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

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Background – heterogeneity in obesity

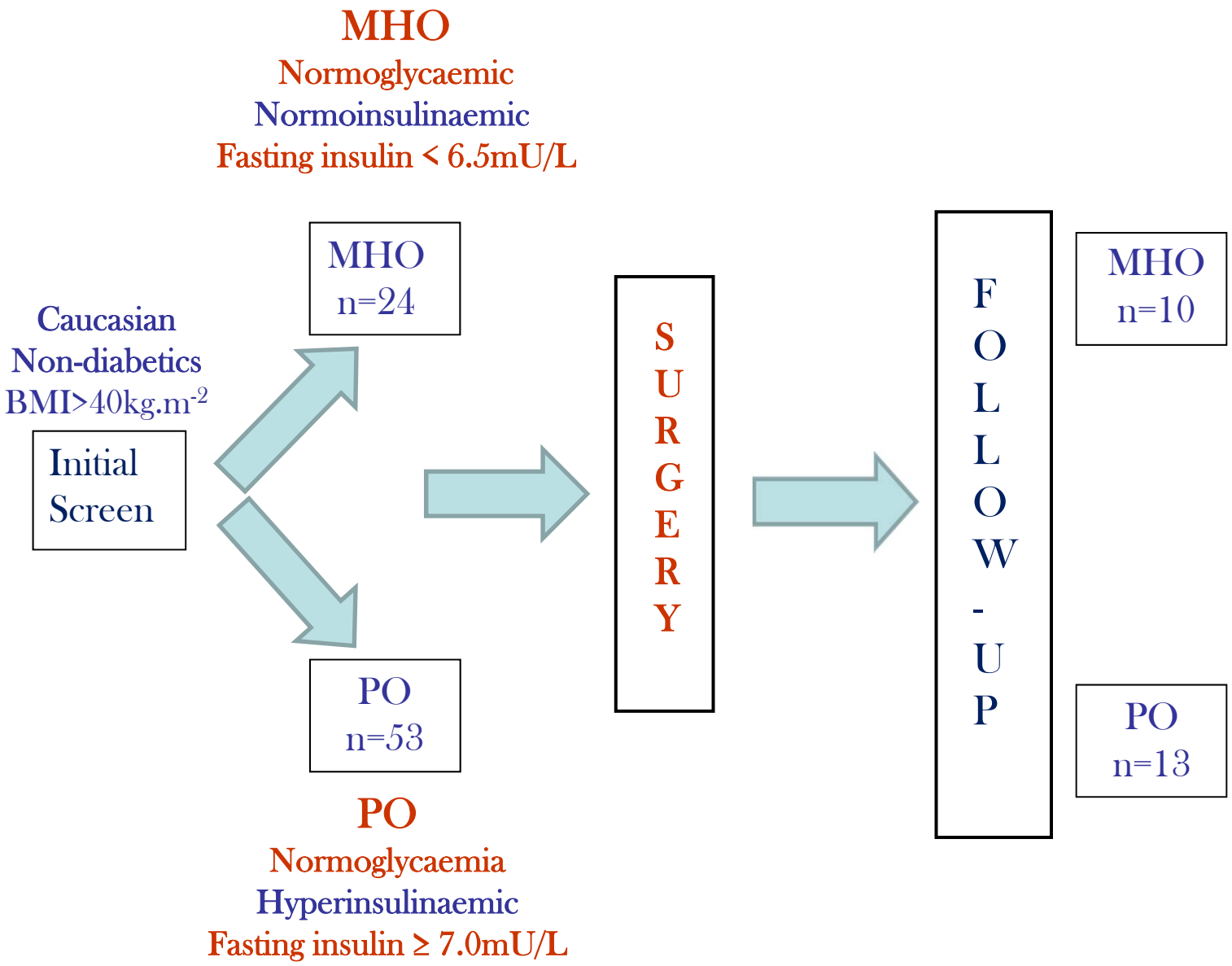
- *Subsets of obese individuals, 20-30% of the Caucasian population, protected from obesity-associated metabolic abnormalities; the 'metabolically healthy but obese' (MHO).* ***Primeau et al. 2011***
- *Display healthy metabolic profile, despite excessive body fat; normal insulin sensitivity, normal 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



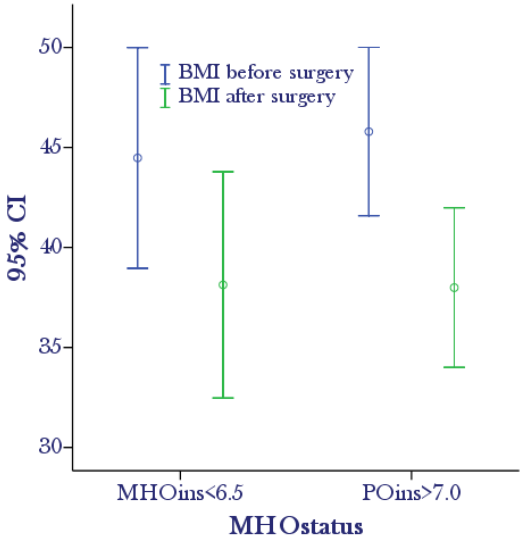
Methods .....

- ***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 ...

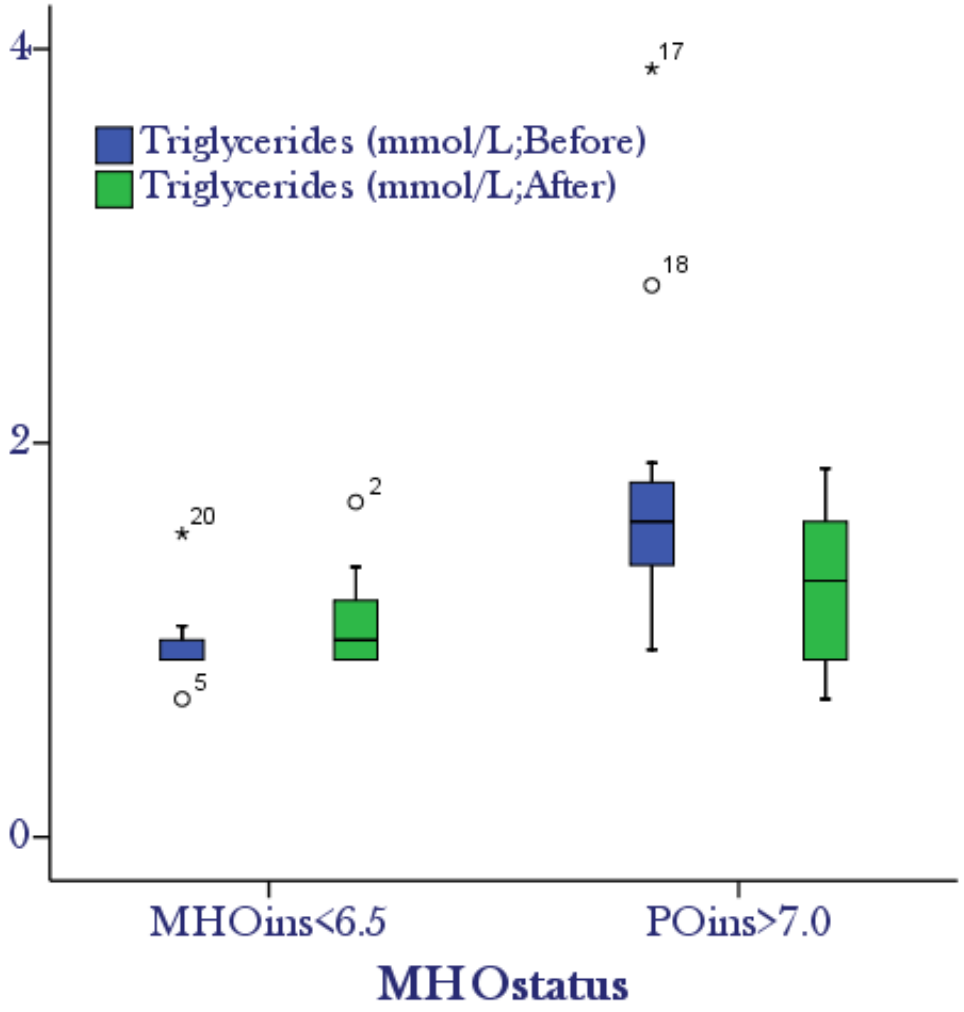


Significant weight loss in both groups 3-6 months post surgery.

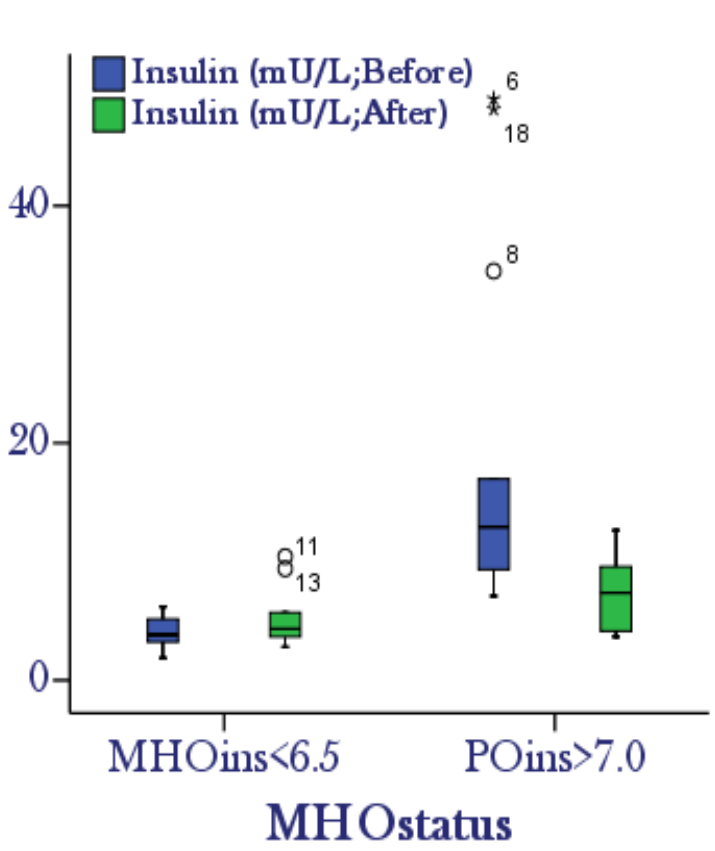
	MHO			PO		
	Median	IQR25	IQR75	Median	IQR25	IQR75
FPG (mmol/L;Before)	5.10	3.90	5.90	5.10	4.65	5.95
FPG (mmol/L;After)	4.80	4.68	5.03	4.60	4.35	5.00
TC (mmol/L;Before)	3.50	3.08	4.03	4.20	3.10	4.70
TC (mmol/L;After)	4.15	3.68	4.65	4.40	4.10	5.00
LDL (mmol/L;Before)	1.90	1.80	2.35	2.40	1.88	2.87
LDL (mmol/L;After)	2.55	1.85	3.08	2.80	2.65	3.37
HDL (mmol/L;Before)	1.03	0.80	1.33	0.90	0.65	1.08
HDL (mmol/L;After)	1.15	1.05	1.50	1.11	0.95	1.20

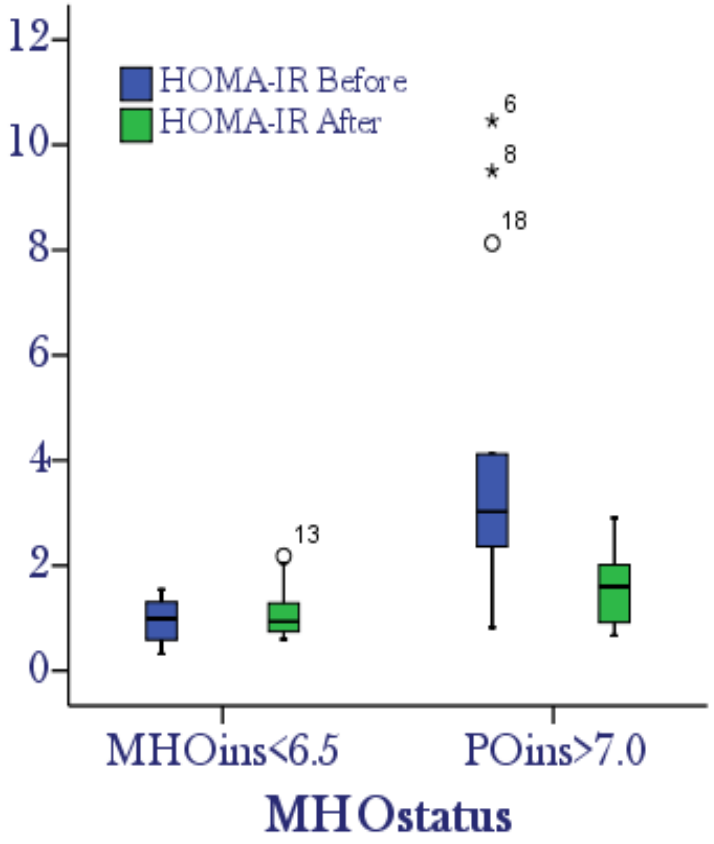
In the Table: Red denotes significant change

Triglycerides

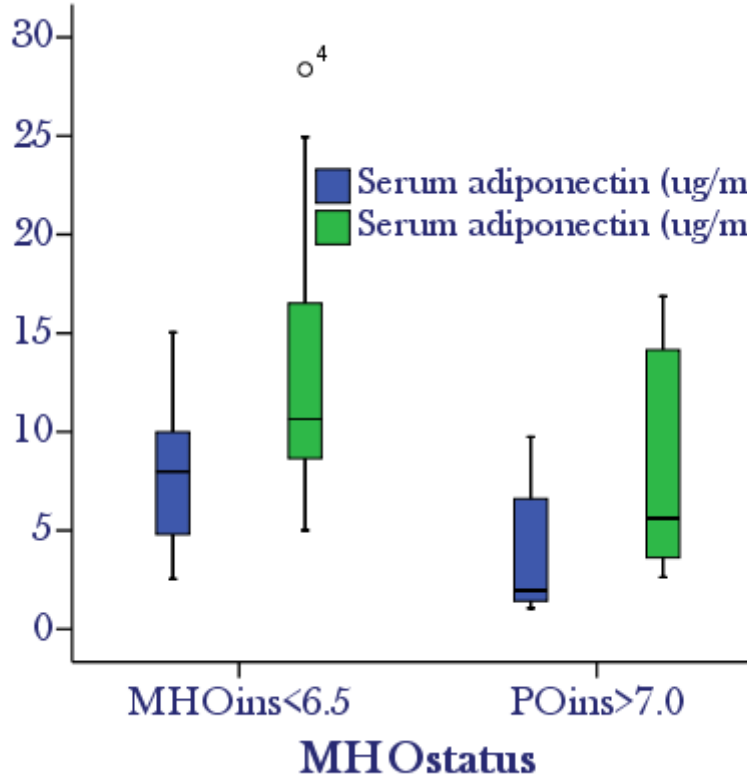


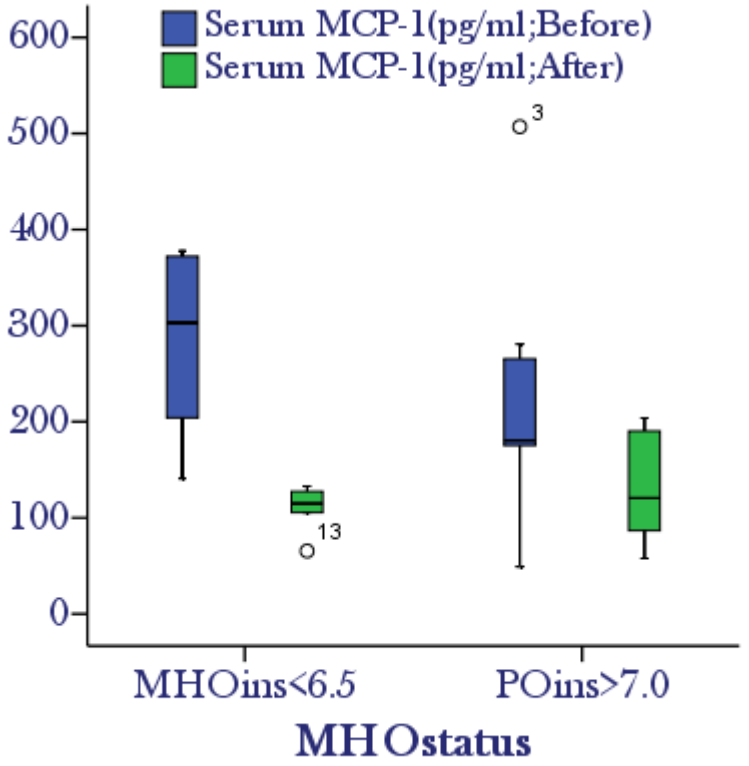
Systemic Insulin and insulin sensitivity





Adipokines/chemokines





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*

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