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Peer Review of *World Journal of Diabetes*, Da-Feng Liu, MD, Doctor, Professor, The First Ward of Internal Medicine, Public Health Clinical Centre of Chengdu, Chengdu 610061, Sichuan Province, China. ldf312@126.com

AIMS AND SCOPE

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EDITORIAL

Effect of bariatric surgery on metabolism in diabetes and obesity comorbidity: Insight from recent research

Hui-Hong Tang, Dong Wang, Cheng-Chun Tang

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Abstract

Obesity is a prevalent cause of diabetes mellitus (DM) and is a serious danger to human health. Type 2 DM (T2DM) mostly occurs along with obesity. Foodborne obesity-induced DM is caused by an excessive long-term diet and surplus energy. Bariatric surgery can improve the symptoms of T2DM in some obese patients. But different types of bariatric surgery may have different effects. There are some models built by researchers to discuss the surgical procedures' effects on metabolism in diabetes animal models and diabetes patients. It is high time to conclude all this effects and recommend procedures that can better improve metabolism.

Key Words: Bariatric surgery; Obesity; Diabetes; Animal models; Diabetes patients

Core Tip: Bariatric surgery is a type of treatment that can improve the metabolic status and prognosis of patients with obesity and diabetes comorbidities. Bariatric surgery could alleviate obesity and has a positive effect on metabolism in diabetes animal models and diabetes patients, suggesting that the recommended frequency of bariatric surgery for diabetic and obese comorbid patients should be increased.

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INTRODUCTION

Obesity and type 2 diabetes mellitus (T2DM) typically co-occur. The pathophysiology of obesity is primarily caused by insulin resistance, hyperinsulinemia, hormonal dysregulation, and systemic inflammation[1]. Bariatric procedures are an option for those who want to help themselves reduce weight. Sleeve gastrectomy (SG), gastric banding, and Roux-en-Y gastric bypass (RYGB) are common bariatric operations performed in clinical practice. Studies have been conducted on how bariatric surgery affects diabetes metabolism. Recently, a journal article published in this journal titled, "Impact of bariatric surgery on glucose and lipid metabolism and liver and kidney function in food-induced obese diabetic rats," conducted basic research on this topic.

Studies on the effect of bariatric surgery on metabolism in diabetes

Several clinical trials have repeatedly demonstrated the critical role that surgery plays in improving glucose homeostasis and initiating remission. Many large cohort studies comparing the two approaches to obesity management indicate that patients undergoing bariatric surgery have a higher chance of achieving remission of diabetes than those who only receive standard obesity treatment[2-6]. Patients with diabetes may undergo a brief course of therapy after bariatric surgery. The factors most frequently associated with remission are younger age, a higher C-peptide level, diabetes for less than 4 years before the surgery, and relying only on diet or oral medication to treat the illness[7-10]. In a joint statement, the American Diabetes Association, Diabetes United Kingdom, the Chinese Diabetes Society, Diabetes India, and the International Diabetes Federation urged patients with class I obesity (body mass index: 30.0-34.9 kg/m^2) and poorly controlled hyperglycemia despite receiving the best possible medical care, including insulin, to consider bariatric surgery [11]. A very small proportion of patients may continue to experience a protracted remission. Research assessing long-term results has shown that individuals who achieve diabetic remission have a recurrence incidence of more than 50%[6,12, 13]. From the above studies, it can be seen that bariatric surgery markedly improves blood sugar control in patients with diabetes, although the improvement is not significant for long-term diabetes management.

Similar to employing calorie restriction to achieve weight loss, bariatric surgery results in an improvement in insulin sensitivity, which is a crucial component of the pathogenesis of diabetes[14-16]. One feature that appears before weight loss after bariatric surgery is the rapid improvement in glucose management. Many patients are discharged insulin-free, even though they had needed hundreds of units of insulin before surgery[17]. The above studies have shown that bariatric surgery can improve the patient's insulin sensitivity, thereby allowing the patient to use a reduced amount of insulin after surgery.

Changes in the repertoire of systemic bile acids and elevated glucagon-like peptide 1, a circulating incretin hormone, have been reported following the surgery[18]. Bariatric surgery preserves β cell function and coordinates islet activity, which partially improves glycemic control. Changes in circulating glucagon-like peptide 1 levels can indirectly affect β cells through changes in body weight, or they can act directly[19]. Bile acids are metabolites generated from cholesterol that act as detergents to facilitate the absorption of vitamins and lipids and act as ligands for host receptors[20]. The etiology of T2DM is linked to chronic inflammation associated with obesity[21]. Furthermore, pancreatic fatty acid production following RYGB surgery is essential for β cell function during calorie restriction[22]. The changes in lipid metabolism and the reduction of inflammation caused by bariatric surgery also have an important impact on remission in patients with diabetes.

Bariatric surgery reverses endothelial dysfunction by improving nitric oxide availability and inhibiting vascular oxidative stress; it also serves as an effective anti-inflammatory strategy by mitigating interferon-γ-mediated adipose tissue inflammation[23]. Changes in the jejunal Roux limb mRNA and lncRNA expression patterns initiate neuromodulation and endocrine-related pathways *via* the gut-brain axis that is essential for remission of T2DM following metabolic and bariatric surgery[24]. In addition, a blood signature of diabetes reversal in mice highlights new miRNA–gene interactions in the pancreatic islets during the resolution of diabetes following bariatric surgery[25,26]. Therefore, it can be seen that oxidative stress, neuromodulation, and endocrine regulation also affect remission in patients with diabetes after bariatric surgery.

Vertical SG surgery in the UC Davis T2DM rat model postponed the onset of diabetes, which is partially independent of a decrease in body weight[27]. Experimental metabolic surgery significantly lowers albuminuria in a rat model of diabetic kidney disease[28,29]. Reductions in podocyte stress, glomerulomegaly, and glomerulosclerosis post-RYGB in Zucker diabetic fatty rats indicate improved glomerular histology. Quantifiable decreases in podocyte foot process effacement indicate an improvement in glomerular ultrastructure post-RYGB and post-SG. Interestingly, a more noticeable decrease in proteinuria is observed when RYGB is used instead of SG. In addition, research on humans suggests that RYGB may better regulate metabolism than SG[30]. RNA sequencing has been used to characterize the transcriptional program underlying these structural changes at the pathway level. This program has been linked to a considerable decrease in the activation of fibrotic and inflammatory responses. In Zucker diabetic fatty rats, weight loss and improvements in glycemia after RYGB surgery are accompanied by normalization of glomerular tuft size, decreases in desmin expression by podocytes, and preservation of the morphology of the podocyte foot process compared to sham-operated control animals[31]. It can be seen that bariatric surgery also improves the renal function in the diabetic obese rat model, which can improve the glomerular structure.

Highlights of the chosen article

This study was selected to provide commentary because it has noteworthy findings with clinical implications. Diabetes mellitus (DM) typically develops in response to obesity and poses a major threat to human health. T2DM often coexists with obesity. Excessive long-term eating and excess energy are the causes of foodborne obesity-induced DM. Some obese people may find that their T2DM symptoms are alleviated after bariatric surgery; however, the outcomes of various bariatric procedures vary. In this study, the effects of various bariatric surgeries on the prognosis of patients with diabetes and obesity were explored.

This study showed that bariatric surgery affects liver and kidney function, as well as glucose and lipid metabolism, by modulating the PKCβ/P66shc pathway in food-derived obese diabetic rats. The PKCβ/P66shc pathway plays a role in intracellular crosstalk and signal transduction[32] and has received considerable attention because of the connection between excess nutrient intake and obesity[33]. Bariatric surgery to alleviate obesity affects metabolism and may provide a new way of solving diabetes and obesity comorbidities and offer a novel treatment for foodborne obesity-induced diabetes. The PKCβ/P66shc pathway explored herein is an extensively studied oxidative stress pathway, suggesting that alleviating oxidative stress may be a possible way to ameliorate diabetes and obesity comorbidities.

This study also analyzed the pros and cons of various bariatric surgeries, which is essential in clinical use when surgeons are choosing surgical modalities. RYGB tends to result in a tiny wound with low risk, favorable prognosis, lower recurrence rate by reducing islet cell apoptosis, an increase in insulin secretion, and restoration of islet function. However, RYGB might lead to excessive blood sugar, anastomosis inflammation locally, and stomach discomfort in mice. Also, it might result in intestinal adhesion, infection, poor closure of the surgical incision, gastric paresis, gastrointestinal dysfunction, abdominal distension, and incapacity to eat. SG can effectively control T2DM, obesity, and the risk of obesity-related cardiovascular and cerebrovascular complications by reducing the volume of the stomach, reducing weight, and improving T2DM. However, SG completely removes the fundus of the stomach and may increase the risk of developing gastroesophageal reflux disease. Gastric banding also reduces weight by reducing food intake. The surgical damage is minimal, and the postoperative recovery is fast. However, the surgical effect is suboptimal, resulting in limited weight loss. The above results suggest that in clinical settings, the selection of the type of bariatric surgery according to the patient's individual situation will result in different postoperative complications and personal perceptions, and may also improve patient surgical satisfaction.

CONCLUSION

Diabetes and obesity are increasingly threatening human health. The traditional five-step approach to diabetes, comprising patient education, dietary control, medication, exercise therapy, and self-monitoring management, is not universally effective due to physiological, behavioral, and economic barriers. Bariatric surgery is increasingly recognized as an effective treatment for patients with T2DM and obesity. While surgery does not solve the underlying problem of oversupply of energy and does not cure the disease, it significantly reduces the burden on patients. Elucidating the mechanisms of metabolic function in patients will improve healthcare professionals' understanding of the disease. Bariatric surgery represents both an enlightening scientific model and an effective treatment to address the diabetes crisis. In conclusion, bariatric surgery alleviates obesity and has a positive effect on metabolism in diabetes animal models and patients with diabetes, suggesting that the recommended frequency of bariatric surgery for patients with diabetes and obesity should be increased.

FOOTNOTES

Co-corresponding authors: Dong Wang and Cheng-Chun Tang.

Author contributions: Tang HH, Wang D, and Tang CC conceived, designed, and refined the study; Tang HH drafted the manuscript; Wang D and Tang CC contributed equally to this work as co-corresponding authors. The reasons for designating Wang D and Tang CC as co-corresponding authors are as follows. First, they both participated in choosing the idea of the study. Second, they both revised the manuscript. Third, they both are responsible for the study. In summary, we believe that designating Wang D and Tang CC as co-corresponding authors of is fitting for our manuscript as it accurately reflects our team's collaborative spirit, equal contributions, and diversity.

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