KRZEMIŃSKA, Katarzyna, KUBAS, Maria, KUSZNERUK, Julia, KŁUSEK, Magdalena and CZERWIK, Julia. Benefits of bariatric surgery on glycemic control in patients with type 2 diabetes mellitus. A narrative review. Quality in Sport. 2024;20:53990. eISSN 2450-3118.
https://dx.doi.org/10.12775/QS.2024.20.53990
https://apcz.umk.pl/QS/article/view/53990

The journal has been 20 points in the Ministry of Higher Education and Science of Poland parametric evaluation. Annex to the announcement of the Minister of Higher Education and Science of 05.01.2024. No. 32553.
Has a Journal's Unique Identifier: 201398. Scientific disciplines assigned: Economics and finance (Field of social sciences); Management and Quality Sciences (Field of social sciences).
Punkty Ministerialne z 2019 - aktualny rok 20 punktów. Załącznik do komunikatu Ministra Szkolnictwa Wyższego i Nauki z dnia 05.01.2024 r. Lp. 32553. Posiada Unikatowy Identyfikator Czasopisma: 201398.
Przypisane dyscypliny naukowe: Ekonomia i finanse (Dziedzina nauk społecznych); Nauki o zarządzaniu i jakości (Dziedzina nauk społecznych).

The authors declare that there is no conflict of interests regarding the publication of this paper.
Received: 01.08.2024. Revised: 21.08.2024. Accepted: 22.08.2024. Published: 23.08.2024.

Benefits of bariatric surgery on glycemic control in patients with type 2 diabetes mellitus. A narrative review

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Abstract

Introduction and purposes:

Obesity is a critical global health challenge, closely linked to a range of serious conditions, including metabolic syndrome, insulin resistance, and an increased likelihood of developing type 2 diabetes. Affecting over two billion people worldwide, obesity necessitates a multifaceted approach to treatment, encompassing lifestyle changes, pharmaceutical interventions, and surgical procedures. Among the surgical options, bariatric surgeries such as sleeve gastrectomy (SG) and Roux-en-Y gastric bypass (RYGB) are particularly prominent.

Materials and Methods: A systematic literature search was conducted using PubMed and Google Scholar. The search employed terms such as 'glycemia', 'bariatric surgery', ‘metabolic surgery’ 'RYGB', 'diabetes type 2’, ‘Postprandial hyperinsulinemic hypoglycemia’ 'hypoglycemia' ‘dumping syndrome’. Articles published between 2019 and 2024 were included in the search.

Results:

Bariatric surgery is well-documented for its significant impact on glycemic control and overall physical health, resulting in substantial reductions in both HbA1c levels and BMI. Remarkably, many patients with type 2 diabetes achieve remission of the disease following surgery, regardless of their pre-surgery BMI. However, the enhanced glycemic control achieved through bariatric procedures can also lead to an increased risk of developing postprandial hyperinsulinemic hypoglycemia (PHH). This condition arises as a complication from the surgery, where blood sugar levels drop excessively after meals due to an overproduction of insulin.

Conclusion:

Despite this potential risk, the overall benefits of bariatric surgery in managing and potentially reversing type 2 diabetes are profound.

Keywords:

Bariatric surgery, glycemia, diabetes mellitus type 2, obesity, hypoglycemia, Roux-en-Y gastric bypass, sleeve gastrectomy, body mass index

Introduction

Elevated body mass index (BMI) is a critical concern for population health. The World Health Organization characterizes obesity as an "abnormal or excessive accumulation of fat that poses a risk to health”. [1] Recent statistics indicate that over 2 billion individuals are affected by excess weight, accounting for around 30% of the global population. As obesity rates rise there is a corresponding increase in the prevalence of metabolic syndrome. Existing theories suggest that insulin resistance plays a key role in causing metabolic syndrome, [2] which is diagnosed when an individual meets at least three out of the following five criteria: abdominal obesity, type II diabetes mellitus (T2DM), hypertension, hyperlipidemia, and low levels of high-density lipoprotein (HDL). [3]

Methods:

A systematic literature review was conducted by searching through databases such as PubMed and Google Scholar. The search included specific terms to ensure a thorough examination of the available research: 'glycemia' 'bariatric surgery,' 'RYGB,' 'diabetes type 2’, ‘hypoglycemia’, ‘metabolic surgery’, 'RYGB', 'diabetes type 2’, ‘Postprandial hyperinsulinemic hypoglycemia’, ‘dumping syndrome’, ‘Sleeve gastrectomy’, ‘Roux-en-Y gastric bypass’, and ‘BMI’. The search included articles published between 2019 and 2024, as well as frequently cited publications from over a decade ago. The inclusion criteria were as follows: papers, case series, meta-analyses, and reports that concentrated on the epidemiology and research concerning type 2 diabetes and bariatric surgery, with a major focus on the impact of surgery on patients' glycemia. Only English-language publications were considered.

Treatment for Obesity

The treatment of obesity should be tailored to the individual patient, taking into account their specific needs, age, gender, condition, and metabolic risk factors, while also considering any concomitant diseases. The management of obesity typically involves three stages: 1. non-pharmacological treatment (diet, exercise, lifestyle changes), 2. pharmacological treatment, and 3. surgical treatment. [4]

While lifestyle interventions and medical therapies can be highly beneficial for many patients, achieving and maintaining significant weight loss can still be a challenge for those struggling with obesity. [5] A considerable number of patients demonstrate a lack of understanding of the fundamental principles of physical exercise, which negatively impacts their condition. However, those who recognized the role of body weight in diabetes progression were more likely to engage in physical activity. Some patients explore different dietary approaches, with intermittent fasting becoming popular. The effects of intermittent fasting on glucose homeostasis appear mixed, and there is some evidence that it could be an option for those with T2DM. Some studies indicate that there may be no significant impact, while others suggest that improvements may be observed in glucose tolerance, insulin levels, and blood glucose, particularly in obese diabetics. [6]

Sustained weight loss is a fundamental aspect of diabetes management, as other approaches, including preventive therapy, lifestyle and diet control, and pharmacological treatments, often prove ineffective in maintaining an optimal weight.

Bariatric surgery has been demonstrated to be an effective means of promoting long-term weight loss, by reducing food intake and addressing the physiological factors that cause weight gain. This approach has been demonstrated to be effective in several trials, with significant and sustained weight loss and a reduction in obesity-related comorbidities being observed. [7] With the increasing prevalence of obesity, particularly in low- and middle-income countries, certain experts view bariatric surgery as a potential solution to address the looming obesity epidemic. [8] Obesity makes clinical and logistical challenges for hospitals. There is a rising need for specialized bariatric beds that support patients up to 454 kg, and larger imaging devices. However, the high cost of this equipment often exceeds the budget of smaller and rural hospitals. [9]

It is estimated that overweight and obesity may contribute to over 40% of the burden of Type 2 diabetes mellitus (T2DM), though further research is needed to confirm this. T2DM is a long-term metabolic condition that can lead to several complications. It is becoming increasingly clear that high glucose levels can have a detrimental impact on glucose homeostasis, with the potential to cause significant damage to vital organs such as the heart, kidneys, blood vessels and eyes. [10] It is worth noting that it stands as one of the significant comorbidities of obesity. A comprehensive model indicated that a body mass index (BMI) above 30 kg/m² may be a major risk factor for Type 2 diabetes mellitus (T2DM). [11]

Bariatric surgery methods

The basic indications for the Metabolic and bariatric surgery (MBS) are:

a) is recommended for individuals with a body mass index (BMI) >35 kg/m2, regardless of the presence, absence, or severity of co-morbidities.
b) MBS should be considered for individuals with metabolic disease and BMI of 30-34.9 kg/m2.
c) BMI thresholds should be adjusted in the Asian population such that a BMI >25 kg/m2 suggests clinical obesity, and individuals with BMI >27.5 kg/m2 should be offered MBS

2022 American Society of Metabolic and Bariatric Surgery (ASMBS) and International Federation for the Surgery of Obesity and Metabolic Disorders (IFSO) Indications for Metabolic and Bariatric Surgery. [12]

In the study of trends in bariatric surgery and its popularity among the United States, results show that surgery rates rose from 43.5 per 100,000 in 2006 to 70.6 per 100,000 in 2009, then plateaued from 2010 to 2015. Sleeve gastrectomy increased significantly from 11% (n = 596) in 2006 to 70% (n = 15,425) in 2015 (P < .001), while Roux-en-Y decreased from 45% (n = 10,129) in 2010 to 24% (n = 5074) in 2015 (P < .001). [13] It is observed that the predominant bariatric procedures performed in current surgical practice are sleeve gastrectomy (SG) and Roux-en-Y gastric bypass (RYGB).

Sleeve gastrectomy (SG) is a common restrictive bariatric surgery for treating obesity, usually performed laparoscopically. This method has the advantage of shortening the length of time spent in the hospital and speeding up the recovery process. The surgery involves removing the fundus and approximately 80% of the corpus of the stomach, leaving a small, sleeve-shaped gastric pouch of 100-150ml with an intact pylorus to regulate emptying. This has the effect of reducing food intake and decreasing hunger by lowering ghrelin secretion. [14]

This means that nutrients are emptied directly into the jejunum, bypassing 95% of the stomach, the duodenum, and the proximal jejunum. [15] It should be noted that sleeve gastrectomy is irreversible.

The Roux-en-Y gastric bypass (RYGB) procedure involves the creation of a 25ml gastric pouch, which is separated from the excluded stomach. The pouch is then connected to the jejunum, thereby circumventing the majority of the stomach. The procedure is concluded with a jejunojejunostomy. [16] It is widely accepted that RYGB is the gold standard bariatric procedure, however, there has been a notable increase in the utilization of SG. SG is now the most widely performed bariatric surgery worldwide it could be argued that this approach has the advantage of being an easier procedure with a shorter operative time than RYGB. [17]

There has been a growing interest in the One Anastomosis Gastric Bypass (OAGB) procedure in recent times. While the use of adjustable gastric bands has seen a decline over time, they still represent a significant proportion of bariatric procedures performed globally, accounting for approximately 5% of all cases. [18] It would appear that RYGB and SG have generally comparable efficacy for weight loss, which may be related to similar physiological responses, including rapid nutrient entry into the intestine, increased postprandial secretion of gut peptides, and increased plasma levels of bile acids. However, emerging evidence suggests that the sleeve procedure is associated with fewer reoperations and the bypass procedure may lead to more sustained weight loss and glycaemic control. Although safety is a concern, current data indicate that perioperative mortality ranges from 0.03% to 0.2%, which has improved significantly since the early 2000s. [19] A pooled analysis revealed an overall mortality rate of 0.08% (95% CI: 0.06-0.10; prediction interval: 0-0.21%). No significant differences were identified in 30-day, 90-day, or in-hospital mortality rates ($P = 0.29$), nor across study types ($P = 0.60$). The mortality rates by the procedure were 0.03% for gastric banding, 0.05% for sleeve gastrectomy, 0.09% for one-anastomosis gastric bypass, 0.09% for Roux-en-Y gastric bypass, and 0.41% for a duodenal switch ($P < 0.001$). In conclusion, bariatric surgery has low perioperative mortality rates and is considered safe. [20]

Post-bariatric surgery

Bariatric surgery has been demonstrated to enhance physical functioning and mobility by reducing disability, joint pain, and the prevalence of arthritis. Additionally, it has been shown to improve musculoskeletal function, walking capacity, exercise efficiency, and endurance. Furthermore, fat loss following bariatric surgery has been observed to increase peak oxygen uptake (VO2peak) relative to body weight, which can confer benefits to weight-bearing activities. [21] The 6-minute walk test provides evidence that weight loss resulting from bariatric surgery enhances an individual's capacity to walk. The 6-minute walk test represents a straightforward, secure, and efficacious methodology for the evaluation of the functional status of obese patients undergoing bariatric surgery. [22]

Post bariatric surgery glycemia

Kleopatra Alexiadou conducted a prospective study to understand batter how proglucagon-derived peptides (glucagon, GLP-1, oxyntomodulin, and glicentin) are secreted following RYGB surgery. It was observed that, after RYGB surgery, fasting glucose levels and glucose tolerance showed a notable improvement in a relatively short time. It would appear that the insulin response to meals increased, along with higher levels of GLP-1, oxyntomodulin, and glicentin. There was a significant drop in fasting glucagon levels at 3 and 12 months after surgery, although the glucagon response to meals and GIP secretion did not change significantly. It seems that changes in proglucagon peptide secretion after RYGB, especially the decrease in fasting glucagon, may potentially contribute to improved blood sugar control. [23] Sandoval Darleen noted that there has been a major increase in the incretin hormone GLP-1 following bariatric surgery, with levels rising more than tenfold. It seems plausible to suggest that the entire range of intestinal peptides rises after a meal, potentially as a result of rapid nutrient entry into the gut and/or changes in intestinal structure or cell differentiation. [15] Petros Katsogiannos conducted a study in which the patients assigned to the surgical intervention (RYGB group) underwent assessments post laparoscopic RYGB. In the surgery group, there was a slight decrease in fasting GLP-1 levels at four weeks, which was not statistically significant, but at 24 weeks, there was a notable decline in these levels, which reached a statistically considerable reduction ($p < 0.01$) compared to the baseline. It is worth noting, that the GLP-1 response during oral glucose tolerance test (OGTT) was higher at both four and 24 weeks post-surgery. It would appear that the control group did not exhibit any notable changes in fasting GLP-1 levels or during the OGTT between visits. In contrast, among the group that underwent surgery, it was observed that there were enhanced incretin and glucagon responses to glucose. This finding could indicate that neurohormonal mechanisms may potentially contribute to the improvement of insulin resistance and glycemia following RYGB in type 2 diabetes. [24] In his study, Salvador Navarrete Aulestia performed OAGB on sixteen patients with BMI < 35 kg/m2 with an average age of 42.9 years who had metabolic syndrome, including conditions like T2DM, insulin resistance, high blood pressure, or dyslipidemia. The study included patients with at least 12 months of follow-up. Patients with a BMI of 30 to 34.9 kg/m² (mean weight 87.7 kg, BMI 32.2 kg/m²) showed significant weight loss and improved metabolic parameters after surgery weight 66.8 kg, BMI 25.4 kg/m² (21.7-26.6). Preoperative values were fasting blood glucose 193.6 mg/dl and HbA1c 8.4%; while postoperative values improved to fasting blood glucose 78.8 mg/dl, and HbA1c 6.1%, and there was 100% remission of T2D comorbidities. [25] On the other hand, Kermansaravi in a study of 197 patients with a BMI ≥ 50 kg/m² who underwent OAGB showed a mean age of 38 years and a pre-operative BMI of 53.7 kg/m². The mean excess weight loss (EWL%) EWL% was 63.7%, 67.8%, and 66.2% at one, two, and five years post-OAGB, respectively, with the highest EWL% of 68.4% achieved at 18 months. Kermansaravi demonstrated that OAGB can be safely performed as a one-stage procedure in these patients, yielding significant weight loss and remission of obesity-related medical issues. The shorter operative time is an added benefit for high-risk obese patients. [26]

A retrospective study conducted at King Abdulaziz Medical City in Riyadh examined 318 patients with obesity (BMI ≥ 30 kg/m²) who underwent laparoscopic sleeve gastrectomy or Roux-en-Y gastric bypass between 1 January 2001 and 31 March 2017. Data were collected both before to surgery and at the 12-month postoperative follow-up. The patients were classified into three categories according to the extent of their BMI reduction. The categories were defined as: 0-9, 10-14, and >14 kg/m². The results show mean postoperative HbA1c was 5.83 ± 0.9, a reduction from the preoperative mean of 6.74 ± 2.1 (P = 0.001). A comparison of preoperative and postoperative HbA1c levels revealed that, while preoperative levels were significantly higher in diabetic patients than in non-diabetics, postoperative differences were insignificant. Those with diabetes who exhibited minimal BMI reduction (0-9 kg/m²) demonstrated significantly elevated HbA1c levels compared to non-diabetics. Conversely, those with larger BMI reductions (10-14 and >14 kg/m²) exhibited no significant differences. In conclusion, the findings of this study indicate that a major reduction of HbA1c was observed in diabetic patients following surgery. A greater reduction in body mass index was associated with a larger decrease in hemoglobin A1c. [27] Mohammed Khaled S Zaki in his study sought to evaluate the impact of laparoscopic sleeve gastrectomy (LSG) on glycemic control in obese patients in Al-Madinah Al-Munawwarah, Saudi Arabia. To this end, the reduction in HbA1c levels associated with weight loss was assessed. In this cross-sectional study, the researchers analysed a total of 102 patients (with a body mass index (BMI) of ≥30 kg/m² and aged ≥18 years) who underwent laparoscopic sleeve gastrectomy (LSG) between January 2017 and December 2019. Data on age, body mass index (BMI), and glycated hemoglobin (HbA1c) were collected at two time points: before and after the surgical procedure. The results demonstrated that post-LSG, there was a 30% reduction in BMI and a 26.4% reduction in HbA1c. Over the course of an average follow-up period of 10 months, 44 patients achieved a BMI of less than 40 kg/m² with an HbA1c of less than 6.5%, and 32 patients reached an HbA1c of less than 5.7%. The short-term effects of laparoscopic sleeve gastrectomy (LSG) on glycemic control in obese patients are evidenced by a significant reduction in weight and HbA1c, which indicates a positive effect on glycemic control. [28] Ahmed Atiah S. Alzahrani conducted a systematic review and meta-analysis on the Saudi-Arabian population, comparing the efficacy of LRYGB and LSG in morbidly obese patients with T2DM. The study analyzed pre-operative and post-operative weight and diabetic control using three high-quality RCTs with 760 patients. The findings highlighted effective management of morbid obesity and diabetes, showing promising results for both diabetic and obese patients.The results were significant (MD 0.30; CI 0.07–0.54; P = 0.010), indicating that both LSG and RYGB positively affect glycemic levels in obese patients with uncontrolled diabetes and HbA1c >5.7. The results were homogeneous (I2 0%; P < 0.073). [29] In his retrospective study, Khalid R. Murshid examined 340 patients aged 15 and older with T2DM and a BMI of ≥35 kg/m² who underwent LSG at King Fahad Hospital Almadinah Almunawwarah, KSA, between January 2015 and July 2019. The preoperative measurement of HbA1c and BMI was followed by subsequent assessments at various intervals up to one year postoperatively. The results demonstrated a consistent reduction in BMI from 49.27 kg/m² preoperatively to 32.72 kg/m² at 10–12 months post-LSG.

A statistically significant reduction in HbA1c levels was observed, from 8.38% to 6.43% over the course of one year ($p = 0.0001$). Of the patients, 75% achieved an HbA1c of 6.5% or lower within a year, while the remaining 25% demonstrated improvement but did not meet the target level. [30]

Positive predictors of postoperative diabetes remission

Bariatric surgery has been demonstrated to result in improvements in microvascular complications and peripheral neuropathy in individuals with diabetes. While it may halt the progression of early-stage retinopathy, bariatric surgery has the potential to exacerbate advanced retinopathy. Furthermore, bariatric surgery has been demonstrated to improve proteinuria and major renal outcomes, irrespective of the severity of chronic renal disease (CKD). [31] Recent randomized studies confirm that bariatric surgery improves or remits major CKD risk factors like type 2 diabetes and hypertension, with observational studies showing enhanced estimated glomerular filtration rate and albuminuria even in patients without preexisting CKD. [32] In a study of 100 patients with severe obesity and type 2 diabetes who underwent RYGB surgery, an attempt was made to identify any potential prognostic factors for type 2 diabetes remission in the three years following surgery. The results indicated that a plasma C-peptide level above 3 ng/dl may be a potential predictor of diabetes remission. This result was subsequently validated in a further study involving 20 patients. [33] All Gastric Bypass (GB) patients and half of Sleeve Gastrectomy (SG) patients achieved T2DM remission, with significant decreases in plasma amylin levels post-OGTT. These findings suggest that post-OGTT amylin levels may be useful for assessing T2DM remission, especially in SG patients. [34]

Postoperative hypoglycemia

Postprandial hyperinsulinemic hypoglycemia (PHH) is a serious complication following bariatric surgery, leading to life-threatening symptoms like seizures, disorientation, vision impairment, and loss of consciousness. Hyperinsulinemic hypoglycemia, occurring after meals, is marked by neuroglycopenic symptoms and aligns with Whipple's triad for hypoglycemia: (1) symptoms of hypoglycemia, (2) low plasma glucose levels, and (3) symptom relief after glucose intake. [35] PHH typically develops several months after RYGB, occurring about an hour after a meal with low blood glucose and inappropriate hyperinsulinemia. Similar to late dumping syndrome, PHH results from procedures that divert nutrients into the mid-small bowel, unlike purely restrictive surgeries like gastric banding and sleeve gastrectomy. Diagnosing PHH requires a detailed patient diary and ruling out conditions like early dumping syndrome, nesidioblastosis, and insulinoma. Key diagnostic tests include measuring plasma glucose, insulin, C-peptide, and proinsulin levels, with a negative 72-hour fasting test being crucial to exclude insulinoma. [36] Managing post-operative hypoglycemia often requires a multidisciplinary approach. Dietary changes are typically the primary treatment, though some patients may need medications like GLP-1 receptor antagonists, and surgery, such as gastric bypass reversal, is considered only for severe cases that don't respond to other treatments. [37]

For those who do not respond to diet, medications like acarbose, somatostatin analogs, and canagliflozin have proven effective, while other drugs like CCBs, diazoxide, and liraglutide have shown promise in case reports. GLP-1 antagonists are still under study but may offer a future treatment option for PPH. [38]

Summary

The global health issue of obesity, defined by a high body mass index (BMI), affects over two billion people. There is a robust correlation between obesity and metabolic syndrome and insulin resistance. The treatment of obesity encompasses a range of strategies, including lifestyle modifications, pharmacological interventions, and bariatric surgery. Surgical options, including sleeve gastrectomy (SG) and Roux-en-Y gastric bypass (RYGB), have been demonstrated to be effective for achieving long-term weight loss and improving related health issues. The popularity of SG is increasing due to its relatively low complexity. A significant body of evidence demonstrates that bariatric surgery markedly improves glycemic control and physical health, with notable reductions in HbA1c and BMI. Patients with type 2 diabetes mellitus who undergo bariatric surgery (BS) experience remission of the disease. The glycemic level is reduced to the point of increasing the risk of postprandial hyperinsulinemic hypoglycemia (PHH), which is a postoperative complication. It can be treated with dietary alterations and pharmacological interventions, or alternatively, surgery may be performed. Further research is being conducted into potential new treatments for postprandial hyperinsulinemic hypoglycemia (PHH). Overall, bariatric surgery remains a safe and effective solution for the management of severe obesity and its associated conditions.

Disclosure

Conceptualization, KK, and MK; methodology, KK; software, JC; check, MK, JC and JL; formal analysis, JL; investigation, MK; resources, JC; data curation, JL; writing - rough preparation, KK, JL, MK; writing - review and editing, JC, MK; visualization, MK, KK, MK, JC, JL; supervision, JC, MK; project administration, KK, JK; receiving funding, MK

All authors have read and agreed with the published version of the manuscript.

Funding

This research received no external funding.

Institutional Review Board Statement

Not applicable.

Informed Consent Statement

Not applicable.

Data Availability Statement

The data presented in this study are available on request from the corresponding author.

Conflicts of Interest

The authors declare no conflicts of interest.

Acknowledgments

None.

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