EDITORIAL (SEE HERRERA ET AL., P. 1413)

Is Visceral Fat Responsible for the Metabolic Abnormalities Associated With Obesity?

Implications of omentectomy

The results from both epidemiological and physiological studies have demonstrated a strong association between excess abdominal adipose tissue and the presence of metabolic risk factors for coronary heart disease (CHD), including insulin resistance, impaired glucose tolerance, type 2 diabetes, dyslipidemia, and increased circulating inflammatory proteins (1–3). Abdominal adipose tissue is a complex organ and is composed of multiple distinct compartments and subcompartments, including subcutaneous fat and intra-abdominal fat, which can be further subdivided into retroperitoneal and intraperitoneal fat, which can be divided again into mesenteric and omental fat masses. Intraperitoneal fat, which is also known as visceral adipose tissue (VAT), is considered a particularly important marker of metabolic risk (4–6).

It has been hypothesized that increased VAT is directly involved in the pathogenesis of metabolic dysfunction because VAT releases free fatty acids (FFAs) and inflammatory proteins into the portal vein, which are delivered to the liver (7). However, most FFAs in the portal circulation are derived from subcutaneous adipose tissue, and <20% of total FFAs delivered to the liver or skeletal muscle originate from lipolysis of VAT in obese people (8,9). Moreover, most inflammatory adipokines in the portal vein are likely derived from subcutaneous fat, which releases adipokines into the systemic circulation that enter the portal vein through the splanchnic bed (10). In addition, increased VAT itself is not associated with insulin resistance or dyslipidemia without a concomitant increase in intrahepatic triglycerides (11). Therefore, these data do not support an obvious causal link between intraperitoneal fat and metabolic disease.

Surgical removal of the greater omentum makes it possible to evaluate the importance of VAT in the pathophysiology of obesity in people. In fact, the results from two randomized controlled studies (12,13) have already been reported that evaluated the effect of surgical removal of the greater omentum on insulin action in obese patients undergoing bariatric surgery. Unfortunately, the data and conclusions from these studies are contradictory. In one study (12), subjects randomized to adjustable gastric banding plus omentectomy had a greater improvement in oral glucose tolerance and insulin sensitivity, assessed by using an intravenous insulin tolerance test, than subjects randomized to adjustable gastric banding alone. However, the omentectomy group also experienced more weight loss than the banding-alone group, which could have contributed to the observed differences in insulin action. In the second study (13), the prevalence of hyperglycemia and hyperinsulinemia 2 years after surgery were not different in subjects randomized to roux-en Y gastric bypass (RYGB) surgery plus omentectomy or RYGB alone, but insulin sensitivity was not directly assessed.

In this issue of *Diabetes Care*, Herrera et al. (14) report the results of a 1-year randomized controlled trial that evaluated whether omentectomy provided additional therapeutic effects on selected metabolic variables and circulating inflammatory proteins and adipokines in obese patients who undergo RYGB surgery (15). Twenty-two subjects were randomized to have RYGB surgery or RYGB surgery plus omentectomy. The rate of weight loss was the same in both groups throughout the study and reached a maximum of ~30% weight loss at 1 year. The amount of VAT removed (~0.8 kg), which presumably represents at least 25% of total VAT, is greater than diet-induced reductions in VAT that is associated with a 25–50% increase in skeletal muscle and liver insulin sensitivity (15–17). In their subjects, surgery-induced weight loss resulted in considerable improvement in most metabolic and inflammatory outcomes (plasma glucose, insulin, adiponectin, and C-reactive protein concentrations; lipid profile; blood pressure; impaired glucose tolerance; and diabetes) but had mixed results in plasma concentrations of several other adipokines. However, there was no significant difference in any outcome measure between groups. In addition, performing an omentectomy was not trivial and had adverse effects; omentectomy increased the duration of surgery by >1 h and caused a serious complication in one subject.

The results from the study by Herrera et al. have important implications regarding the role of VAT in the pathophysiology of obesity and suggest that increased VAT does not directly cause metabolic dysfunction. However, limitations in study design leave two important questions unanswered. First, is it possible that the overwhelming effect of weight loss induced by RYGB surgery masked the potential therapeutic effects of removing VAT? Second, were the outcome measures sensitive enough to detect metabolic improvements, particularly in insulin sensitivity, which is probably the most common metabolic abnormality associated with increased VAT? Additional studies are still needed that use more sensitive methods to assess insulin action and that evaluate the effect of omentectomy alone without concomitant weight loss surgery.

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