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Association between Bariatric Surgery and Major Adverse Diabetes Outcomes in Patients with Diabetes and Obesity: A Systematic Review

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ABSTRACT

Introduction: While significant randomized clinical trials have demonstrated the efficacy of bariatric surgery in the treatment of type 2 diabetes, there remains a notable gap in research exploring the potential risks associated with this procedure in patients with both diabetes and obesity. Despite the compelling evidence of its benefits, the associated risks and mortality outcomes specific to this patient population have not been extensively investigated. To better understand the relationship between bariatric surgery and these potential risks, as well as mortality among individuals with type 2 diabetes, comprehensive observational studies are essential.

Method: This systematic review was conducted following the PRISMA guidelines for article selection. Relevant articles were identified by searching keywords related to bariatric surgery, metabolic surgery, diabetes, and type 2 diabetes. These keywords were combined and searched across databases including Google Scholar, PubMed, and ScienceDirect, in accordance with the inclusion and exclusion criteria. A total of 4 articles met the criteria and were included in the final analysis.

Result: Among the 4 articles related to bariatric surgery and adverse diabetes outcomes in patients with diabetes and obesity, it can be concluded that although bariatric surgery offers many advantages, including a significant reduction in blood glucose levels and the achievement of stable glycemic control, it also has certain disadvantages.

Conclusion: Although bariatric surgery offers many benefits, it also presents significant risks for patients with diabetes and a BMI of 35 or higher. These risks may lead to various complications, including worsening of diabetic retinopathy and severe hypoglycemia.

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Introduction

The prevalence of obesity has risen sharply in recent decades, becoming a critical global public health issue (1). The worldwide epidemic of overweight and obesity, as measured by body mass index (BMI), now affects approximately 1.7 billion people, with this concerning trend particularly evident among adults (2). Health experts widely consider bariatric surgery the primary treatment option for individuals with clinically severe obesity who are at a heightened risk of morbidity and mortality from obesity-related conditions (3).

Bariatric surgery, a gastrointestinal procedure designed to achieve and sustain significant weight loss, has proven to be an effective preventive and therapeutic approach for managing type 2 diabetes and reducing cardiovascular risk factors. Studies have consistently demonstrated that gastric bypass and sleeve gastrectomy outperform intensive medical therapy (4).

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Bariatric surgery can be performed using various techniques, with several factors influencing the choice of approach. These surgeries are associated with a range of obesity-related medical conditions, including diabetes, nonalcoholic fatty liver disease, gallbladder disease, cardiovascular disease, hypertension, dyslipidemia, endocrine changes, musculoskeletal disorders, cancer, and pulmonary complications (5).

These conditions contribute to over 2.5 million deaths worldwide annually. Additionally, individuals with obesity have a reduced life expectancy compared to those with a normal weight (6).

Diabetes poses a substantial global healthcare challenge, with projections suggesting it could reach pandemic levels by 2030. In 2014, an estimated 387 million people worldwide were affected by diabetes. Additionally, approximately 316 million individuals with impaired glucose tolerance are at high risk of developing the disease, with this figure expected to increase to 471 million by 2035. Without prompt and effective interventions, it is estimated that around 592 million people will be affected by diabetes in the next 25 years (7).

Several epidemiological studies have consistently shown a parallel increase in obesity and diabetes. The enteroinsular axis is a key physiological system that includes glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic peptide (GIP), both of which are gut hormones. These incretin hormones are produced by L and K cells in the intestinal tract in response to nutrient presence and stimulate insulin secretion (8).

Additionally, various bariatric procedures can influence the secretion of other gastrointestinal hormones that regulate insulin sensitivity, such as ghrelin and peptide YY (PYY). These procedures have demonstrated significant effects on the metabolic state of individuals with diabetes. However, due to the heterogeneity and progressive nature of type 2 diabetes, relying solely on any single therapeutic intervention, or even a combination of interventions, is impractical for its effective management (9).

Numerous studies have assessed the association between bariatric surgery and major adverse diabetes outcomes in patients with both diabetes and obesity. While substantial evidence suggests the benefits of bariatric surgery in improving type 2 diabetes, standardized studies evaluating the potential risks associated with this procedure in this specific patient cohort are lacking. This systematic review aims to investigate the relationship between bariatric surgery, mortality, and diabetes complications in patients with diabetes who have undergone bariatric surgery. The review will analyze data from various studies to assess the impact of bariatric surgery on mortality rates and the incidence of diabetes-related complications.

Materials and Methods

This systematic review was conducted in accordance with PRISMA guidelines (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) and was registered in PROSPERO (ID=3317). The study included randomized controlled trials (RCTs), both double-blinded and single-blinded. The eligibility criteria for included studies were based on the PICO (Population, Intervention, Comparison, Outcome) framework, defined as follows:

P: Patients with diabetes and obesity; I: Bariatric surgery; O: Major adverse diabetes outcomes, diverse risks, and mortality; C: No specific comparison group was included.

The investigation aimed to examine the association between bariatric surgery (I) and major adverse diabetes outcomes in patients with diabetes and obesity. The study population consisted of individuals diagnosed with type 2 diabetes and obesity. The intervention was bariatric surgery (O), and the primary outcomes included major adverse diabetes events, various risks, and mortality (P).

The studies were limited to English-language publications, with publication dates ranging from 2005 to 2020. Two reviewers independently assessed the abstracts and titles, while one reviewer evaluated the full text of each study. A comprehensive search was conducted from June 2023 to December 2023.

Data Sources and Research

Data sources were searched across multiple databases, including the National Library of Medicine PubMed/MEDLINE, SpringerLink, and EMBASE. The search utilized specific keywords related to bariatric surgery, metabolic surgery, diabetes, type 2 diabetes, diabetes mellitus, medical treatment or therapy, conventional treatment/therapy, diabetes remission, and diabetes complications. Additionally, Medical

Subject Headings (MeSH) terms were incorporated to refine the search process.

Data Extraction

Data extraction and quality assessment involved collecting information from the primary research articles using various parameters, including the primary author's surname, publication date, country, patient BMI and age before surgery, sample size, duration of follow-up, treatment outcomes, and any statistical adjustments made for confounding variables.

Result

Description of Studies

A total of 454 prospective articles were identified through the updated electronic search in our study. After a thorough review of the titles and abstracts, a comprehensive evaluation of the full-text articles was conducted, resulting in the inclusion of 4 trials [Figure 1]. The studies included participants of all genders, with a mean age of approximately 50 years. In all studies, subjects in the comparison cohort received non-surgical treatments for type 2 diabetes, including oral hypoglycemic agents and insulin.

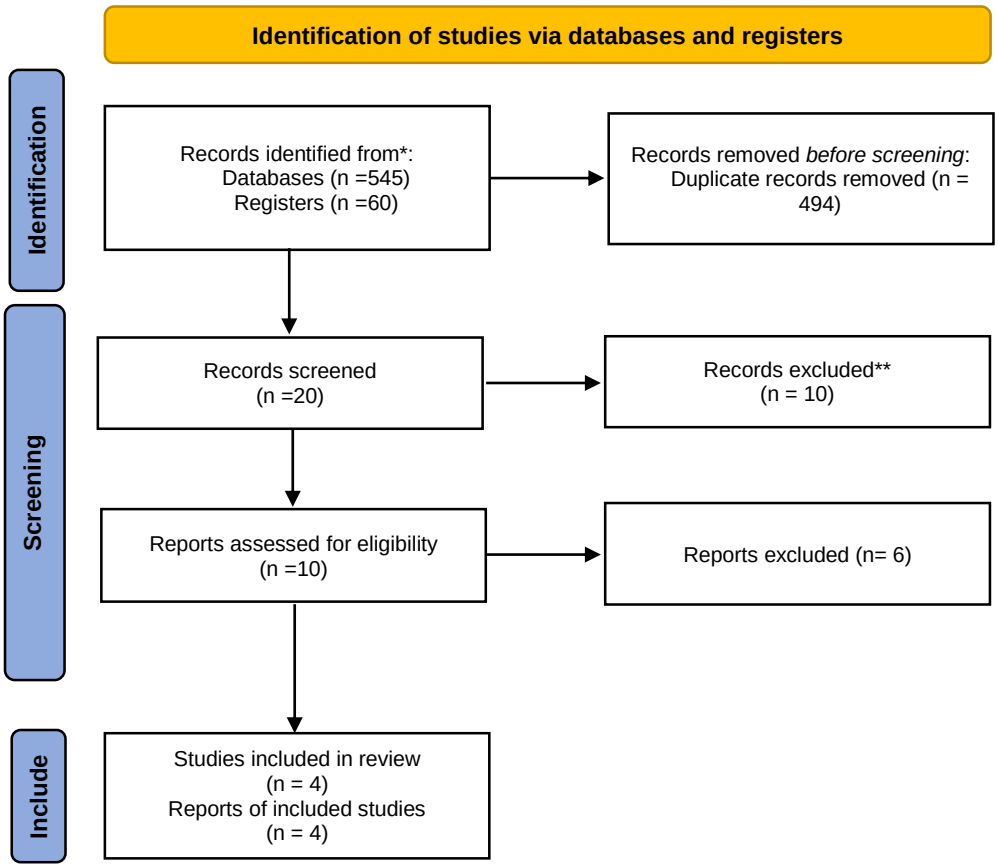

Figure1. Study flow diagram

Included Studies

To identify research directly related to the central theme of the study, specific selection criteria were applied. These criteria included only original articles that featured randomized clinical trials, as well as prospective, retrospective, or cohort studies with accessible full-texts, rather than abstracts alone. Furthermore, it was essential to include studies on bariatric surgery encompassing all genders. In each study, data collected included details such as author/year, age group, male-to-female ratio, and total patient count.

Excluded Studies

Studies with the following characteristics were excluded: non-English publications, non-original research articles, including systematic or literature reviews, and case reports.

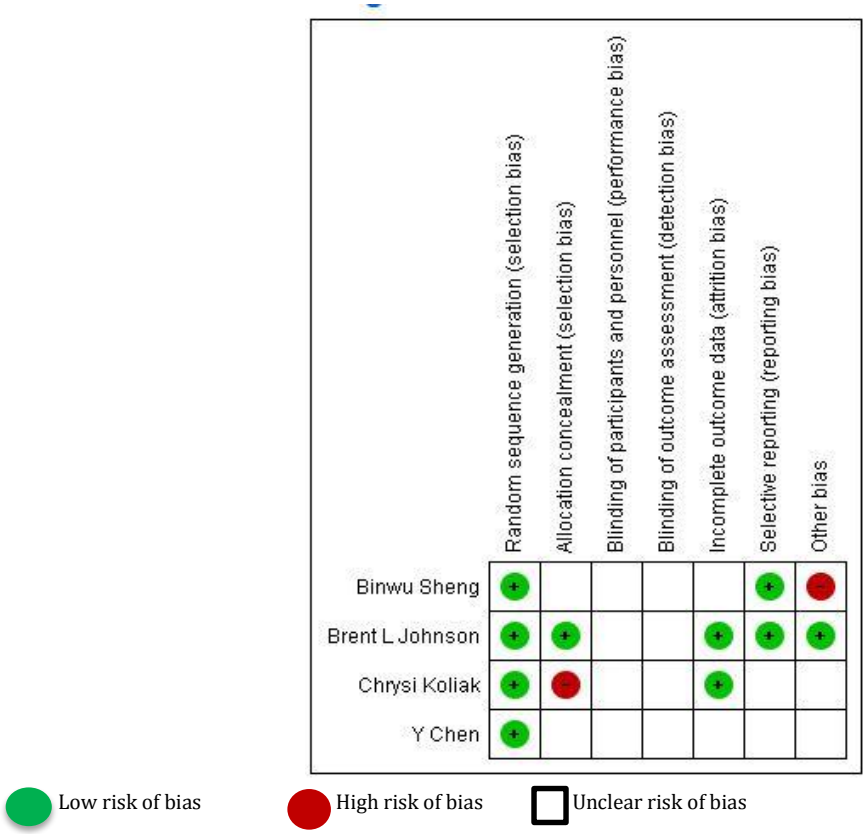

Figure 2. Risk of bias summary: review authors' judgments about each risk of bias item for each included study

Risk of Bias in Included Studies

The 'Risk of Bias' assessment is presented in Figure 2. All four studies were considered to have a low risk of bias (10, 11, 12, 13).

Allocation

All four included studies reported a randomization procedure (10, 11, 12, 13). Of these, only one study adequately described the concealment of treatment allocation (12).

Blinding

The other six trials did not implement blinding for patients, care providers, or outcome assessors, or they did not report on blinding procedures.

Incomplete Outcome Data

Two studies reported incomplete outcome data (12,13).

Selective Reporting

Only two RCTs were registered in an accessible clinical trial registry and were deemed to have a low risk of reporting bias (10, 12).

Other Potential Sources of Bias

Two articles discussed other potential sources of bias; however, one of them did not provide a complete and clear explanation (10, 12).

Table 1. Variables of different researches

No	Country	Authors	Study design and sample size	Purpose of the study	Main of finding	Dependent Variables	Independent Variable
1	USA	David P Fisher, et al. (2018)	Retrospective, matched cohort study. 5,301 patients	Investigate the relationship between bariatric surgery and incident macrovascular events in patients with severe obesity and type 2 diabetes	Bariatric surgery was associated with a lower incidence of macrovascular events and coronary artery disease at 5 years	Major adverse diabetes Outcomes macrovascular disease	Bariatric surgery
2	Greece	Chrysi Koliaki, et al. (2017)	-	Examined surgical procedures, pathophysiological mechanisms, and clinical outcomes of bariatric surgery for obese patients with T2DM*.	Bariatric surgery is an effective treatment for severe obesity and T2DM.	Major adverse diabetes outcomes: Remission of type 2 diabetes mellitus sensitivity Weight loss	Bariatric surgery
3	USA	Brent L Johnson, et al. (2013)	Retrospective cohort design. The BAR was 2,580, and for the CON* group was 13,371	Investigate the mid- to long-term outcomes of bariatric surgery in obese patients with T2DM, specifically examining the major macrovascular and microvascular complications compared to nonbariatric surgery controls.	Bariatric surgery was associated with a significant reduction in major macrovascular and microvascular events in moderately and severely obese patients with T2DM.	Major adverse diabetes outcomes: Major macrovascular events: Myocardial infarction Stroke All-cause death	Bariatric surgery treatment group)
4	UK	Y Chen, et al. (2017)	Retrospective observational study. 102 patients	Assess the changes in DR* in T2DM* patients after undergoing bariatric surgery and identify potential risk factors associated with it	Bariatric surgery does not prevent the progression of DR in patients with T2DM	Changes in diabetic retinopathy	The level of HbA1c* before the bariatric surgery

*** DR:** diabetic retinopathy *** T2DM:** Type 2 diabetes *** HbA1c:** glycated hemoglobin *** CON:** nonbariatric surgery control

Discussion

Fisher et al. conducted a study to examine the relationship between bariatric surgery and macrovascular disease outcomes in patients with type 2 diabetes and severe obesity. The study results demonstrated a significant association between bariatric surgery and improvements in diabetes management, a reduction in the incidence of both microvascular and macrovascular events, and decreased mortality rates compared to non-surgical interventions. The evidence indicated that patients with type 2 diabetes who underwent bariatric surgery had higher remission rates and a lower occurrence of microvascular and macrovascular diseases, as well as reduced mortality, following a minimum five-year follow-up period (10).

While bariatric surgery is generally associated with improved glycemic control and a reduced onset of diabetic retinopathy over time, concerns have been raised about an initial worsening of diabetic retinopathy following the procedure. This may be attributed to the rapid decrease in blood glucose levels induced by the surgery (10). However, certain aspects of the research yield varied findings. Koliaki et al. highlighted the growing recognition of bariatric surgery as an effective treatment for severe obesity and type 2 diabetes. Given the gastrointestinal tract's crucial role in metabolic regulation, it has become an important target for addressing type

2 diabetes. Bariatric surgery, also referred to as metabolic surgery, exerts effects beyond weight loss through multiple mechanisms. These mechanisms include changes in tissue-specific insulin sensitivity, beta-cell function, incretin responses, alterations in bile acid composition and flow, modifications in gut microbiota, adjustments in intestinal glucose metabolism, and increased metabolic activity in brown adipose tissue. However, determining the optimal timing for intervention to achieve long-term type 2 diabetes remission remains a challenge. Additionally, the relationship between the duration of type 2 diabetes remission and the progression of microvascular and macrovascular complications remains unclear in current research (11).

Bariatric surgery (BAR) has emerged as a recognized and effective intervention for individuals with clinical obesity and type 2 diabetes mellitus (T2DM). In a study by Johnson et al., researchers investigated the intermediate-to long-term effects of bariatric surgery on diabetic populations. The study findings demonstrated a significant association between bariatric surgery and a reduction of up to 65% in the incidence of major macrovascular and microvascular events among patients with T2DM and moderate-to-severe obesity (12).

These findings provide compelling evidence supporting the efficacy of bariatric surgery in improving outcomes related to type 2 diabetes and obesity. However, it is important to note that post-bariatric surgery patients are at risk of hypoglycemia, a condition characterized by low blood glucose levels (12).

The studies by Fisher, Koliaki, and Johnson underscore the effectiveness of bariatric surgery as an intervention for individuals with T2DM and clinical obesity, demonstrating substantial improvements in reducing the incidence of major macrovascular and microvascular events. Nonetheless, the potential risk of hypoglycemia following surgery should be carefully managed and monitored to ensure optimal patient outcomes.

The efficacy of metabolic surgery (also known as bariatric or obesity surgery) as a therapeutic approach for type 2 diabetes is well-established. Data from several randomized controlled trials indicate that, when combined with optimal medical therapy, surgery is superior to medical therapy alone in achieving glycemic and metabolic targets in diabetes management. Consequently, metabolic surgery is now recommended as a viable therapeutic option for type 2 diabetes mellitus associated with obesity (13).

However, it is important to note that certain postoperative complications are commonly observed shortly after bariatric surgery, including leakage, wound complications, and ulcer/reflux. In contrast, complications such as hernia, intestinal obstruction, and gallstones typically emerge 1–2 years after the procedure (14,15).

Furthermore, bariatric surgery can result in anatomical and physiological changes that may contribute to long-term deficiencies in essential vitamins and minerals. Although this investigation lacked access to primary care data, which typically includes follow-up procedures beyond 2 years post-surgery, it observed that occurrences of malnutrition and anemia were twice as frequent following bariatric surgery (16,17,18).

Several factors have been identified as potential risk factors or predictors of adverse outcomes in patients with diabetes undergoing bariatric surgery. Age is one such factor, although existing studies offer conflicting evidence on the association between older age and mortality risk in bariatric surgery. However, our study found a significant increase in mortality risk for older patients with diabetes who underwent bariatric surgery over a medium-term period of 4.7 years (19, 20). Additionally, bariatric surgery in patients with a diabetes duration of more than 15 years was associated with elevated mortality risks (21).

Gender has also been shown to potentially influence the risk of adverse outcomes following bariatric surgery in patients with diabetes. Some studies suggest, for example, that men may face higher surgical risks than women (22, 23). Additionally, the use of specific medications, pre-existing cardiac conditions, recent revascularization surgery within six months prior to the procedure, and severe hepatic dysfunction with ascites within one year of the procedure are recognized as factors that increase the risks associated with bariatric surgical interventions (24, 25, 26).

Overall, these studies collectively strengthen the evidence supporting bariatric surgery as a therapeutic approach for individuals with type 2

diabetes and obesity, underscoring its potential benefits in diabetes management and reduction of related complications. However, they also highlight concerns, such as the risk of hypoglycemia following surgery, which necessitates careful monitoring and management. Each study examines different aspects of the relationship between bariatric surgery and outcomes related to type 2 diabetes and obesity. While all demonstrate positive outcomes associated with bariatric surgery, their specific findings vary. For instance, Fisher et al. report significant improvements in diabetes management, along with reductions in microvascular and macrovascular events and decreased mortality. Koliaki et al. discuss various weight loss-independent effects of bariatric surgery but note the uncertainty regarding remission duration and complication development. Johnson et al. report a substantial reduction in major incidences of both macrovascular and microvascular events.

Conclusion

This study demonstrated that although bariatric surgery offers numerous benefits, it also carries significant risks for patients with diabetes and a BMI of 35 or higher. These risks may lead to various complications, including worsening of diabetic retinopathy, severe hypoglycemia, and episodes of low blood glucose levels.

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Conflict of Interest

There is no conflicts of interest in this work.

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