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### ORAL PRESENTATION SESSION

OP01

#### PREDICTORS OF WEIGHT LOSS OUTCOMES IN OBESITY CARE

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**Background** Clinically meaningful, sustained weight loss (WL), is achievable for some, but challenging for most people with obesity (PwO). To better understand factors contributing to WL outcomes, we examined attitudes and behaviors related to obesity care in a nationally representative sample of PwO from the ACTION (Awareness, Care, and Treatment In Obesity management) Study.

**Methods** 3008 US adult PwO in a stratified cross-sectional sample completed survey assessing recent WL outcomes and associated attitudes and behaviours. A multivariate logistic model compared variation in WL success (10% of sample; defined as  $\geq 10\%$  WL in previous 3 years and self-reported success in weight management over previous year (PwO-S) with seven characteristics taken from demographic, attitudinal and behavioural survey domains.

**Results** WL success by our definition was consistent with PwO-reported WL history. PwO perceived that support, motivation for WL, and reinforcement and engagement with HCPs, are associated with WL success, even after controlling for weight history. This study underscore the potential role of motivation and engagement of PwO in WL success and provide a strong foundation for exploring mechanism for these factors to predict success.

Understanding these mechanism should help identify important targets to enhance obesity treatment outcomes.

OP02

#### EARLY RESPONDERS TO LIRAGLUTIDE 3.0 MG AS ADJUNCT TO DIET AND EXERCISE FROM THE SCALE MAINTENANCE TRIAL

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**Aim** This is a post-hoc analysis of the SCALE Maintenance trial comparing outcomes in liraglutide 3.0 mg early responders (ERs) vs. early non-responders (ENRs) who completed 56 weeks of treatment (ERs vs. ENRs;  $\geq 5\%$  vs.  $< 5\%$  weight loss at week 16 after randomisation).

**Methods** Efficacy outcomes for liraglutide 3.0 mg ERs vs. ENRs are reported as observed means or proportions for individuals completing 56 weeks of treatment. The safety analysis set was used for adverse events.

**Results** Mean characteristics at randomisation ( $n = 212$ ) for participants on liraglutide 3.0 mg were: 46 years of age, 84% female, BMI  $36 \text{ kg/m}^2$ . Of those who completed 56 weeks of treatment ( $n = 159$ ), 108 (68%) were ERs to liraglutide 3.0 mg and 51 (32%) ENRs.

91.7% of ERs maintained their run-in weight loss (or lost further weight) during 56 weeks of treatment vs. 47.1% of ENRs. The percentage of individuals who had regained all weight loss achieved during the run-in period by week 56 was 0.0% for ERs vs. 3.9% for ENRs. At week 56, greater mean and categorical weight loss and similar improvements in cardiometabolic risk factors were observed in ERs vs ENRs (Table). Adverse events (AEs) were reported in 92.7% of ERs vs. 91.0% of ENRs. For serious AEs, proportions were 4.9% vs. 0.0% and for gastrointestinal AEs 78.9% vs. 62.7% for ERs vs. ENRs respectively.

**Discussion** Among those who completed 56 weeks of treatment, liraglutide 3.0 mg ERs achieved greater mean and categorical weight loss than liraglutide 3.0 mg ENRs, following  $\geq 5\%$  weight loss prerandomization.

## OP03

## TRI-PONDERAL MASS INDEX VS BODY MASS INDEX IN DISCRIMINATING ABDOMINAL FATNESS IN OVERWEIGHT ADOLESCENTS

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**Background and aims** Recently Peterson's group proposed that the tri-ponderal mass index (TMI), which is weight divided by height cubed, may be a valid alternative to BMI when measuring body fat in adolescents. Therefore, in addition to BMI, quantifying body fat distribution with waist-to-height ratio (WHtR), a proxy for abdominal obesity, could improve efficacy in clinical practice, especially in children classed as overweight by BMI. Taking this into account, this study examined whether TMI has better accuracy than BMI in discriminating abdominal fatness in overweight adolescents

**Methods** This cross-sectional study included 3749, 1889 males and 1860 females, aged 12–13. BMI was calculated and expressed as z-scores using CDC growth charts. TMI was calculated and expressed as percentile scores, 85th and 95th, to classify overweight and obesity respectively. Abdominal obesity defined as WHtR  $\geq$  0.5.

Regression analysis was used to investigate the association between WHtR and BMI and TMI separately. The discriminant ability of TMI, BMI z-score, with respect to abdominal obesity was investigated using non-parametric receiver operating characteristic analysis.

**Results** TMI correlation with WHtR was stronger than that of BMI ( $R^2 = 0.79$  vs  $0.72$  in boys and  $R^2 = 0.78$  vs  $0.72$  in girls for TMI and BMI respectively).

In boys, TMI area under the curve (AUC) was 0.960 versus BMI z-score AUC of 0.950 ( $P < 0.005$ ). In girls, TMI AUC was 0.972 versus BMI z-score AUC of 0.958 ( $P < 0.0001$ ).

The overall misclassification rate was only 7.49% for TMI vs 14.92% for BMI z scores ( $P < 0.001$ ).

**Conclusion** TMI is a superior body fat index and discriminated body fat distribution more accurately than BMI; so, this data support the proposal of the use, in association with the WHtR, of TMI rather than BMI to characterize overweight adolescents with high cardiometabolic risk.

Our analysis needs to be extended to other ethnic groups and replicated in a wider age range and in longitudinal studies.

## OP04

## KETOGENIC DIET-INDUCED WEIGHT LOSS IS ASSOCIATED WITH AN INCREASE IN VITAMIN D LEVELS IN OBESE ADULTS

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Vitamin D is an important micronutrient involved in calcium homeostasis, musculoskeletal health and in the pathophysiology of different organ systems. Recent data showed a strong association between hypovitaminosis D and different cardio-metabolic diseases. Several studies have identified that obesity is associated with vitamin D deficiency, although there is no consistent evidence for the causal relationship between these events. The four proposed mechanisms are: reduced sun exposure, sequestration in adipose tissue, negative feedback from 1,25-dihydroxyvitamin D<sub>3</sub>, volumetric dilution. Ketogenic diet has proven to be very effective for rapid weight loss, especially in reducing fatty mass while preserving free-fatty mass.

We investigated the effect of ketogenic diet-induced weight loss on vitamin D levels in a population of obese adults.

We enrolled 56 obese outpatients, prescribed with either traditional low calories diet (LCD) or very low calories ketogenic diet (VLCKD). 25(OH)D levels were measured by competitive immunoassay with chemiluminescence. We also measured: fasting plasma glucose and insulin, total, LDL- and HDL-cholesterol, triglyceride, creatinine, e-GFR, HOMA, uric acid, hsCRP. Body composition was evaluated by bioimpedentiometry. The mean value of 25(OH)D in the whole population at baseline was  $17.8 \pm 5.6$  ng/ml, without difference between groups. After 12 months of dietetic treatment, in VLCKD patients 25(OH)D levels increased from  $18.4 \pm 5.9$  to  $29.3 \pm 6.8$  ng/ml ( $P < 0.0001$ ), vs  $17.5 \pm 6.1$  to  $21.3 \pm 7.6$  ng/ml ( $P = 0.067$ ) in the LCD group. At multiple regression analysis fatty mass resulted the strongest independent predictor of vitamin D levels, explaining 15.6, 3.3, 9.4% of its variation in the whole population, in LCD and VLCKD groups, respectively.

These data suggest that a dietetic regimen which implies a great reduction of fat mass can restore vitamin D levels in obese.

## OP05

## PREVALENCE OF SARCOPENIA IN YOUNG ADULTS WITH SEVERE OBESITY FROM SOUTHERN ITALY

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Sarcopenic obesity (SO) is a condition where fat mass (FM) excess and muscle mass depletion coexist and it is usually described in the elderly. A clear definition for SO is currently lacking and there is therefore a need to develop a standardised approach of defining SO using body composition assessment. The aim of this study is to evaluate the prevalence of sarcopenic obesity in young adults with

severe obesity (BMI > 40) using bioimpedance analysis (BIA) as screening tools.

We studied 225 men (age  $33 \pm 9.4$  years; weight  $147 \pm 22$  kg, BMI  $48.7 \pm 6.63$  kg/m<sup>2</sup>, fat free mass (FFM)  $79.9 \pm 12.2$  kg, FAT  $67.6 \pm 15.1$  kg, PFAT  $45.5 \pm 5.3\%$ ) and 363 females (age  $34 \pm 9.9$  years; weight  $126 \pm 19.3$  kg, BMI  $48.2 \pm 6.72$  kg/m<sup>2</sup>, FFM  $61.2 \pm 9.04$  kg, FAT  $65.2 \pm 13.6$  kg, PFAT  $51.3 \pm 4.75\%$ ).

Anthropometric measurements and (BIA) at 50 kHz (DS Medica) were performed early in the morning; skeletal mass was calculated according to Janssen equation  $SM$  (kg) = ( $h^2/BIA$  resistance \* 0.401) + (sex \* 3.825) + (age \* 0.071) + 5.102; where height (h) is in cm, BIA resistance is in ohms; as concerning sex, male = 1 and female = 0. SO was defined with three different criteria:

- (1) Lowest tertile SM of the group;
- (2) SMP INDEX = SM (kg)/body mass (kg) × 100;
- (3) 25th percentile of the distribution of residual SM in the group.

Based on SM tertiles, 67 males and 109 females were defined SO and 158 males and 254 females non sarcopenic obese (NSO). According to SMP, 160 males and 269 females were defined SO and 65 males and 93 females were NSO; based on residual SM, 91 males and 57 females were defined SO and 272 males and 168 females NSO. However, 35 males (15.6%) and 66 females (18.2%) only fulfilled all three criteria and were defined SO.

Sarcopenia rates vary widely based on different definitions. When SMP is used, we have observed the highest prevalence of SO. Anyway, a correct diagnosis of sarcopenia needs to be confirmed with functional data, particularly in severe obese young adults.

## OP06

### EFFECT OF MEDICAL NUTRITIONAL TREATMENT OF OBESITY ON FIBROSCAN MEASURES OF LIVER STEATOSIS AND FIBROSIS

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**Background and aims** Non-alcoholic fatty liver disease (NAFLD) is referred to as the presence of fat in the liver in absence of a chronic alcohol consumption and is often associated with obesity, insulin-resistance, diabetes and metabolic syndrome. NAFLD is recognized as an important health problem and due to both inflammation and genetic factors, it may complicate with fibrosis, cirrhosis and even cancer. Actually, no pharmacological treatment is available for NAFLD and weight loss combined to lifestyle changes is the only acknowledged management. Recently, Fibroscan, an ultrasonographic imaging technique, has been used to assess the presence of liver steatosis and fibrosis, through the measurement of Controlled Attenuation Parameter (CAP) and stiffness respectively. In this study we investigated the changes of Fibroscan measurements in patients with NAFLD who underwent a hypocaloric medical nutritional treatment (MNT).

**Materials and methods** We enrolled 68 consecutive overweight/obese individuals. 50 healthy normal weight people were investigated as control group. Inclusion criteria were age 18–75 years and BMI > 25.0 kg/m<sup>2</sup>, exclusion criteria were habitual alcohol consumption (> 30 g/day for men and 20 g/day for women), chronic HBV or HCV infection, MNT in the last 6 months.

**Results** Obese/overweight patients had significantly higher CAP ( $320 \pm 56$  vs  $203 \pm 47$  Db/m;  $P < 0.001$ ) and stiffness values ( $7.2 \pm 4.4$  vs  $4.2 \pm 1.1$  kPa;  $P < 0.005$ ) compared to control group. Success of a MNT was achieved in 45 patients (71%). The prevalence of NAFLD (CAP > 248 dB/m) after successful MNT reduced to 61% ( $p < 0.001$ ), whereas it was unchanged (96%;  $p$  ns) in the subgroup with MNT failure. The subgroup with successful MNT reported a CAP reduction of  $15.4 \pm 20.2\%$  ( $P < 0.001$ ) while that of stiffness was  $18.0 \pm 32.5\%$  ( $P < 0.001$ ).

**Conclusions** This study suggests that obesity treatment with hypocaloric diet induces favorable changes of Fibroscan measures in people with NAFLD.

## OP07

### OBESITY AND DIFFERENTIATED THYROID CANCER (DTC): LACK OF CORRELATION BETWEEN BODY MASS INDEX (BMI) AND HISTOPATHOLOGICAL FEATURES

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The prevalence of obesity is associated with an increased incidence of DTC. Whether higher BMI is associated with more aggressive presentation of DTC is still unknown. The aim of this study was to investigate the relationship between BMI and histopathological features of DTC in a consecutive series of patients.

We retrospectively evaluated the data of 805 DTC patients who underwent total thyroidectomy (TTx) and radioiodine remnant ablation (RRA) in years 2010–2011. Patients were divided into three groups accordingly to their BMI [normal weight (Nw), overweight (Ow), obese (Ob)], at the time of the first control after TTx (median 5 months). For each group clinico-pathological and histological features and risk of recurrence (according to 2009 ATA Guidelines) were evaluated.

Out of 805 pts, 360 were Nw, 285 were Ow and 160 were Ob. Age and BMI were positively associated ( $p < 0.05$ ) in 5.3% of Nw, in 8.9% of Ow, and in 10.1% of Ob. DTC was multifocal in 56.6% of Nw, 55.6% of Ow and 59.9% of Ob. Metastatic lymph nodes (N1a a/o N1b) were observed in 24.3% of Nw, 23.2% of Ow and in 18.4% of Ob. Accordingly to the ATA 2009, about one half of the pts had an intermediate risk of recurrence (51.4% of Nw, 51.2% of Ow, 50% of Ob) and the other half had low risk (46.9% of Nw, 47.4% of Ow, 48.1% of Ob); as expected, very few were the high risk patients. The post therapeutic whole body scan (ptWBS) showed the presence of metastasis in 3.3% of N, 4.9% of Ow and 1.2% of Ob. The above reported differences among the three groups were not statistically significant. In our series increased BMI was significantly associated with older age. In conclusion, no significant differences in the histological presentation of DTC could be demonstrated among Nw, Ow and Ob patients.

## OP08 GENDER DIFFERENCES IN THE MEDITERRANEAN DIET IN HEALTHY ADULT PATIENTS

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Gender and age exert important influences on food preferences. Mediterranean diet (MD) is a healthy dietary pattern characterized by a high consumption of vegetables, fruits, grains, legumes, fish, eggs, along with a moderate intake of meat, oil and wine. The aim of this observational study was to evaluate the adherence to the MD in a sample of adult population, stratified according to categories of sex, age, and body mass index (BMI).

**Materials and methods** Cross-sectional study on 1013 healthy adult patients (461 males; 45.5%), largely representative of the adult population living in the Campania Region with regard to gender ( $\chi^2 = 0.08$ ,  $p = 0.777$ ) (<http://www.istat.it/campania>). Patients were divided into five BMI categories and four age groups for each gender. The adherence to the MD was evaluated using the PREVENCIÓN con Dieta MEDiterránea (PREDIMED) questionnaire.

**Results** The majority of subjects reached a high-average adherence to the MD, while only one third of the subjects were low adherers. Across all BMI categories, females showed an overall higher adherence to MD compared with males up to 18–28 age years. Within each sex and BMI group, we observed a significant increase of the adherence to the MD up to 29–38 years, with a subsequent decline along with increasing age. Within each sex and age group, the adherence to the MD tended to decrease with increasing BMI. A significant positive correlation was observed between PREDIMED score and BMI in normal weight in both genders. This association became negative along with increasing BMI.

**Conclusion** Our findings showed that there is a clear gender difference in the association between the adherence to the MD and BMI, as female participants showed an overall higher adherence to the MD compared with male counterpart. However, in both gender this association showed a biphasic trend, which is characterized by a positive association in normal weight categories, and a negative association in the other BMI categories.

## OP09 THE EFFECTS OF RYGB ON TISSUE INSULIN SENSITIVITY, BETA CELL FUNCTION AND POST- MEAL GLUCOSE FLUX ARE MAINTAINED 7 YEARS AFTER SURGERY IN BOTH DIABETIC AND NON DIABETIC PATIENTS

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The improvement in Type 2 Diabetes (T2D) after gastric bypass (RYGB) is accompanied by change in insulin sensitivity (IS), B-cell function, post-meal glucose flux. Long-term studies indicate that the remission rate of T2D was higher at 2 than 10 years post-surgery. Most

of the studies analysed the effects of surgery on glucose metabolism in the early years after surgery. Our aim was to determine if the effects of surgery on tissue IS, post meal glucose flux and B-cell function (B-GS) are maintained long term after surgery.

**Methods** We studied 14 T2D and 10 nondiabetic (ND) patients before (B), 1 (1 year) and 7 years (7 years) after RYGB with a mixed meal test (MTT) and euglycaemic-insulin-clamp combined with tracer technique to measure B-cell function (B-GS), glucose fluxes, adipose-IR, hepatic-IR, muscle IS (M/I).

**Results** Both ND and T2D patients at 7 years regained  $15 \pm 6\%$  of weight lost by after RYGB. T2D was resolved 1 year post-surgery and this outcome was maintained at 7 years (HbA1c  $56 \pm 6$  vs  $36 \pm 1$  vs  $41 \pm 2$  mmol/mol; B, 1y and 7 years). M/I improved at 1y (from  $7.1 \pm 1.5$  to  $13.5 \pm 1.0$  in ND and from  $5.4 \pm 0.8$  to  $13.8 \pm 1.4$  in T2D),  $p < 0.001$ , and maintained at 7 years in both ND and T2D ( $16.5 \pm 2.5$  in ND to  $13.5 \pm 1.5$  nmol. kgffm<sup>-1</sup>. min<sup>-1</sup>. PM<sup>-1</sup> in T2D;  $p = ns$  vs 1 year). Hepatic-IR and Adipose tissue-IR improved at 1y ( $p < 0.03$ ) and maintained at 7 years in both ND and T2D ( $p = ns$ ). Plasma glucose profile and the dynamic of the oral glucose Ra were similar in ND and T2D at 1 year and 7 years. Post meal suppression of Endogenous glucose production during the first 90 min was improved in both groups at 7 years compared to 1y. (AUC of EGP 0–90  $p < 0.05$ , 1 vs 7 years, for both group). In T2D, the improvement in B-GS seen at 1y ( $33 \pm 5$  to  $64 \pm 8$  pmol min<sup>-1</sup> m<sup>-2</sup>. mM<sup>-1</sup>,  $p = 0.001$ ) was maintained at 7 years ( $79 \pm 15$ ) at a similar level as in ND ( $136 \pm 16$  vs  $88 \pm 8$  vs  $83 \pm 9$ , B, 1- and 7 years).

**Conclusion** In both ND and T2D, RYGB induces marked improvements in glucose tolerance, insulin sensitivity (muscle, liver, adipose tissue) and B-cell function that are maintained 7 years after surgery. Research grant of Italian Ministry of Health {RF-2011-02348446}.

## OP10 OCCURRENCE OF THE IMMUNE NON-NEURONAL CHOLINERGIC SYSTEM IN THE INFLAMED ADIPOSE TISSUE OF OBESE MICE

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A key feature of morbid obesity is white adipose tissue (WAT) inflammation. In obese animals and humans, WAT is infiltrated by immune cells, mainly macrophages, which are mainly found at sites where adipocytes die by pyroptosis, forming distinctive crown-like structures. Acetylcholine (ACh) was the first neurotransmitter to be discovered. However, within the past decades increasing evidence has shown that ACh is also produced by non-neuronal cells and tissues, including the immune cells, where it acts as a secreted messenger with anti-inflammatory properties. Here we evaluated whether the non-neuronal cholinergic system occurs in obese and inflamed fat. By RT-qPCR, we found that all the components of the non-neuronal cholinergic system molecular machinery significantly increased in subcutaneous and visceral WAT from high-fat diet obese mice compared with mice fed a normal diet. By immunohistochemistry and confocal microscopy, we found that about 40–50% of macrophages infiltrating obese WAT did express choline acetyltransferase (ChAT), choline transporter-1 (ChT-1) and the vesicular ACh transporter

(VACHT), whereas the white adipocytes expressed the butyrylcholinesterase (BChE). In vitro studies showed that white adipocytes differentiated from hMADS cells not only produced BChE but also, and to a larger amount, acetylcholinesterase (AChE). Collectively, these data suggest that a consistent proportion of macrophages infiltrating obese WAT produce and secrete ACh that in turn acts on ACh receptor-bearing adipocytes. The diffusion of this potent molecule is prevented by ACh re-uptake by macrophages (through VACHT) or by adipocyte ACh degradation (through BChE and AChE) into acetate and choline, which is quickly taken up by the macrophages expressing the ChT-1. Promoting the anti-inflammatory effect of the non-neuronal cholinergic system recruited in the inflamed obese fat could represent a novel and effective therapeutic approach to obesity and associated diseases.

## OP11

### EXTRACELLULAR VESICLES (EVS) RELEASED FROM ADIPOSE TISSUE OF OBESE INDIVIDUALS REDUCE SURVIVAL AND FUNCTION IN HUMAN PANCREATIC $\beta$ -CELLS

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Extracellular vesicles (EVs) play a major role in cell-to-cell communication by transferring proteins, RNAs and microRNAs to recipient cells. Few studies have described the characterization of EVs derived from white adipose tissue (WAT) and their association with obesity and diabetes. In fact, EVs have been implicated in the crosstalk between adipocytes and macrophages; moreover, an increase in EVs from omental WAT has been described in insulin resistant individuals. However, to date the role of EVs in the crosstalk between adipocytes and pancreatic  $\beta$ -cells remains to be defined. We hypothesized that in pathophysiologic conditions, adipocyte-derived EVs would regulate the survival and function of pancreatic  $\beta$ -cells. We show here that EVs derived from mouse 3T3-L1 adipocytes increased survival and proliferation and reduced apoptosis in INS-1E  $\beta$ -cells and human pancreatic islets, treated with cytokines (CKs) or palmitate/high glucose.

Conversely, EVs from 3T3-L1 cells treated with CKs exerted opposite effects and enhanced  $\beta$ -cell death and apoptosis. Interestingly, NGS analysis showed that EVs from control and CK-treated 3T3-L1 adipocytes contained a different expression pattern of microRNAs implicated in  $\beta$ -cell survival and function. Importantly, in humans, EVs released from subcutaneous and omental AT of obese individuals reduced cell survival and insulin secretion in human pancreatic  $\beta$ -cells (EndoC- $\beta$ H3), suggesting that in obesity and type 2 diabetes (T2D) WAT reduces  $\beta$ -cell mass and function. Overall, the results of this study indicate the existence of an EV-mediated cross-

talk between WAT and pancreatic  $\beta$ -cells, and suggest new avenues for identifying therapeutic strategies in obesity and type 2 diabetes.

## OP12

### UPREGULATED MACROPHAGES EXPRESSION OF PLIN2 IS ASSOCIATED WITH EARLY ATHEROSCLEROSIS IN OBESE CHILDREN

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**Background** Perilipin (Plin) 2 regulates net balance between macrophage intake and efflux of fat within artery fatty streaks and is overexpressed in human carotid lesions. Since the atherosclerotic process begins in childhood and obesity accelerates it, we investigated monocyte Plin2 expression in obese versus normal-weight children and its correlates with early atherosclerosis as estimated by carotid intima media thickness (cIMT).

**Methods** Sixty-three overweight/obese children and 21 age- and sex-matched normal-weight controls were enrolled. Plin2, proteasome subunits (PSMD3, PSMC4) mRNA expression were determined by RealTime PCR in monocytes; Plin2, LAMP2A and hsc70 protein expression were assessed by western blot analysis. cIMT was estimated by carotid ultrasonography.

**Results** Plin2 protein levels were significantly higher in obese children than in controls [66.6 (3.45) vs 45.12 (4.46),  $p = 0.001$ ] and expression correlated with cIMT in the former group after adjusting for variables known to affect cIMT, ( $\beta$ -coeff = 0.39;  $p = 0.02$ ). There was negative correlation between Plin2 protein expression and mRNA levels of subunits PSMC4 and PSMD3 ( $r = -0.42$ ,  $p = 0.003$  and  $r = -0.32$ ,  $p = 0.02$  respectively). mRNA expression of proteasome subunits PSMC4 and PSMD3 were both reduced in obese children as compared to controls [105.8 (8.6) vs 155.1 (16.8);  $p = 0.006$  and 8.6(0.66) vs. 11.7 (1.5);  $p = 0.03$ ]; LAMP2A and Hsc70 expressions did not differ between cases and controls. Plin2 and LAMP2A levels were inversely correlated in lean subjects ( $r = -0.75$ ;  $p = 0.0004$ ).

**Conclusions** A childhood obesity dependent impairment of Plin2 expression is dysregulated monocytes of obese children and contributes to enhanced atherosclerosis.

## OP13

MINOR ROLE OF MATURE ADIPOCYTE  
MINERALOCORTICOID RECEPTOR IN OBESITY

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Obesity is a major risk factor contributing to the development of Cardiovascular Disease and type 2 Diabetes. Mineralocorticoid Receptor (MR) expression is increased in adipose tissue of obese patients and, in the last years, several studies provided evidence that MR pharmacological antagonism improves glucose metabolism in genetic and diet-induced mouse models of obesity.

In order to investigate if the lack of adipocyte MR is sufficient to explain these beneficial metabolic effects, we generated a mouse model with inducible adipocyte-specific deletion of MR gene (adipo-MRKO).

We observed a significant, yet not complete, reduction of MR transcript and protein expression in subcutaneous and visceral depots of adipo-MRKO mice. Notably, only mature adipocyte fraction lacks MR gene, whereas, stromal vascular fraction keeps normal MR expression in our mouse model.

Adipo-MRKO mice fed a 45% high fat diet for 14 weeks did not show any significant difference in body weight and fat mass compared to littermates controls. Glucose and insulin tolerance tests revealed that mature adipocyte MR deficiency did not improve insulin sensitivity in response to a metabolic homeostatic challenge. Accordingly, no significant changes were observed in gene expression profile of adipogenic and inflammatory markers in adipose tissue of adipo-MRKO. Moreover, differentiating preadipocytes, pharmacological MR antagonism in mature primary murine adipocyte differentiated *ex vivo* from wild type mice did not display any effect on adipogenic and inflammatory markers.

Taken together, these data demonstrate that MR deletion in mature adipocytes displays a minor role in diet-induced obesity and metabolic dysfunctions.

## OP14

STUDY OF PSYCHOLOGICAL AND PSYCHIATRIC  
PREDICTORS OF SUCCESS IN THE TREATMENT  
OF OBESITY

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Many therapeutic approaches, such as lifestyle interventions, weight-reducing drugs, and bariatric surgery, have been developed through the years to treat obesity, although success rates, especially long-term, remain modest. Our group has previously worked on identifying possible psychological and psychopathological features associated with a good response to a program of multidisciplinary therapy aimed at weight loss in obese patients. Results obtained so far confirm a modest efficacy of such programs and failed in identifying any convincing predictor of success. However, this preliminary study allowed us to develop a new psychometric test (Grandangle Overview Defining Obesity Treatment—GODOT) based on the most predicting 23 items we selected out of all the questionnaires we used to assess the sample. We then conducted a new prospective study on 213 obese patients referring to the Obesity Agency of the University of Florence, Italy that were assessed by the means of the new instrument GODOT. At the 6 month follow-up, only 52 patients (24.4%) reached the pre-defined therapeutic target of 5% weight loss. Out of all the instruments used, GODOT total score was the only psychometric tool significantly associated with treatment success. However, the test showed a modest sensibility and specificity. Despite these results are only preliminary, the present work provides an interesting starting point for future research on predictors of therapeutic success in obesity, which are crucial for a more specific identification of patients with a higher chance of succeeding in weight loss programs.

## POSTER SESSION

### Epidemiology and prevention

P01

#### PRESENTATION OF AN INNOVATIVE INTERNATIONAL QUESTIONNAIRE ON EATING HABITS AND ATTITUDES AMONG ITALIAN AND SOUTH AMERICAN TEENAGERS

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Many studies on children and teenagers have shown the correlation between eating habits, lifestyle and present and future health status. It has been shown in children a strong influence by their parents on their eating patterns and weight; in teenagers, who are close to adulthood, we have less evidences. The aim of this questionnaire is exploring the eating habits and lifestyle among teenagers of different cultures, aged between 16 and 18, to highlight the main factors that influence their choices and to compare them in two different communities such as the Italian and Peruvian one. It is a semi-quantitative questionnaire, web administrated and filled out by teenagers who attend high school in South Italy (Campobasso), North Italy (Bologna), and Peru (Lima). It consists of two sections, the first one investigates: (1) the main socio-demographic features of the subjects and their family; (2) some attitudes such as the involvement of managing one's own nutrition; (3) if subjects have a particular diet; (4) the attitude towards emerging issues like the sustainability in the agricultural and food production; (5) physical activity. The second session deals with the food questionnaire which is divided into nine food groups, results of an accurate study of the Guide Lines and Italian and Peruvian food habits found in literature. The portions are expressed in medium saized-portions in g/ml, or translated in term of standard unit and homemade unit of measurement for each food; the frequency of consumption is referred to the frequency on a monthly, weekly and daily basis of each food and drink in the past 4 weeks. The questionnaire has been validated in Italian and Spanish languages and tested on a group of subjects in Italy and Peru, which has shown a good reproducibility and reliability in the results. If the next study should confirm a good subjects' compliance, besides bringing interesting results, it could be taken as a model also in other European and non-European countries.

P02

#### EVALUATION OF RESULTS IN THE USE OF A VERY LOW-CALORIE KETOGENIC DIET (VLCKD) VS A VERY LOW-CALORIE NON-KETOGENIC DIET (VLCNKD) IN A 4-WEEK PREOPERATIVE PERIOD, IN PATIENTS UNDERGOING BARIATRIC SURGERY

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The aim of this study is to evaluate whether a diet with a very low caloric ketogenic intake has the ability to reduce body weight and to

modify the body composition favourably compared with a non-ketogenic diet with the same caloric intake.

We enrolled 94 patients (39 M, 45 F, mean age  $45 \pm 12$  years, mean BMI  $47.5 \pm 8$ ) consecutively affiliated to our Unit candidates for bariatric surgery who agreed to undertake a weight loss programme in a preoperative 4-week period. Patients were assigned alternatively to the ketogenic or non-ketogenic arm. The 47 patients of the ketogenic arm (28 M, 19 F, mean age  $45 \pm 11$  years, mean BMI  $49 \pm 8$ ) received a VLCKD with the following components: Protein 85 g. Lipids 30 g. Carbohydrates 30 g Kcal, 730 for 28 days. This treatment involved the combination of natural foods with hypoglycemic replacement meals. The 47 patients of the non-ketogenic arm (20 M, 27 F, mean age  $45 \pm 14$  years, mean BMI  $46 \pm 9$ ) received a VLCnKD with the following nutritional components: Protein 75 g. Lipids 30 g. Carbohydrates 65 g Kcal, 830 for 28 days. This treatment included the combination of natural food with two oral supplements per day, Glucerna SR. At t0 and at t1, the following parameters were evaluated: weight, Body Mass Index (BMI), waist circumference (WC), Hand Grip Strength Fatty Liver Index (FLI), and through mono-frequency bioimpedance method for deteminated body composition.

The VLCKD patients had significantly higher starting BMIs than the VLCnKD patients and both groups achieved a significant weight loss from T0 to T1, which was greater in the VLCKD group, although not significantly different from the VLCnKD group. For the other parameters taken into consideration, there was a significant difference between T0 and T1 in both groups as regards WC, FLI, FM, FFM, ECW and ICW. the ketogenic regime. seems more effective in reducing the parameters related to FLI and FM with a greater maintenance of MM and FFM.

### Obesity and diabetes

P03

#### VISCERAL ADIPOSE TISSUE-DERIVED INFLAMMATORY ENVIRONMENT AFFECTS CD4 T CELL PHENOTYPE AND FUNCTION IN OBESE PATIENTS WITH AND WITHOUT T2D

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Visceral adipose tissue (VAT) functions not only as a passive fat storage depot, but also as an endocrine and immunological organ. Indeed, in preclinical models of obesity, T cells localized in the VAT display significant changes compared to the physiological condition (leanness); in humans, there is scarce knowledge regarding T cell profile in obesity-driven inflamed VAT, especially in the presence of type 2 diabetes (i.e. diabetes), and compared to leanness. Here, we aimed to determine the profile of CD4 T cells in the VAT of obese patients -with (OB/D) and without type 2 diabetes (OB/ND)- and lean controls (LC).

The phenotype of conventional CD4 T cells (Tconv)—obtained by excluding regulatory T cells by the analysis—was assessed by flow cytometry in the stromal vascular fraction (SVF) obtained from the VAT of OB/D, OB/ND undergoing bariatric surgery and LC undergoing kidney living donation. Serial concentrations of supernatant

pre-conditioned with 20 mg of fat were used in co-culture assays with peripheral blood mononuclear cells to assess cell differentiation.

Shortage of a subset of CD4 Tconv expressing PD-1 is evident in OB/D, which is accompanied by partial impaired production of inflammatory cytokines and elevated proliferative capacity compared to LC, and reduced cytotoxic ability compared to the diabetes-free condition. Interestingly, inhibition of PD-1 + expression on CD4 T cells was found to be induced by the VAT environment coming from OB/D patients. Regardless the diabetes status, elevated PD-1 + CD4 T cell recirculation was evident in obesity, suggesting high local turnover. Of note, the frequency of tissue-resident PD-1 + cells in the VAT positively correlated with the % of fat mass loss 2 months after bariatric surgery, suggesting that their enrichment may promote early weight loss.

PD-1 + CD4 Tconv in the VAT show altered phenotype and function in obesity and may be potential targets for diabetes immunotherapy.

#### P04

### EFFECT OF GLP-1 RECEPTOR AGONISTS IN REPLACEMENT OF INSULIN MEALS BOLUS, IN ADDITION TO BASAL INSULIN, IN ELDERLY PATIENTS WITH TYPE 2 DIABETES

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**Background and aims** Type 2 diabetes (DT2) is an obesity associated condition with an increasing prevalence, especially among elderly people. “Basal-bolus” insulin treatment (BBIT) is often the best choice in elderly patients with comorbidities and complication, but it is associated with both high risk of hypoglycaemia and management difficulties. The glucagon-like peptide 1 receptor agonist (GLP-1 RA) has been shown to promote weight loss in obese patients and reducing HbA1c without causing hypoglycaemia.

**Materials and methods** This retrospective and longitudinal study evaluated the clinical effect of the switch from BBIT ( $\pm$  metformin) to GLP-1 RA + basal insulin (BI) in a group of elderly (> 65 years old) patients with uncompensated DT2 identified from medical records of the outpatients of 2 Italian anti-diabetic centres. Evaluations were performed at time of switch (T0), and at 6 (T6), 12 (T12) months.

**Results** Among 639 patients, 16 cases of switch from BBIT were identified. Treatment failure with GLP-1 RA was detected in 4 (1m/3f) cases (3 cases at T6, 1 at T12). This group was 68 years old (65–72), had a BMI of 40.0 kg/m<sup>2</sup> (37.8–42.2), a waist circumference of 124.5 cm (116.0–130.0) and an HbA1c of 8.2% (7.9–8.5). In 12 (5m/7f) cases the treatment was successful. This group was 70 years old (65–86), had a BMI of 34.7 (27.9–51.6), a waist circumference of 117.5 cm (95.0–130.0), and a HbA1c of 7.9% (7.5–9.6). In the successful switch group, significant reductions of body weight (T0: 92.3; T6: 87.6; T12: 88.0 kg; p.

#### P05

### EFFECT OF PERIODONTAL DISEASE ON GLUCOREGULATORY HORMONES IN INDIVIDUALS WITH MORBID OBESITY

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A few studies have addressed the link between periodontitis (PD) and obesity; the influence of PD on the glucoregulatory hormone pattern has never been explored. We measured clinical periodontal parameters (probing pocket depth, PPD, bleeding on probing, BOP, clinical attachment level, CAL) in 110 severely obese, non-diabetic subjects. Insulin, glucagon, GLP-1 and GIP were assessed after 3 days of standardized diet. 47 subjects had periodontitis (PD+) and 63 did not (PD−). PD + had a mean number of teeth of 26, 30.3% of gingival sites with PPD > 4 mm, 55.2% of BOP sites and a mean CAL loss of 4.1 mm, indicating a generalised tissue loss. hsCRP was high in both groups (4.31  $\pm$  3.80 vs 3.67  $\pm$  2.62 mg/l, p = 0.29). PD + showed higher IL-6 levels (3.4  $\pm$  3.9 vs 5.2  $\pm$  4.1 pg/ml, p = 0.02); IL-1 $\beta$  did not differ. No direct relationship emerged between cytokines and hormones. Compared with PD−, PD + had higher glucagon (26.60[25.22] vs 3.93[7.50] ng/l, p < 0.0001) and GIP levels (10.56[13.30] vs 6.43[8.43] pmol/l, p < 0.001), and lower GLP-1 (11.78[10.07] vs 23.34[16.80] pmol/l, p < 0.0001). Insulin did not differ. In PD +, after adjustment for confounders, PPD was directly related to glucagon ( $\beta$  = 0.424, p = 0.002) and inversely to GLP-1 ( $\beta$  = −0.159, p = 0.044). In PD +, CAL and PPD correlated with glucagon (r = 0.404, p = 0.003 and r = 0.456, p < 0.001 respectively). For PPD, such relationship held at multiple regression analysis ( $\beta$  = 0.431, p = 0.002); when adding incretins in the model, both glucagon and GLP-1 were associated (fullmodel R<sup>2</sup> = 0.30). In comparing different stages of PD, glucagon was related with the severity of periodontitis (16.17  $\pm$  9.95 ng/l, 25.25  $\pm$  4.34 ng/l, 39.24  $\pm$  4.45 ng/l from stage I to III; p = 0.03). We describe here for the first time an impaired incretin axis coupled with a relative hyperglucagonemia in obese non-diabetic individuals with PD and subclinical inflammation, that might contribute to deteriorate their glucose tolerance and partially explain the higher risk of diabetes observed in these patients.

#### P06

### THE EMPOWERMENT ON MEDITERRANEAN DIET AS A POSSIBLE TOOL TO TACKLE PREDIABETES ASSOCIATED TO OVERWEIGHT OR OBESITY: A PILOT STUDY

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The most important therapeutic strategy to prevent the progression from prediabetes (PD) to overt type 2 diabetes (T2DM) is lifestyle intervention focused on a healthy diet.



However, there is no specific dietary pattern recommendation to prevent T2DM in both general and at risk population. The objective of this study was to investigate the effect of the short-term empowerment on Mediterranean Diet (MD) adherence on metabolic and anthropometric parameters in PD overweight or obese subjects. Patients and Methods: Forty-two subjects with PD, aged 18–75 years, and BMI > 25 kg/m<sup>2</sup> that received dietary advice on MD by nutritionists during session groups every 2 weeks for 4 months. Data on energy caloric intake and macronutrient consumption were collected using a 7-days food diary record. The adherence to MD was investigated through the PREDIMED questionnaire. No advice were given regarding to caloric restriction and physical activity. At the baseline and at the end of the study each subject underwent anthropometric, metabolic, and nutritional assessment. Results: About 40.5% of subjects restored their normal glucose tolerance at the end of the study. Fasting plasma glucose, glycosylated haemoglobin (HbA1C), BMI, waist circumference, visceral adiposity index, triglycerides, total and LDL cholesterol levels were significantly decreased, while HDL-cholesterol significantly increased at the end of the study.

The subjects significantly increased the adherence to MD as assessed by PREDIMED questionnaire at the follow up. A reduction of prevalence of the metabolic syndrome was also reported. Interestingly the PREDIMED score correlated with HbA1C values at the follow up, after adjusting for BMI and total caloric intake. Conclusion: The short-term empowerment on MD adherence improves anthropometric and metabolic parameters in PD overweight or obese subjects. This takes great importance given that diet must be the cornerstone of treatment of patients at high risk of developing T2DM.

## Obesity and chronic diseases

P07

### DIETARY SUPPLEMENTATION WITH A SPECIFIC AMINO ACID FORMULA SUSTAINS MITOCHONDRIAL BIOGENESIS AND REDUCES HEPATIC STEATOSIS IN A HIGH-FAT DIET MOUSE MODEL OF NON-ALCOHOLIC FATTY LIVER DISEASE

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Non-alcoholic fatty liver disease (NAFLD) encompasses a wide spectrum of liver disorders characterized by hepatocyte fat accumulation and damage and inflammation, in the absence of alcohol abuse. The increasing prevalence of NAFLD correlates to the rise of obesity and predisposes susceptible individuals to cirrhosis, hepatocellular carcinoma and cardiovascular diseases. Due to the lack of approved drugs, diet and lifestyle modification are the only recommended options for NAFLD patients. Mitochondrial dysfunction and oxidative stress take part to NAFLD pathogenesis. We asked whether dietary supplementation with an amino acid mixture, enriched in BCAAs (BCAAem) and able to induce mitochondrial biogenesis and function in various tissues and to protect liver from EtOH-driven damage

(Tedesco et al., Am J Physiol Gastrointest Liver Physiol 314:G566–82, 2018) would prevent mitochondrial dysfunction and liver steatosis in mice models of dietary-induced NAFLD. Four-month old male C57BL/6 J mice (n = 6/group) were fed 6 months with high-fat diet containing 45% kcal fat (D12451, Research Diet Inc, New Brunswick, NJ). Increased body weight was paralleled by histological evidence of liver steatosis, ballooning, inflammation and fibrosis resulting in increased NAFLD Activity Score (NAS). Administration of BCAAem (1.5 mg/g body weight/day in tap water for 6 months) significantly reduced NAS and elicited a scaling down of hepatic lipid droplets (LD) diameter in HFD-fed mice. A significant increase of liver mitochondrial DNA content was observed in BCAAem-treated vs. untreated HFD-fed mice. Taken together, these data suggest a potential role of a specific amino acid formula in slowing down the progression of NAFLD, modulating the complex homeostasis of hepatic LD and sustaining mitochondrial biogenesis.

This work was supported by SEELN project (Brescia University 2015 Health&Wealth call, cofinanced by Molise University and Professional Dietetics SpA).

P08

### THYROID FUNCTION AND PREVALENCE OF THYROID DISORDERS IN MORBIDLY OBESE PATIENTS

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**Introduction** Contrasting data exist concerning the relationship between thyroid function and obesity. Objective: to investigate the prevalence of thyroid disease and alterations of thyroid function and morphology in morbidly obese patients, who are candidates to bariatric surgery, compared to normal-weight patients.

**Materials and methods** we retrospectively evaluated 391 obese patients (310 females and 81 males, mean age 38 years, range 18–66, mean BMI 45.75 ± 6.86 kg/m<sup>2</sup>), and 438 normal-weight patients referred to our Department for non-thyroidal disease (95 adrenal incidentalomas, 117 polycystic ovary syndrome, 36 idiopathic hirsutism, 30 primary hyperparathyroidism, 160 subjects in whom no endocrinopathy was detected). In all patients, TSH, FT3, FT4, anti-thyroglobulin and anti-thyroperoxidase antibodies and thyroid ultrasound was performed, identifying 255 obese and 361 normal-weight patients without thyroid disease.

**Results** the prevalence of thyroid disease was 34.78% in obese group compared to 27.7% in normal-weight group (p < 0.0001), with a significant  $\mu\text{UI/ml} \pm 1.22$ ) than in normal-weight patients (1.80  $\mu\text{UI/ml} \pm 1.0$ ) (p < 0.0001) and there was a positive correlation between TSH levels and BMI (p = 0.01). Obese patients had higher FT3 levels (3.63 ± 1.22 pg/ml) than normal-weight (3.20 ± 0.43 pg/ml) (p < 0.0001). Thyroid volume was significantly higher in obese patients (13.07 ± 8.27 ml) compared to normal-weight (9.52 ± 3.21 ml) patients (p = 0.01). No correlation was found between thyroid volume and BMI, TSH and insulin.

**Conclusion** A higher TSH associated to increased thyroid volume (TSH-unrelated) could account for the increased prevalence of thyroid disease in obese patients.

P09  
1-H POST-LOAD PLASMA GLUCOSE LEVELS  
AND INFLAMMATORY PROFILE IN OBESE  
SUBJECTS WITH NORMAL GLUCOSE TOLERANCE

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**Introduction** Recent evidences showed that glucose tolerant non-obese subjects with 1-h post-load glucose > 155 mg/dl (NGT-1 h-high) exhibit an unfavorable inflammatory profile as compared with NGT individuals with 1-hour post-load plasma < 155 mg/dl (NGT-1 h-low).

**Aim** To evaluate the inflammatory profile of obese subjects with NGT 1 h-high as compared with obese subjects with NGT 1 h-low.

**Methods** The study group consisted of 586 (228 M and 358 F) non-diabetic subjects. On the first day, after 12-h fasting, subjects underwent anthropometrical evaluation, including body mass index (BMI) and waist circumference, and a venous blood sample was drawn for laboratory determinations including inflammatory profile [high sensitivity C-reactive protein (hsCRP), erythrocyte sedimentation rate (ESR), fibrinogen, serum uric acid, PLT and WBC]. On the second day, a 75 g OGTT was performed. Insulin resistance was evaluated HOMA-IR.

Subjects were divided into two groups based on BMI value: obese subjects (BMI > 30 kg/m<sup>2</sup>, n = 264) and non-obese subjects (BMI < 30 kg/m<sup>2</sup>, n = 322). Also, we divided the obese subjects with NGT into two groups: 193 subjects with 1-h post-load plasma glucose < 155 mg/dl (NGT 1 h-low), and 71 individuals with 1-h post-load plasma glucose > 155 mg/dl (NGT 1 h-high).

**Results** There were no differences in age and sex in the study groups. BMI and body weight were significantly higher in obese subjects when compared with the non-obese subjects (P < 0.001 and P < 0.001, respectively). Obese subjects also exhibited significantly higher levels of ESR (P < 0.001), CRP (P < 0.001), serum uric acid (P < 0.001), WBC (P < 0.001) and fibrinogen (P < 0.001). HOMA-IR was significantly higher in obese subjects compared with non-obese subjects.

In the NGT obese subjects, between obese subjects with NGT 1 h-high and obese subjects with NGT 1 h-low no significant differences in ESR, CRP, WBC and fibrinogen were observed. Serum uric acid, was significantly higher in obese subjects with NGT 1 h-low.

There was no difference in the HOMA-IR value in the two groups.

**Conclusion** Our data confirm that the obese subjects have an unfavorable inflammatory profile when compared with non-obese subjects. Conversely, no differences in inflammatory profile between obese subjects with NGT 1 h-high or NGT 1 h-low were observed.

## Obesity and cardiovascular diseases

P10  
DIETARY INDUCTION OF MITOCHONDRIAL  
BRANCHED-CHAIN AMINO ACID OXIDATION  
BOTH PREVENTS AND AMELIORATES HEART  
FAILURE IN MICE

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Obesity and its associated diseases, such as coronary artery disease, diabetes mellitus, hypertension, dyslipidemia, and insulin resistance, are major risk factors for heart failure (HF). Several lines of evidence highlight a causal role of the obesity-linked metabolic alterations in the HF development, where altered cardiac metabolism and decreased mitochondrial substrate oxidation are important hallmarks. A nutritional approach to improve HF is still lacking. Recent research points towards an important role for dysregulated branched-chain amino acid (BCAA) metabolism in cardiac adaptation in HF. We explored the ability of a diet rich in saturated fatty acids (SFA diet) in which casein, the main protein source in rodent diet, was substituted with a specific mixture of soluble essential amino acids enriched in BCAA (SFA-EAA diet) to both prevent and improve HF. To this end, mice were subjected to cardiac hypertrophy by means of transverse aortic constriction (TAC) and were fed with either diet, starting before (preventive experiment) and after TAC (therapeutic experiment). As expected, TAC decreased fractional shortening rate (FS) in both experiments. On the contrary, mice fed with SFA-AA showed a significantly improved FS as compared to TAC mice fed with control SFA diet. Gene expression also showed that SFA-AA diet blunted the upregulation of several cardiac hypertrophy markers all of which were induced in TAC mice fed with SFA. Also, the downregulation of mitochondrial fatty acid oxidation genes induced by TAC was prevented by SFA-AA diet. Notably, the SFA-EAA-induced recovery from TAC was impaired in PP2Cm knockout mice. PP2Cm is a mitochondrial phosphatase that promotes the BCAA catabolism, leading to metabolic utilization of these amino acids. Together, our results strongly suggest that a diet enriched in specific essential aminoacids prevents and ameliorates HF by promoting expression of genes which are key regulators of BCAA oxidation.

P011  
KETOGENIC DIET IMPROVES ARTERIAL  
STIFFNESS IN OBESE ADULTS

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**Background** Obesity is often associated with several cardio-metabolic diseases such as insulin resistance, diabetes mellitus, arterial hypertension, atherogenic dyslipidemia, etc. The coexistence of obesity with one or more of these clinical conditions contributes to increase the cardiovascular risk of obese patients.

Ketogenic diet has proven to be very effective for rapid weight loss. It is a very-low-carbohydrate, normo-proteic and normal/high-fat diet. Arterial stiffness evaluated as pulse wave velocity (PWV) is an early marker of vascular damage and an independent predictor for

cardiovascular events. It is associated with normal vascular aging as well as with several morbid conditions, including obesity.

**Aim** We sought to investigate if weight loss obtained with a ketogenic diet could influence arterial stiffness.

**Materials and methods** We enrolled 56 obese outpatients (32 men and 24 women, mean age  $46.75 \pm 11.05$  years), prescribed with either traditional low calories diet (LCD) or with very low calories ketogenic diet (VLCKD). Pulse wave velocity was evaluated by a validated system employing high-fidelity applanation tonometry.

We also measured: fasting plasma glucose and insulin, total, LDL- and HDL-cholesterol, triglyceride, creatinine, e-GFR, HOMA, uric acid, hsCRP. Body composition was evaluated by bioimpedentiometry. **Results** After 12 months of dietetic treatment, VLCKD patients exhibited a greater even if not statistically significant weight loss compared with LCD patients ( $43.6 \pm 12.6$  vs  $38.8 \pm 9.9$  kg,  $P = 0.064$ ) as well as a greater loss of fatty mass ( $35.7 \pm 8.4$  vs  $23.5 \pm 6.1$  kg,  $P = 0.002$ ). PWV reduced from  $10.6 \pm 2.4$  to  $7.5 \pm 1.9$  m/s ( $P = 0.007$ ) in VLCKD group vs  $10.4 \pm 2.1$  to  $9.8 \pm 1.9$  m/s in LCD group.

**Conclusion** Our data, even if obtained in a small population, allow to hypothesize a direct role of ketogenic diet in improving PWV that goes beyond weight loss.

P012

### BODY MASS INDEX STRATIFICATION IN ITALIAN ADULTS WITH CONGENITAL HEART DISEASE IN RELATION TO DIAGNOSIS

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**Background and aims** Adults with congenital heart disease (ACHD) are at risk of overweight and obesity, two major health problems, though underweight can be a negative prognostic factor too. Awareness of the body mass index (BMI) in ACHD is very limited. The present study describes the use and prevalence of BMI in Italian hospitalized ACHD patients in relation to diagnosis, sex and age.

**Methods and results** We classified 1420 ACHD patients, aged 18–69 years, on the basis of their BMI, and compared them to the Italian reference population. We found a significantly higher prevalence of underweight compared to the Italian reference population (6.20% vs 3.20%). ACHD women were more underweight than ACHD men.

Underweight decreased with older age. Overweight was significantly less frequent in the total ACHD population (26.90%), compared to 31.70% in the Italian reference population. Men were more likely to be overweight than women. In statistical terms obesity was similar in the Italian reference population (10.50%) and our ACHD population (9.93%). Both overweight and obesity increased with age.

**Conclusions** In our cohort of ACHD the prevalence of underweight was double that of the Italian reference population. The prevalence of overweight was lower, while obesity was similar. Since BMI does not account for differences in body fat distribution, a future aim will be to

quantify the visceral component of the adipose tissue in ACHD patients and examine their body composition in order to reflect their risk of acquired cardiovascular disease better, and either to maintain or achieve an adequate visceral component.

### Obesity complications

P013

### SEVERE OBESITY AND THE FOOT: A TRUCK ON SCOOTER'S WHEELS

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**Aim** to test the modification induced on foot shape, joints, tendons and skin by severe obesity.

**Methods** all the patients admitted for bariatric surgery in our hospital between March and June 2018 (Group A) were compared to normal controls (Group B) for: foot and leg circumferences, skin hardness and temperature, skin and tendons thickness and radiographic evaluation of bone structures, measuring Costa-Bertani and Kite angles and Astragalic inclination.

**Results** Group A (n 36, M/F 17/19, mean age  $45.1 \pm 8.2$  years, BMI  $43.4 \pm 2.2$  kg/m<sup>2</sup>) significantly differed from Group B (n 36, M/F 20/16, mean age  $42.1 \pm 7.9$  years, BMI  $22.8 \pm 1.9$  kg/m<sup>2</sup>) for foot dimension (Dorsal foot  $26.2 \pm 1.8$  in Group A vs  $20.6 \pm 1.4$  in Group B— $p < 0.01$ , Overmalleolar  $27.4 \pm 1.0$  in Group A vs  $20.9 \pm 1.6$  in Group B— $p < 0.01$ , Underknee  $43.1 \pm 3.0$  in Group A vs  $33.6 \pm 1.1$  in Group B— $p < 0.01$ ), foot temperature ( $33.9 \pm 3.9$  in Group A vs  $27.9 \pm 2.9$  in Group B— $p < 0.02$ ) and skin and tendon thickness (Heel skin  $1.39 \pm 0.24$  in Group A vs  $1.11 \pm 0.23$  in Group B— $p < 0.01$ , Scaphoid skin  $0.67 \pm 0.25$  in Group A vs  $0.57 \pm 0.12$  in Group B— $p = 0.03$ ; Heel fascia  $0.35 \pm 0.13$  in Group A vs  $0.28 \pm 0.05$  in Group B— $p = 0.01$ , Scaphoid region fascia  $0.23 \pm 0.07$  in Group A vs  $0.15 \pm 0.04$  in Group B— $p = 0.02$ ). Both Costa-Bertani angle ( $130 \pm 7$  in Group A vs  $120 \pm 5$  in Group B— $p = 0.02$ ) and Astragalic inclination ( $29.1 \pm 5.2$  in Group A vs  $23.0 \pm 3.1$  in Group B— $p < 0.02$ ) were higher in Group A compared to Group B.

**Conclusions** Severe obesity significantly affect both shape and structure of the foot possibly exposing these patients to a higher risk of biomechanical stress.

P014

### OPHTHALMOLOGIC EVALUATION OF SEVERELY OBESE PATIENTS UNDERGOING BARIATRIC SURGERY: A PILOT, MONOCENTRIC, PROSPECTIVE, OPEN-LABEL STUDY

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Ophthalmologic abnormalities affecting the optic nerve head, the lens, and the fovea have been described in severely obese patients.

The aim of this study was to investigate whether body weight reduction and/or improvement of comorbidities observed after gastric bypass surgery may influence various ophthalmologic parameters in severely obese subjects.

This was a pilot, monocentric, prospective, and open label study. Fifty-seven severely obese patients with a mean body mass index value of  $44.1 \pm 6 \text{ kg/m}^2$  were recruited and received a complete ophthalmological evaluation (RE = right eye, LE = left eye). Twenty-nine patients who underwent gastric bypass were evaluated 3 months, and 1 year after surgery.

**Results** At baseline, blood pressure values were directly and significantly related with intraocular pressure values ( $p < 0.05$ ,  $R 0.35$ ). Blood pressure values were also significantly and inversely related to retinal nerve fiber layer thickness, particularly in the temporal sector (RE  $p < 0.05$   $r -0.31$ ; LE  $p < 0.01$   $r -0.43$ ). Moreover, minimum foveal thickness values were significantly and inversely associated with body mass index (RE  $p < 0.02$   $r -0.40$ ; LE  $p < 0.02$   $r -0.30$ ). A significant reduction of body mass index ( $p < 0.05$ ) and a significant ( $p < 0.05$ ) improvement of blood pressure was observed 3 months and 1 year after gastric bypass, which were associated with a significant increase in retinal nerve fiber layer thickness and minimum foveal thickness values in both eyes ( $p < 0.05$ ).

**Conclusions** The results of this study suggest that severely obese patients may have a greater susceptibility to glaucomatous optic nerve head damage and atrophic age related macular degeneration. Weight reduction and the consequent amelioration of blood pressure observed after gastric bypass surgery are associated with an improvement of ophthalmologic parameters.

## Pediatric obesity

### P015

#### TRENDS OF THE PREVALENCE OF OVERWEIGHT/GENERAL OBESITY AND ABDOMINAL OBESITY IN AN ADOLESCENT POPULATION OF AN URBAN AREA AROUND MILAN FROM 2009 TO 2017

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**Background and aim** A recent ISTAT survey shows a slowly decreasing trend of the prevalence of overweight (OW) and general obesity (OB) among Italian adolescents.

However, there are no reports on the trend of the prevalence of abdominal obesity—a predictor of cardiometabolic risk—in Italian adolescents.

The aim of this study was to evaluate the trends of the prevalence of overweight (OW), general obesity (OB) and abdominal obesity from 2009 to 2017 in a wide school-based population of adolescents in an urban area around Milan.

**Methods and results** Every year all the pupils had anthropometric measurements taken (weight, height and waist circumference). Body

Mass Index and waist-to-height-ratio (WHtR) were calculated. Pupils were stratified as subjects with normal weight, overweight, and general obesity according to the International Obesity Task Force age- and sex-specific BMI cut-offs. Abdominal obesity was defined as  $\text{WHtR} \geq 0.5$ .

A total of 5,480 adolescents, aged 12–13, were analyzed over the years (2009  $n = 487$ ; 2010  $n = 363$ ; 2011  $n = 384$ ; 2012  $n = 455$ ; 2013  $n = 520$ ; 2014  $n = 474$ ; 2015  $n = 739$ ; 2016  $n = 984$ ; 2017  $n = 1078$ ).

The prevalence of OW plus OB, considered together for our analysis, decreased from 2009 to 2017 (30.8% vs 26.2%), although it remained higher in boys than in girls over time (35.9% vs 25.5% in 2009; 29.9% vs 21.9% in 2017, respectively).

Moreover, as regards the prevalence of abdominal obesity, we observed a constant reduction from 2009 to 2017 (24.6% vs 18.1%). Yet again, the prevalence of abdominal obesity was higher in boys than in girls (30.6% vs 18.4% in 2009 and 23.0% vs 12.4% in 2017, respectively).

**Conclusions** Our findings confirm ISTAT 2018 data and show an overall decrease in the prevalence of OW/OB, with the strongest improvements mainly in boys, from 2009 to 2017.

For the first time, we remark, as in the general obesity, a constant reduction of abdominal obesity in adolescents of both sexes.

### P016

#### CARDIOMETABOLIC RISK PROFILE IN A POPULATION OF YOUNG ADULTS WITH PREVIOUS CHILDHOOD OBESITY: METABOLIC LEGACY

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Childhood obesity (OB) predicts adult OB with a higher risk of OB-associated comorbidities during adulthood. Less is known about the impact of childhood OB on cardiometabolic risk factors and its role in early development of a cardiovascular (CV) risk profile. Aim of our study was:

- (1) to determine the prevalence of overweight (OW)/OB;
- (2) to evaluate CV risk factors;
- (3) to determine the impact of childhood OB on risk profile, in young adults previously obese children. We studied 46 adults (23M/23F, age  $20.7 \pm 2.2$  years, mean  $\pm$  SD) from a database of prepubertal obese children (age  $10.2 \pm 1.7$  years) from the Pediatric Endocrinology Unit. All subjects underwent thorough metabolic evaluation: anthropometric features, blood pressure (BP), EKG, biochemical parameters, HOMA-IR, thyroid function, carotid Doppler ultrasonography (US), liver US, bioelectrical impedance analysis (BIA). 80% percent of subjects were OW (26%) or OB (54%), 26% showed metabolic syndrome (MS), and 53% presented with 1 or 2 criteria of MS; 72% percent had NAFLD including 33% of actual normal weight subjects. The degree of children OB (BMI SDs), correlates with adult BMI ( $r = 0.34$ ,  $p < 0.01$ ), waist circumference (WC) ( $r = 0.34$ ,  $p < 0.01$ ) and Intima media thickness (IMT) ( $r = 0.28$ ,  $p < 0.05$ ). Actual BMI correlates with WC ( $r = 0.84$ ,  $p < 0.0001$ ), Systolic BP ( $r = 0.49$ ,  $p = 0.0003$ ) and IMT ( $r = 0.41$ ,  $p < 0.005$ ); SBP ( $r = 0.533$ ,  $p < 0.0001$ ) and IMT ( $r = 0.5$ ,  $p = 0.0002$ ) showing a stronger correlation with WC. Thus, childhood

OB predicts adult OB and is associated with early end-organ damage such as endothelial dysfunction (ED) and fatty liver only partially reversible with OB correction. In our population 80% of subjects already showed OB-related conditions, either alone or in combination, with a strong impact on cardio-metabolic outcome such as abdominal OB, hypertriglyceridemia, atherogenic dyslipidemia, hypertension, NAFLD, IFG, early ED. Childhood OB.

## Obesity, nutrition and lifestyle

P017

### A NUTRITIONAL ONLINE PLATFORM TO IMPROVE EATING HABITS: IS IT EFFECTIVE

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**Background** In the last years, the population growth led to an organizational redesign of the health care services network promoting remote ones as viable alternative of the widespread face-to-face clinical approach. Thanks to the rapid technology progress, online tools have been introduced to remotely support patients in their care pathway. In this context, a responsive web application (FoodCoach, FC) for mobile devices and PC providing to patients a Personalized Nutritional Plan (PNP) has been developed at San Raffaele Hospital (OSR). The aim of this study was to assess the efficacy of FC in improving the eating habits in a sample population.

**Methods** Forty healthy subjects aged between 18 and 65 were enrolled in a two arms RCT study where an Intervention Group (IG) used FC (i.e. receiving a PNP compliant with the Mediterranean Diet (MD) released by a dietitian) and a Control Group (CG) received the INRAN Guidelines on good nutrition. Anthropometric indices were collected at the start and at the end of the experimental period (40 days), together with the assessment their eating habits through a Food Frequency Questionnaire. During the 40 days, subjects were asked to follow the nutritional suggestions and fill a food diary (in FC for IG and in a paper format for CG). The MD Score by A. Trichopoulos was used to evaluate the subjects' adherence to the MD. **Results** A trend for the IG in improving MD adherence and eating habits has been found. Instead, the CG showed a trend in worsening MD adherence. Moreover, IG lost more weight than CG (mean and SD IG = 1.5 ± 1.6 vs CG = 0.5 ± 1.5) and significant differences in anthropometric indices changes have been found only for IG (p < 0.005). The engagement level was also evaluated to validate the hypothesis that a high engagement eases the compliance.

**Conclusions** FC brought to a positive outcome, especially in losing weight, showing that it could have a greater impact in improving people's eating habits on a large scale.

P018

### INTERMITTENT VERSUS CONTINUOUS ENERGY RESTRICTION ON WEIGHT LOSS AND CARDIOMETABOLIC OUTCOMES. A SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

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Increasing evidence suggests that the intermittent energy restriction (IER) may be an effective strategy to reduce body weight and improve cardiovascular risk factors.

However, available results are still contradictory. This systematic review and meta-analysis summarized recent evidence on the efficacy of IER versus continuous energy restriction (CER) on weight-loss, body composition, blood pressure and other cardiometabolic risk factors. Randomized controlled trials were systematically searched from MEDLINE, Cochrane Library, and TRIP databases. Effect size was expressed as weighted mean difference (WMD) and 95% confidence intervals (CI). Ten trials were finally included (duration range 8–24 weeks). The IER regimens varied across the studies and involved from 1 to 3 "fast" days per week, providing ≤ 25% daily energy requirements, and from 3 to 6 "feed" days per week, which could be ad libitum (4 trials) or based on balanced energy consumption (6 trials). Findings showed that the intermittent approach determined higher weight-loss (WMD: -4.25 kg, 95% CI -7.39 to -1.11; p = 0.008, I<sup>2</sup> = 79.5%) than the continuous one, with stronger results after balanced eating pattern (WMD = -5.98 kg 95% CI -10.41 to -1.56; p = 0.008; I<sup>2</sup> = 68.9%). There were no differences between-arms in the other variables, except for a small effect on triglyceride levels (WMD: -13.43 mg/dl; -22.14 to -4.72; p = 0.003, I<sup>2</sup> = 0%). However, the heterogeneity across-studies was high. In conclusion both intermittent and continuous energy restriction achieved a comparable effect in promoting metabolic improvements, but IER was slightly superior for weight-loss and triglyceride reduction in the short term. Further long-term investigations are needed to draw definitive conclusions.

P019

### SPECIFIC AMINO-ACID REPLACEMENT OF DIETARY PROTEIN PROMOTES THERMOGENESIS AND ENERGY EXPENDITURE IN DIFFERENT MODELS OF OBESITY

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Long-term exposure to diets containing high ratios of saturated to unsaturated fatty acids (SFA diets) increases body weight and fat accumulation, impairs glucose metabolism, leading to obesity and type 2 diabetes (T2D), and reducing health span. Here, we tested the metabolic effects of a balanced SFA diet (20% protein, 70% carbohydrate, and 10% fat, half of which was lard) compared to those of an isocaloric, isolipidic, and isonitrogenous diet, in which casein was

almost completely (93.5%) replaced by purified essential amino acids (SFA-EAA diet). The amino acid composition of SFA-EAA diet was modelled according to a formula stoichiometrically similar to one previously found to promote mitochondrial biogenesis in skeletal muscles of middle-aged mice when supplemented to daily diet with drinking water. We demonstrated that the SFA-EAA diet was able to revert obesity and T2D induced either by long-term consumption of SFA diet or in a model of genetic obesity (i.e., in leptin-deficient ob/ob mice), and to prevent obesity development in 8-week-old male and female mice fed with both diets for 6 weeks. Moreover, the SFA-EAA diet extend survival of mice. Conversely, such effects were not observed with an SFA diet whose protein content was substituted with a purified amino acid mixture designed on the amino acid profile of casein (SFA-CAA diet), supporting the specific effect of the amino acid composition of SFA-EAA. We showed that the SFA-EAA was able to promote thermogenic energy expenditure, without changing food intake, food absorption, and gut microbiota. Mechanistically the effects of SFA-EAA diet were likely due to brown fat activation, through a direct action on the mechanistic target of rapamycin complex 1 in brown adipocytes, independent of the sympathetic nervous system. Together, our results suggest that specific amino-acid replacement of dietary protein might be a valid therapeutic strategy to maintain metabolic health in mammals.

#### P020

### ADHERENCE TO MEDITERRANEAN DIET AND NAFLD DIAGNOSIS: PRELIMINARY RESULTS FROM AN ITALIAN PROSPECTIVE COHORT STUDY

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**Background** NAFLD (Non Alcoholic Fatty Liver Disease) is the most common liver disorder in Western countries; its pathogenesis and progression are associated with unhealthy lifestyles.

**Methods** In order to assess the association between dietary and physical activity patterns and the presence of NAFLD, we performed a prospective cohort study with a lifestyle intervention (1-year long) for patients with NAFLD. All the recruited subjects, aged 18–59 years old, without overt clinical illness, underwent liver ultrasound (US), clinical evaluation and laboratory blood tests. According to the results of US, subjects were classified in two cohorts: NAFLD patients (NP) and healthy controls (HC). Dietary habits were collected by a standardized self-administered FFQ, with validation process as a part of the study. Among 148 food items, we identified those presumed to be closer to Mediterranean Diet (MD) and assigned a score according to their frequency consumption. Higher values of the score indicate greater adherence to MD. The study was supported by Brescia University 2015 Health&Wealth call [ClinicalTrials.gov identifier number NCT0330061].

**Results** From July 2017 to April 2018 155 subjects were enrolled: 73 NP and 82 HC. Mean age and gender distribution were similar in the two cohorts. At baseline statistical differences among NP and HC

were detected in BMI and waist circumference ( $31.5 \pm 5.5$  vs.  $23.8 \pm 3.7$  kg/m<sup>2</sup> and  $105 \pm 13$  vs.  $87 \pm 10$  cm) and in most of laboratory tests: HDL cholesterol  $51.1 \pm 11.7$  vs.  $65.5 \pm 18.3$  mg/dL, LDL cholesterol  $127.9 \pm 28.9$  vs.  $114.3 \pm 3.1$  mg/dL, triglycerides  $142.5 \pm 88.8$  vs.  $81.7 \pm 38.6$  mg/dL, HOMA IR  $3.7 \pm 1.0$  vs.  $1.1 \pm 0.9$  and ALT  $40.9 \pm 21.1$  vs.  $29.4 \pm 21.7$  U/L. Adherence to MD was scored  $5.5 \pm 3.5$  (range 0–11) among NP and  $8.7 \pm 3.9$  (range 1–19,  $p < 0.0001$ ) among HC.

**Conclusions** Patients with NAFLD showed a lower score of adherence to MD than healthy controls, suggesting the importance of structured interventions to enhance this dietary pattern as the first line treatment.

#### P021

### NEW PREDICTIVE EQUATION IN A LARGE COHORT OF ITALIAN ADULTS WITH SEVERE OBESITY

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An accurate prediction of resting energy expenditure (REE) is crucial for assessing energy needs in obese individuals. The aim of the present study was to develop and validate new equations for predicting REE in a large cohort of Italians with severe obesity by using bioimpedance analysis (BIA) raw variables.

Obese patients, consecutively referred to the outpatient clinics and aged 18–65 years, were recruited.

Beside anthropometry, REE was measured by indirect calorimetry and BIA performed at 50 kHz. New equations were generated using two models: Model 1 with age, weight, height and BMI, and Model 2 with previous variables plus raw BIA variables such as bio-impedance index (BI-index) and phase angle (PhA) (Model 2). A total of 2712 obese outpatients were used to develop ( $n = 2255$ ; weight = ; BMI =) and validate ( $n = 457$ ; weight = ; BMI =) new predictive equations.

Our results showed that REE was directly correlated with all anthropometric variables, and inversely with age. REE was also moderately correlated with raw-BIA variables. Overall, the strongest association was observed between REE and weight (males  $r = 0.783$  and females  $r = 0.825$ ). The following predictive equations were obtained by multiple regression analysis.

#### Model 1

Males: REE=  $13.4 \times \text{Weight} - 2.50 \times \text{Age} + 854$ ;  $R^2=0.617$ ; SEE=260 kcal.  
Females: REE=  $14.0 \times \text{Weight} - 2.60 \times \text{Age} + 931$ ;  $R^2=0.688$ ; SEE=208 kcal.

#### Model 2

Males: REE=  $11.6 \times \text{Weight} - 3.17 \times \text{Age} + 45.1 \times \text{PhA} + 6.04 \times \text{BI-index} + 313$ ;  $R^2=0.642$ ; SEE=252 kcal.  
Females: REE=  $12.2 \times \text{Weight} - 2.76 \times \text{Age} + 39.7 \times \text{PhA} + 6.50 \times \text{BI-index} + 797$ ;  $R^2=0.707$ ; SEE=202 kcal.

The results of the study show an association between REE and raw BIA variables. However, from a practical point of view, the addition of raw BIA variables improves to a small extent the prediction power of the equations.

P022

### RELATIONSHIP AMONG FATTY LIVER INDEX, VISCERAL ADIPOSITY INDEX AND HOMA-IR AND MEDITERRANEAN DIET AS A MODIFIABLE ENVIRONMENTAL FACTOR IN OBESE PATIENTS

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**Background** Unhealthy lifestyle, including diet and obesity are the most probable causes of fatty liver (FL), a source of inflammatory factors. The Mediterranean Diet (MD), a healthy dietary pattern characterized by high consumption of vegetables and low consumption of full fat dairy products and red meat, is associated with a better insulin sensitivity. Adherence to MD is a significant predictor of changes in the fat content of the liver in overweight patients with FL. Fatty Liver Index (FLI) has proposed as a surrogate parameter for liver fat content in the general population. Visceral adiposity Index (VAI) is a gender-specific index of adipocyte dysfunction highly correlated with cardiometabolic risk. The aim of this observational study was to evaluate the correlations between the adherence to the MD with endocrine-metabolic indices in obese patients.

**Patients and Methods** Fifty obese individuals (19 M and 31 F, mean age  $36.9 \pm 8.3$  and  $36.1 \pm 10.1$  yrs, respectively) were included in this study. The adherence to the MD was evaluated using the PRE-vencción con Dieta MEDiterránea (PREDIMED) questionnaire. HoMA-IR, FLI and VAI were calculated.

**Results** Forty-six individuals presented poor adherence to the MD, 46% average adherence and 8% high adherence. FLI and HoMA-IR values higher than cut offs were found in all the subjects, while VAI score higher than age and gender-specific cutoff values was evidenced in 92% subjects. MD adherence was significantly correlated with BMI ( $r = -0.541$ ,  $p < 0.001$ ), waist circumference ( $r = -0.660$ ,  $p < 0.001$ ), HoMA-IR ( $r = -0.531$ ,  $p = 0.014$ ), FLI ( $r = -0.617$ ,  $p < 0.001$ ), and VAI ( $r = -0.323$ ,  $p = 0.022$ ). After adjusting for BMI, MD adherence and FLI remained still significantly correlated ( $r = -0.488$ ,  $p = 0.001$ ). At multiple regression analysis, MD adherence was the major predictor of FLI ( $\beta = -0.621$ ,  $t = -5.3$ ,  $p < 0.001$ ).

**Conclusions** Besides the well-known relationship between MD and insulin resistance, our data evidences the negative association among MD adherence, FLI and VAI in obese subjects. The independent association between MD adherence and FLI further supports the key role of diet in FL pathogenesis.

P023

### DIETARY INTRODUCTION OF BERGAMOT FRESH FRUIT IMPROVES BODY COMPOSITION IN OBESE SUBJECTS DURING METABOLIC REHABILITATION

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Clinical use of Citrus x bergamia has a wide scientific literature testifying to its phytotherapeutic properties: lipid-lowering, hypoglycaemic and protective vessel effects. In addition to the most known effect on cholesterol HMG CoA reductase, Bergamot juice inhibits hepatic synthesis of triglycerides through the inhibition of the

ACAT enzyme and develops an hypoglycemic activity through the increase of the AMPK enzyme, improving the sensitivity to insulin.

Aim of the present study is to evaluate the effects on body composition measured by bioelectrical impedance in a group of hospitalized obese subjects for a metabolic psychological nutritional rehabilitation cycle. They had an hypocaloric menu with an average energy intake of 1350 kcal daily during an observation period of 21 days. In a period of about 6 months 51 patients were enrolled, 18 males and 33 females, age between 18 and 65 years, BMI medium  $56 \pm 8$  kg/m<sup>2</sup> to which a bergamot was administered daily. In no case has the study been suspended for compar side effects or hypersensitivity phenomena, but 14 subjects (27%) abandoned the study for taste incompatibility. Our data show that total body water falls in absolute value and in a percentage value in all the subjects studies and in the control population: from  $67 \pm 11$  to  $59 \pm 9$  L that is from  $43 \pm 5$  to  $40 \pm 6\%$  in the study group, from  $49 \pm 12$  to  $45 \pm 10$  L that is from  $39 \pm 6$  to  $38 \pm 5\%$  in the control group. Extracellular water gets down in both groups, just in absolute and in percentage from  $32 \pm 6$  to  $26 \pm 5$  L that is from  $47 \pm 6$  to  $44 \pm 4\%$  in the study group and from  $25 \pm 7$  to  $23 \pm 6$  L from  $51 \pm 6$  to  $50 \pm 7\%$  in the control group. Intracellular water (ICW) even if it shows a slight deflection in absolute value, both in the treated subjects (from  $35 \pm 6$  to  $33 \pm 5$  L) and in the control subjects (from  $24 \pm 6$  to  $23 \pm 6$  L), it increases in percentage from  $53 \pm 6$  to  $56 \pm 4\%$  in the study, while from  $49 \pm 6$  to  $50 \pm 7$  in the control group. The BCM not changes in absolute value in the two groups (from  $44 \pm 9$  to  $44 \pm 7$  kg and from  $30 \pm 8$  to  $30 \pm 9$  kg), but increases in percentage value in study subjects (from  $52 \pm 6$  to  $55 \pm 5\%$  vs from  $49 \pm 7$  to  $49 \pm 8$ ). Our results confirm the effectiveness of the use of bergamot also as fresh fruit (and not as an extract, already studied in literature) in promoting weight loss and improving body composition.

### Eating behavior disturbances

P024

### IMPROVEMENT OF FOOD CRAVING AND EMOTIONAL EATING TWO YEARS AFTER GASTRIC BYPASS AND SLEEVE GASTRECTOMY

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**Abstract** Bariatric surgery is the most effective procedure to achieve a stable reduction of body weight in morbidly obese subjects. Furthermore, several studies indicate that bariatric surgery may have favourable effects on dysfunctional eating. The aim of this study was to test the hypothesis that gastric bypass and sleeve gastrectomy can induce a decrease in food craving and emotional eating.

**Methods** 43 obese females (mean age  $41.6 \pm 11.3$  SD years; pre-surgery BMI  $46.8 \pm 7.5$  SD, postsurgery BMI  $30.4 \pm 5.4$  SD) and 10 obese males (mean age  $47.8 \pm 8.8$ ; presurgery BMI  $50 \pm 9$ , postsurgery BMI  $35.4 \pm 9.2$ ) were administered the Food Cravings Questionnaire-Trait (FCQ-T) and Emotional Eating Scale (EES), before and 2 years after bariatric surgery (gastric bypass and sleeve gastrectomy). Statistical: Paired Sample T-test.

**Results** After bariatric surgery, obese subjects exhibited an improvement in all scales of FCQ-T and EES.

Factors (FCQ-T), <i>EES</i>	Presurgery (mean ± SD)	Postsurgery (mean ± SD)	p<
Intent (Plans)	4,27 ± 3,2	3,06 ± 3,09	0,01
Positive Reinforcement	8,1 ± 5,96	5,5 ± 4,06	0,01
Negative Reinforcement	4,48 ± 3,36	3,2 ± 2,81	0,05
Loss of Control	7,44 ± 6,6	2,64 ± 3,18	0,001
Thoughts	4,83 ± 5,44	2,58 ± 3,74	0,01
Hunger/Physio	7,62 ± 5,22	4,98 ± 3,03	0,001
Emotions	6,81 ± 4,97	4,36 ± 3,6	0,001
Cues/Environment	7,56 ± 4,83	3,46 ± 3,34	0,001
Guilt	5,1 ± 4,19	3,2 ± 3,31	0,01
Anger	11,12 ± 8	5,53 ± 6,67	0,001
Anxiety	8,17 ± 5,97	4,67 ± 5,32	0,01
Depression	5,76 ± 4,89	3,55 ± 3,24	0,01

**Conclusion** favourable effects of bariatric surgery include stable body weight reduction and improvement of dysfunctional eating, with an overall amelioration of the quality of life.

## P025

### FOOD ADDICTION AND ATTACHMENT STYLES: A PRELIMINARY INVESTIGATION

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The construct of “Food Addiction” (FA) has been introduced in recent years to better understand obesity and dysfunctional eating patterns.

Despite the interest in FA, the link between attachment style and FA is still little explored although it could help to legitimize FA as a psychopathological disorder of eating behavior. Therefore the purpose of this study was to investigate insecure attachment styles, in particular anxious and avoiding, within the construct of FA. The research was conducted on a clinical sample of 60 patients enrolled in a medical center of Rome for the treatment of overweight, obesity and eating disorders. All participants were administered the Yale Food Addiction Scale (YFAS), the Binge Eating Scale (BES), the Style Questionnaire Attachment (ASQ), the Body Uneasiness Test-A (BUT-A) and the Teate Depression Inventory (TDI). FA was diagnosed in 25 subjects (41.7%).

Statistical analyzes showed a correlation between FA and BED ( $r = 0.75$ ;  $p < 0.01$ ) and FA and Depression ( $r = 0.54$ ;  $p < 0.01$ ) in line with the literature, but an interesting data concerned the positive relationship between FA and Body Image disorder ( $r = 0.64$ ;  $p < 0.01$ ).

The study of attachment style showed that FA was positively correlated with anxious and avoidant attachment. A partial correlation was also conducted, and it was found that the relationship between FA and the anxious attachment style remained significant ( $r = 0.33$ ;  $p < 0.05$ ) even after controlling for potentially disturbing variables (age, BMI, positivity to BES, BUT and TDI), while that between avoidant attachment style was no longer significant. The results of the research increase the knowledge on the etiopathogenesis of FA highlighting the relationship with anxious attachment style and support the acknowledgment of FA in the spectrum of eating psychopathology.

## Physiopathology of energy balance

### P026

#### PREVALENCE OF ORGAN AND NON ORGAN-SPECIFIC AUTOANTIBODIES IN PATIENTS WITH LIPODYSTROPHY

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Lipodystrophy syndromes are a group of rare disorders characterized by the complete or partial deficiency of adipose tissue. Lipodystrophy can be classified according to the extent of fat loss in generalized or partial forms, or based on the pathogenetic mechanisms in genetic or acquired. The aim of this study was to assess the prevalence of organ and non-organ specific autoimmunity in our cohort. We evaluated 33 patients: 11 affected by acquired forms of lipodystrophy (AL) and 22 affected by genetic forms (GL). In all subjects organ-specific autoantibodies (anti thyroglobulin-AbTg, anti-thyroperoxidase-AbTPO, anti-gastric parietal cells-APCA, anti 21-hydroxylase-21OHAb, anti-transglutaminase, ab anti endomysium, anti-glutamic acid decarboxylase-GAD Ab) and non organ-specific autoantibodies (anti nuclear antibodies-ANA titre > 1:160, anti-extractable nuclear antigens-ENA, anti-native DNA, anti-neutrophil cytoplasmic, Immunoglobulin M rheumatoid factors, anti-cardiolipin antibodies, anti-liver kidney microsome-LKM, anti-smooth muscle-ASMA, anti-antimicrobial antibodies-AMA, lupus anticoagulant, Coombs test) were assessed. In AL patients, AbTg and AbTPO were present in 3/11 (27%); 1/11 patient (9%) was positive for 21OH-Ab. APCA were positive in 5/11 patients (45%); GAD-Ab were positive in 1/11 patient (9%). In GL patients, APCA were detected in 2/22 (9%). Among non-organ specific antibodies, ENA and Coombs test were positive in 3/11 (27%) of patients with acquired lipodystrophy. 10/33 patients presented ANA, 4/7 (57%) patients with AL compared with 6/14 (42%) patients with GL. In conclusion the prevalence of organ and non-organ specific autoantibodies is significantly higher in acquired lipodystrophy when compared with the prevalence in genetic forms. It is important to analyze autoantibody profiles for the assessment and management of the disease. The presence of auto-antibodies might support a role for autoimmunity in the pathogenesis of acquired lipodystrophy.

### P027

#### RECOMBINANT LEPTIN TREATMENT FOR METABOLIC COMPLICATIONS ASSOCIATED WITH LIPODYSTROPHY: RESULTS FROM THE FIRST ITALIAN EXPERIENCE

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Lipodystrophies are rare syndromes characterized by an irreversible loss of subcutaneous adipose tissue and are conventionally distinct in partial (PL) or generalized forms (GL) based on the pattern of adipose tissue disappearance. Lipodystrophy is associated with leptin deficiency, resulting in a host of metabolic abnormalities (severe insulin resistance, diabetes, hyperlipidemia, hepatomegaly and nonalcoholic steatohepatitis) and treatment with recombinant-methionyl human leptin (metreleptin), as an adjunct to diet, reduces food intake and improves the metabolic abnormalities associated with the disease.

We herein report the results of the first Italian experience of treatment of a cohort of patients affected by lipodystrophy. This is a retrospective data collection conducted from a single Center. Six patients (3 diagnosed with PL and 3 diagnosed with GL) were started to treatment based on the severity of the metabolic co-morbidities. Prior to metreleptin treatment, patients had at least TG > 200 mg/dL and/or HbA1c > 8% under standard pharmacological treatment. The duration of exposure to metreleptin varied across patients, up to 5.5 years (mean 30 months, SD 25). Following treatment a mean 70% decrease of HbA1c and a 60% reduction of TG were observed. These changes occurred in the face of reduction/withdrawal of treatment for diabetes and hyperlipidemia. A 40% reduction of transaminase levels and a mean 45% reduction in hepatic left volume size (measured by ultrasound) were also observed. Only one patient experienced a minor adverse event (transient skin reaction after subcutaneous injections).

In conclusion, the response to treatment with metreleptin in real-life patients affected by lipodystrophy and followed at our Center, was consistent with published results reported in clinical trials confirming that treatment with metreleptin in the context of lipodystrophy is effective and safe.

## Rehabilitation

P028

### NUTRITIONAL LEARNING HAS AN IMPORTANT RELEVANCE DURING THE REHABILITATION OF THE OBESE SUBJECTS AND IS ASSOCIATED WITH WEIGHT LOSS

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This study investigated the nutrition knowledge of obese subjects and the relation between the improvement in nutrition knowledge and weight loss obtained with a 3-month outpatient metabolic-nutritional-psychological rehabilitation. Food knowledge and levels of physical activity were assessed with Moynihan Questionnaire (MQ) and IPAQ before and after rehabilitation in 189 obese subjects (81.5% women, 58.6 ± 12.3 years, 37% class I, 38% class II, 22% class III obesity). MQ was developed in UK to assess the nutrition knowledge of elderly subjects and validated for Italian food habits in non-obese patients. The MQ consists of 15 items and has 4 main subject domains: 1) dietary recommendations, 2) nutrient sources (omega 3 and fibres), 3) healthiest meal option and 4) associations between diet and disease. The total score ranges from 15 (greatest nutritional knowledge) to 30 (lowest nutritional knowledge). At baseline, mean total score was 21.3 ± 2.6: nutritional knowledge was high in 8.5% of subjects (score 1–17), good in 50.3% (score 18–21), sufficient in 37.6% (score 22–25) and poor in 3.7% (score > 26). Answers were more frequently correct and wrong on the domain 3 and 2 respectively. The lowest scores were observed in subjects with the highest degree of education

( $p < 0.0001$ ) and the longest duration of obesity ( $p < 0.0005$  adjusted for education). The total score was unaffected by gender, age and class of obesity. The rehabilitation induced a 5.1% decrease in weight and an increase in physical activity (from 32 to 108 min/week,  $p < 0.0001$ ) and an improvement in nutrition knowledge (mean score 18.7 ± 2.4,  $p < 0.0001$  vs baseline). Changes in nutrition knowledge were correlated with weight changes ( $r 0.231$ ,  $p < 0.01$  adjusted for physical activity changes) and the attendance to the educational sessions ( $r 0.171$ ,  $p < 0.05$ ). Results show that nutritional learning (particularly on nutritional sources) is relevant in the rehabilitation of obese subjects and MQ may be a useful indicator.

P029

### KETOGENIC DIET, WEIGHT LOSS AND BODY COMPOSITION

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In recent years, there has been increased interest in very low carbohydrate ketogenic diets (VLCKD) that have undoubtedly been shown to be effective, at least in the short to medium term, as a tool to tackle obesity, hyperlipidemia and some cardiovascular risk factors. Ketogenic diets are characterized by a reduction in carbohydrates (usually less than 50 g/day) and a relative increase in the proportions of protein and fat. After a few days of such a nutritional regimen there is an increase of the “so called” ketone bodies that can be used by tissues for energy as an alternative to glucose. This kind of mild ketosis should not be confused with the pathological ketosis of diabetes, indeed Hans Krebs called it “physiological ketosis”, to reinforce this difference. Through a network of weight loss centers we have recruited 25 subjects (5 males and 20 female; mean age 44.1 years, SD 12). The subjects were divided into three groups based on the duration of the weight reduction protocol (15 days, 20 days, 30 days) and analyzed at the beginning (T0) and at the end (T1) of the protocol with multi-frequency bioimpedentiometry. Inclusion criteria were: BMI ≥ 25, age > 20 years and < 70 years, currently on a carbohydrate rich diet (> 50% energy), desire to lose weight and health status suitable for a VLCKD i.e. normal renal function, not pregnant or lactating. At the first visit it was explained that during the diet protocol it was necessary to almost totally exclude carbohydrates and a detailed menu containing permitted and non-permitted foods was provided to each participant, along with the components of the VLCKD. Subjects received no monetary compensation for their participation and signed a voluntary consent form before starting the diet. The permitted foods were: cooked or raw green vegetables, meat, fish and eggs, olive oil and a supplement dish composed of proteins and zero carbohydrate, that was provided for every meal, for a maximum of 4 per day. Despite for none of the variables analysed the variation turns out to be statistically significant, probably due to the limited number, the VLCKD confirms the effectiveness as tool for rapid weight reduction, mainly at the expense of the FM. A larger cohort would certainly have been decisive in confirming the result obtained.

## Pharmacological treatment

P030

### AGE NO IMPEDIMENT TO EFFECTIVE WEIGHT LOSS WITH LIRAGLUTIDE 3.0 MG: DATA FROM TWO RANDOMIZED TRIALS

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**Background** Older people are believed to achieve lower weight loss than younger people on a given therapy. We describe a post hoc analysis of the efficacy and safety of liraglutide 3.0 mg in people aged  $\geq 65$  years (y) vs those  $< 65$  years from the two largest 56 week randomized, controlled, double-blind SCALE trials with liraglutide 3.0 mg.

**Methods** Individuals with BMI  $\geq 30$  kg/m<sup>2</sup> or  $\geq 27$  kg/m<sup>2</sup> with hypertension or dyslipidemia or BMI  $\geq 27$  kg/m<sup>2</sup> with type 2 diabetes were randomized to once-daily subcutaneous liraglutide 3.0 mg or placebo, with a 500 kcal/day deficit diet and 150 min/week exercise, and divided into baseline age subgroups:  $\geq 65$  y vs  $< 65$  years. **Results** No significant interaction between treatment and baseline age subgroup was seen in either trial for mean body weight or weight-related endpoints, indicating consistent treatment effects in both age subgroups: SCALE Obesity and Prediabetes:  $\geq 65$  years (−8.4% vs −4.2% for liraglutide 3.0 mg vs placebo,  $< 65$  years: −8.0% vs −2.5% for liraglutide vs placebo,  $p = 0.38$ . SCALE Diabetes:  $\geq 65$  years (−7.2% vs −2.5% for liraglutide vs placebo,  $< 65$  years −5.6% vs 1.9% for liraglutide vs placebo,  $p = 0.34$ . Similar effects on glycaemic endpoints were seen in each age subgroup in SCALE Diabetes.

**Conclusion** Liraglutide 3.0 mg showed similar efficacy in individuals  $\geq$  and  $< 65$  years, though elderly individuals in both groups tended to report more side effects.

P031

### BASELINE CLINICAL CHARACTERISTICS OF OBESE PATIENTS RESPONDER AND NON-RESPONDER TO LIRAGLUTIDE THERAPY

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Liraglutide is a glucagon-like peptide 1 receptor agonist, which acts through peripheral and central pathways affecting food intake, satiety and glucose homeostasis. The aim of this study was to evaluate efficacy of the treatment and the characteristics of responder patients. **Methods:** we retrospectively studied a cohort of 98 patients treated with liraglutide, who had previously failed multiple lifestyle. Each obese patient was evaluated also by a Psychiatrist. Patients were evaluated after 4, 12 and 24 weeks of treatment to assess efficacy and safety. These patients suffered also of hypertension, dyslipidemia, impaired glucose tolerance, type 2 diabetes. **Results:** we followed 98

patients at the 1 month, 83 patients after 3 months and 59 patients after 6 months (75 female, 23 male; mean age  $51 \pm 14$  years; mean BMI  $38.49 \pm 6.35$  kg/m<sup>2</sup>). 48 patients were considered free from psychiatric disorders, 21 patients were affected by binge eating disorder and 29 patients by other psychiatric diseases (schizophrenia, bipolar disorder, depression or anxiety). There was a significant weight loss from baseline after 30 days of therapy as well as after 3 and 6 months ( $p < 0.0001$ ). After 4 weeks all patients were using liraglutide 1.2 mg once daily and they had lost  $3.05 \pm 0.35$  kg of their initial body weight. After 3 months 48% and after 6 months 63% patients lost at least 5% of their initial body weight. We evaluated demographic variables (age, gender, marital/working status and education), metabolic variables, intake behavior and daily habits, smoking and physical activity. The only variable that differed significantly between responders and non-responders groups was the weight loss at the first 4 weeks of the treatment ( $p < 0.0001$ ).

**Conclusions** Our preliminary data didn't show any significant difference between responders and non responders groups at the baseline. The only predictive factor for a successful weight loss.

P032

### LIRAGLUTIDE FOR THE TREATMENT OF OBESITY: A “REAL LIFE” EXPERIENCE IN A SINGLE OBESITY CENTER

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Randomized Controlled Trials (RCTs) have shown that Liraglutide (L), compared to dietary behavioral changes, leads to a greater, dose dependent, weight loss. Results obtained in real life may not reflect those observed in RCTs because of differences in selection of patients, follow-up protocols and dose scheduling of the drug.

Aim of the study was to evaluate the effect of L treatment L in a series of consecutive obese subjects (OB) referred to a single obesity center from March 2016 to February 2018. 69 OB (49 F, 20M), aged 18–78 years, BMI 30–55 who completed at least 1 month of L treatment were included. L was assigned at the starting dose of 0.6 mg and increased up to 3 mg/day with various regimens of dose escalation. Body weight was assessed at various time points. Data recorded at the last observation (35–505 days after treatment initiation) were compared to baseline values. Data obtained 3 months after L withdrawal were also analyzed. Weight loss occurred in 59/69 OB; in 6/69 body weight increased and in 4/69 there were no body changes. Mean weight loss in OB on L 3 mg (41 patients) was  $7 \pm 5\%$ . 65% and 25% OB treated with L 3 mg for more than 6 months achieved a weight loss more than 5% and 10%, respectively. Higher drug doses and longer treatment duration were associated with greater weight reduction. In a multivariate analysis, after adjustment for age and sex, only duration of treatment remained associated with weight loss. Mean weight regain 3 months after L withdrawal was 2.1% and it was positively associated with the extent of previously achieved weight loss.

**Conclusions** Real life L treatment of OB in a single obesity center, yielded results comparable to those reported in RCTs. The association between weight loss and weight regain following L withdrawal suggests variable degrees of responsiveness to the drug. Combining results of RCTs with those observed in real life may increase their power and overcome their limitations.

P033

## USE OF LIRAGLUTIDE 3.0 MG AND NALTREXONE/BUPROPION IN PATIENTS WITH WEIGHT REGAIN AFTER BARIATRIC SURGERY

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Bariatric surgery results in greater improvement in weight loss outcomes and weight associated comorbidities compared with non-surgical interventions, regardless of the type of procedure used. Nevertheless weight regain (WR) is an important issue after bariatric surgery. We here report our experience on pharmacological treatment in patients who regained weight after bariatric surgery.

24 female patients (pts; aged 22–57 years,  $43.3 \pm 11$ ) who had been undergone elsewhere to bariatric surgery (14 laparoscopic adjustable gastric banding (LAGB), 2 Roux-en-Y gastric bypass (RYGB), 8 laparoscopic sleeve gastrectomy (LSG); mean BMI before surgery  $44.6 \pm 10.1$  kg/m<sup>2</sup>; minimum BMI after surgery  $30.5 + 8.4$  kg/m<sup>2</sup>, came to our observation  $62.5 \pm 37.3$  months (range 12–144 months) after surgery because of weight regain. After surgery the patients were following dietary and behavior counseling. At the first observation mean BMI was  $35.5 \pm 8.6$  kg/m<sup>2</sup> (range 26.4–43.0). Liraglutide was administered once-daily sc; starting dose was 0.6 mg with weekly 0.6 mg increments to 3.0 mg. The mean follow-up was  $11 \pm 4.5$  months (range 6–18). Other three female patients (mean age 49.6 years), previously undergone LAGB at a mean BMI of  $43.7$  kg/m<sup>2</sup> and achieved a minimum mean BMI after surgery of  $32.41$  kg/m<sup>2</sup>, came to our observation 70–99 months: mean BMI  $38.4$  kg/m<sup>2</sup>. These pts were treated with 32 mg/360 mg Naltrexone/Bupropion (N/B; dose increase every week 8/90 mg).

After liraglutide treatment, BMI average reduction was  $-5.1$  (at the end, mean BMI:  $30.4 \pm 4.5$ , range 24.8–39.4). BMI reached on pharmacological treatment was lower than the minimum BMI achieved after surgery. The three patients treated for 6 months with N/B, achieved a mean BMI of  $34.18$  kg/m<sup>2</sup> (range 33.2–36.0).

Our data show the usefulness of pharmacological approach in obese subjects who showed weight regain after initially successful bariatric surgery.

(Policaptil Gel Retard and placebo) while, among them, 57 were randomized (32 and 25 to Policaptil Gel Retard and placebo, respectively) and completed all study procedures. Chronic treatment was defined as a  $30 \pm 2$  days administration of Policaptil Gel Retard /placebo (3 tablets BID) associated to a balanced normocaloric diet and physical activity (7000 steps/day). The following parameters were recorded at baseline and after treatment period: anthropometric parameters, fasting insulin, homeostasis model assessment of insulin resistance (HOMA-IR), postprandial glycaemic (t0, 30, 60, 90, 120, 150, 180) and lipid [t0, 60, 120, 180, 240, 300; total, LDL, HDL cholesterol (CHL) and triglycerides] profile after a standard normocaloric meal (599 kcal: 44.3% carbohydrates, 23.1% proteins, 32.6% fat).

**Results** In single-dose assessment (n = 63) Policaptil Gel Retard, compared to placebo, showed a statistically significant postprandial blood glucose (BG) profile improvement in the 30–60 timeframe after baseline measurement (Policaptil Gel Retard BG at t30-BG at t60  $0.45 \pm 0.65$  vs Placebo  $0.67 \pm 0.76$  mmol/L,  $p < 0.05$ ). At the same time, probably due to the restricted population (n = 32 Policaptil Gel Retard, n = 25 placebo), no differences in fasting and postprandial glycemia and HOMA-R were recorded after 30-days treatment. Prolonged intake of Policaptil Gel Retard decreased postprandial level of LDL-CHL 300' after standard meal in comparison with Placebo ( $p = 0.04$ ). Moreover, intra-group analysis reveals that Policaptil is able to significantly decrease post-prandial levels of LDL-CHL and total CHL at all timepoints ( $p < 0.001$ ). In Placebo group none of the LDL-CHL measurements showed a significant variation, while a decrease was observed in HDL-CHL levels ( $p < 0.001$ ) and, consequently, in total CHL ( $p < 0.05$ ). Reduction of triglyceride level didn't show significant changes in both groups. Finally, prolonged Policaptil Gel Retard/placebo intake led to significant weight loss as well as in hip and waist circumference reduction.

**Conclusions** Despite no major differences between Policaptil Gel Retard and placebo were recorded in anthropometric parameters, Policaptil Gel Retard exerts specific beneficial effect on LDL metabolism independently from weight loss. Finally, single dose intake of Policaptil Gel Retard showed preliminary promising findings on glycaemic profile, paving the way for subsequent investigations. **Disclosure** Trial funded by Aboca Spa Società Agricola. A.B. and M.S. received a fee for their collaboration with Aboca Spa.

**Bariatric surgery**

P034

## ASSESSMENT OF THE EFFECTS OF POLICAPTIL GEL RETARD ON THE GLYCEMIC, LIPID AND WEIGHT PROFILE IN OVERWEIGHT AND MILD OBESE SUBJECTS

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**Background** Obesity represents a health/economic burden whose prevalence is constantly growing worldwide. Few therapeutic options are currently available and, in many cases, treatment compliance is affected by high therapy costs. This trial aims at evaluating acute (single-dose) and chronic (30-days) Policaptil Gel Retard (Libramed) activity on weight, glycaemic and lipid metabolism in overweight and mild obese subjects.

**Materials and methods** In the present randomized, double blinded, placebo-controlled clinical trial, 63 normoglycaemic and overweight/mild obese patients were enrolled and underwent acute treatment

P035

## DYNAPENIA IN OBESE PATIENTS WHO ARE CANDIDATES TO BARIATRIC SURGERY

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**Background** Handgrip strength (HGS) reflects the higher isometric strength of the muscles responsible for the flexion of the hand. In the clinical setting, HGS is evaluated, as a proxy of muscle strength, for identifying low muscle strength (dynapenia) and sarcopenia. A few data are so far available in the literature on HGS variability in obese individuals.

**Aim** To evaluate the prevalence of dynapenia in obese individuals according to different sets of criteria.

**Methods** We carried out a cross-sectional study in 175 obese patients candidates to bariatric surgery, with no major comorbidities, aged 18–58 years: 70 males ( $34.5 \pm 10.2$  years; BMI  $39.3 \pm 5.2$  kg/m<sup>2</sup>) and 105 females ( $35.9 \pm 10.4$  years; BMI  $40.1 \pm 5.7$  kg/m<sup>2</sup>). HGS was measured using a Takei dynamometer, with three trials from each hand. The highest value among the six measurements was considered for statistical analysis. Four different sets of diagnostic criteria for dynapenia (i.e. cutoffs for low HGS) were considered as follows: two sets, Lauretani (2003) and Alley-1 (2004), which are independent of BMI, and other two sets, Fried (2001) and Alley-2 (2004), with cutoffs depending on BMI.

**Results** Dynapenia was more prevalent according to Alley-2 (11.4% females and 28.6% males) and Fried criteria (4.8% and 4.3%), while prevalence was very low when Lauretani criteria (1.9% and 4.3%) or Alley-1 criteria (0% and 2.9%) were used. Values (in kg) of lower HGS percentiles were calculated in obese patients aged 18–50 years. They were as follows: in females, 3rd = 21.0, 5th = 21.4, 10th = 22.9, 15th = 24.7 and 25th = 25.9; in males 3rd = 32.5, 5th = 33.5, 10th = 35.1, 15th = 36.8 and 25th = 40.1. These values were slightly higher compared to the percentiles calculated in non-obese controls. **Conclusion** The prevalence of dynapenia in the obese differ according to the criteria used, being higher when cutoffs vary depending on BMI. Specific percentiles and/or clinical cutoffs are needed to identify low muscle strength in obese and very obese patients.

P036

### HANDGRIP STRENGTH AND RAW “QUALITY” BIA VARIABLES IN OBESE PATIENTS CANDIDATES TO BARIATRIC SURGERY

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Hand grip strength (HGS) is assumed to be a marker of muscle strength, while impedance ratio (R) and phase angle (PhA) are raw bioimpedance analysis (BIA) variables proxy of extracellular/intracellular water ratio, body cell mass, cell membrane integrity, etc. All these variables could be useful for assessing muscle quality.

**Aim** To evaluate in obese and very obese patients the relationships of HGS with anthropometric variables and raw “quality” BIA variables.

**Methods** One hundred fifty seven obese individuals candidates to bariatric surgery (age 18–58 years) participated in the study: 62 males (age  $34.9 \pm 10.6$  years; BMI  $39.3 \pm 5.1$  kg/m<sup>2</sup>) and 95 females (age  $36.0 \pm 10.5$  years; BMI  $40.1 \pm 5.7$  kg/m<sup>2</sup>).

HGS was measured using a Takei dynamometer, with three trials from each hand. The highest value among the six measurements was considered for statistical analysis. Multi-frequency BIA (impedance-Z and PhA) was performed on the whole body at 5–10–50–100–250 kHz (HUMAN IM-TOUCH analyzer, DS Medica, Milano). BI index was calculated by dividing stature squared by Z. IR was calculated as the ratio Z at 250 kHz/Z at 5 kHz.

**Results** HGS was  $45.7 \pm 8.4$  kg in males and  $29.5 \pm 5.4$  kg in females. IR was lower in males ( $0.736 \pm 0.020$ ) than females ( $0.760 \pm 0.019$ ), while the opposite was true for PhA ( $7.2 \pm 0.7$  vs.  $6.2 \pm 0.7$  degrees).

After adjusting for gender, HGS weakly correlated with stature, but not with weight and BMI. On the contrary, there was a significant association with BI indexes especially at higher frequencies, and a stricter association with IR250/5 ( $r = -0.433$ ,  $p < 0.001$ ) and PhA ( $r = -0.508$ ,  $p < 0.001$ ).

Multiple regression analysis indicated that, in addition to sex, BI indexes at higher frequencies are significant predictors of HGS in obese patients combined with IR or PhA (adjusted R<sup>2</sup> = 0.688 and 0.704, respectively,  $p < 0.001$ ).

**Conclusions** The present study show that in obese and very obese patients there are quite significant relationships of HGS with raw “quality” BIA variables such as IR or PhA.

P037

### SLEEVE GASTRECTOMY AND GASTRO-OESOPHAGEAL REFLUX: THE 24-HOUR PH-IMPEDANCE AS AN OBJECTIVE METHOD FOR PRE- AND POST-OPERATIVE EVALUATION

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Sleeve Gastrectomy and gastro-oesophageal reflux: the 24-h pH-impedance as an objective method for pre- and post-operative evaluation.

**Aims** In literature there are conflicting data about the effect of Sleeve Gastrectomy in gastro-oesophageal reflux disease. The objective of this study is to evaluate changes of gastro-oesophageal reflux after Sleeve Gastrectomy by pre and post-operative 24-h PH-impedance.

**Materials and methods** From 2014 to 2017, 30 patients undergoing Sleeve Gastrectomy were enrolled. The pre- and post-operative evaluations, in addition to the normal bariatric assessment included: oesophagogastroduodenoscopy (OGD), questionnaires for GERD (FOREGUT), questionnaires for quality of life (SF36) and 24 h pH-impedance at baseline and 9 months after the operation.

**Results** From the results obtained, it was shown that there is no correlation between patient-reported reflux symptoms (FOREGUT questionnaires) and the amount of reflux measured by 24 h pH-impedance and OGD. The sample at 9 months after Sleeve Gastrectomy showed a tendency towards worsening of gastro-oesophageal reflux and in some cases the onset of “de novo” reflux. The results show that there is a deterioration of the Demeester score and the Reflux Index Score (RIS) and a numerical increase in the episodes of reflux. In all patients, the questionnaires for the evaluation of the quality of life showed a clear improvement of the same.

**Conclusions** Based on the data extrapolated from this preliminary study, we can conclude that Sleeve Gastrectomy remains an effective bariatric procedure both in terms of weight loss and improvement in comorbidity with consequent improvement in quality of life, but with 24-h pH-impedance is possible to objectify a worsening of gastro-oesophageal reflux despite weight loss.

**P038**  
**EFFICACY OF SUBLINGUAL SUPPLEMENTATION OF VITAMIN B<sub>12</sub> IN PATIENTS UNDERGOING BARIATRIC SURGERY**

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**Introduction** The aim of the study was to test the efficacy of sublingual supplementation of vitamin B<sub>12</sub> following bariatric surgery. Patients that undergo bariatric surgery are at risk of vitamin B<sub>12</sub> deficiency, caused by a reduced intake and malabsorption. Guidelines consider intramuscular vitamin B<sub>12</sub> as the gold standard therapy for a vitamin B<sub>12</sub> deficiency, our approach was to try the efficacy of a sublingual vitamin B<sub>12</sub>.

**Patients and methods** We assessed the effectiveness of daily sublingual supplementation dose of 500 µg of cyanocobalamin (Barilife Bidodici<sup>®</sup>) administered over a period of 12 weeks on biochemical markers of vitamin B<sub>12</sub> in 37 patients who underwent bariatric surgery (26 Laparoscopic Gastric Bypass-GBP- and 11 Sleeve Gastrectomy-SG-) between January 2018 and April 2018 and had a minimum follow up of 3 months.

Hemoglobin, plasma iron, mean corpuscular volume (MCV) and cobalamin levels before surgery and 3 months after the surgery were analyzed.

**Results** In the GBP group, there were 18 women and 8 men (BMI average of 46.05) with a mean age of 47 years. Before surgery, three patients presented mediterranean anemia. After 3 months, the hemoglobin levels decreased by 1.30%, the MCV levels decreased by 5.39%, plasma iron decreased by 0.33%, and the B<sub>12</sub> levels increased by 116.93%. In the SG group, there were 10 women and 1 man (BMI average of 43.82) with a mean age of 42 years. After 3 months, the hemoglobin levels decreased by 3.49%, the MCV levels decreased by 1.42%, plasma iron increased by 5.14%, and the B<sub>12</sub> levels increased by 160.08%.

**Conclusions** The purpose of the present study was to assess the efficacy of daily cobalamin sublingual supplementation in patients that underwent bariatric surgery.

Administration was efficacious and convenient, and compliance was high. However, these patients need a continuous follow-up after the surgical procedure to prevent and treat vitamin deficiencies.

**P039**  
**VITAMIN DEFICIENCIES IN OBESE PATIENTS SUBMITTED TO ROUX-EN-Y GASTRIC BYPASS, MINI GASTRIC BYPASS AND BILIOPANCREATIC DIVERSION**

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Bariatric surgery has been considered a long-term effective treatment for severe obesity. Alteration of gastrointestinal physiology by bariatric procedures affects the nutritional intake and absorption.

Aim of this study is to assess nutritional deficiencies in patients undergoing bariatric surgery (malabsorptive procedures) and to identify predictors of postoperative nutritional status.

**Methods** We retrospectively analyzed 315 patients (245 females, 70 males) undergoing to bariatric surgery at Bariatric Surgery Department of Siena with minimum 1-year follow-up: 196 Roux-en-Y gastric bypass surgery (RYGB), 83 mini gastric bypass, 35 biliopancreatic diversion (DBP). Patients were evaluated baseline and after surgery. All were advised to take multivitamins (Bariatric<sup>®</sup>) and vitamin D was supplied based on serum levels. At each time of follow up we evaluated weight, EWL%, nutritional complications (hemoglobin, iron, ferritin, transferrin, pre-albumin, electrolytes) and annually vitamins (vitamin B<sub>12</sub>, folic acid, vitamin A, D and vitamin E).

**Results** Mean age 40.7 ± 9.57 years (range 18–66), mean pre-operative BMI was 47.32 ± 6.47 kg/m<sup>2</sup> (range 33.7–74.6). EWL% at 1 year was 67.61 ± 27.38%, at 2 years 73.79 ± 37.30%, at 5 years 64.88 ± 39.96%. Vitamin B<sub>12</sub> and vitamin E levels significantly reduced in the RYGB after 1, 2 and 5 years (p < 0.05). Vitamin A levels significantly reduced at 1 and 2 years in the gastric minibypass (p < 0.05) and at 5 years in the RYGB and the DBP. Folic acid and vitamin D levels significantly increased at 1 and 2 years (p < 0.05) in the RYGB and minibypass. We found a positive correlation between vitamin A and cholesterolemia, HDL, LDL, triglyceridemia and prealbumin (p < 0.05), between vitamin E and cholesterolemia, HDL and LDL (p < 0.05).

**Conclusions** The risk of nutritional deficiencies increases over time. Fat-soluble vitamins levels (vitamin A and E) correlate positively with lipids, which could be a good predictor of their.

**Nutraceuticals**

**P040**  
**SERUM VITAMIN D INCREASE AFTER DAILY USE OF A BUCCAL SPRAY COLECALCIFEROL NEW FORMULATION**

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Vitamin D (VD) is essential for active intestinal calcium absorption and plays a central role in maintaining calcium homeostasis and skeletal integrity. Considering the possibility of reduced VD levels in normal subjects and in patients with malabsorption, we assessed the efficacy of daily administration of a buccal spray formulation containing colecalciferol for 2 months in 14 patients (12F and 2M), with basal low levels of VD. The patients studied were: 4 after bariatric surgery (3 Roux-en-Y gastric bypass (RYGB) and 1 laparoscopic adjustable gastric banding (LAGB)), 4 with controlled hypothyroidism (HY), 3 with type 2 Diabetes mellitus (DM), 3 with normal-functioning multinodular goiter (G). The exclusion criteria were:

malignant disease, hepatic or renal failure or the use of bisphosphonates, glucocorticoids and anticonvulsants. Fasting blood samples were collected to measure baseline vitamin 25(OH)D, calcium, parathyroid hormone (PTH) levels in all participants at day 0 and at day 60. The buccal VD spray was supplied by Nestlé Health Science (Meritene VITAD + Spray). All participants were instructed to take 2000 IU day (3 sprays each of 333 IU) twice daily for 2 months. The normal values in our laboratory are: vitamin 25(OH)D: 75–250 nmol/L, serum calcium 8.40–10.20 mg/dL, PTH 10.8–79.4 pg/mL. The results are summarized in the table:

	Vitamin 25(OH)D nmol/L	Serum total calcium mg/dL	PTH pg/mL
	33,64 ± 13,18	9,42 ± 0,31	91,11 ± 49,78
	54,35 ± 13,85	9,42 ± 0,19	76,46 ± 33,36
	p < 0,01	NS	NS (p = 0,40)

These results confirm the efficacy of buccal spray colecalciferol to increase the vitamin 25(OH)D levels in all patients examined ( $p < 0.01$ ). It can be concluded that this buccal colecalciferol spray formulation produce a significantly increase of serum vitamin 25(OH)D concentration in all subjects examined, including those with previous bariatric surgery, over a period of 60 days treatment.

## Obesity and microbioma

P041

### GUT MICROBIOTA ANALYSIS IN OBESE PATIENTS BEFORE AND AFTER LIFE-STYLE INTERVENTION

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**Introduction** Several studies report that the major factor influence in gut microbiota composition is the food habits. The aim of the present study is to analyze the characteristics of gut microbiota in a group of adult obese patients before and after a multi-disciplinary treatment including a nutritional intervention.

**Materials and methods** Stool samples from 10 diet-free obese patients, were collected before (BT; BMI = 36.4 ± 5.7), and after treatment (AT; BMI = 34.4 ± 5.8). Barcoded amplicon libraries for the bacterial community analysis were generated using primers targeting the V3 and V4 hypervariable region of the bacterial 16S rRNA gene and Nextera XT index kit (Illumina, Inc.). Samples were sequenced and analysed with Illumina MiSeq platform and the 16S metagenomics app and the MiSeq Reporter software.

**Results** Analysis of bacterial complexity revealed a statistically significant decrease at Actinobacteria phylum ( $p = 0.03$ ), Bifidobacteriaceae family ( $p = 0.008$ ), Bifidobacterium genus ( $p = 0.01$ ) and an increase in Clostridiaceae family ( $p = 0.003$ ) in AT. No statistically significant differences was revealed in species. Furthermore, the ratio Firmicutes/Bacteroidetes was not significantly reduced.

**Conclusion** Reported results are preliminary and referred to a limited group of patients. We consider collected data as a good starting point to the follow up of the study. The ambition is to identify microbial profile involved as casual and/or promoting obesity factors, with the purpose to modify selectively gut microbiota and improve healthiness, with long time dietary interventions.

P042

### GUT MICROBIOTA ANALYSIS IN A GROUP OF DIET-FREE OBESE PATIENTS

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**Introduction** Aim of this study is to characterize the gut microbiota in of obese patients, diet-free (DF) for at least 12 months.

**Materials and methods** Stool samples from 18 DF patients (BMI = 35.4 ± 5.3) were compared to 10 normal weight (NW; BMI = 22.2 ± 2.0) and 10 obese weight cycling (WC; BMI = 34 ± 7.6). IBD and recent antibiotic treatment were considered as exclusion criteria. In DF patients, anthropometric, nutritional and clinical parameters were related to microbiota composition. Barcoded amplicon libraries for bacterial community analysis were generated using primers targeting the V3 and V4 hypervariable region of the bacterial 16S rRNA GENE AND Nextera XT index kit (illumina,inc.). Samples were sequenced and analysed with illumina MiSeq platform and the 16S metagenomics app and the MiSeq Reporter software.

**Results** Bacterial analysis revealed an increase in Chloroflexi in DF group compared to NW and WC ( $p = 0.01$ ), and a depletion of Actinobacteria compared to NW ( $p = 0.048$ ), of Oscillospira compared to NW ( $p = 0.02$ ), of *B. rodentium* compared to WC ( $p = 0.002$ ), of *B. uniformis*, *P. merdae* and *L. pectinoschiza* compared to NW ( $p = 0.001$ ;  $p = 0.03$ ;  $p = 0.001$ ). No significant differences were detected at family level. We found a positive correlation between protein intake and both Chloroflexi and Oscillospira, between fasting glycaemia and *B. uniformis* and between LDL and *P. merdae* and a negative correlation between LDL and Cyanobacteria, *B. rodentium* and *B. uniformis*. A negative correlation was found between body weight, abdominal circumference, fat mass, BMI and Chloroflexi, and between BMI and Oscillospira.

**Conclusion** Our data confirm in part some already known results but they will be implemented and compared with those obtained after weight loss.

## Obesity and cancer

P043

### A SPECIFIC AMINO ACID MIXTURE PREVENTS MITOCHONDRIAL DAMAGE IN DOXORUBICIN CARDIOTOXICITY

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Obese women have increased incidence of breast cancer than normal weight subjects. Anthracycline anticancer drugs (e.g., doxorubicin) are mainly used in these patients, and can induce cardiotoxicity,

which is due to mitochondrial damage. Recent evidence demonstrate that branched-chain amino acids-enriched mixture (BCAAem) supplementation increases mitochondrial biogenesis in cardiac and skeletal muscle. This study hence aimed to verify and compare in vitro effects of different amino acid formula supplementations on mitochondrial biogenesis markers in HL-1 cardiomyocytes treated with doxorubicin (DOX). In particular, we show here that exposure of doxorubicin-treated HL-1 cells to BCAAem, unlike to CAAem (a mixture that reproduces the amino acid profile of casein) was able to counteract the mitochondrial biogenesis damage induced by anthracycline. Moreover, to evaluate the in vivo effects of DOX on mitochondrial biogenesis, and to verify whether the BCAAem supplementation rescued the DOX-induced mitochondrial damage, we analyzed morphology and morphometry of mitochondria in the heart of mice treated with DOX plus BCAAem. We tested also the gene expression of the main mitochondrial biogenesis and function markers, including COX IV and Cyt c, in addition to mtDNA amount, in these animals. Our results confirmed that BCAAem supplementation was able to selectively ameliorate mitochondrial biogenesis and cardiac toxicity in mice. Finally, we investigated the involvement of endothelial nitric oxide synthase (eNOS) in the process of mitochondrial biogenesis, and showed that BCAAem stimulated protein kinase B (AKT) and mammalian target of rapamycin (mTOR) signaling pathway. Taken together, our results demonstrate that while mitochondrial biogenesis and function are down-regulated in heart of DOX-treated mice, the BCAAem supplementation prevents the mitochondria damage. These results could be relevant to prevent cardiac toxicity in chemotherapy-treated humans.

## Genetics

P044

### DESCRIPTION OF A NOVEL AGPAT2 MUTATION (Q144X) IN A CHILD AFFECTED BY BERARDINELLI–SEIP CONGENITAL GENERALIZED LIPODYSTROPHY (TYPE 1 CGL)

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Type 1 CGL is a rare autosomal recessive disorder associated with a near total absence of adipose tissue. Other features include insulin resistance, hypertriglyceridemia, hepatic steatosis, muscle pseudo-hypertrophy, acanthosis nigricans and acromegaloid appearance. Type 1 CGL is due to mutation of the AGPAT2 gene. AGPAT2 protein, 1-acyl-sn-glycerol-3-phosphate acyltransferase beta (also known as lysophosphatidic acid acyltransferase beta), is a 278 amino acids protein and belongs to the family of acyltransferases. This enzyme catalyzes an essential reaction in the biosynthetic pathway of

glycerophospholipids and triacylglycerol. In this report we describe a novel pathologic allelic variant Q144X in exon 3 of AGPAT2 gene that results in a premature stop codon and in a truncated non functional protein.

The proband, a 7-years old male child, was born from unrelated parents in a small village in the Northern area of Italy. Few days after birth, elevated levels of triglycerides (1565 mg/dl), AST (543 U/L), ALT (667 U/L) and an enlarged liver were detected. In 2010 BSCL Syndrome was diagnosed after genetic analysis that revealed a novel nonsense homozygous mutation (Q144X) in exon 3 of the AGPAT2 gene. The allelic variant in the heterozygous form was found in both parents and in 3 additional family members of the maternal side (see pedigree below; M mutant allele, N normal allele).

In conclusion we describe a novel nonsense AGPAT2 variant (Q144X) in a child affected by Berardinelli–Seip Congenital Generalized Lipodystrophy (type 1 CGL). The occurrence of this unique variant on both sides of the paternal families, suggests a founder effect from an ancestor of this resident community.

## Adipose organ and obesity

P045

### BODY FAT INDEX (BFI) VERSUS BODY MASS INDEX (BMI), WAIST CIRCUMFERENCE (WC) AND WAIST-TO-HEIGHT RATIO (WHTR) IN FAT MASS (FM) EVALUATION

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**Background** In Obesity it is important to have accurate and inexpensive clinical tools that can correctly estimate the amount of fat mass in patients, thus allowing a correct quantification of the entity of adipose organ.

**Aim** To evaluate if BFI (BMI × Waist) is able to accurately identify overfat and obese patients based on the percentage of FM (measured by Bioimpedance Analysis, BIA) in comparison with BMI, WC, WHtR. Patients and method: The database includes 2400 outpatients attending the Program of Obesity treatment (SODcDiabetes at the Careggi University Hospital), 684 men (28.5%) and 1716 women (71.5%), with an average age of 47.2 ± 14.8 years. A univariate and a multivariate statistical analysis was performed separately by gender and implemented through the analysis of the Receiver Operating Characteristics Curve (ROC), followed by the analysis of the area under the curves (AUC) and by the comparison of the sensitivity and specificity of the four indices.

**Results** The indicators under evaluation show a strong positive correlation with the percentage FM (p-Value < 0.001) both in univariate and multivariate correlation. The AUC of the ROC shows that the index with greater diagnostic accuracy for the condition of overfat is WHtR (AUC = 0.890) for men and BFI (AUC = 0.923) for women, while in obesity WHtR (AUC = 0.891) for men and BFI (AUC = 0.922) for women.

**Conclusions** BFI is the best tool to discriminate between overfat and obese subjects on the basis of the percentage of FM in females while, WHtR is the indicator with the greatest diagnostic accuracy in males, having in addition a good diagnostic accuracy even in females. Present results enable clinicians to have an indirect measure of FM in those setting in which BIA is not available.

## Metabolic workings in bariatric surgery

P046

### SERUM IGF-BINDING PROTEIN 2 (IGFBP-2) CONCENTRATIONS CHANGE EARLY AFTER GASTRIC BYPASS BARIATRIC SURGERY REVEALING A POSSIBLE MARKER OF LEPTIN SENSITIVITY IN OBESE SUBJECTS

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Essential obesity is characterized by “leptin resistance” but no reliable in vivo marker of leptin activity have been so far described. Expression of IGFBP-2 in mice is regulated by leptin and its over-expression is associated with reduced caloric intake, resistance to weight gain and to hepatic steatosis. Gastric bypass bariatric surgery is effective in inducing stable weight loss and resolution of co-morbidities associated with obesity.

Hormonal variations contributing to these effects occur very early after surgery but have not been fully elucidated.

We aimed at evaluating IGFBP-2 serum changes (measured by ELISA assay) early after bariatric surgery and their relationship with variations of leptin (measured by RIA assay) to test the hypothesis that an early increase of leptin sensitivity may explain some of the effects of gastric bypass. Fifty-one obese patients (41 women and 10 men), 9 non-obese surgical controls and 41 lean matched controls were studied. IGFBP-2 was measured at time 0, 3 days, 1 month, 3 months, 6 months, 12 months, 18 months after bariatric bypass surgery and at time 0 and 3 days after non-bariatric laparoscopic surgery in a lean control group.

Leptin was measured at time 0 day, 3 days, 1 month and 12 months after bariatric bypass surgery and at time 0 and 3 days after non-bariatric laparoscopic surgery. Obese patients showed low serum levels of IGFBP-2. After gastric bypass, IGFBP-2 serum levels significantly increased at 3 days and became normal before the occurrence of relevant changes in body weight, serum concentrations were stable up to 18 months from surgery. IGFBP-2/leptin ratio increased early after surgery and became normal 1 year after.

In conclusion, IGFBP-2 serum levels increased early in a window of time when variations of hormones mediating the effects of bariatric surgery occur. We speculate that IGFBP-2, a leptin-regulated protein, might be a reliable in-vivo marker of leptin action and that gastric bypass might improve leptin sensitivity contributing to weight loss.

## Metabolic regulatory mechanisms

P047

### PLASMA UNACYLATED GHRELIN LEVELS PREDICT 5-YEAR MUSCLE MASS IN HUMANS

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**Introduction** Unacylated ghrelin (UnAG) is an emerging modulator of skeletal muscle metabolic pathways with antioxidative, anti-inflammatory and insulin-sensitizing actions observed both in rodent healthy and disease models. Importantly, sustained UnAG administration was reported to normalize low muscle mass in chronic disease experimental conditions. Potential associations between UnAG and muscle mass in humans remain however currently unknown.

**Methods** In 235 individuals from the North-East Italy MoMa population study (age 52 ± 16 years; M/F: 122/113) we investigated prospective associations between baseline ghrelin profile (UnAG as well as acylated hormone) and 5-year body composition with particular regard to muscle mass. Body composition and muscle mass were measured by bioelectrical impedance; muscle strength was measured at the 5-year evaluation by hand-grip strength assessment. **Results** In all subjects, circulating UnAG levels were positively associated with 5-year muscle mass (P < 0.01). Total ghrelin but not the acylated form also positively predicted 5-year muscle mass, while additional negative associations were observed between 5-year muscle mass and age, female gender and baseline BMI (P < 0.05). Conversely, no associations were observed between any variables and muscle strength. In multiple regression analysis, UnAG was found to be still significantly associated with muscle mass after multiple adjustments for confounding variables.

**Conclusions** In a North-East Italy general population cohort, UnAG selectively and independently predicts 5-year muscle mass. Based on available knowledge from animal studies, UnAG could contribute to maintenance of muscle mass by modulating muscle oxidative stress, inflammation and insulin action.

P048

### IMPROVED INSULIN SENSITIVITY FROM DIET-INDUCED WEIGHT LOSS IN OBESE HUMANS IS ASSOCIATED WITH INCREASED CIRCULATING UNACYLATED GHRELIN LEVELS

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**Introduction** Unacylated ghrelin (UnAG) is an emerging modulator of insulin action with beneficial effects reported in skeletal muscle in rodent models. Obesity is characterized by low plasma UnAG and



may potentially contribute to obesity-associated low insulin action. Effects of dietary treatment through moderate caloric restriction (CR) on plasma UnAG as well as on the potential involvement of UnAG modifications in diet-induced changes in insulin action in obesity are currently unknown.

**Methods** The impact of 16-week caloric restriction [ObCR,  $n = 11$ ; age =  $55 \pm 2$  years; body mass index (BMI) =  $35 \text{ kg/m}^2$ ] or control diet (ObCon;  $n = 9$ ; age =  $53 \pm 2$ ; body mass index =  $34$ ) on plasma circulating total (TotalG[KSN1]), acylated (AG) and unacylated ghrelin (UnAG) was investigated in obese individuals. Insulin sensitivity was measured through the hyperinsulinemic-euglycemic clamp technique as area under the curve (AUC) of glucose infusion to maintain euglycemia.

**Results** Compared to ObCon, ObCR reduced body weight and BMI in association with improved whole-body insulin sensitivity (all  $P < 0.05$ ). No changes in TotalG, AG or UnAG were detected in ObCon. In contrast, TotalG and UnAG selectively increased in ObCR with no changes in AG ( $P < 0.05$  vs Baseline and ObCon). In all subjects, changes in UnAG were positively associated with changes in AUC ( $n = 20$ ;  $P < 0.01$ ); this association remained statistically significant ( $P < 0.05$ ) after adjustment for treatment (Con vs CR) and BMI changes.

**Conclusions** Dietary treatment and weight loss in obese individuals modify circulating ghrelin profile with selective increase in unacylated but not acylated hormone. The current results indicate that higher unacylated ghrelin likely contributes to metabolic benefits and may explain improvements in insulin sensitivity during diet-induced weight loss in human obesity.

P049

## ASSOCIATION BETWEEN TSH LEVELS AND BODY MASS INDEX (BMI) IN SUBJECTS WITH NORMAL THYROID FUNCTION

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Overt hyperthyroidism is known to be associated with weight loss and hypothyroidism with weight gain. Little is known about weight changes within the normal range of thyroid function. Aim of this study was to evaluate the relation between the values of TSH and some obesity indices (BMI and body weight) in adult subjects with normal thyroid function. The study was performed in 794 subjects (387 M and 407 F). Height, weight and thyroid function (TSH, FT3, FT4) were measured in all subjects. Only subjects with normal thyroid function have been included ( $n = 524$ ). Subjects were divided into two groups based on BMI value: obese subjects (BMI  $> 30 \text{ kg/m}^2$ ,  $n = 256$ ) and non-obese subjects (BMI  $< 30 \text{ kg/m}^2$ ,  $n = 268$ ). There were no differences in age and sex in the two groups. BMI and body weight were significantly higher in obese subjects when compared with the non-obese subjects ( $P < 0.001$  and  $P < 0.001$ , respectively). Obese subjects showed significantly higher values of TSH ( $P < 0.001$ ) and significantly lower values of FT4 ( $P < 0.01$ ) when compared with non-obese subjects. There were not differences in the levels of FT3 in the two groups. Linear regression analysis showed a positive correlation between values of TSH and BMI ( $r = 0.115$ ,  $P < 0.004$ ) and between values of TSH and body weight ( $r = 0.241$ ,  $P < 0.001$ ). We observed a negative correlation between values of FT4 and BMI ( $r = -0.223$ ,  $P < 0.0001$ ). Obese subjects have been stratified in quartiles according to levels of TSH. Subjects in the 4th quartile (higher levels of TSH) presented more elevated values of BMI than the 1st quartile (lower levels of TSH). In a logistic regression model, subjects with normal thyroid function and levels of TSH in the 4th quartiles showed an increased risk of having obesity compared to the 1st quartile (OR 1.97;  $P < 0.05$ ). In conclusion, our data seem to indicate a positive association between TSH values and BMI in adult subject with normal thyroid function.