Obesity, Type 2 Diabetes, and the Metabolic Syndrome

Pathophysiologic Relationships and Guidelines for Surgical Intervention

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KEYWORDS

• Obesity • Metabolic syndrome • Diabetes • Bariatric metabolic surgery
• Insulin resistance • Gut • Microbiota

KEY POINTS

- Visceral obesity is associated with systemic low-grade inflammation leading to insulin resistance, β-cell dysfunction, and cardiometabolic diseases.
- The gastrointestinal tract is a key organ in metabolic regulation; hence, it is a biologically rational target for interventions aimed at treating metabolic syndrome, obesity, and type 2 diabetes (ie, metabolic surgery).
- Recent randomized clinical trials show that bariatric/metabolic surgery causes greater improvement of type 2 diabetes and reduction of cardiovascular risk compared with lifestyle modification and medical therapies.
- Based on such clinical and mechanistic evidence, several international professional organizations and government agencies have recently suggested expanding the indications for bariatric/metabolic surgery to include patients with inadequately controlled type 2 diabetes and a body mass index as low as 30 kg/m^2 and 27.5 kg/m^2 for Asians.

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INTRODUCTION

Obesity represents one of the primary causes of preventable deaths. In 2014, an estimated 1.9 billion adults were considered overweight and more than 600 million were obese, translating to 13% of the worldwide adult population.[1,2] Also, the prevalence of morbid obesity (defined by a body mass index [BMI] >40 kg/m^2) has almost doubled since 1980.[1] Such increase in the prevalence of obesity and morbid obesity has been related to a variety of factors including sedentary lifestyle, disproportionate caloric intake, stress, socioeconomic status, in addition to ethnicity and genetic susceptibility. Obese men and women are at significantly higher risk of developing type 2 diabetes mellitus (T2DM).[3,4] In fact, the prevalence of T2DM has increased in parallel with the augmented prevalence of obesity. Currently, T2DM affects about 285 million people worldwide, a number predicted to almost double by 2030.[5]

The term "metabolic syndrome" (MS) is generally used to indicate the cluster of central obesity, insulin resistance (IR), hypertension, and hyperlipidemia. Metabolic syndrome results in a greater risk of developing T2DM and cardiovascular disease, 2 of the principal causes of death worldwide.[6]

Bariatric surgery causes significant and sustained weight loss and can considerably reduce IR, with dramatic clinical improvement or remission of insulin-resistant states (ie, dyslipidemia, hypertension, hyperuricemia, sleep apnea). Experimental evidence from animals shows that the effects of bariatric surgery on insulin sensitivity and glucose homeostasis are not just the consequence of mechanical reduction of food intake or energy absorption but derive from a variety of physiologic mechanisms, including changes in gut hormones, biliary acids metabolism, nutrient sensing, and microbiota.[7]

This knowledge corroborates evidence of a critical role of the gut in glucose and energy homeostasis and supports consideration of the gastrointestinal (GI) tract as a rational biological target for interventions aimed at treating obesity, diabetes, and metabolic disorders.[8] Recent randomized clinical trials show that bariatric surgery results in better control of T2DM and greater reduction of cardiovascular risk factors compared with a variety of lifestyle interventions and medical therapies.[9–12] Based on such mounting mechanistic and clinical evidence, conventional bariatric procedures are now increasingly being proposed not only as mere surgical management of obesity but also as a valuable approach to intentionally treat T2DM—a new concept and practice referred to as "metabolic surgery."[13–15]

Obesity and the Adipose Tissue

Obesity has become a pandemic and has received increasing attention over the past decades for the implications it carries in the development of numerous chronic diseases. In the last 30 years, the average BMI has increased at a rate of 0.4 kg/m^2 per decade worldwide.[16] Among high-income countries, the United States has the highest prevalence of obesity, with one third of the population having a BMI of 30 or greater.[17] Even though the prevalence of obesity in the United States tended to stabilize after 2005, the prevalence of severe (BMI >35 kg/m^2) and morbid (BMI >40 kg/m^2) obesity has continued to increase. Between 1986 and 2000, the prevalence of subjects with a BMI of 40 or greater quadrupled and that of subjects with a BMI of 50 or greater quintupled.[17,18]

Obesity is a condition characterized by an excess of body adiposity and for practical reasons is commonly measured by BMI, an expression of body weight as a nonlinear function of height. A BMI $\geq$30 kg/m^2 indicates the presence of obesity; when BMI exceeds 40 kg/m^2, the subject is regarded as morbidly obese.[19]