pathways included: Inflammatory (NFκB associated) and Insulin receptor signaling which both play key roles in protein flux.
Conclusions: Sarcopenic obese mice exhibit altered gene expression compared to sarcopenic lean mice. Our findings have shown that key cellular signaling pathways associated with protein synthesis and degradation have been altered between lean and obese sarcopenic mice.

Acknowledgements: This study was funded by the Arkansas Bioscience Institute, the major research component of the Arkansas Tobacco Settlement Proceeds Act of 2000.

5-21
Optimized Grip Testing and Comparison with In Vivo Muscle Contractility in Dynapenic Aged Mice

Greg Owendoff, Alissa Ray, Prameela Bobbili, W. David Arnold
Ohio State University Department of Neurology, Columbus, Ohio, USA

Background: Dynapenia, or age-related loss of muscle strength, is a major contributor to loss of function in older adults. Dynapenia has been shown to disproportionately affect the hindlimb in rodents and the lower limbs in older adults. Grip testing is a standard preclinical assessment of muscle strength due to simplicity and non-invasive nature. Despite ease of use, many potential sources of confounding variability may impact grip testing. Our goal was to assess different grip methods for sensitivity, reliability, and relationships with muscle contractility.
Methods: Grip strength [all limb, AL; forelimb, FL), bilateral hindlimb (HL), and unilateral hindlimb (RHL, LHL)] and plantarflexion muscle contractility were normalized to body weight and compared in C57BL/6J mice aged 6 and 24 months (n = 10 per age, 50% female). Tests were repeated to assess intrarater reliability.
Results: Both AL and HL grip showed strong differences in old versus young mice ($p<0.0001$). FL, RHL, and LHL were more variable and showed differences in female ($p=0.0006$, $p=0.0043$, $p=0.0001$) but not male ($p=0.2605$, $p=0.9528$, $p=0.6153$) mice. Coefficients of variability on repeated testing were as follows: AL 7%, HL 14%, FL 19%, RHL 15%, and LHL 10%. Correlations with tetanic torque was strongest at 75 Hz stimulation rate for AL ($r=0.7559$, $p<0.0001$) and HL ($r=0.7112$, $p=0.0004$) and at 45 Hz for RHL ($r=0.5167$, $p=0.0197$).
Conclusion: AL and HL grip show the best performance and reproducibility in aging mice. Both AL and HL correlated with 75 Hz stimulation contractility suggesting an assessment of near maximal muscle function. Forelimb muscles showed less dynapenia, but this discrepancy was only obvious in males. The correlation of RHL testing with contractility at more submaximal rates suggests that UHL may not assess maximal muscle function, and this may be related to how the mouse is immobilized during unilateral hindlimb testing.

5-22
Electrical impedance myography correlates with muscle mass and neuromuscular deficits during aging: a potential instrument for sarcopenia?

Carlos J. Padilla[1], Markus Harrigan[1], Hallie Harris[1], Seward B. Rutkove[2], Brian C. Clark[3], and W. David Arnold[1]
[1]Department of Neurology, The Ohio State University, Wexner Medical Center, Columbus, Ohio, USA; [2]Department of Neurology, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, Massachusetts, USA; [3]Ohio Musculoskeletal and Neurological Institute and the Department of Biomedical Sciences, 250 Irvine Hall, Athens, Ohio, USA

Introduction: Sarcopenia, or pathological age-related loss of muscle mass and strength, is a major contributor to loss of physical function in older adults. The goals of this study were to investigate neuromuscular deficits in an aged rat model of sarcopenia and to assess the relationships of these changes to Electrical Impedance Myography (EIM).
Methods: Young [6 months of age: n=8 (3 females, 5 males)] and old F344 rats [(26 months of age: n=8 (3 female, 5 male)] were assessed with hindlimb grip strength and plantarflexion muscle contractility and the following assessments of the gastrocnemius: motor unit number estimation (MUNE), repetitive nerve stimulation (RNS), single fiber electromyography blocking (SFEMG), EIM, and wet weights.
Results: Grip strength (absolute: $p=0.0228$ and normalized (NL): $p=0.0168$), muscle contractility (5-150 Hz nerve stim) (rate: $p<0.0001$, age: $p=0.0260$, and rate X age: $p=0.0004$), MUNE ($p=0.0134$), and gastrocnemius weights (per body weight) ($p<0.0001$) were all reduced in old versus young rats. RNS decrement at 10, 20, 30, 40, 50 Hz stimulation rates (frequency: $p=0.6070$, age: $p=0.0099$, interaction: age X frequency: $p=0.0695$) and SFEMG ($p=0.0015$) showed increased neuromuscular junction transmission failure in old rats. EIM showed reduced 50 kHz EIM reactance ($p=0.0076$) and phase ($p=0.0002$) but not resistance ($p=0.1207$) in old rats. EIM showed the following correlations: phase versus normalized gastrocnemius ($r=0.8412$; $p=0.0001$), normalized max torque ($r=0.6562$; $p=0.0079$), normalized hindlimb grip ($r=0.6551$; $p=0.008$); reactance versus normalized gastrocnemius ($r=0.7672$; $p=0.0008$), normalized max torque ($r=0.7502$; $p=0.0013$), normalized grip ($r=0.7349$; $p=0.0018$) and resistance versus absolute gastrocnemius ($r=-0.6931$; $p=0.0042$), and absolute grip ($r=-0.576$; $p=0.0246$).
Conclusions: Sarcopenia is a complex and likely multifactorial syndrome, and our data suggest that age-related loss of muscle function is associated multiple neuromuscular deficits. EIM is sensitive to age-related change and is correlated with age-related neuromuscular defects. Therefore, EIM may be a promising biomarker for age-related muscle status.

5-23
Co-application of Oral Magnesium Supplementation and Low-Magnitude, High-Frequency Vibration Treatment Attenuates Sarcopenia via PI3k/Akt/mTOR Pathway

Can Cui[1], Zhengyuan Bao[1], Yuning Chim[1], Ling Qin[1], Simon Kwoon-ho Chow[1], Wing-hoi Cheung[1]
[1]Department of Orthopaedics & Traumatology, Faculty of Medicine, The Chinese University of Hong Kong, Shatin, N.T., Hong Kong

Introduction: Sarcopenia which is coded recently in the International Classification of Disease, Tenth Revision (ICD-10) Clinical Modification (CM), is characterized by the gradual

loss of muscle mass, muscle strength, and muscle quality in aging. Sarcopenia is a muscle disease (muscle failure) rooted in adverse muscle changes that accrue across a lifetime. The pathogenesis of sarcopenia is quite complicated, and anabolic and catabolic process play important roles in the development of sarcopenia. Currently limited options were offered to counter muscle failure during sarcopenia, except for lifestyle therapies like healthy nutrition and exercise training, combined treatment of exercise and nutritional supplements (protein, vitamin D, creatine, amino acid and so on) showed some promising effects on muscle regeneration. Although community-based, well-rounded exercise programs have been proven to improve muscle mass and functional fitness, their efficacy in reversing sarcopenia has not been documented. Furthermore, the beneficial effects of a combination of well-rounded exercise and protein supplementation in improving body composition, physical function, and oxidative stress among sarcopenic elderly has yet to be determined. As reported in previous studies, Low-Magnitude, High-Frequency Vibration (LMHFV) and dietary Mg both showed positive effects on muscle metabolism, increase muscle mass and physical performance in elderly patients. Also, LMHFV and Mg were reported to have potential relationships with muscle hypertrophy pathway, suggesting some underlying mechanism of LMHFV and Mg on muscle maintenance may exist through medicating anabolic and catabolic process during sarcopenia. This study aims to assess comprehensively the combined effect of dietary nutrition intake (Mg) and mechanical loading to attenuate age-related loss of skeletal muscle mass, power, and strength directly through physiological mechanisms.

Methods: Senescence-accelerated mouse P8 (SAMP8) mice at month 6 were randomized into control (Con), vibration (VIB), Mg or Mg+VIB groups. The mice in the VIB group were given LMHFV (0.3g, 35Hz, 20min/day, 5days/week) treatment. Mg was administered to animals through oral gavage of 0.2ml Mg solution in water at the dosage of 98mg/ml/day, 5 days/week. Both LMHFV and Mg supplement were given in the Mg+VIB group. Ex-vivo functional assessment, immunohistochemical staining of myofibers (myosin heavy chain expression) and Dual Energy X-ray Absorptiometry (DXA) measurements were performed at month 0,2,3,4 post-treatment for all groups. In vitro, C2C12 myoblasts were cultured on 30mm dishes and divided into 10 groups in this study: (1) control, (2) LMHFV only, (3) Mg only, (4) Mg+LMHFV, (5) Mg+Rapamycin, (6) Mg+LY294002, (7) LMHFV+Rapamycin, (8) LMHFV+LY294002, (8) Mg+LMHFV+Rapamycin (10) Mg+LMHFV+LY29402. The transcriptional expression levels of IGF1, myoD, Myf4, Myf5, myogenin, FOXO-3, MuRF1 and MAFbx were assessed by qPCR; the translational level of p85, Akt, pAkt, mTOR, eIF4EBP1, S6K1, myoD and myogenin were detected by Western Blot. Data analysis was done with one-way ANOVA, and the significant level was set at $p \leq 0.05$.

Results: *In vivo*, at late stage in month 3 and 4, lean mass percentage and appendicular lean mass percentage in VIB groups were higher than control group. The mice in the VIB, Mg and combination groups showed significantly higher muscle strength and contractibility at month 3 (Figure A). In MHC staining, the combination group showed showed significantly fewer type I muscle fibers and more type IIa and IIb muscle fibers than the control group at 2. Also the combination group could highly increase the expression level of myoD, Myf-5, Myf-6, and myoG at month 2. Mg and combination groups increased mTOR, p85, Akt, pAkt translational expression significantly at month 3 and 4. (Figure C). *In vitro*, co-application of Mg and LMHFV did not show synergistic effect for increasing myotube formation. With the inhibition of PI3k/Akt/mTOR, both LY294002 and Rapamycin groups showed significantly lower myotube formation compared with Mg and LMHFV groups. Western blot results further substantiated the findings. Inhibition of p85 and mTOR abolished the enhancement effects of treatments.

Discussion and Conclusions: In this study, the results showed that LMHFV treatment could effectively increase muscle mass and enhance muscle function in SAMP8 sarcopenia mice, particularly showing dominant effect on muscle mass compared with other treatment groups. Oral Mg supplements did not show any changes in muscle mass, but could continuously increase muscle function and enhance type II muscle hypertrophy and suppress type I muscle fiber atrophy during sarcopenia. LMHFV or Mg treatment could enhance muscle proliferation and stimulate muscle growth by increasing MyoD and Myf5 expression via PI3k/Akt/mTOR pathway, but suppressing MAFbx and MuRF1 *in vivo* and *in vitro*. Combined treatment of LMHFV and Mg could show an addictive effect on suppressing type I fiber atrophy but increasing type II muscle hypertrophy, and no synergistic or addictive effect was shown on muscle contractile function, *In vitro*, Combination of LMHFV and Mg could enhance myoblast differentiation with acute effect on Myf5 and Myf6, inhibit upregulation of MAFbx and MuRF1 via PI3k/Akt/mTOR pathway, which was consistent with LMHFV or Mg individually.

Significance/Clinical Relevance: The combined treatment of Mg and LMHFV could be potential resolution on sarcopenic muscular changes, targeting muscle atrophy related PI3K/Akt/MTOR pathway.

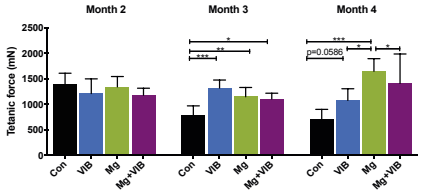


Figure A: Ex-vivo functional test results at month 2,3,4 post treatments.

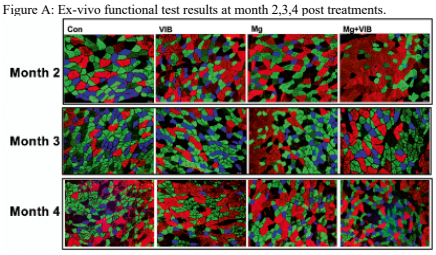


Figure B: IHC staining at month 2,3,4 post treatments.

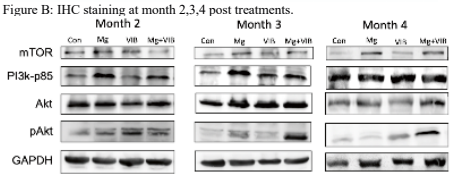


Figure C: WB results of PI3k/Akt/mTOR at month 2,3,4 post treatments.

5-24

Follistatin-induced Muscle Hypertrophy in Aged mice Improves Neuromuscular Junction Form and Function

Chitra C. Iyer[1], Deepti Chugh[1], Prameela J. Bobbili[1], Anton J. Blatnik III[1], Alexander E. Crum[1], Allen F. Yi[1], Brian K. Kaspar[2], Kathrin C. Meyer[2], Arthur H.M. Burghes[1], W. David Arnold[1]

[1]The Ohio State University, Columbus, USA; [2]Nationwide Children's Hospital, Columbus, USA

Introduction: Sarcopenia, or age-related loss of muscle mass and strength, is associated with physical frailty, disability and mortality, and contributes to loss of physical function in older adults. Current interventions include exercise and improved nutrition; however, the former may not be feasible or effective for all older adults. Hence, there is a need to explore additional treatment strategies. We were interested in investigating the effects of increasing the muscle mass in aged C57Bl/6J mice via overexpression of follistatin, a known antagonist of myostatin which is a negative regulator of muscle mass.

Methods: 24-month old C57BL/6J mice received a one-time intramuscular injection of follistatin (AAV9-FS-344). Assessments of motor unit electrophysiology and muscle physiology were performed every two weeks until the endpoint of 27 months of age. Neuromuscular junction (NMJ) transmission and morphology were assessed at endpoint. Levels of endogenous follistatin and myostatin were measured via ELISA in gastrocnemius muscle homogenates.
Results: Follistatin overexpression improved the muscle mass and tetanic torque production (**Figure 1A** and **1B** respectively). There was no improvement in age-related loss of motor units. Interestingly, the NMJ transmission significantly improved as indicated by a decrease in blocking from 25% to 4% in treated mice (**Figure 1C**). Follistatin overexpression also resulted in a significant (~10%) increase in NMJ innervation as shown in **Figure 1D**. Additionally, endogenous follistatin levels increased at 27 months, as compared to 12 and 24 months of age. There was no change in endogenous myostatin levels between the ages of 12 to 27 months. Overexpression of human follistatin did not change the levels of endogenous follistatin and myostatin.
Conclusions: Our results suggest that follistatin increases muscle mass and torque production and counters the age-related decline in NMJ transmission and innervation in aged mice.

Figure 1: Overexpression of follistatin results in increased muscle mass, and improvement in tetanic torque, NMJ transmission and morphology. (*$p<0.05$, **$p<0.01$)

6-01
Nutrition status and sarcopenia in discharged hospital patients in Iceland

Alfons Ramel
Faculty of Food Science and Nutrition, University of Iceland, Iceland

Background: Nutritional status of hospitalized old adults is often inadequate after discharge. The aim of the study was to assess sarcopenia, dietary intake, food security and nutritional status of old adults after discharge.
Methods: In this pilot study community-dwelling old adults (N=13; 87.7±5.6yrs; MMSE≥20; no catabolic diseases) discharged from the Acute Geriatric Unit of the National University Hospital of Iceland were included. Anthropometrics, dietary intake, food security and quality of life (QoL) were assessed at discharge, one week (home) and two weeks later (home).
Results: At discharge, 50% of women and 57% of men were sarcopenic. Baseline BMI was 24.7±5.1 kg/m2 and there was significant weight loss during the 2 weeks period in participants (-2.6 kg, P=0.0001) resulting in an endpoint BMI of 23.8 ±4.7 kg/m2. Actual daily energy-(759.0±183.4 kcal) and protein intake (35.1±7.5 g) were significantly lower (both P<0.001) than the corresponding estimated requirements (2061.6±kcal; 82.4±g). Kitchen assessment at the participants' homes revealed that 33% of all foods were expired and 24% of all foods had visible mold. Of the participants, 75% experienced loneliness and QoL (31.5±8.6) was significantly lower than the age and gender adjusted reference values of 50.
Conclusion: Loneliness, malnutrition, inadequate dietary intake and food insecurity are serious problems in discharged old adults in Iceland. There is a great need for individualized nutritional therapy, during and after hospital stays to ensure proper dietary intake with the aim to reduce malnutrition and re-admissions as well as to increase the quality of life of old adults.

6-02
Weight loss, malnutrition and physical function in community dwelling old adults in Iceland

Alfons Ramel
Faculty of Food Science and Nutrition, University of Iceland, Iceland

Background: Body weight loss and malnutrition have been thoroughly investigated in patients and nursing home residents and often to be found to be related to morbidity and mortality. However, little is known on the prevalence of such nutrition related problems in the community of old adults. The aim of this study was to investigate associations between weight loss, malnutrition and physical function in community dwelling Icelandic old adults.

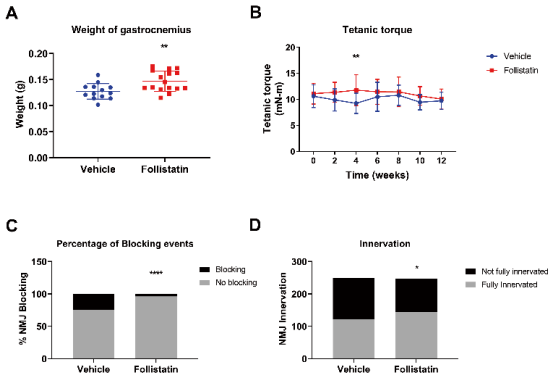


Figure 1: Overexpression of follistatin results in increased muscle mass, and improvement in tetanic torque, NMJ transmission and morphology. (*$p<0.05$, **$p<0.01$)

Methods: A cross-sectional study of 5764 Icelandic older adults from the AGES-Reykjavik study was conducted. Participants underwent a detailed clinical examination in the time period 2002-2006 and were asked retrospectively about weight change during the last 12 months.
Results: Mean age of the participants at baseline was 76.3 years. Of the participants, 1.5% were underweight, 32.3% normal weight, 43.9 overweight and 22.3% obese. During 12 month previous to assessment, 10.9% lost > 5 kg body weight, 46% gained weight and 43.1% were weight stable. Participants with weight loss rated their health poorer and reported more frequently loss of appetitie and disphagia than weight stable participants (all P < 0.001).
According to a multivariate general linear models weight loss was associated with slower timed-up-and-go (0.7sec,P=0.001), slower 6-m-walk-test (0.3sec,P=0.001) and weaker leg strength (-1.7kg,P=0.001) but not grip strength (-0.7kg,P=0.151) when compared to weight stable. These associations were independent from BMI but partly explained by lower fat free mass in the weight loss category.
Conclusion: Weight loss is prevalent in community dwelling old adults and is associated with poorer muscular strength and physical function. These associations are independent from BMI.

6-03

Nutritional signature and body composition adaptations at high-altitude: Western trekkers vs Eastern porters

Danilo Bondi[1], Vittore Verratti[2], Anna Maria Aloisi[3], Raffaela Piccinelli[4], Tereza Jandova[5], Stefano Pieretti[6], Cinzia Le Donne[4], Mattia Taraborrelli[7], Carmen Santangelo[7], Tiziana Pietrangelo[1]

[1]Department of Neuroscience, Imaging and Clinical Sciences, University "G. d'Annunzio" of Chieti – Pescara, Italy; [2]Department of Psychological, Health and Territorial Sciences, University "G. d'Annunzio" of Chieti – Pescara, Italy; [3]Department of Medicine, Surgery and Neuroscience, University of Siena, Italy; [4]Council for Agricultural Research and Economics, Research Centre for Food and Nutrition, Rome, Italy; [5]Faculty of Physical Education and Sport, Charles University, Prague, Czech Republic; [6]National Center for Drug Research and Evaluation, Istituto Superiore di Sanità, Rome, Italy; [7]Department of Medical, Oral and Biotechnological Sciences, University "G. d'Annunzio" of Chieti – Pescara, Italy

Introduction: High-altitude exposure leads many physiological challenges such as weight loss and dehydration. However, little attention has been posed to the role of nutrition into the topic of high-altitude adaptations. Considering also that altitude traveling is increasing nowadays, we aimed to identify the nutritional signature during an altitude expedition, with an ecological study design, comparing two different ethnic groups.
Methods: Five Italian trekkers and 7 Nepalese porters, all males, recorded all foods, beverages and supplements ingested in diaries, during the "Kanchenjunga Exploration & Physiology" expedition (300 Km distance in 19 days); average daily intake of micro and macro-nutrients was then calculated by the *FOODCONS* software. Participants were tested for bioelectrical impedance analysis (BIA) five times during the trek. Italians only were tested 10 days before and 7 days after the expedition using muscle ultrasound (MU).
Results: Nepalese consumed more rice than the Italians; only Italians consumed cheese and substitutes. Water intake was 3099 g/d for Italians and 3240 g/d for Nepalese. Nepalese diet had a higher density of dietary fibre. Mean intake of vitamin A, K, B12 and riboflavin was lower for Nepalese. Intake of calcium was lower than recommended levels. BMI and waist circumference, as well as fat free mass and total body water, decreased in both groups in respect to baseline. Rz increased during the trek. About Xc, Italians increased only at day 9, whereas Nepalese at day 5, 9, and 16. Cross-sectional area of *vastus lateralis* was reduced after the expedition.
Conclusions: Specific nutritional and food-related risk factors advices for the diverse expeditioners should support altitude expeditions. Balance of fluids and hydration status deserves a special focus at altitude. Loss of muscle mass in response to hypobaric hypoxia, despite an adequate protein intake, poses altitude expeditions as an ecological model to study sarcopenic pathways.

6-04

Association between changes in nutrients intake and changes in muscle strength and physical performance in the SarcoPhAge cohort

Laetitia Lengelé[1], Pauline Moehlinger[3], Olivier Bruyère[1], Médéa Locquet[1], Jean-Yves Reginster[1, 2], and Charlotte Beaudart[1]

[1]WHO Collaborating Centre for Public Health Aspects of Musculoskeletal Health and Aging, Division of Public Health, Epidemiology and Health Economics, University of Liège, CHU—Sart Tilman, Quartier Hôpital, Avenue Hippocrate 13 (Bât. B23), 4000 Liège, Belgium; [2]Chair for Biomarkers of Chronic Diseases, Biochemistry Department, College of Science, King Saud. University, Riyadh 11451, Saudi Arabia; [3]Paris Institute of technology for life, food and environmental sciences, Engineering and health field: people, bioproducts, environment. 16 Claude Bernard street, F-75231 Paris Cedex 05.

Introduction: Muscle weakness and physical performance impairment are common geriatric conditions that raise morbidity and mortality. They are known to be affected by nutrition, but although a few longitudinal studies exist, more are needed to investigate the impact of dietary intake changes on muscle parameters changes. This study aims to fill this gap by exploring the association, over 3 years, between variations of nutrients intakes and, on one side, the variations of handgrip strength, as a surrogate of muscle strength, and on the other side, the physical performance, assessed by gait speed.
Methods: Participants from the SarcoPhAge study, a Belgian cohort of people aged 65 years and older, were asked to complete a self-administered Food Frequency Questionnaire (FFQ) at the second (T2) and the fifth (T5) year of follow-up. Daily macro- and micronutrients intakes were measured and their changes in consumption over the three years of follow-up was then calculated. The association between changes in nutrients consumption and the variations in muscle parameters were investigated through multiple linear regressions.
Results: Out of the 534 participants included in the cohort, 238 had complete data at T2 and T5 (median age of 72.0 years [70.0-78.0 years], 60.9% women). In the cross-sectional analysis, calories, omega-3 fatty acids, potassium and vitamins D, A and K intakes were positively correlated with muscle strength. In the longitudinal analysis, after adjustment for confounding variables, neither the variation of gait speed nor the variation of muscle strength were significantly impacted by the variations in nutrients consumption.
Conclusion: Muscle strength is positively associated with dietary consumption at a given time. When studying variations over a period of three years, no association is found between nutrient intake and either gait speed or muscle strength. Other longitudinal investigations with longer follow-up are required to improve knowledge about these interrelations.

6-05

Resting Energy Expenditure changes after 2 weeks of Very Low-Calorie Diet are associated with baseline production rates of specific amino acids

Raven A. Wierzchowska-McNew, Marielle P.K.J. Engelen, Sunday S. Simbo, Nicolaas E.P. Deutz

Health and Kinesiology, Texas A&M University, College Station, United States

Introduction: Loss of body weight (BW) after prolonged dietary energy restriction results in a lower Resting Energy Expenditure (REE) due to a decrease in lean body mass (LBM). However, post-intervention REE values obtained by indirect calorimetry are often lower than those obtained by prediction models, suggesting that other factors, unrelated to body composition, contribute to the magnitude of REE reduction among participants. We studied whether changes in REE after a Very Low-Calorie Diet (VLCD) can be explained by individual differences in baseline protein and amino acid metabolism.
Methods: 35 morbidly obese adults (11 males, 24 females), age 49.2±1.9 y, and BMI 41.8±0.9 kg/m^2 underwent a VLCD of 820 kcal/day for 2 weeks. Subjects were studied pre- and post-VLCD in the postabsorptive state. REE was measured by indirect calorimetry and body composition by dual-energy X-ray absorptiometry. In addition, whole-body production (WBP) rates of multiple amino acids involved in protein metabolisms (Phenylalanine (PHE), Tyrosine (TYR), arginine (ARG)) and their interconversions were measured after IV pulse administration of their stable tracers. Baseline plasma enrichments were measured by LC-MS/MS. Data presented as means±SE. Statistics by ANCOVA adjusted for baseline measurement, age, and an additional confounder (when indicated). Correlations by Pearson correlation coefficient.

Results: Two weeks of VLCD resulted in BW-loss of 4.8±0.3 kg (p=0.0178), LBM-loss of 2.8±0.5 kg (4.8% baseline weight; p=0.0147), and a 5.2±2.5% decline in REE (106±50 kcal/day, p=0.0004, adjusted for baseline LBM). We found moderate to strong correlations between post-intervention REE and baseline net protein breakdown (r: 0.5982, p=0.0006), and WBP rates of PHE (r: -0.3482, p=0.0393) and ARG (r:-0.5996, p=0.0005).
Conclusion: The magnitude of REE reduction after very low-calorie restriction in obese subjects can be predicted by the baseline metabolic rates of specific amino acids.

6-06
Impairments in small intestinal function are associated with reduced muscle quality in a group of Congestive Heart Failure and healthy participants

Sarah K. Kirschner, Nicolaas E. P. Deutz, Clayton L. Cruthirds, Marielle P. K. J. Engelen
Center for Translational Research in Aging & Longevity, Department of Health & Kinesiology, Texas A&M University, College Station, TX, USA

Introduction: Congestive Heart Failure (CHF) is associated with multiple systemic features including compromised muscle health. We and others previously observed small intestinal dysfunction in CHF patients but whether impairments in measures of intestinal and muscle function are linked (gut-muscle axis) remains to be explored.
Methods: We studied 14 clinically stable CHF patients (LVEF: 35.5(2.1)%) and 16 healthy controls. After ingestion of a complete high protein meal containing L-PHE-[1-^{13}C] and spirulina-[U-^{15}N], protein digestion and absorption was calculated as spirulina degradation ratio (L-PHE-[^{15}N]/[1-^{13}C] in plasma). Small intestinal membrane integrity and active carrier-mediated glucose transport were measured by urinary recovery of the orally ingested inert sugars lactulose, rhamnose, and 3-O-methyl-glucose. Handgrip and leg muscle strength were determined by handgrip and isokinetic dynamometry and corrected for lean mass (by DXA) to obtain muscle quality. Group differences were analyzed by ANCOVA adjusted for age, gender, bmi, and/or hsCRP concentration. Association between intestinal and muscle function were analyzed by partial correlation and adjusted for group, age, gender, and/or hsCRP concentration. Values are estimated mean differences [95% CI].
Results: Protein digestion and absorption was reduced in CHF patients (-0.24 [-0.37, -0.11], P=0.0006), and active carrier-mediated glucose transport lower in CHF (-19.4 [-6.1, -32.6]%, P=0.006) compared to controls. Small intestinal permeability was comparable between the groups. In addition, CHF patients had a reduced handgrip (-58.4 [-94.1, -22.6]N, P=0.003) and leg muscle strength (-91.8 [-159.5, -24.0]N, P=0.003). Handgrip and leg muscle quality were lower in participants with lower protein digestion and absorption (P=0.0006 and P=0.003, resp.), impaired glucose absorption (P=0.017 and P<0.0001, resp.) and higher small intestinal permeability (P= 0.038 and P=0.002, resp.).
Conclusions: Impairments in small intestinal function are strongly linked to disturbed muscle quality in CHF. The clinical relevance of this observed relation needs to be further established.

6-07
Elevated meal-induced anabolic response after four weeks of ω3 fatty acid supplementation in Chronic Obstructive Pulmonary Disease (COPD)

Mariëlle PKJ Engelen, Renate Jonker, Rajesh Harrykissoon[2], Anthony J Zachria[2], Nicolaas EP Deutz
Center for Translational Research in Aging & Longevity.' Dept. Health and Kinesiology, Texas A&M University, [2]Pulmonary and Critical Care, Scott & White Medical Center, College Station, TX

Introduction: We recently found that a lower net whole-body protein breakdown in the overnight fasted state (NetPB) in COPD is strongly linked to presence of muscle weakness. The eicosapentaenoic (EPA) and docosahexaenoic (DHA) acids are ω3 fatty acids known to positive influence muscle health. This study investigates whether 4 weeks of EPA+DHA supplementation restores postabsorptive NetPB and improves the anabolic response to feeding in COPD in a dose-dependent way.
Methods: In 32 COPD patients (GOLD: II-IV) and 34 healthy controls, Phenylalanine-[ring-$^{2}H_5$] and Tyrosine-[$^{13}C_9$,^{15}N] isotopes were administered to measure protein synthesis (PS) and breakdown (PB) to calculate postabsorptive NetPB and anabolic response to a standard meal (NetPS). COPD subjects received daily for 4-weeks, according to RCT three-group design, a dose of high (3.5g, n=10) or low (2.0g, n=10) EPA+DHA or placebo (n=12) *via* gel capsules. NetPB and meal-induced NetPS were assessed pre- and post-intervention. Plasma enrichments by LC-MS/MS, statistics by ANCOVA, controlling for confounders sex, age, BMI. Data are estimates (mean [95% CI]).
Results: Lower NetPB was present in the COPD group (p=0.01). The high but not low dose EPA+DHA increased NetPB (51.3 umol/h [25.5, 77.0],p=0.0004) in COPD. Both low and high dose of EPA+DHA increased meal-induced NetPS (37.1 umol/h [9.5, 64.7],p=0.01 vs. 70.9 umol/h [30.5, 110.9],p=0.001, respectively). The EPA+DHA induced increase in NetPB and meal-induced NetPS was strongly related (r=0.48,p=0.008).
Conclusions: Daily intake of oral ω3 fatty acids for 4 weeks positively influences postabsorptive and prandial protein metabolism in patients with COPD, suggesting higher metabolic cycling throughout the day which results in an improved meal-induced net protein anabolism.

6-09
Presence of cachexia and impaired appetite in hospitalized elderly cancer patients

Rayne de Almeida Marques[1], Thamirys de Souza Chaves Ribeiro[2], Vanusa Felício de Souza[2], Maria Claudia Bernardes Spexoto[3], Taisa Sabrina Silva Pereira[4], José Luiz Marques Rocha[1,2], Valdete Regina Guandalini[1,2]
[1]Graduate program in Nutrition and Health. Federal University of Espirito Santo, Vitoria, Espırito Santo, Brazil; [2]Department of Integrated Education. Nutrition Course. Federal University of Espirito Santo, Vitoria, Espırito Santo, Brazil; [3]Faculty of Pharmaceutical Sciences. Nutrition Course. Federal University of Grande Dourados. Dourados, Mato Grosso do Sul, Brazil; [4]Universidad de las Américas Puebla, Cholula, Puebla, México, Ex Hacienda Sta. Catarina Mártir S/N, San Andrés Cholula, Puebla, México

Introduction: Cancer cachexia is described as a multifactorial syndrome characterized by involuntary weight loss, with continuous loss of skeletal muscle mass accompanied or not by loss of fat mass. In elderly cancer patients, the prevalence of cachexia reaches approximately 60.0%, compromising quality of life, response to treatment and survival. Objectives: To investigate the presence of cachexia and impaired appetite in hospitalized elderly cancer patients.
Methods: This observational cross-sectional study was carried out with elderly (≥60 years) subjects of both sexes, diagnosed with malignant neoplasia and admitted to a public tertiary hospital in Vitoria-ES/Brazil, from July 2017 to March 2019. The presence of cachexia was diagnosed using the following diagnostic criteria: a) unintentional weight loss ≥ 5% in the last six months, or b) unintentional weight loss > 2% in the last six months plus BMI < 20kg/m^2. Appetite was assessed through the Cancer Appetite and Symptom Questionnaire (CASQ) and classified into three categories: low (≤ 1 point); moderate (1-3 points) and severe (>3 points). For this study, moderate and severe impairment were

grouped together. The results were evaluated using the SPSS program, version 22.0. This study was approved by the Ethics and Research Committee of the Federal University of Espirito Santo (nº: 27954014.0.0000.5060).
Results: Ninety elderly subjects aged in average 68.8 ± 7.0 years participated in the study. Of these, 56.7% were men and 56.7% declared themselves non-white. The most prevalent type of cancer was that of the gastrointestinal tract (52.9%). Cachexia was present in 54.4% of the elderly evaluated here, with 75.6% of them presenting moderate to severe appetite impairment. There was an association between cachexia and impaired appetite (p= 0.05).
Conclusion: The elderly cancer patients evaluated here had a high prevalence of cachexia and impaired appetite. The association between these parameters indicates the need for multimodal care.

6-10
Hospitalized cancer patients with high neutrophil to lymphocytes ratio had lower calf circumference and increased risk of malnutrition

Jéssika M Siqueira[1], Jéssika D P Soares, Thaís C Borges[1], Tatyanne L N Gomes[1], Claude Pichard[2], Alessandro Laviano[3], Gustavo D Pimentel[1]
[1]Laboratory of Research in Clinical Nutrition and Sports (Labince), Faculty of Nutrition, Federal University of Goiás, Goiânia, Brazil; [2]Clinical Nutrition, Geneva University Hospital, Geneva, Switzerland; [3]Department of Translational and Precision Medicine, Sapienza University of Rome, Rome, Italy

Introduction: This study aimed i) to identify the cut-off value of NLR that best predicts malnutrition by nutritional risk screening (NRS 2002) and ii) whether there is an association between NLR and nutritional risk screening.
Methods: A cross-sectional study enrolled 119 patients with advanced cancer undergoing chemotherapy and/or surgery. NRS 2002 was applied within 24 hours hospitalization to assess the nutritional risk. Calf circumference was assessed using a measuring tape. Systemic inflammation was assessed as C-reactive protein (CRP) and NLR using the neutrophils and lymphocytes count. To identify the best cut-point for NLR value predict the nutritional risk using ROC curve. Differences between groups were tested using T Student, Mann Whitney or Chi Square tests. Logistic regression analyzes were performed to evaluate the association between NLR and nutritional risk.
Results: The ROC curve showed that the best cut-point for predicting nutritional risk was NLR >5.0 (sensitivity 60.9% and specificity of 76.4%). The NLR ≥5.0 group had a higher prevalence of risk of malnutrition (NLR ≥5.0: 73.6% *vs*. NLR <5.0: 37.9%, p = 0.001) than the NLR <5.0. The NLR group ≥5.0 showed lower body weight, BMI, and calf circumference in the NLR ≥5.0 group (NLR ≥5.0: 30.6± 4.3 *vs*. NLR <5.0: 32.6± 4.4, p = 0.01) than the NLR <5.0 group. In contrast, the NLR ≥5.0group had higher CRP and NLR levels than in the group NLR <5.0. In addition, we found an association between the NRS and NLR values in the Crude model (OR: 1.73 (95%CI: 1.23-2.42), p = 0.001) and when adjusted for sex, age, physical activity, alcohol intake, smoking status, BMI, cancer and treatment type and performance status (OR: 1.57 (95%CI: 1.07-2.31), p = 0.019).
Conclusion: In hospitalized advanced cancer patients with high NLR values had lower body weight, BMI and calf circumference. In addition, high NLR was associated with risk of malnutrition in 1.5 times.

7-01
Country- and gender-specific cut points for low allometrically adjusted grip strength from 13,235 older adults of low- and middle-income countries

Pedro Pugliesi Abdalla[1], Lucimere Bohn[2], André Pereira dos Santos[1], Marcio Fernando Tasinafo Junior[1], Leonardo Santos Lopes da Silva[3], José Augusto Gonçalves Marini[1], Ana Claudia Rossini Venturini, Anderson dos Santos Carvalho[3], Gustavo André Borges[4], Dalmo Roberto Lopes Machado[1]
[1]University of São Paulo, Ribeirão Preto, Brazil; [2]University of Porto, Porto, Portugal; [3]Paulista University, [4]State University of Western Paraná

Introduction: Grip strength values to identify geriatric syndromes are based in absolute way or adjusted by body mass index. These might result in inaccurate classification of extreme body size older adults (i.e., light or tall), once relationship between grip strength and height and body weight are non-linear. Allometry might overcome this constraint. We aim to determine the risk threshold for geriatric syndromes of older adults using allometric coefficients to normalize grip strength by body size.
Methods: 13,235 older adults of Study on Global Aging and Adult Health (SAGE) carried out in China, Ghana, India, Mexico, Russia and South Africa were analyzed. Dispersion plots were employed to check relationship between grip strength and body size (body mass, height and appendicular skeletal muscle mass [ASM]). Country- and gender-specific allometric exponents for body size were computed with log linear models. Partial correlation was used to observe if the allometric normalization removed the effect of body size on grip strength. Cut points for low allometrically adjusted grip strength were fixed in first quintile. Frequencies of low grip strength according to EWGSOP2 and our criteria was compared with chi-square test.
Results: A non-linear trend between grip strength and body mass and ASM was observed. Body mass, height and ASM allometric exponents vary between 0.19 and 2.16. Allometric normalization removed effect of body size on grip strength. Frequency of low strength was significantly higher with the EWGSOP2 (female: 29.3%; male: 40.4%) compared to our criteria (female: 20.0%; male: 20.0%; p<0.001), with the exceptions of Russian older males and South African older females, where opposite trend was observed (p<0.05).
Conclusions: The proposed allometric exponents normalize grip strength according to body size variables. The cut points proposed for low muscular strength will improve the accuracy in determining geriatric syndromes of older adults living in low- and middle-income countries.

7-02
Influence of a movement program on mobility in very elderly individuals – quasi experimental study

Ana Gonçalves[1], Luísa Veiga[2], Maria Teresa Tomás[2]
[1]Centro de Bem-Estar Social Lar Padre Tobias, Samora Correia, Portugal; [2]Escola Superior de Tecnologia da Saúde de Lisboa (ESTeSL) – IPL, Portugal

Introdution: Physical activity is of major importance for a healthy ageing. Physical inactivity is negative for all health components specially muscle strength and for ageing process this is even more negative with sarcopenia as a major factor of impairment. The decrement in functional fitness that occurs with aging is widely studied, but studies regarding relationships between physical fitness and exercise training in very old and institutionalized adults are scarce.
Objective: Our purpose was verify the influence of a movement program in handgrip and mobility in very old adults living in a nursing home.
Methods: This is a quasi-experimental study, with a control group. A group of 14 very older adults, aged between 75 and 94 years (4 males; 10 females) and living in a nursing home

were divided in two groups. The intervention group (IG) participated in a 45 minutes twice a week exercise training program of moderate intensity during 8 weeks, aiming at increase her mobility and strength. Exercises where done using body weight and small materials such as Thera Band® elastic bands. The usual care group (UCG) performed only usual care activities that included one time a week one session of playful activities. Both groups performed a set of functional tests: TUG test, sit to stand, Gait Speed (6m), handgrip.
Results: Results showed an increment in walking speed only ($p<0,05$) (7,3±1,1 seconds to 3,7±0,4 sec for IG; 19,0±10,8 to 11,6±7,2 for UCG). Although some clinical improvements in the other variables, results were not significant, which could be due to the duration and frequency of exercise program.
Conclusion: Exercise training programs are of major importance for very older adults living in nursing homes but it seems that duration should be higher than 8 weeks and frequency higher than twice a week.

7-03
Integrating a preventive care path into daily life of older adults with mobility disability risk: introducing a predictive model to the exercise response

Leo Delaire[1], Aymeric Courtay[1], Joannes Humblot[1], Mathieu Fauvernier[2, 3], Marc Bonnefoy[1]
[1]Service de médecine du vieillissement – Hôpital Lyon Sud – Hospices Civils de Lyon; [2]UMR CNRS 5558, Université Lyon 1; [3]Service de Biostatistique – Bioinformatique, Hospices Civils de Lyon

Introduction: The higher proportion of elders makes mobility disability prevention an uppermost issue. There is a consistent need for implementing multimodal care paths in community-dwelling. Exercise is a very good candidate for the care of sarcopenia and frailty. However, exercise response is under the condition of multiple factors which cause heterogeneity. Our main goal was to identifying the best responders to exercise to designed specific care orientations in prevention programs. Our secondary goal was to propose a structured multicomponent exercise training. We assumed to observe improvements in both physical and functional performance and strength.
Method: 104 participants (82.1±5.7) recruited among the "Comfortable on my legs" program, who engaged in a multicomponent group-based training consisting on 20 sessions (2x per week) during 10 weeks. Training involved 3 phases of evolution based on intensity augmentation and execution modes. Exercises involved resistance and functional tasks. We performed a multivariate model to highlight the best responders to our exercise intervention in our program. Model was based on the likelihood of at least 1 point of SPPB gain.
Results: Exercise intervention show significant improvements in physical and functional performance (TUG $p<.001$; gait speed $p<.001$; SPPB $<.001$) as well as in strength in women (grip strength; GS $p<.01$) Model shows interactions between baseline SPPB (OR=0.31; $p<0.001$), BMI (OR=0.78; $p<0.001$) and grip strength (GS; OR=1.22; $p<0.003$). Best responders are participants with low SPPB, normal BMI (20) and normal grip strength (27).
Conclusions: A structured multicomponent exercise intervention reduces mobility disability risk by enhancing physical performance and muscle efficiency. Elders with low SPPB, high grip strength and normal BMI are more likely to respond to this type of intervention. Our results provide important issues for the development of targeted-interventions and specific care orientations.

7-04
Does the presence of abdominal obesity impact physical-functional parameters in community-dwelling elderly women?

Patricia Parreira Batista[1], Jéssica Rodrigues de Almeida[1], Stephanie Aguiar[1], Cláudia Venturini[1], Juleimar Soares Coelho de Amorim[2], Leani de Souza Máximo Pereira[1]
[1]Postgraduate Program in Rehabilitation Sciences - Department of Physiotherapy - Universidade Federal de Minas Gerais, Belo Horizonte, Minas Gerais, Brazil; [2]Federal Institute of Education, Science and Tecnhonology of Rio de Janeiro, Physical Therapy Course- IFRJ, Rio de Janeiro, RJ, Brazil

Introduction: The decline in muscle performance with aging, in part, proceeds through the infiltration of intra and intermuscular adipose tissue and through endocrine and inflammatory pathways arising from abdominal adipose tissue. Independent conditions, sarcopenia and abdominal obesity (AO), are associated with an increased risk of functional disability in older adults. As follows, the aim of the study was to compare physical-functional parameters in community elderly women with and without AO.
Methods: Cross-sectional study with women community-dwelling (≥65 years), sedentary, with reduction of muscle function walking speed (WS≤0.8 m/s) and/or handgrip strength (HGS<20 kg). Participants were excluded with impairment cognitive (MMSE, according to schooling level), inability to walk, acute pain, neurological and/or rheumatological disease, history of cancer (last 5 years) and lower limb fractures in the last year. Clinical and sociodemographic data, performed tests of HGS (Jamar® dynamometer), muscle mass (DXA), WS (4 mts) and Short Physical Performance Battery (SPPB), and presence of AO given by waist circumference (WC≥88cm) were collected to participants. Comparison between the groups was by independent Student T test (α=0.05). Approval by the Research Ethics Committee/UFMG (CAAE:14129513.7.1001.5149).
Results: 103 elderly participated, with a mean age of 76±6.65 years. Of these 60 women (76.08±6.7 years) with AO (GAO), BMI of 26.08±6.73 Kg/m^2 and WC of 100.66±10.26 cm. Group without AO (GNAO) were 43 women (41.75%), 75.88±6.6 years, BMI of 26.74±5.47 kg/m^2 and WC of 81.06±5.15 cm. Significant deleterious difference only for WS (GAO =0.74±0.15 m/s; GNAO =0.8±0.17 m/s; p=0.04) and trend towards SPPB (GAO =7.28±2.15; GNAO=8.09±1.99; p=0.054). Significant difference for HGS (GAO=18.08±4.68 kg; GNAO=15.58±3.78 kg; p=0.005) and muscle mass (GAO=6.44±1.12; GNAO=5.39±0.62; p<0.001), but without negative catabolic impact.
Conclusion: The presence of AO in elderly women has a negative impact on mobility and function. Longitudinal studies are necessary to identify early factors determinants and mediators involved.

7-05

Muscle architectural changes in Response to Eight-Week Neuromuscular Electrical Stimulation Training in Healthy Older People

Danilo Bondi[1], Tereza Jandova[1], Marco Narici[2], Michal Steffl[3], Michele D'Attilio[4], Moreno D'Amico[1], Dagmar Pavlu[3], Vittore Verratti[5], Stefania Fulle[1], Tiziana Pietrangelo[1]

[1]Department of Neuroscience, Imaging and Clinical Sciences, University "G. d'Annunzio" of Chieti – Pescara, Italy; [2]Department of Biomedical Sciences, University of Padova, Italy; [3]Faculty of Physical Education and Sport, Charles University, Prague, Czech Republic; [4]Department of Medical and Oral Sciences and Biotechnologies, University "G. d'Annunzio" of Chieti - Pescara, Italy; [5]Department of Psychological, Health and Territorial Sciences, University "G. d'Annunzio" of Chieti – Pescara, Italy

Introduction: Loss of muscle mass of the lower limbs and of the spine extensors markedly impairs locomotor ability and spine stability in old age. Strength training is effective in counteracting age-related postural impairments in elderly.
Methods: For the first study, eight volunteers (≥ 65 years) performed neuromuscular electrical stimulation NMES 3 times/week for 8 weeks on quadriceps and lumbar paraspinal muscles (combined training: CT). Eight sex- and age-matched individuals served as controls. Functional tests (Timed Up and Go test (TUG) and Five Times Sit-to-Stand Test (FTSST)), VL muscle architecture (muscle thickness (MT), pennation angle (PA), and fiber length (FL)), along with VL cross-sectional area (CSA) and both sides of lumbar multifidus (LM) and vastus lateralis (VL) were measured before and after the training period by ultrasound. For the second study, eleven healthy elderly following CT or training only quadriceps (QT) with NMES were tested for functional balance, static stabilometry, and isometric strength.
Results: By the end of the training period, MT and CSA of VL increased by 8.6% and 11.4%, respectively. LM CSA increased by 5.6% (left) and 7.1% (right). Interestingly, all VL architectural parameters significantly decreased in the control group. Training had a significant effect on TUG ($r = 0.50$, $p = 0.046$). The CT group showed a greater improvement than QT group in static balance control, i.e. reducing the CEA of the CoP displacement from 99±38 to 76±42 mm^2 (Cohen's $d=0.947$).
Conclusions: These results extend previous findings on the hypertrophic effects of NMES, suggesting this passive training to be an useful mean for combating age-related sarcopenia. Benefits for improving static balance through CT were possibly due to the effectiveness of NMES training for improving spinal stabilization. Passive training should be used in the elderly who cannot perform active training modalities.

7-06

Six minute walk test performance in Chronic Obstructive Pulmonary Disease is related to oxygen use, muscle strength, and the production of specific muscle related amino acids

Clayton L Cruthirds, Jaekwon K. Park, Nicolaas E.P. Deutz, Marielle P.K.J. Engelen
Center for Translational Research in Aging & Longevity, Dept. Health and Kinesiology, Texas A&M University, College Station, TX, USA

Introduction: Reduced six minute walk test (6MWT) is a powerful clinical marker in Chronic Obstructive Pulmonary Disease (COPD) which has been linked to impaired quality of life and mortality. As the role of impaired muscle health remains unclear, we studied whether 6MWT in COPD can be explained by individual differences in disease severity, muscle function and mass, and muscle related protein and amino acid metabolism.
Methods: 46 COPD (GOLD 1-4) patients were studied. 6MWT was completed on a standardized 65 meter circular course in a climate controlled hallway. Disease severity was assessed by medical screening, lung function by spirometry, muscle strength by isokinetic dynamometer, and body composition by DXA scan. Whole body production rate (WBP) of multiple amino acids including tau-methylhistidine (mHis) and glutamine (GLN) were assessed by pulse IV tracer infusion, and tracer enrichment analysis by LC-MS/MS. Data are mean [95% CI]. Statistics by Pearson correlation or multiple linear regression to explain 6MWT distance with covariates GOLD stage, continuous oxygen use, total lean mass, WBP of mHIS and WBP of GLN.
Results: Mean 6MWT distance was 332.8 [335.3, 386.6] m. Reduced 6MWT distance was not associated with muscle mass ($r=0.22$, $p=0.14$) but was associated with lower strength ($r=0.48$, $p<0.001$), and presence of oxygen use ($r=-0.61$, $p<0.0001$). Oxygen users walked 62 meters less than non-oxygen users ($p<0.05$). Furthermore, reduced 6MWT distance was associated with higher WBP of mHIS ($r=-0.31$, $p<0.05$) and lower WBP of GLN ($r=0.49$, $p<0.001$).
Conclusion: These data suggest that 6MWT performance is mainly influenced by oxygen use, muscle strength, and metabolism of specific muscle related amino acids.

7-07

Assessing the impact of inpatient rehabilitation on functional recovery from cachexia/muscle wasting in cancer – a combinatorial approach

Ishan Roy, Kevin Huang, Akash Bhakta, Emily Marquez, Jacqueline Spangenberg, Prakash Jayabalan
Shirley Ryan AbilityLab (SRAlab, formerly known as Rehabilitation Institute of Chicago); Department of Physical Medicine and Rehabilitation, Northwestern University, Chicago, Illinois, USA

Introduction: Inpatient rehabilitation (IPR) is often indicated for cancer patients with significant physical and functional decline. However, there is limited understanding of the impact of IPR on functional outcomes for cancer patients with cachexia/muscle wasting.
Objective: To determine the functional recovery of cancer patients in IPR with cachexia using cachexia/muscle wasting associated markers, (including serum markers, weight loss, or changes in body composition).
Methods: Data was collected from 330 admissions to oncologic IPR units at SRAlab. Using a retrospective cohort study design, patients at risk of cachexia/muscle wasting syndrome were: chronic weight loss (CWL, >5% body weight loss in 6 months), rapid weight loss (RWL, >5% body weight loss during acute care hospitalization), serum creatinine<0.60 mg/dL (LC), and serum albumin<3.5 g/dL (LA). In addition, we examined standard Body Mass Index thresholds including under-weight (UW), normal-weight (NW), over-weight (OW), and obese (OB). Functional recovery was measured using the 13-item motor Functional Independence Measure (FIM) and 5-item cognitive FIM sub-scales, validated for assessing function in IPR.
Results: The total cancer population in IPR made significant positive motor gains (+13.6, $p<0.0001$) and cognitive gains (+1.9, $p<0.0001$). However, in a multivariate analysis, LC was independently associated with lower motor recovery ($p=0.003$). In a combinatorial approach, LC+LA, LC+RWL, and LC+OW combinations each had lower motor recovery by at least 4 points ($p=0.03$). For cognition, LA was independently associated with lower recovery ($p<0.0001$), while the LC+RWL, LA+RWL, LC+LA+RWL, LA+RWL+CWL, LC+LA+RWL+CWL, UW+LC, and UW+LA combinations were also associated with lower cognitive recovery by at least 2 points ($p=0.03$).
Conclusion: To our knowledge, this is the first study to investigate the role of IPR in functional recovery in patients at risk of cachexia/muscle wasting. Importantly, we identified single serum markers and combination markers of serum and

body composition that distinguish motor and cognitive functional recovery.

7-08
Interest and faisability of intra-dialytic resistance work sessions in the fight against dynapenia in elderly, high comorbidity patients

Damien Paris[1,2], Bruno Beaune[1,2], Giorgina B. Piccoli[2], Antoine Chatrenêt[1,2]
[1]Laboratory "Movement, Interactions, Performance" (EA 4334), Le Mans University, Le Mans, France; [2]Nephrology, Le Mans Hospital, Le Mans, France

Introduction: End stage renal disease treated by dialysis, induces many physical and social derangements. Many patients have a very low level of physical activity which is reflected by low muscle strength (dynapenia), frequent sarcopenia and low quality of life. Thus, the aim of the study was to assess the impact of a pilot physical activity program on dynapenia, quality of life and level of physical activity in a group of elderly haemodialysis patients, usually excluded by training programs.
Methods: The study included 24 patients which were randomly divided into 2 groups, composed of one activity group and one control group. The study intervention lasted 5 weeks, within which the activity group performed supervised intradialytic sessions of strengthening two times per week, and a control group without supervised physical activity. Grip strength was assessed through handgrip dynamometer and functional tests was composed of a five time sit to stand test. Questionnaires were used to quantify quality of life (World Health QoL), and level of physical activity by means of (Physical Activity Scale for the Elderly (PASE)).
Results: Mean age was 62.4 years old and mean Charlson score was 8 (high comorbidity). After the intervention, in the activity group the grip strength increased by 3.6 kg (28-31.6) and time of STS-5 decreased by 2.7 s (14.5-11.8) ($p < 0.001$), while control group showed no evolution. In addition, only the activity group highlighted a better quality of life for the Physical and Psychological domains (+ 16.8% for $p = 0.013$ and +20.9% for $p < 0.001$ respectively). Finally, the level of physical activity increased only for the activity group ($p = 0.033$).
Conclusion: This study demonstrated the feasibility of a supervised intradialytic program of 5 weeks dedicated to end stage renal disease, even in elderly, high comorbidity patients.

8-01
SARA-OBS study: natural progression of sarcopenia and sarcopenic obesity in older adults

Waly Dioh[1], Cendrine Tourette[1], Anait Azbekyan[1], Rene Lafont[1,2], Pierre Dilda[1], Jean Mariani[2], Stanislas Veillet[1], Sam Agus[1]
Biophytis, Paris, France; Sorbonne Université, CNRS, France

Introduction: SARA-OBS is an observational study, designed to characterize older adults with sarcopenia including sarcopenic obesity, and at risk of mobility disability. Gait speed, muscle strength, and self-administered quality-of-life questionnaires were assessed along with exploration of sarcopenia biomarkers, and their correlation with changes of physical function and actimetry.
Methods: A single-arm observational study, of 6 months duration, with main inclusion criteria for Sarcopenia, according to FNIH criteria (appendicular lean body mass (ALM)/ body mass index (BMI) <0.789 in men and <0.512 in women or ALM <19.75kg in men and <15.02kg in women) and short physical performance battery (SPPB) ≤8/12 in men and women aged ≥ 65 years.
Results: 185 participants were recruited with a majority of female (111 [60.0%] participants). Participants were 79.238 (±7.510) years old with a BMI of 29.581 (±6.982) in average.
A trend for a deterioration in gait speed was observed in the primary end-point: 400-meters walk test (400MWT), 0.027[0.171] m/sec, $p=0.064$). A statistically significant deterioration ($p=0.006$), was also observed in the secondary end-point: 6-minute walk distance (6MWD) with the mean change from baseline to Month 6 being of -16.655 meters. The mean walked distance ranged from 297 at baseline to 284 meters at Month 6. A non-significant deterioration was noted in co-primary end-point: Physical Function Domain (PF-10) of the Short Form Health Survey (SF-36) and secondary end-points on physical performance: chair stand and power stair climb tests.
Inflammatory biomarkers Interleukin-6 and high sensitivity CRP showed a slight non-significant increase over 6 months. 15 adverse events of special interest (falls) were observed in 14 out of 185 participants.
Conclusion: The SARA-OBS data shows a significant deterioration of walking ability with the 6MWD and a trend towards deterioration in several functional parameters, within 6 months. A further work, to better characterize responders is ongoing.

8-02
Changes in Plasma and Urinary Metabolites After Elamipretide in Barth Syndrome Patients: Analyses from the TAZPOWER study

David A. Brown[1], Hilary J. Vernon[2]
[1]Stealth BioTherapeutics, Newton, MA, USA; [2]Johns Hopkins University, Baltimore, MD, USA

Introduction: Barth Syndrome (BTHS) is a rare X-linked genetic disorder that results in a deficiency of mature cardiolipin, which manifests as cardiomyopathy, skeletal myopathy, neutropenia, and growth abnormalities. TAZPOWER evaluated the effects of elamipretide on functional outcomes in a placebo-controlled, crossover study design in patients with BTHS. Elamipretide localizes to the inner mitochondrial membrane and associates with cardiolipin to improve mitochondrial membrane stability and ATP production.
Methods: Plasma and urinary concentrations of key metabolites from BTHS patients (N=11) were analyzed following 12 weeks of placebo and 12 weeks of daily subcutaneous doses of elamipretide (40 mg). We focused on metabolites previously seen to be altered in BTHS, including acylcarnitines, β-hydroxybutyrate, 3-methylglutaconic acid, and selected circulating amino acids.
Results: Increased plasma levels of short- and medium-chain acylcarnitines (C2 to C16) are frequently observed biomarkers of mitochondrial dysfunction, and are commonly seen across myopathic diseases and muscle wasting. Acylcarnitines were elevated by 15% at baseline; elamipretide treatment significantly reduced levels of these acylcarnitines ($P<0.05$) in plasma and urine. In addition, elamipretide reduced plasma levels of β -hydroxybutyrate (β -OHB) and lowered plasma and urinary 3-methylglutaconate (3-MGC). Plasma taurine, an indicator of mitochondrial, muscular and cardiovascular function, was also elevated in BTHS patients following the elamipretide arm of the study.
Conclusions: Alterations in several metabolic biomarkers were observed in TAZPOWER, and are reflective of impaired mitochondrial function in BTHS. In this study, disruptions in fat catabolism (reflected by elevated acylcarnitines) were prominent in BTHS, and improved with elamipretide. Heightened ketone body formation (β -OHB) and elevated 3-MGC corroborated our previous BTHS studies, and were lowered after the elamipretide arm. Taken together, these data show that treatment with elamipretide improves these key biomarkers of mitochondrial dysfunction. These data further highlight the potential of elamipretide to treat skeletal muscle wasting and cardiomyopathies.

8-03

Investigating a multimodal nutrition and exercise intervention for the treatment of cachexia in patients with Lung and GI cancers: a randomized clinical trial in Progress.

Richard F. Dunne[1], Elizabeth Cej[1], Michelle C. Janelsins[1], Luke J. Peppone[1], Aram F. Hezel[1], Aminah Jatoi[2], Mozhgan Dorkhan[3], David C. Linehan[1], Supriya G. Mohile[1], Karen M. Mustian[1]

[1]University of Rochester Medical Center, Rochester, USA; [2]The Mayo Clinic, Rochester, USA; [3]Lund University, Lund, Sweden

Background: Cancer cachexia (CC) is a common debilitating syndrome characterized by symptoms of weight and muscle loss, reduced physical function, poor quality of life, and increased mortality. Research suggests exercise is a highly promising treatment for CC: exercise increases lean mass, improves physical function and can elicit a powerful anti-inflammatory response. Combining exercise with nutritional supplementation is a preferred approach as it addresses the negative energy balance that patients with CC suffer from. We are conducting a randomized clinical trial investigating a combined intervention of Remune™, a juice-based supplement with whey protein, omega-3-fatty acids, and vitamin D, and EXCAP©®, a home-based tailored low-to-moderate intensity exercise regimen, in patients with Lung and Gastrointestinal Tract (GI) cancers and cachexia.
Methods: In this three-arm, 12-week study, 45 pts will be randomized to Remune™ alone, Remune™ and EXCAP©®, or usual care (UC). Subjects with a diagnosis of incurable Lung or GI cancer with plans to begin chemotherapy and >2% weight loss are eligible. The primary aim is to determine the feasibility and safety of the combined intervention of Remune™ plus EXCAP©® as measured by recruitment rates, adherence to interventions, and adverse events. Secondary aims include assessing body mass by Computed Tomography (CT), the 6-minute walk test, changes in weight, and patient-reported CC symptoms.
Results: This study is in first month of enrollment, but patient enrollment and enthusiasm has been positive thus far. Fifteen patients have been screened and four were deemed eligible and were approached for consent. Three of four patients approached signed consent and have been randomized.
Conclusions: We are conducting a three arm randomized controlled trial investigating the feasibility of a multimodal intervention of a novel nutritional supplement (Remune™) and a home-based exercise regimen (EXCAP©®). Interim results will be updated at SCWD in 2021. Goal is to complete enrollment by early 2022.

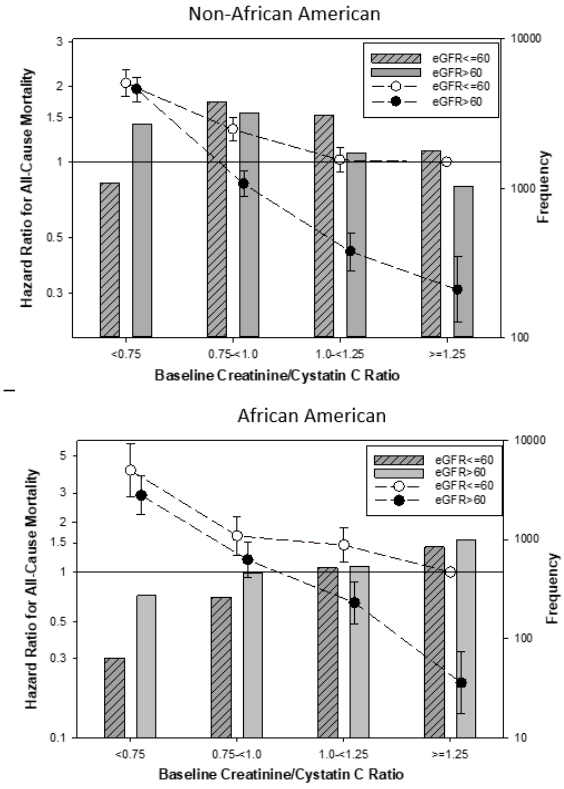
8-04

Serum creatinine to Cystatin C ratio as a potential muscle mass surrogate unfolds racial differences in kidney function assessments and outcomes among Black and non-Black US Veterans

John G. Rizk[1], Susan T Crowley[2], Cachet Wenziger[3,4], Kamyar Kalantar-Zadeh[3,4], Elani Streja[3,4]

[1]Edson College, Arizona State University, Phoenix, AZ; [2]West Haven VA Med. Center, West Haven, CT; [3]Division of Nephrology, Hypertension and Kidney Transplantation, Univ. California, Irvine, School of Medicine, Irvine, CA, USA;[4]Long Beach VA Med. Center, Long Beach, CA, USA

Background: Serum creatinine-based estimated glomerular filtration rate (eGFR) equations (e.g. MDRD and CKD-EPI) include a race correction index for Black versus non-Black patients to account for presumed higher muscle mass in Blacks. Serum Cystatin C (CysC) is a marker of renal function independent of muscle mass. Therefore, a serum creatinine (Cr) to CysC ratio (CrCyR) ratio may provide insight on patient on over or under estimate of renal function based on Cr and the amount of muscle mass in a patient. We hypothesize that a greater CrCyr may confer better survival in patients with and without kidney disease independent of race.
Methods: In a retrospective cohort study of 22,316 US Veterans with baseline CysC and Cr data between October 2004 and September 2019, we examined associations of eight groups of CrCyr (<0.75, 0.75-<1.00, 1.0-<1.25, ≥1.25 for eGFR ≤ or >60 ml/min/1.73m^2) with all-cause mortality among African-American (AA) and non-African-American (non-AA) patients. Model adjustments included age, gender, race, smoking status, and comorbidities.
Results: The mean (±SD) age of the cohort was 67±14 years, 5% were female, 69% were non-AA, and 18% were AA. The median (IQR(interquartile range)) for CysC was 1.40 (1.03-1.93) mg/L, for creatinine 1.30 (0.90-1.80) mg/dL and for CrCyR 0.96 (0.75-1.16). The proportion of AA patients increased across CrCyR groups, suggesting AA have higher muscle mass per renal function. Compared to the reference, a CrCyR<0.75 (suggesting lower muscle mass) had the highest mortality risk among both AA and non-AA patients in both eGFR strata (non-AA: HR(95%CI): 2.06(1.83-2.33) and 1.95(1.74-2.18) for eGFR≤60 and eGFR>60, respectively; non-AA: HR(95%CI(Confidence Interval)): 4.12(2.83-5.99) and 2.91(2.23-3.79) for eGFR≤60 and eGFR>60, respectively). In the highest CrCyR group (CrCyR≥1.25, indicating more muscle mass), the normal eGFR group had the lower death risk compared to the reference for both AA and non-AA patients (non-AA: HR(95%CI): 0.31(0.23-0.42); AA: HR(95%CI): 0.215(0.14-0.33)).
Conclusions: A higher CrCyR indicating a higher Cr relative to CysC level is observed in more AA than non-AA and strongly associated with better overall survival in both race groups of US Veterans regardless of kidney function level. Future studies should examine the clinical utility of CrCyR as a potential surrogate of muscle and overall health over creatinine or CysC alone when evaluating risk in patients with and without kidney disease regardless of race.



8-05
Modulation of AMPK activity and protein turnover signaling in disused rat soleus muscle

Timur Mirzoev, Natalia Vilchinskaya, Inna Paramonova, Svetlana Belova, Ekaterina Mochalova, Boris Shenkman
Institute of Biomedical Problems of the Russian Academy of Sciences, Moscow, Russia

Introduction: Currently there are no good therapies to treat disuse-induced muscle wasting, in part, due to a lack of understanding of the molecular mechanisms responsible for the induction and maintenance of muscle atrophy. AMP-activated protein kinase (AMPK) is able to negatively regulate protein synthesis and activate proteolysis. Since AMPK activity in rat soleus muscle increases from 7- to 14-day hindlimb unloading (HU), we hypothesized inhibition of AMPK activity during this period of unloading would affect anabolic or catabolic pathways regulating muscle mass.
Methods: HU was used as a rodent model of disuse-induced muscle atrophy. Wistar rats were randomly divided into 4 groups: 1) vivarium control (C), 2) 14-day HU (14HU), 3) dorsomorphin (AMPK inhibitor) administration from 7- to 14-day HU (Dors), 4) creatine administration from 7- to 14-day HU (Creat) (AMPK inhibition via an increase in phosphagens occurs). Anabolic and catabolic markers were assessed using WB and RT-PCR.
Results: Treatment with creatine partly attenuated disuse-induced decrease in rat soleus dry weight. Both dorsomorphin and creatine administration resulted in a full prevention of HU-induced increase in AMPK (Thr172) and ACC (Ser79) phosphorylation. Moreover, both AMPK inhibitors prevented a disuse-induced increase in ULK1 (Ser 555) phosphorylation (a marker of autophagy initiation) but did not affect markers implicated in the regulation of protein synthesis (p70S6K, 4E-BP1, GSK3beta). Creatine treatment slightly attenuated a decrease in phospho-AKT (Ser473) content and an increase in E3-ubiquitin ligase MuRF1 mRNA expression after 14-day HU.
Conclusion: Treatment of rats with creatine during HU partly prevented soleus muscle atrophy presumably by AMPK dephosphorylation and subsequent suppression of autophagy initiation. The study was supported by the Russian Science Foundation (RSF) grant No. 17-75-20152.

8-06
Metformin administration mitigates disuse-induced rat soleus muscle wasting

Timur Mirzoev, Inna Paramonova, Sergey Rozhkov, Svetlana Belova, Natalia Vilchinskaya, Boris Shenkman
Institute of Biomedical Problems of the Russian Academy of Sciences, Moscow, Russia

Introduction: It is well established that prolonged disuse results in a significant skeletal muscle wasting. Currently, no ideal treatment exists to inhibit disuse-induced catabolic state in skeletal muscles. Because the activity of AMP-activated protein kinase (AMPK) in rat soleus muscle is suppressed at the early stages of hindlimb unloading (HU) we hypothesized that pre-treatment of rats with metformin (AMPK activator) would exert beneficial effects on skeletal muscle during disuse.
Methods: Mechanical unloading was performed via HU. Wistar rats were randomly divided into 4 groups: 1) intact control (C), 2) control rats treated with 300mg/kg/day of metformin for 10 days (C+Met), 3) HU for 7 days (HU), 4) rats treated with 300mg/kg/day of metformin for 7 days before HU and during the first 3 days of 1-week HU (HU+Met). Anabolic and catabolic markers were assessed using WB and RT-PCR. Diameter of slow and fast muscle fibers was determined by immunohistochemical analysis.
Results: Treatment with metformin partly prevented disuse-induced decrease in rat soleus muscle weight and the size of slow-twitch muscle fibers. Moreover, metformin administration fully prevented unloading-induced slow-to-fast fiber transformation. In comparison with the HS group, maximum absolute twitch and tetanic force of isolated soleus muscle in the HU+Met group was increased. AMPK (Thr172) phosphorylation was significantly increased in the HU+Met group vs. the C group and GSK-3β (Ser9) phosphorylation was significantly increased in the HU+Met group vs. the HS group. Treatment with metformin did not affect the rate of protein synthesis and mTORC1-signaling, however partly prevented disuse-induced upregulation of calpain-1 and ubiquitin genes.
Conclusion: Pre-treatment of rats with metformin can attenuate disuse-induced soleus muscle atrophy presumably by partial prevention of proteolytic pathways activation.

The study was supported by the Russian Science Foundation (RSF) grant No. 17-75-20152.

8-07
Ageing-related Neuromuscular Junction Degeneration in Sarcopenia is Attenuated by Vibration Treatment

Zhengyuan Bao[1], Can Cui[1], Simon Kwoon-ho Chow[1], Ling Qin[1], Wing-hoi Cheung[1]
[1]Department of Orthopaedics & Traumatology, Faculty of Medicine, The Chinese University of Hong Kong, Shatin, N.T., Hong Kong

Introduction: Neuromuscular junction (NMJ) degeneration has been proven one critical pathophysiological factor of sarcopenia. Our previous studies confirmed that low-magnitude high-frequency vibration (LMHFV) treatment could enhance muscle performance in the elderly and improve skeletal muscle function in sarcopenic SAMP8 mice. This study aims to investigate the effects of LMHFV on NMJ degeneration in sarcopenia and the related mechanisms of Agrin-Lrp4-MuSK-Dok7-Rapsyn pathway.
Methods: SAMP8 mice at month 6 were allocated into either control (CTL) or vibration (VIB) group. The mice in the VIB group were given LMHFV (35Hz, 0.3g) 20 min/day and 5 days/week. Functional and morphological assessments of NMJ were evaluated at month 0,2,4,6 post-treatment with n=5/group/timepoint. $p<0.05$ as significant difference.
Results: Tetanic force triggered by either muscle or nerve stimulation started to decrease significantly from 8 months old ($p<0.05$), while NMJ function started to reduce early from 6 months old ($p<0.05$). Endplate AChRs showed significant discrete and fragmented appearance from 6-8 months old ($p<0.05$). Tetanic and specific tetanic force triggered by both muscle and nerve stimulus were significantly increased in VIB group compared with CTL group at months 4 post-treatment ($p<0.05$). But NMJ function was only improved at months 6 post-treatment ($p<0.05$). Morphologically, VIB treatment could significantly alleviate AChRs discrete and fragmented appearance at months 4 post-treatment ($p<0.05$). Protein expression level of Dok7 was significantly increased in VIB group at months 4 post-treatment ($p<0.05$).
Conclusion: SAMP 8 mice could be taken as an animal model of NMJ degeneration. NMJ deterioration precedes the appearance of sarcopenia in SAMP8 mice. LMHFV treatment could preserve NMJ integrity and thus performance of NMJ function. Dok7 mRNA and protein expression were shown to be increased by LMHFV, indicating it was important for the maintenance of NMJ function and morphology in muscle regeneration and may be the key factor in the process of LMHFV treatment.

8-08

Voluntary wheel running with and without follistatin overexpression improves neuromuscular junction transmission but not motor unit loss in aging C57BL/6J mice

Deepti Chugh[1], Chitra C. Iyer[1], Prameela Bobbili[1], Anton J. Blatnik III[1], Brian K. Kaspar[2], Kathrin Meyer[2], Arthur HM Burghes[1], Brian C. Clark[3], W. David Arnold[1]
[1]The Ohio State University, Columbus, USA; [2]Nationwide Children's Hospital, Columbus, USA; [3]Ohio Musculoskeletal and Neurological Institute, USA

Introduction: Factors intrinsic to muscle as well as upstream neurobiological factors have both been implicated in age related loss of muscle mass and strength. Exercise is an effective intervention for sarcopenia, but the long-term impact of exercise in maintaining neuromuscular integrity is not fully understood. The aims of this study were to investigate the effects of long-term voluntary running wheel exercise either alone or in combination with follistatin (antagonist of myostatin to increase muscle size) on neuromuscular junction (NMJ) and motor unit function in mice between 22-27 months of age.
Methods: Baseline and repeated monthly assessments of frailty, motor unit number and muscle contractility were performed on C57BL/6J mice (n= 50; balanced for gender). Mice were randomized to housing with or without voluntary running wheels and injection with adeno-associated virus to overexpress follistatin (FST) or vehicle. Animals were classified as good or poor runners based on running wheel compliance. Three groups were compared: 'sedentary' (poor runners and mice without wheels; n= 26), 'running' (good runners; n=8), and 'running plus FST' (good runners plus FST injection; n=10).
Results: The 'running plus FST' group showed increased muscle mass and tetanic torque (**Fig. 1A and 1B, respectively**) but running alone or in combination with follistatin did not affect motor unit degeneration (**Fig. 1C**). Yet, running, with and without follistatin, demonstrated pronounced improvement in NMJ transmission as shown by a significant reduction in blocking when compared to the sedentary group (**Fig. 1D**).
Conclusion: Chronic voluntary running with or without follistatin treatment, started in late life, improves NMJ transmission but does not appear to have an overt impact on motor unit loss. Antagonism of myostatin via follistatin overexpression improves muscle size and contractility but does not provide added neurobiological benefit when combined with exercise.

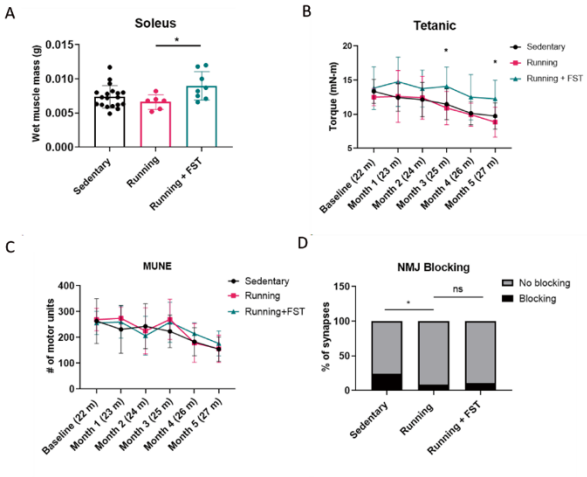


Figure 1: Effect of voluntary wheel running and follistatin overexpression on muscle mass (A), tetanic torque (B), motor unit number (C), and NMJ transmission fidelity (D). * denotes statistical significance; $p < 0.05$, ns: not significant.

9-01

Growth differentiation factor 15 (GDF-15) blockade restores muscle function and physical performance in a mouse model of cancer-induced cachexia.

Brianna LaCarubba[1], Xiangping Li[1], Anthony Rinaldi[1], Stephanie Joaquim[1], Abdul Sheikh[1], John Stansfield[2], Donald Bennett[2], Danna Breen[1], Bei Zhang[1], Zhidan Wu[1], Ja Young Kim-Muller[1]
[1]Internal Medicine Research Unit, Pfizer Inc., Cambridge, MA, USA, [2]Biostatistics, Early Clinical Development, Pfizer Inc., Cambridge, MA, USA

Introduction: Cachexia is a multifactorial metabolic disease that induces continuous muscle and adipose tissue wasting, frequently accompanied by loss of appetite and concomitant reduction of calorie intake. Growth differentiation factor 15 (GDF-15) is a stress-induced hormone whose circulating levels associate with cachexia and poor survival of cancer patients. In preclinical cancer cachexia models, tumor derived GDF15 induces anorexia and body weight loss (muscle and fat mass), which is fully reversed by neutralizing antibodies against GDF15. However, it remains to be determined whether the increased skeletal muscle mass also results in restoration of muscle function and physical performance. Therefore, we examined the effect of GDF15 neutralization using an in vivo muscle function and physical performance in a mouse model of cancer cachexia using in vivo muscle function and exercise platforms, including voluntary wheel-running and involuntary treadmill exercise.
Methods: A cachectic mouse tumor model was established with ectopically implanted human TOV21G ovarian cancer cells to SCID mice. Body weight, food intake, muscle mass and function and physical activity endpoints were measured in cachexia animals treated either with control IgG or anti-GDF-15 antibody (mAB2).
Results: mAB2 treatment partially reversed weight loss in cachectic tumor-bearing mice while skeletal muscle mass was completely restored. Consistent with the muscle mass improvement, mAB2 also dramatically increased muscle function as determined by maximum force. Moreover, engaged in voluntary exercise by a running wheel, mAB2 treatment significantly restored running wheel activity to levels of non-tumor bearing animals. Furthermore, mAB2 markedly improved treadmill running distance, time spent running, the speed at exhaustion, and work output in cachectic mice, subjected to a graded exercise test to exhaustion after 4 weeks of treadmill training.
Conclusions: Our findings demonstrate that GDF-15 neutralization may be an efficacious therapeutic intervention to improve body weight, muscle mass as well as restore physical performance in cachexia patients.

9-02

Growth differentiation factor 15 (GDF-15) inhibition attenuates platinum-based chemotherapy-induced emesis, anorexia and weight loss and increases survival

Danna M. Breen, Kevin Beaumont, Donald Bennett, Julia Brosnan, Roberto Calle, Jeffrey R. Chabot, Susie Collins, Teresa Cunio, Ryan M. Esquejo, Stephanie Joaquim, Alison Joyce, Hanna Kim, Laura Lin, Betty Pettersen, Shuxi Qiao, Michelle Rossulek, Brendan Tierney, Karen M. Walters, Gregory Weber, Zhidan Wu, Bei B. Zhang, Morris J. Birnbaum
Pfizer Worldwide Research, Development & Medical, Cambridge, USA

Introduction: Platinum-based chemotherapy is associated with nausea/emesis, anorexia and weight loss which lead to poor quality of life and outcomes. Cisplatin increases circulating growth differentiation factor 15 (GDF-15), a cytokine that induces conditioned taste aversion, anorexia and weight loss. We examined whether GDF-15 inhibition can

prevent platinum-based chemotherapy-induced emesis, anorexia and weight loss, and increase survival in mice and non-human primates.
Methods: GDF15 concentrations from plasma was using ELISA. Body weight, food intake and other parameters were measured in animal models.
Results: In cancer patients, platinum treatment increased circulating GDF-15 in NSCLC, CRC, and ovarian cancer (~1.5 fold) compared to those receiving a non-platinum-based therapy. Cisplatin, oxaliplatin and carboplatin administered individually all increased circulating GDF-15 (≥ 5-fold) in wildtype mice (but not in knockout mice) and induced anorexia, skeletal muscle wasting, and weight loss. GDF-15 mRNA was increased in kidney, liver, brain and white adipose tissue. In non-human primates, cisplatin treatment for 5 days (96% of the daily recommended clinical dose) also increased circulating GDF-15 (> 5-fold), and induced anorexia and emesis. Treatment with the anti-GDF-15 monoclonal antibody (mAB1) resulted in no detectable circulating levels of free GDF-15 and attenuated both cisplatin-induced anorexia and emesis. Furthermore, in a mouse cachectic tumor model, cisplatin treatment inhibited tumor growth; however, GDF-15 levels were still elevated, and additional weight loss occurred compared to vehicle control. When mAB1 was given in combination with cisplatin, weight loss was reversed and tumor growth inhibition was maintained, resulting in greater survival compared to cisplatin alone.
Conclusions: These data support the notion that GDF-15 inhibition with mAB1 holds the potential as an effective therapeutic approach to alleviate GDF-15 mediated emesis, anorexia and weight loss with the aim to enable optimal cancer treatment as well as to improve patient quality of life and potentially survival.

9-03
Folfox Chemotherapy induces Chronic Metabolic Dysfunction and Fatigue in Mice

Brittany R. Counts, Jessica L. Halle, and James A. Carson
Integrative Muscle Biology Laboratory, Division of Rehabilitation Sciences, College of Health Professions, University of Tennessee Health Science Center, Memphis TN, USA

Chemotherapy mitigation of cancer progression is associated with well-described acute toxicities; patients commonly exhibit body mass loss, muscle weakness, and whole-body metabolic dysfunction. There is growing evidence that chemotherapy's adverse effects can be progressive and chronic after treatment completion. However, the mechanistic understanding of persistent metabolic and functional toxicities associated with chemotherapy is limited.
Purpose: Investigate the long-lasting effects of Folfox chemotherapy on metabolic function and fatigue in mice.
Methods: Male and female C57BL/6J mice (B6; N=55), at 12 weeks of age, were injected with four cycles (1 cycle = 1 injection every other week) of either Folfox (FOL; 5-Fluroracil 30mg/kg, Oxaliplatin 6mg/kg, and Leucovorin 90mg/kg) or phosphate-buffered saline (PBS; 100ul). At either 14 (n=16), 28 (n=23), or 70 days (n=16) after the 4th FOL cycle, a treadmill run to fatigue test was performed, and mice sacrificed. A subset of mice was placed in metabolic cages for five days, 28 days after the 4th FOL cycle was completed. The gastrocnemius muscle was used for protein analysis.
Results: FOL attenuated fat and lean mass increases during treatment, despite no food intake changes. However, neither body weight nor lean mass was different from controls at 70 days post-chemotherapy. FOL decreased treadmill run time to fatigue after the 4th FOL cycle (-53%), which remained reduced 28 (-45%) and 70 days (-39%) after completing FOL treatment. Systemic carbohydrate oxidation was greater in FOL mice 28 days post-FOL, and glucose intolerance was present in FOL mice 70 days post-FOL. Muscle AMPK phosphorylation (p=0.038) was induced, and rpS6 phosphorylation (p=0.045) was decreased 28 days after FOL treatment.
Discussion: Repeated FOL chemotherapy administration in mice can induce progressive and chronic metabolic dysfunction associated with increased fatigue long that persist long after completing treatment.

Acknowledgments: NCI R21-CA231131

9-04
Dietary EPA and DHA restore altered lipid metabolism pathways associated with chemotherapy-induced myosteatosis in a preclinical model of colorectal cancer: a skeletal muscle transcriptomic analysis

Peter Isesele[1], Alaa Almasud[1], Bhumi Bhatt[2], Sambasivarao Damaraju[2], Vickie Baracos[3,] Vera C Mazurak[1]
[1]Department of Agricultural Food and Nutritional Science, University of Alberta, Edmonton, Alberta, Canada. T6G 2P5; [2]Department of Laboratory Medicine and Pathology, Faculty of Medicine and Dentistry, University of Alberta, Edmonton, AB T6G 2R3; [3]Division of palliative Care Medicine, Department of Oncology, University of Alberta, Edmonton, AB, Canada

Introduction: Myosteatosis is independently prognostic for survival in cancer patients. Prior work has revealed that dietary EPA and DHA (fish oil) reverse chemotherapy-induced myosteatosis in an experimental model of colorectal cancer, but the mechanisms by which EPA and DHA mitigate this effect are not known. This study aimed to identify the differentially regulated transcripts associated with fatty acid uptake and storage in the skeletal muscle in response to tumor, chemotherapy, and the effects of dietary EPA and DHA.
Methods: Female Fischer 344 rats fed control diet were compared with experimental groups provided EPA and DHA (2.0 g /100 g of diet) initiated on the first day of chemotherapy. Rats received chemotherapy (irinotecan + 5-fluorouracil) 2 weeks after tumor implantation (1-cycle). Total RNA was extracted from gastrocnemius muscle and subjected to transcriptomic analysis using RNA-Seq. Differentially expressed genes were subjected to Ingenuity Pathway Analysis (IPA). Genes enriched in a pathway were identified and annotated for their putative functional role.
Results: Transcripts of adipogenesis (*Pparg*[p=1.39E-02, fc=1.6], *Fabp4* [p=0.069, fc =1.6], *Lep* [0.005, fc =13.8], *Scd1* [0.0017, fc = 6.8], *Plin1* [0.0033, fc = 4.2], *Klf5* [0.0046, fc = 1.6), fatty acid activation (*Slc27a1* [p =2.3E-02, fc = 1.54], *Slc27a6* [p = 0.012, fc = 4.1), and acetyl-CoA biosynthesis (*Dld* [p=0.033, fc = 1.5], *Phda1* [p=0.014, fc =1.5]) were activated in tumor bearing and chemotherapy treated animals compared to reference animals (no tumor/chemotherapy). Dietary EPA and DHA restored these transcripts to levels not different from reference animals
Conclusions: Lipid synthesis and storage appear to be driven by tumor and chemotherapy, contributing to myosteatosis. Provision of dietary EPA and DHA restored transcripts in these pathways to levels similar to reference animals. Collectively, these findings offer a potential mechanistic insight on the role of EPA and DHA in mitigating myosteatosis.

9-05

Protection Against Doxorubicin-Induced Cardiac Dysfunction is Not Maintained Following Prolonged Autophagy Inhibition

Ryan N. Montalvo[1], Vivian Doerr[1], Oh Sung Kwon[2], Erin E. Talbert[3], Jeung-Ki Yoo[1], Moon-Hyon Hwang[1], Branden L. Nguyen[1], Demetra D. Christou[1], Andreas N. Kavazis[4], and Ashley J. Smuder[1]

[1]University of Florida, Department of Applied Physiology and Kinesiology; Gainesville, FL, USA; [2]University of Connecticut, Department of Kinesiology, Storrs, CT, USA; [3]University of Iowa, Department of Health and Human Physiology, Iowa City, IA, USA; [4]Auburn University, School of Kinesiology, Auburn, AL, USA

Introduction: Doxorubicin (DOX) is a highly effective chemotherapeutic agent used in the treatment of various cancer types. Nevertheless, it is well known that DOX promotes the development of severe cardiovascular complications. Therefore, investigation into the underlying mechanisms that drive DOX-induced cardiotoxicity is necessary to develop therapeutic countermeasures. In this regard, autophagy is a complex catabolic process that is increased in the heart following DOX exposure. However, conflicting evidence exists regarding the role of autophagy dysregulation in the etiology of DOX-induced cardiac dysfunction.
Methods: This study aimed to clarify the contribution of autophagy to DOX-induced cardiotoxicity by specifically inhibiting autophagosome formation using a dominant negative ATG5 adeno-associated virus construct (rAAV-dnATG5). Acute (2-day) and delayed (9-day) effects of DOX (20mg/kg i.p.) on the hearts of female Sprague-Dawley rats were assessed.
Results: Our data confirm established detrimental effects of DOX on left ventricular function, redox balance, and mitochondrial function. Interestingly, targeted inhibition of autophagy in the heart via rAAV-dnATG5 in DOX-treated rats ameliorated the increase in mitochondrial reactive oxygen species emission and the attenuation of cardiac and mitochondrial function, but only at the acute timepoint. Deviation in the effects of autophagy inhibition at the 2- and 9-day timepoints appeared related to differences in ATG5-ATG12 conjugation, as this marker of autophagosome formation was significantly elevated 2 days following DOX exposure but returned to baseline at day 9.
Conclusion: DOX exposure may transiently upregulate autophagy signaling in the rat heart; thus, long-term inhibition of autophagy may result in pathological consequences.

9-06

Alterations in hepatic fatty acids in chemotherapy-associated steatohepatitis (CASH) reveal depletion of total polyunsaturated fatty acids following irinotecan plus 5-fluorouracil treatment in an animal model of colorectal cancer

Md monirujjaman[1], Asha Pant[1], Karen Kelly[1], Randy Nelson[1], Oliver Bathe[2], Rene Jacobs[1], Vickie Baracos[3], Vera C Mazurak[1]

[1]Alberta Institute for Human Nutrition, Department of Agricultural Food and Nutritional Science, 4-126 Li Ka Shing Centre for Health Research Innovation, University of Alberta, Edmonton, Alberta, Canada. T6G 2P5; [2]Department of Surgical Oncology, University of Calgary; [3]Department of Oncology, Cross Cancer Institute, University of Alberta

Introduction: Chemotherapy-associated steatohepatitis (CASH) is a well-known toxicity that commonly appears following treatment with Irinotecan(CPT)+5-fluorouracil(5-FU) for metastatic colorectal cancer (CRC). Fatty liver is a side effect of chemotherapy that limits the ability to treat CRC patients in the most effective way. Alterations in hepatic fatty acid metabolism in CRC patients treated with CPT+5-FU have not been well defined. The aim of this study was to determine hepatic fatty acid composition and expression of genes involved in lipid metabolism, after receiving CPT+5-FU in an animal model of CRC.
Methods: Female Fischer 344 rats were provided a semi-purified AIN-76 basal diet with modified fat component. One cycle of chemotherapy consisted of CPT+5-FU and was initiated 2 weeks after tumor implantation; a second cycle was given one week later. Two and 9 days after each cycle, animals were killed, and livers collected. Fatty acids in the triglyceride and phospholipid fractions were isolated using thin layer chromatography and quantified using gas chromatography. Expression of 44 lipid metabolism genes were analyzed by qPCR.
Results: Total liver triglycerides and phospholipid level was lower in D9 animals compared to animals of D0 and D2. Total PUFA both in phospholipid and triglycerides was declined at D9. Of 44 genes analyzed, 13 genes were altered with treatment. Expression of genes VLCAD and DGAT1 involved in fatty acid oxidation were significantly elevated after each cycle, whereas expression of genes ELOVL2 and FADS2 involved in fatty acid elongation and desaturation were significantly lower at D9 compared to D2 and D0 (P<0.03).
Conclusions: Hepatic total PUFA was depleted and genes involved in pathways of PUFA synthesis were down-regulated by chemotherapy treatment. This observation is especially important given the current interest in fish oil supplementation for cancer patients to restore PUFA content and improve the therapeutic index of many current cytotoxic drugs.

9-07

Atenolol improves skeletal muscle architecture and inhibits immobilization-induced muscle atrophy

Sapana Kushwaha, Deepak Rawat, Anand Kumar
Department of Pharmaceutical Sciences, School of Biomedical and Pharmaceutical Sciences Babasaheb Bhimrao Ambedkar University (A Central University), Vidya Vihar, Lucknow, INDIA

Introduction: Disuse atrophy (also called as Immobilization) is defined as the loss of skeletal muscle mass due to inactivity or lower activity than 'normal or routine' use. It occurs in case of a cast application in fracture management or permanent bed rest due to some disease. In the present study, we investigate the atenolol, a cardio-selective beta blocker as a possible therapeutics in cast immobilization-induced muscle atrophy.
Methods: For conducting study, Wistar rats were randomized into three groups. Group I was served as control group. Group II was immobilized (IM) control group and served as IM control. Group III was received the atenolol (10 mg/kg) in IM group. Atenolol was freshly prepared in water and was given intraperitoneally for 14 days. Immobilization was done in one hindlimb of all rats in plantar flexion with plaster. Plaster cast was applied from trunk to middle of left hind paw under mild anesthesia. Without casting hindlimb was served as contralateral limb. Endpoints parameter includes behavioural test, creatine kinase (CK), oxidative stress (GSH, MDA, SOD) and histopathological analysis.
Results: Results of rotarod, foot print and swimming test analysis showed that immobilized group has lesser physical activity and work strength as compared to the control group and intervention of atenolol treatment significantly improved muscle strength. Further results showed that atenolol significantly increase the myofibrillar protein content in gastrocnemius muscle of IM group. Atenolol also restored the oxidative stress levels (MDA, SOD and GSH) when compared to immobilized group. Histopathological findings confirmed that the atenolol markedly increased the cross sectional area and minimum Feret's diameter in myofibres of gastrocnemius muscle as compared to IM group.
Conclusions: In conclusion, atenolol restored the immobilization-induced muscle atrophy. Further, detailed molecular studies are required to decipher the exact

mechanism of atenolol mediated protection disuse skeletal muscle atrophy

FACULTY

Swarnali **Acharyya**, USA
Chair I

Volker **Adams**, Germany
Chair E, Poster Session 7

Stefan **Anker**, Germany
Chair A, A1, Chair Joint Session SCWD - MASCC - EONS, Chair O

Markus **Anker**, Germany
M3

Hidenori **Arai**, Japan
B3

Josep **Argiles**, Spain
Poster Session 4, Chair I, Poster Session 8

Didier **Attaix**, France
Poster Session 5, Chair G

Vickie **Baracos**, Canada
A3, D3

Miguel L **Batista** Jr., USA
E2

Jürgen **Bauer**, Germany
Poster Session 4, N4, Poster Session 8

Mauricio **Berriel Diaz**, Germany
Poster Session 6, M4

Olivier **Bezy**, USA
Chair N

Andrea **Bonetto**, USA
Chair F

Marc **Bonnefoy**, France
Chair N, Poster Session 11

Scott **Brakenridge**, USA
Poster Session 3, Chair H

Ruta **Brazauskas**, USA
Statistical Seminar

Bette **Caan**, USA
J3

James **Carson**, USA
Chair K, Poster Session 12

Andreas **Charalambous**, Cyprus
Chair + Talk Joint Session SCWD - MASCC - EONS

Andrea L **Cheville**, USA
Talk Joint Session SCWD - MASCC - EONS

Jesper **Christensen**, Denmark
P2

Andrew **Coats**, Australia
Chair A, B4, Chair O

Paola **Costelli**, Italy
Chair B, Poster Session 6

Jeffrey **Crawford**, USA
Chair D, Chair F, Chair O

Srinivasan **Dasarathy**, USA
Poster Session 10, P1

Edwin de **Wit**, Switzerland
O3

Hans **Degens**, UK
H2

Egidio **Del Fabbro**, USA
Talk Joint Session SCWD - MASCC - EONS

Cynthia **Delgado**, USA
L4

Nicolaas **Deutz**, USA
Poster Session 2, Chair P

Wolfram **Doehner**, Germany
B2

Jason **Doles**, USA
Chair C, Poster Session 3

Gustavo **Duque**, Australia
Chair B

Bill **Evans**, USA
D4, Chair N, O2

Mirza **Faisal Beg**, Canada
J4

Jerome **Feige**, Switzerland
Chair J

Luigi **Ferrucci**, USA
Chair L

Roger **Fielding**, USA
Chair M, Poster Session 12

Kevin M **Flanigan**, USA
C2

Jose **Garcia**, USA
Poster Session 9, Chair O

Sven **Geißler**, Germany
Chair H

David **Glass**, USA
Chair K, P4

Marcus **Goncalves**, USA
I3

Theresa **Guise**, USA
I2

Denis **Guttridge**, USA
Chair E

Stephan **Herzig**, Germany
A4, Chair M

Steven **Heymsfield**, USA
Chair D

T Alp **Ikizler**, USA
E1

Richard **Jaspers**, The Netherlands
H1

Aminah **Jatoi**, USA
Chair I, O

Kamyar **Kalantar-Zadeh**, USA
L2

Masaaki **Konishi**, Japan
N3

Mitja **Lainscak**, Slovenia
Chair A, Poster Session 9, N1

Francesco **Landi**, Italy
Chair J, Poster Session 11

Alexandro **Laviano**, Italy
Poster Session 2, Chair O

Jennifer **Le-Rademacher**, USA
Statistical Seminar

Stef **Levolger**, The Netherlands
K4

Yi-Ping **Li**, USA
K2

Hanns **Lochmüller**, Canada
Chair C

Gordon **Lynch**, Australia
H3

Andrea **Maier**, Australia
Chair J

Robert **Mak**, USA
L1

Michelangelo **Mancuso**, Italy
O4

Daniel **Marks**, USA
K1

Emanuele **Marzetti**, Italy
J1

Asmita **Mishra**, USA
D1

Frank **Misselwitz**, Germany
Chair O

John **Morley**, USA
B1, Chair H

Kate **Murphy**, Australia
F4

Mauricio **Muscaritoli**, Italy
P3

Gustavo A **Nader**, USA
Poster Session 1, G4

Fabio **Penna**, Italy
Poster Session 7, Chair P

Mathias **Plauth**, Germany
Chair P

Joanne **Reid**, USA
L3

Maria **Rohm**, Germany
M1

Giuseppe **Rosano**, UK
Chair B, N2

Dmitry **Rozenberg**, Canada
D2

Maurilio **Sampaolesi**, Belgium
Chair E, Poster Session 5

Marco **Sandri**, Italy
G1

Roberta **Sartori**, Italy
F3

Jens **Schmidt**, Germany
Chair C

Annemie **Schols**, The Netherlands
Chair D

Marilia **Seelaender**, Brazil
M2

Richard **Skipworth**, UK
I1

Adrian **Slee**, UK
J2

Ashley **Smuder**, USA
F1

Wei Roc **Song**, China
G2

Pietro **Spitali**, The Netherlands
C1

Jochen **Springer**, Germany
Poster Session 1, Chair M, O1

Florian **Strasser**, Switzerland
Talk Joint Session SCWD - MASCC - EONS

Erin **Talbert**, USA
F2

Francesco Saverio **Tedesco**, UK
C4

Stephan **von Haehling**, Germany
A2, E4, Chair L

Hidetaka **Wakabayashi**, Japan
Chair L

Xiaonan **Wang**, USA
Chair G

David **Waning**, USA
Chair G, Poster Session 10

Jochen **Weishaupt**, Germany
C3

Tobias **Winkler**, Germany
H4

Joachim **Wiskemann**, Germany
Talk Joint Session SCWD - MASCC - EONS

Zhidan **Wu**, USA
K3

Bei **Zhang**, USA
I4

Teresa **Zimmers**, USA
E3, Chair K

Antonio **Zorzano**, Spain
G3

SUPPORT

Gold sponsor

Pfizer

Silver sponsors

HELSINN

Stealth BIOTHERAPEUTICS

Bronze sponsors

Faraday PHARMACEUTICALS

Further sponsors

Actimed Therapeutics

biophytis

ThermoFisher SCIENTIFIC

With the support of

CHARITÉ UNIVERSITÄTSMEDIZIN BERLIN