



COMMENT ON SJÖHOLM ET AL.

Weight Change–Adjusted Effects of Gastric Bypass Surgery on Glucose Metabolism: 2- and 10-Year Results From the Swedish Obese Subjects (SOS) Study. *Diabetes Care* 2016;39:625–631

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We read with interest the article by Sjöholm et al. (1) in *Diabetes Care* on the effect of Roux-en-Y gastric bypass (RYGB) on glucose metabolism 2 and 10 years following surgery. The authors used data from the Swedish Obese Subjects (SOS) study and compared fasting glucose, insulin, and HOMA of insulin resistance (HOMA-IR) in patients who underwent gastric banding (GB), RYGB, or vertical banded gastroplasty (VBG). To evaluate for procedure-specific effects of RYGB, they compared groups on the basis of percent total body weight loss and concluded that weight loss is more important than procedure type for long-term improvements in glucose metabolism. The authors hypothesized that short-term and long-term improvements in glucose metabolism are different. We fully agree with this concept. In our studies (2), early improvements in glucose metabolism after RYGB occurred before any change in peripheral tissue insulin resistance. Although the study by Sjöholm et al. is based on this observation and attempts to address a fundamental question in metabolic surgery, several limitations challenge the conclusions therein.

The use of fasting samples to assess glucose metabolism is a primary flaw of the study. Although the calculation of HOMA-IR is readily and commonly performed, it represents a simplistic assessment of actual glucose metabolism; its correlation with clamp-based glucose

disposal can be significantly impacted by sex and race (3). Furthermore, multiple studies have suggested that HOMA-IR can be inaccurate in assessing insulin resistance, with a 14% false-negative rate compared with intravenous glucose tolerance testing (4). It is important that the validity of HOMA-IR in post-bariatric surgery patients has not been established. Although HOMA-IR can certainly be used in clinical studies with a secondary interest in glucose metabolism, its inaccuracies compared with minimal model or clamp-derived indices challenge the conclusions of the study (5). In the data presented by Sjöholm et al. (1), insulin levels and HOMA-IR in normoglycemic patients were significantly different based on procedure type. In contrast, in patients with impaired glucose metabolism, weight-adjusted coefficients for HOMA-IR were smaller for RYGB patients, although this was not statistically significant. It seems counterintuitive that RYGB would improve insulin resistance in a weight-independent manner in normoglycemic patients but not in patients with impaired glucose metabolism.

There is also a valid concern about statistical power in the study by Sjöholm et al. The results were based on the 10-year follow-up of 60 GB and 61 RYGB patients with impaired glucose metabolism (impaired fasting glucose or type 2 diabetes). In addition to the variations between individuals, the weight-loss

grouping further diluted the sample size. This limited the evaluation for linear association between weight loss and insulin resistance per procedure type. Finally, although the SOS study is of unique value for research on bariatric surgery, it has serious inherent limitations: 1) the inclusion of patients who mostly underwent VBG, a procedure abandoned due to poor long-term results; 2) the 40% of patients lost to follow-up at 10 years; 3) the 17% procedural conversion rate during follow-up; and 4) the limited number of biologic specimens. This lack of data restricts the ability to address mechanistic questions in terms of diabetes resolution and control.

In addition, the conclusion of the study by Sjöholm et al. is in contrast to recent report from Mingrone et al. (6), which found no difference in percent total body weight loss between patients who developed diabetes remission at 5 years following RYGB or biliopancreatic diversion compared with the ones who did not.

Despite these limitations, the study documents again that weight loss is a key factor in the success of metabolic surgery. The benefit of weight loss in improvement of glucose metabolism is indisputable and clearly demonstrated by the results of the study. This is in accordance with the results of the Diabetes Prevention Program (DPP) and adds to the current recommendations for weight loss in patients with type 2 diabetes (7). The study by Sjöholm et al.

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adds valuable information in that regard and delineates an area in metabolic surgery where further mechanistic research is needed.

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