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Review

Bariatric Surgery as Immunometabolic Therapy: A Narrative Review of Mechanisms, Clinical Outcomes, and Future Precision Approaches

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Abstract: Obesity is a global health and economic burden that affects disadvantaged groups and increases healthcare use. It involves adipocyte hypertrophy/hypoxia, adipokine imbalance, immune cell recruitment, pro-inflammatory polarization, signaling activation, systemic inflammation, oxidative stress, insulin resistance, and a higher cardiometabolic risk. This review synthesizes bariatric surgery as an immunometabolic intervention, integrating mechanistic, clinical, and translational findings. A literature search of PubMed/MEDLINE, Scopus, and Web of Science (through 2025), supplemented by Google Scholar, included peer-reviewed human and animal studies on metabolic or immunological mechanisms; technical surgical reports and non-peer-reviewed sources were excluded. Bariatric surgery consistently achieves broader metabolic and immunomodulatory, sustained weight loss and improved glycemic control and comorbidity profiles. Diabetes improvements partially preceded major weight loss via enhanced enteroinsular signaling, altered bile acid pathways, and microbiome remodeling. Surgery reduces systemic inflammation, reprograms cytokines, improves immune cell phenotypes, and lowers oxidative stress, leading to antioxidant status recovery. Comparative evidence indicates an efficacy–risk gradient: laparoscopic adjustable gastric banding is least effective; laparoscopic sleeve gastrectomy offers intermediate benefits with favorable safety; Roux-en-Y gastric bypass is widely supported with strong outcomes and manageable risks; and biliopancreatic diversion with duodenal switch yields maximal benefit but higher adverse-event and malabsorption burden. Bariatric surgery is an immunometabolic intervention that induces immune and metabolic remodeling, disrupting the obesity–inflammation–insulin resistance cycle via multi-system remodeling.

Keywords: Obesity; Public Health; Chronic Disease; Lifestyle Changes; Pharmacotherapy; Inflammation

1. Introduction

Obesity is a significant global public health issue, with its prevalence increasing across regions, countries, and age groups. Recent data show a substantial increase, affecting hundreds of millions to over a billion adults worldwide. High rates are notable in Europe and the Americas, with growth in many low- and middle-income areas [1,2]. Urbanization, dietary changes, and lack of physical activity heavily influence these trends. Socioeconomic disparities worsen the issue, as obesity is more common among disadvantaged groups and is linked to lower education and socioeconomic status [3,4]. The economic impact is significant: obesity raises healthcare costs through increased

outpatient services, hospitalizations, medications, and indirect costs from decreased productivity, lost income, disability, and social transfers [5,6]. Consequently, healthcare systems face increasing pressure from obesity-related services and chronic disease management, with obesity significantly impacting national health expenditures and public budgets [5,6].

Obesity is a chronic disease affecting multiple systems and is associated with higher illness and death rates, especially cardiometabolic diseases and cancer [2]. Cardiovascular implications and mortality risks have been highlighted in a review of obesity phenotypes and cardiovascular risk [7]. Obesity-related metabolic issues, such as insulin resistance, high blood pressure, and abnormal lipid levels, are associated with coronary heart disease in an earlier cardiovascular metabolic syndrome analysis [8]. For children, a review of severe obesity underscores the development of type 2 diabetes (T2D) and its consequences, including stroke, heart attack, and sudden death [9]. Regarding cancer, inflammatory pathways linking obesity to liver and colorectal cancers have been explored in the Tumor Necrosis Factor-alpha (TNF-α)/interleukin-6 (IL-6) review [10], and the obesity-breast cancer connection has been examined [11]. An economically focused modeling study in Türkiye revealed significant costs and a notable portion of national health expenditure due to obesity [12].

Lifestyle changes are crucial for managing obesity; however, biological and environmental factors hinder their long-term effectiveness. Diet, exercise, and self-discipline can lead to short-term improvements, but weight regain is common, and maintaining these changes is challenging once support ends [13]. Obesity is a chronic condition in which appetite regulation, stress, and metabolic responses disrupt adherence, and environments that promote obesity hinder sustained changes [14]. Even when lifestyle interventions improve weight and risk factors, the benefits may fade, indicating that lifestyle therapy alone is often inadequate for lasting metabolic normalization [15]. Behavioral interventions support lifestyle changes but are limited by variability, accessibility, and sustainability. Self-monitoring, goal setting, feedback, and social support can enhance outcomes; however, the effects vary, and the optimal combinations for severe obesity remain unclear [16]. Behavioral programs often require ongoing clinician involvement, multidisciplinary support, and reinforcement, which are not easily accessible [16]. Disparities in participation, adherence, dropout rates, and effectiveness suggest that individuals with fewer resources benefit less, potentially worsening health disparities [17]. Even in successful studies, metabolic improvements may diminish post-intervention, with weight maintenance and insulin sensitivity gains often not persisting [18]. Thus, although beneficial, behavioral interventions are limited by relapse, implementation challenges, and varying responses.

Pharmacotherapy enhances outcomes and often leads to more significant short-term weight reduction than lifestyle changes alone; however, it has limitations. An ideal anti-obesity medication is still lacking, and long-term use requires oversight due to side effects, adherence challenges, and the need for lifestyle modification [19]. Weight regain is common after stopping treatment, even with drugs, highlighting the chronic suppressive nature of most pharmacological treatments [14,20]. Some medications may inconsistently affect metabolic outcomes, and certain treatments for diabetes management may cause weight gain [15]. Pharmacotherapy should be considered beneficial yet incomplete; it supports weight loss and metabolic regulation but does not address weight regain and rarely provides a lasting solution [21,22]. The primary limitation of all three approaches is that obesity is a chronic, biologically defended condition. Lifestyle modifications, behavioral therapy, and pharmacotherapy offer significant benefits, but long-term success relies on continuous support, personalized treatment, and combined strategies rather than any single approach [23].

Obesity is now understood as an immunometabolic condition characterized by inflammation and metabolic imbalance. Enlarged fat cells experience local hypoxia, stress, and dysfunction, which alter the stromal-vascular environment. This recruits and activates macrophages, T cells, dendritic cells, and other immune cells, thereby enhancing inflammatory signaling. In obese adipose tissue, pro-inflammatory mediators such as TNF-α, IL-6, interleukin-1β (IL-1β), and monocyte chemoattractant protein-1 (MCP-1) increase, whereas anti-inflammatory adipokines such as adiponectin decrease, promoting inflammation [24, 25]. This is not just local; adipose-derived cytokines and adipokines have systemic effects, linking excess fat to insulin resistance and metabolic issues [26]. Adipose tissue functions as an endocrine-immune center, converting excess nutrients into inflammatory and metabolic signals. Enlarged adipocytes emit signals that attract pro-inflammatory macrophages and promote pro-inflammatory (M1) macrophages-like polarization, while immune cell interactions strengthen pathways that sustain cytokine production and fibrosis [25]. Hypoxia-inducible pathways worsen adipokine imbalance and impair insulin signaling, cre-

ating a cycle in which inflammation and metabolic stress exacerbate each other [27]. Thus, obesity is a chronic inflammatory disease in which adipose tissue orchestrates endocrine, immune, and metabolic dysfunction [24,28].

Bariatric surgery is the most effective solution for severe obesity, achieving greater and longer-lasting weight loss than traditional treatments. Surgery recipients lose more weight than those who only make lifestyle changes or receive medical care, with one study noting a 29.6% weight reduction post-surgery versus 11.3% with lifestyle changes and 1.6% with conventional therapy over two years [29]. Other studies have highlighted bariatric surgery as the most powerful obesity treatment, with modern metabolic surgery resulting in sustained weight loss of 20–30% [30]. This is crucial in severe obesity cases, where non-surgical methods often lead to modest weight loss. In addition to weight loss, bariatric surgery offers better metabolic outcomes by modifying the disease. Clinical trials have shown higher remission rates for T2D, better glycemic control, and reductions in hypertension, dyslipidemia, and metabolic syndrome postoperatively [31,32]. The benefits include improvements in insulin sensitivity, β-cell function, gut hormone signaling, bile acid metabolism, and glucose regulation [33]. The literature supports bariatric surgery as the preferred treatment for morbid obesity, surpassing conservative methods [29,30]. Yadav et al. showed improvements in insulin resistance and endothelial dysfunction after RYGB [34]. Iqbal et al. noted the metabolic and cardiovascular benefits of this diet, such as T2D remission and reduced inflammation [35]. Guo et al. provided evidence that surgery alters the gut microbiome [36]. Kruljac et al. discuss its metabolic benefits involving hormonal and gut mechanisms [37]. A significant gap is the focus on clinical outcomes, such as weight reduction, while immunological impacts are less examined. Surgery reduces chronic inflammation, with decreases in CRP, IL-6, leukocytes, ferritin, and cytokines [38,39]; however, the biological basis is not fully understood. Reviews highlight the unclear mechanisms linking surgery to adipokines, inflammatory signaling, and insulin resistance, indicating more progress in documenting outcomes than in elucidating processes [40]. More studies are needed to investigate immune modulation and related biological processes after surgery.

This narrative review compiles and analyzes the latest evidence on bariatric surgery from an immunometabolic perspective, merging mechanistic insights with clinical outcomes. This review clarifies how bariatric procedures influence inflammatory pathways, immune cell behavior, and metabolic signaling, thereby improving obesity-related health issues. By connecting surgical practices with immunological insights, this review highlights the systemic immunomodulatory approach of bariatric surgery rather than just a weight-loss method. It explores new directions in precision medicine, such as biomarker-driven patient selection, microbiome-based treatments, and artificial intelligence, to enhance results. This comprehensive approach aims to establish a foundation for future research and clinical advancements, promoting bariatric surgery as an immunometabolic therapy.

2. Methods

This narrative review synthesizes evidence on the immunometabolic effects of bariatric surgery in obesity, integrating mechanistic studies, clinical trials, observational research, and translational immunology findings. This approach provides a comprehensive understanding of metabolic, endocrine, and immune interactions, beyond a purely systematic framework.

A literature search in PubMed/MEDLINE, Scopus, and Web of Science identified studies published from January 2000 to June 2025. Publications were also sought through manual searches of reference lists and Google Scholar. This process yielded 512 records in total. After duplicate removal and title/abstract screening, 420 records were evaluated for eligibility. Among these, 62 articles were assessed, and 22 studies were selected for narrative synthesis. Additional searches using Google Scholar revealed emerging evidence. Keywords and MeSH terms such as "obesity," "immunometabolism," "adipose tissue inflammation," "bariatric surgery," "Roux-en-Y gastric bypass," "laparoscopic sleeve gastrectomy," "cytokines," "gut microbiome," "GLP-1," and "insulin resistance" were used to search the literature. Boolean operators refined the search results, and reference lists of the selected studies were reviewed for additional publications.

Studies were selected based on specific criteria, including immunometabolic processes, inflammatory pathways, metabolic results, and recovery post-bariatric surgery. Evidence synthesis merged clinical, molecular, and translational insights into inflammation linked with obesity and metabolic changes. Emphasis was placed on randomized controlled trials, prospective cohort studies, systematic reviews, meta-analyses, and high-quality mechanistic investigations for evidence of metabolic and immunological effects. Emerging experimental studies were included if they provided insights not covered by clinical studies. Studies focusing solely on surgical techniques

without metabolic or immunological outcomes, case reports, editorials, and non-peer-reviewed sources were excluded from the review. The selection process began with a review of the titles and abstracts, followed by an examination of the full texts. The data were categorized into thematic areas: immunopathogenesis of obesity, immune cell dynamics, inflammatory signaling pathways, gut hormone modulation, microbiome changes, cytokine reprogramming, oxidative stress, and comparative outcomes of bariatric procedures. The findings, mechanisms, and clinical implications were organized into thematic sections and summary tables.

The qualitative synthesis method merged findings from various studies. The evidence was divided into mechanistic, clinical, and translational categories to provide a comprehensive view of bariatric surgery as an immunometabolic intervention. A comparative analysis of common bariatric procedures, including RYGB, laparoscopic sleeve gastrectomy (LSG), laparoscopic adjustable gastric banding, and biliopancreatic diversion with duodenal switch (BPD/DS), focused on metabolic effectiveness, immunological impact, and safety profiles.

We focused on randomized controlled trials and prospective cohort studies with follow-up periods of over six months. The lack of a formal risk of bias assessment is a limitation, as discussed in the limitations section. Priority was given to randomized controlled trials, meta-analyses, and recent publications with clear methodologies and reproducible results, ensuring reliable and clinically relevant evidence was obtained.

This review relied solely on previously published literature; therefore, no ethical approval or informed consent was required. However, narrative designs may introduce selection bias and limit quantitative comparability due to variations in study designs, populations, and outcome measures. Despite these limitations, this methodology provides a solid framework for integrating diverse evidence and offers valuable insights into the immunometabolic mechanisms underlying the effects of bariatric surgery.

3. Immunopathogenesis of Obesity

3.1. Adipose Tissue Dysfunction and Hypoxia

Obesity is a chronic inflammatory condition in which adipose tissue acts as an endocrine and immune organ, not just for energy storage. Enlarged adipocytes experience hypoxia, activating pathways such as Hypoxia-inducible factor-1α (HIF-1α) (**Table 1**). This stress alters adipocyte function, shifting the adipokine profile to a pro-inflammatory state with increased IL-6, leptin, MCP-1, and TNF-α, and reduced adiponectin levels [28]. These changes contribute to the chronic, low-grade systemic inflammation typical of obesity.

Table 1. Immunopathogenesis of obesity.

Mechanism	Key Features	Immunological Impact	Metabolic Consequences
Adipocyte hypertrophy with secondary local hypoxia	Enlarged fat cells	Activation of HIF-1α signaling, adipokine dysregulation, macrophage recruitment, and pro-inflammatory cytokine production	Adipokine imbalance
Hypoxia (Consequence of hypertrophy)	Enlarged adipocytes outgrow capillary supply; HIF-1α activation	Activation of inflammatory pathways	Insulin resistance
Macrophage infiltration	Crown-like structures	M1 polarization	Chronic inflammation
Cytokine release	↑ TNF-α, IL-6, IL-1β, MCP-1	Systemic inflammation	Metabolic syndrome
Adipokine dysregulation	↓ Adiponectin, ↑ leptin	Loss of anti-inflammatory signaling	Endothelial dysfunction

Note: HIF-1α = Hypoxia-inducible factor 1-alpha; TNF-α = Tumor Necrosis Factor-alpha; IL-6 = Interleukin-6; IL-1β = Interleukin-1β; MCP-1 = Monocyte Chemoattractant Protein-1.

A crucial aspect of this process is the recruitment of immune cells, particularly macrophages. Dysfunctional adipocytes emit signals that attract monocytes to the adipose tissue, forming crown-like structures around dying adipocytes with a pro-inflammatory phenotype [41]. These macrophages produce TNF-α, IL-1β, IL-6, and MCP-1, intensifying inflammation and adipocyte dysfunction [41,42]. Evidence suggests that macrophage buildup results from bloodstream recruitment and local proliferation during early obesity.

Inflammation is heightened by communication between adipocytes and immune cells. Pro-inflammatory pathways, such as Nuclear Factor kappa B (NF-κB) and c-Jun N-terminal Kinase (JNK), encourage cytokine release and im-

mune activation, while macrophage polarization shifts from anti-inflammatory/pro-resolving (M2) macrophages-like to M1-like in obesity [43] (**Table 2**). Hypoxia alters macrophage metabolism, increasing glycolytic activity and cytokine production, with HIF-related pathways regulating inflammation [44, 45]. This interaction between stressed adipocytes and immune cells creates a self-sustaining inflammatory cycle that worsens adipose dysfunction [46].

Table 2. Key immunometabolic pathways in obesity.

Pathway	Trigger	Effect
Nuclear Factor kappa B	Cytokines, stress	Pro-inflammatory gene activation
c-Jun N-terminal Kinase	Lipotoxicity	Insulin resistance
Toll-like Receptor 4	Free fatty acids	Innate immune activation
NOD-, LRR- and pyrin domain-containing protein 3	Metabolic stress	Interleukin-1β production
Mitogen-Activated Protein Kinase	Cellular stress	Cytokine signaling

The effects of adipose inflammation extend systemically. Pro-inflammatory cytokines and adipokines enter the bloodstream, causing chronic, low-grade systemic inflammation that contributes to insulin resistance, dyslipidemia, endothelial dysfunction, and cardiometabolic risk. Obesity represents immunometabolic dysregulation, where hypertrophy, hypoxia, macrophage infiltration, cytokine release, and systemic inflammation are interconnected, linking excess adiposity to T2D, cardiovascular disease, and other complications [41,47].

3.2. Immune Cell Dynamics in Obesity

In obesity-related adipose tissue inflammation, immune cell behavior reveals how excess nutrient storage causes ongoing metabolic problems. Healthy adipose tissue macrophages are M2-like and anti-inflammatory, aiding tissue repair and insulin sensitivity through IL-4 and IL-10 signaling (**Table 3**). Obesity promotes pro-inflammatory M1-like macrophages that release TNF-α, IL-6, IL-1β, and MCP-1, increasing insulin resistance and tissue damage [47]. This polarization shift is driven by lipid-filled adipocytes emitting free fatty acids and chemotactic agents, attracting monocytes, raising the M1/M2 macrophages ratio, and forming crown-like structures around dying adipocytes [25,48]. An imbalance in adaptive immunity supports macrophage reprogramming: obesity increases T helper 1 (Th1) cell and T helper 17 (Th17) cell responses, whereas Th2 and Treg populations decrease, weakening anti-inflammatory signals for M2 polarization [49,50]. Other immune cells, such as B cells, neutrophils, mast cells, eosinophils, and Natural Killer T cells, alter cytokine availability and antigen presentation, perpetuating inflammation [50].

Table 3. Immune cell dynamics in obesity.

Cell Type	Lean State	Obese State	Functional Outcome
Macrophages	M2 (anti-inflammatory)	M1 (pro-inflammatory)	Insulin resistance
T cells	Th2, Treg dominant	Th1, Th17 dominant	Chronic inflammation
B cells	Regulatory	Pro.-inflammatory	Cytokine amplification
Neutrophils	Low activity	Increased recruitment	Tissue damage
Natural Killer T cells	Balanced	Dysregulated	Immune imbalance

3.3. Inflammatory Signaling Pathways

Cellular immune reorganization is sustained by inflammatory signaling pathways, notably NF-κB, JNK, Mitogen-Activated Protein Kinases, IκB kinase β, Toll-like Receptor 4-related signaling, and NOD-, LRR- and pyrin domain-containing protein 3 inflammasome [51]. These pathways merge metabolic stress signals, such as saturated fatty acids and adipokine imbalance, with immune activation, maintaining cytokine production, oxidative stress, and disrupted insulin signaling in adipocytes and immune cells [52]. This feedback loop attracts and activates immune cells, exacerbating adipose tissue inflammation and systemic low-grade inflammatory responses. These processes suggest that obesity is not just excess energy but an immunometabolic disease marked by leukocyte reprogramming and chronic inflammatory pathway activation [48,53].

4. Mechanisms of Bariatric Surgery-Induced Immunometabolic Remodeling

4.1. Gut Hormonal Modulation after Bariatric Surgery

Bariatric surgery alters gut hormone signaling to enhance metabolic health beyond that achieved by weight reduction. After RYGB and LSG, postprandial glucagon-like peptide-1 (GLP-1) levels significantly increase, boosting the incretin response, promoting insulin secretion, enhancing β-cell function, and reducing postprandial blood sugar spikes [54]. Concurrently, ghrelin levels generally decrease, reducing hunger and calorie intakes [55]. Gastric bypass studies show that the swift increase in GLP-1 decreases appetite, and inhibiting gut hormone responses can restore appetite and food intake, underscoring their role in post-surgical metabolic regulation [56] (**Table 4**). These changes in GLP-1 and ghrelin explain why bariatric surgery improves insulin sensitivity, glucose regulation, and diabetes outcomes through neurohormonal remodeling of the enteroinsular axis [57].

Table 4. Mechanisms of bariatric surgery in immunometabolism.

Mechanism	Biological Effect	Clinical Outcome
Gut hormones (increased glucagon-like peptide-1 and ghrelin)	Improved insulin secretion, appetite suppression	Diabetes remission
Microbiome remodeling	Increased beneficial bacteria	Reduced inflammation
Bile acid signaling	Farnesoid X Receptor/Takeda G Protein-Coupled Receptor 5 activation	Improved glucose metabolism
Adipose tissue reduction	Decreased inflammatory cytokines	Improved insulin sensitivity
Immune modulation	Shift to anti-inflammatory profile	Reduced systemic inflammation

4.2. Gut Microbiome and Bile Acid Remodeling

Bariatric surgery rapidly alters the gut microbiome by changing nutrient flow, stomach acidity, and bile acid circulation, thereby creating a unique microbial community post-surgery. Reviews and studies consistently show an increase in Bacteroidetes, Fusobacteria, Verrucomicrobia, and Proteobacteria, while Firmicutes-associated groups such as Clostridiales, Blautia, and Dorea decrease, although the extent of diversity change is debated [36,58]. These changes are metabolically significant, affecting short-chain fatty acids and bile acids, which influence energy expenditure, glucose metabolism, and adipose tissue function [59,60]. The rise in circulating bile acids post-surgery is linked to higher GLP-1 levels and better postprandial blood sugar control, suggesting that microbial changes enhance incretin signaling and insulin sensitivity via FXR and TGR5 pathways [61, 62]. Immunologically, the post-surgery microbiome may lower inflammation by improving gut barrier integrity, reducing bacterial product translocation, and decreasing innate immune activation. Bile acids also participate in immune system communication, aiding immune surveillance and inflammation regulation [36,63]. Bariatric surgery reconfigures the gut ecosystem, linking microbial, endocrine, and immune pathways, leading to lasting improvements in metabolic balance [58,64].

4.3. Cytokine Reprogramming and Immune Modulation

Bariatric surgery reduces systemic inflammation by counteracting obesity-related immune triggers, notably from visceral fat, and by altering cytokines to a less inflammatory state. Prospective studies have shown postoperative decreases in hs-CRP, TNF-α, IL-1β, IL-6, IL-8, and Th1- and Th17-related mediators, such as IFN-γ, IL-12, IL-18, and IL-23, indicating subdued innate and adaptive immune responses [65] (**Table 5**). Anti-inflammatory effects follow metabolic improvements: insulin resistance and lipid profiles improve within 3 months, while significant inflammatory marker reductions occur at 6 months, showing that metabolic balance restoration aids in systemic inflammation resolution. Long-term data show sustained decreases in CRP and IL-6 levels years post-surgery, with better oxidative stress profiles [66], and broader inflammation assessments show significant cytokine reductions 12 months post-RYGB or LSG [67]. On a cellular level, bariatric surgery normalizes immune cell composition: T and B cell phenotypes shift towards lean individuals, although some cytokine-producing abilities recover more slowly, suggesting that complete immunological remodeling takes time [68]. Overall, bariatric surgery mitigates chronic low-grade inflammation by reducing adipose tissue cytokine production, enhancing insulin sensitivity, and rebal-

ancing circulating cytokines and immune cell function [34,38].

Table 5. Effects of bariatric surgery on cytokines and inflammation.

Marker	Pre-Surgery	Post-Surgery	Effect
CRP	High	Reduced	Lower systemic inflammation
TNF-α	Elevated	Decrease following surgery but magnitude varies by procedure and follow-up duration	Reduced insulin resistance
IL-6	Elevated	Decrease following surgery; however, some studies report persistent elevation during early postoperative periods	Improved metabolic profile
IL-1β	Elevated	Reduced	Decreased inflammation
IL-10	Tends to increase	Tends to increase following surgery, although findings are not uniform across studies	Anti-inflammatory shift

Note: T2D = Type 2 diabetes; CRP = C-reactive protein; TNF-α = Tumor Necrosis Factor-alpha; IL-6 = Interleukin-6; IL-1β = Interleukin-1β; IL-10 = Interleukin-10.

4.4. Reduction of Oxidative Stress

Bariatric surgery reduces oxidative stress by disrupting the obesity-induced cycle of excessive reactive oxygen species, weakening antioxidant defenses, and causing tissue damage, thereby enhancing redox balance and metabolic function. Longitudinal studies have shown that patients have increased total antioxidant status post-surgery and reduced inflammatory markers, such as CRP and IL-6, indicating decreased oxidative load on the adipose tissue, liver, and blood vessels [66]. Research shows declines in lipid peroxidation and protein carbonylation, along with changes in glutathione and ascorbic acid levels, suggesting that the antioxidant system recovers as the pro-oxidant environment of severe obesity diminishes [69,70]. This is crucial because oxidative stress worsens insulin resistance and liver stress; when oxidative damage decreases post-surgery, insulin sensitivity and glycemic control improve, and features of metabolic syndrome often decrease [71]. Thus, a reduction in oxidative stress after surgery is a significant factor in improving long-term cardiometabolic health.

5. Comparative Effectiveness of Bariatric Procedures

5.1. Comparative Analysis of Bariatric Procedures

RYGB, LSG, laparoscopic adjustable gastric banding (LAGB), and BPD/DS differ in their effects on gastrointestinal structure and nutrient flow, which affect their effectiveness (**Table 6**). RYGB and BPD/DS are the most transformative, combining restriction with foregut exclusion and distal nutrient delivery, rapidly changing incretin secretion, bile acid signaling, and nutrient processing. LSG is mainly restrictive but triggers significant endocrine effects, whereas LAGB is the least disruptive to intestinal physiology [72,73]. Studies have shown that RYGB and LSG enhance glucose regulation, with RYGB often yielding stronger initial insulin responses. The literature on insulin resistance places RYGB and BPD ahead of LSG and LAGB in terms of early metabolic improvements [73].

Table 6. Comparative analysis of bariatric procedures.

Procedure	Mechanism	Weight Loss	Metabolic Effect	Immunological Effect	Risk Profile
RYGB	Restrictive + malabsorptive	High (20–30%)	Strong diabetes remission	Strong anti-inflammatory	Moderate risk
LSG	Restrictive + hormonal	Moderate-high	Good metabolic effect	Moderate immune modulation	Lower risk
LAGB	Restrictive	Low-moderate	Limited	Minimal	Lowest short-term risk
BPD/DS	Strong malabsorptive	Very high	Most potent	Strong immune modulation	Highest risk

Note: RYGB = Roux-en-Y Gastric Bypass; LSG = Laparoscopic Sleeve Gastrectomy; LAGB = Laparoscopic Adjustable Gastric Banding; BPD/DS = Biliopancreatic Diversion with Duodenal Switch.

Immunologically, all procedures reduce obesity-related inflammation; however, bypass surgeries have broader effects on adipose tissue biology, gut signaling, and microbiome-related metabolites. Reviews have reported re-

ductions in inflammatory markers and improved organ communication post-surgery, with benefits beyond weight loss [72]. This results in reduced systemic inflammation, decreased cytokine signaling, and improved metabolic tone, especially after RYGB and BPD/DS, which alter nutrient exposure more significantly than LAGB [74,75]. LSG enhances inflammatory status; however, lacking a major malabsorptive component, its effects are intermediate between bypass procedures and LAGB [76].

RYGB and BPD/DS typically surpass LSG and LAGB in terms of weight loss and diabetes remission, despite increased nutritional and surgical complexity. Long-term studies have shown that RYGB results in more weight loss than LAGB and better resolution of metabolic syndrome. Network meta-analyses ranked RYGB above BPD and LSG, with LAGB ranked lowest for cardiometabolic outcomes [32,77]. BPD/DS is often most effective for severe obesity, leading to greater body mass index reduction and improved glycemic and lipid control than RYGB, although with more adverse events [78]. LSG provides sustained weight loss and glycemic benefits, sometimes nearing RYGB in mid-term outcomes, but is generally less effective for advanced metabolic diseases [76]. LAGB aids in weight reduction and comorbidity improvement; however, its impact is smaller and more reliant on long-term adherence and device management [79].

However, their safety profiles differ. LAGB is the least invasive and historically safest short-term procedure; however, device-specific complications such as slippage, erosion, and reoperation reduce its long-term appeal [79]. LSG has a more favorable safety profile than RYGB, with fewer long-term reinterventions and reduced nutritional risk, although it still involves surgical risks and may require revision for inadequate weight loss or reflux issues [76,79]. RYGB is more technically challenging, posing a higher risk of micronutrient deficiency, particularly vitamin B12, with internal hernia and bowel complications. It remains effective with acceptable risk in experienced centers [79,80]. BPD/DS offers the strongest metabolic effect but the highest malabsorption-related concerns and adverse events, and is suitable for patients needing maximal weight loss and glycemic benefits with lifelong follow-up [78,81].

Overall, the comparison shows a classic efficacy-versus-risk gradient: LAGB offers procedural simplicity but the weakest metabolic impact; LSG is intermediate with good durability and safety; RYGB is balanced, offering strong metabolic benefits with manageable risk; and while BPD/DS often results in significant, lasting weight loss and metabolic enhancements, its malabsorptive aspect increases the risk of serious nutritional issues, such as protein-calorie malnutrition, deficiencies in fat-soluble vitamins (A, D, E, and K), iron deficiency, calcium imbalance, and secondary metabolic bone disease. Therefore, thorough long-term nutritional monitoring and supplementation are crucial after the procedure [72,77,78].

5.2. Roux-en-Y Gastric Bypass as a Widely Established Procedure

RYGB is a leading bariatric surgery due to its lasting weight loss, metabolic enhancement, and changes in the endocrine and immune systems. Unlike procedures that only restrict food intake, RYGB alters nutrient pathways, enhancing glucose metabolism and appetite control. It is often regarded as a benchmark bariatric procedure for severe obesity because of its extensive evidence base and durable metabolic outcomes, surpassing less effective procedures such as gastric banding. Its superiority stems from the metabolic reprogramming of the gut, liver, fat tissue, and pancreas [82].

RYGB is metabolically effective because it boosts incretin signaling and insulin dynamics. In a study comparing RYGB with LSG, RYGB showed a faster insulin response, indicating unique metabolic benefits. The metabolic benefits of bariatric surgery are partly due to increased GLP-1 secretion post-meals, enhancing insulin secretion, satiety signaling, and blood sugar control. However, fasting GLP-1 levels may remain stable or vary across studies [83]. Long-term research has shown sustained benefits in diabetes management, body weight, and metabolic syndrome markers, reinforcing its status as the standard treatment [84].

Immunologically, RYGB reduces inflammation associated with severe obesity and shifts immune cell function to a less proinflammatory state. Postoperative studies have shown reduced inflammatory cytokine levels and increased IL-10-associated regulatory B cells [85]. RYGB partially reprograms immune cell interactions towards regulation, disrupting the obesity–inflammation–insulin resistance cycle [86].

The combined metabolic and immunological effects of RYGB make it highly effective and enduring. Its benefits stem from integrated mechanisms, including changes in GLP-1 and peptide tyrosine tyrosine, bile acid signaling, gut microbiota, nutrient sensing, and improved insulin sensitivity, beyond mere restriction [82,83]. It has a more established evidence base than newer procedures, reinforcing its status in severe obesity and diabetes remission.

Despite the nutritional and surgical risks, its effectiveness, durability, and safety are persuasive, especially for patients prioritizing metabolic benefits [87].

6. Clinical Immunometabolic Outcomes

6.1. T2D Remission

A comprehensive examination of the impact of bariatric surgery on diabetes remission shows that initial glucose regulation improvements occur before significant weight loss and are linked to changes in gastrointestinal hormone secretion. Later effects result from reduced body fat and improved insulin sensitivity [88]. Another review outlined the roles of intestinal hormones, bile acids, gut microbiota, adipose tissue, and inflammatory pathways in post-surgery diabetes remission [89].

Review by Hutch and Sandoval of GLP-1 highlights how RYGB and LSG increase post-meal GLP-1 levels, improving glucose metabolism before major weight loss [90]. Research on GLP-1 physiology emphasizes its role in normal glucose tolerance and metabolic response after surgery [91].

Liu et al.'s review argues that bariatric surgery addresses obesity and T2D through microbiota-bile acid interactions and FXR signaling [82]. Similarly, Tu et al. emphasized the role of bile acids, GLP-1/PYY, and gut microbiota as key metabolic effect mediators after RYGB and LSG [92].

6.2. Hypertension and Cardiovascular Health

Bariatric surgery improves hypertension and cardiovascular health by reversing chronic inflammation linked to severe obesity. Visceral adipose tissue releases cytokines and adhesion molecules, causing endothelial dysfunction, vascular stiffness, renal stress and sympathetic activation. Surgery reduces this inflammatory burden, with studies showing improvements in blood pressure and inflammatory biomarker levels. A study found that RYGB reduced mean arterial pressure and inflammatory mediators such as CRP, MCP-1, and MIF, indicating that blood pressure improvements are linked to reduced inflammation, not just weight loss [93].

These immune changes restore vascular homeostasis. By reducing inflammation, bariatric surgery enhances endothelial signaling and may decrease immune cell-driven vascular remodeling, thereby improving vascular reactivity. A study showed that RYGB reduced CRP, MCP-1, ICAM-1, E-selectin, and P-selectin levels, with improved insulin resistance and endothelial dysfunction, especially in the first six months [40]. Zhou et al. reported decreases in hs-CRP and ICAM-1, reinforcing that bariatric surgery reduces vascular inflammation and enhances endothelial health [94].

The importance of immune modulation in the cardiovascular system is significant. Reviews note that bariatric surgery resolves comorbidities such as hypertension, left ventricular hypertrophy, nephropathy, and other cardiovascular risks, extending benefits beyond weight loss [79]. Recent evidence has shown that surgery lowers the odds of hypertension and cardiovascular disease, reducing all-cause and cardiovascular mortality [95]. These data support a model in which bariatric surgery shifts the body from a proinflammatory state to a less inflammatory vascular phenotype, improving blood pressure control and reducing long-term cardiovascular risk [34].

6.3. Systemic Benefits beyond Weight Loss

Bariatric surgery offers systemic benefits beyond weight loss by altering the inflammatory and metabolic environments in patients with severe obesity (**Table 7**). Obesity is driven by immune activation in adipose tissue and disrupted adipokine signaling, fostering insulin resistance and cardiometabolic issues [40,96]. adaptive immunity, with reduced CD4+ and CD8+ T-cell counts, a lower Th1/Th2 ratio, increased regulatory B cells, and diminished cytokine secretion [40]. These shifts are linked to better insulin sensitivity, glucose regulation, and reduced oxidative stress, suggesting that bariatric surgery is a metabolic-immune intervention rather than just restrictive [40].

Table 7. Systemic benefits of bariatric surgery.

System	Effect
Metabolic	Improved insulin sensitivity, glucose control
Cardiovascular	Reduced blood pressure, endothelial function improvement
Immune	Reduced chronic inflammation

Table 7. *Cont.*

System	Effect
Endocrine	Hormonal normalization
Gastrointestinal	Microbiome restoration

These effects clarify the stabilization of cardiometabolic health after surgery. Reviews have highlighted reduced systemic and tissue inflammation, improved dyslipidemia and hypertension, slower atherosclerosis, and reduced cardiovascular and all-cause mortality after the procedures [35]. Initially, postoperative changes in gut hormone signaling, bile acid metabolism, glucose transporter expression, and microbiome remodeling occur, while long-term benefits are due to sustained adiposity and reduced inflammatory load [35,97]. Thus, bariatric surgery transitions the body from a proinflammatory, insulin-resistant state to a stable metabolic profile with reduced cardiovascular risk and enhanced long-term health [35,98].

7. Bariatric Surgery as an Immunometabolic Immunotherapy

7.1. Immunometabolic Mechanisms

Bariatric surgery, a non-drug immunotherapy, reduces fat mass and disrupts pathways that maintain chronic inflammation in patients with severe obesity. Obesity is linked to chronic immune activation, pro-inflammatory T and B cells, increased cytokine levels, and oxidative stress, contributing to insulin resistance and cardiometabolic issues [96]. Post-surgery, inflammation shifts to a less active state: research shows decreases in inflammatory biomarkers and partial normalization of lymphocyte composition, including recovery of CD4+ Treg levels and changes in B-cell and T-cell phenotypes, although some cytokine functions may take longer [65, 99]. Bariatric surgery also enhances intestinal immune regulation by boosting IgA responses to pro-inflammatory microbial components, suggesting a strengthened mucosal immune defense [100]. These findings support the notion that bariatric surgery acts as an upstream partial immune remodeling, reducing immune dysfunction triggers rather than targeting a single inflammatory mediator [101].

7.2. Comparison of Pharmacological Therapies

Compared to traditional immunomodulatory therapies, bariatric surgery is broader, systemic, and potentially more durable (**Table 8**). Pharmacological immunomodulators target one cytokine, receptor, or pathway, whereas bariatric surgery affects adipose tissue inflammation, gut hormone signaling, bile acid metabolism, microbial ecology, and immune cell metabolic programming [102, 103]. This multifaceted remodeling is crucial, as the reduction in inflammatory markers is accompanied by improved metabolic stability, endothelial function, and insulin sensitivity, indicating that immune modulation is part of a broader restoration of homeostasis [39]. Furthermore, microbiome-linked metabolites post-surgery can re-educate immunity; post-bariatric microbial communities and their branched-chain amino acid metabolites enhance antitumor immunity and improve the response to immune checkpoint blockade in preclinical models [104,105]. Thus, bariatric surgery should be considered not only as a weight-loss procedure but also as a potent immunometabolic therapy, broader than conventional immunomodulatory approaches, targeting the pathological host state [96,105]. The interplay between visceral adiposity, obesity, and insulin resistance forms a self-sustaining pathological cycle that conventional treatments fail to adequately interrupt (**Figure 1**).

Table 8. Bariatric surgery versus immunometabolic intervention.

Feature	Bariatric Surgery	Pharmacotherapy
Target	System-wide	Specific pathway
Duration	Long-term	Temporary
Mechanism	Multi-pathway	Single pathway
Effect on inflammation	Broad suppression	Selective
Sustainability	High	Moderate
Cost-effectiveness	Generally favorable long-term cost-effectiveness in many healthcare system, although results vary by region and healthcare model	Variable

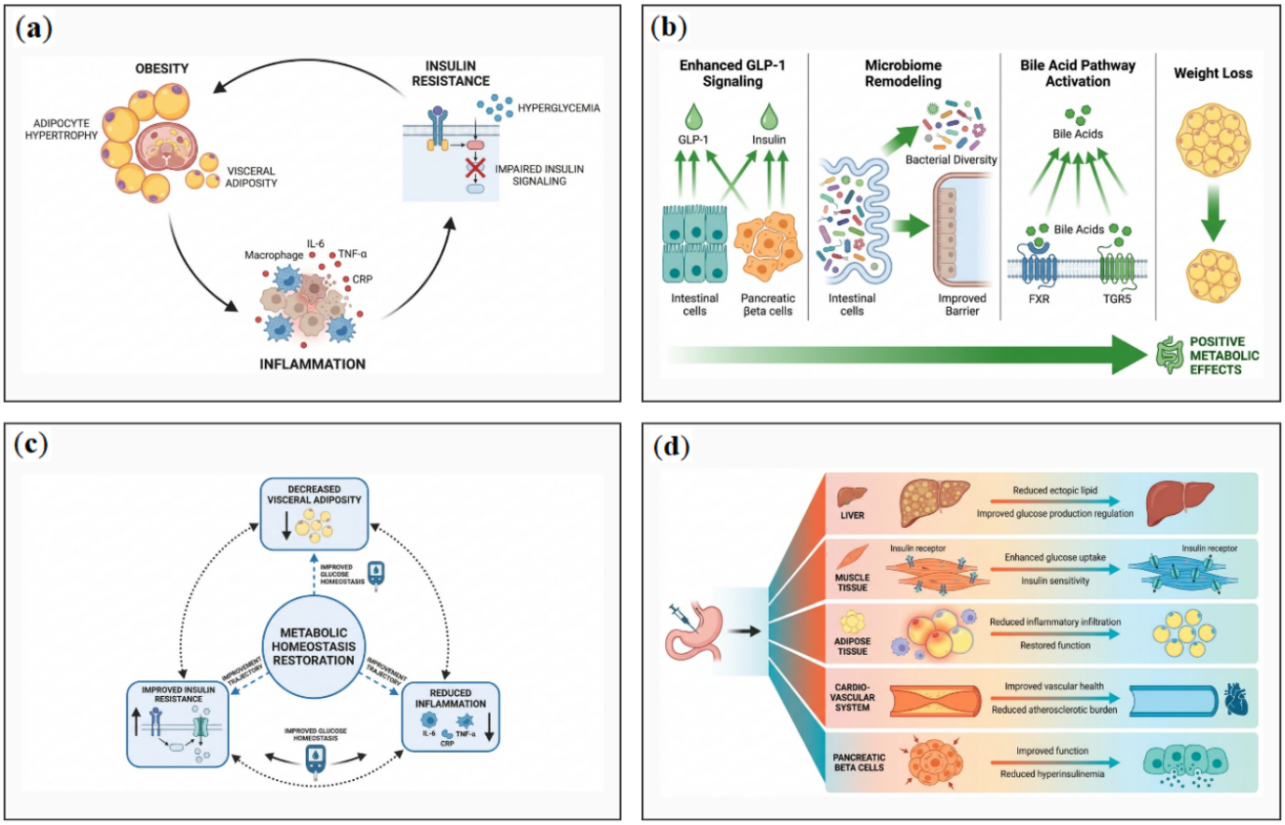

Figure 1. Immunometabolic pathways linking obesity, inflammation, insulin resistance, and the impact of bariatric surgery. (**a**) Obesity-linked dysfunction. Adipocyte enlargement and visceral fat increase cause low-grade inflammation, marked by macrophage infiltration and pro-inflammatory agents like IL-6, TNF-α, and CRP. This hinders insulin signaling, causing insulin resistance and hyperglycemia and creating a cycle of metabolic dysfunction. (**b**) Post-bariatric pathway. Interventions boost GLP-1 signaling and insulin release, alter the gut microbiome, enhance the intestinal barrier, elevate bile acid signaling via FXR and TGR5, and support weight loss, thereby fostering positive metabolic outcomes. (**c**) Restoration of homeostasis. Decreased visceral fat correlates with reduced systemic inflammation, improved insulin sensitivity, and better glucose regulation, culminating in metabolic recovery. (**d**) Organ-specific effects Surgery reduces ectopic lipid buildup in the liver, improves skeletal muscle glucose absorption and insulin sensitivity, restores adipose tissue function, enhances vascular health, and improves pancreatic β-cell function. These modifications collectively reduce the obesity-related cardiometabolic risk.

8. Special Populations and Emerging Applications

8.1. Immunocompromised Patients

While bariatric surgery benefits obese individuals metabolically, its effects on immunocompromised patients vary because of immune dysfunction affecting recovery [106]. Individuals with compromised immunity, such as chronic corticosteroid users or individuals with autoimmune diseases, human immunodeficiency virus, cancer, transplants, or genetic disorders, often have impaired immune regulation and tissue repair [107]. Surgery improves insulin resistance, adipokine balance, and reduces inflammation; however, immunological recovery may differ from that in immunocompetent individuals [108]. Bariatric surgery reduces inflammation by decreasing adipose tissue and modulating hormone levels; however, immunocompromised patients may have reduced immune adaptability, affecting macrophage polarization, T-cell regulation, and cytokine balance [109]. Postoperative complications, such as infections, delayed healing, and micronutrient deficiencies, may be more pronounced, especially after RYGB or BPD/DS [110]. Obesity exacerbates immune dysfunction; thus, selected immunocompromised patients may benefit from surgery. Emerging research suggests that metabolic health improvements may partially restore immune balance; however, the evidence is limited and mostly observational, with few studies on long-term outcomes in

immunocompromised groups.

8.2. Precision Medicine and Artificial Intelligence

Precision medicine and artificial intelligence offer the potential for personalized metabolic surgery plans but face implementation challenges. Integrating datasets such as biomarkers, genomics, microbiomes, imaging, and clinical variables requires a standardized infrastructure, validated models, and comprehensive datasets [111]. Challenges include data privacy, algorithmic bias, limited resource access, regulatory issues, and ensuring that artificial intelligence recommendations are clinically interpretable. Future efforts should focus on developing clinically relevant and ethically scalable precision frameworks for personalized surgical decisions and postoperative monitoring.

8.3. Tissue Repair and Systemic Recovery

Recovery after surgery involves managing inflammation and supporting tissue repair, neuromuscular health, and functional adaptation. Research has shown that modifying inflammatory and cellular pathways aids skeletal tissue and muscle function by maintaining neuromuscular junctions and reducing stress-related tissue issues. Recovery after bariatric surgery is influenced by localized inflammation and broader systemic responses that regulate tissue remodeling and mobility restoration. Thus, early mobilization and better recovery may result from coordinated inflammation control, tissue repair, and systemic metabolic adaptation.

9. Critical Analysis of Conflicting Findings

Table 9 summarizes the variations in the evidence supporting immunometabolic outcomes after bariatric surgery. Long-term weight loss, remission of T2D, improved insulin sensitivity, and lower cardiovascular risk are supported by randomized controlled trials, prospective cohort studies, and meta-analyses, inspiring high confidence. In contrast, immune cell remodeling, cytokine reprogramming, gut microbiome changes, bile acid signaling, and reduced oxidative stress rely on mechanistic, translational, and observational studies, yielding moderate evidence despite consistent results. The weakest evidence concerns immunocompromised groups and precision medicine applications, where data are limited by small sample sizes, retrospective designs, and brief follow-up. These disparities contribute to contradictory findings and underscore the need for standardized methodologies and longer follow-up periods in prospective studies.

Table 9. Strength of evidence supporting major immunometabolic outcomes of bariatric surgery.

Immunometabolic Outcomes	Principal Evidence Sources	Overall Strength of Evidence*	Key Limitations
Sustained weight loss	Randomized controlled trials, prospective cohorts, meta-analyses	High	Heterogeneity in procedure type and follow-up duration
T2D remission and glycemic improvement	Randomized controlled trials, long-term cohort studies, systematic reviews	High	Variable remission definitions and patient populations
Improvement in insulin sensitivity	Randomized controlled trials, mechanistic studies, prospective cohorts	High	Differences in assessment methods
Reduction in systemic inflammatory markers (CRP, IL-6, TNF-α)	Prospective cohort studies, longitudinal studies, meta-analyses	Moderate-High	Limited long-term immunological follow-up
Cytokine reprogramming and immune-cell remodeling	Mechanistic human studies, translational studies, observational cohorts	Moderate	Small sample sizes and inconsistent immune profiling
Gut hormone modulation (GLP-1, PYY, ghrelin)	Randomized trials, physiological studies, mechanistic investigations	High	Procedure-specific variability
Gut microbiome remodeling	Human cohort studies, translational studies, animal experiments	Moderate	Significant methodological heterogeneity and limited causal evidence
Bile acid signaling and metabolic regulation	Mechanistic studies, translational research, observational studies	Moderate	Limited long-term clinical validation
Reduction in oxidative stress	Prospective cohort studies, biochemical analyses	Moderate	Small study populations and variable biomarkers

Table 9. *Cont.*

Immunometabolic Outcomes	Principal Evidence Sources	Overall Strength of Evidence*	Key Limitations
Hypertension improvement and cardiovascular risk reduction	Long-term cohort studies, meta-analyses, observational studies	High	Limited randomized cardiovascular outcome data
Immunometabolic effects in immunocompromised patients	Observational studies, retrospective analyses, small cohorts	Low	Scarcity of prospective studies and long-term follow-up
Artificial intelligence and precision medicine applications	Pilot studies, predictive modeling studies, emerging translational research	Low	Limited clinical implementation and validation

Note: T2D = Type 2 diabetes; CRP = C-reactive protein; TNF-α = Tumor Necrosis Factor-alpha; IL6 = Interleukin-6; GLP-1 = Glucagon-Like Peptide-1; PYY = Peptide YY. *Evidence strength was qualitatively assessed based on the study design, result consistency, sample size, follow-up length, and reproducibility of published data. High indicates support from several randomized trials and extensive prospective studies. Moderate is supported by observational, mechanistic, or translational studies with consistent outcomes. Low is based on limited observational data and new research.

Many studies have shown decreased systemic inflammation and improved metabolism post-bariatric surgery, with results varying by procedure, patient demographics, and biomarkers. Differences in cytokine reactions, adipokine control, microbiota changes, and metabolic adjustments were observed across the surgical methods and follow-up periods. While many studies report reductions in IL-6, TNF-α, and CRP levels, some have found ongoing inflammation despite weight loss. Variations in GLP-1 signaling, microbiome structure, and insulin sensitivity depend on the initial metabolic conditions, surgery type, and patient's immune characteristics. These discrepancies highlight the complex nature of immunometabolic changes and the need for standardized, long-term studies.

10. Limitations

Despite evidence supporting bariatric surgery, several factors limit the strength and applicability of the current findings. A major issue is the short follow-up period in many studies (12–36 months), which hinders the assessment of long-term weight loss maintenance, metabolic disorder remission, and delayed complications. The narrative approach lacks a formal bias assessment, which may positively skew the results. Variations in surgical techniques, patient criteria, procedures, and outcome definitions cause inconsistent results, complicating the comparisons. There are also limited data on immunological biomarkers, which hinders the understanding of immunometabolic mechanisms. Addressing these issues requires standardized methods, extended follow-up, and comprehensive immunological evaluations. Most immunological studies track patients for 24 months or less, leaving it unclear whether changes in cytokine profiles, immune cell phenotypes, and inflammatory markers indicate lasting remodeling or temporary responses. Publication bias undermines the confidence of the evidence, as studies with null or adverse findings are underrepresented. The absence of sham-controlled trials prevents distinguishing the impact of gastrointestinal rerouting from weight loss effects, which is crucial for understanding immunometabolic mechanisms. Isolating immunometabolic effects from fat mass reduction suggests that reported immune benefits may result from adiposity reduction rather than surgery-specific reprogramming. Variability in surgical techniques, such as pouch size and Roux limb length, reduces cross-study comparability, potentially explaining inconsistencies in the immunological outcomes.

11. Future Directions

Future bariatric research should adopt a precision immunometabolic approach. Obesity involves adipose changes, cytokine imbalance, endocrine disruption, gut-immune interactions, oxidative stress, and altered energy processes. Therefore, studies should prioritize personalized immunometabolic profiling over body mass index.

Precision frameworks should incorporate inflammatory biomarkers, adipokines, metabolomics, gut microbiome patterns, genetics, nutritional status, immune profiling, and metabolic indicators. This profiling could guide procedure selection based on obesity severity, inflammatory load, metabolic phenotype, immune capability, cardiovascular risk, microbiota, and nutritional vulnerability. Studies should assess whether personalized immunometabolic alignment enhances recovery, inflammation resolution, remission sustainability, and quality of life.

The integration of translational immunology into bariatric surgery is crucial. Studies should use advanced immunophenotyping techniques, including single-cell transcriptomics, cytokine network mapping, macrophage po-

larization, T-cell profiling, and inflammatory trajectory monitoring. These methods may reveal how surgery affects immune regulation, tissue remodeling, endothelial function, oxidative stress, and organ-specific inflammation beyond the effects of caloric restriction.

Further research should explore microbiome changes, intestinal barrier integrity, bile acid signaling, incretin physiology, and host-microbiota interactions during immunometabolic recovery after surgery. Longitudinal trials with microbiome data may identify microbial signatures predictive of sustained weight loss, diabetes remission, inflammation resolution, nutritional complications, and metabolic resilience.

AI and machine learning can transform metabolic surgery by enabling personalized care. AI platforms that integrate clinical data, imaging, biomarkers, genomic information, microbiome profiles, wearable monitoring, and health records could aid in predicting complications, nutritional monitoring, procedure selection, response forecasting, and relapse risk assessment. Challenges include algorithmic bias, data harmonization, regulatory oversight, ethical governance, model explainability, cybersecurity, and limited access to resource-constrained systems.

Attention is needed for vulnerable groups, including those with compromised immune systems, older adults, and patients with sarcopenic obesity, autoimmune diseases and chronic inflammatory disorders. These groups may exhibit unique inflammatory patterns and metabolic adaptations after surgery. Immune-stratified trials are necessary to understand how baseline immune dysfunction affects postoperative remodeling, nutritional risk, infection susceptibility and outcomes.

Research should emphasize regenerative strategies to minimize inflammatory damage while maintaining metabolic efficacy. Exploring biomaterials with reduced reactivity, inflammatory signaling modulation, microbiome therapies, neuromuscular preservation, and anti-fibrotic approaches may enhance tissue adaptation and recovery after surgery. The future of bariatric surgery lies in transforming it into a systems-level therapeutic platform that integrates surgery, immunology, microbiome science, computational medicine, precision nutrition, and personalized care.

12. Conclusions

Obesity is a multifaceted immunometabolic disorder characterized by chronic low-grade inflammation, adipose dysfunction, immune dysregulation, oxidative stress, and metabolic imbalance. Interactions between enlarged adipocytes, inflammatory cytokines, hormonal disturbances, and insulin resistance drive T2D and cardiovascular complications. Although lifestyle interventions and medications are standard, they often struggle with long-term compliance and incomplete metabolic recovery.

Bariatric surgery may offer metabolic and inflammatory benefits to immunocompromised patients; however, the evidence is limited to retrospective studies and cohorts. Although fat, inflammation, and metabolic problems may improve balance, the extent and durability remain unclear. Postoperative complications, including infections, delayed wound healing, and nutritional deficiencies, may differ; therefore, decisions should be individualized through assessments. However, more studies are needed to clarify its safety, immunological effects, and benefits.

Procedures such as RYGB, LSG, and BPD/DS vary in effectiveness and safety, necessitating personalized selection based on patient profiles and treatment goals. However, gaps remain regarding the durability of immunological changes, specific procedural mechanisms, and their impact on vulnerable populations.

Bariatric surgery is a powerful immunometabolic intervention that disrupts the obesity-inflammation-insulin resistance cycle. Future prospective, mechanistic, and precision medicine research is essential to identify patient-specific response predictors, clarify long-term immunological effects, and optimize personalized obesity care.

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Conflicts of Interest

The authors declare no conflict of interest.

AI Use Statement

While drafting this manuscript, the authors used Paperpal solely to refine the language, grammar, spelling, and scientific readability. No AI tools were used for data generation, statistical analyses, result interpretation, content fabrication or conclusion formulation. All scientific interpretations, clinical analyses, and final revisions were independently reviewed and approved by the authors, who assumed full responsibility for the manuscript's integrity, originality, and accuracy.

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