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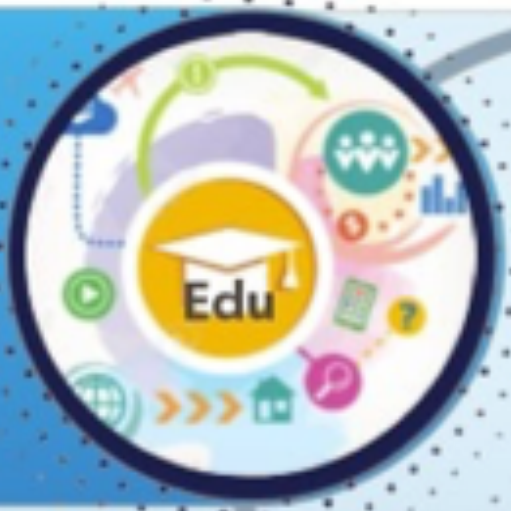

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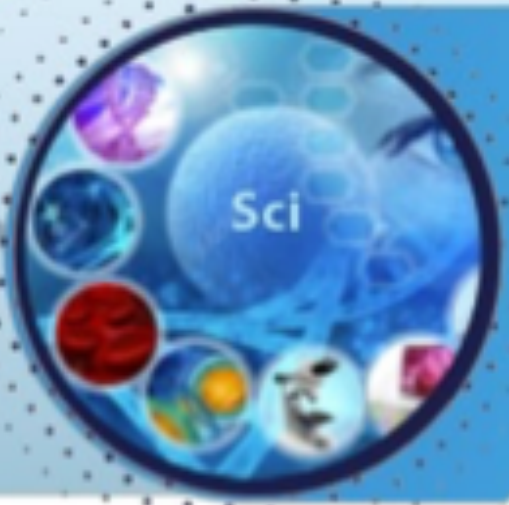

Issue 3 | 2025

OAK.uz
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ISSN: 2181-3175

Journal of Education & Scientific Medicine

ISSN 2181-3175

Tashkent Medical Academy

Review Article

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Metabolic Surgery for Complex Phenotypes of Metabolic Syndrome: from obesity index to hormonal and gastrointestinal profiles

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ABSTRACT

Background: *Metabolic syndrome (MetS) is a heterogeneous condition influenced by diverse endocrine, anatomical, and inflammatory profiles. As bariatric surgery evolves into metabolic surgery, understanding patient-specific phenotypes becomes essential for personalized treatment.*

Objective: *To review and analyze current evidence on how metabolic surgery outcomes are affected by individual variations in insulin resistance, GERD, NAFLD, gut hormone response, and anatomical gastric parameters.*

Methods: *A narrative literature review was conducted using PubMed, Scopus, and Embase, including clinical trials and cohort studies from 2005 to 2024. Key search terms included «metabolic syndrome», «bariatric surgery», «phenotypes», «GERD», «NAFLD», and «gut hormones».*

Results: *Evidence shows that patients with high HOMA-IR and low C-peptide respond better to malabsorptive procedures like OAGB or RYGB, while those with mild insulin resistance and active GLP-1 signaling benefit from restrictive options such as LSG. The presence of GERD and anatomical variation in stomach axis influences surgical choice, with anti-reflux modifications proving superior in high-risk patients. NAFLD, increasingly viewed as a «hepatocentric» component of MetS, may also require tailored surgical strategies. Gut hormone dynamics and microbiota profiles are emerging as key modifiers of metabolic outcomes.*

Conclusion: *Metabolic surgery should no longer be viewed as a singular approach. Recognizing and stratifying phenotypic complexity in MetS patients allows for more rational procedure selection and improved long-term outcomes. A shift toward algorithm-driven, phenotype-adapted surgery is both necessary and imminent.*

Keywords: *Metabolic syndrome, bariatric surgery, phenotyping, insulin resistance, GERD, NAFLD, GLP-1.*

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INTRODUCTION

Metabolic syndrome (MetS) is a multifactorial clinical entity characterized by central obesity, insulin resistance, dyslipidemia, hypertension, and low-grade systemic inflammation [1]. It affects over one-quarter of the global adult population and is associated with a markedly increased risk of type 2 diabetes mellitus (T2DM), cardiovascular disease, and non-alcoholic fatty liver disease (NAFLD) [2]. Although initially considered a nutritional and lifestyle disorder, recent research underscores the importance of underlying hormonal, genetic, and anatomical factors that shape its clinical course and treatment response.

The success of bariatric surgery in achieving weight loss and improving metabolic markers in obese patients has led to its redefinition as "metabolic surgery" [3]. However, mounting evidence suggests that outcomes vary widely depending on individual phenotypic characteristics such as insulin secretion capacity, the presence and severity of gastroesophageal reflux disease (GERD), visceral fat distribution, and gastrointestinal hormone profiles [4-6].

Standard surgical techniques such as laparoscopic sleeve gastrectomy (LSG), Roux-en-Y gastric bypass (RYGB), and one-anastomosis gastric bypass (OAGB) have demonstrated high efficacy overall. Yet, a uniform approach may not be ideal. For example, patients with advanced insulin resistance and low beta-cell reserve tend to benefit more from procedures with greater malabsorptive effects, while those with early-stage metabolic impairment and strong GLP-1 signaling respond well to restrictive techniques [7]. Similarly, patients with baseline GERD may experience worsening symptoms after LSG unless anti-reflux adaptations are made [8].

Anatomical factors - including stomach axis deviation, hiatal hernia, and variable gastric volumes - also affect procedure selection and postoperative satisfaction. Recent advances in imaging and 3D modeling have enabled more precise characterization of upper gastrointestinal anatomy, opening the door for anatomy-driven surgical planning [9].

Moreover, emerging studies indicate that gut microbiota composition and incretin hormone response play an integral role in postoperative metabolic shifts, further emphasizing the need for individualized intervention [10].

This review explores the growing recognition of phenotypic diversity in MetS patients undergoing metabolic surgery. We examine how factors such as insulin resistance, GERD, NAFLD, gut hormones, and gastric anatomy can be used to stratify surgical decision-making and improve long-term metabolic outcomes.

MAIN TEXT

1. Metabolic Phenotypes and Their Surgical Implications

Metabolic syndrome is not a uniform diagnosis but rather a spectrum of interrelated disturbances that manifest differently across patient populations. Increasingly, researchers and clinicians have begun to classify patients into functional phenotypes based on the severity of insulin resistance, residual beta-cell function, degree of hepatic steatosis, and inflammatory load [1].

Patients with severe insulin resistance, typically defined by HOMA-IR values >5.0, often exhibit poor glycemic response to restrictive surgeries alone. In these individuals, C-peptide levels may be suppressed, and incretin response blunted. For such patients, malabsorptive procedures - such as one-anastomosis gastric bypass (OAGB) or Roux-en-Y gastric bypass (RYGB) - are generally associated with more robust improvement in glycemic control, even in the absence of significant weight loss [2].

By contrast, individuals with mild-to-moderate insulin resistance, preserved pancreatic beta-cell function, and elevated GLP-1 activity tend to benefit sufficiently from restrictive operations such as laparoscopic sleeve gastrectomy (LSG). These patients often demonstrate earlier satiety and stronger postprandial incretin effects, supporting less invasive procedures [3].

In recent studies, the use of C-peptide levels as a stratification tool has been proposed. Cummings et al. observed that patients with low fasting C-peptide (<1.5 ng/mL) had inferior outcomes with LSG but responded favorably to bypass operations, likely due to greater enhancement of distal gut hormone signaling [4].

This growing body of evidence supports a phenotype-adapted surgical approach, wherein procedure type is selected based not only on BMI, but on endocrine and biochemical markers that more accurately reflect metabolic dysfunction.

2. Gastroesophageal Reflux Disease (GERD): Structural and Functional Considerations

GERD is highly prevalent in obese patients and often coexists with other features of metabolic syndrome. Its presence significantly influences surgical decision-making, as certain bariatric procedures can exacerbate reflux symptoms. Sleeve gastrectomy (LSG), although widely used, has been shown to worsen GERD in up to 30% of

patients due to increased intragastric pressure, loss of the angle of His, and decreased compliance of the gastric conduit [5].

Several anatomical factors contribute to reflux exacerbation, including axial rotation of the stomach, hiatal hernia, and pre-existing lower esophageal sphincter incompetence. Patients with these features may be better candidates for anti-reflux-modified LSG or gastric bypass procedures, which have shown more favorable outcomes in this subgroup [6]. OAGB, while effective metabolically, can also lead to bile reflux in a small but significant proportion of patients unless limb length and anastomosis configuration are carefully selected [7].

Recent studies suggest that including GERD severity and anatomical markers in preoperative stratification improves postoperative satisfaction and reduces the need for revisional surgery [8].

3. Non-Alcoholic Fatty Liver Disease (NAFLD) and Hepatocentric Stratification

NAFLD is now recognized as both a consequence and driver of metabolic syndrome. It is present in more than 70% of obese individuals and is strongly associated with insulin resistance and inflammatory dysregulation [9]. The extent of hepatic steatosis and fibrosis influences not only surgical risk but also the metabolic benefits derived from different bariatric procedures.

Bypass surgeries, particularly RYGB and OAGB, have been associated with superior histological improvement in hepatic steatosis and inflammation compared to LSG [10]. The mechanisms include enhanced GLP-1 and FGF-19 signaling, improved bile acid metabolism, and greater insulin sensitization in hepatocytes.

Patients with moderate-to-severe NAFLD, especially those with elevated liver enzymes and imaging-confirmed steatosis, may thus benefit from bypass-based procedures. In contrast, patients with mild or reversible fatty liver may respond well to restrictive techniques.

Incorporating hepatic profile data into surgical algorithms may allow for a «hepatocentric» approach to metabolic surgery, wherein liver status directly informs the procedural plan.

4. Gut Hormone Profiles and the Emerging Role of Microbiota

The gastrointestinal tract is not only the site of mechanical digestion but also a major endocrine organ that regulates appetite, glucose homeostasis, and lipid metabolism. Gut hormones such as GLP-1, GIP, PYY, and ghrelin play key roles in the metabolic effects observed after bariatric surgery [1]. The extent and nature of hormonal changes vary depending on the procedure.

Bypass procedures (e.g., OAGB, RYGB) induce distal gut stimulation, markedly increasing GLP-1 and PYY levels, which enhance insulin sensitivity and promote satiety [2]. Restrictive operations such as LSG primarily reduce ghrelin levels via fundus resection, leading to appetite suppression. These hormonal shifts are particularly relevant in stratifying patients: those with impaired GLP-1 response may benefit more from bypass surgery, while ghrelin-sensitive individuals may respond better to LSG [3].

In addition to hormonal alterations, gut microbiota composition undergoes profound changes after bariatric surgery. Studies have shown that OAGB and RYGB promote microbial diversity and increased abundance of beneficial bacterial strains linked to improved glucose and lipid metabolism [4]. The impact of these microbial shifts is being actively investigated as a factor in inter-individual variability of metabolic outcomes.

Emerging research suggests that microbiota profiling may one day be used to predict surgical responsiveness and tailor postoperative care, although clinical integration remains premature at this stage [5].

Overall, the evolving understanding of gut endocrine and microbial ecology supports a paradigm shift from anatomy-based surgery toward physiology-informed.

CONCLUSION

As bariatric surgery continues to evolve into a discipline of metabolic intervention, recognition of phenotypic heterogeneity among patients with metabolic syndrome is essential. Evidence increasingly supports that variables such as insulin resistance severity, beta-cell reserve, GERD status, NAFLD burden, gut hormone profiles, and gastric anatomy all influence postoperative outcomes.

Restrictive procedures may be appropriate for patients with mild metabolic dysfunction and favorable hormonal profiles, while those with advanced insulin resistance or hepatic involvement often benefit more from bypass-based approaches. GERD and anatomical variation further modulate procedural selection and long-term satisfaction.

Incorporating this complexity into surgical decision-making calls for a shift toward phenotype-guided, algorithm-driven planning. While randomized trials and biomarker validation are still evolving, the future of metabolic surgery clearly lies in individualized therapy rooted in integrated clinical, biochemical, and anatomical data.

Ethical Approval:

Not applicable. This article is a narrative review of published literature and does not involve human or animal subjects.

Conflict of Interest:

The author declares no conflict of interest.

Funding:

No external funding was received for the preparation of this manuscript.

Author Contributions:

Khamdamov I.B. – Literature review, data synthesis, critical analysis, manuscript drafting and revision.

Acknowledgements:

The author expresses gratitude to the academic staff of Tashkent Medical Academy for their support and valuable discussions during the preparation of this work.

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How to Cite: *Khamdamov I.B. Metabolic Surgery for Complex Phenotypes of Metabolic Syndrome: from obesity index to hormonal and gastrointestinal profiles // Journal of Educational & Scientific Medicine, 2025. Vol. 1, Issue 3, P. 89–93.*

METABOLIK SINDROMNING MURAKKAB FENOTIPLARI UCHUN METABOLIK JARROHLIK: SEMIZLIK KO‘RSATKICHI, GORMONAL VA ME’DA-ICHAK PROFILLARIGA ASOSLANGAN YONDASHUV

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ANNOTATSIYA

Metabolik sindrom bir xildagi emas, balki endokrin, anatomik va yallig‘lanish holatlariga bog‘liq holda har xil ko‘rinishda namoyon bo‘ladi. Maqolada insulinga chidamlilik, GERD, NAJBP, ichak gormoni profillari va me’da anatomiyasi asosida fenotipik stratifikatsiya orqali metabolik jarrohlik yondashuvini individualizatsiya qilish imkoniyatlari yoritiladi. Kuchli HOMA-IR va past C-peptidga ega bemorlar ko‘proq malabsorbtiv usullarga (OAGB, RYGB) mos keladi, yengil metabolik buzilish va yuqori GLP-1 faoliyati bo‘lganlar esa LSG kabi cheklovchi amaliyotlardan foyda ko‘radi. GERD va NAJBP mavjudligi ham jarrohlik usulini tanlashga ta’sir qiladi. Ichak gormonlari va mikrobiotaning o‘zgarishi esa natijalarning individual farqini tushuntirishda muhim bo‘lishi mumkin.

Kalit so‘zlar: Metabolik sindrom, bariatrik jarrohlik, fenotiplashtirish, insulin rezistentligi, GERD, NAJBP, GLP-1.

МЕТАБОЛИЧЕСКАЯ ХИРУРГИЯ ПРИ СЛОЖНЫХ ФЕНОТИПАХ МЕТАБОЛИЧЕСКОГО СИНДРОМА: ОТ ИНДЕКСА ОЖИРЕНИЯ ДО ГОРМОНАЛЬНОГО И ЖЕЛУДОЧНО-КИШЕЧНОГО ПРОФИЛЯ

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АННОТАЦИЯ

Метаболический синдром представляет собой гетерогенное состояние, при котором исходы метаболической хирургии зависят от множества факторов, включая степень инсулинорезистентности, остаточную функцию бета-клеток, наличие ГЭРБ, степень НАЖБП, анатомические особенности желудка и профиль кишечных гормонов. В обзоре обобщены современные данные о том, как эти фенотипические особенности влияют на выбор между рестриктивными и шунтирующими методами. Пациенты с тяжёлой инсулинорезистентностью и низким уровнем С-пептида получают наибольшую пользу от операций типа OAGB или RYGB, в то время как при лёгком метаболическом нарушении и выраженной GLP-1 активности эффективны методы, подобные LSG. Наличие ГЭРБ и выраженного стеатогепатита требует модификации техники вмешательства. Авторы подчёркивают необходимость перехода к алгоритмически управляемой и фенотипически ориентированной хирургии.

Ключевые слова: Метаболический синдром, бариатрическая хирургия, фенотипирование, инсулинорезистентность, ГЭРБ, НАЖБП, GLP-1.