a continuous outcome, reflecting severity, using the method of Gurka and DeBoer.[1] IR was calculated with the homeostatic model assessment (HOMA-IR) and modeled as a continuous variable. An OLS regression model predicting MetS as a function of HOMA-IR, BMI, and their interaction, along with key covariates was used to test whether HOMA-IR moderates the relationship between BMI and MetS severity, independent of GDM. **Results:** The association between BMI and MetS severity was significantly modified by HOMA-IR (b=0.008, p<0.001), independent of GDM status during pregnancy, such that the positive association between BMI and MetS severity was stronger among individuals with higher HOMA-IR. For example, among women with HOMA-IR values 1-standard deviation below the mean, the estimated association between BMI and MetS severity was (b=0.0394, p<0.001); however, among women with a HOMA-IR value 1-standard deviation above the mean, the association between BMI and MetS severity was (b=0.0745, p<0.001). **Conclusion**: IR after pregnancy was a significant moderator of the association between BMI and MetS severity. Future studies should explore whether interventions to improve IR can reduce MetS severity independent of BMI and prior GDM.

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Adipose Tissue, Appetite, and Obesity

INTEGRATED PHYSIOLOGY OF OBESITY AND METABOLIC DISEASE

Insulin Resistance Shows Stronger Correlation With Ectopic Liver Fat Instead of Visceral Fat in Asian Indians

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Introduction: Insulin resistance (IR) is associated with abdominal obesity. Asian Indians have higher insulin resistance at lower abdominal obesity levels as compared to the western population. However, the relative association of various compartments of abdominal fat, i.e., Subcutaneous Fat (SCAT), Visceral fat (VAT), and ectopic Liver Fat, is not very clear. Our study's objective was to look for the association of abdominal fat composition in Asian Indians with IR level and gender and diabetes status. **Methodology**: Our study is an analytical cross-sectional study conducted from 2018–2020 at SMS Hospital located in northwest India. 91 subjects were studied during the study period and underwent MRI for SCAT, VAT, and Liver fat estimation. We divided subjects into tertile groups, based on HOMA-IR levels, and statistical analysis for SCAT, VAT, and Lipid fat in each tertile and as a whole group carried out. Similarly, we analysed data in male and female and diabetic and non-diabetic groups, as tertiles and as a whole. **Results:** Of the recruited subjects 49 were diabetics (M: F=23:26) and 42 were non-diabetic (M: F=12:30). In the overall group, HOMA-IR has a weak positive association with VAT and Liver Fat and a weak negative association with SCAT (R=0.28,0.38 and -0.11, respectively). From tertile1 to tertile3, there was a consistent increase in VAT and Liver fat (119.3, 121.1, 156.6 cm^2 and 8.18, 10.02, 10.89% respectively), so that R value increases from -0.24 to 0.21 for VAT and -0.195 to 0.58 for Liver Fat. On the other hand, the SCAT levels were not different and correlation with IR declined from -0.299 to -0.39. On Sex wise analysis negative correlation of SCAT with IR become substantial from tertile1 to tertile3 in both males and females but strong correlation was seen in females (-0.189 to -0.515) though amount of SCAT was not different among tertiles. Both VAT and Liver Fat increased with tertile1 to terrtile3; IR was very strongly correlated with Liver Fat in both the sexes at higher tertiles (0.91 for males and 0.71 for females). In the diabetic group, liver fat was significantly associated with IR at higher tertile (R=0.9). The SCAT was negatively associated with IR, and a further decline in correlation coefficient with each tertile, became significant at 3rd tertile (-0.41) with a weak correlation of IR with VAT. These relations have similar SCAT and Liver fat trends but a strong correlation not seen in the non-diabetic group. **Conclusion:** Insulin resistance strongly correlated with ectopic liver fat in Asian Indians including diabetics with no gender disparity which became significant at higher tertile. As compared to ectopic liver fat, VAT has only a minor role in development of IR. SCAT has a protective role against IR in both diabetics and non-diabetics.

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Is Insulin Resistance at Baseline a Predictor of Weight Loss After Bariatric Surgery?

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Background: Obesity is a multifactorial disease that is strongly associated to other metabolic disorders, such as insulin resistance and type 2 diabetes. Bariatric surgery is nowadays considered the most effective treatment of morbid obesity. The role of insulin resistance (IR) in weight loss after bariatric surgery is highly unknown.

Aim: To evaluate the association between Insulin Resistance (IR) and percentage of excess weight loss (EWL%) one, two, three and four years after bariatric surgery in patients with morbid obesity. **Methods:** Retrospective longitudinal study in patients with morbid obesity followed in our centre between January 2010 and July 2018 were included.

Patients were excluded if they had diabetes. We evaluated baseline Homeostatic Model Assessment of IR (HOMA-IR), Homeostatic Model Assessment of β-cell function (HOMA-beta), Quantitative Insulin Sensitivity Check Index (QUICKI) and Matsuda and DeFronzo index, and performed a linear regression concerning each year's EWL%.
Results: After applying the exclusion criteria, 1723 patients were included in this analysis. The logarithm of HOMA-beta was negatively associated with EWL% at second-, third- and fourth-years post-surgery (β=-1.04 [-1.82 to -0.26], p<0.01; β=-1.16 [-2.13 to -0.19], p=0.02; β=-1.29 [-2.64 to 0.06], p=0.061, respectively), adjusting for age, sex, body mass index and type of surgery. This was not observed in the first-year post-surgery nor for the other indexes. Glycaemia at baseline was also positively associated to EWL% at second- and third-years post-surgery.
Conclusion: IR at baseline seems to be associated to long term weight loss, explicitly after the first year post bariatric surgery.

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INTEGRATED PHYSIOLOGY OF OBESITY AND METABOLIC DISEASE

L-Leucine Supplementation for Preserving Lean Mass During Low Calorie Diet in Sarcopenic Obese Women: A Pilot Study

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Background: In sarcopenic obese subjects it is essential to reduce body weight and to preserve lean mass, in order to avoid a worsening of muscle function (1). Several studies have shown that leucine supplementation can be useful to improve skeletal muscle mass in sarcopenic patients (2). **Aim:** Evaluate the effectiveness of a short-term low calorie diet (LCD) combined with combined supplementation with whey protein, leucine and vitamin D on weight loss, lean mass and muscle strength in sarcopenic, obese, hyperinsulinemic and menopause women. **Materials and methods:** 16 female with mean age: 58.1 years (range: 47–69 years), BMI 37.6 Kg/m^2 (range: 31,7 - 44,1 Kg/m^2), HOMA-index ≥ 2.5, were assigned to an LCD regimen (1000 kcal/day) with supplementation of 18 g protein, 4 g leucine and 5 mcg vitamin D for 45 days. Anthropometric indexes, blood and urine chemistry, body composition by DEXA, muscle strength by handgrip test and Short Physical Performance Battery (SPPB) were assessed at baseline and at the end of the treatment. **Results:** A significant reduction of BMI (35,7 vs 37,6 Kg/m^2), waist circumference (102,4 vs 107 cm), HOMA index (2,3 vs 4,8) and fasting insulin (10,4 vs 17,4 μIU/ml) was observed in all patients. Women preserved total lean body mass (57 vs 55 %) and improved significantly muscle strength, as measured by handgrip (22,2 vs 18,6 Kg) and SPPB (8,9 vs 7,5). **Conclusion:** We conclude that LCD with adequate protein intake and a supplementation with whey protein, leucine and vitamin D should be promoted to maintain muscle mass and improve muscle strength in menopause women with sarcopenic obesity.
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Adipose Tissue, Appetite, and Obesity
INTEGRATED PHYSIOLOGY OF OBESITY AND METABOLIC DISEASE

Leptin Decreases Energy Expenditure but Increases Thyroid Hormone in Patients With Lipodystrophy

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Leptin is an adipokine that signals energy sufficiency. In rodents, leptin deficiency is associated with decreased body temperature and energy expenditure (EE), which is reversed with leptin replacement. Leptin's role in EE in humans is unclear; however, one study of 10% weight-reduced healthy subjects suggested that leptin replacement to pre-weight loss levels restored the decline in EE, thyroid hormone, and catecholamines associated with weight loss. Patients with lipodystrophy (LD) are characterized by deficiency of adipose tissue and can serve as models to study effects of leptin deficiency and replacement in humans. We hypothesized that treatment with recombinant leptin (metreleptin) in patients with LD would increase EE, thyroid hormone, and catecholamines. We conducted a non-randomized crossover study of 25 patients with LD who were hospitalized for 19 days on an iso-caloric diet. The initiation cohort consisted of 17 patients with no prior exposure to metreleptin, who were first studied for 5 days without metreleptin (period 1), then were treated with metreleptin for 14 days (period 2). The withdrawal cohort consisted of 8 previously metreleptin-treated patients who were continued on metreleptin for the first 5 days of the study (period 1), then were taken off metreleptin for 14 days (period 2). At the end of each period, we measured 24-hour EE (TEE) and resting EE (REE) using indirect calorimetry and free T3, T4, epinephrine, norepinephrine and dopamine after an 8–12 hour fast. In the leptin initiation cohort, TEE and REE decreased from 2402±383 kcal/day and 1805±332 kcal/day to 2272±396 kcal/day (p=0.003) and 1688±318 kcal/day (p=0.03), respectively. Free T3 increased from median (IQR) 248 (200, 270) pg/mL to 295