

# 11º Simpósio de Metabolismo da Faculdade de Medicina da Universidade do Porto

## – Palestras, Comunicações Orais e Posters



### > SESSION I – METABOLIC FITNESS AND AGEING

#### Skeletal muscle ageing: from a transcriptome and metabolome perspective

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**Background:** Age-related skeletal muscle loss (sarcopenia) increases the risk of frailty and mortality. Within the skeletal muscle, fast and slow muscles seem to be differently susceptible to age-related changes. Here, we set to understand how the transcriptome and metabolome change in pre-sarcopenic muscle types and how this relates to human muscle ageing.

**Methodology:** We extracted *Soleus* (slow, oxidative) and *Extensor Digitorum Longus* (EDL, fast, glycolytic) muscles from young (4 months old, n=6-8) and pre-sarcopenic (no muscle weight loss) old (25 months old, n=6-7) C57BL/6 mice and performed gene expression and metabolite analyses employing RNA-seq and UHPLC, respectively. Human RNA-seq counts were obtained from GTEx database (*Gastrocnemius*, fast muscle type), with age groups (in years) defined as 20-29 for young and ranging from 30-39, 40-49 and up to 70-79 for old depending on the analysis. Statistical analyses were performed using custom R scripts.

**Results:** Gene expression profiling revealed 229 differentially expressed genes (FDR<0.05) in ageing EDL (young vs old), and 131 genes were found to change (FDR<0.05) in ageing *Soleus*. Genes down-regulated in aged EDL were enriched for mitochondria-related processes, including "NADH dehydrogenase complex", "mitochondrial translation" and "mitochondrial gene expression". In *Soleus*, downregulation was related to extracellular matrix including "collagen trimer" and "focal adhesion". Differences in metabolite levels were also more pronounced in ageing EDL (192, p<0.05), enriched for "sphingolipid" and "nicotinamide" metabolism, than in ageing *Soleus* (132, p<0.05), enriched for "diacylglycerol metabolism". Overall, EDL seems to be more susceptible to age-related changes than *Soleus*.

Human data analyses revealed downregulated processes related to mitochondria in all age-group comparisons similar to what was observed for EDL. These age-related changes include detrimental, neutral and adaptive processes.

**Conclusions:** Different muscle types exhibited distinct age-related changes. Common to mice and humans were alterations related to mitochondria, which might be relevant to fast muscles atrophy.

**Keywords:** Ageing; Skeletal muscle; Transcriptome; Metabolome; Mitochondria

#### Nutritional and functional status in the elderly, a picture of the Portuguese elderly population

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Older adults present a higher risk of nutritional and functional status dysfunctions. The Nutrition UP 65 Project aimed to study the association between the nutritional and functional status of the Portuguese older population, based on anthropometric parameters, vitamin D, hydration status, handgrip strength (HGS) and gait speed (GS). This was a cross-sectional study that included 1,500 Portuguese older adults ≥ 65 years old, and the sample was representative of Portuguese older adults in terms of sex, age, educational level and area of residence. Results have shown that 44.3% of the elderly were overweight and 38.9% were obese. Approximately 14.8% were at risk of undernutrition and 1.3% were undernourished. In addition, among individuals identified at risk of undernutrition, more than 30% presented simultaneously overweight/obesity. Low values of HGS (<18 kgf in women and <30.3 Kgf in men) and of GS (>0.8 m/s) were observed.

ness nutritional status, the Global Subjective Assessment (SGA) was used. Readmission was considered to be those patients coming from the hospital itself, from home care or transferred from another hospital unit. It was evaluated the association between nutritional status and readmission rate with the occurrence of death.

**Results:** The average age was  $85.4 \pm 4.5$  years, of which 200 (62.4%) were female. The data showed that there was a worsening in nutritional status in the percentage of severe malnourished patients during hospitalization (24.2% vs. 31.4%;  $p < 0.001$ ). The readmission and death rates were 33% ( $n = 115$ ) and 30.4% ( $n = 96$ ), respectively. Severe malnourished elderly people were twice more likely to die than those without this nutritional status (61.4% vs. 38.5%; OR 2.17 95% CI 1.3 - 3.55;  $p = 0.002$ ). The data also showed a significant increase in the chance of death in those patients who were readmitted (39% vs. 25.8%; OR 1.8 95% CI 1.12-3.02;  $p = 0.016$ ).

**Conclusions:** About a quarter of critical octogenarian elderly hospitalize severely malnourished, the readmission rate was 33% and there is an increased chance of death for these severely malnourished and readmissioned patients.

**Keywords:** Octogenarians; Intensive care units; Critically ill patient

### 13 – Low skeletal muscle function, but not mass, is associated with the presence of type 2 Diabetes

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**Background:** The pathophysiology of type 2 Diabetes mellitus (T2DM) is intimately connected to the skeletal muscle (SkM). SkM affects insulin resistance and is, in turn, affected by the metaflammation, microvascular disease and ectopic fat deposition of T2DM. SkM mass can be inferred by the waist-to-calf ratio (WCR) and its function by the Short Physical Performance Battery (SPPB). The aim of this study was to determine the association between SkM mass and function with T2DM in patients with Metabolic Syndrome (MetS).

**Methodology:** Patients with MetS, aged 18 to 75 years-old, attending an outpatient clinic from April 15<sup>th</sup> to September 30<sup>th</sup> 2019, were consecutively included. Exclusion criteria comprised type 1 Diabetes, secondary hypertension, active neoplasia, autoimmune disease, HIV or hepatitis virus B or C infection and end-stage renal disease and/or liver disease. History and anthropometric data were collected, including weight, height, waist circumference (WC) and WCR; the SPPB was applied.

**Results:** A total of 81 patients were included, of which 58.0% had T2DM; most patients were female (55.6%) and the median age was 65 (interquartile range 16.5) years. Patients with T2DM were older (64.1 vs. 56.5 years,  $p = 0.001$ ) and more likely to have concurrent hypertension (96% vs. 65%,  $p < 0.001$ ) and dyslipidemia (96% vs. 56%,  $p < 0.001$ ). In univariate analysis, WC [odds ratio (OR) 1.1, 95% confidence interval (CI) 1.0-1.1], WCR (OR 146.2, 95% CI 9.9-2159.0) and SPPB (0.6, 95% CI 0.4-0.8) were associated with T2DM. In multivariate analysis, only SPPB maintained its association (OR 0.65, 95% CI 0.44-0.97).

**Conclusions:** Poorer muscle function, as determined by the SPPB, was associated with the presence of T2DM, even when considering body composition, per WCR. Longitudinal and mechanistic studies are warranted to best characterize this relationship.

**Keywords:** Diabetes; Sarcopenia; Muscle function; Muscle mass

### 14 – Acute effect on glycolytic involvement after resistance training sessions differing in set configuration

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**Background:** Resistance training (RT) is currently recommended by health organizations as a significant component of a healthy fitness lifestyle and many prevention programs for several diseases<sup>1</sup>. Loading parameters can be manipulated in different ways, providing different effects. In order to prescribe RT with safety and maximal efficiency, the effects of loading parameters should be clarified. A parameter that could modulate the RT effects is the set configuration. Set configuration refers to the repetitions actually performed with regard to the maximum possible number of repetitions in a set<sup>2</sup>. The aim of this study was to analyze the acute effects on glycolytic involvement of two RT sessions differing in set configuration.

**Methodology:** 41 sport science students (29 males, 12 females) performed in a random order two RT sessions (leg extension, leg curl, lat pull, bench press and parallel squat). Experimental sessions were equated for intensity, volume and total resting time (40 repetitions with the 15RM load with 360 sec of total resting time between sets for each exercise) and differed by set configuration: 4 sets of 10 repetitions with 2 min-rest between sets (Traditional Session: TS) and 8 sets of 5 repetitions with 51 sec-rest between sets (Cluster Session: CS). In both training sessions, 3 min-rest between exercise were performed. Before and after the sessions, capillary blood lactate concentration (BL) was obtained and a two-way repeated-measures analyses of variance (ANOVA) was used to evaluate the effect of session (TS or CS) and time (Pre-Post) on lactatemia.

**Results:** For BL, main effects of time and session and time x session interaction were found ( $p < 0.001$ ). After TS and CS, higher values were observed compared with baseline values. For comparison between values after RT, TS showed higher values in comparison with CS ( $p < 0.001$ ).

**Conclusions:** These data shown that both RT sessions increased BL. However, the BL increments are mitigated by CS. In conclusion, set configuration can modulate the glycolytic response after RT sessions.

**Keywords:** Set configuration; Cluster configuration; Resistance training; Glycolytic involvement; Blood lactate

### 15 – Obesity/type 2 diabetes mellitus biomarkers induce changes in nutrient transport that can promote breast cancer progression

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**Background:** Obesity and type 2 diabetes mellitus (T2DM) associate with increased incidence and mortality from many cancers, including breast cancer. We investigated the effect of obesity/T2DM biomarkers (hyperinsulinemia, hyperleptinemia, and increased levels of inflammation and oxidative stress) upon uptake of two important nutrients (glucose and glutamine) by breast cancer cells.

**Methodology:** Breast cancer cells (MCF-7 and MDA-MB-231) were exposed to high levels of the oxidative stress inducer *tert*-butylhydroperoxide (TBH; 0.5-2.5  $\mu$ M), insulin (1-50 nM), leptin (10-500 ng/ml) and pro-inflammatory cytokines (TNF- $\alpha$  or INF- $\gamma$ ; 1-100 ng/ml) for 24 h, and 3H-deoxy-D-glucose (<sup>3</sup>H-DG) and <sup>3</sup>H-glutamine (<sup>3</sup>H-GLN) uptake (6 min) were then quantified.

**Results:** TBH, insulin and INF- $\gamma$  induced a concentration-dependent increase in 3H-DG (10 nM) uptake in both cell lines, and leptin only in MCF-7 cell line. By examining the influence of a selective GLUT1 transport inhibitor (BAY-876 500 nM) on the stimulatory effect of these compounds, we con-