Effect of surgical weight loss on insulin sensitivity and lipid profiles in MHO subjects.

Sufi P.¹
Malik S.N.², Lei S.², Casale C.², Heath D.¹, Gray R.¹, Mohamed-Ali V.²

¹Whittington Hospital, North London Obesity Surgery Service (NLOSS), London, UK
²Adipokines and Metabolism Research Group, Research Division of Metabolism & Experimental Therapeutics, Division of Medicine, University College London, London, UK
Background – heterogeneity in obesity

- Subsets of obese individuals, 20-30% of the Caucasian population, protected from obesity-associated metabolic abnormalities; the 'metabolically healthy but obese' (MHO). Primeau et al. 2011
- Display healthy metabolic profile, despite excessive body fat; normal insulin sensitivity, normal lipid and inflammatory profiles, no hypertension.
- Unlike the pathologically obese (PO), the metabolic profiles of MHO are comparable to normal weight subjects, with lower incidences of type 2 diabetes and cardiovascular diseases.
- Whether MHO individuals would gain any extra metabolic benefit from weight loss is unclear.
- Also no universally agreed definition of MHO as yet
Objectives

- to assess the effect of surgical weight loss on insulin sensitivity and lipid metabolism in MHO and PO subjects

- A simple, but, stringent, circulating biomarker to identify MHO

- Cross-sectional characterization of MHO versus PO, identified with this marker

- Effect of weight loss
Schema of Study and definition of patients

**MHO**
- Normoglycaemic
- Normoinsulinaemic
- Fasting insulin < 6.5mU/L

**PO**
- Normoglycaemia
- Hyperinsulinaemic
- Fasting insulin ≥ 7.0mU/L

Caucasian
Non-diabetics
BMI > 40kg.m⁻²

Initial Screen

MHO
n=24

PO
n=53

Surgery

Follow-up

MHO
n=10

PO
n=13
Methods ..... 

- **Anthropometric measures** - Height (m), weight (kg), BMI m.kg$^{-2}$, blood pressure, CPEX
- **Laboratory parameters** - lipid profile, inflammatory markers (IL-6, MCP-1), adipokines (adiponectin)
- **Insulin sensitivity** - fasting plasma glucose and serum insulin used to calculate HOMA-IR index - product of fasting plasma glucose (mmol/l) and insulin (mIU/L) divided by 22.5.
Baseline.....

- At baseline, using our criteria MHO (n=24) and PO (n=53) patients were identified and found to be matched for:
  - age (MHO vs. PO 40.6(9.5) vs 41.1(11.3) years, 
  - body mass index, aerobic fitness, fasting plasma glucose, total-cholesterol, LDL-cholesterol and HDL-cholesterol.

- However, MHO patients had significantly lower systolic (p=0.03) and diastolic (p=0.05) blood pressure, circulating insulin levels (p<0.001) and triglycerides (p<0.001)

- MHO significantly more insulin sensitive (0.84 {0.59-1.2} vs 2.4 {1.7-4.1}, p<0.001) HOMA-IR index.
Following surgery ...

Significant weight loss in both groups 3-6 months post surgery.

In the Table: Red denotes significant change
Triglycerides

![Chart showing the distribution of triglyceride levels before and after treatment for patients with different MHO status. The chart includes box plots and individual data points with annotations for each group.](chart)

- **Triglycerides (mmol/L;Before)**
- **Triglycerides (mmol/L;After)**

**MHOstatus**
- **MHOins<6.5**
- **POins>7.0**
Systemic Insulin and insulin sensitivity
Adipokines/chemokines

![Box plot](image)

- **Serum adiponectin (ug/mL)**
- **Serum MCP-1 (pg/mL)**

**MHO status**
- MHOins<6.5
- POins>7.0

- **MHOins<6.5**
- **POins>7.0**
Follow-up summary.....

- At 3-6 months after surgery all patients lost weight significantly (p< 0.001).
- In the PO subjects this was associated with an increase in HDL-cholesterol (p< 0.001) and a significant reduction in plasma triglycerides, insulin and HOMA-IR.
- However, in the MHO group weight loss was accompanied by an increase in plasma total-cholesterol, triglycerides and insulin, as well as HOMA-IR.
- Adiponectin increased and MCP-1 decreased in both groups.
Conclusions ....

- The metabolic effects of weight loss in MHO and PO patients appear to vary significantly.
- In the PO patients weight loss has the expected favourable metabolic profile.
- However, in MHO individuals, given their favorable metabolic profile prior to surgery, no additional metabolic gain is associated with weight loss.
- However, markers of adipose tissue health improved in both groups.
Discussion....

- A single fasting serum glucose and insulin concentration is able to identify the MHO and PO cohorts described in this study.

- Following weight loss there still appears to be heterogeneity in the response of these two groups, to some extent confirming recent results from Sesti et al., 2011.

- However, more systemic anti-inflammatory (adiponectin) and less pro-inflammatory (MCP-1) adipokines after weight loss in both groups suggest improved adipose tissue health.

- Thus, much of the MHO/PO phenotype may be mediated by differences resident in the skeletal muscle and/or liver.
Funding

European Commission FP6 - EXGENESIS
(LSHM - CT- 2004 - 005272 )

The Whittington Hospital NHS

Translational Research Small Grants Scheme