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Review article

Long-term systemic effects of metabolic bariatric surgery: A multidisciplinary perspective

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ABSTRACT

Background: Obesity is a global health crisis with profound implications on various body systems, contributing to a series of comorbidities. Metabolic Bariatric Surgery (MBS) has emerged as an effective treatment option for severe obesity, with significant weight reduction and potential systemic physiological alterations.
Objectives: This narrative review aims to provide a comprehensive analysis of the long-term effects of MBS on a wide array of body systems, including the heart, liver, kidneys, reproductive system, skin, lungs, digestive tract, pancreas, and blood, as well as related cancers of these organs.
Methods: A systematic search was conducted in academic databases (PubMed, ISI Web of Science, and Scopus) for observational studies and reviews published between July 2000 and December 2023, investigating the association between MBS and the subsequent function of different organ systems. High-quality studies were prioritized to ensure reliable evidence synthesis.
Results: MBS has demonstrated favorable outcomes in reducing cardiovascular disease risk, improving cardiac function, and alleviating heart failure symptoms. It has also been associated with improved respiratory function, remission of obstructive sleep apnea, and reduced cancer incidence and mortality. Additionally, MBS has shown benefits in managing gastrointestinal disorders, enhancing glycemic control, and promoting pancreatic beta-cell regeneration in type 2 diabetes mellitus. However, some methods of MBS are associated with a higher risk of cholelithiasis, GERD, and pancreatic exocrine insufficiency.
Conclusion: MBS has far-reaching systemic effects beyond weight loss, offering potential long-term benefits for various organ systems and comorbidities associated with obesity. For many patients with severe obesity, the potential benefits of Metabolic and Bariatric Surgery (MBS) can outweigh the associated risks. However, careful evaluation by a qualified healthcare professional is crucial

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to determine candidacy and ensure a successful outcome. Further research is needed to fully elucidate the long-term impacts and tailor personalized treatment approaches.

1. Introduction

Obesity is a global health crisis with profound implications on various body systems, contributing to a series of comorbidities ranging from cardiovascular diseases to metabolic dysfunctions. The most recent guidelines recommend metabolic bariatric surgeries (MBS) to be considered as a treatment option for individuals with a body mass index (BMI) greater than or equal to 35 kg/m2, regardless of the presence, absence, or severity of co-morbidities and for individuals with a BMI between 30 and 34.9 kg/m2 who also have metabolic diseases [1].

The term “Metabolic surgery” was introduced in 1972 by HW. Scott to describe the impact of ileal bypass on hypercholesterolemia and arteriosclerosis [2] and in 2016, Rubino et al. suggested the term “Metabolic Bariatric Surgery” for modern practice [5]. Over time, bariatric procedures evolved from their initial classification (restrictive, malabsorptive, or combined) to include intricate metabolic effects, signifying a paradigm shift [3,4].

The development of laparoscopic approaches further enhanced surgical management, making these procedures safer and quicker. Recently, numerous endoscopic techniques like Endoscopic Sleeve Gastroplasty (ESG) and Orbera Gastric Balloon have been developed for personalized patient care [5]. Non-surgical weight loss methods such as the Obalon Balloon System [6], cryolipolysis [7], and AspireAssist [8] offer lower risks, shorter recovery times, fewer dietary restrictions, and higher cost-effectiveness compared to surgery. Additionally, robotic surgeries provide superior visualization, more degrees of freedom, and better ergonomics [9]. However, to this date, MBS remains the most common approach for severe obesity worldwide [1]. IFSO Worldwide Survey, have shown that the number of bariatric procedures performed annually has consistently increased, reflecting its widespread adoption as the primary approach to managing severe obesity globally [10].

While the primary outcome of MBS has traditionally been viewed as weight reduction, emerging evidence suggests a complex interplay between weight loss and systemic physiological changes. Recent studies have begun to uncover the broader systemic effects of MBS, suggesting impacts that extend far beyond mere weight loss to reduce the burden of morbidity and mortality due to severe obesity [11,12]. Research has documented improvements in cardiovascular risk factors, insulin sensitivity, and hormonal balances post-surgery [13–15]. However, the extent and nature of these changes in organs such as the heart, liver, kidneys, and beyond remain incompletely understood.

Despite the growing body of literature, there remains a significant gap in comprehensive, system-wide studies that elucidate the long-term effects of MBS on various organs. This narrative review aims to address this gap by providing a thorough analysis of the long-term effects of MBS on a wide array of body systems. Specifically, it will explore the impacts of MBS on the heart, liver, kidneys, reproductive system, skin, lungs, digestive tract, pancreas, and blood, as well as related cancers of these organs. This holistic approach will enhance our understanding of MBS as a multifaceted intervention that may influence the incidence or prognosis of various comorbidities.

2. Methods

2.1. Objective

The primary objective is to assess the long-term influence of MBS on a wide range of bodily systems beyond weight loss, comprehensively. This study will investigate its potential impact on the heart, liver, kidneys, reproductive system, skin, lungs, digestive tract, pancreas, and blood through meticulous analysis of observational studies and meta-analyses. This review will critically analyze the findings from the included studies, highlighting potential benefits, limitations, and areas requiring further investigation. This narrative review is structured according to SANRA guidelines (the Scale for the Assessment of Narrative Review Articles) [16].

2.2. Search strategy

To investigate this relationship, these academic databases were searched comprehensively: PubMed, ISI Web of Science, and Scopus. The search strategy focused on studies published between July 2000 and December 2023, encompassing a substantial timeframe within the evolving field of MBS. The null hypothesis was that there was no association between undergoing MBS and the subsequent function of different organ systems within the body. We employed a combination of search terms related to both bariatric procedures and potential health outcomes:

1 Metabolic Bariatric Surgery Terminology: We included terms encompassing a broad range of bariatric interventions, including “bariatric surgery,” " sleeve gastrectomy,” “Adjustable Gastric Banding,” “Roux-en-Y gastric bypass,” “Biliopancreatic diversion with duodenal switch,” and the abbreviation “BPD/DS."
2 Health Outcomes of Interest: To capture the potential influence of MBS on various organ systems, we incorporated terms like “Cancer”, “Tumor”, “Malignancy” “Heart”, “Cardiovascular” “Kidney”, “Renal”, “Nephrological” “Liver”, “Hepatic” “Reproductive”, “Fertility” “Skin” “Respiratory”, “Pulmonary”, “Gastrointestinal”, and “Digestive”.

2.3. Study selection and quality assessment

Studies investigating the potential link between undergoing MBS and its subsequent effect on various body organs were included. We excluded letters, comments, non-English and animal studies. This systematic search and selection process is designed to provide a comprehensive narrative review of the current evidence regarding the long-term effects of MBS on diverse organ systems.

We did not conduct a formal risk of bias assessment using tools like the Cochrane Risk of Bias (RoB) or other RoB tools. Instead, they prioritized studies considered higher quality based on the evidence hierarchy. This included meta-analyses, systematic reviews, multicenter studies, prospective studies, and randomized controlled trials. This strategic approach aimed to ensure the analysis included the most reliable and robust evidence. By focusing on studies with strong methodologies and minimizing the inclusion of lower-quality evidence, we aimed to mitigate potential biases that could compromise the validity of the findings.

3. Results

3.1. Cardiovascular system

Obesity is a well-known risk factor for cardiovascular diseases (CVD). Various pathological processes, such as dyslipidemia and insulin resistance, promote the development of CVD. In a study by Powell-Wiley et al., more than 189,000 patients were evenly divided between MBS patients and matched hospitalized control individuals, with 78 % of patients in each group having Class III obesity. Patients who underwent MBS had 37 % lower all-cause mortality and were significantly less likely to have admissions for new-onset heart failure (64 % risk reduction), myocardial infarction (37 % risk reduction), and ischemic stroke (29 % risk reduction) as compared to the control group [17].

In a meta-analysis, researchers presented findings from 80 studies, showing that MBS has favorable outcomes in patients with severe heart failure, offering potential benefits such as weight reduction, improved cardiac function, decreased heart failure symptoms, and reduced hospitalization rates [18]. These improvements include a 12.2 % (95 % CI 0.096–0.149; $p < 0.001$) decrease in left ventricular (LV) mass index, an increase of 0.155 (95 % CI 0.106–0.205; $p < 0.001$) in E/A ratio, a reduction of 2.012 mm (95 % CI 1.356–2.699; $p < 0.001$) in left atrial diameter, a decrease of 1.16 mm (95 % CI 0.62–1.69; $p < 0.001$) in LV diastolic dimension, and an increase of 1.636 % (95 % CI 0.706–2.566; $p < 0.001$) in LV ejection fraction after the surgical procedure [18]. Moreover, the improved effect of MBS on the cardiac structure has been documented in the improvement in epicardial fat reduction, reduced ventricular interaction, LV reverse remodelling, and improved longitudinal biventricular mechanics, but LA myopathy and hemodynamic congestion still progressed [19]. The enhancement in other cardiac indexes has also been observed as indicated by significant improvement of left ventricular ejection fraction (LVEF) (10.0 $\pm$ 11.9 %, $p < 0.001$) and significant reduction of 0.5 New York Heart Association (NYHA) classification (0–2, $p < 0.001$) post-MBS in patients with obesity [20].

In a recent study of patients with concomitant non-alcoholic fatty liver disease (NAFLD) and obesity, researchers have shown that the overall risks of major adverse cardiovascular events and all-cause mortality were significantly reduced in patients who underwent MBS [21].

This finding has also been observed in nonalcoholic steatohepatitis (NASH) patients, where the cumulative incidence of major adverse cardiovascular events at ten years was 8.5 % in the MBS group and 15.7 % in the nonsurgical group, representing the favorable effect of MBS on adverse cardiovascular events in NASH patients [13].

Among other evaluated effects, studies have shown that MBS has decreased hospital length of stay, caused a 50 % reduction in in-hospital mortality after heart failure admissions, and significantly, reduced overall hospital stay expenses of patients admitted due to heart failure [22,23]. A large observational study investigated the long-term benefits of metabolic surgery for patients with type 2 diabetes and obesity [24]. The study followed over 13,700 participants for a median of nearly four years and showed that patients who underwent surgery had a significantly lower risk of experiencing a major adverse cardiovascular event (MACE) compared to those who did not have surgery (cumulative incidence at 8-years, 30.8 % vs. 47.7 %, $p < 0.001$) [25]. This benefit included a reduced risk of death (OR 0.59, 95 % CI 0.48–0.72) [24]. All seven pre-specified secondary outcomes, including mortality, showed statistically significant differences in favor of MBS [24].

Another study involving Medicare beneficiaries (189,770 patients) with obesity found that bariatric surgery significantly reduced the risk of several serious health issues compared to a control group of patients with obesity, matched for age, sex, and body mass index [25]. Specifically, the surgery was associated with a lower mortality rate (9.2 deaths per 1000 person-years compared to 14.7), a decrease in new cases of heart failure (OR 0.46, 95 % CI 0.44–0.49), a lower risk of myocardial infarction (OR 0.63, 95 % CI 0.59–0.68), and a reduced chance of stroke [25].

Heart transplantation among patients with obesity is of great concern due to the high prevalence of severe cardiovascular issues in this population. In a long-term survival study of patients with congestive heart failure, researchers have indicated that patients who underwent sleeve gastrectomy or Roux-en-Y gastric bypass experienced a gain of 5.3 and 7.4 additional years of survival compared to patients with medical weight management due to having a higher chance for heart transplantation [26].

3.2. Gastrointestinal system

The impact of obesity on the gastrointestinal system through both chronic low-grade inflammation and alterations in gut microbiota composition, has been studied extensively.

Obesity affects gut microbiota composition, potentially leading to further inflammation and metabolic disturbances [27]. Dysbiosis in the gut microbiota, particularly an increased Firmicutes/Bacteroidetes (F/B) ratio, is observed in individuals with obesity and contributes to heightened energy extraction from the diet, inflammation, and metabolic disturbances [27]. Therefore, bariatric surgeries, by altering the gut microbiota, and reducing adipose tissue, can be beneficial in improving dysbiosis and inflammation status in individuals with obesity [28].

Obesity also triggers chronic low-grade inflammation, activating proinflammatory pathways and recruiting immune cells in adipose tissue. This contributes to insulin resistance, metabolic dysfunction, and a pro-inflammatory immune system phenotype [29]. Chronic inflammation and structural changes in the esophagus due to obesity and GERD may promote malignant transformation and tumor progression [30].

The role of MBS in GERD treatment is complex and requires individual assessment. A systematic review underlined the complex relationship between obesity, GERD, and MBS procedures [31]. It found that surgical choice should be tailored to the individual, with thorough preoperative investigation (including a 24-h pH study and high-resolution manometry) to identify the most suitable option and effectively manage GERD post-surgery [31].

On the contrary, a report has been published that Laparoscopic SG (LSG) negatively influenced GERD symptoms because SG could not make any guarantee to relieve or improve GERD as well as cause it in some patients who used this procedure and was compensated in asymptomatic individuals [32]. Further, GERD before surgery was related to poorer outcomes and reduced weight loss with LSG, indicating that it may be a relative contraindication for this procedure [32]. Comparing the impact of different bariatric surgeries on GERD, it has been found that RYGB is more effective in alleviating GERD symptoms. At the same time, LSG appeared to increase the incidence of GERD, and adjustable gastric banding initially improved symptoms but led to new onset GERD symptoms during long-term follow-up [33,34].

In terms of drug absorption, MBS can influence the pharmacokinetics of orally ingested drugs. Bariatric surgeries result in anatomical and physiological changes, reducing the oral bio-accessibility of drugs [35]. Following malabsorptive procedures, the levels of metabolic enzymes present in the upper small intestine (i.e., CYP3A4) alter from their original status, thereby affecting drug availability for several drugs [35].

3.3. Respiratory system

Obesity is associated with altered lung mechanics, reduced lung volumes, and increased airway resistance, leading to impaired lung function and the development of respiratory distress syndrome, and systemic inflammation and oxidative stress further contribute to lung injury [36–38]. In the recent pandemic, it was observed that patients with obesity faced a higher risk of severe illness and mortality when infected with COVID-19 [39].

As reported, the sleeve gastrectomy improved ventilation in patients with severe obesity, which has been attributed to increased ventilatory efficiency and decreased oxygen demands [40]. Meanwhile, MBS enhances functional capacity and lung function in women with obesity [41]. The effect of MBS on respiratory improvement has been indicated in various studies; it has been shown that the dynamic inspiratory capacity improves (0.13 L–0.21 L), and the shortness of breath was reduced post- MBS among patients with obesity class III [42].

Obesity strongly contributes to the pathogenesis of obstructive sleep apnea (OSA) by increasing the mechanical load on the upper airway, exacerbating respiratory complications [43,44]. MBS proves to have advantageous outcomes for individuals with obesity induced OSA [45,46]. A 2023 meta-analysis by Oweidat et al. involving 2310 patients with OSA from 32 studies found that MBS significantly improved several health markers [46]. Patients experienced a notable decrease in body mass index (BMI), apnea-hypopnea index (AHI), and respiratory disturbance index (RDI). Additionally, the study showed a 65 % remission rate for OSA following surgery [46]. In addition, in another meta-analysis by Qin et al., using 24 studies, the researcher reported that notable enhancements in forced vital capacity (FVC), mean oxygen saturation (SpO_2), nadirSpO2, sleep efficiency (SE), N3%, rapid eye movement (REM%), and Epworth sleepiness scale (ESS) were noted when compared to the initial measurements in patients undergoing bariatric surgeries [45].

Studies have also documented the effect of MBS on improving acoustic parameters. It has been revealed that individuals with obesity who underwent weight loss surgery exhibited neck circumference, fundamental frequency, and maximum phonation time values that were more similar to the average values of individuals with normal weight [47].

3.4. Skin

While the direct effect of obesity on skin tissue has not been studied, there are potential mechanisms through which obesity may impact skin health. Chronic inflammation as a result of severe obesity, can impair skin tissue healing and regeneration, potentially compromising overall skin health [48]. There are several other factors that contribute to increased susceptibility to skin infections and hinder the healing process of wounds in patients with obesity. There's a potential link between obesity and changes in the skin microbiome, along with reduced oxygen supply to the skin tissues due to excess adipose tissue, which is crucial for proper wound healing [49,50].

The positive effects of MBS on skin manifestations were documented in a prospective controlled intervention study, where successful weight loss post-surgery correlated with a significant reduction in skin conditions such as acanthosis nigricans and keratosis pilaris [51]. However, dermatological concerns are a prevalent issue post-MBS. The effect of weight loss on skin tissue has been evaluated in numerous studies. In a case report, the risk of severe malnutrition and resultant complications, such as extensive dermatitis due to zinc and vitamin deficiencies following malabsorptive MBS, has been highlighted [52]. This underscores the critical need for lifelong nutritional support and supplementation to prevent such complications [52]. Additionally, loose and irritated skin negatively impacts the quality of life, indicating the need for increased dermatological care post-operation [53]. Studies proved that massive weight loss following MBS induces significant changes in the skin's collagen system, which could affect the results of subsequent contouring surgeries [54,55]. Skin protein profiles and their role in body contouring surgery have also been investigated after major weight loss. High expression of haptoglobin associated with a decrease of collagen XIV, vinculin, and periplakin in groups after significant weight losses was confirmed, indicating that the inflammatory lesion remains active in the skin and causes changes in its structural organization, with severe repercussions on its clinical characteristics and physical properties [56].

3.5. Cancer

Extensive research has explored the link between weight loss interventions and cancer risk and mortality. A meta-analysis of 32 studies found that MBS was associated with better cancer prognosis [57]. They have concluded that MBS was associated with a reduced overall incidence of cancer (OR 0.62, 95 % CI 0.46–0.84, $p < 0.002$), obesity-related cancer (OR 0.59, 95 % CI 0.39–0.90, $p = 0.01$) and cancer-associated mortality (OR 0.51, 95 % CI 0.42–0.62, $p < 0.00001$) [57]. In this study, they have cleared out that MBS was associated with a reduction in the future incidence of hepatocellular carcinoma, colorectal cancer, pancreatic cancer and gallbladder cancer, breast cancer, endometrial cancer and ovarian cancer [57].

While research on the impact of MBS (Metabolic Bariatric Surgery) on existing gynecological cancers is ongoing, its effectiveness in preventing these cancers in high-risk obese women is well-supported which makes MBS a promising strategy for reducing cancer risk and potentially improving overall survival rates [58]. Moreover, a multinational study has found out that MBS led to a decreased overall cancer risk in women, including specific cancers like breast and endometrial cancer and the protective effect of this intervention was primarily observed within the first five postoperative years [59]. Similarly, in an extensive cohort of 58, 667 Post-menopausal women, women with intentional weight loss had lower obesity-related cancer risk (OR 0.88, 95 % CI 0.80–0.98) compared to women with stable weight; and among all cancers, intentional weight loss was most strongly associated with endometrial cancer (OR 0.61, 95 % CI 0.42–0.88) [60]. In the Splendid (Surgical Procedures and Long-term Effectiveness in Neoplastic Disease Incidence and Death) matched cohort study, researchers investigated whether bariatric surgery could reduce cancer risk and mortality in adults with obese [61]. The study included 30,318 with a median follow-up of 6.1 years. Patients who underwent bariatric surgery ($n = 5053$, including Roux-en-Y gastric bypass and sleeve gastrectomy) were matched 1:5 to patients who did not undergo surgery for their obesity ($n = 25,265$). The findings revealed that bariatric surgery was associated with a significantly lower risk of developing obesity-related cancers and dying from cancer compared to no surgery [61]. The risk of obesity-associated cancer was 3.0 events vs 4.6 events per 1000 person-years in the surgery and control groups respectively ($p = 0.002$) [61]. This translates to 32 % lower chance (OR 0.68, 95 % CI 0.53–0.87) for developing obesity-related cancer following bariatric surgery. Similarly, cancer-related mortality also showed a benefit, with 0.6 events vs 1.2 events per 1000 person-years in the surgery and control groups ($p = 0.01$) [61].

However, the relationship between weight loss from MBS and cancer progression is complex. While the overall trend suggests a protective effect, particularly for obesity-related cancers, continuous research and vigilance in post-surgery care are essential due to the nuanced outcomes for different types of cancer and the long-term impact. For instance, a retrospective study highlighted the concerning trend of increasing esophageal cancer rates after MBS, underlining the need for tailored treatment strategies in such cases [62]. In summary, MBS is linked with a net reduction in cancer risk and mortality for certain cancers. Yet, the potential increased risk for others emphasizes the need for ongoing surveillance and patient-specific considerations.

3.6. Biliopancreatic system

The pancreas plays a crucial role in glucose metabolism and the development of metabolic disorders like T2DM. Obesity has been found to significantly impact pancreatic function, leading to an imbalance in insulin secretion, insulin resistance, and disturbances in glucose homeostasis [63]. Adipose tissue, which acts as a secretory organ in obesity-related metabolic disorders, produces various adipokines, such as adiponectin and leptin, that can influence pancreatic function and insulin sensitivity [63].

Chronic low-grade inflammation, commonly associated with obesity, may also contribute to pancreatic β-cell dysfunction and the development of T2DM [64].

The relationship between weight loss and pancreatic function is multifaceted, involving physical changes in body composition, as well as metabolic and physiological implications. MBS appears to significantly impact the pancreas, altering both fat content and blood flow in ways that contribute to improved blood sugar control and potential reversal of T2DM. Studies have shown that these procedures reduce pancreatic fat while preserving blood flow to the organ, both of which are linked to better glucose management [65]. Notably, even independent of weight loss and insulin sensitivity, maintaining adequate pancreatic blood flow after surgery is strongly associated with improved glucose control in diabetic patients [65]. A recent long-term study by Purnell et al. has reported a T2DM remission rate of 57 % after RYGB (46 % complete, 11 % partial) [66]. This suggests that MBS may directly influence how the pancreas functions. In addition, Schauer et al., in a five-year follow-up analysis of the STAMPEDE trial, reported the absolute superiority of MBS over medical treatments in achieving HbA1c less than 6 % with or without medication in patients with T2DM [67]. Courcolas et al. compared the effectiveness of MBS to medical treatments for obesity [68,69]. They investigated patients in two-time intervals: the first 5 years and 7–12 years after bariatric surgery. Their findings showed that patients who underwent MBS achieved superior glycemic control [68,69]. This was evidenced by lower use of diabetes medication and higher rates of diabetes remission compared to those who received medical/lifestyle intervention [68,69]. Furthermore, specific procedures like RYGB and SG have been shown to promote the regeneration of pancreatic beta cells and enhance islet function, further contributing to the resolution of T2DM [70,71]. Lastly, in a three-year follow-up of the largest cohort of patients ever randomized in the STAMPEDE, TRIABETES, SLIMM-T2D, and CROSSROADS trials, Kirwan et al. demonstrated that metabolic/bariatric surgery is more effective and durable than medical/lifestyle intervention for achieving remission of type 2 diabetes, and this benefit extends even to individuals with class I obesity, a group for whom surgery is not typically recommended [72].

Obesity, particularly with a high BMI before the age of 50, is linked to an increased risk of pancreatic ductal adenocarcinoma (PDAC) [73]. MBS may offer a protective effect against the development, progression, and mortality of PDAC through mechanisms that could potentially lead to novel therapeutic avenues [73]. A comprehensive study on 160,129 MBS participants and 1,263,804 individuals in the control group with 5.2 ± 1.9 and 6.0 ± 1.9 years of follow-up; found a significant decrease in the likelihood of developing pancreatic cancer during the follow-up period for those who underwent MBS (OR: 0.567) [74].

While MBS offers significant benefits, it can also lead to complications like pancreatic exocrine insufficiency (PEI), a condition characterized by impaired exocrine pancreatic function. Research indicates that bariatric procedures like Roux-en-Y gastric bypass can cause PEI in a significant portion of patients, with studies reporting up to 31 % experiencing this issue after surgery [75,76]. The altered anatomy resulting from bypass surgery can disrupt the proper mixing of food with pancreatic enzymes and bile, leading to malabsorption and maldigestion [76,77]. This can manifest as symptoms like steatorrhea, weight loss, and malnutrition [76,77].

A cohort study comparing different surgery procedures, including OAGB, SG, and SASI (Single Anastomosis Sleeve Ileal Bypass), found that 23.5 %, 17.2 %, 14.3 %, and 20.0 % of patients in the respective groups experienced moderate exocrine pancreatic insufficiency (EPI), with no statistically significant differences in gastrointestinal quality of life index (GIQLI) [78]. Supplementing with pancreatic exocrine replacement therapy (PERT) is an important part of the treatment for confirmed PEI or suggestive symptoms. It has been shown to treat this complication without affecting weight loss [75,76]. However, in methods such as SG, exocrine pancreatic function remains normal [79].

Pancreatitis is a rare but serious complication following MBS, which can occur due to various factors such as small bowel obstructions from blood clots. Studies have found that the incidence of acute pancreatitis increases significantly after MBS, with a 7-fold increase after RYGB and a 4-fold increase after SG [80].

Despite the benefits, the association between MBS and the subsequent development of cholelithiasis is a concern. Crystalline deposits within the gallbladder or biliary tract are more commonly observed in individuals with obesity [81,82], with the risk further exacerbated following bariatric procedures [83–85]. In addition, the management of potential gallstone-induced pancreatitis is also crucial [86].

In conclusion, the relationship between MBS and the pancreas is a complex and multifaceted topic. Understanding the impact of weight loss and bariatric procedures on pancreatic function, cancer risk, and potential complications is essential for providing comprehensive care to patients undergoing these interventions.

3.7. Renal system

Metabolic bariatric surgeries can be beneficial for patients with obesity and chronic kidney disease (CKD). Studies have shown that MBS might prevent kidney damage by reducing glomerular hyperfiltration and improving metabolic and inflammatory parameters [87]. Additionally, some researchers have reported that MBS was associated with an improvement in CKD risk categories in a large proportion of patients [88–90]. These surgeries also appears to be safe and effective for patients with kidney transplantation. It does not negatively affect kidney transplant outcomes and can enable previously ineligible patients with severe obesity to become transplant candidates [91]. However, there is a tendency for weight regain in those receiving surgery post-transplant [92]. On the other hand, patients with chronic kidney disease and End-Stage Renal Disease (CKD & ESRD) may have a higher risk of postoperative complications such as reoperation and readmission [93,94]. This is an important consideration when evaluating the risks and benefits of MBS for this patient population.

Hypoabsorptive bariatric procedures may increase kidney stone formation due to changes in urine composition. Researchers have reported that various surgical methods, including RYGB, SG, and BPD/DS, were associated with an increased risk for kidney stones [95]. However, dietary management, including a low-oxalate diet and fluid intake, can help mitigate these risks [96].

In conclusion, while MBS can lead to improvement in conditions associated with CKD and enhance the viability of kidney transplant candidacy, it also requires careful management to mitigate complications such as kidney stones and to monitor postoperative outcomes.

3.8. Coagulation and hemostasis

Obesity is associated with a hypercoagulable state, characterized by stronger and more quickly-formed blood clots and resistance to fibrinolysis. However, studies have shown that MBS can help improve these coagulation abnormalities. Patients with morbid obesity have been found to present with these tendencies towards hypercoagulability prior to surgery, but these issues improve substantially after undergoing bariatric procedures [97]. Furthermore, bariatric patients generally exhibit a trend towards improved coagulation, with female patients and those with higher BMIs particularly displaying reduced hypercoagulability [98]. Specific studies have examined the effects of MBS on coagulation markers. For example, a study on LSG found that it could induce a hypercoagulable state in the short-term, with increased prothrombin time (PT) and D-Dimer, and decreased activated partial thromboplastin time (APTT) after the surgery [71]. On the other hand, MBS appears to have a beneficial impact on fibrinolysis. One study reported that reductions in plasmin inhibitor and fibrinogen after Roux-en-Y Gastric Bypass (RYGB) contributed to improved fibrin clot lysis, suggesting a pro-fibrinolytic effect. These positive changes were also linked to reductions in metabolic factors like cholesterol, glucose, and the inflammatory marker interleukin-6 (IL-6) [99]. Global coagulation assays, such as Thrombin Generation Assay (TGA) and TEG®, have been used to identify hypercoagulability in patients with obesity, which could serve as predictive markers for thrombotic events [100]. In summary, MBS appears to have a complex effect on coagulation, initially inducing a hypercoagulable state but ultimately leading to improved fibrinolysis and reduced overall hypercoagulability in patients with morbid obesity. These alterations in hemostatic parameters necessitate a careful postoperative management plan to mitigate the risk of thromboembolic events.

3.9. Hepatic system

While the procedure is not explicitly recommended for the treatment of nonalcoholic fatty liver disease (NAFLD) or compensated liver cirrhosis, the weight loss and metabolic improvements facilitated by MBS can have a profound impact on liver health. A meta-analysis involving over 16 million patients has shown that MBS can reduce the risk of adverse liver outcomes, including nonalcoholic cirrhosis and liver cancer [101]. However, it is important to note that the procedure may also increase the risk of alcoholic cirrhosis post-surgery, highlighting the need for careful patient selection and close monitoring [101]. Metabolic bariatric surgery facilitates weight loss and metabolic improvements, which can potentially eliminate NAFLD, nonalcoholic steatohepatitis (NASH), and liver fibrosis. While there is a noted risk of liver failure post-surgery, the overall benefits appear to outweigh this risk [102]. For patients with obesity and early-stage (Child A) liver cirrhosis, MBS can be an effective intervention, as it may prevent the progression of NAFLD and even reverse existing liver changes. However, it is important to recognize that while MBS leads to weight loss and metabolic improvement, it can also carry rare risks for patients with chronic liver disease, such as deterioration of liver function and the need for liver transplantation [103,104]. It is reported that using preoperative transjugular intrahepatic portosystemic shunt (TIPS) can help reduce the postoperative risks in these patients [105,106]. Research has shown that bariatric surgeries, such as Sleeve Gastrectomy (SG) and Adjustable Gastric Banding (AGB), can significantly affect key metabolic and inflammatory markers (such as GLP-1) that are crucial in the development and progression of NAFLD and NASH [107]. Histological improvements in NASH after MBS are common, though some patients may experience worsening of liver fibrosis [107]. In summary, while MBS is not a panacea for liver disease, it can be a valuable tool in the management of obesity-related liver conditions, provided that the risks and benefits are thoroughly evaluated for each patient.

3.10. Fertility and reproductive system

MBS has been studied for its effects on reproductive health in both men and women.

Obesity can have a significant impact on male reproductive health, as it is associated with decreased sperm quality [15]. For men, while hormonal status generally improves after MBS, there have been observations of reductions in sperm parameters following the procedure [108–110]. This indicates a necessity for further investigations to understand the comprehensive implications of MBS on

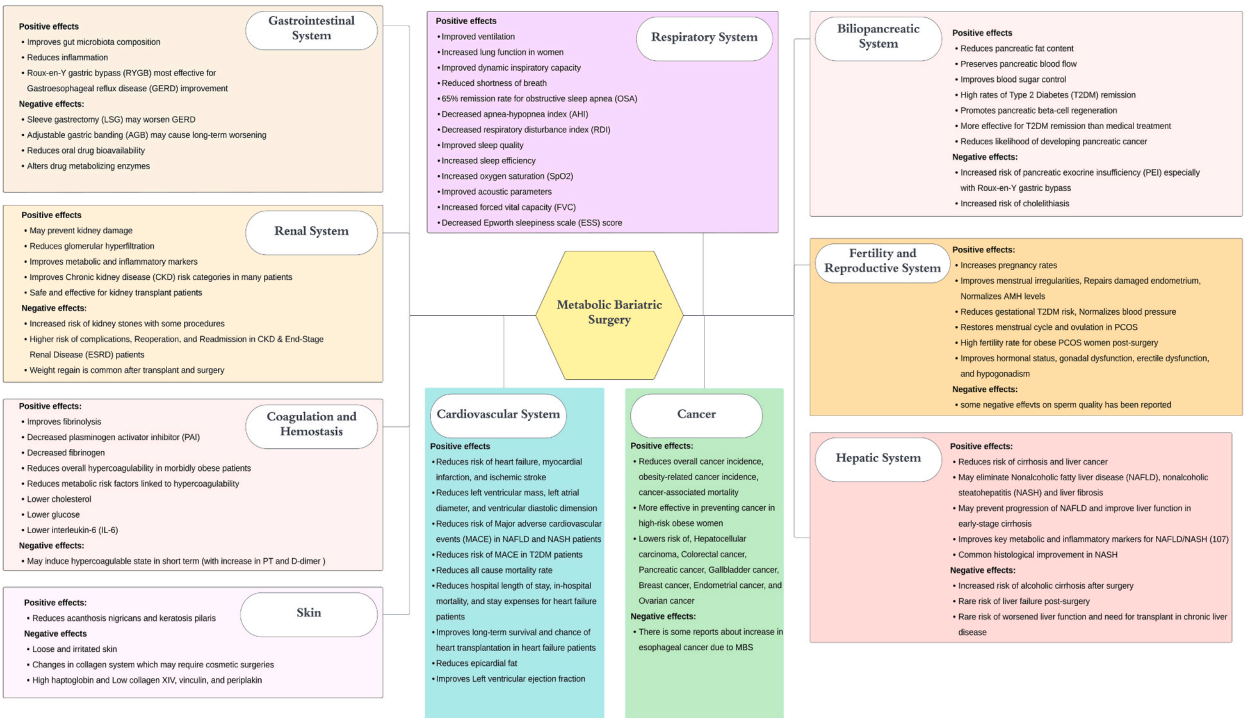

Fig. 1. Summary of the long-term effects of MBS on various body organs and diseases.

male reproductive health. In addition, obesity-associated gonadal dysfunction has been shown to improve post-surgery, with positive effects on hormonal, metabolic, and erectile dysfunction, as well as hypogonadism [111].

Obesity can have a significant impact on female reproductive health, as it is associated with menstrual cycle disturbances and exacerbation of Polycystic Ovary Syndrome (PCOS) symptoms [15]. MBS has been studied for its positive effects on reproductive health in women. Surgical interventions like MBS are considered beneficial for obese patients facing fertility issues [112–115]. MBS can improve a range of negative reproductive outcomes associated with obesity, such as menstrual irregularities, damage to the endometrium, and it can normalize Anti-Müllerian Hormone (AMH) levels, which are important for assessing ovarian reserve [112–115]. It also increases pregnancy rates, reduces the risk of gestational T2DM, and normalizes blood pressure [112–115]. Specifically addressing women with PCOS, MBS has demonstrated improvements in restoring the menstrual cycle and regular ovulation. The study showed a high fertility rate in obese women with PCOS post-surgery [116]. MBS is considered an effective treatment option for obese individuals with infertility [117]. However, risks such as malnutrition and non-adherence to postoperative guidelines can complicate outcomes [117].

4. Discussion

Metabolic bariatric surgery, while demonstrably effective in combating severe obesity and its associated comorbidities, extends beyond its primary function of weight reduction. Its impact transcends the gastrointestinal system, influencing various organ systems with both significant benefits and potential complications. This necessitates a comprehensive understanding of its multifaceted effects on the body, acknowledging both the potential for significant health improvements and the spectrum of potential adverse outcomes. To fulfill the goals of this research, Fig. 1 details the long-term impacts of bariatric surgery.

Bariatric surgery dramatically reduces the risk of heart failure, stroke, and myocardial infarction [17]. It improves heart function, lowers blood pressure, and even increases the chance of receiving a heart transplant for individuals with severe obesity [18,19,26]. Sleep apnea, a common and debilitating consequence of obesity, is effectively treated through bariatric surgery, leading to substantial improvements in sleep quality and breathing [46]. In overall, lung function also improves, reducing respiratory complications [45]. These procedures also positively impact the liver, reducing the risk of nonalcoholic cirrhosis and liver cancer [101].

MBS offers a good chance for type 2 diabetes remission [66]. Weight loss and metabolic changes improve pancreatic function, potentially reversing the disease and enhancing blood sugar control [65,66]. However, PEI is also a significant concern after bariatric procedures, particularly RYGB. Although studies have approved PERT for management of PEI [75,76], Research indicates that a substantial portion of patients might experience PEI following surgery, with studies reporting up to 31 % grappling with this issue [75,76]. Furthermore, the association between bariatric surgery and the development of cholelithiasis cannot be ignored. Individuals with obesity are already at a higher risk for gallstones, and bariatric procedures appear to exacerbate this risk further [81–85].

There are several reports that the risk of certain cancers, such as pancreatic ductal adenocarcinoma [73], hepatocellular carcinoma, colorectal cancer, pancreatic cancer and gallbladder cancer, breast cancer, endometrial cancer and ovarian cancer [57], decreases significantly after MBS. Conversely, a Study by Plat et al. suggests an increased risk of esophageal cancer development following bariatric surgery, particularly after RYGB, with a trend observed over recent decades [62]. The specific types of esophageal cancer observed, such as adenocarcinoma of the distal esophagus and Barrett's esophagus, point towards a potential link with GERD. While some patients experience GERD relief after bariatric surgery, others may see a worsening of this condition. The emergence of GERD is reported to be 9.3 % after LSG and 2.3 % after RYGB(32). It was also mentioned that LSG has been linked to a higher incidence of GERD than RYGB (OR = 5.2, $p < 0.001$) [32].

While successful weight loss after bariatric surgery often leads to a welcome improvement in skin conditions like acanthosis nigricans and keratosis pilaris [51], various dermatological concerns remain prevalent. Dermatological issues secondary to malnutrition and vitamin deficiency are important concerns [52]. The significant changes in skin tissue resulting from rapid weight loss require careful attention and management because loose and irritated skin may necessitate contouring surgeries, thus subjecting the patient to another surgical procedure.

Regarding kidneys, while it is reported that renal function improves, the risk of chronic kidney disease is reduced [88–90]; hypo-absorptive bariatric procedures may increase kidney stone formation [95].

For women facing fertility challenges due to obesity, bariatric surgery can regulate menstrual cycles, improve PCOS symptoms, and increase fertility rates [15,116]. On the contrary, there have been observations of reductions in sperm counts following MBS [108–110], although enhancements in hormonal, metabolic, and erectile dysfunction, as well as hypogonadism, have also been reported by other studies [111]. While the effects on sperm quality in men are still under investigation, hormonal improvements offer potential benefits.

5. Future directions

Long-term studies can assess the surgery's lasting impact, while personalized medicine approaches can tailor treatment plans. Mechanistic studies will improve our understanding of how surgery affects the body, and comparative studies can identify the most effective procedures. Integrating bariatric surgery with other therapies and addressing the obesogenic environment hold promise for a more multifaceted approach. Future research should also focus on psychological and social aspects, potential risks, quality of life, and economic implications to optimize patient care and healthcare resource allocation. Additionally, research into other novel non-surgical methods is crucial to identify long-term effects and provide an even wider range of options for personalized weight loss plans.

6. Conclusion

In conclusion, Metabolic Bariatric Surgery (MBS) impact extends far beyond weight loss, offering several improvements across various organ systems, leading to a healthier and more fulfilling life for individuals with severe obesity. However, potential risks and complications exist and these potential downsides highlight the importance of thorough pre-operative counseling and ongoing monitoring of patients who undergo these procedures. Careful patient selection, thorough preoperative evaluation, and meticulous and multi-disciplinary postoperative monitoring are crucial for maximizing positive outcomes and ensuring long-term health.

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Declaration of AI and AI-assisted technologies in the writing process

During the preparation of this work, the author(s) utilized Quillbot in scientific writing to enhance the readability and language of the manuscript. The author(s) applied human oversight and control throughout the process, carefully reviewing and editing the AI-generated content. After using this tool/service, the author(s) reviewed and edited the content as needed and take(s) full responsibility for the content of the publication.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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List of Abbreviation

AGB: Adjustable Gastric Banding
AHI: Apnea-Hypopnea Index
AMH: Anti-Müllerian Hormone
CHF: Congestive Heart Failure
CKD: Chronic Kidney Disease
CVD: Cardiovascular Disease
ESRD: End Stage Renal Disease
ESS: Epworth Sleepiness Scale
FVC: Forced Vital Capacity
GERD: Gastrosophageal Reflux Disease
HCC: Hepatocellular Carcinoma
LSG: Laparoscopic Sleeve Gastrectomy
LVEF: Left Ventricular Ejection Fraction
MACE: Major Adverse Cardiovascular Events
MBS: Metabolic Bariatric Surgery
MI: Myocardial Infarction
NAFLD: Nonalcoholic Fatty Liver Disease
NASH: Nonalcoholic Steatohepatitis
NYHA: New York Heart Association
OSA: Obstructive Sleep Apnea
PAI: Plasminogen Activator Inhibitor
PERT: Pancreatic Enzyme Replacement Therapy
PEI: Pancreatic Exocrine Insufficiency
PI: Prothrombin Time
RDI: Respiratory Disturbance Index
RYGB: Roux-en-Y Gastric Bypass
Sp02: Oxygen Saturation
T2DM: Type 2 Diabetes Mellitus