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Metabolic surgery: who and when? Is there a good answer?

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Abstract
Currently there is little doubt that the body mass index (BMI) is not an appropriate tool to grant access to metabolic surgery, especially in type 2 diabetics (T2D).
Several studies are pointing towards other parameters that should go along with BMI in the treatment decision tree in non morbidly obese diabetics.
Insulin resistance, fat distribution among others are considered good tools to predict favorable outcomes in medically non controlled diabetics if sent to surgery.
The bottom line in good T2D control is to decrease cardiovascular mortality. Using adequate tools to screen patients to the appropriate surgical treatment may favor patients that are not under control after lifestyle changes and best medical treatment, thus decreasing longterm cardiovascular mortality secondary to type 2 diabetes.

Introduction
Currently, there is little doubt that the body mass index (BMI) is not an appropriate tool to grant access to bariatric and or metabolic surgery, especially in type 2 diabetics (T2D). And it is of little argument that it is not even a good tool for choosing the best therapeutical option for a diabetic patient, medical or surgical. BMI alone does not reflect the degree or distribution of adiposity; it discriminates unfairly on the basis of gender, race, age, fitness, and body fat composition.
But, if BMI alone should not be the only tool for the adequate patient’s screening for their best treatment, what should we pursue as ancillary tools for the best therapy for diabetic patients?

How to identify candidates?
It is clear that T2D is a primary medical disease, but it is a very expensive one, as it consumes around 11% of the US healthcare budget. This devastating disease has a 10-year mortality of 51%, it is responsible for 68% of fatal cardiovascular events and stroke, it is a major cause of limb’s amputation and the main cause of blindness and new cases of renal failure. Finally, the overall risk of dying among people with diabetes is at least double the risk of their peers without diabetes. The continuing morbidity and mortality in persons with diabetes is a sign that the answer as to the best management for type 2 diabetes in terms of maxi-
mizing metabolic control is still elusive. Given this scenario, the option of bariatric/metabolic intervention needs to be considered in appropriately selected individuals.

A recent report by Lopez-Jimenez et al, from the Mayo Clinic, showed that regardless of BMI, visceral fat is the worst predictor for cardiovascular events and death, and it is clearly associated to the insulin resistance syndrome.3

There are 2 kinds of obese individuals, the malignant and the benign phenotype.4 Stefan et al., described at the same BMI there are some conditions that augment the metabolic risk. They defined that at any given amount of total body fat, metabolically benign obese was not accompanied by insulin resistance and early atherosclerosis. Ectopic fat in the liver rather than visceral fat may be more determinant for insulin resistance, thus defining metabolically malignant obesity.

What parameters should be used with BMI?

Wajchenberg in 20025 demonstrated visceral adipose tissue imaged by computed tomography (CT) or magnetic resonance imaging (MRI) is associated with the metabolic syndrome features, being morphologically and functionally different from subcutaneous adipose tissue (SAT). By pooling all data, correlation analysis indicated that VAT contributes more to insulin resistance (HOMAIR) than SAT does.

Stefan again, in 20116 highlighted the importance of non-alcoholic fat liver disease (NAFLD). It is the emerging observation that NAFLD without any liver-specific consequences is often already strongly associated with metabolic alterations, most importantly with insulin resistance, which plays an important role in the pathophysiology of dyslipidemia, type 2 diabetes, and cardiovascular disease. Fabbrini in 20107 stressed as well the importance of NAFLD and insulin resistance. Interesting was the correlation of the ectopic liver fat accumulation with HOMA IR, aspartate aminotransferase (AST) and alanine aminotransferase (ALT) and magnetic resonance. There was little correlation with ultrasound.

Stern in 20058 suggests how to identify patients with insulin resistance based on routine clinical measures. Insulin resistance was defined based on BMI, HOMA IR, family history and triglycerides. Insulin resistance patients were identified if BMI was over 28.7 or BMI > 27 with a positive family history or HOMA IR over 4.6 or BMI higher than 27 plus HOMA IR greater than 3.6. And if BMI followed the same criteria above, but family history was negative, insulin resistance (metabolic malignant profile) would be diagnosed if triglycerides levels were over 216 mg/dl. Those parameters are relatively easy and quick to achieve.

Besides ectopic liver and musculoskeletal fat distribution and the clinical parameters described above, some studies revealed interesting markers for metabolic syndrome severity and cardiovascular mortality.

Fasting insulin levels were predictors of the severity of metabolic syndrome.9

In a recent study about bariatric surgery and long-term cardiovascular events,7 baseline insulin level was the strongest predictor of cardiovascular events. Surprisingly in this study, BMI levels did not predict any cardiovascular events after 20 years follow up. And in the same BMI range, there was a direct relation between the carotid artery intima thickness and atherosclerosis. Seeking for other alternatives than BMI to spot the severity of metabolic syndrome, a mathematical model was developed based on the hip and height, the body adiposity index (BAI) = Hip/Height1.5 (fig. 1). BAI is strongly associated body fat mass regardless of BMI.

The BAI correlate with the percentage of body fat mass, body mass composition measured by Dual-energy X-ray absorptiometry (DXA), and predicts the severity of the metabolic syndrome components.

Other parameters

Fasting C peptide over 1 ng/dl and qualitative response after a mixed meal challenge may reflect the β cell function and should be tested before any therapeutic option is offered.10 Waist circumference11 and adiponectin levels (higher in insulin sensitive patients) are good tools to be eventually used in new perspectives in the treatment of T2D patients.

Conclusions and future directions

It is clear that BMI alone is not a good tool to screen candidates that can benefit from the good outcomes after metabolic/bariatric surgery.12 Visceral fat, mainly ectopic hepatic fat play a major role in the determination of metabolically malignant obesity. Baseline fasting insulin levels are the mostly important isolated factor that predicts cardiovascular events and mortality. Worldwide healthcare policy makers are urged to reevaluate the older BMI centered criteria.

Randomized controlled trials (RCTs) are important to determine the adequate role of gastrointestinal surgery and T2D control. Recently, 2 RCTs were published13,14 that showed the superiority of surgery when compared to medical treatment.

But we need to move forward. RCTs are needed to prove real “hard points” benefits of surgery over

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\begin{align*}
\text{BAI} & = \frac{\text{Hip}}{\text{Height}^{1.5}} - 18 \\
\text{BAI} & = \frac{\text{Hip}}{\text{Height} \times \text{Height}} - 18
\end{align*}
\]

Fig. 1.—BAI - body adiposity index.
medical treatment, such as micro vascular disease control. Other than this, RCTs should focus on the best timing for surgery (the sooner the better?), selecting the appropriate candidates and finding if there is any place for surgery as the first line of treatment for T2D. It is unquestionable that metabolic surgery has definitively its role for the treatment of diabetes and/or metabolic syndrome.

References


Table I: Summary of other tools that may help for the indication of metabolic surgery

- High fasting insulin level
- Thicker carotid artery intima media
- High HOMA IR
- Lipid profile (high triglycerides)  
- Positive family history
- 4 to 5x higher levels of AST/ALT
- High BAI (hip circumference)
- Large waist circumference

AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; BAI: Body adiposity index.