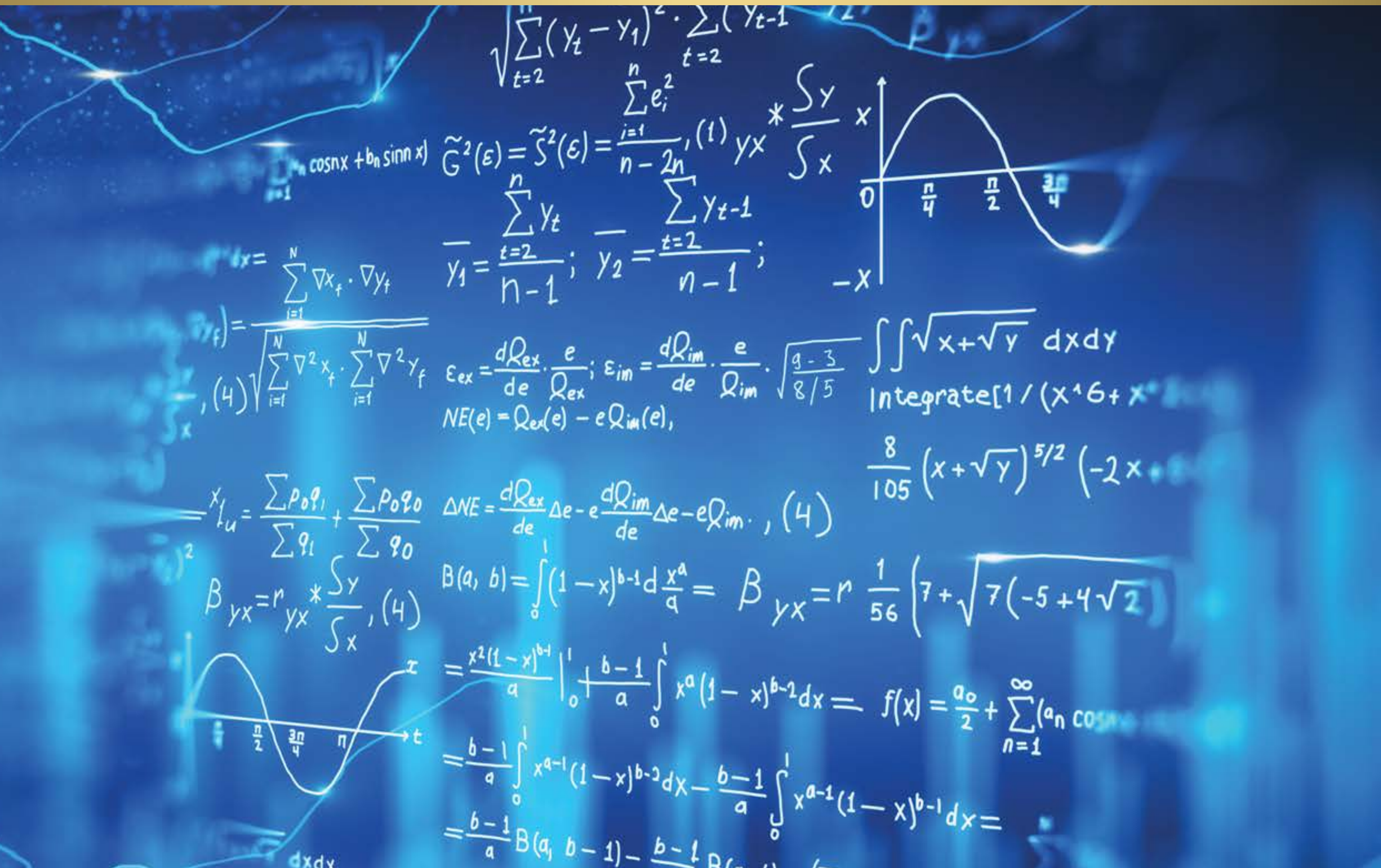
IFSO

CONSENSUS ON DEFINITIONS AND CLINICAL PRACTICE GUIDELINES FOR PATIENTS CONSIDERING METABOLIC-BARIATRIC SURGERY



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INTRODUCTION

It would not be an exaggeration to state that severe obesity adversely affects every organ system of the body. Once a problem predominately seen in the developed world, and in particular, the United States, severe obesity is now a public health crisis throughout the world. Recent estimates suggest that the prevalence of overweight and obesity world-wide is over two billion people or 30% of the world's population (Lancet). As such, obesity threatens to bankrupt the healthcare systems of many countries.

Fortunately, the recent introduction of several new treatments, the newly-published updated guidelines for metabolic/bariatric surgery (MBS), and the increased understanding of the disease referred to as severe obesity have improved our options for combating this incurable disease epidemic.

In the past, the treatment of patients with obesity was restricted to those with a body mass index (BMI) > 35 kg/m^2 who also suffered from one or more associated conditions such as type 2 diabetes, or patients with a BMI of > 40 kg/m^2 with or without comorbid conditions. Treatments were limited to diet, exercise, behavioral therapy, a few open-access gastrointestinal operative procedures, and a narrow selection of medications that achieved marginal weight loss results.

Currently, we are blessed with a wide range of treatment options, all of which have greater safety and efficacy than the previous generation of treatments. These include several new operative procedures, mediations, and the introduction of endoscopic procedures. In addition, clinicians now have a greater appreciation for nutritional surveillance and supplementation and the need to have behavioral therapy available for those patients who may require it.

To better apply these new treatment options, IFSO, the predominant international medical society dealing with the obesity epidemic, recognized that there was no uniformity in how we define the disease or its treatments, and no unified clinical practice guidelines for the best use of these treatments. To overcome these shortcomings, IFSO leadership decided to orchestrate a consensus conference comprised of clinical leaders from around the world, guided and assisted by an internationally-recognized, MD-PhD expert in

The working group included not only bariatric surgeons, but other clinicians involved in the care of patients with severe obesity, including endoscopists, physicians, dieticians, behavioral therapists, and others. The conference was held in Hamburg Germany, March 9-10, 2023, and lasted two full days.
Prior to the meeting, participants were given topics to present in their areas of expertise. They were 45 oral presentations given followed by ample discussion, questions, and answers.

Subject material presented was broken down into five modules. The first module included the standardized reporting of definitions. The second module covered diet, exercise, and lifestyle. The third concerned medical treatment, while the fourth addressed endoscopic procedures. The fifth module was the largest and was split into two: the first one being the surgical treatment of obesity and the second the treatment of metabolically-challenged patients and other high-risk patients.

A modified Delphi study was then performed to assist in the creation of new guidelines. Prior to the meeting, 138 statements were created by the group at large. A 70% level of inter-voter agreement was considered consensus. All told, there were three rounds of voting. These results then were combined with an exhaustive review of published scientific literature to generate the current clinical practice guidelines.

Severe obesity remains an incurable, unrelenting disease. Its prevalence and costs for care are large and getting larger. This consensus publication represents the experienced opinons of many of the most highly regarded bariatric experts from around the world. Hopefully, the clinical use of this consensus paper by clinicians will improve the success of the current armamentarium of treatment options.

The meeting and all subsequent publications have been endorsed by the World Obesity Federation, World Gastroenterology Organization, and the International Diabetes Federation.

Scott A. Shikora, MD, FACS, FASMBS
President, International Federation for the Surgery of Obesity and Metabolic Disorders

FOREWORD

One of the most interesting, gratifying, and appealing situations in our daily lives as physicians derives from our basic need to communicate and discuss with peers, around the world, the many clinical issues we face in our own established healthcare settings.

Obesity is an ongoing health condition that produces a myriad of clinical consequences affecting nearly all the various organ systems. At the same time, it challenges most clinicians due to its complexity. Currently, we are in the early stages of our knowledge as it relates to our patients' psychosocial needs, behaviours, nutritional requirements, alterations in digestion, and more.

Enthusiasm, curiosity, and expectations about the role of Gastroenterology tackling the wide spectrum of obesity-associated diseases correlates with our understanding about the impact of obesity on digestive oncology and liver disease, and how one of our prime- time tools – digestive endoscopy – is playing a decisive role in managing these patients. The need for multimodal treatment nourishes the concepts that WGO has been developing with IFSO, constructing a narrative throughout the medical and surgical communities that there are complementary roles, delivered by different insights and perspectives, and that we are all crucial to linking the various pieces of the obesity-management puzzle. This multimodal approach, for us, is not a battlefield pitting experts against experts, but an inspirational drive for all disciplines involved in the care of patients with severe obesity to contribute with timely, safe, and empirically-validated knowledge, not just to be shared globally during these exciting times, but also to be updated steadily through our joint, evolving expertise.

Guilherme Macedo, MD
President of the World Gastroenterology Organization (WGO)

PREFACE

Obesity, a multifaceted and complex condition, has become one of the most pressing health challenges of the 21st century. As our understanding of this chronic disease deepens, it becomes increasingly apparent that a coordinated and evidence-based approach is crucial for addressing this crisis.

The IFSO Consensus on Definitions and Clinical Practice Guidelines is the culmination of a collaborative effort by a diverse group of researchers, clinicians, and healthcare professionals, who have endeavored tirelessly to establish a unified consensus on the therapeutic alternatives for the treatment of obesity and all associated complications. The book covers various treatment modalities, including lifestyle modifications, medications, endoscopic procedures, metabolic bariatric/ surgery, and combination strategies.

All the chapters in this book are written by experts in the field who have contributed their knowledge and expertise to provide a balanced and evidence-based overview of the current state of the art for treating severe obesity. Each chapter is designed to be informative and practical, providing valuable insights into implementing these strategies in clinical practice.

All the sections of the book delve into evidence-based approaches to treat this incurable and progressive disease. Moreover, the book helps to define the disease and clinical responses with much-needed definitions that are current and free of both bias and patient humiliation. Moreover, this book covers the recent advancements in the various therapeutic modalities for specific patients such as adolescents, seniors, and high clinical risk patients like those with heart failure or having a BMI greater than 50 kg/m^2. Lastly, the book will address the benefits of combination strategies.

The ultimate goal of this consensus document is to foster a compassionate, evidence-based approach that acknowledges the complexity of obesity, while empowering healthcare professionals to deliver the highest quality of care to their patients. While this book is a significant step forward in our collective understanding of obesity treatment, it is essential to recognize that our knowledge of this subject continues to evolve. As such, we encourage healthcare professionals to stay informed about new developments in the field and to adapt their practices as new evidence emerges. We hope this book serves as a valuable resource and a catalyst for continued growth and collaboration in the ongoing fight against obesity.

Together, we can make a difference in the lives of millions of individuals affected by obesity and help shape a healthier future for generations. We hope this book will contribute to greater consensus on the definitions and clinical practices used for treating obesity, ultimately leading to better outcomes for those affected by this complex disease.

Ricardo V. Cohen, MD
On behalf of the World Obesity Federation (WOF)

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This book is the result of a working process that lasted for several months and culminated in a 2-day "IFSO Consensus conference on definitions and clinical practice guidelines", followed by a 3-round Delphi survey of 43 multi-disciplinary experts from every continent.

These experts – who included surgeons, physicians, endoscopists and integrated health professionals – worked together in close partnership to create this book. Each of them participated in the conference, many giving presentations, and the Delphi survey that followed. Most also contributed sections to the book, without which the book would never have come to fruition.

Special thanks to our partner organizations – WGO, WOF and IDF – that participated in this ambitious project.

We also give thanks to all members of the organizational team, with special thanks to:

- Professor Paulina Salminen, who was the main driving force behind revising and collecting the different chapters.
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- Dr. Kevin P. White for his assistance planning and orchestrating the Delphi study and analysing its results, and for being the final editor of this book.

Special thanks also to Manuela Mazzarella, our IFSO Chief Operating Officer, for her incredible work on this project, organizing countless duties, while addressing and solving every problem that arose with a smile on her face. No one else could do what she does. She is truly one in a million.

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Last but not least, we thank the Johnson & Johnson company for their continued great interest in continuing medical education, as well as for the educational support they have given us throughout the current process.

CHAPTER 1

REPORTING DEFINITIONS AND STANDARDS FOR MANAGING OBESITY

Lee M. Kaplan, MD, PhD

As it is well-described elsewhere in this volume, metabolic-bariatric surgery (MBS) is a highly effective means of inducing and maintaining long-term weight loss. Both as a result of the weight loss, and in many cases through additional metabolic mechanisms, MBS has been shown to improve many of the metabolic complications of obesity, including type 2 diabetes, atherosclerotic cardiovascular disease, non-alcoholic steatosis and steatohepatitis, and chronic kidney injury. It also reduces the risk of several forms of cancer. In the face of these many substantial benefits, however, it is important to recognize that the efficacy of surgery varies substantially from patient to patient.

With respect to weight loss itself, multiple studies have demonstrated that the percentage total body weight loss (%TWL) varies in a normal distribution around the mean and that the observed variability in response to MBS is substantial, with a standard deviation generally in the range of 10 to 12%. Despite the substantially greater effect that MBS has on average weight loss, relative to all other obesity treatments, the degree of variability is similar to that seen after lifestyle-, medication- and medical device-based therapies. The observed variability means that the middle 95% of the weight loss response distribution (i.e., within two standard deviations of the mean) encompasses a greater than four-fold variation in maximum initial post-operative weight loss (typically the maximal weight loss within two years of the surgical procedure). As an example, for Roux-en-Y gastric bypass (RYGB), which induces an average of 34% maximal initial weight loss and a standard deviation of 11%, the 95% confidence interval for initial post-operative weight loss varies from 12% to 56% total body weight loss!

The normal, bell-shaped distribution of initial post-operative total body weight loss strongly suggests that the patient-to-patient variation primarily reflects underlying biological heterogeneity. There is no evidence of a skewed or bimodal distribution that might result from important interindividual differences in postoperative adherence to recommended lifestyle changes. Support for a biological basis for the variable response is further supported by recent studies demonstrating a strong genetic contribution to the weight loss response to RYGB and other MBS procedures. While not all biological determinants need to have a genetic basis, the strength of the genetic determinants implies that biology plays an important, if not dominant, role in determining weight loss – and potentially other beneficial responses – achieved after MBS in individual patients.

Large variability in the weight loss response means that a small, but significant portion of patients undergoing MBS will experience a substantially less robust benefit from these procedures. People at the low end of the weight loss distribution often experience less substantial improvement in obesity complications and measures of quality of life than those who have a greater response. These individuals have long been characterized as "non-responders" as a means of defining their need for additional treatment or support for the management of their obesity. However, the categorical differentiation between MBS responders and non-responders has, by necessity, been somewhat arbitrary. There is no clear demarcation between patients who respond effectively to MBS and those who do not (i.e., no second grouping within the weight loss distribution curve). While some studies suggest that 20% total body weight loss is the minimum required to achieve substantial metabolic and cardiovascular benefit from MBS procedures, even these observations provide no clear criteria for clinical effectiveness. From evaluations of multiple clinical trials and observational studies, it appears that the greater the weight loss, the greater the likelihood of improving both the severity and clinical outcomes of virtually all obesity complications and comorbidities studied. Thus, the binary distinction between "responders" and "non-responders" appears inadequate as a guide to ongoing management.

While even arbitrary criteria can serve a useful role for the development of clinical practice guidelines and medical coverage determinations, the degree to which the clinical response to MBS is suboptimal appears to be an even more useful driver of appropriate ongoing clinical practice. Moreover, given the high prevalence of stigmatization of people with obesity and the health care providers who treat them, it is particularly important not to infer that some misbehavior – by either the patient or the surgeon – is responsible for a less robust, or suboptimal, outcome.

In recent decades, numerous studies have advanced the understanding of the pathophysiology underlying obesity and the mechanisms by which MBS induces weight loss and leads to long-term improvement in obesity and its complications. Taken together, this research clearly supports several important conclusions:

1. **The elevated body fat that is the hallmark of obesity results primarily from disruption of the normal physiological regulation of body fat (often induced by the modern obesogenic environment), which causes the body to seek and defend an excessively high fat mass.** These pathophysiological effects induce changes in appetite and energy expenditure regulation to achieve these abnormal fat mass targets. The purposeful consumption of excess calories (or purposeful reduction in physical activity) appears to play much less of a role than previously thought.

2. **MBS acts primarily by improving the underlying pathophysiology of obesity, causing improved regulation of body fat, and lowering the sought and defended fat mass.** As a result of these physiological effects, the initial effects of MBS are to reduce appetite (often dramatically), while preserving energy expenditure. As MBS achieves maximal effects – marked by reaching body fat and weight plateaus – the initial changes in appetite abate and all components of appetite and energy expenditure regulation move back toward normal.

3. **Both the mechanical restriction of food intake and macronutrient malabsorption, even when present, appear to contribute little or nothing to observed improvements in obesity or its complications, particularly over the long term.** Indeed, the ability of pregnancy to cause women to increase their appetite, their food consumption, and their weight – allowing the pregnancy to support the development of a healthy baby, despite the growing foetus restricting stomach expansion increasingly – demonstrates not only that MBS improves obesity through physiological re-regulation, but that the critical physiological effects of pregnancy are able to overcome those of MBS. In other words, the mechanical restriction of food intake and macronutrient malabsorption, even when present, appear to contribute little or nothing to improvements in obesity or its complications, particularly over the long term.

The biological basis of obesity and the response to MBS underscore the importance of recognizing that a suboptimal clinical response rarely reflects either substandard surgical skill or technique. Similarly, though patients' post-operative compliance with dietary recommendations is considered important, a suboptimal clinical response is rarely caused by noncompliance or any other aberrant or inadequate behavior by the patient. Thus, the language that we use to describe less robust or effective clinical outcomes needs to avoid ascribing blame, making pejorative implications, and drawing unproven, causal inferences. Consequently, in the consensus statements accompanying this volume, we recommend that less than ideal weight loss or clinical improvement after MBS be described as a "suboptimal clinical response" or "suboptimal weight loss" rather than "non-response" or an "inadequate" response to treatment.

As noted earlier, with the normal distribution of weight loss response to MBS, there is no specific magnitude of weight loss that clearly differentiates between treatment success and suboptimal response. There is some evidence that 20% total body weight loss is associated with reduced cardiovascular risk, so many clinicians and investigators have used this criterion to assess the clinical response to MBS. We recognize, however, that the magnitude of weight loss has widely different clinical effects in different patients and should not be used as the single determinant of the need for additional clinical intervention. In this regard, the magnitude of weight loss is like a patient's body mass index (BMI). BMI, while a good tool to assess clinical risk across populations, is of far less value estimating obesity-associated risk or determining appropriate treatment for individual patients. In addition, as discussed elsewhere in this volume, the recent development and availability of more effective anti-obesity medications has broadened the range of treatment opportunities for patients who experience a suboptimal response to MBS. Because treatments for suboptimal weight loss differ in their efficacy, side effects, cost, and availability, the choice of which approach to use in an individual patient needs to consider the overall clinical presentation of the patient including, most importantly, the degree to which the patient's response to MBS was suboptimal.

In the accompanying consensus statements, we have maintained the 20% weight loss criterion as the one with the greatest amount of supporting evidence. However, we recommend that it be used only as a guide for evaluating the patient and instituting additional therapy, not as the sole criterion for doing so, or as the basis for choosing among the available options for further treatment.

One of the prominent features of clinical obesity care is that, while most healthcare providers recognize that obesity is a disease, we have varying perspectives on what makes it a disease, and rarely treat obesity in the same way we treat other chronic diseases. This inconsistent behavior and messaging is often confusing for patients, public health officials, payers, and the general public. In the accompanying consensus statements, we have included recommendations for specific language standards that reflect the most up-to-date scientific and clinical developments, improve message accuracy and consistency, and attempt to avoid stigmatization of people with obesity or those whose careers are devoted to improving such individuals' health and quality of life.

In particular, we have developed consensus definitions of different types of MBS procedure, recommending that they not be characterized by assumed mechanisms of action, but by descriptions of anatomical manipulations. We have recommended more standardized and consistent means of assessing the magnitude of weight loss that can reasonably be attributed to MBS (vs. other interventions that a patient may have been undertaken sequentially or in parallel). Moreover, as noted above, we have recommended the terms "suboptimal initial weight loss" for those patients whose postoperative weight loss in the first two years is less than typical, and "recurrent weight gain" for those who experience significant weight gain after initial postoperative weight loss.

We have worked to ensure that each of the consensus statements employs the recommended language standards. However, we recognize that in some cases, there is still a need to modernize the statements further as they undergo regular review over time. No consensus effort is perfect, and none is ever complete. It is just the next step in advancing the science and art of good patient care.

In a recently-completed three-round Delphi survey of 43 international, interdisciplinary experts in obesity management, the following 15 consensus statements – pertaining to reporting definitions and reporting standards – all reached consensus (Table 1-1). It is noteworthy that coming to consensus on these reporting definitions and standards was considered pivotal by the advisory board of the current guidelines. For this reason, voting on these 15 statements was afforded most of the first day of the two-day consensus conference held on March 8-9th, 2023 in Hamburg, Germany. This permitted several hours of open discussion. Even with this, further on-line discussion and voting conducted after the two-day consensus meeting were required to achieve these final statements. Further details regarding the consensus survey methods and results are available elsewhere [1].

Table 1-1: Reporting definitions and standards achieving at least 70% consensus in a three-round Delphi survey of n=43 multi-disciplinary experts in obesity management

REPORTING DEFINITIONS
A suboptimal initial response to metabolic/bariatric surgery (MBS) is demonstrated either by inadequate weight loss OR by an unusually modest improvement in a significant obesity complication.
A late post-operative clinical deterioration is demonstrated either by recurrent weight gain OR by worsening of a significant obesity complication that occurs after an initially adequate post-operative clinical response.
The degree to which the clinical response to MBS is suboptimal or there is a late post-operative clinical deterioration can vary widely from patient to patient. The severity of the suboptimal response should guide clinical treatment.
The baseline weight for assessing weight loss after MBS should be a weight determined before starting preoperative weight reduction.
In patients who have been treated with AOM before undergoing MBS, who STOP it at the time of or shortly after surgery, the baseline weight for assessing the effect of surgery on bodyweight should generally be a weight determined BEFORE the AOM was started.
In patients who have been treated with AOM before undergoing MBS and CONTINUE this medication post-op., the baseline weight used to assess the effect of surgery on body weight should generally be measured on the day of surgery.
The initial surgical weight loss (defined as maximum weight loss within the first 2 years after MBS) should be determined in a manner that excludes any post-plateau weight loss caused by adding AOM, any endoscopic intervention, or any calorie-restricted diet.
Surgical or endoscopic procedures to convert to a new type of metabolic/bariatric operation (conversion surgery) and those to re-establish normal anatomy (reversal surgery) should be clearly distinguished and considered separately from procedures to modify or enhance the effects of a previous operation (revision or modification surgery).
Modification or revision procedures are typically designed to optimize the effectiveness of previous operations, while conversion procedures most commonly introduce additional mechanisms of therapeutic action.
The term "obesity complication" mostly describes diseases, conditions, and symptoms for which there is published evidence that obesity is a contributing cause or exacerbating factor. When such a causative relationship has not been established or accepted, the associated disorder is more accurately labelled an obesity comorbidity.
When considering the effects of MBS on intestinal nutrient absorption, diminished absorption (hypo-absorption or malabsorption) of micronutrients should be clearly distinguished from the hypo-absorption or malabsorption of macronutrients or ingested calories.
Characterization of the absorptive effects of an MBS procedure should not be used to imply that these effects are the mechanisms of action of weight loss associated with the operation. It is preferable to describe such procedures by their anatomical features (e.g., "bypass," "diversion," or more generally, "gastrointestinal") rather than by their inferred mechanism of action.
Characterization of the changes in the physical structure of the gut produced by an MBS procedure – including the size & shape of GI segments or anastomoses – should not be used to imply that these changes "restrict" food intake as a mechanism of associated weight loss. It is preferable to describe such procedures by their anatomical features (e.g., "gastrectomy," "banding" or, more generally, "gastric") rather than by their inferred mechanism of action.
REPORTING STANDARDS
In general, a suboptimal initial clinical response to MBS is demonstrated either by total body weight or BMI loss of less than 20% OR by inadequate improvement in an obesity complication that was a significant indication for surgery.
In general, a late post-operative clinical deterioration after MBS is demonstrated either by recurrent weight gain of more than 30% of the initial surgical weight loss OR by worsening of an obesity complication that was a significant

MBS = metabolic-bariatric surgery; AOM = anti-obesity medication; GI = gastrointestinal; BMI = body mass index.

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CHAPTER 2

DIET, LIFESTYLE AND EXERCISE

2.1. The need for dietary, lifestyle and exercise changes to achieve sustainable success - Barbara Andersen and Silvia Leite Faria, Ph.D

Obesity is a chronic disease that requires long-term clinical management. Metabolic-bariatric surgery MBS is the most effective tool for controlling this progressive disease. However, although MBS produces excellent results, weight recurrence occurs in 20-30% of MBS patients. As obesity is a multifactorial disease, possible causes of weight recurrence include endocrine/metabolic alterations; anatomical changes during surgery that fail to provide the desired effects; dietary indiscretions that include inadequate dietary adherence (e.g., excessive calorie, carbohydrate, and/or alcohol intake) and maladaptive eating behaviours (e.g., grazing, bingeing); lack of ongoing follow-up with the bariatric team; mental health issues; and physical inactivity [1, 2]. Recognizing these underlying aetiologies early is critical for effective management [1].

A complex interplay between biological, societal, socioeconomic, socialization-related, psychological, physiological, and personal lifestyle factors – to name just a few essential elements – can contribute to less than satisfactory post-operative results [3]. In addition, each individual's weight maintenance is complicated by the nature, causes, and distribution of their hyper-adiposity, societal and cultural food beliefs and practices, and the complex peripheral and central mechanisms that both increase food intake through reduced feelings of satiety and increased feelings of hunger and minimize energy expenditure [4].

Efforts to promote increased physical activity (PA) and reduce sedentary behaviour (SB) should begin before MBS [5]. Studies show that higher levels of PA and lower levels of SB lead to physical and mental health benefits [5]. Simple validated assessment tools and specific PA prescriptions should aim towards progressively increasing PA. More studies are required to ascertain which conditions and interventions could contribute to helping patients make sustainable PA and SB changes that optimize their clinical outcomes and achieve lifelong success with their plans for sustained weight loss.

Anatomical changes created during MBS limit both energy and nutrient intake, by restricting food intake (early satiety), reducing absorption, or both, all of which predispose patients to nutrient deficiencies. Such nutrient deficiencies, if not prevented or treated, may lead to health problems that can be severe and even fatal. Specific steps should be taken with certain populations, notably pregnant women, children/adolescents, and elderly adults. Other crucial points to consider are the importance of nitrogen balance and protein content in the diet, the latter related to lean body mass retention. As such, proper nutritional monitoring and management are crucial [6, 7].

Lifestyle modification interventions are also needed to avoid weight regain. Studies remain necessary to provide precise and reliable guidelines for dietary changes, eating habits, supervised use of anti-obesity medication (AOM), and the increased incorporation of PA into MBS patients' routines both before and (especially) after surgery Patients' success achieving their weight loss targets is essentially rooted in their adherence to the ongoing guidance provided by the multidisciplinary team, particularly pertaining to lifestyle modifications that include reduced caloric intake, increased PA, and compliance with other evidence-based recommendations from the team [8].

For all these reasons, sustainable therapeutic success requires a multidisciplinary treatment program for people living with obesity, and this should include medical, dietary, psychological, and exercise therapy, as well as social work services. It also must be tailored to each individual patient's needs.

2.2. Behavioural variables that contribute to suboptimal postoperative outcomes - David B. Sarwer, Ph.D

Weight regain after MBS is often attributed to physiological, behavioural, and psychosocial factors. Such behavioural factors include increased daily caloric intake, grazing, loss of control over eating, low physical activity, and loss to follow-up [3, 9-12]. Preoperatively, patients are taught the basic dietary and behavioural changes that will be followed after surgery. Postoperatively, however, there is a tendency for patients to receive little to no ongoing instruction. Thus, patients are vulnerable to returning to maladaptive eating and activity behaviours that may threaten long-term weight control.

Success following MBS requires chronic adherence to a rigorous, reduced-calorie diet [13]. Unfortunately, many patients exhibit poor dietary compliance. The presence of postoperative binge eating, night eating, and lost control over eating is fairly common [14-16] and each is associated both with less weight loss in the first postoperative year and with weight regain over time [17, 18]. Failure to increase physical activity after surgery also has been associated with postoperative weight gain [19, 20]. These data underscore how imperative postoperative behaviour change is for sustained success.

Postoperative interventions to reverse weight regain

Lifestyle modification interventions

Lifestyle modification interventions that emphasize caloric restriction, increased physical activity, and instruction in behavioural modification, are the cornerstone of obesity treatment. In efficacy studies, they typically produce 5-10% weight loss over a period of six months [8]. A number of studies have evaluated the efficacy of adaptations of these interventions to improve MBS outcomes. One meta-analysis of the major clinical trials found minimal differences in weight loss between treatment and a range of control or comparison conditions 6-12 months following the onset of the intervention [21]. This observation suggests that teaching lifestyle modification skills alone is not enough to substantially improve weight outcomes.

Acceptance-based behavioural treatments for weight loss

Recently, acceptance-based behavioural treatments ABT for weight loss have grown in popularity and may address some of the limitations of traditional lifestyle modification ¬approaches. Such ABT emphasizes engaging in goal-directed behaviours that are in line with a person's values (weight maintenance and improved health) despite uncomfortable internal experiences (hunger and food cravings). In a departure from traditional behavioural interventions, the goal is not to reduce these negative internal experiences, but rather to develop a willingness to experience these thoughts, feelings, emotions, and sensations in "the service of" a valued action—weight loss.

While ABTs have been shown to be efficacious for weight loss in persons with obesity who have not undergone MBS, a number of small studies have also investigated their use in MBS patients. Weineland and colleagues reported decreases in disordered eating behaviour in those treated with ABT relative to those who received treatment as usual[22]. Two other studies have revealed that teaching patients mindfulness skills promotes postoperative weight loss[23, 24].

Bradley and colleagues have conducted three studies examining the feasibility, acceptability, and preliminary efficacy of ABT in persons who have regained weight postoperatively[25-27]. The first study was an open trial of an acceptance-based, in-person group treatment for individuals (n = 11) who had regained at least 10% of their weight[26]. Preliminary efficacy was demonstrated as weight regain stopped, and even reversed, with an impressive mean percentage weight loss of 3.6% ± 3.0% total body weight during the 10-week intervention.

In the second study, the intervention was delivered online[27]. In 16 patients, weight regain was reversed with a mean percentage weight loss of 5.1% ± 5.5%. This weight loss was maintained at 3-month follow-up. The third study was a randomized controlled trial (RCT) comparing the intervention against a waiting-list control condition[25]. Participants who received the intervention reversed their weight regain trajectory from their lowest weight (which was sustained at 3-month follow-up), while controls continued to regain weight. Percentage weight loss in the intervention group also was significantly greater than in controls. Collectively, these studies show great promise for the use of ABT, delivered remotely, as a way to reverse postoperative weight regain.

Remote delivery of postoperative interventions

There are numerous barriers to patients engaging in postoperative interventions delivered in person. More frequent postoperative follow-up and/or attendance at support groups is associated with greater weight loss[28]. However, regular follow-up and attendance at support group meetings tends to decrease over time. Moreover, patients often come to the MBS program from great distances away, challenging their ability to return regularly for recommended postoperative visits or additional treatment.
Remote, and, in particular, online delivery of interventions appears well-suited to address these issues. Online treatments can include video modules demonstrating session content, as well as interactive features. Such interventions are particularly desirable, reduce participant burden, and are cost effective[29].

Summary

The great majority of individuals who undergo MBS experience sizable weight loss and improvements in weight-related comorbidities that endure throughout the first decade after surgery, if not longer. However, 20-30% of patients experience suboptimal weight loss and/or sizable weight regain over that time. The field of MBS has been slow to address these challenges to long-term success, likely because of the need to focus on increased utilization of surgery around the world. There is some evidence to suggest that traditional lifestyle modification interventions may be beneficial for some patients, while others likely need novel approaches, such as ABT or the use of platforms that promote remote delivery. Early evidence supports the efficacy of such novel approaches, though additional study is needed. The worldwide growth in rates of clinically-severe obesity and utilization of MBS necessitate the development of novel strategies to promote lifelong success.

2.3. Short and long-term nutritional considerations after metabolic-bariatric surgery - Violeta Moizé Arcone, MSc, PhD, RDN

Introduction

The health benefits of MBS are associated not only with improvements in the severity of comorbidities but also with reductions in their incidence and mortality rates [30, 31]. Such enhanced health outcomes have contributed to the increase in the use of this therapeutic approach in patients with severe and complex obesity [31, 32]. However, food restrictions and the anatomical changes created during surgery mean that the risk of nutritional complications must always be considered [7, 33].

This section summarizes the mechanisms by which different types of MBS can be associated with an increased risk of nutritional complications that, if not treated, can trigger grave health consequences both short- and long-term. In addition, specific nutritional management in older adults (>65 years old), adolescents, and pregnant women undergoing MBS will be briefly considered.

Nutritional considerations associated with metabolic and bariatric surgery

The risk of developing nutritional deficiencies (ND) is influenced by pre-surgical, surgical, and post-surgical factors. Impaired pre-operative nutritional status is a risk factor for both postoperative ND and metabolic complications [34, 35]. This supports the need to identify and correct ND preoperatively as part of the comprehensive preoperative intervention [6, 7, 36]. Bariatric surgery results in major changes in gastrointestinal anatomy that affect gut physiology. Regardless of the surgical procedure, the development of new eating behaviours and the changes in anatomical conditions after MBS limit total energy intake, placing patients at risk of nutritional deficiencies. The impact on nutrient absorption varies by procedure, whether the stomach pouch is reduced or bypassed, changes in the length of the small intestine (afferent/efferent), and length of a common channel [7, 37]. Specifically, food-related behavioural changes and meal patterns – including reduced portion size, early satiety experienced after the meal, changes in taste preferences, and the potential for repeat emesis – can contribute to a negative energy balance and limited vitamin, mineral, and protein intake [38, 39]. Along with these changes, impaired acid secretion, because of gastric resection, may further impair nutrient extraction and the modifications needed for nutrient absorption [37] (See Figure 2-1, below). Although the degree of impact on nutrition absorption may vary between different surgical procedures, all of them have been shown to negatively affect serum levels of iron, folate, vitamin B12, and vitamin D, increasing patients' risk of developing deficiencies [7]. It is important to note that lack of adherence to nutritional supplementation and low-level commitment to medical follow-up appointments after MBS are significant risk factors ND development [6, 40]. Bariatric surgery itself can contribute to nutritional issues through gastro-intestinal symptoms – like dumping syndrome and gastro-oesophageal reflux – and other gastro-intestinal changes like delayed exposure of food to bile and pancreatic juices, thereby diminishing completeness of digestion and absorption [41]. Although there are more data on the nutritional impact of the most popular procedures – like sleeve gastrectomy SG and Roux-en-Y gastric bypass (RYGB)[6, 7, 40] – others procedures like single-anastomosis duodenal-ileal bypass with sleeve gastrectomy (SADI-S) and one-anastomosis gastric bypass (OAGB) require further research [7].

Protein (intake and status): the main actor

A sustained negative energy balance is needed to promote weight loss, and dietary changes after MBS entail calorie restriction [40]. The protein content of a patient's diet is potentially important during surgical weight loss, since protein intake is associated with lean body mass (LBM) retention during weight loss and weight maintenance, satiety, thermogenesis, glucose homeostasis (specifically circulating levels of branched-chain amino acids after MBS) and, if insufficient, malnutrition [42]. It is well known that protein is one of the main nutrients affected by MBS [40]. Exclusion of the duodenum and proximal part of the jejunum, where protein is mainly absorbed, together with anatomical changes in the gastric pouch (affecting the secretion of gastric acid and pepsin) negatively impact protein uptake[42]. It is generally accepted that not only the absolute amount of protein, but dietary content encompassing all the essential amino acids is required for optimal protein synthesis and balance [43, 44]. The decrease in lean body mass during weight loss may affect the regulation of metabolic processes, such as protein turnover and basal metabolic rate, thereby compromising long-term healthy weight management [45]. On the other hand, long-term negative energy and nitrogen balance can be associated with the loss of lean tissue [42]. This is especially important in adults who are particularly susceptible to developing sarcopenia, which will be discussed briefly, later in this section. As shown in Figure 2-2, the equilibrium and status quo of various key bodily systems can be altered and must be monitored carefully to prevent complications and optimize MBS outcomes [42].

Nutritional management after MBS: the importance of an integrated program

Patients undergoing MBS should be invited to participate in a specifically-structured and well-designed interdisciplinary patient-centred program [7, 46]. Nutritional complications can be prevented or managed with preoperative assessments and patient education, using evidence-based information to enhance patient empowerment and promote self-management [47]. A preoperative nutritional assessment by a specialist dietitian/nutritionist allows for the correction of identified deficiencies [40, 46]. It also is recommended that patients take a complete multivitamin and mineral supplement (containing thiamine, iron, selenium, zinc, and copper) daily after all MBS procedures [40, 46]. Based on limited evidence, current MBS guidelines for the SG and the RYGB suggest a minimum of 60-80g/day of dietary protein or 1.0-1.5g/kg Ideal Body Weight as an achievable and meaningful target to minimize post-surgical complications [6]. Procedures with a higher associated risk of protein-energy malnutrition require a dietary protein intake of 90g/day or as high as 2.1g/kg Ideal Body Weight. However, the limited volume of the stomach and the higher satiety experienced after a meal following MBS could make this recommendation unrealistic. Consequently, dietary protein supplementation has been postulated to be a useful tool to meet daily protein needs [40, 46].

To help patients living with obesity optimize MBS outcomes and prevent complications, it is important to ensure access to specialist-delivered dietetic support to (1) allow regular monitoring of the patient's laboratory tests and, by doing so, adjustments to nutritional supplementation, as required [6, 40]; and (2) enhance patients' commitment to the MBS program for a minimum of two years [7]. After discharge from the program, patients should undergo monitoring of their nutritional status at least once every year as part of a shared care model of management [7]. Longer-term adherence to bariatric support group meetings has been shown to benefit weight loss outcomes [48].

As with other chronic conditions, obesity requires interdisciplinary care [6, 7, 40, 42], which is the cornerstone of life-long bariatric care. Specifically, a dietitian specialising in obesity management is integral to the assessment and ongoing nutritional care of patients undergoing MBS [7].

Special populations undergoing MBS

Pregnant women

Weight loss and the reduced adiposity induced by MBS in women of reproductive age significantly enhances fertility [49]. On the other hand, compromised nutrient absorption after MBS, in combination with increased demands for nutrients and energy during pregnancy, can exacerbate deficiencies affecting the mother and, thus, foetal growth and development [50]. Although some nutrient-specific interventions help to ensure normal, safe development of the foetus – including vitamins A, D, C, and E, Zinc, vitamins B9 and B12, thiamine, iodine, and omega-3 supplements [51] – no consensus yet exists on what constitutes adequate supplementation. Considering the first year after MBS critical to ensuring nutrient status adequacy, current guidelines recommend avoiding pregnancy until 12-18 months after MBS until maximal weight loss and weight stabilization are achieved [6, 40]. It also is preferable for women to plan gestation before undergoing MBS to ensure not only nutrient sufficiency, the timely commencement of additional folic acid [49], and adherence to prescribed supplements, but also that the gestational woman comes to adopt a healthy eating pattern [52]. Supplementation must be tailored and prescribed by a specialist based on a comprehensive evaluation and follow-up, since both the excess and lack of certain micronutrients could have detrimental effects [51]. Nutritional status should be monitored closely for the safety of the mother and baby starting before pregnancy and continuing through lactation [53].

Adolescents

Well-designed, prospective, observational studies suggest that weight loss surgery is safe and effective for paediatric patients in comprehensive, multidisciplinary MBS settings where team members have experience working with youth and their families [54]. Adolescents should be monitored for dietary adherence and nutritional status and receive suitable education on a regular basis, due to the numerous changes that may occur in their body composition, growth, and sexual development as they move towards adulthood [55]. Prospective data from a Swedish cohort revealed multiple micronutrient deficiencies following MBS, an observation that highlights the need for routine and long-term monitoring [56]. It is particularly important to consider that, because malabsorptive procedures are associated with an especially-high prevalence of post-surgery nutritional deficiencies, the care of patients undergoing such procedures should continue indefinitely at a centre specializing in MBS28. Longitudinal, non-stigmatizing, shared decision-making with patients and families – which includes planning the adolescent's transition to adult care – is important to help address obesity as a chronic condition that will persist throughout each patient's lifespan [54].

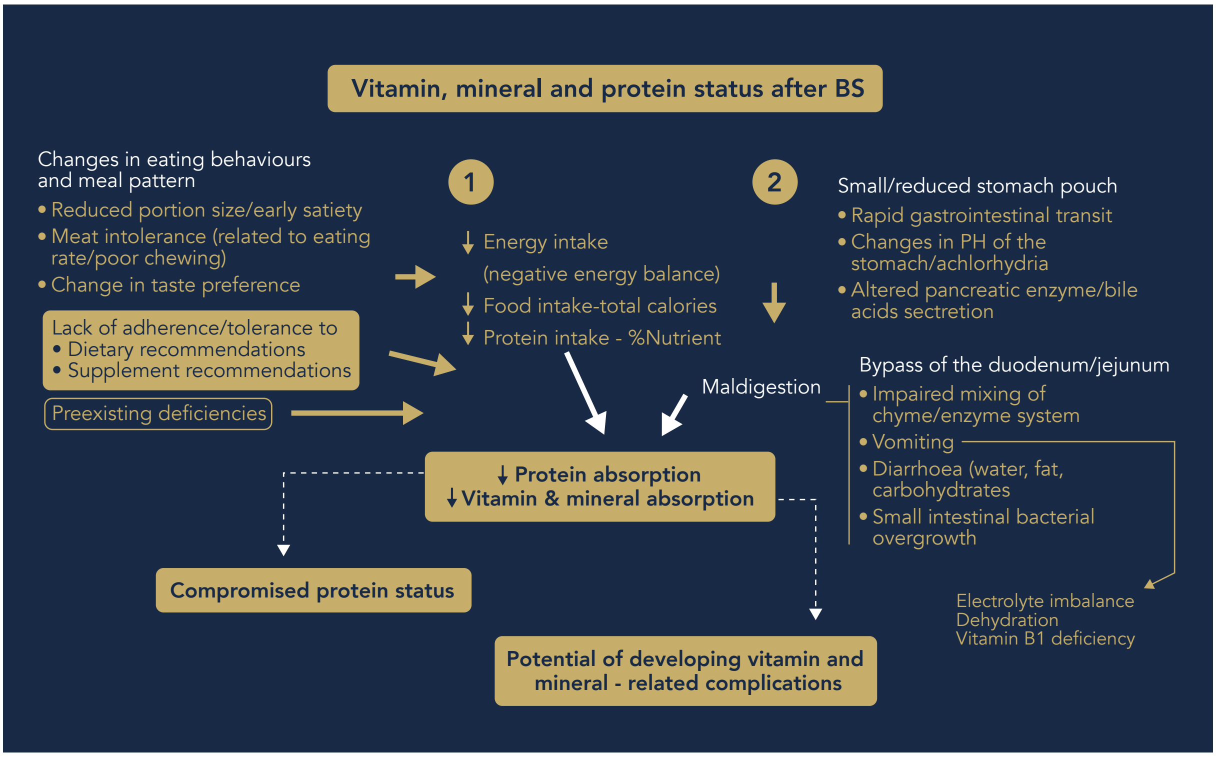
Older adults

Older age is a risk factor for sarcopenic obesity in MBS candidates and is fairly common in female candidates for MBS over 60 years of age [57]. Sarcopenia may have profound implications in older adults seeking MBS, due to the marked alterations that can occur in their body composition. It is associated with physical disability, frailty, reduced quality of life, and even death [58]. Patients undergoing MBS average roughly 8 kg of lean body mass (LBM) loss within one year of surgery, and the optimal time window to intervene is during the first few weeks post-operatively, since 55% of lean body mass (LBM) is lost within three months, coinciding with the period of major reduction in energy and protein intake [59]. During the preoperative evaluation, a "pre-habilitation" and/or rehabilitation program that considers protein intake along with strength training should be prescribed individually for each patient [60]. Considering the implications for overall health, it would be valuable for such programs to include clinical outcomes like physical rehabilitation, muscle strength, and muscle function.

Conclusions

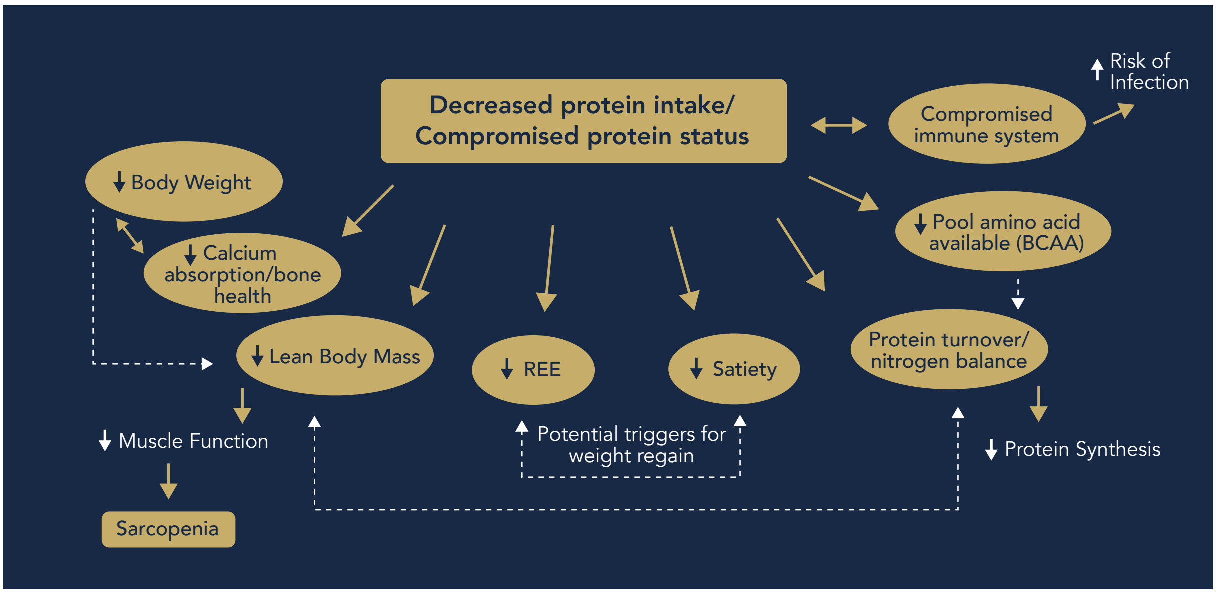
Nutritional education, as well as the management and resolution of nutrition-related problems, should be integrated into every interdisciplinary patient-centred bariatric program curriculum. Patients should have access to follow-up with a specialist dietitian/nutritionist for support with dietary and lifestyle changes, to challenge barriers that might adversely influence patients' adherence to supplementation, and to promote their commitment to the program. Continued long-term patient empowerment, behavioural medicine education, and the transfer of skills to manage complications are essential. The evaluation and follow-up of people living with obesity who undergo MBS should consider the prevention, identification, and long-term management of nutritional deficiencies, especially in those who have undergone procedures that predominantly impact nutrient absorption. Although discussed only briefly in this chapter, the prevention, evaluation, and treatment of deficits is especially important for patients who have undergone malabsorptive procedures, adolescent and elderly patients, and patients before and during pregnancy and lactation.

Figure 2-1: Anatomical, meal pattern, and behavioural changes potentially contributing to the development of nutrient abnormalities after MBS



Source: Adapted from Moizé V, Vidal J. Laferrère B. Protein nutrition and status. Chapter 49 in: Metabolism and Pathophysiology of Bariatric Surgery Nutrition, Procedures, Outcomes and Adverse Effects-1st Ed. Nov.26, 2016 [42].

Figure 2-2: Complications associated with compromised protein status after bariatric surgery



REE: resting energy expenditure; BCAA: Branched chain amino acids
Source: Adapted from Moizé V, Vidal J. Laferrère B. Protein nutrition and status. Chapter 49. in: Metabolism and Pathophysiology of Bariatric Surgery Nutrition, Procedures, Outcomes and Adverse Effects-1st Ed. Nov.26, 2016 [42].

2.4. Introducing physical activity and reducing sedentary behaviours in people living with obesity before and after metabolic and bariatric surgerys
- Dale S. Bond, PhD

Introduction

Higher levels of physical activity (PA) and lower levels of sedentary behaviour (SB), which displace time that could be spent performing PA, can confer numerous physical and mental health benefits before and after MBS. Yet, many patients spend too little time being active and too much time being sedentary to fully attain these benefits. Thus, while MBS has substantial and durable effects on body weight, multiple comorbidities, and physical function for the majority of patients, it appears to have little impact on patients' objectively-measured PA and SB. Thus, the integration of routine PA and SB assessments into clinical practice to identify patients who need additional behavioural counselling and strategies is warranted. Moreover, there is need for greater insights into which patients and under what conditions such interventions are needed, and into how these interventions can be most successful at helping patients to make sustainable PA and SB changes to optimize their clinical outcomes and achieve lifelong success after MBS.

PA and SB before MBS

Patients who undergo MBS, like all individuals, should be encouraged to: (1) increase their PA, especially PA performed at moderate-to-vigorous intensities (i.e., MVPA); and (2) replace time spent in SB (i.e., waking behaviours characterized by low energy expenditure and sitting, reclining or lying posture) with light- and moderate-intensity physical activities [61-63]. Increasing PA via increasing MVPA or reducing SB carries multiple health benefits, especially for individuals with chronic conditions, including obesity [64-66].

Efforts to promote PA should occur before MBS. Increasing PA before MBS contributes to significant improvements in health-related quality of life and higher PA levels before MBS and are a strong predictor of higher PA levels after MBS [67, 68]. However, patients on average engage in low levels of MVPA and high levels of SB before MBS, when measured objectively via wearable sensors (e.g., accelerometers) [69-71]. To date, the Longitudinal Assessment of Bariatric Surgery (LABS)-2 multi-site consortium is the largest study involving sensor-based measurements of physical activity and sedentary behaviours among MBS (N=473) patients. In this study, patients averaged accumulating 77 minutes/week of MVPA before MBS, with 76% of patients falling far below guidelines to improve health (≥150 MVPA minutes/week) [69]. Moreover, less than 10% of the MVPA was accumulated in bouts lasting ≥10-minutes (so called "bouted MVPA", a proxy for exercise). While some other studies using different objective devices or measurement protocols have identified higher total MVPA estimates in MBS patients [72-75], the proportion of waking hours spent in MVPA (4%-5%) and pattern of MVPA accumulation (minimal MVPA accrued in longer bouts indicative of exercise) are similar.

Regarding SB, results from the LABS-2 study showed that before MBS, patients averaged spending nearly two-thirds (64%) of their waking hours in SB, with 59% of participants falling into either the high or very high sedentary category [69]. Other studies that used device-based activity measures suggest that this percentage may be as high as 81% [76]. Importantly, data also suggest that patients, on average, accumulate 30% of SB in prolonged bouts ≥ 30 minutes that are associated with cardiometabolic risk [73, 77, 78]. Taken together, the above data suggest that patients average spending too little time in MVPA and too much time in SB, resulting in low overall movement during the day.

Changes in PA and SB after MBS

Despite MBS producing large reductions in body weight, increases in physical function, and improvements in multiple physical and psychological comorbidities for a majority of patients, MBS appears to have little impact on patients' physical activity and sedentary behaviours. In the LABS-2 study, patients on average increased their MVPA minutes/week from 77 minutes prior to surgery to 106 minutes when reassessed one year after surgery [69]. While this change was statistically significant, the clinical importance of this modest improvement is unclear, as patients still below minimum-recommended guidelines to improve health, let alone those recommended for weight management (≥250 minutes/week) [61, 79]. Other studies involving smaller samples have detected similar findings with small or no changes in MVPA during the first post-surgical year [19, 71, 80-82]. Additionally, most patients make no further changes in MVPA beyond one year post surgery [69].

In the LABS-2 study, post-operative changes in SB followed a pattern similar to those observed for MVPA, with a small, statistically-significant improvement (i.e., decrease of ~30 minutes/day) in time spent in SB during the initial postoperative year, but minimal changes beyond this point [69]. Moreover, a majority (59%) of participants fell into either the "high" or "very high" SB trajectory group from pre- to 3-years post-surgery [69]. Other, smaller studies have yielded similar findings, with patients averaging small, statistically non-significant changes in SB after MBS [70, 71, 81, 82]. Moreover, in the recent Oslo Bariatric Study, MBS patients actually increased their time spent in SB by more than one hour per day between one and five years after surgery [83].

The above findings indicate that most MBS patients make modest to no changes in MVPA or SB. Furthermore, after MBS many patients continue to engage in levels of MVPA that fall below guidelines to improve health and spend a large majority of their waking hours in SB.

Higher levels of PA can confer numerous health benefits in MBS patients

Spending too little time in MVPA and too much time in SB before and after MBS is problematic, because there is growing evidence that higher levels of PA can confer numerous physical and mental health benefits for patients undergoing MBS. These benefits, often superimposed on surgery effects, include improved physical fitness, cardiometabolic health, and physical function; reduced bone loss; and enhanced weight regulation and body composition [84-95]. Research also shows that PA may assist with regulating appetite and eating, reducing depression, and enhancing certain aspects of health-related quality of life, such as energy and vitality [67, 80, 96, 97]. As shown in Figure 2-3 (below), nearly all PA-related benefits are supported by observational and experimental evidence. However, it should be noted that the quality and quantity of experimental evidence remains limited. For example, in a recent meta-analysis of RCTs involving PA interventions that included both information on PA prescription and weight measurement beyond one year post-surgery, only a small, non-statistically significant effect on weight recurrence was observed [98]. However, the small number of trials (N=5) and several methodological issues (e.g., only 2 of the 5 trials assessed interventions designed to prevent weight recurrence) undermined the investigators' ability to draw definitive conclusions regarding the efficacy of PA interventions for counteracting weight recurrence. Thus, rigorous, appropriately-designed trials examining interventions to help patients achieve both higher levels of PA and related health benefits clearly remain necessary.

Figure 2-3: Benefits of increased level of physical activity in MBS patients

Higher levels of PA can confer numerous health benefits in MBS patients

- ↑ CR Fitness
- ↑ Muscle Strength
- ↓ Cardiometabolic risk
- ↓ Bone loss
- ↑ Physical function
- ↑ Body composition
- ↑ Weight loss / ↓ weight recurrence
- ↑ Appetite & eating regulation
- ↓ Depression symptoms
- ↑ Energy/vitality

Evidence includes observational and experimental in all categories
with the exception of experimental for 'Appetite & eating regulation'.

Patients choosing to undergo MBS need additional pre- and post-surgical interventions to make PA changes

To achieve PA-related health benefits, patients choosing to have MBS need some additional intervention to help them make sustainable changes in PA. While several interventions involving supervised PA have been tested to demonstrate any effects of PA on a variety of fitness and health outcomes after MBS, only a few behavioural interventions have specifically focused on helping patients achieve PA changes in daily life [99-102]. One example is the Bari-Active trial, in which a 6-week behavioural counselling intervention produced large, objectively-measured increases in pre-surgical bouted MVPA compared to standard care (+16.6 minutes/day vs. -0.3 minutes/day, $p = 0.001$) [99]. Additionally, intervention participants reported statistically-significant ($p < 0.05$) improvements in multiple aspects of health-related quality of life, especially those related to physical health, whereas controls' health-related quality of life did not change and remained below population norms [67]. Finally, intervention participants reported large increases in psychosocial mechanisms of PA behaviour change, including PA enjoyment, self-efficacy, and autonomous motivation [103]. These findings suggest that patients can make clinically-meaningful changes in PA and achieve related health benefits even before MBS and its associated weight loss and health improvements occur. Yet, because intervention participants did not achieve additional PA increases at post-surgical follow-up [104], patients need additional support and strategies to achieve sustainable increases in PA for general health and optimize short- and long-term MBS outcomes.

PA should be a standard component of multidisciplinary MBS care

Many patients undergoing MBS have low PA levels before surgery and do not make clinically-meaningful changes in PA after surgery, increasing their risk of suboptimal MBS outcomes and undermining overall health. Thus, at a minimum, routine PA screening, assessments, prescription, and counselling should be standard components of multidisciplinary MBS pre- and post-surgical care [98, 105]. Use of simple, validated assessment tools can help to identify patients who have low PA and barriers to increasing their PA. Physical activity prescriptions should target gradual increases in MVPA and replacing SB with light- and higher-intensity physical activities to increase overall daily PA. Brief counselling delivered in-person or through telehealth methods [101] that involves teaching standard behavioural strategies (e.g., self-monitoring, goal-setting, problem-solving) and other newer therapeutic strategies (e.g., acceptance and values-based interventions and positive psychological skill-building [106, 107]) may help to address barriers to achieving the objectives of PA prescriptions. Such efforts are essential to improve patients' overall health and optimize MBS outcomes.

2.5. Results of a consensus survey - Silvia Leite Faria, PhD

Patients living with obesity who are candidates for MBS need assistance from a variety of healthcare professionals. For this reason, bariatric service centres have organized multidisciplinary teams to attend to these needs. Nutritional supplementation is a cornerstone for maintaining patients' quality of life. Nutrient deficiencies are a risk after MBS and, if not treated, can lead to serious and even life-threatening health problems. Specific steps should be taken, and hypo-absorptive procedures should have higher doses of protein and liposoluble vitamins. Maintaining adequate protein intake is another key issue. Inadequate protein intake jeopardizes lean body mass retention, which is directly correlated with weight maintenance. In summary, the need for proper nutritional management should be emphasized. Increased physical activity also should be encouraged, starting even in the early preoperative stage. Besides leading to mental health improvements, higher levels of PA also helps to ensure lean body mass preservation during weight loss. This, in turn, impacts body composition, which correlates with basal metabolic rate improvements, thereby helping to maintain weight loss.

Lifestyle modification interventions should be introduced in a clear and well-organized manner to assist patients in their understanding of the need to follow the instructions given. This information should also serve to encourage patients as they face the challenges of changing their lifestyles while avoiding any forms of stigma.

It was for all the above-noted reasons that (1) a multi-disciplinary team of international experts in obesity management were asked to participate in a 3-round Delphi consensus survey in the winter and spring of 2023 to assist in drafting MBS guidelines; (2) the panel included, in addition to bariatric surgeons and endoscopists, experts in nutrition, psychology, and exercise for persons with obesity; and (3) in addition to statements on MBS, the survey included statements on patient preparation for surgery and management after surgery by nutritionists and both psychology and exercise counsellors. Results of these statements serve to supplement those of an earlier 3-round Delphi consensus survey of 94 international interdisciplinary experts, conducted jointly by IFSO and the World Gastroenterology Organization (WGO) in 2022, in which the primary focus was on the non-surgical management of obesity, including pre- and post- MBS care.

In terms of psychological assessments prior to an MBS procedure, our current experts could not come to consensus that every patient should undergo an evaluation by a mental health professional. However, they almost unanimously agreed that all patients with a known or suspected mental health diagnosis should undergo an assessment with a mental health professional prior to MBS, even if that condition is currently being treated.

Our experts similarly agreed that individuals need some form of behavioural intervention to modify physical activity and sedentary behaviours, both before and after MBS. They also agreed that increasing physical activity and exercise has clinically-significant physical and psychological benefits for MBS patients; and that, when measured objectively, most individuals who engage in low levels of moderate-to-vigorous intensity physical activity and have high levels of sedentary time before surgery make only modest improvements in these during the initial year after MBS.

In terms of nutrition in the post-operative period, due to the significant caloric restriction that individuals experience after MBS and to minimize any muscle loss associated with weight loss, the experts agreed that a minimum of 60 grams of dietary protein is required daily after all MBS procedures. Besides this, since hypo-absorptive MBS procedures result in more significant protein loss, it is essential to ensure that patients undergoing such procedures consume a minimum of 80 to 100 grams of dietary protein each day.

Focusing on body composition, experts agreed that performing diagnostic studies to identify sarcopenia is advisable in at-risk individuals both before and after MBS. Meanwhile, considering intrinsic characteristics related to individuals over 65 years of age, a rehabilitation program managing protein intake along with strength training should be prescribed individually both before and after MBS to prevent sarcopenia and related complications among individuals considered at particular risk.

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2.6. **Final conclusions** - Silvia Leite Faria, PhD

Several common denominators have been highlighted by healthcare professionals in this chapter.

- Weight loss success is directly connected to continual adherence to a rigorous, integrated, specifically-structured, well-organized, interdisciplinary, patient-centred program.
- Such programs should aim to prevent, identify, and manage the risks of short-term and long-term complications of MBS.
- Education to guide patients' dietary practices, physical activity, and other influential lifestyle behaviours should be provided both prior to and after MBS.
- Patients also must have access to specialists who will promote adherence and commitment to the weight loss program and accompany these patients over time. Such experts should also transfer skills to patients which they will need to manage complications that may arise.
- Studies support the use of acceptance-based behavioural treatment (ABT) as an aid for MBS patients.
- Goal-directed guidance in line with patient values, and online sessions using videos with interactive activities, are additional innovations currently being suggested.
- The worldwide growth in obesity rates requires serious attention through further studies that continually search for surgical and non-surgical solutions that may contribute to successful lifelong outcomes for patients who have undergone MBS.

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CHAPTER 3

MEDICAL TREATMENT OF OBESITY

3.1. Introduction: current status of pharmaco-modulation and mechanisms of action - Alex Miras MD, PhD

Since the 1960s, obesity pharmacotherapy has experienced some successes, but appreciably more failures. One reason for this is that, while medications have been reasonably effective at inducing weight loss, their safety has been an Achilles heel. Fenfluramine/phentermine, rimonabant, and sibutramine are examples of such medications that were eventually withdrawn due to their deleterious effects either on the cardiovascular system or mood, the latter to the point of suicidal ideations. Up to 2017, the only medication that had survived the test of time was orlistat, which is still available and can be effective for those who can tolerate it.

What has changed since 2017 is the application of our knowledge on how the gut "talks" to the brain. The discovery of native hormones that signal hunger and satiety has revolutionised the way obesity is treated. Gut hormone analogues, predominantly of the hormone GLP-1, were initially introduced for the clinical treatment of type 2 diabetes mellitus (T2DM) 10 years earlier. Their effectiveness in glucose regulation in the context of clinically-meaningful weight loss and a very favourable safety profile have led to their use for obesity at higher doses. Gut hormones do not behave like other hormone systems in the body, such as cortisol or even insulin, for which higher doses can be lethal. In contrast, treatment even with high doses of GLP-1 only causes transient side effects that include nausea, diarrhoea, and constipation. The worst-case scenario is the development of pancreatitis or cholecystitis, both of which are rare. There also is no evidence of tachyphylaxis of the GLP-1 receptor to high doses of treatment or of any increased risk of malignancy.

All these factors have led to the rapid uptake and refinement of this technology to develop increasingly-effective and longer-acting treatments that are more convenient for patients. The next step in this revolution is combining two or more gut hormones, either in the same or in different molecules, to cause additive, if not synergistic, effects on body weight regulation. What remains unclear are whether these treatments can impact hard clinical outcomes, what their long-term safety is, and how their use can be personalised to individuals. Hopefully, all these questions will be answered in this new and exciting era.

3.2. Who should be prioritized for medical weight management?
- Arya M. Sharma, MD

Given the vast number of individuals living with obesity both for practical and economic reasons, the question of whom to prioritize for treatment with anti-obesity medications (AOM) is of considerable significance. Traditionally, guidelines have recommended different levels of treatment based on BMI class, with or without the presence of comorbidities. However, given that BMI is merely a measure of patient size, it does not reflect any given individual's actual health status. This has led to the development of several disease-staging systems, which further characterize the severity of disease based on the presence of obesity-related complications or comorbidity. These include the Edmonton Obesity Staging System (EOSS) [1], the King's Obesity Staging System [2], and the Cardiometabolic Staging System endorsed by the American Association of Clinical Endocrinologists and American College of Endocrinology [3]. Of these, EOSS, which defines obesity stage based on the presence of varying degrees of mental, medical, and functional impairments of health, has been shown to be a better predictor of mortality than BMI or waist circumference alone [4]. Indeed, within a given EOSS stage, individual mortality risk appears to be independent of BMI. Higher EOSS stages have also been associated with greater peri-operative risk in individuals with similar BMI [5]. Given the higher risk of individuals with higher obesity stages, it is likely that these individuals will stand to benefit most and should therefore be prioritised for obesity treatment, including the use of AOM.

However, several other issues may warrant consideration when prioritizing patients for treatment with AOM. Such issues include individuals who meet the criteria for surgery but are not suited for, do not have access to, or do not want surgery, as well as individuals who are too heavy/sick for surgery and might benefit from pre-surgical weight loss. There also is evidence now showing that AOMs may have an important role preventing and reversing post-surgical weight gain [6]. One may perhaps also consider prioritizing individuals who require weight loss for other procedures (e.g. transplantation, fertility treatments, etc.). Ultimately, the decision regarding which patients to prioritise for treatment with AOM will depend on availability, access, and resources, as well as the expected benefits as part of a personalized obesity management plan.

3.3. Weight management pharmacotherapy in children and adolescents
- Claudia K. Fox, MD, MPH

The use of anti-obesity medication (AOM) for the pediatric population is a rapidly evolving field. Born out of the poor outcomes of lifestyle therapy, particularly in adolescents [7], and the recognition that obesity in children and adolescents tracks strongly to adulthood [8], several recent clinical trials have examined the safety and efficacy of AOMs in this population. These include three large randomized, double-blinded, placebo-controlled clinical trials in adolescents with obesity. Of these, the most favorable outcomes were seen with semaglutide 2.4mg, which induced a mean 16.7% placebo-subtracted BMI reduction over 68 weeks among 201 adolescents with obesity. Additionally, again compared to placebo, semaglutide improved cardiometabolic risk factors and quality of life [9]. Extended-release phentermine/topiramate outcomes also appear to be robust, including a 10.4% placebo-subtracted BMI reduction over 56 weeks in 223 adolescents with obesity [10]. Finally, liraglutide 3mg resulted in a 4.6% placebo-subtracted BMI reduction over 56 weeks in 251 adolescents with obesity [11]. Although the safety profiles of each of these AOMs were deemed acceptable by the researchers, it should be noted that these studies were deemed insufficient to garner universal approval by prescription drug regulatory agencies such as the Federal Drug Administration (FDA) and Europena Medical Association (EMA). Only liraglutide 3mg and semaglutide 2.4mg are approved by both EMA and FDA for youth ≥12 years old. More trials are needed, including those that examine the safety and efficacy of AOMs in children younger than 12 years of age.

3.4. Efficacy and safety of the long-term use of pharmacotherapy for obesity
- Josep Vidal, MD

The American Society of Metabolic and Bariatric Surgery (ASMBS) recommend reporting follow-up after metabolic-bariatric surgery (MBS) as short-term, medium-term, or long-term if the length of follow up is <3 years, 3-5 years, or > 5 years, respectively [12]. It could be argued that the same standard should be used when addressing the issue of pharmacotherapy for obesity. Unfortunately, no study is yet published in which the efficacy and safety of pharmacotherapy as a treatment modality for obesity have been evaluated beyond five years of follow up.

Currently-available prescription drugs – namely orlistat, phentermine-topiramate, naltrexone-bupropion, liraglutide, semaglutide, and tirzepatide – have all been evaluated in well-defined RCTs [13]. Among these, four RCTs with ≥ 2 years of active drug therapy have been published [14-17]. As shown in Table 3-1, the XENDOS trial detected the superiority of orlistat 120mg TID over placebo in the two main outcome measurements: achieving weight loss (WL) and reducing the incidence of type 2 diabetes at four years of follow up [14]. Similarly, in the SCALE-Prediabetes trial, even greater WL and a reduced incidence of T2D were observed in subjects on liraglutide 3.0mg OD, relative to placebo, at three years follow-up [15]. A sustained WL-effect over two years also was demonstrated in the SEQUEL trial which assessed the combination drug phentermine-topiramate [16]. More recently, two-year data from the STEP-5 RCT have been published, which demonstrate the durability of the WL effect of semaglutide 2.4 OD over two years [17]. Of note, the proportion of subjects with double-digit weight loss has consistently been higher in semaglutide trials than in those involving orlistat, phentermine-topiramate, or liraglutide. The observed WL in these trials has nonetheless been associated with improvements in several metabolic derangements (glucose, lipid, blood pressure, C-reactive protein) included either as secondary or exploratory endpoints. Unfortunately, data on the efficacy of naltrexone-bupropion and tirzepatide in RCTs with follow up of one or more years have not been published.

Importantly, however, no major safety issues were identified in any of the above-mentioned RCTs [14-17]. Although gastrointestinal side effects were common, they were usually mild. Use of liraglutide for three years was associated with a higher proportion of gallbladder-related events (5%) than with placebo (2%) [15]. Of note, an additional RCT using semaglutide 2.4mg with two years of follow up has been published [17]. In the STEP-1 trial extension, semaglutide 2.4mg was used for one year, while a second year without active drug therapy was included [18]. Weight recurrence was observed following drug discontinuation after 52 weeks of use.

Unfortunately, data on the long-term use of pharmacotherapy for obesity outside RCTs also are unavailable. Follow up data from real-world data studies are scarce and limited to follow up under one year [19]. In the near future, new RCTs may shed light on the health impact of long-term pharmacotherapy for obesity. The ongoing SELECT RCT aims to evaluate the effect of semaglutide 2.4mg versus placebo on cardiovascular (CV) event reduction in people with overweight or obesity [20]. Similarly, the effect of tirzepatide on CV event reduction is being evaluated in the SURMOUNT-MMO RCT (ClinicalTrials.gov Identifier: NCT05556512), with both studies having intended follow up for up to five years. According to information listed at clinicaltrials.gov, these two studies are scheduled for completion in the last quarter of 2023 and in 2027, respectively.

3.5. Personalisation of pharmacotherapy for obesity - Alex Miras, MD, PhD

Obesity is a highly-heterogeneous set of different diseases, and our understanding of the pathophysiology and phenotypes of its subpopulations is improving slowly. Due to persistent pushback from the scientific and clinical communities regarding the biological underpinnings of obesity, our understanding of its subpopulations is far behind that of other diseases, like cancer and even diabetes. There are numerous benefits to acquiring this knowledge, however, one of them being that we can then use such knowledge to personalise treatments for the disease. Such treatments include nutritional, physical activity, psychological, pharmacological, endoscopic, and surgical therapies. Application of precision medicine in this field will mean that we prioritize people who either already have or are most likely to develop obesity complications, and offer them the most effective therapy that will cause the fewest side effects in a manner that is cost-effective both to them and to the healthcare system.

The revolution in pharmacotherapy for obesity has drawn considerable focus on the need for optimal use of newer medications which are relatively expensive. At the moment, there are no known baseline patient characteristics that predict long-term weight loss. Baseline psychological profiling and measurements of "engagement" or "motivation" have demonstrated no predictive value. Currently, the best predictor of response with any class of medication is the presence of weight loss three months either after its initiation or after the maximum dose of drug has been reached [21]). The usual threshold for a good response at three months is >5% of total body weight loss, as this predicts weight loss responses at 12 months and beyond.

Evidence on responses to specific medications remains limited. Most of the evidence stems from small clinical trials or experimental medicine studies. For orlistat, people who reduce their fat consumption after 72 weeks of treatment lose >10% of their total body weight, versus those who do not change their food preferences who lose <5% of their total body weight [22].

Based on the results of participants in double-blind RCTs receiving the combination of naltrexone and bupropion, patients who experience an increase in "craving control", measured using the Control of Eating Questionnaire after eight weeks of treatment, lose more weight at 56 weeks than those who do not [23]. While naltrexone/bupropion improves binge eating psychopathology, this has not translated into superior weight loss so far [24]. In patients who use naltrexone/bupropion whilst trying to stop smoking, use of the medication causes weight stability [25]. The Taq1A polymorphism of the dopamine receptor density 2 gene is associated with the density of striatal dopamine D2 receptors and thought to influence the neural response to food and the development of obesity. In one study, short-term treatment with naltrexone/bupropion caused significantly greater weight loss at 16 weeks in people carrying the A allele than in those without it (5.9% vs. 4.2%) [26].

Whether liraglutide reduces the rewarding value of food and might, therefore, be more effective in people who consume energy-dense food remains unclear, based on human neuroimaging studies (e.g. [27]). People with high baseline emotional eating scores seem to be more resistant to the effects of short-term liraglutide on brain responses to food in neuroimaging studies, but this has not been shown to translate to less weight loss [28]. The only predictor of response to liraglutide at 16 weeks is a reduced rate of gastric emptying after five weeks of treatment.

Supportive evidence for semaglutide is gradually emerging [29]. One nested study within the STEP-5 double-blind RCT demonstrated that people with a higher baseline craving for sweets, using the Control of Eating Questionnaire, lose significantly more weight (17.5% vs. 11.6%) at 106 weeks of treatment than those without [30].

Finally, in an experimental medicine study of extended-release phentermine-topiramate using a randomised double-blinded design, greater baseline consumption of calories at an ad libitum test meal was associated with superior short-term weight loss after two weeks of treatment [31].

3.6. Setmelanotide and future combination treatments - Caroline M. Apovian, MD

Obesity is a complex disease that is multifactorial in origin. However, severe early-onset obesity may be due to rare genetic variants that result in dysfunction in the melanocortin pathway, which is a central pathway for energy homeostasis and appetite regulation. When the body is satiated, leptin binds to the leptin receptor that is expressed on pro-opiomelanocortin (POMC) neurons in the hypothalamus, which in turn increases the expression of POMC. Then POMC is cleaved by proprotein convertase subtilisin/kexin type 1 (PCSK1) into α and β- melanocyte-stimulating hormones (MSH). These peptides bind and activate the melanocortin-4 receptor (MC4R), which promotes satiety and increases energy expenditure [32].

Rare human genetic mutations in the POMC, LEPR and PCSK1 pathways block MC4R signalling, which causes unopposed hunger or hyperphagia and severe, early-onset obesity. Setmelanotide [33] is an MC4R agonist which was approved by the FDA in 2020 for paediatric and adult patients with obesity due to POMC, LEPR, or PCSK1 deficiency. In June 2022, the indication for setmelanotide was extended by the FDA to include patients with Bardet-Biedl syndrome. Several trials of this agent in patients with this and other similar syndromes have been conducted, with setmelanotide found to help achieve meaningful weight loss at one year and to generally be well tolerated, with hyperpigmentation the most common adverse effect [34, 35]. Further research with setmelanotide in patients with other genetic variants that are more common may expand the use of this anti-obesity agent in the future.

3.7. Use of adjuvant pharmacotherapy before and after metabolic-bariatric surgery - Rachel L. Batterham, MD, MSc, PhD

A suboptimal response to MBS is common, with a prevalence estimated as high as 25%, depending on which procedure the patient has undergone and the definition of suboptimal response used [36]. The parameters most commonly used to define suboptimal response are percentage total body weight loss (%TWL), T2DM remission, and change in serum HbA1c level. The mechanisms underlying suboptimal response after surgery remain elusive, with only a small number of studies indicating that patients with insufficient weight loss have blunted post-prandial levels in gut hormones like GLP-1 and PYY [37, 38].

Patients typically undergo assessments for nutritional, psychological, and social causes that may be contributing to insufficient weight loss. Surgical causes, including a gastro-gastric fistula and a candy-cane formation at the gastro-jejunal anastomosis are uncommon, whilst dilatation of the gastric pouch after RYGB is not thought to contribute to inadequate weight loss [39].

The use of modern pharmacotherapy for obesity is an attractive option for many patients, due to the excellent safety profile and efficacy of several drugs. In terms of evidence, in the only double-blind, placebo-controlled RCT assessing the post-MBS use of an AOM, the adjuvant use of liraglutide 1.8mg daily in patients without T2DM remission after RYGB or Vertical Sleeve Gastrectomy (VSG) was associated with an absolute mean HbA1c reduction of 13.3 mmol/mol (-1·22%, 95% CI -19·7 to -7·0; p=0·0001) from baseline and 5% weight loss at six months [40]. Results from case series using liraglutide at a daily dose of either 1.8mg or 3mg are consistent with these findings [41, 42]. In one, recent double-blind, placebo-controlled RCT that evaluated liraglutide 3mg daily for people with suboptimal weight loss and post-prandial GLP-1 responses, use of the medication was associated with approximately 9% total body weight loss at 24 weeks and had a safety profile similar to when the medication is used in non-surgical patients [Mok et al, JAMA surgery, in press]. Another similar trial testing semaglutide 2.4mg weekly is ongoing (ClinicalTrials.gov NCT05073835). Case-series using non-GLP-1 based therapies have yielded mixed, but overall encouraging results (e.g. [43]).

What is intriguing with these findings is that, with the use of GLP-1-based adjuvant therapies at least, the weight loss and glycaemic outcomes of patients who have undergone MBS are similar to those of people who have not had previous MBS. This is an exciting finding that opens many mechanistic research questions. In addition to the identification of baseline markers that predict response to MBS and pharmacotherapy after surgery, such experimental medicine studies are needed to fill a key gap in knowledge. These studies will not only be of academic interest, but have important clinical implications in the era of personalized interventions for obesity. In addition, the long term-safety of pharmacotherapy needs to be established through RCTs and large registries.

3.8. Results of a consensus survey

- Alex Miras, MD, PhD; Rachel L. Batterham, MD, MSc, PhD

This initiative by IFSO represents a fundamental shift in the way obesity is treated. It also is a new way of thinking about the disease that highlights its biological diversity. As part of this, an expert panel was recruited comprised of a wide range of multidisciplinary professionals treating the disease, and not just bariatric surgeons. The language used in the statements also is more consistent with that used by other professions in the field.

The medical aspects of obesity care attracted a lot of attention by both surgeons and non-surgeons during the consensus survey process, due to the recent major advances in obesity pharmacotherapy. The rates of agreement with the proposed statements were generally high, with 72.5% the lowest rate of agreement. Statements focused on the importance of delivering pharmacotherapy on a long-term basis, which is common practice for virtually all chronic diseases. The expert panel also agreed that the use of obesity pharmacotherapy can be considered both before and after bariatric surgery. There was an emphasis on the use of medications for young people from 12-18 years old, and on the need for genetic screening for children, young adults, and adults who may have monogenic causes of obesity. A number of medications – like liraglutide 3.0mg daily – have been approved in many countries for the treatment of obesity in young adults with good results, in terms of safety and efficacy, both of which are critical during this sensitive time in someone's life. Setmelanotide is also available in many countries for people with specific monogenic causes of obesity and can be initiated in children over the age of 6. There was a high level of agreement regarding the use of medications in this age group.

With regards to adults, there were various levels of agreement that obesity pharmacotherapy should be considered based not only on the patient's BMI and previous weight loss attempts, but also depending on their obesity-related complications. The panel agreed that these medications should be used long term, as discontinuation typically leads to rapid weight regain. The panel also agreed that these medications can be considered as a bridge to surgery for some people and as an adjunct to surgery in those who have not responded adequately, in terms of weight loss or improvements in obesity-related complications. At the moment, there are no good baseline predictive markers of response, so patients should be reassessed three months or so after the initiation of treatment, as this early response predicts longer-term outcomes. Whilst the experts agreed that these medications can have transient side effects upon initiation, they also recognised that long-term safety data are lacking and urgently needed to increase confidence in their use by both healthcare professionals and patients.

Table 1: Categorical weight loss and other pre-specified metabolic efficacy measures in participants in randomized clinical trials of pharmacotherapy for obesity with at least 2 years duration

Acronym of the RCT	Length of FU	Study Drug	>5% WL	>10% WL	>15% WL	>20% WL	Other pre-specified primary end points at the end of the study (active drug versus placebo)
XENDOS (3)	4yrs	Orlistat 120mg TID	52.8%	41.0%	NR	NR	↓ Incidence of T2DM
		Placebo	37.3%	20.8%	NR	NR	
SCALE Prediabetes (4)	3yrs	Liraglutide 3.0mg OD	49.6%	24.8%	11.0%	NR	↓ Incidence of T2DM
		Placebo	23.7%	9.9%	3.1%	NR	
SEQUEL (5)	2yrs	Phen/Top 15/92mg OD	79.3%	53.9%	31.9%	15.3%	None
		Phen/Top 7.5/46mg OD	75.2%	50.3%	24.2%	9.2%	
		Placebo	30.0%	11.5%	6.6%	2.2%	
STEP-5 (6)	2yrs	Semaglutide 2.4mg OW	77.1%	61.8%	52.1%	36.1%	None
		Placebo	34.4%	13.3%	7.0%	2.3%	

RCT: randomized clinical trial. FU: follow up. Phen/Top: phentermine-topiramate.
WL: weight loss. TID: three times per day. OD: once daily. OW: once weekly.
T2DM: type 2 diabetes mellitus. CRP: C-reactive protein.

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CHAPTER 4

ENDOSCOPY FOR THE TREATMENT OF OBESITY

4.1. Introduction: Where is the endoscopic management of obesity heading?

- Christine Stier, MD

In recent years, the field of obesity and metabolic disease management has witnessed significant advancements in endoscopic bariatric and metabolic therapies (EBMTs). These advancements have increased patient access to care and expanded the therapeutic armamentarium for the management of excess adiposity and its metabolic complications. The value propositions for EBMTs include anatomy preservation, reduced short and long-terms risks, shorter recovery times, potential reversibility, minimal disruption of patient lifestyles, and potential cost-effectiveness, together making them a viable option for the management of obesity in patients who either do not qualify for bariatric surgery or do not wish to pursue a surgical intervention. In addition, these interventions, in certain clinical situations, can be utilized as a bridge to bariatric surgery or to revise bariatric surgery; for example, utilizing endoscopic techniques to decrease the volume of a dilated laparoscopic sleeve gastrectomy (SG) or reduce a dilated gastro-jejunal anastomosis after Roux-en-Y gastric bypass (RYGB) for recurrent weight gain [1-6].

Current EMBT can be divided into those procedures that target the stomach, which predominantly work by impacting appetite pathways controlling satiety and satiation via alterations in gastric accommodation and emptying. These include intragastric balloons (IGBs) and gastric remodelling techniques, such as endoscopic sleeve gastroplasty [7, 8]. Other EMBTs target the proximal small intestines, thereby affecting the metabolic dysregulation associated with obesity. Procedures like a duodenal-jejunal bypass liner and endoscopic duodenal resurfacing or regeneration can restore metabolic homeostasis and improve insulin sensitivity, which is responsible for the management of obesity, type 2 diabetes, metabolic syndrome, and non-alcoholic fatty liver disease [9-12].

The field of EBMT continues to evolve rapidly. Technological advancements continue to drive innovation and push the boundaries of efficacy, safety, and durability. In the future, new platforms will emerge, such as endoscopic gastric remodelling for weight loss; non-thermal endoscopic energy modalities to regenerate aberrant metabolic signalling in the small intestine; and modular anatomy preserving endoscopic or hybrid laparoscopic and endoscopic devices and techniques that combine gastric and small intestinal interventions for weight-loss-dependent and weight-loss-independent metabolic benefits like traditional bypass procedures.

However, while EMBTs offer promising solutions, they are not without limitations. Patient selection, procedure availability, and long-term outcomes are areas that require further investigation and refinement. Nonetheless, as the evidence-base grows and experience accumulates, these therapies are increasingly being incorporated into clinical practice as valuable options for managing obesity and metabolic diseases.

4.2. RCT for class I and II obesity for endoscopic sleeve gastroplasty (ESG)

- Barham K. Abu Dayyeh, MD, MPH

Endoscopic sleeve gastroplasty (ESG) is an endoscopic bariatric and metabolic therapy (EBMT) that has gained global clinical adoption. The gastric remodelling form, physiology, and nomenclature of ESG were first described in 2013 after previous advances in gastric endoscopic suturing techniques for weight loss [13-15]. In its current, clinically-adopted, and regulatory-approved form, ESG employs a full-thickness endoscopic suturing device to create apposition of the anterior against the posterior wall of the stomach, passing through the greater curvature [16]. Suturing starts at the transition between the gastric body and antrum, moving proximally toward the fundus, which is typically partially reduced with preservation of a small pouch to allow fundal accommodation. Thus, it transforms the gastric body into a narrow tube, thereby altering satiety and satiation [7]. The above-mentioned anatomic principles are consistent across centres and providers; thus, the procedure is clinically mature, homogeneous, and reproducible.

Since 2013, the amount and quality of evidence concerning the efficacy and safety of ESG has been mounting. As of December 2022, more than 200 international peer-reviewed medical articles had been published on the procedure, with study designs varying from large case series to prospective and retrospective studies, culminating in a large US multi-centre randomized trial with mid-term follow-up; the MERIT Trial [17]. In a meta-analysis of observational studies that included 1859 patients prior to the MERIT Trial, the pooled means for percentage total weight loss (%TWL) at 6, 12, and 24 months were 14.86% (95% confidence interval [CI]: 13.83-15.90%), 16.43% (15.23-17.63%), and 20.01% (16.92-23.11%), respectively. Pooled means for percentage excess weight loss at 6, 12, and 24 months were 55.75% (50.61-60.89%), 61.84% (54.75-68.93%), and 60.40% (48.88-71.92%). The pooled incidence of serious adverse events was 2.26% (1.25-4.03%) and no deaths were reported [18]. At this time, ESG is being utilized clinically on all continents of the world, with more than 40000 clinical procedures performed to date.

The primary objective of the MERIT trial was to evaluate the efficacy and safety of ESG at achieving weight loss and improving metabolic parameters. The trial was powered to meet the safety and efficacy endpoints determined by two governing societies: the American Society for Metabolic and Bariatric Surgery [19] and the American Society for Gastrointestinal Endoscopy [20]. The trial's results are generalizable, as it was conducted at nine US centres, representing academic and community bariatric surgery and gastroenterology practices with variable prior expertise in the ESG procedure. The study enrolled a total of 209 patients with a body mass index (BMI) ranging from 30 to 40 kg/m² and age from 21-65 years. The patients were randomized to either ESG with moderate-intensity lifestyle modification (ESG arm) or moderate-intensity lifestyle modification alone (LS). At 52 weeks, the primary endpoint of mean %EWL was

49.2% (SD = 32.0) for the ESG group and 3.2% (SD = 18.6) for the control group ($p<0.0001$). Mean %TBWL was 13.6% (SD = 8.0) for the ESG group and 0.8% (SD = 5.0) for the LS group ($p<0.0001$), and 77% of participants in the ESG group reached 25% or more EWL at 52 weeks, versus just 12% in the LS group ($p<0.0001$). At 52 weeks, 80% of the participants in the ESG group also had experienced improvement in one or more metabolic comorbidities, while 12% worsened; this compared with 45% of controls who experienced similar improvement, but 50% who worsened. At 104 weeks, 41 (68%) of the 60 participants in the ESG group had maintained 25% or more EWL. The ESG group also exhibited significantly-greater improvements in objective measures of glucose homoeostasis, insulin resistance, inflammatory markers, and measures of visceral adiposity and non-alcoholic fatty liver disease, relative to the LS group. Serious ESG-related adverse events - requiring surgical, endoscopic, or radiological intervention – occurred in three (2%) of 131 patients who underwent ESG either during the RCT or afterwards in a crossover trial, without mortality or the need for either intensive care or surgery [17].

Such convincing results explain the consensus of 94 international, inter-disciplinary obesity management experts in a recently-completed Delphi survey co-orchestrated by IFSO and the World Gastroenterology Organization (WGO) in 2022 [21]. In this survey, consensus was reached by 85.2% of the experts that ESG should be considered for patients who are in the overweight category and have obesity-related comorbidities, while 72.7% agreed that ESG should be considered in patients with Class 3 obesity when they are not good surgical candidates or have declined surgery [21]. As noted in section 4.5 at the end of this chapter, similar favourability of ESG was expressed by 43 inter-disciplinary obesity-management experts in the most recent 2023 IFSO survey [22].

4.3. Endoscopic treatments in adolescents

- Christine Stier, MD

Background

There is a rapidly growing burden of obesity and associated comorbidities in adolescents. To investigate the prevalence and incidence of childhood obesity and identify risk factors for the development of metabolic syndrome in childhood, the European epidemiological study IDEFICS was launched in 2006. Four risk factors were identified predicting the development of metabolic syndrome in childhood and adolescence, which were obesity, hypertension, dyslipidaemia and dysglycemia [23]. In addition, according to the WHO publication of June 2021, 39 million children under the age of 5 were overweight or obese in 2020, and more than 340 million children and adolescents aged 5-19 were already overweight or obese in 2016 [24].

As anticipated, the prevalence of obesity in childhood and youth is associated with a parallel increase in the prevalence of type 2 diabetes mellitus (T2DM) in the same age group. Already between 2002 and 2012, the incidence of T2DM among young people in the USA increased from 9 to 12.5 per 100.000, with similar trends in both Europe and Asia. Ethnic populations are particularly affected [25]. Accordingly, an American registry study has shown that the prevalence of dysglycaemia increases to 23.1% when only one of the four above-listed risk factors is present (e.g. obesity), and to 44% when all four risk factors exist [26]. In this regard, it should be stressed that the morbidity and mortality rates from T2DM in children and adolescents is higher than that of T1DM in their peers [27]. Paediatric type 2 diabetes is also associated with an increased mortality rate when compared with the longer duration of the disease in adults (25-30% ß-cell loss versus 7-10% ß-cell loss per year). This highlights how juvenile T2DM is a rapidly-progressive disease characterized by the early onset of complications and rapid ß-cell deterioration [28]. To make matters worse, in this population, pharmaceutical options are limited and metformin is associated with a treatment failure rate of 50%. In addition, it was only recently that another drug, a GLP-1 analogue that also has an anorectic effect, was approved for use in adolescents [29].

In summary, childhood/adolescent obesity and associated conditions – like dysglycaemia and T2DM – are not fully comparable to adult obesity and require even more effective and timely treatment to meet pressing medical needs. The hope of being able to treat obesity in adolescents without additional medication or invasive therapies is currently untenable. However, it is often feared that drastic weight loss during growth could affect bone metabolism. Thus, EMBTs may be the treatment of choice for successfully managing adolescents with obesity and associated comorbidities, as they are effective, appear less invasive, and can be repeated. For the purpose of evaluating the strength of currently-published evidence, a literature review was performed. This included assessing the evidence that has already been generated and is available on the subject in peer-reviewed scientific journals.

Methods

Search

Electronic databases were searched for articles that met the inclusion criteria without date restriction. Reference lists were searched manually. For this review, study inclusion was limited to papers that reported on any type of endoscopic treatment for obesity in adolescents. Excluded from inclusion were duplicate publications of the same study.

Assessing the evidence

Evidence was assessed according to GRADE guidelines [30, 31]. By these guidelines, meta-analyses of randomized controlled trials (1a), followed by individual RCTs (1b), provide the highest level of evidence. Grade 2 evidence includes systemic reviews (2a) and prospective cohort studies (2b). By the same classification system, class 3 includes systematic reviews of case-control studies (3a) and individual case-controlled studies (3b), while case series count as class 4 and expert opinions as class 5 evidence. Class 1 evidence, either A or B, leads to a level A recommendation, while class 2 and 3 evidence, either A or B, leads to a level B recommendation in the medical field. The grade of C or D level recommendations corresponds to levels 4 and 5 evidence. GRADE criteria for the identification of bias also were taken into account, with the consequence that any identification of significant bias risk led to downgrading the level of evidence. Examples of bias include stopping a trial because of an apparent outcome benefit and selectively reporting favourable endpoints[32].

Statistics

As the number of studies found was limited, continuous variables are presented as means and ± one standard deviation (1SD) with corresponding ranges (min/max), if available. The homogeneity of results was taken into account in the case of multiple studies on one particular EBMT tool. All adverse events (AEs) are listed.

Results

Intragastric balloon

The largest number of publications was found for the use of an intragastric balloon (IGB) [33-41]. An IGB results in functional restriction of the stomach volume, due to its specific filling volume (see Figure 4-1).

Of the ten trials identified, two were found to be duplicates [37, 39]. After excluding these duplicates, a further subdivision was made according to the type of balloon used. Accordingly, six studies with fluid-filled balloons and two studies with gas-filled balloons were evaluated. One particularity was one trial that explicitly included adolescents with obesity due to a genetic defect (Prader-Willi Syndrome) [34]. The hyperphagia associated with this syndrome resulted in a higher rate of adverse events, which could not be considered a normal distribution and therefore necessitated considering this study in isolation, with further subdivision of the fluid-filled balloon cohort.

Intragastric fluid-filled balloons adjusted for hyperphagia are summarized in Table 4-1. The first publication on this topic was by Vandenplas et al. in 1999 and was in absolute contradiction to all the other studies [41], in that the investigators failed to identify any effect of the implanted balloon in five adolescents. Given that this study was published more than 20 years ago, had only five patients, and exhibited marked inhomogeneity (chi-square model), it was excluded from pooled analysis. Thus, the adjusted pooled cohort had 74 adolescents, extracted from four studies [35, 38, 40] with a mean age of 16.25 ± 2.05 years. The same IGB was used in all cases. Inflation volume varied from 500-700 mL, and treatment duration was six months. All but one of the trials [35] were prospective. On overall analysis and on individual analyses, both the reduction in BMI (baseline: 39,85 ± 4,50 kg/m^2 result: 35,90 ± 5,97 kg/m^2) and reduction in weight (baseline: 119,55 ± 14,84 kg; result: 108 ± 18,46 kg) from baseline to six-month follow-up were statistically significant. No balloon-related adverse events (AEs) were observed. Mild AEs included nausea and epigastric pain and may have been caused by the medication used. Due to the specific nature of the patient population, all trials with more than 10 people were classified as cohort studies, three of which were prospective and, therefore, graded as 2b evidence [38, 40, 42]. The Fittipaldi study, which had 27 patients, was retrospective [35] and is, therefore, considered 3b evidence.

In 2008, DePeppo published a prospective cohort study of 12 adolescents with obesity and hyperphagia caused by Prader-Willi syndrome [34]. To date, this is the only published study on IGBs that has looked at such a highly-specific group of patients. The study is summarized in Table 4-2 and is considered level 2b evidence. The balloon used had a filling volume of 500 – 700 mL. Baseline BMI decreased significantly from 47.9 ± 7.8 kg/m^2 to 41.3 ± 9.3 kg/m^2 after six months of ICG implantation ($p < 0.005$). Weight reduction also was significant ($p < 0.005$) falling from 105.6 ±17.2 kg to 92.5 ± 20.6 kg. It is noteworthy that the underlying hyperphagia in Prader-Willi syndrome appeared to lead to an increase in adverse events (AEs) compared to adolescents with obesity treated with a gastric balloon without hyperphagia. In five out of 12 adolescents with Prader-Willi syndrome, IGB implantation resulted in four non-fatal but severe AEs (food impaction, a fibrous bezoar, aerophagy, acute gaseous distention) and one death due to stomach perforation [34].

Table 4-3 summarizes two studies in which 27 adolescents with obesity were implanted with a 250cc nitrogen-filled (Obalon 3M) intragastric balloon [33, 36]. In 2015, Nobili et al. published the results of a series of 10 adolescents, among whom three were female [36]. The youths started with a BMI of 36.73 kg/m^2 and achieved a non-significant decline to 35.68 kg/m^2 after three months of treatment. A significance-level of $p=0.005$ was achieved only by excluding three individuals who were classified as non-adherent. In principle, this study would be classified as a prospective cohort study with 2b class evidence, However, according to GRADE bias identification, only selective endpoints were reported to reach significance, which must lead to downgrading the evidence obtained.

Similarly, DePeppo excluded nine of 17 individuals (11 females) who had a baseline BMI > 35 kg/m^2 from analysis [33]. The overall cohort showed a non-significant reduction in BMI from 35.27 ± 5.89 kg/m^2 to 32.25 ± 7.1 kg/m^2 with treatment. However, a subgroup of eight individuals with a baseline BMI of 33.71 ± 2,17 kg/m^2 were able to lose significant weight with treatment, achieving a final mean weight of 28.84 ± 3.42 ($p=0.004$). This represented weight reduction from 84.44 kg to 75.19 ± 12.48. However, the selective reporting conducted to achieve a desired result downgrades the class of evidence from 2b to 4, following GRADE guidelines [32].

Endoscopic sleeve gastroplasty

In endoscopic sleeve gastroplasty (ESG), stomach volume is reduced endoscopically by performing plications with full-thickness sutures (see Figure 4-2). This is tantamount to restriction. The impressive work of Alqathami, involving more than 1000 individuals, is also reported in his prospectively-designed analysis of 109 adolescents treated with ESG for obesity [43] (Table 4-4). This constitutes class 2b evidence and is by far the largest group of adolescent patients included in a trial. None of them experienced severe AE, and only 14 of the 109 patients reported epigastric pain after the procedure. This clearly demonstrates the safety of the procedure in the treatment of this particular patient population. There is also information on follow-up of two-years duration. In addition, the intervention was found to be very effective. The initial BMI was significantly reduced from 33.0 ± 74.7 to 29.5 ± 3.7 kg/m^2 after six months and further to 27.6 ± 6.2 kg/m^2 after one year, representing %EWL of 87.1 ± 59.5%. However, some weight gain was reported at two years, with %EWL reduced to 63.8 ± 52.3% [44].

Duodeno-jejunal bypass liner (DJBL)

The EndoBarrier is a thin-walled, flexible Teflon tube that is inserted endoscopically as a capsule into the duodenum and unfolds to a length of approximately 60 cm in the upper small intestine. It acts as an impermeable membrane, preventing food flowing strictly inside the tube from coming into contact with the intestinal wall and digestive juices. This results in altered hormone release in the duodenum, which results in an anti-diabetogenic effect on metabolism. Currently, DJBL is not available for clinical use due to its confirmed side effect profile. One prospective cohort study (class 2b evidence) has been published in which 19 adolescents (13 females) ranging in age from 16 years to 20 (mean =17,3 years; 16,7-17,9) were treated with a DJBL [45]. In addition to weight loss, improvements in metabolic parameters were observed. Although there was a significant reduction in weight from 125.3 ± 4.2 kg to 110.4 ± 3.5 kg (p=0,0038), the overall reduction in a measure of insulin resistance - mean homeostatic model assessment insulin resistance HOMA-IR – was striking, declining from 5.4 to 3.2 (p= 0,0034). On the other hand, weight regain and the recurrence of previously-observed metabolic complications occurred after device removal [45].

Discussion

There has also been an increase in the prevalence of obesity among adolescents in Germany, with a doubling of the prevalence among children from 6-11 years old and a tripling of the prevalence among those 12-17 years old. Impaired glucose tolerance with the inherent progression described above was found in 38% of those affected [46]. The management of adolescents with obesity, both in terms of assessment and indications for intervention, requires the special care of a multidisciplinary team, including substantial support from paediatricians and psychotherapists.

In addition, the published data presented here suggest that genetic testing is essential to identify whether an underlying genetic syndrome of hyperphagia (e.g., Prader-Willi-Syndrome) exists, since it appears to be associated with a higher risk of interventional therapy [34]. Thus, any kind of appetite stimulation disorders with the unstoppable sensation of hunger – such as proopiomelanocortin (POMC) deficiency - a genetic disorder of the leptin-melanocortin transduction pathway - must be ruled out before an interventional approach is adopted. Such pathways are uncontrollable by the interventional manipulation of signalling in the gastrointestinal tract. Note that genetic syndromes are present in approximately 5% of youths with severe, early-onset obesity [46, 47].

In principle, EMBTs appear to be particularly suitable for treating obesity in adolescents when an interventional approach is indicated. In general, EMBTs are minimally-invasive procedures with no long-term sequelae like nutritional deficiencies or persistent reflux disease, making them ideal for the anticipated long remaining lifespan of youths. These interventions also preserve the stomach and are, therefore, organ-sparing; and they are adjustable in terms of their effectiveness, since they can usually be repeated easily at any time [43]. That said, extensive experience of the interventionist is essential.
Practitioners who utilize EMBTs believe that they are a suitable intervention for most adolescents. On the other hand, before the adoption of such interventions can be considered standard of care in clinical practice, further empirical support is necessary.
Overall, there is still a limited body of literature on the use of EMBTs in adolescents with obesity [33-36, 38-40, 44, 45]. Fluid-filled balloon results are available for just 74 adolescents and the ESG experience for just 109 adolescents. However, the quality of the evidence in this very specific and vulnerable population of patients is not poor.

Given the urgent need for treatment explained above, the evidence found for ESG and fluid-filled balloon implantation, even with such limited numbers of subjects, permits a Grade B recommendation (based mainly on 2b and 3b class evidence). This suggests that these procedures 'should' be considered in the treatment of adolescents with obesity. This cannot be concluded for gas-filled balloons, however. According to GRADE criteria, no significant weight loss was achieved with this intervention if data selection biased towards favourable results are afforded the class 4 evidence status they warrant. Finally, DJBL is not currently available for clinical use as an EBMT, even though it has been shown to be effective in the treatment of pre-diabetes and T2DM in adolescents. This leaves only two empirically-supported interventions and suitable for use in adolescents: fluid-filled IGBs and ESG. Compared to IGB, an ESG is characterized by greater durability (2-year follow-up) and, above all, by the relative simplicity of repeating the procedure.

4.4. Endoscopic treatments for metabolically-challenged patients

- Christopher Thompson, MD, MSc

Endoscopic metabolic and bariatric therapies (EMBTs) include a wide range of procedures and devices. These can be broadly classified into gastric and enteric procedures. The gastric procedures are thought to alter digestive physiology and typically delay gastric emptying. The procedures hence encourage weight loss by inducing early satiation and/or prolonged satiety. They are associated with improvements in glycaemic indices and other obesity-related comorbidities. However, it is thought that this improvement is indirect and secondary to weight loss. It is well established that a percentage of total body weight loss (%TWL) exceeding 5-10% is associated with improvements in glycated haemoglobin (HbA1c), insulin resistance, total and visceral adiposity, and non-alcoholic steatohepatitis (NASH), and this has been a weight loss target for many of these procedures [48].

Enteric or small bowel procedures have direct metabolic effects, independent of weight loss. They are designed with a particular focus of treating type 2 diabetes (T2DM) and other metabolic conditions. However, they are often associated with more limited weight loss. These small bowel devices are an emerging class of procedures, with none yet having US Food and Drug Administration (FDA) approval, and they will not be the focus of this brief review.

Gastric EMBTs, such as endoscopic gastric remodelling procedures (EGR) and intragastric balloons (IGBs), have been assessed for metabolic outcomes. There are many different types of IGB. However, because they are all proposed to work by the same mechanisms and have similar outcomes, they can be considered together. The level of evidence for these procedures ranges from Level 4 to Level 1b.

A meta-analysis by Popov, et al. reviewed 40 IGB studies specifically focusing on metabolic outcomes [49]. This included 10 randomized controlled trials (RCTs) and 30 observational studies, encompassing a total of 5,688 patients. The overall decrease in HbA1c was 0.6%. However, there was a reduction of 1.1% in patients with a baseline HbA1c of >6.5%. There were also significant improvements in fasting blood glucose, hypertension, liver function tests, and dyslipidaemia. The odds ratios (ORs) for resolution and improvement in T2DM were 1.4 and 9.3, respectively ($p < 0.001$), and the ORs for resolution of hypertension and dyslipidaemia were 2.0 and 1.7 ($p < 0.001$) [49]. This comprehensive meta-analysis including 10 RCTs provides level 1b evidence for the resolution or improvement of obesity-related metabolic comorbidities.

The use of IGB in the treatment of NASH has also been explored in a prospective randomized sham-controlled pilot study, published by Lee, et al.[50]. Liver biopsies were performed within six months prior to randomization and one month following repeat endoscopy (6 months following the study procedure involving IGB placement or a sham intervention). A total of 21 subjects were enrolled, among whom three withdrew due to early IGB intolerance. Eighteen subjects completed the study, with eight in the IGB arm and 10 in the sham arm. There were no differences in baseline characteristics, including BMI, presence of T2DM, NAFLD activity scores, steatosis scores, and fibrosis scores between the IGB and sham groups. At the end of treatment, median NAFLD activity scores were significantly lower in the IGB than sham group (median = 2 [0.75] vs. 4 [2.25]; $p = 0.03$). There also was a trend toward improvement in the median steatosis scores (1 [0.75] vs. 1 [1]; $p = 0.075$). There was no change in the median (IQR) for lobular inflammation, hepatocellular ballooning, or fibrosis scores in either group following treatment.

These studies provide high-class evidence supporting the use of IGB in the treatment of obesity-related metabolic disease. Of note, long-term efficacy following IGB removal remains dependent on a longitudinal management plan, which should include ongoing lifestyle intervention, anti-obesity medications, and potentially repeat IGB or some more invasive intervention, as indicated.

Endoscopic gastric remodelling (EGR) procedures include endoscopic sleeve gastroplasty (ESG) and endoscopic gastric plication (EGP). Both types of procedure focus on shortening the width and length of the stomach to reduce gastric volume and alter digestive physiology. They are functionally similar and are often referred to as plication or sutured ESG, as this term is more established. The first study to evaluate metabolic outcomes for ESG was reported by Sharaiha et al. in 2017 [51]. It was a prospective series of 91 patients with two years of follow up. The investigators reported 20.9% total weight loss at 24 months with a rate of 1.1% severe adverse events (SAEs), including one gastric leak. Of note, HbA1c decreased by 0.6% across the entire cohort, and more significantly decreased by 1.0% in patients with diabetes or prediabetes ($p = 0.02$). The investigators also reported significant improvements in waist circumference, triglycerides, and liver transaminases.

The above-described study was followed by a larger, 1000-patient prospective observational study reported by Alqahtani et al. in 2019 [52]. They reported 76.5% resolution of T2DM with no recurrence, while the remaining patients exhibited improvement defined as a reduction in medication dosage. There was also 100% improvement in hypertension and 56.3% improvement in dyslipidaemia.

The MERIT Trial, conducted by Abu Dayyeh et al., was the pivotal RCT that provided de novo marketing status for ESG [43]. The study also examined metabolic outcomes. This RCT involved 209 patients, 85 undergoing ESG and 124 lifestyle modification alone. The %TWL one year after randomization was 13.6% for ESG and 0.8% for controls. A "response" was defined as at least 25% EWL at one year, and this definition was met by 77% in the ESG group versus just 12% of controls. Comorbidities also favourably improved in the active treatment group. Specifically, diabetes, hyperlipidaemia, and metabolic syndrome improved to a statistically-significant degree in the ESG group relative to controls [43].

Analysis of a prospective ESG registry including 118 patients with NAFLD and underlying obesity also demonstrated improvements in hepatic steatosis and fibrosis following ESG [53]. At two years, the %TWL was 15.5%. The Hepatic Steatosis Index score decreased by 4 points per year ($p <0.001$), while the NAFLD fibrosis score decreased by 0.3 points per year ($p = 0.034$). Additionally, 24 patients experienced a reduced risk of hepatic fibrosis, declining from F3-F4 or indeterminate to F0-F2, whereas only one patient (1%) experienced an increase in the estimated risk of fibrosis ($p = 0.02$).

Newer EGP procedures also have emerging data on metabolic outcomes. Jirapinyo and Thompson reported the efficacy of plication ESG in 110 patients, identifying significant improvements in insulin resistance (HOMA-IR), HbA1c, AST, ALT, and HTN ($p < 0.01$) [54]. A follow-up study by the same group evaluated the effect of plication ESG on liver fibrosis in 45 patients with at-risk NASH (F2-F4)[55].9 At 12 months, patients experienced an average of 15.5% ± 7.9% TWL, with 63% reaching at least 10% TWL. There were also significant improvements in a composite fibrosis score (NAFLD fibrosis score: 0.48 ± 1.51 to -1.18 ± 1.56, $p < 0.0001$), a fibrosis-4 index (1.4 ± 1.2 to 1.2 ± 0.7; $p = 0.03$), imaging-based markers of fibrosis (vibration-controlled transient elastography: 13.9 ± 7.5 kPa to 8.9 ± 4.8 kPa; $p < 0.0001$) and the Agile 3+ (0.53 ± 0.28 to 0.37 ± 0.28, $p = 0.001$). In addition, the investigators noted significant reductions in a controlled attenuation parameter (HOMA-IR), as well as in haemoglobin A1c and liver transaminases ($p < 0.05$ for all).

There is considerable evidence confirming improvements in metabolic conditions following gastric EMBTs. Nevertheless, there is currently no evidence of weight loss-independent mechanisms with these gastric procedures. This is unlike the emerging small bowel EBMTs that specifically target metabolic conditions, and it is likely that the improvements observed following gastric EBMTs are solely due to weight loss. Overall, these endoscopic interventions appear to be an acceptable treatment option for the metabolically-challenged patient with underlying obesity. Furthermore, it is likely that these outcomes will continue to improve with various personalized strategies and combination therapies that are on the horizon.

4.5. Results of a consensus survey

- Barham K. Abu Dayyeh, MD; Christine Stier, MD

The consensus group described in previous chapters of these guidelines voted on 13 statements related to endoscopic bariatric and metabolic therapies. Consensus was reached on seven of these 15 statements, as listed in Table 4-6, below. With the credo that only four of the 43 participating experts were endoscopists only, and only 11 of the 28 surgeons performed EBMT procedures, the experts seemed overall quite supportive of ESG in various clinical settings, from class 1 to 3 obesity, in adults and adolescents, and both before or after metabolic and bariatric surgery. On the other hand, no consensus was reached on any one of the five statements on intragastric balloons.

Table 4-1: Studies assessing use of the 6M BIB (Bioenterics) intra-gastric balloon

1st author (Year)	Volume	Study design	N	Gender M/F	Mean age	Baseline BMI	Final BMI	P value	Baseline weight	Final weight (kg)	P value	Adverse events (AE)
Sallet [40] (2004)	500 - 700 mL	Prospective mulicentre cohort study	21	NA	NA	36,5 ± 8,4	31,5 ± 9,1	0,006	NA	NA	NA	NA
Karagiozoglou-Lampoudi [42] (2009)	700mL	Prospective cohort study	14	6/8	18,5 ± 2,5	39,1 (33-54)	37 (26-50)	0,001	118 (80-174)	108 (62-162)		0/14 balloon-related AE 1/14 non-balloon-related AE
Fittipaldi-Fernandez [35] (2017)	600 - 700 mL	Retrospective cohort study	27	4/23	17,41	37,04 ±6,29	31,18 ±7,46	0,001	102,21 ± 25,8	86,23 ± 27,34	0,0001	None
Reece [38] (2017)	500 mL	Prospective pilot study	12	5/7	15 Tanner Score ≥ 4	BMI z-score 4 ± 0,29	BMI z-score 3,8 ± 0,32	0,002	138,45 ± 23,97	131,43 ± 23,10	0,006	NA
Means			74			39,85	35,90		119,55	108		
Standard deviations						4,40	5,97		14,84	18,46		No serious AE

N = number of patients; M = male; F = female; BMI = body mass index; NA = not applicable; AE = adverse events.

Table 4-2 Studies assessing 6M BioEnterics fluid-filled intragastric balloon in patients with syndromic hyperphagia

1st author (Year)	Filling volume	Study design	N	Gender M/F	Mean age	Baseline BMI	Final BMI	P value	Baseline weight	Final weight (kg)	P value	Adverse events (AE)
DePeppo [34] (2008)	500 - 700ml	Prospective, cohort study	12	4/8	18,5 ± 2,5	47,9 ± 7,8	41,3 ± 9,3	0,005	105,6 ± 17,2	92,5 ± 20,6	0,005	1/12 death due to gastric perforation 1/12 acute gaseous distension 1/12 aerophagy 2/12 food impaction

N = number of patients; M = male; F = female; BMI = body mass index; NA = not applicable; AE = adverse events.

Table 4-3: Studies assessing a nitrogen-filled Obalon 3M intragastric balloon

1st author (Year)	Filling volume	Study design	N	Gender M/F	Mean age	Baseline BMI	Final BMI	P value	Baseline weight	Final weight (kg) 12/24 months	P value	Adverse events (AE)
Nobili [36] (2015)	250mL Nitrogen	Prospective cohort study	10	7/3	13,34 ± 2,5	35,68	35,68	NS	98,79	93,04	NS	5/10 epigastric pain
DePeppo [33] (2017)	250mL Nitrogen	Prospective cohort study	17	6/11	18,5 ± 2,5	35,27 ± 5,98	32,25 ± 7,1	NS	90,8 ± 18,4	83,6 ± 27,1	NS	5/17 epigastric pain 2/17 spontaneous balloon emission
Means			27			30,00	31,75		94,79	80,77		
Standard deviations						2,22	54,11		7,01	7,88		No serious AE

N = number of patients; M = male; F = female; BMI = body mass index; NA = not applicable; AE = adverse events.

Table 4-4: Studies assessing a nitrogen-filled Obalon 3M intragastric balloon

1st author (Year)	Filling volume	Study design	N	Gender M/F	Mean age	Baseline BMI	Final BMI 6/12/24 months	P value	Baseline weight	Total body weight loss (kg)	P value	Adverse events (AE)
Alqahtani[44] (2019)	NA	Prospective cohort study	109	10/99	17,6 ± 2.2	33,0 ± 74,7	29,5 ± 63,7 27,6 ± 6,2 30,0 ±6,8	0,05	14,4 ±6,5 16,2 ± 8,3 13,7 ± 8.0		0,05	14/109 epigastric pain No serious AE

N = number of patients; M = male; F = female; BMI = body mass index; NA = not applicable; AE = adverse events.

Table 4-5: Studies assessing duodenojejunal bypass liner in prediabetic or diabetic adolescents

1st author (Year)	Filling volume	Study design	N	Gender M/F	Age Range (years)	Baseline BMI	Final BMI	P value	Baseline weight	Final weight (kg) 12/24 months	P value	Adverse events (AE)
Homan [45] (2019)	NA	Prospective, non-randomized, open-label study	19	6/13	17-20	NA	NA	NA	125,3 ± 4,2	110,4 ±3,5 120 ±3,8	0,0038 NS	No premature explantion Decreases in iron, selenium, Vitamin A, D3, E, ferritin, haemoglobin. Decrease in triglycerides No serious AE

N = number of patients; M = male; F = female; BMI = body mass index; NA = not applicable; AE = adverse events.

Table 4-6: Endoscopic Metabolic and Bariatric Therapy (EMBT)

Statements (N = 15)	N	Rounds required	Most common selection	Percentage consensus	Consensus achieved
ESG combined with lifestyle intervention is preferable to lifestyle interventions alone, for the management of adults with class II obesity.	39	1	Agree	89.7%	Yes
ESG combined with lifestyle intervention is an acceptable management option for adults with class III obesity who either do not qualify (given medical or psychological comorbidities) or do not wish to pursue MBS.	42	1	Agree	87.5%	Yes
ESG combined with lifestyle intervention is preferable to lifestyle interventions alone, for the management of adults with class I obesity.	38	1	Agree	78.9%	Yes
In individuals with class I obesity and comorbidities, ESG is effective at inducing sustained weight loss that remains at 12-24 months follow-up.	38	1	Agree	76.3%	Yes
In individuals with class I obesity and comorbidities, ESG is superior to LIFESTYLE CHANGES/AOM/NEITHER/BOTH.	39	1	Lifestyle changes	74.4%	Yes
ESG combined with lifestyle intervention is preferable to lifestyle interventions alone, for the management of adolescents with class II obesity.	40	1	Agree	72.5%	Yes
In individuals with class I obesity and comorbidities, ESG is not suitable if an individual does not want surgical treatment.	39	1	Disagree	71.8%	Yes
IGB therapy combined with lifestyle intervention is preferable to lifestyle interventions alone, for the management of adolescents with class II obesity.	42	2	Disagree	59.5%	No
ESG combined with lifestyle intervention is preferable to lifestyle interventions alone, for the management of adolescents with class I obesity.	41	2	Agree	56.1%	No
IGB therapy combined with lifestyle intervention is preferable to lifestyle interventions alone, for the management of adolescents with class I obesity.	42	2	Disagree	54.8%	No
IGB therapy combined with lifestyle intervention is preferable to lifestyle interventions alone, for the management of adults with class II obesity.	41	2	Agree	53.7%	No
IGB therapy combined with lifestyle intervention is preferable to lifestyle interventions alone, for the management of adults with class I obesity.	41	2	Disagree	51.2%	No
IGB therapy combined with lifestyle intervention is an acceptable management option for adults with class III obesity who either do not qualify (given medical or psychological comorbidities) or do not wish to pursue MBS.	41	2	Disagree	51.2%	No

N = number of voters in deciding round; ESG = endoscopic sleeve gastroplasty; LGB = laparoscopic gastric banding; IGB = intra-gastric balloon; MBS = metabolic and bariatric surgery; AOM = anti-obesity medication. Shaded cells indicate non-consensus.

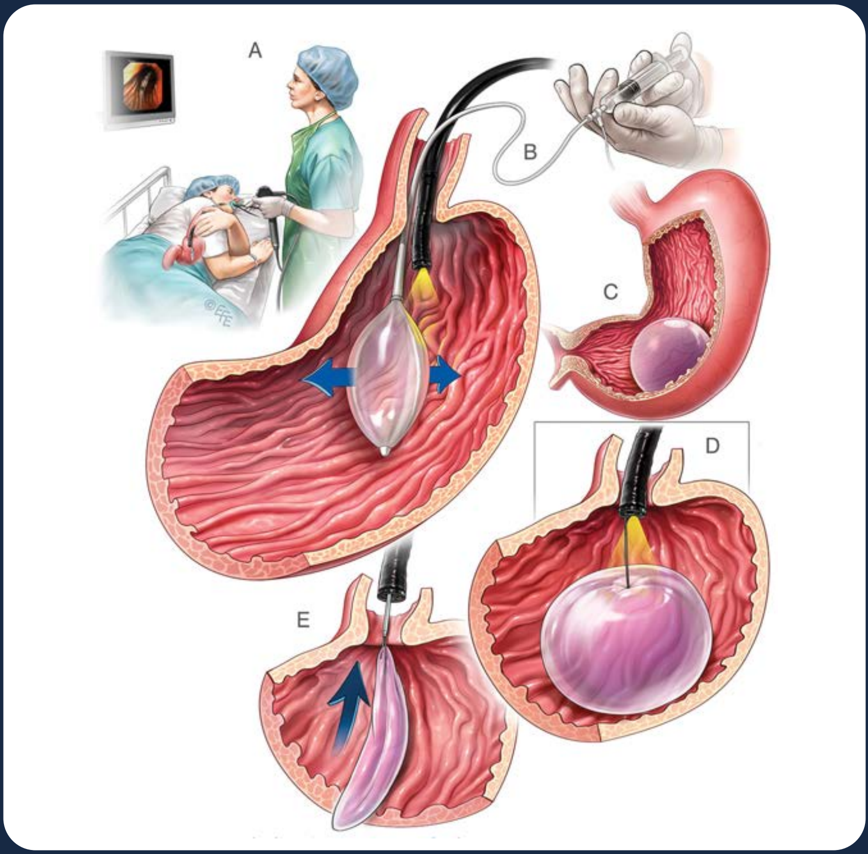

Figure 4-1: Intragastric Balloon

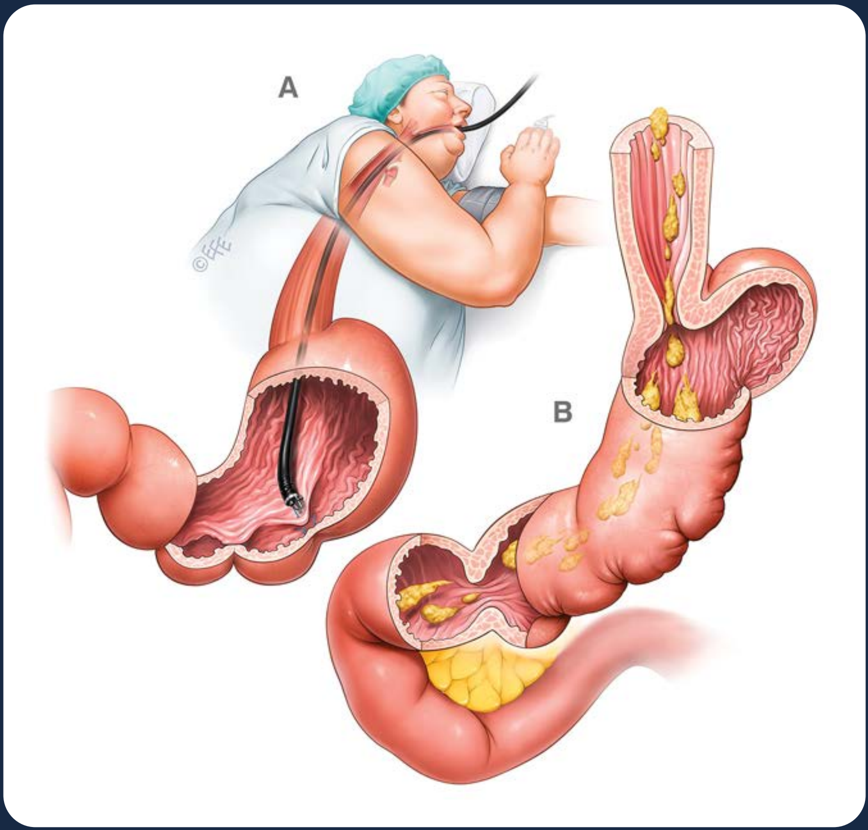

Figure 4-2: Endoscopic Sleeve Gastroplasty

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CHAPTER 5

SURGICAL TREATMENT OF OBESITY

5.1. Primary rationale behind these guidelines

- Marina Kurian, MD

Obesity is a complex disease that requires interdisciplinary care. The current IFSO consensus statement on obesity definitions and clinical practice guidelines is designed to help define optimal and suboptimal outcomes, remove stigmatizing language, and provide clinicians with guidance on clinical care pathways. This chapter will focus on the different MBS procedures and what the expected outcomes are, based on the current literature. A balanced assessment of the risks and benefits of the different MBS procedures will be provided, with the overriding goal of guiding clinicians in their selection of approaches so significant improvements in overall health, longevity, and obesity-associated medical conditions are achieved. As detailed in the final Section 5.9, during a consensus survey of surgeons and non-surgeons with internationally-recognized expertise in obesity management, we were able to reach consensus in many areas and identify the indications, contraindications, and expected outcomes for all the commonly-used MBS procedures.

We will compare randomized controlled trials (RCTs) evaluating different MBS procedures including Roux-en-Y gastric bypass (RYGB), sleeve gastrectomy (SG), one-anastomosis gastric bypass (OAGB), and sleeve gastrectomy with single anastomosis duodeno-ileostomy (SADI-S). Moreover, as Dr. Buchwald has said: "it is our moral imperative to perform revisional surgery for patients with this chronic disease"[1] Hence, we also will review the most up-to-date literature on conversion/revision surgery after gastric bypass and sleeve gastrectomy.

Historically, MBS procedures have been tailored to each individual patient's metabolic condition [2]. In this book's summary chapter, we also will provide what we consider a "best practices algorithm" to assist clinicians in identifying the most appropriate operation for patients on a patient-by-patient basis. Some of the discussion will focus on the best and/or least invasive operation for a given patient, given whatever obesity-related medical conditions they have. In this era of newer procedures that may be less technically difficult as well as other novel procedures, consensus guidelines like this one are vital to help guide surgeons towards optimizing weight loss and obesity-related complication outcomes.

5.2. Introduction to the long-term results of various metabolic-bariatric procedures - Ahmad Bashir, MD; Jaime Ponce, MD

Metabolic-bariatric surgery is currently having a vast, enhancing impact on the science of obesity. Over the past few decades, MBS has evolved and markedly improved its outcomes, so now it provides the best chance most persons living with obesity have at achieving long-term weight loss and either full remission or improvements in obesity complications. Throughout the current process, IFSO and other associations dedicated to obesity management having been working to provide clinicians with the most up-to-date guidelines based on the highest-quality published empirical data available. By doing this, IFSO and others have been striving to increase patient and clinician awareness regarding the potential benefits and risks of surgery, so more patients will have access to MBS and MBS procedures are more optimally suited to help them achieve their weight-loss and complication/comorbidity-management goals.

Naturally, many MBS procedures have evolved over time. Such evolution has primarily aimed towards simplifying the surgical technique, while delivering similar if not superior outcomes at less risk. The main shift has been to deliver one-anastomosis versions of commonly-known Roux-en-Y (RY) procedures. Consequently, for the long-established Roux-en-Y gastric bypass (RYGB), there has been a full-circle return to one-anastomosis gastric bypass (OAGB) over the past few years. Similarly, single-anastomosis duodeno-ileostomy with sleeve gastrectomy (SADI-S) has evolved from a Roux-en-Y duodenal switch (RY-DS). Contrary to this evolution, adjustable gastric banding (LAGB) has experienced a dramatic decline [3], almost completely being abandoned by the surgical community due to concerns regarding long-term complications and a high need for re-operations [4]. These major shifts ultimately were due to concerns regarding the procedures' long-term outcomes.

Over the next few pages, we will discuss in greater detail the best published long-term evidence on the outcomes of OAGB, SADI-S and, to a lesser extent given its now infrequent use, LAGB, highlighting the highest-level evidence presently available.

One-anastomosis gastric bypass (OAGB)

In 2021, Jain et al followed up their initial randomized controlled trial (RCT) comparing OAGB (with a biliopancreatic limb length of 150-180 cm) to laparoscopic sleeve gastrectomy (LSG), with 5-year outcomes on 73 vs. 71 available patients [5]. The 73 OSGB patients experienced 65.28 ± 13.98% excess weight loss (EWL%), 37.35 ± 16.49 kg total weight loss (TWL), and 62.09 ± 12.72% excess BMI loss (EBMIL%). Corresponding outcomes for the 71 LSG patients were 55.95 ± 27.01%, 31.40 ± 18.00, and 50.60 ± 26.04. The rate of type II diabetes (T2DM) remission was higher in OAGB than LSG patients, being achieved in 85% versus just 57% of the OAGB and LSG patients, respectively ($p = 0.022$), with clinical improvement in T2DM observed in an additional 7.5 vs. 22.3% ($p < 0.022$). Quality of life scores also were higher in OAGB patients [5]. Surgical complications occurred in 6.8% of OAGB patients: marginal ulcer presenting as perforation or bleeding in two patients, while three others required cholecystectomy for gallstones. On the other hand, medical complications were encountered in 28.8%, with anaemia, hypoalbuminemia resolving with protein supplements, and marginal ulcers or gastro-oesophageal reflux disease (GERD) controlled with proton pump inhibitors (PPIs) accounting for the majority of these. No patients encountered macronutrient malnutrition, while one patient died for unknown reasons two years after surgery.

The IFSO update on OAGB position statement, published by De Luca et al. in 2021, highlighted similar outcomes on short to mid-term (up to 5 years) follow up [6]. The authors concluded that OAGB still requires further, longer-term, well-designed studies, especially RCTs targeting standardization of the technique, particularly the biliopancreatic limb length relative to total small bowel length.

Single-anastomosis duodeno-ileal bypass with a sleeve gastrectomy (SADI-S)

In 2022, Verhoef et al published their meta-analysis on the best available evidence on SADI-S [7]. With follow up as long as 29 months, the best available accumulative evidence identified a mean %TWL of 37.3% and T2DM remission rate of 62.9%, with similar remission or improvements in other obesity-related medical conditions, including hypertension, hyperlipidaemia, and obstructive sleep apnoea. Micronutrient deficiencies were most common for vitamins D & A (32.1 and 12.6%, respectively). Hypoalbuminemia (5%) seemed to occur in patients who had a common channel of 200cm, but not encountered in patients with a common channel of 250-300 cm. Sanchez-Pernaute et al published their 10-year prospective outcomes on 80 available patients (75% follow up) with similar results [8].

Again, the focus of future research on SADI-S should be on high-quality RCTs with long-term follow-up that compare this procedure to its Roux-en-Y counterpart: RY-DS (duodenal switch).

Laparoscopic adjustable gastric banding (LAGB)

Gastric banding lost its appeal amongst the surgical community starting in about 2010, given the rapid and steady emergence of sleeve gastrectomies and concerns over the high frequency of long-term re-operations and device re-implants with banding [4, 9]. In 2019, O'Brien et al. performed a systematic review and meta-analysis examining the available literature beyond 10 years, while comparing it to their own 20-year outcomes [10]. In 1002 patients with available follow up from 10-16 years, the %EWL among LAGB patients was 45.9% (27-66%). However, the mean reoperation rate was 47.8% (range = 8-78%), mostly due to pouch enlargement or port/tubing complications, with conversions and erosions less frequent. Among patients with 20-year data, the %EWL among LAGB patients was better at 63%; however, 29.8% of such patients developed complications, with 26.0% requiring a reoperation, more than 35% either not experiencing an improvement in obesity complications or losing <25% of the initial %EWL, and 6.7% developing new obesity complications. Several single studies have similarly identified high rates of re-operations and inadequate weight loss (<30% EWL) in LAGB patients followed beyond 10 years [11-13]. Moreover, direct comparisons between LAGB and LSG generally show superior weight loss, diabetes remission rates, and overall outcomes with LSG [14, 15].

Given these results, as reported in the final section of this chapter (section 5.9), a multi-disciplinary panel of 43 experts in obesity management was asked to vote on two statements pertaining to LAGB's place in current obesity management. Members of the panel reached almost unanimous agreement (94.7%) that long-term follow-up of 10 years and beyond reveals a high-rate of band-related reoperations and device explants after LAGB. Meanwhile, though no consensus was reached on whether the procedure is an effective treatment option for suitable patients with obesity, 60.0% of the experts voted that LAGB is NOT. Based upon these results and its decline from accounting for roughly 30% of all MBS procedures in 2010, making it the most commonly-performed MBS procedure worldwide in 2008 [9], to under 1.0% of all MBS procedures performed in 2022 [3], LAGB will not be discussed further in the current guidelines. Both OAGB and SADI-S will be discussed in greater detail in later sections.

5.3. Sleeve gastrectomy versus Roux-en-Y gastric bypass

- Paulina Salminen, MD, PhD; Ali Aminian, MD

Long-term results from RCTs comparing sleeve gastrectomy (SG) and Roux-en-Y-gastric bypass (RYGB) are limited. In the recent years, SG has become the most common MBS procedure, accounting for up to 60% of all procedures both globally and in the US [16, 17] given its good clinical outcomes, safety profiles, and technical ease, relative to RYGB [16, 18-20]. The long-term results of different MBS techniques are of vital importance, given the ever-increasing obesity pandemic and MBS being the only treatment documented to be effective for patients with severe obesity, in terms of providing long-term, substantial weight loss, remission of obesity-related comorbidities, improved quality of life (QOL), and longer life expectancy [19-26]. On the other hand, recent case series have been plagued by a high incidence of worsening or de novo GERD and esophagitis, and alarming rates of Barrett's oesophagus (BE) after SG [27-30].

Randomized clinical trials: SG versus RYGB

Table 5-1 characterizes currently published RCTs, while Table 5-2 summarizes their main outcomes [19, 20, 31-35]. It must be noted that all these trials were underpowered to detect differences in the trials' secondary outcomes (e.g., T2DM remission, complications). In addition, many of the trials had methodological issues that must be taken into consideration when interpreting the results.

10-year outcomes of the SLEEVEPASS RCT

The SLEEVEPASS trial [36] is the only currently-published RCT comparing SG and RYGB with 10-year outcomes. In the SLEEVEPASS trial, the outcomes analysed were weight loss, remission of obesity-related comorbidities, and long-term GERD symptoms, endoscopic esophagitis, and Barrett's oesophagus. Prior to randomization to either SG or RYGB, all trial patients underwent upper gastrointestinal endoscopy (UGE). Although it was not part of the initial study protocol, long-term follow-up endoscopy at 10 years was offered to all patients, enabling comparison to the patients' preoperative endoscopic findings. Esophagitis was classified according to the Los Angeles classification system [37] and any endoscopic diagnosis confirmed by histopathology. Histopathological confirmation of Barrett's oesophagus required the presence of columnar intestinal metaplasia with goblet cells, in accordance with the American Society for Gastrointestinal Endoscopy (ASGE) definition [38, 39]. Out of the 228 available patients, 193 (84.6%) had 10-year follow-up data on weight loss, comorbidity remission, quality of life, and GERD symptoms, and 176 (77.2%) underwent follow-up upper endoscopy.

The results of this 10-year follow-up analysis of the SLEEVEPASS RCT revealed significant and sustained long-term weight loss in both the SG and RYGB patient groups. The weight loss trajectories in the SG and RYGB groups were very similar at all data collection points up to 10 years. The procedures did not meet the prespecified %EWL criteria for equivalence, with RYGB associated with greater weight loss at 10 years, similar to the 5-year [20] and 7-year [24] follow-up results. However, based upon the study's design and prespecified equivalence margins, any superiority of one procedure over the other could not be detected. The prevalence of de novo Barrett's oesophagus was similar after SG (4%) and RYGB (4%), but both rates were significantly lower than those reported for earlier studies, which were as high as 17% after SG in case series [29, 30]. Oesophagitis, reflux symptoms and proton-pump inhibitor use were significantly more prevalent after SG than after RYGB. There were no statistically-significant differences in either long-term complication rates or remission rates for T2DM, dyslipidaemia, or obstructive sleep apnoea between the procedures, but remission of hypertension was more commonly observed after RYGB.

Observational studies: SG versus RYGB

None of the RCTs published, to date, have had the sample size and statistical power to assess safety or the differential impact of each procedure on clinical outcomes. In the absence of adequately-large RCTs, well-designed observational studies can help with such issues. Large observational studies with long-term follow-up clearly show that both SG and RYGB are safe, effective, and durable metabolic procedures.
Since MBS is generally an extremely safe approach to obesity management and adverse event rates are very low, thousands of patients are required to compare safety outcomes between SG and RYGB. This said, observational and cross-sectional studies involving large databases have consistently shown that the risk of serious adverse events is less after SG than after RYGB [40-42]. On the other hand, in well-designed large comparative studies, RYGB has appeared to generate greater weight loss [40, 41], a greater impact on glucose metabolism and improvements in T2DM including higher remission and lower relapse rates [40, 41, 43, 44], a higher incidence of discontinuation of diabetes and cardiovascular medications [45, 46], and a lower risk of adverse cardiovascular and renal outcomes [40] than SG has.

Table 5-1. Study characteristics of randomized clinical trials comparing SG and RYGB

1st author/country (year)	Number of patients (Enrolment period)	Follow-up rate	Primary endpoint	Primary endpoint analysis time point Other longer-term follow-up	Main inclusion criteria
Kehagias [33] / Greece (2011)	60* (2005 – 2007)	57/60 (95%)	Weight loss (%EWL)	3 years	Severe obesity
Keidar [34] / Israel (2013)	41* (2008 – 2010)	37/41 (91%)	HbA1c	1 year	Severe obesity and T2DM
Zhang [35] / China 2014	64* (2007 – 2008)	24/64 (37%)	Weight loss (%EWL)	5 years	Severe obesity
Ignat [32] / France 2016	105* (2009 – 2012)	71/105 (68%)	Weight loss (%EWL)	5 years	Severe obesity
Peterli [19] / Switzerland 2018	225 (2007 – 2011)	205/225 (91%)	Weight loss (%EBMIL)	5 years	Severe obesity
Salminen [20] / Finland (2018)	240 (2008 – 2010)	193/240 (80%)	Weight loss (%EWL)	5 years /7[24] 10[36] years	Severe obesity
Hofso [31] / Norway (2019)	109 (2012 – 2014)	107/109 (98%)	T2DM remission and disposition index (β-cell function)	1-year	Severe obesity and T2DM

%EWL = percentage of excess weight loss; %EBMIL = percentage of excess body mass index loss; T2DM = type 2 diabetes mellitus. * No power calculation or sample size estimate was done

Table 5-2. Primary endpoint results in randomized clinical trials comparing SG and RYGB

1st author (Year)	Primary endpoint	Primary endpoint results
Kehagias [33] (2011)	Weight loss (%EWL)	SG 68% vs. RYGB 62% (p=0.13)
Keidar [34] (2013)	HbA1c	Similar* HbA1c normalization and weight loss
Zhang [35] (2014)	Weight loss (%EWL)	SG 63% vs. RYGB 76% (p=0.02)
Ignat [32] (2014)	Weight loss (%EWL)	SG 65% vs. RYGB 75% (p=0.017)
Peterli [19] (2018)	Weight loss (%EBMIL)	SG 61% vs. RYGB 68% (p=0.22)**
Salmine n[20] (2018)	Weight loss (%EWL)	SG 49% vs. RYGB 57%^
Hofso [31] (2019)	T2DM remission and disposition index (β-cell function)	SG 48% vs. RYGB 75% (p=0.0036) and similar beneficial effect on β-cell function

%EWL = percentage of excess weight loss; %EBMIL = percentage of excess body mass index loss; T2DM = type 2 diabetes mellitus; SG = sleeve gastrectomy; RYGB = Roux-en-Y gastric bypass.
* No inter-group statistical comparisons (SG vs. RYGB); only within-group comparisons (baseline vs. follow-up).
** After adjusting for multiple comparisons.
^ Equivalence trial. Procedures non-equivalent; but based on prespecified equivalence margins, this difference was not clinically significant.

5.4. Long-term results after one-anastomosis gastric bypass (OAGB)

- Jean Marc Chevallier, MD, PhD

Introduction

In 1997, surgeon R. Rutledge described a procedure he called a mini-gastric bypass [47]. In 2018, IFSO recommended that the name to be changed to one-anastomosis gastric bypass (OAGB) and deemed the procedure suitable as a standalone MBS procedure in 2018 [48]. The progressively increasing popularity of OAGB led IFSO, in 2019, to organize a Consensus Conference in Hamburg, Germany, at which 52 internationally-recognized bariatric surgeons from 28 countries convened to vote on 90 statements [49]. Among these 90 statements, at least 70% consensus was achieved for 65. Among the consensus reached was regarding OAGB's effectiveness helping individuals with obesity and severe obesity to lose weight and achieve improvement or even resolution of numerous obesity-linked disorders, like T2DM and hypertension, all of which is supported by published literature [50-67]. There nonetheless was concern regarding the relative shortage of level 1 evidence supporting OAGB's efficacy, relative to other more established procedures like RYGB and SG. In addition, since OAGB was initially described, concerns have been expressed regarding the at least theoretically-increased risk of gastric and esophageal cancer due to bile reflux [68] and regarding the empirically-documented risk of malabsorption that may lead to severe malnutrition [69-71].

Evidence on OAGB efficacy

Over the past few years, four systematic reviews/meta-analyses have been published examining the long-term results achieved after OAGB, one of these meta-analyses having two subsequently-published updates [6, 60, 61, 63, 72, 73]. As well, a single, multi-centre RCT with five years of post-operative follow up, called the YOMEGA trial, was published in 2019 [74].

The review by de Luca et al. was presented as part of a 2021 update of a 2020 IFSO Position Statement by the IFSO task force [6]. In this review of 95 quantitative studies (randomized and non-randomized) and 15 qualitative studies with follow-up of one to three years, the %EWL ranged from 64.0 to 75.6%, while the percentage of excess BMI lost (%EBMIL) lost ranged from 69.5 to 87.8%, and T2DM and hypertension resolution rates ranged from 60 to 100% and from 40.0 to 74.0%, respectively.

In the met a-analysis of 25 articles by Parmar et al., in which 12807 patients were followed for from six months to 12 years, the pooled %EWL again was high, at 76.4% overall and from 70.0% to 85.0% after five years of follow-up [63]. Likewise, the pooled mean resolution rates for T2DM and hypertension were 83.7% and 66.9%.

The meta-analysis published in 2019 by Magouliotis compared OAGB and RYGB in 11 studies encompassing 12445 patients followed for up to five years [72]; and in this analysis, the pooled %EWL and T2DM resolution rates both were higher in OAGB than RYGB patients.

In the one RCT with five-years of follow-up, OAGB and RYGB again were compared, with patients receiving either procedure achieving excellent %EWL at five years (87.9 vs. 85.8%, respectively) [74]. However, more patients undergoing OAGB experienced adverse side effects (35.9 vs. 20.5%, respectively, $p = 0.042$), mostly related to malabsorption in patients whose OAGB involved a 200 cm biliopancreatic limb. The authors concluded that further research was necessary to determine if altering the biliopancreatic limb length during OAGB might lower the rate of malabsorptive adverse effects without jeopardising weight loss and weight-loss-associated outcomes.

In a 2019 IFSO-orchestrated Delphi survey of 51 internationally-recognized experts in MBS surgery, 96% consensus was reached that OAGB generally results in greater weight loss than a sleeve gastrectomy [49]. Such sentiments have been born out in a just-published (2023) meta-analysis comparing OAGB and SG in patients with a BMI >50 kg/m^2, the extracted data drawn from nine retrospective studies encompassing 2332 patients [73]. On meta-analysis, OAGB was found to be superior to SG in %EWL [weighted mean difference (WMD): 8.52%; 95% CI: 5.81-11.22; p<0.001), %TWL (WMD: 6.65%; 5.05-8.24; p<0.001), and the odds of hypertension remission (OR = 1.63; 1.06-2.50), with no significant differences observed in operating time, hospital length of stay, or complications, or in the rate of T2DM remission (OR: 0.72; 0.18-2.94).

Late complications

In the 2021 IFSO Update Position Statement on OAGB, among 18763 patients there have been 1025 late complications (5.46%) and 1.33% of patients have required some reoperation [6]. The main reason for revisional surgery was malnutrition, which accounted for more than a third (36.5%) of the revisions. Moreover, there was a clear correlation between biliopancreatic limb (BPL) length and the incidence of malnutrition, with 92.3 % of the reoperations for malnutrition occurring in patients with a BPL length >200 cm. Gastroesophageal reflux, including bile reflux, was the second most common reason for revisional surgery, occurring in 18.3% of these patients, with acid reflux slightly more frequent than bile reflux [75]. That said, in the de Luca et al. meta-analysis, no difference was identified in the rate of histologically-proven bile reflux between OAGB and RYGB [6]. Similarly, the marginal ulcer rate in OAGB patients was 2.7%, which was comparable to the rate documented in the RYGB patients. Internal hernias also were rare in OAGB patients, due to the apparent absence of mesenteric defects that occur with OAGB, while herniation through Petersen's space was not reported at all. On the other hand, anaemia was more common in OAGB than RYGB patients.

Bilio-pancreatic limb length

As stated in the previous paragraph, in the meta-analysis published by de Luca et al., over 90% of the reoperations for malnutrition were associated with a BPL length over 200 cm [6] and a BPL ≥200 cm was present in all nine OAGB patients who developed severe post-operative malabsorption in the YOMEGA RCT [74]. In a recently-published matched, propensity-score analysis that we performed comparing two types of OAGB – OAGB with a BPL = 150 cm (n=392) and OAGB with a BPL = 200 cm (n =392) – there was no significant difference in the percentage of excess BMI lost at 1, 2, 3, 4, and 5 year s[76]. However, in patients with a BPL = 150 cm, there was a significantly-reduced rate of marginal ulcers (OR = 0.4, CI 95% [0.2; 0.8], p = 0.006) and significantly fewer patients with hypoalbuminemia (OR = 0.3, CI 95% [0.2; 0.7], p = 0.006). Reoperations also were significantly more frequent in the OAGB-200 versus OAGB-150 group [76]. These results are summarised in Figure 5-1.

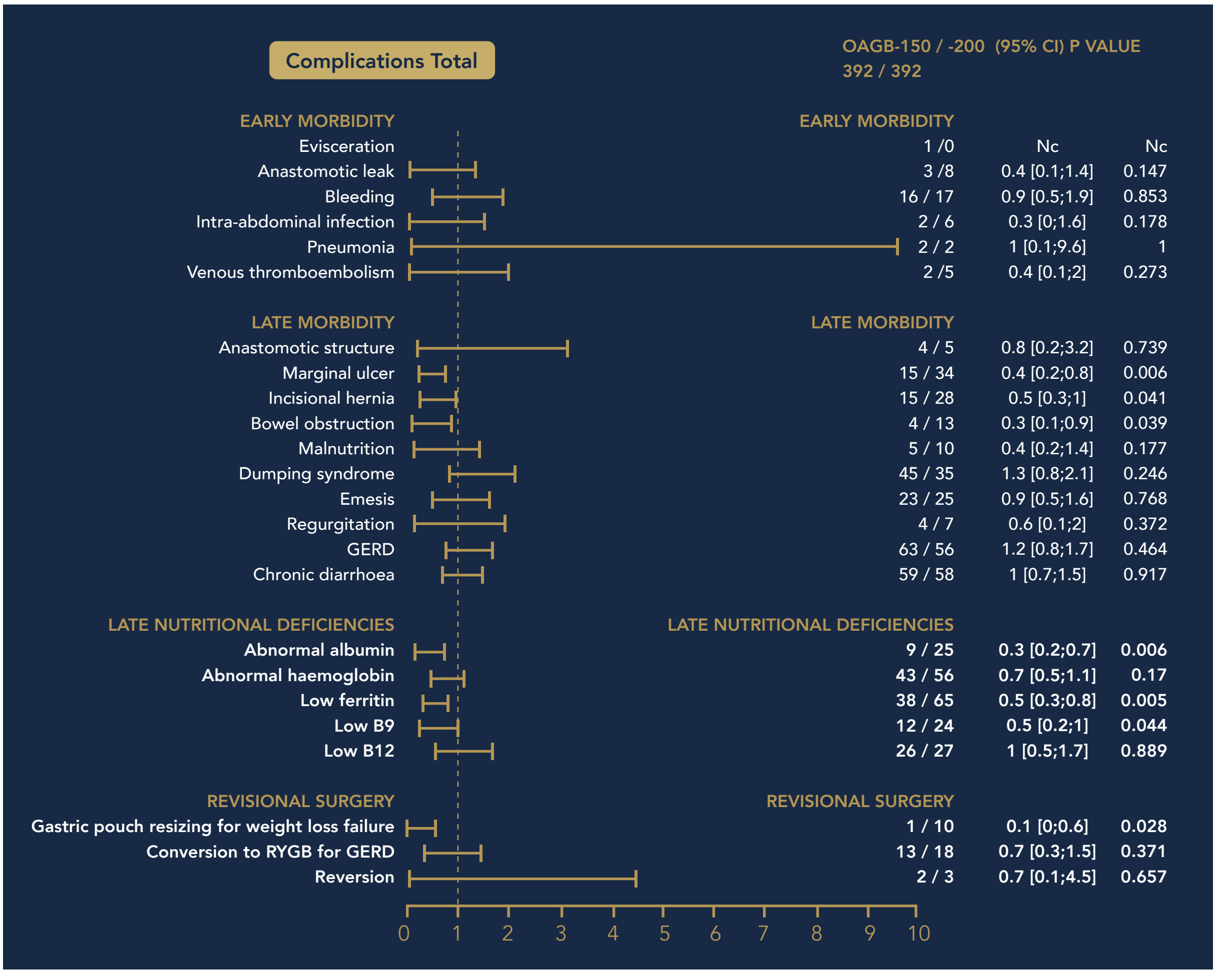


Figure 5-1: Comparing early and late morbidity in OAGB patients with a 200 cm versus 150 cm BPL (borrowed from Bertrand et al, 2022) [76].

Bile reflux and potential carcinogenic risk

Many have likened the OAGB procedure to Billroth II reconstruction and postulated a similar risk of bile in the afferent limb being carcinogenic to the stomach, oesophagus, or both. The suggested time lapse to detect gastric stump cancer following a Billroth II reconstruction has been estimated to be from 17.5 to 34.6 years [77]. To generate a quicker answer to this long-held question, we performed experimental studies in a rat model of OAGB that we developed. We have, to date, published two of these studies, in which we kept some rats alive for 16 weeks, which is equivalent to 16 years in a man's life; and others for 30 weeks, equivalent to 30 years of human life. After 16 weeks, molecular analysis consisting of quantitative real-time PCR was performed on the following markers of interest:

- The Barrett's ulcer markers MUC-1 and MUC-4
- The esophago-gastric carcinogenic markers p53, Cyclin D1, EGF-R, and NF-kB

As a first step, we looked for any significant increase in any of these markers in the 16-week-old OAGB versus SHAM rats, and failed to identify any such increase [78]. We then examined the 30-week-old OABG and SHAM rats histologically, and failed to detect any Barrett's lesions or oesophageal ulcers [79]. In the 30-week OAGB rats, 16.7% had histological evidence of oesophagitis. In both the 2019 IFSO Delphi survey of 51 international bariatric surgeons [49] and the just-completed IFSO-orchestrated Delphi survey of 43 multi-disciplinary obesity-management experts [80], moderate to strong consensus was reached that the OAGB procedure should NOT be considered carcinogenic. That said, in the former survey, 78% of the experts agreed that OAGB should be considered contraindicated in patients with pre-existing Barrett's oesophagus [49].

Conclusions

Published evidence suggests that OAGB is at least as good as RYGB and superior to SG at inducing weight loss and improvements in at least some obesity-associated diseases (particularly hypertension and T2DM), but that surgeons need to be cautious and avoid using a BPL length >150 cm, as it is associated with increased rates of malabsorption and potentially-serious malnutrition. That said, other than a single RCT, published level-1 data remain sparce, with the most-recent meta-analysis comparing OAGB and SG based entirely upon retrospective studies. Consensus is, however, that any concerns that OAGB is a carcinogenic procedure due to the increased risk of bile reflux are unfounded.

5.5 Single anastomosis duodeno-ileostomy with or without sleeve gastrectomy (SADI and SADI-S) - long-term results - Andrés Sánchez-Pernaute, MD, PhD

Introduction

The single-anastomosis duodenal switch (SADI-S) procedure was introduced in Spain in 2007 as a simplified form of the duodenal switch [81] (Figure 5-2). The operation provided two important theoretical advantages over the one-anastomosis gastric bypass (OAGB): first, it preserves the pylorus, which avoids pathologic biliary reflux into the stomach and oesophagus; and second, measurements are of the common channel length, instead of the biliary limb with the OAGB [47]. The initial common channel length with SADI-S was 200 cm. In a short series of 50 patients with 98% follow up, initial studies revealed impressive short-term weight loss, with mean %EWL > 100%, meaning that the average patient actually overshot their initial target weight [82, 83]. However, 8% of the patients developed clinical manifestations of hypoproteinaemia, and 4% required revision to elongate the common limb length. This motivated a change to the current standard 250 cm common limb length. In the longer-term, the revisional rate for patients with a 200 cm common channel was reported to be 16%, so procedures using that common limb length are no longer performed.

More than 120 papers on SADI-S have been published so far in peer-reviewed journals, and there are three ongoing prospective randomized control trials, one comparing SADI-S with RYGB in France [84]; one comparing SADI-S with standard Roux-en-Y duodenal switch and OAGB in Spain; and the last comparing SADI-S with duodenal switch as either primary or revisional surgery in Portugal. There also is one ongoing prospective non-randomized cohort study comparing SADI-S with duodenal switch in Canada. And there are at least six systematic literature reviews/metanalyses that analyse different topics, from bile reflux to metabolic outcomes and comparisons against other techniques [7, 85-89].

Safety of the procedure

The technique has been demonstrated to be safe, with a low rate of postoperative complications. Operating times also are significantly shorter than for Roux-en-Y duodenal switch. Surve et al. reported the results of a multi-institutional series with more than 1300 patients, which included a 0.6% anastomotic leak rate, anastomotic ulcers in 0.1%, and bile reflux in 0.1% [90]. These results were reported in 2018, and included a learning curve for most of the surgeons. The same research group reported on a significantly-higher complication rate after RYGB at three years follow-up, complications that included reoperations, ulcers, small bowel obstruction and upper gastrointestinal symptoms [91]. Surve et al. also conducted a matched-cohort comparison, drawing from a total series of 1254 MBS patients, from which they extracted and compared 61 patients with SADI-S and 61 patients with RYGB [92]. Emergency room visits and readmissions were comparable with the two procedures. The early reoperation rate was higher after RYGB (3.2% vs 1.6%), while the overall rates of complications were similar. The total long-term complication rate, including all events, from dumping syndrome to diarrhoea, was 62% after gastric bypass and 19.2% after SADI-S. The most common complications after RYGB were ulcers (16.3%), dumping

(11.4%), small bowel obstruction (11.4%), internal hernia (9.8%), and anastomotic stricture (8.1%). After SADI-S, 6.5% of the patients developed a gastric-incisura and upper third stricture, while 4.9% developed diarrhoea[92]. The same research group conducted a similar matched cohort study to compare the results of SADI-S and those of Roux-en-Y duodenal switch [93]. The complication rate after duodenal switch was double the rate observed after SADI-S: 20% vs 10%. There was only one reported case of new intestinal obstruction caused by an internal hernia after SADI-S [94].

Managing an anastomotic leak after SADI-S can be challenging due to the confluence of bile and pancreatic juices with saliva and gastric secretions at the anastomotic site. To date, however, there have been no published reports and scarce communications about how stenting is virtually impossible and the requirement for nutritional support to compensate for this complication.

Long-term weight loss and metabolic results

The longest follow up for SADI-S was reported by our group [8]. Weight loss results included 87% EWL and 38% total weight loss (TWL) at 5 years, and 80 and 34%, respectively, at 10 years with a 75% follow-up rate. At five years, Surve et al reported 38% TWL and 73.5% EWL rates [92]. Other studies and meta-analysis have generated similar outcomes, with scarce differences in outcomes after standard duodenal switch [87].

There are no randomized comparisons with RYGB. Surve et al reported the results of a retrospective analysis comparing weight loss after the two operations at three years, and a matched comparison with results at five years [91, 92]. In the mid-term, SADI-S patients showed slightly better weight loss, 86 vs 79% EWL, albeit a non-statistically significant difference. However, in the matched study, five-year results were significantly better for SADI-S, in terms of %EWL, %TWL, final BMI, and change in BMI from pre-operatively [92].

Metabolic results after SADI-S appear promising. The first report of SADI-S for diabetic patients included 97 patients with a mean preoperative glucose level of 167 mg/dl and glycated haemoglobin of 7.6%; 40 of these patients were insulin dependent [95]. In the long-term, overall remission rate (normal laboratory and no treatment) was achieved in 52% of the patients, including 75% of the patients initially on oral hypoglycaemic medication and 38% of those requiring insulin. Remission rates appear to be superior to those achieved after gastric bypass with normalization of glycaemia and a more physiologic postprandial response observed, without the severe variations in continuous glycaemia observed after gastric bypass procedures [96, 97].

This promising metabolic response has been explained by Pereira et al [98]. The increased length of the common limb of the single-anastomosis procedure increases the potential interaction of bile acids and food with the ileal mucosa, enhancing stimulation of the surface and the nuclear receptors TGR5 and FXF, thereby increasing the secretion of different gastrointestinal hormones and peptides, including GLP-1 and PYY. The authors of this study demonstrated higher peaks of secretion of glucagon, insulin, GLP-1, GIP. and total bile acids after SADI-S, temporally linked to the aforementioned enhanced metabolic response [98].

SADI-S as a second-step or revisional operation

Whilst SADI-S can be considered a second step towards achieving resolution of metabolic disorders or as a revisional surgery for suboptimal weight loss or weight recurrence after a sleeve gastrectomy, the literature is scarce. Sánchez-Pernaute et al. reported 72% EWL at two years in an initial small cohort of patients [99], and 79% EWL and 41% TWL at five years in a later series of 51 patients [100]. Comparable results have been reported by Balibrea et al. [101].

Two interesting papers from the Netherlands compared patients who underwent conversion of a sleeve gastrectomy to either SADI-S or RYGB at four institutions [102, 103]. In the short term, TWL was 10% better for SADI-S patients than for gastric bypass patients; initial mean BMIs were 45 and 42 kg/m^2, respectively, reduced at two years to 32.7 and 39.5 kg/m^2, respectively. The authors followed up with a larger number of patients with five years of follow up, among whom TWL was 29.4% after SADI-S and 17.9% after gastric bypass. The second revisional procedure also resulted in a 15% increase in TWL for SADI-S versus just 2% for gastric bypass.

Conclusions

Studies that have emerged over the past 15 years have demonstrated SADI-S to be a simpler, safer, and at least as effective alternative to older malabsorptive operations. For this reason, it has been accepted, by both the IFSO and ASMBS, as an effective MBS technique [104, 105]. Nonetheless, since the highest level of evidence available in currently-published studies is 2a, further long-term results and prospective randomized trials are necessary.

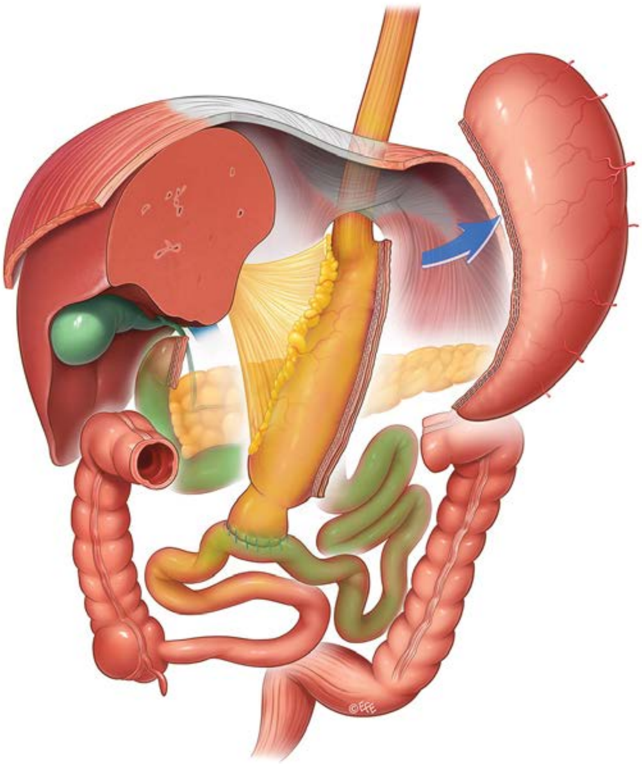


Figure 5-2. SADI-S scheme.
The common limb is usually 250 to 300 cm in length.

5.6. Choosing the most appropriate metabolic-bariatric procedure: an algorithm
- Jacques Himpens, MD, PhD

According to the IFSO registry, the vast majority of primary MBS procedures involve one of the following four procedures, in decreasing order of frequency: laparoscopic sleeve gastrectomy (SG), Roux-en-Y gastric bypass (RYGB), one-anastomosis gastric bypass (OAGB), and biliopancreatic derivation with duodenal switch, using either a single anastomosis (SADI-S) or double anastomosis (DS). The procedure chosen mostly depends on the surgeon's and/or patient's preference, and this unscientific basis most likely explains the high frequency of SG worldwide [106]. It is the aim of the current section to provide guidance for decision-making based on high-quality evidence in the literature, so the surgical procedure that is selected is best suited to the patient deemed suitable for MBS. Note that the algorithm proposed here does not address patients with a BMI >50 kg/m^2 or above 60 years of age, both patient populations discussed at length in the next chapter.

The most important objective in all surgery is to not harm the patient (noli me tangere). Hence, bariatric surgeons must avoid procedures that endanger patients despite proven success achieving weight loss and/or improved metabolic outcomes.

Along these lines, it is pivotal to evaluate each patient's Helicobacter pylori status, especially when the procedure being considered involves exclusion of the gastric body, thereby jeopardizing access for endoscopic diagnostic and therapeutic work. H. pylori has been shown to facilitate the development of gastric carcinoma, atrophic gastritis, ulcers, gastro-intestinal stromal tumours [107]. It is important that H. pylori is eradicated before MBS because – as a rule – its eradication reduces the risk of carcinoma of the stomach [108]. Conversely, however, it appears that H. pylori is actually protective against oesophageal carcinoma [109]. Hence, in cases where HP appears to be extremely resistant, SG should be considered.

The presence of H. pylori infection can be assessed by upper gastro-intestinal endoscopy (UGD) provided that well-established biopsy protocols are respected. Alternatively, H. pylori can be detected in stools, but UGD has been proven to provide additional essential information, and hence is considered an essential part of the MBS patient work-up [107]. The risk of severe gastric disease and oesophagitis, including Barrett's oesophagus, may be either accentuated or diminished by certain MBS procedures (such as LSG). Such conditions – which might otherwise remain asymptomatic and undetected, with the potential to induce severe disease at a later stage – can usually be assessed adequately by UGD [110].

According to most publications, the prevalence of Barrett's oesophagus after LSG is high and increases year by year. However, because there is no evidence that this pejorative evolution happens after a gastric bypass [111], one may decide to forego LSG in patients with severe esophagitis or Barrett's oesophagus.

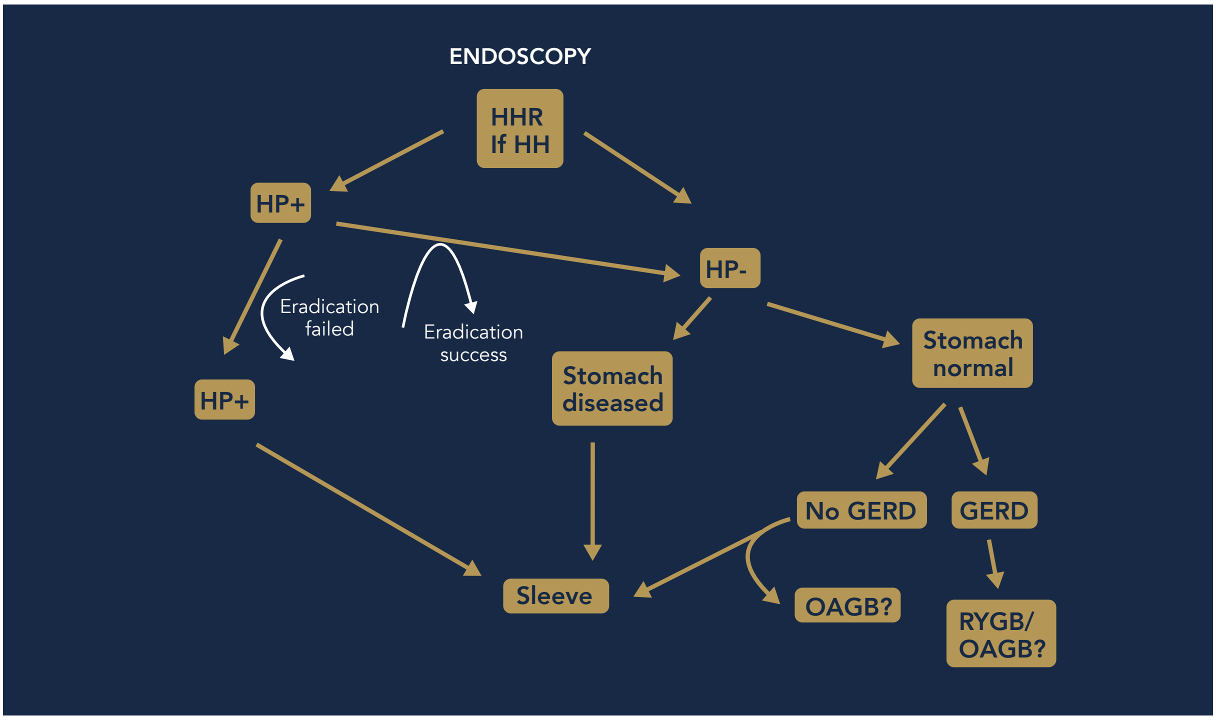
A peculiar situation occurs in patients with a hiatal hernia, which may or may not coincide with severe oesophagitis. The surgical option is to include hiatal hernia repair (HHR) concomitantly with LSG (provided no severe oesophagitis is involved); but this strategy has no proven benefit over LSG without HHR [112]. Nevertheless, substantial evidence exists that performing hiatal hernia repair at the same time as LSG improves oesophagitis and GERD [113]. Hence, when a hiatal hernia is present in the absence of severe oesophagitis, combining LSG and a hiatal hernia repair may still be recommended. Alternatively, RYGB can be chosen, since it is the procedure of choice in most series involving patients with a hiatal hernia [114].

In many cases, the main patient issue is overweight, with or without T2DM. In such instances, three surgical options generally prevail: LSG, RYGB, and OAGB. Indeed, while BPD-DS has been documented to yield excellent clinical results, the high rate of complications makes this procedure less attractive.

The outcomes achieved with SG and RYGB are quite comparable, in terms of weight loss and diabetes control [36]. However, though the prevalence of oesophagitis is higher on long-term follow-up after LSG, relative to RYGB, this is not the case for Barrett's oesophagus.

In terms of weight loss and glucose control, OAGB is non-inferior to RYGB, but OAGB is easier to perform and associated with similar outcomes for up to five years post-operatively [115]. The above-noted recommendation are summarized in Figure 5-3, below.

Figure 5-3: Algorithm for MBS in patients with obesity.
(Patients with a BMI ≥50kg/m² and/or age >65 years excluded).



HP: Helicobacter Pylori, HH: Hiatal Hernia, HHR: Hiatal Hernia Repair
OAGB: One anastomosis gastric bypass; RYGB: Roux en Y Gastric Bypass
T2DM: case by case SG vs RYGB (Aminian) vs OAGB (Robert)

5.7. Revisional surgery after RYGB - Jacques Himpens, MD, PhD

Roux-en-Y gastric bypass (RYGB) is currently the second most frequently performed metabolic-bariatric surgery procedure. The sheer volume of procedures alone renders it hardly surprising that bariatric surgeons are sometimes called to perform revisional surgery to deal with less-than-optimal outcomes (e.g., suboptimal weight loss, excessive weight loss, weight recurrence after initial satisfactory weight loss), or to adjust aberrations that were caused either at the time of surgery or that developed with time and interfere with the correct physiology of RYGB, resulting in marginal ulcers, dumping syndrome, GERD, persistent or recurrent pain, meteorism, flatulence, and diarrhoea. Perhaps the most difficult aspect of revisional surgery after RYGB is determining IF and WHEN one should intervene surgically [116], since most undesired outcomes can be adequately treated by non-surgical means (e.g., dietary, genetic, psychiatric) [117].

When the primary goal is to correct weight issues, several options are possible, none of which has demonstrated clear superiority [86]. Possible techniques include distal Roux-en-Y gastric bypass (DRYGB), conversion to a duodenal switch with the one-anastomosis procedure SADI-s or the two-anastomosis procedure BPD-DS, and resizing the gastric pouch and/or gastro-jejunal anastomosis via either a laparoscopic or endoscopic approach. However, based on the findings in the above-noted systematic review, it seems that malabsorption-enhancing procedures – like DRYGB or the duodenal switch with one (SADI-s) or two anastomosis (BPD-DS) – are the most effective procedures in the long-run.

Despite the results of the above-noted meta-analysis, Mahawar et al., in their systematic review, concluded that interventions involving the gastric pouch and/or the size of the gastro-enterostomy did not have a significant impact on weight loss [118]. While none of the studies analysed by these authors detected better outcomes with larger pouches or wider gastro-jejunostomies, nine of 14 and six of 10 did not identify any influence on weight loss by larger pouches or wider stomas, respectively. According to another recent meta-analysis [119], inadequate weight loss after RYGB is best approached by lengthening the biliopancreatic limb at the expense of the common limb (i.e., distalising the bypass), while preserving a safety margin so the combined alimentary limb length and common limb length remain greater than 350 cm. (Figure 5-4). Further shortening the limbs was not associated with greater %EWL (P = 0.9), but was significantly associated with severe protein malnutrition (p = 0.01) [119].

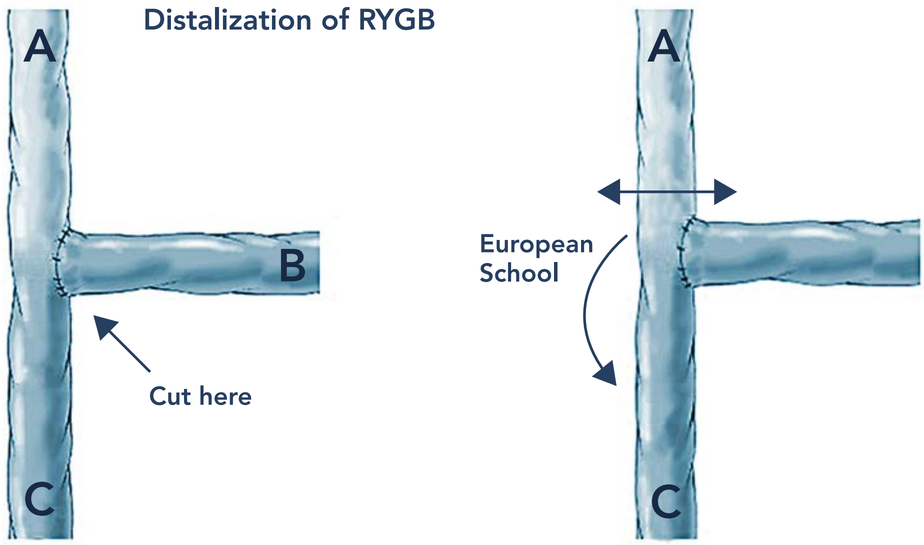


Figure 5-4: Schematic of distalisation by lengthening the biliary limb (transection of distal end of alimentary and reimplantation more distally on the common limb).

A = alimentary, 150cm, B = Biliary, C=common

The technique shown above represents lengthening the biliopancreatic limb at the expense of the common limb (i.e., distalising the bypass), while preserving a safety margin so the combined alimentary limb length + common limb length remain >350 cm.

Either SADI-s or DS are viable options when weight loss is deemed suboptimal after RYGB. However, in a recent expert consensus survey, revisions using BPD-DS were considered limited because of the procedure's technical difficulty. In that same survey, 86.2% of the experts claimed they would routinely recommend or consider the procedure if it were more technically feasible after a failed gastric bypass [120].

When the multidisciplinary advisory team decides to select surgery as an option for non-weight related issues after RYGB – such as for the dumping syndrome or GERD – ad hoc treatment must be chosen because evidence-based treatment modes are lacking. Using the ligamentum teres hepatis to reinforce a hiatal hernia repair, radiofrequency ablation of the distal oesophagus, and employing the upper part of the remnant to create a sling at the gastro-oesophageal junction have all been described for patients with GERD after RYGB. Meanwhile, endoscopic or laparoscopic trimming of the gastro-jejunal anastomosis or even placement of a loose non-adjustable band distally around the gastric pouch may result in slowing down gastric pouch emptying, thereby potentially reducing dumping syndrome.

Conclusions

Pouch volume and gastro-jejunal anastomosis size are "probably" not all that important when revising RYGB. Limb lengths may be altered to improve weight loss, but one should be wary of the risk of malnutrition. Total alimentary limb length is the most important determinant in terms of avoiding protein malnutrition. Dumping symptoms and GERD can both be problematic after RYGB, but treatment options convincingly supported by scientific evidence remain missing .

5.8. Conversion or revision surgery after a sleeve gastrectomy

- Estuardo Behrens (Guatemala)

Sleeve gastrectomy (SG) is the most frequently performed (67%) of all of the primary MBS procedures worldwide, as reported in the IFSO Global Registry Report 2022 [3]. The popularity of SG can be attributed to several factors, which include it being, relative to most other MBS procedures:

1) More economical
2) Technically simpler to perform
3) Free of any surgical anastomoses
4) Free of the risk of internal hernias
5) Easier to learn, with a shorter learning curve
6) Faster to perform, with shorter operating times
7) Feasible and relatively safe in patients considered at higher surgical risk; and
8) Comparable to RYGB in terms of weight loss and metabolic outcomes [121].

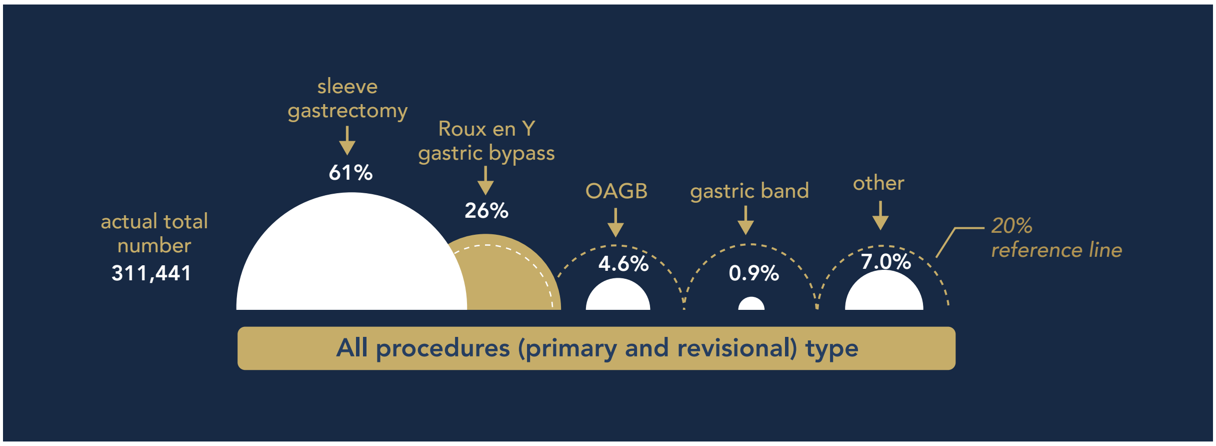


Figure 5-5: Frequency of use of various MBS procedures, as reported in the 7th IFSO Global Registry Report – 2022. (Borrowed with permission from Brown et al., 2022 [3])

Obesity can be considered the pandemic of the 21st century. It is a chronic, noncommunicable disease that does not respect age, sex, or ethnicity and appears to be a global phenomenon. Metabolic and bariatric surgery is the only treatment option that has been shown to cause sustainable weight loss and remission of the metabolic syndrome [122]. The MBS procedures – SG and RYGB – are the two most frequently performed MBS procedures in the world (see Figure 5-5). Both also are the procedures with the most published supportive evidence.

Despite its worldwide high acceptance, SG has post-operative issues that oblige MB surgeons to sometimes perform revisions or conversions. The principal causes for reoperation in these patients are GERD, leaks, and either suboptimal weight loss or weight recurrence.

The main objective of this section is to describe these three primary reasons for revision and conversion after SG, understanding what Ricardo V. Cohen said once, that "The pinnacle of evidence-based medicine today is the randomized control trial (RCT), surpassed only by meta-analysis of randomized control trials" [123]. For this reason, predominantly meta-analyses and systematic reviews were reviewed.

GERD

Several meta-analyses considered level 1 evidence have examined the issue of GERD after SG. In one, Yeung et al [121] used electronic searches in EMBASE, Medline, the Cochrane Library, and Psychinfo from 2000 to 2018 to ultimately identify 35 studies for analysis. In another, Sharples and Mahawar [122] restricted their analysis to just five studies, using Medline, EMBASE, Cochrane Library and NHS evidence to identify these five. Pooled data in these two meta-analyses revealed GERD symptoms in 19% – 31.8% and de novo GERD in 23% - 31.6% of patients post SG. On the other hand, in the latter meta-analysis, a 25% rate of GERD remission also was identified [122].

Barrett's oesophagus (BE) was also seen in 8-11% of patients spanning two meta-analyses[121, 124]. In the latter paper, by Qumseya et al., ten studies were included totalling 680 patients. In this latter paper, the pooled prevalence of Barrett's oesophagus was 11.6%, but there was no correlation with GERD symptoms and most BE was observed beyond three years of follow-up [110].

After SG, 3.1 – 4.0% of patients will need revisional surgery for GERD [121, 125] (Level 1 evidence). In 2019, Guan et al. published their meta-analysis on mid- to long-term outcomes (≥3 years follow-up) after SG, identifying 32 studies for review through PubMed, EMBASE and CENTRAL. They concluded that both bariatric surgeons and patients need to fully understand and deal with the occasional need for revisions after SG [125]. Up to 30% of the patients requiring revisional surgery after SG do so because of GERD, as identified in a meta-analysis published by Matar et al. [126] when they examined indications for and the outcomes of conversion of SG to RYGB. For this review, electronic searches were performed on multiple search engines, including Ovid MEDLINE(R), Epub Ahead of Print, InProcess & Other Non-Indexed Citations, Ovid Embase, the Ovid Cochrane Central Registry, the Ovid Cochrane Database of Systematic Reviews, and Scopus, among others, ultimately identifying 25 articles warranting a full review, but only selecting 17 articles that met the eligibility criteria (n = 556, 68.7% female). Pooled analysis revealed that GERD symptoms resolved in 79% of patients after conversion of SG to RYGB. The authors hence concluded that GERD after SG is a strong indication for conversion to RYGB [126] (Level 1 evidence).

Leaks

In 2020, the ASMBS reported that 61% of MBS procedures performed in the USA and Canada that year were SG. They estimated the incidence of staple-line leaks after SG to be from 0.75 – 7% [127] (Level 1 evidence). In 2017, in a multi-centre German trial, Benedix et al. identified a leak in 241 of 15,756 patients (incidence = 1.53%) [128]. The authors concluded that postoperative staple line leaks after primary SG significantly increases postoperative morbidity and mortality. Risk factors associated with leaks were longer operating time, conversion surgery, intraoperative complications, hypertension, and degenerative joint disease. Other risk factors that were identified were SG stenosis and SG torsion [128].

Staple-line leaks are the second most common cause of death after MBS [129] (Level 3 evidence), as reported in the 5th International Consensus Conference report: Current Status of Sleeve Gastrectomy, published by Gagner et al. in 2016 [129]. In this same report, the mortality rate from leaks after SG was estimated to be from 0 -1.4%. The most frequent time when a leak is diagnosed is three weeks after surgery (88.9%) and the most frequent site is the upper third of the staple line, which is involved in 94% of cases [130], due to various mechanical factors and ischaemia.

Suboptimal weight loss and weight recurrence

Suboptimal weight loss and weight recurrence are, collectively, the most common indication for revisional surgery after SG, estimated to account for 52% of revisions [126]. Following their systematic review and meta-analysis of data, Matar et al. concluded that conversion of SG to RYGB is a conversion option that yields good weight loss and potential resolution of the symptoms of both metabolic syndrome and GERD (Level 1 evidence). Guan et al. identified insufficient weight loss or weight recurrence as the indication for revisional surgery after SG in up to 30% of patients [125] (Level 1 evidence) Fortunately, when converting from an SG, almost any procedure is an option, from a technical standpoint. Hence, the choice of procedure selected is again determined based upon the indication for revision or conversion, the patient, and the surgeon's experience and expertise with different procedures.

Re-operative surgery following a primary MBS procedure is increasing due to insufficient weight loss and weight recurrence. In 2017, Pinto-Bastos et al. performed a systematic review of the reasons for re-operations after MBS, looking at such factors like suboptimal weight loss, weight recurrence, GERD, and staple-line leaks, but also behavioural factors [131]. Analysing data from 29 studies, they found that poor adjustment to lifestyle changes, the postoperative re-emergence of maladaptive eating, difficulty embracing the required lifestyle changes, and the reappearance of depressive and anxiety symptoms were linked to both suboptimal weight loss and weight recurrence [131]. Because of all the above-mentioned behavioural factors, largely reliant on patient compliance, the role of an interdisciplinary team is crucial.

It has also been found that increased gastric volume is one of the factors that predicts weight recurrence after SG. In their meta-analysis, Athanasiadis et al. screened 272 papers identified through PubMed, EMBASE and the Cochrane Library in July of 2019, among which only 32 were included in their systematic review [117]. Risk factors related to weight recurrence fell into five categories: anatomical, genetic, dietary, psychiatric, and temporal. Hormonal changes were not identified as predictive in patients with weight recurrence. Dietary risks factors identified included sugar consumption, portion size, emotional eating, and loss of control/disinhibition when eating. There also was evidence that patients with weight recurrence had lower levels of physical activity than patients without weight recurrence [117]. The one psychiatric risk factor that has been consistently identified as associated with weight recurrence is anxiety.

Conclusions

The use of sleeve gastrectomy is continuing to grow worldwide, but surgeons and patients must communicate to decide what type of surgery is best in each case. Preoperative endoscopy must be performed in all cases, and when severe GERD is identified, the best option for patients is almost inevitably RYGB. At a centre of excellence for MBS, it also is recommended that routine preoperative video-cineradiography and manometry are performed. When revision or conversion are required after an SG, once again the choice of surgery largely depends on the indication for revision, though RYGB is by far the most commonly selected revision procedure. Whatever procedure is selected, all patients must be followed long-term by an interdisciplinary team.

5.9. **Results of a consensus survey** - Lilian Kow, MD,PhD; Ali Aminian, MD

For this section on the general principles of bariatric surgery, there were 26 surgeons among 43 multi-disciplinary experts in obesity management who attended a consensus conference that occurred over two days in Hamburg, Germany in March 2023. The attendees voted on a total of 135 statements that included preoperative decision making and care, indications and contra-indications for MBS, specifics on and comparisons between various MBS procedures (SG, RYGB, OAGB, SADI, LAGB), and follow-up and outcomes. Thirty-eight statements pertained either to the specific primary MBS procedures or re-operations, with consensus reached on 31 (81.6% of the statements). The average level of consensus reached was 80.2%. These results are summarized in Table 5-3. Artist dipictions of the various procedures voted on and discussed in this chapter are found in Figures 5-7 to -5-13.

Further areas of consensus were as follows:

Suitability for MBS

Overall, there was consensus that MBS should be offered to individuals with the following:

- BMI 30-35 kg/m^2 and T2DM who do not achieve substantial, durable weight loss and diabetes improvement with reasonable nonsurgical methods.
- BMI 30-35 kg/m^2 and obesity-related complications, but no T2DM, who do not achieve substantial, durable weight loss and improvement in their complications with reasonable nonsurgical methods.
- BMI 30-35 kg/m^2 and no obesity-related complications who do not achieve substantial, durable weight loss with reasonable nonsurgical methods.

Choice of procedure

Recent trends have led to SG being the most commonly chosen procedure, followed by the RYGB, OAGB, and biliopancreatic diversion with duodenal switch. However, our experts reached consensus that, for individuals with evidence of a large hiatal hernia and/or severe gastro-oesophageal disease or Barrett's oesophagus, RYGB is preferable to SG to control reflux symptoms and decrease the risks of worsening Barrett's oesophagus.

In adult patients with T2DM and obesity, gastric bypass (including RYGB & OAGB) is generally preferable to SG. Our experts reach almost unanimous consensus that OAGB should NOT be considered a carcinogenic procedure. However, for patients undergoing OAGB, there was consensus that a biliopancreatic limb of 200 cm or longer may increase the risk of protein deficiency.

Whilst there was consensus that the indications for a primary SADI-S could include poorly-controlled T2DM, consensus was not reached as to whether a primary SADI-S should be offered to individuals with a BMI ≤ 45kg/m^2 or that it provides a better quality of life than the classic Roux-en-Y Duodenal Switch.

Preoperative preparation

In addition to lower extremity compression, there was consensus that all MBS patients must have perioperative chemoprophylaxis against venous thromboembolism (VTE).

There was consensus that, for the preoperative workup of patients being considered for MBS, improved patient selection for GERD risk will significantly reduce the rate of sleeve gastrectomy conversions to bypass; that preoperative gastroscopy should be performed routinely for individuals considering sleeve gastrectomy; and that a hiatal hernia assessment requires laparoscopic evaluation at the start of MBS.

Follow-up

For sleeve gastrectomy patients, there was concern about the risk of SG-associated reflux.

For long-term follow-up, the main concern pertaining to the risk of sleeve gastrectomy-associated reflux was the endoscopic findings of esophagitis or Barrett's oesophagus, rather than GERD symptoms, like heartburn or regurgitation.

Since most post-MBS VTE events occur after hospital discharge, there was consensus that patients with known risk factors for VTE would likely benefit from extended pharmaco-prophylaxis after discharge. In addition, currently-published data do not support routinely measuring anti-factor-Xa levels post-operatively to monitor the adequacy of VTE thromboprophylaxis.

Individuals who undergo SADI-S must be under surveillance and supplemented for life.

For RYGB patients who develop persistent hypoglycaemia syndrome despite adequate nutritional counselling, there was consensus that treatment with medications like diazoxide, acarbose, octreotide, and a GLP1-mimetic is preferred over reducing the pace of gastric pouch emptying either endo- or laparoscopically and preferred over performing surgical reversal to normal anatomy.

Outcomes

There was consensus that patients experiencing weight recurrence after weight loss require a thorough, multidisciplinary workup before any decision on revisional MBS surgery is made.

There was consensus that patients with suboptimal weight loss following their initial MBS surgery can be considered for revisional surgery. In the absence of GERD symptoms or Barrett´s oesophagus, patients with suboptimal weight loss after a sleeve gastrectomy can be treated by either adding anti-obesity medication (AOM) or converting the SG to some other MBS procedure, or both. For patients with suboptimal weight loss after RYGB, there was consensus that revisional surgery may include pouch trimming (with or without band placement), gastro-jejunal anastomosis size reduction, or limb length modification.

However, more specifically, consensus was not reached for patients with suboptimal weight loss after RYGB on whether revising pouch size or the GJ anastomosis should be performed during the same operation as limb length modification. In addition, no consensus was reached on the most appropriate surgical option for patient with suboptimal weight loss after SG in the absence of GERD symptoms or Barrett´s oesophagus, when experts were offered the options of RYGB, OAGB, or SADI-DS.

There was consensus that patients can be considered for modification of a prior MBS procedure based on weight issues alone (e.g., BMI>35 kg/m^2), even when pre-existing obesity-related complications have resolved or are in remission.
However, no consensus was reached on whether SADI-S outcomes are generally superior to, inferior to, or roughly the same as those achieved with Roux-en-Y DS.

Voting on the treatment of recurrent anastomotic (marginal) ulcers after a RYGB was considered invalid, because open discussion between consensus attendees resulted in too many options to consider (e.g., accurate vagotomy or reducing pouch size; resecting the anastomosis and creating a new one (preferably by hand); resecting the remnant; none of the above).

Full results of the consensus survey are in the process of being submitted for publication [80].

Table 5-3: Results of a 2023 IFSO Delphi survey on metabolic and bariatric surgery

Statements	N	Rounds required	Most common selection	Percentage consensus
ROUX-EN-Y GASTRIC BYPASS (RYGB)				
In individuals with evidence of a large hiatal hernia and/or severe gastro-oesophageal disease or Barrett's oesophagus, RYGB IS/IS NOT preferable to SG.	40	1	Is	97.5%
The best option to treat medically-uncontrolled GERD after a SG is conversion into a RYGB.	38	1	Agree	97.4%
In individuals with class 1 obesity and early-stage diabetic kidney disease, with poor control despite medical treatment, RYGB SHOULD/SHOULD NOT BE recommended.	36	1	Should	91.7%
Revision of RYGB to address suboptimal weight loss would include pouch trimming (with or without band placement), GJ anastomosis size reduction, or limb length modification.	37	1	Agree	78.4%
Unless contraindicated, gastric bypass (including RYGB & one-anastomosis procedures) is generally preferable to SG for adults with T2DM and obesity.	41	1	Agree	78.0%
Preferred treatment for hypoglycaemia syndrome after RYGB, persisting despite adequate nutritional counselling, consists of: Medication (e.g., diazoxide, acarbose, octreotide, GLP1-mimetic)/Reducing the pace of gastric pouch emptying endo- or laparoscopically/Reversal to normal anatomy/None of the above	37	1	Medication	75.7%
Recurrent anastomotic (marginal) ulcers after a RYGB should be treated surgically by: Accurate vagotomy/Reducing pouch size, resecting anastomosis & creating a new anastomosis (preferably by hand)/Resecting the remnant/None of the above.	27	1	Reducing pouch…	74.1%
For a revisional surgery to address suboptimal weight loss after RYGB, given the risk of nutritional adverse events, revising the size of pouch and GJ anastomosis should NOT be done during the same operation as limb length modification.	32	2	Disagree	67.7% (NC)
In the absence of GERD symptoms or Barrett´s oesophagus, the most appropriate surgical option for suboptimal weight loss after a sleeve gastrectomy would be conversion to: RYGB/OAGB/DS-SADI.	36	2	RYGB	60.5% (NC)

N = number of voters in deciding round; AOM = anti-obesity medication; BMI = body mass index; DS = duodenal switch; GERD = gastro-oesophageal reflux disease; GJ = gastro-jejunal; MBS = metabolic and bariatric surgery; OAGB = one-anastomosis gastric bypass; RYGB = Roux-en-Y gastric bypass; RY-DS = Roux-en-Y duodenal switch; SADI = single-anastomosis duodenal-ileal bypass; SADI-S = SADI with sleeve gastrectomy; LGB = laparoscopic gastric banding; T2DM = type 2 diabetes mellitus; VTE = venous thromboembolism. NC = no consensus.

Table 5-3: Results of a 2023 IFSO Delphi survey on metabolic and bariatric surgery

Statements	N	Rounds required	Most common selection	Percentage consensus
SLEEVE GASTRECTOMY (SG)				
Gastroesophageal reflux disease, suboptimal weight loss, and recurrent weight gain are the main reasons for revisions after SG.	37	1	Agree	100.0%
Sleeve gastrectomy is a suitable procedure for high-risk individuals as the first step of a staged surgical approach.	42	1	Agree	95.2%
Sleeve gastrectomy is a suitable procedure for high-risk individuals as a stand-alone procedure.	41	1	Agree	92.7%
Individuals experiencing T2DM recurrence without suboptimal weight loss or recurrent weight gain after a SG are candidates for optimized adjuvant medical treatment.	35	1	Agree	91.4%
In the absence of GERD symptoms or Barrett´s oesophagus, suboptimal weight loss after sleeve gastrectomy can be treated by... Adding an AOM/converting the SG to some other MBS procedure/BOTH/NEITHER.	40	1	Both	87.5%
Improved patient selection preoperatively for GERD risk WILL/WILL NOT significantly reduce the rate of sleeve gastrectomy conversions to bypass.	37	1	Will	83.8%
Sleeve gastrectomy is not the ideal procedure for individuals with severe T2DM on insulin.	35	1	Agree	80.0%
At long-term follow-up, the main concern, pertaining to the risk of sleeve gastrectomy-associated reflux is… GERD symptoms, like heartburn or regurgitation/endoscopic findings, like esophagitis or Barrett's oesophagus.	38	1	Endoscopic findings	76.3%
A preoperative gastroscopy SHOULD/SHOULD NOT be performed routinely for individuals considering sleeve gastrectomy.	40	1	Should	75.0%
Generally, sleeve gastrectomy is the preferred procedure for elderly individuals (>65 years old) because of its excellent safety profile.	40	1	Agree	75.0%

N = number of voters in deciding round; AOM = anti-obesity medication; BMI = body mass index; DS = duodenal switch; GERD = gastro-oesophageal reflux disease; GJ = gastro-jejunal; MBS = metabolic and bariatric surgery; OAGB = one-anastomosis gastric bypass; RYGB = Roux-en-Y gastric bypass; RY-DS = Roux-en-Y duodenal switch; SADI = single-anastomosis duodenal-ileal bypass; SADI-S = SADI with sleeve gastrectomy; LGB = laparoscopic gastric banding; T2DM = type 2 diabetes mellitus; VTE = venous thromboembolism. NC = no consensus.

Table 5-3: Results of a 2023 IFSO Delphi survey on metabolic and bariatric surgery

Statements	N	Rounds required	Most common selection	Percentage consensus
SINGLE-ANASTOMOSIS DUODENO-ILIAL BYPASS (SADI) + DUODENAL SWITCH = SADI-S				
Individuals who undergo SADI-S must be under surveillance and supplemented for life.	36	1	Agree	100.0%
In a metabolically-challenged patient, hypo-absorptive procedures – especially those involving a duodeno-ileostomy – should only be performed by experienced surgeons at high-volume centres (≥ 25 cases per year)	34	1	Agree	88.2%
Suitable candidates for classic Duodenal Switch or SADI-S would be individuals with a BMI >50 kg/m² and previous SG / severe or uncontrolled T2DM / Both / Neither.	35	2	Both BMI>50 & severe DM	77.1%
Indications for a primary SADI-S include poorly-controlled T2DM.	35	1	Agree	71.4%
Indications for a primary SADI-S include a BMI ≤ 45kg/m².	36	2	Agree	66.7% (NC)
Considering that hypo-absorptive MBS procedures are associated with a higher risk of malnutrition, they SHOULD NOT BE/CAN STILL BE undertaken in adolescents (< 18 years old).	42	2	Should not be	66.7% (NC)
Comparing weight loss outcomes between SADI-S (with a common limb length of 250 - 300 cm) and classic Roux-en-Y DS... SADI-S is superior/Classic DS in superior/Weight loss is comparable	36	2	SADI-S & RYDS comparable	63.0% (NC)
Compared with classic Roux-en-Y Duodenal Switch, SADI-S provides a better quality of life.	33	2	Agree	51.5% (NC)
ONE-ANASTOMOSIS GASTRIC BYPASS (OAGB)				
With OAGB, a biliopancreatic limb of 200 cm or longer may increase the risk of protein deficiency.	39	1	Agree	100.0%
OAGB SHOULD/SHOULD NOT be considered a carcinogenic procedure.	37	1	Should NOT	83.8%
OAGB IS/IS NOT better than RYGB for individuals with a BMI >50 kg/m².	31	1	Is NOT	80.6%
Unless contraindicated, gastric bypass (including RYGB & one-anastomosis procedures) is generally preferable to SG for adults with T2DM and obesity.	41	1	Agree	78.0%

N = number of voters in deciding round; AOM = anti-obesity medication; BMI = body mass index; DS = duodenal switch; GERD = gastro-oesophageal reflux disease; GJ = gastro-jejunal; MBS = metabolic and bariatric surgery; OAGB = one-anastomosis gastric bypass; RYGB = Roux-en-Y gastric bypass; RY-DS = Roux-en-Y duodenal switch; SADI = single-anastomosis duodenal-ileal bypass; SADI-S = SADI with sleeve gastrectomy; LGB = laparoscopic gastric banding; T2DM = type 2 diabetes mellitus; VTE = venous thromboembolism. NC = no consensus.

Table 5-3: Results of a 2023 IFSO Delphi survey on metabolic and bariatric surgery

Statements	N	Rounds required	Most common selection	Percentage consensus
LAPAROSCOPIC GASTRIC BANDING (LGB)				
Long-term follow-up (>10 years) after LGB reveals a high-rate of band-related reoperations and device explants.	38	1	Agree	94.7%
Laparoscopic gastric banding (LGB) is an effective treatment option for suitable individuals with obesity.	40	2	Disagree	60.0% (NC)
OTHER				
Weight gain recurrence requires a thorough evaluation before even considering a patient a candidate for modifying a prior MBS procedure.	37	1	Agree	100.0%
Suboptimal weight loss has different implications than recurrent weight gain when considering which type of intervention to consider next.	35	1	Agree	85.7%
A hiatal hernia assessment REQUIRES/DOES NOT REQUIRE laparoscopic evaluation at the start of MBS.	32	1	Requires	81.3%
Modification of a prior MBS procedure can be considered for weight issues alone (e.g., when BMI>35 kg/m^2), even when preexisting obesity-related complications are cured or are in remission.	40	1	Agree	80.0%
OVERALL MEAN LEVEL OF CONSENSUS = 80.2% RYGB = 80.1%; SG = 82.4%; SADI-S = 71.7%; OAGB = 85.6%; LGB = 77.4%; OTHER = 86.8%				

N = number of voters in deciding round; AOM = anti-obesity medication; BMI = body mass index; DS = duodenal switch; GERD = gastro-oesophageal reflux disease; GJ = gastro-jejunal; MBS = metabolic and bariatric surgery; OAGB = one-anastomosis gastric bypass; RYGB = Roux-en-Y gastric bypass; RY-DS = Roux-en-Y duodenal switch; SADI = single-anastomosis duodenal-ileal bypass; SADI-S = SADI with sleeve gastrectomy; LGB = laparoscopic gastric banding; T2DM = type 2 diabetes mellitus; VTE = venous thromboembolism. NC = no consensus.

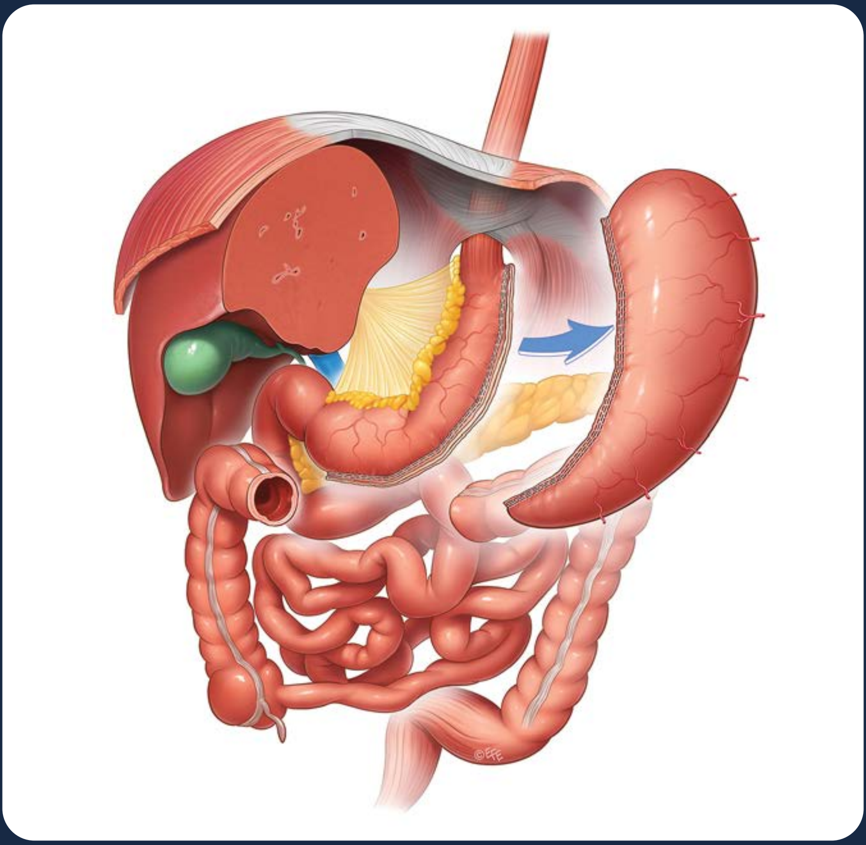


Figure 5-7: Sleeve Gastrectomy

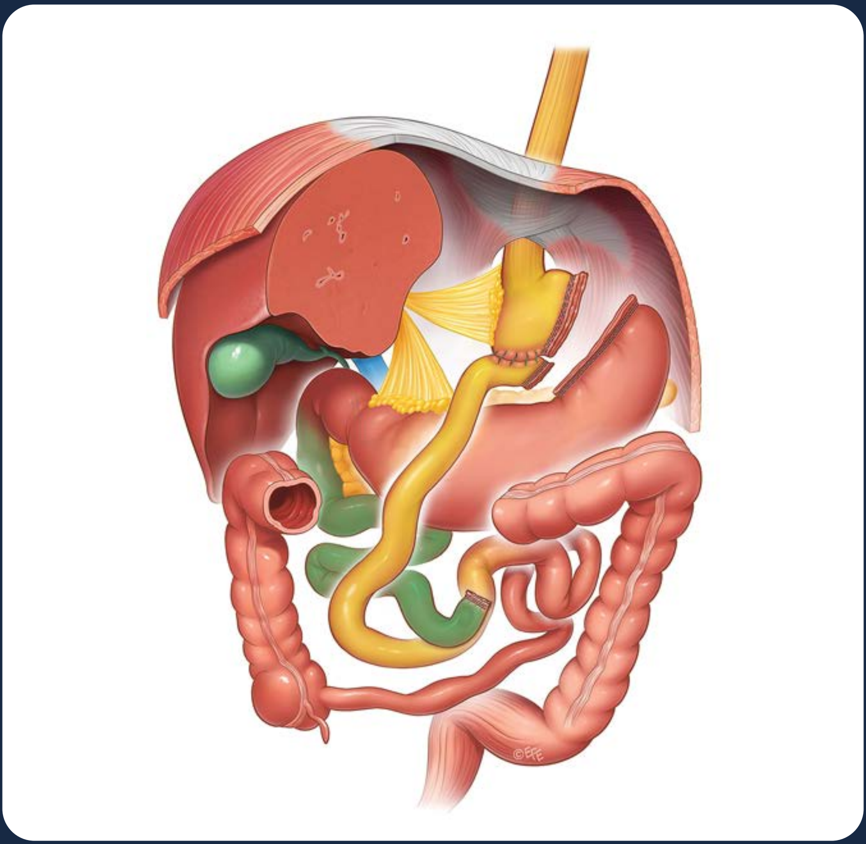


Figure 5-8: RYGB

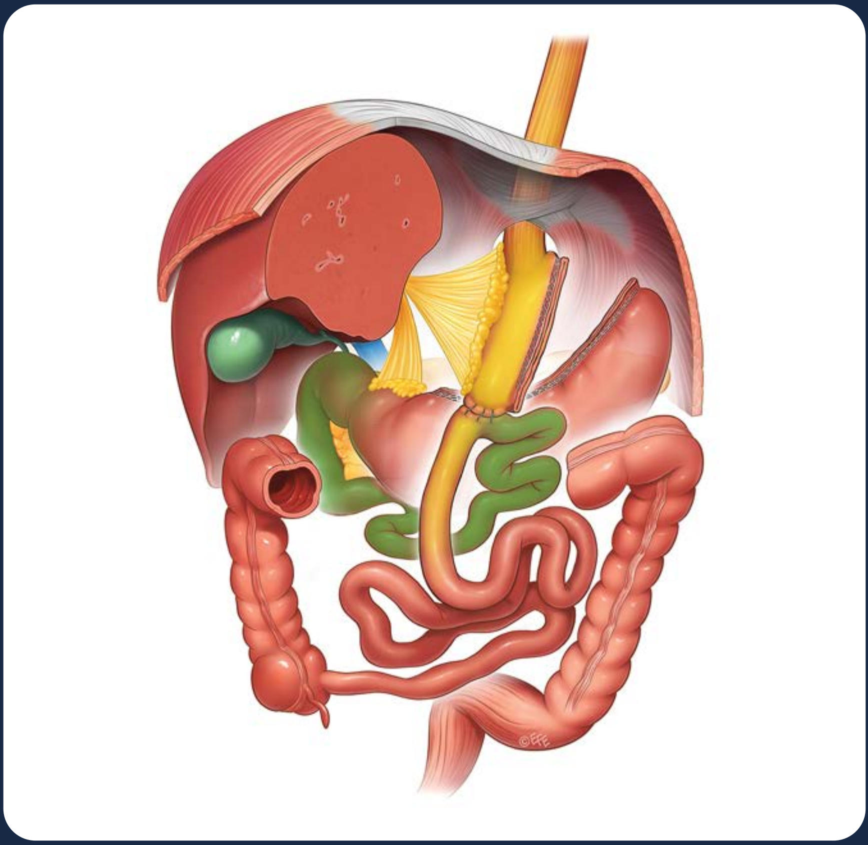


Figure 5-9: OAGB

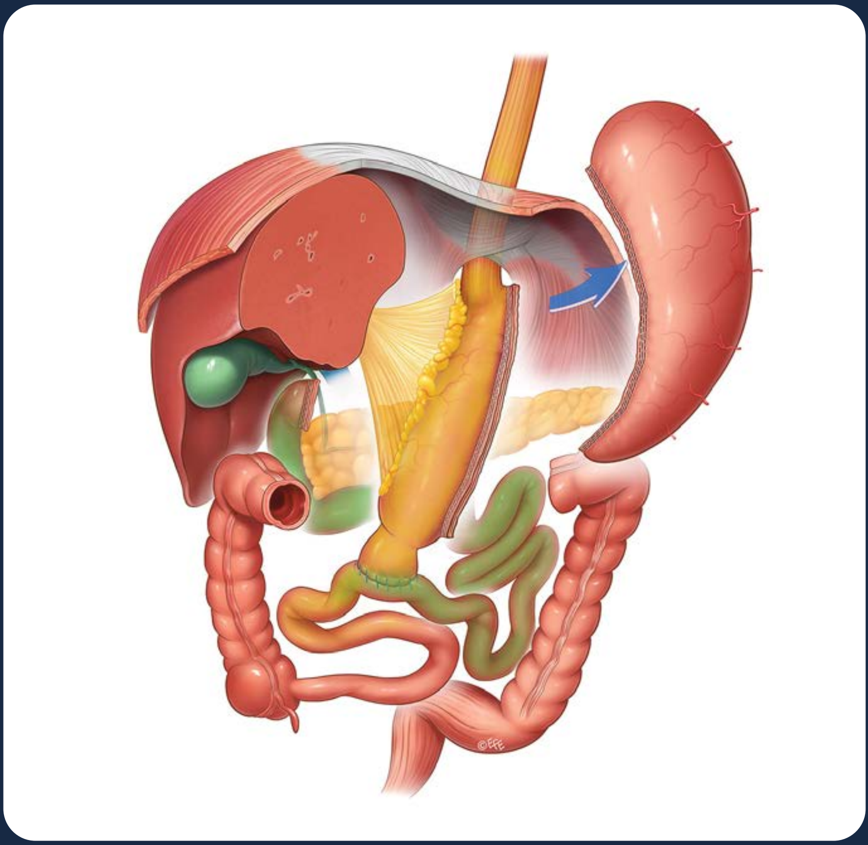


Figure 5-10: SADI-S

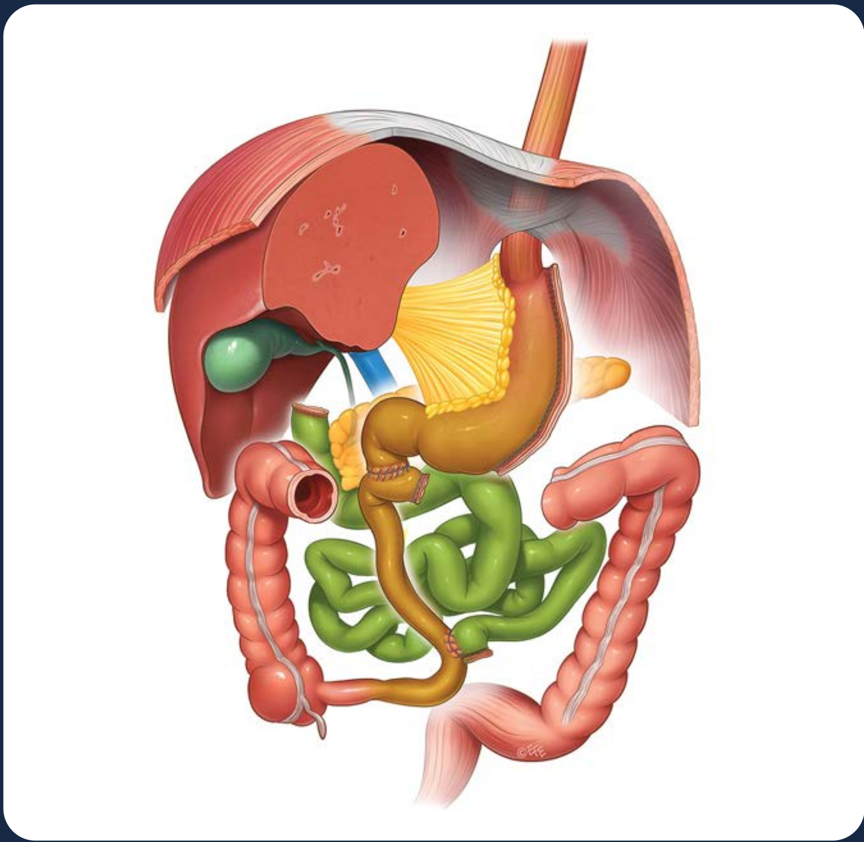


Figure 5-11: Duodenal Switch

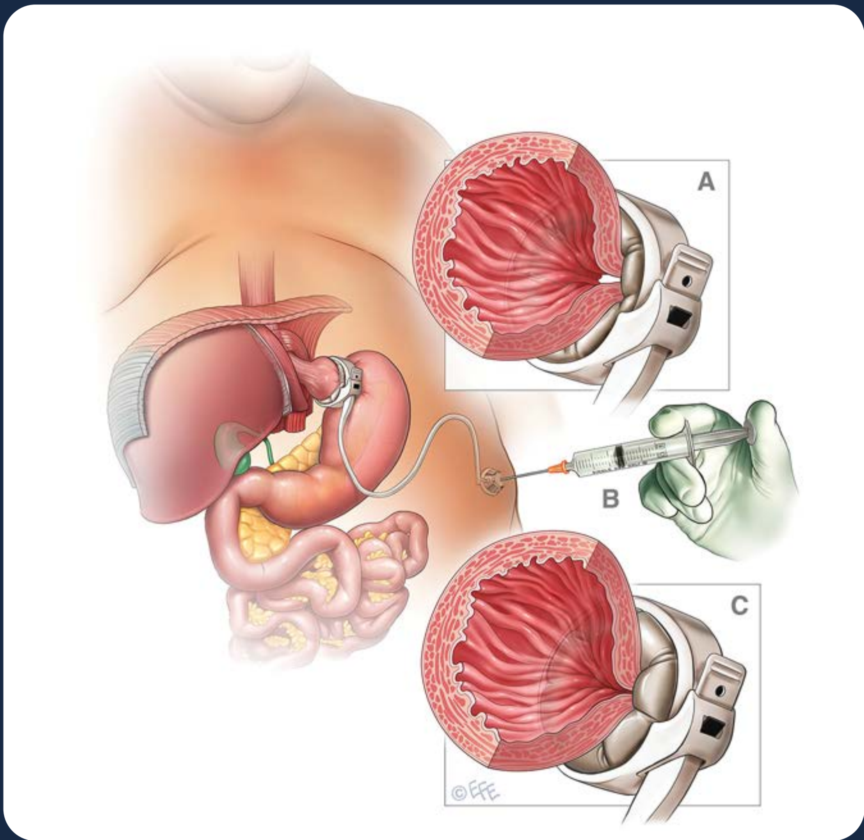


Figure 5-12: Adjustable Gastric Banding

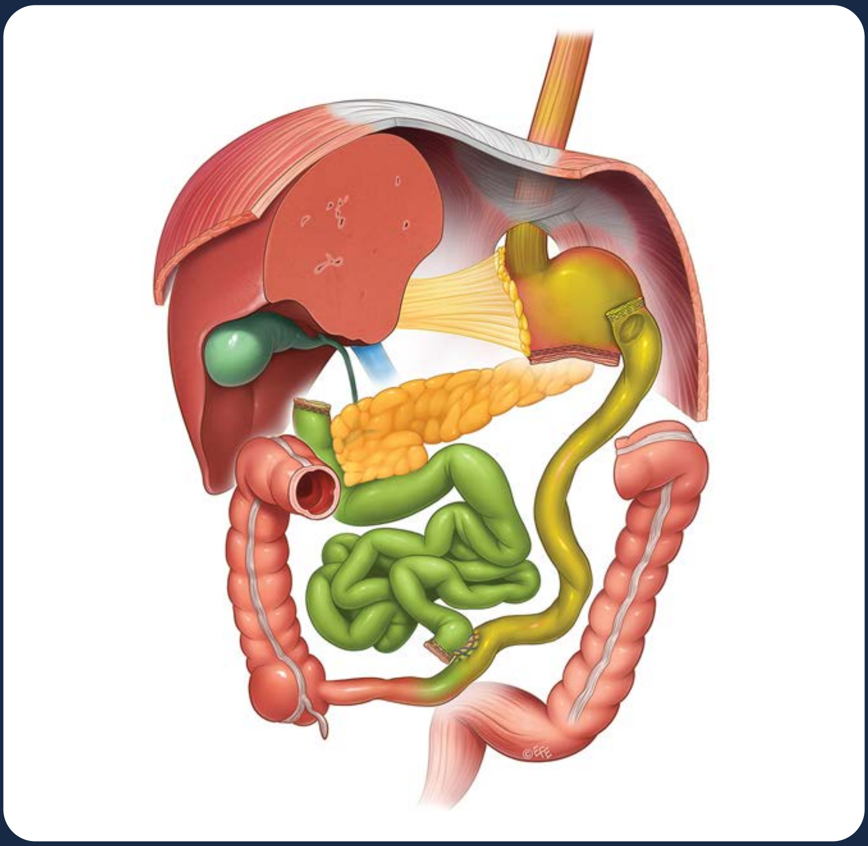


Figure 5-13: Biliopancreatic Diversion

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CHAPTER 6

METABOLIC-BARIATRIC SURGERY IN METABOLICALLY-CHALLENGED PATIENTS

6.1. Introducing the concept of the metabolically-challenged patient

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Metabolically-challenged patients are patients who have a BMI > 50 kg/m^2 or high burden of obesity-associated diseases such as type II diabetes, obstructive sleep apnoea, hypertension, and non-alcoholic fatty liver disease NAFLD. Currently, the prevalence of a BMI >50 kg/m^2 is increasing at a faster pace than either class I (BMI > 30 kg/m^2) or class III obesity (BMI > 40 kg/m^2) [1]. In addition, metabolically-challenged patients are a group of patients with a more severe form of obesity and may need special consideration when deciding management strategies. This is similar to what is often done for patients with stage III cancer. They are managed differently than patients with stage I or II cancer [1]. Metabolically-challenged patients are at higher risk of having or acquiring the complications of obesity and may have worse short- and long-term outcomes after metabolic and bariatric surgery (MBS)[2, 3]. Having a BMI > 50 kg/m^2 is an independent risk factor for venous thromboembolism (VTE), the leading cause of death after MBS [2]. In addition, a BMI > 50 kg/m^2 is an independent risk factor for complications and mortality after MBS [3].

Like short-term outcomes, long-term adverse outcomes of MBS are also more common for metabolically-challenged patients than patients even with class III obesity (BMI 40-49.9 kg/m^2) [4-8].

Procedure selection is paramount for metabolically-challenged patients, since they are inevitably a higher risk group [4]. In addition, weight recurrence after sleeve gastrectomy and Roux-en-Y gastric bypass is highest in patients with a BMI > 50 kg/m^2, when compared to patients with class III obesity (BMI 40-49.9 kg/m^2) [4, 5]. Additionally, procedures at higher risk for early and late complications, like biliopancreatic diversion +/- duodenal switch, provide more durable weight loss for metabolically-challenged patients [9, 10]. However, despite having more severe disease and worse short- and long-term complications, this cohort of especially-high-BMI patients should not be denied MBS. Rather, it is all the more reason to offer them lifesaving MBS. Moreover, biased language and stigmatizing terms like "superobese" should not be used to describe patients who have a BMI > 50 kg/m^2 [11].

6.2. Metabolic and bariatric surgery for class I obesity

- Ali Aminian, MD

Introduction

The International Federation for the Surgery of Obesity and Metabolic Disorders [12], the American Society for Metabolic and Bariatric Surgery (ASMBS), and the American Diabetes Association (ADA) have issued guidelines and position statements on the role of MBS in patients with class 1 obesity (body mass index [BMI] = 30.0–34.9 kg/m^2) [13-15]. This section reviews those guidelines.

Scientific data have clearly shown that BMI alone is a poor indicator of adiposity, metabolic dysregulation, and cardiovascular risk. The health consequences of obesity in a patient with a BMI = 32 kg/m^2 with visceral and ectopic fat accumulation and metabolic disease are significantly higher than those of a metabolically-healthy individual with a BMI = 40 kg/m^2. However, though the latter patient has been historically considered a candidate for MBS and the former not, there is no evidence on clinical efficacy or cost-effectiveness that would justify patients with class 1 obesity being excluded from MBS [13, 14].

Extensive literature indicates that class I obesity can cause or exacerbate several other diseases and negatively impact quality of life and longevity. Therefore, individuals with class I obesity deserve effective and durable treatment for their obesity. Current nonsurgical treatments for class I obesity are often ineffective at achieving major sustained weight reduction and the resolution of comorbidities [13, 14].

There are three subgroups of patients with class I obesity in whom the indications for MBS can be considered separately.

1. Patients with type 2 diabetes

There is compelling evidence from several randomized clinical trials and meta-analyses on the efficacy of MBS at improving or even achieving remission of type 2 diabetes in patients with class 1 obesity [16]. According to the second Diabetes Surgery Summit (DSS-II), the International Diabetes Federation (IDF), and the ADA, MBS may be considered an option to treat type 2 diabetes in adults with a BMI from 30.0–34.9 kg/m^2 (27.5–32.4 kg/m^2 in Asian individuals) who do not achieve durable weight loss and improvement in comorbidities (including hyperglycaemia) with nonsurgical methods (level A evidence) [15]. In addition, the 2022 ASMBS and IFSO updated guidelines recommend that MBS be offered to patients with type 2 diabetes and a BMI ≥30 kg/m^2 [14].

2. Patients with other obesity complications but no type 2 diabetes

Several prospective and retrospective observational studies have revealed improvements in hypertension, dyslipidaemia, fatty liver disease, obstructive sleep apnoea, asthma, joint pain, urinary incontinence, reflux disease, and quality of life following MBS in individuals with class I obesity. The surgical risk, weight loss outcomes, and co-morbidity reductions are consistent with what has been reported in patients with class II and III obesity. Nonetheless, most of these observational studies are limited by small numbers of patients, lack of control data, and short-term follow-up [13].

According to the 2022 ASMBS and IFSO updated guidelines, MBS should be considered in individuals with a BMI of 30–34.9 kg/m^2 who do not achieve substantial or durable weight loss or co-morbidity improvement using nonsurgical methods.

3. Patients without apparent obesity complications

The safety and efficacy outcomes of MBS in this subgroup without apparent obesity complications have been less studied. There are several points that must be considered when evaluating the role of MBS in patients with class I obesity who do not have apparent obesity complications.

- Obesity is a chronic progressive disease. Most individuals with obesity gain weight over time. Even if they have class I obesity at this moment, they will probably progress to class II or III obesity within a few years.
- Even if a patient does not have clinically-apparent obesity complications, they may already have an asymptomatic or mild, subclinical form of one or several obesity complications. Furthermore, these patients are at risk of developing apparent and more severe obesity complications in the future if they continue to carry their weight.
- As explained above, the BMI cut-off of 35 is an arbitrary threshold that has not been empirically validated [13]. From a scientific and medical standpoint, there is no clear reason why a patient with a BMI of 36 kg/m^2 would be eligible for MBS while a patient with a BMI of 34 would not be.
- Current options for the nonsurgical treatment of obesity are generally ineffective, not durable, or not accessible.
- Surgical risk in these patients would be consistent with what has been reported for severe obesity; and we know that MBS is generally a very safe intervention [17].
- Patients with class I obesity typically do not lose excessive weight after MBS, and their BMI usually stabilizes around 25 kg/m^2.

Therefore, even patients with class I obesity without diabetes or other clinically-apparent obesity complications can be offered MBS as an option if they are otherwise suitable and have not been able to achieve substantial and durable weight loss with reasonable nonsurgical methods.

Conclusions

In summary, according to available literature and guidelines, MBS should be considered in individuals with class I obesity who do not achieve substantial or durable weight loss or co-morbidity improvement using nonsurgical methods.

6.3. Venous thromboembolism (VTE) prophylaxis in bariatric surgery

- Ashraf Haddad, MD

Introduction

The incidence of venous thromboembolism (VTE) has been reported to be approximately 0.3% after MBS [18]. After discharge from the hospital, VTE has been reported to occur in as high as 1.3% of patients[19]. Although this rate is extremely low overall, any reduction in the rate of VTE is important, regardless of how minute the reduction is, since VTE is one of the most common causes of morbidity and mortality after MBS.

When researchers analysed data retrieved from the Metabolic and Bariatric Surgery Accreditation and Quality Improvement Program (MBSAQIP), VTE was discovered to have the greatest effect on readmission and mortality. Thus, targeting VTE reduction has a huge potential to reduce readmission and mortality rates [18].

Literature

To write this section we examined review articles, systematic reviews, and meta-analyses addressing the subject of post bariatric surgery VTE prophylaxis over the past 10 years. These articles are summarized below in Table 6-1.

Table 6-1: Summary of key points on venous thromboembolism management

Study (Year)	Type	Highlights
ASMBS position statement (2022) [20]	Review article	• High-quality data are sparce. RCTs are lacking. • VTE is a strong predictor of mortality. • Most VTE happens after discharge. • MBS patients are considered at least at moderate risk.
Amaral et al (2022) [21]	SR+MA Included seven RCTs totalling 1045 participants.	• Higher-dose chemoprophylaxis may result in little or no difference in the risk of VTE or major bleeding. • There is no difference if prophylaxis is started • 12 hours before or after surgery.
Zhao et al (2022) [22]	SR+MA 15 studies (3 RCTS and 12 observational studies) 72,393 participants	• LMWH and fondaparinux may be equally effective. • The effects of augmented dosing on VTE prophylaxis are uncertain. • The effect of extended prophylaxis on VTE prophylaxis remains uncertain.
Brotman et al (2013) [23]	SR+MA Included 8 studies in pharmacotherapy. Included 5 studies on IVC filter.	• LMWH may be more efficacious than UFH. • One study suggested that prolonged therapy (after discharge) with enoxaparin sodium may prevent VTE better than inpatient treatment only. • Using an IVC filter may be associated with higher mortality and DVT rate.
Kaw et al (2014) [24]	SR+MA Examined the use of IVC filters. Included 6 studies 102,767 participants.	• Use of filters increases the risk of DVT (RR=2.81). • PE rate is not increased. • Mortality is increased insignificantly.
Ikesaka et al (2014) [25]	SR 6 studies Pooled proportions were calculated.	• Dose adjusted regimens may be associated with a lower VTE rate (not significant) without significantly increasing the rate of major bleeding events.

SR: Systematic review, MA: Meta-analyses, LWHH: Low molecular weight heparin, UFH: Unfractionated heparin, DVT: Deep venous thrombosis, PE: Pulmonary embolism, IVC : Inferior vena cava, RR: Relative risk

Mechanical Prophylaxis

Mechanical prophylaxis serves to enhance blood flow in the lower extremities. This can be applied as intermittent pneumatic devices, compression stockings, or venous foot pumps. The ASMBS position statement concluded that mechanical prophylaxis is indicated for all MBS patients, as mechanical prophylaxis without chemoprophylaxis carries a higher VTE rate [20]. Similarly, in a recent Cochrane review, adding pharmacological to mechanical prophylaxis appeared to reduce the VTE rate compared to using mechanical prophylaxis alone [21].

It is commonly recommended that mechanical prophylaxis be used for all patients after MBS, as this is a low-risk intervention with an extremely-important potential benefit.

Efficacy and safety of pharmacological prophylaxis

High-quality data regarding the safety, efficacy, and dosing of pharmacological agents are lacking. Low molecular weight heparin (LMWH) is the most commonly used agent. However, it has been suggested that fondaparinux is equally effective [20, 22].

Birkmeyer et al. and the Michigan Collaborative examined three different regimens combining LMWH and unfractionated heparin (UFH). Using LMWH pre- and post-operatively was associated with a lower VTE rate than either using UFH pre-and post-operatively or using UFH pre-operatively and LMWH post-operatively, with no significant differences in bleeding rate [26].

A recent meta-analysis also found that LMWH and fondaparinux are equally effective and more efficacious than UFH at preventing VTE [22]. The authors also reported that there was no evidence to support using oral anticoagulants perioperatively to prevent VTE after MBS.

Augmented and extended dosing

A recent survey of MBSAQIP program directors and ASMBS members identified huge variations in the dosing, timing, and duration of VTE prophylaxis [27]. The two agents used most commonly were LMWH (56.5%) and UFH (38.1%). For LMWH, the most commonly used regimens were 40 mg once daily (32.4%) and 40 mg twice daily (22.7%). For UFH, it was using 5000 units every 8 hours (46.1%), followed by 5000 units every 12 hours (22.6%). The survey also highlighted the use of extended prophylaxis post discharge, with just 13.7% of survey respondents reporting not using extended regimens, while 12.5% used it routinely and 73.8% used it selectively. As for augmented dosing based on weight or body mass index, these regimens were used by 24.4% of surgeons [27].

In their meta-analysis, Brotman and colleagues reported that, with regards to extended regimens, extended prophylaxis with enoxaparin was found to be superior to inpatient treatment only, but just in one study [23]. Augmented dosing (defined as enoxaparin >30 mg or >40 mg twice daily) was not more efficacious at reducing the incidence of VTE, but a trend was noted towards increased bleeding.

In their meta-analysis, Zhao et al examined seven studies assessing the use of augmented VTE prophylaxis regimens, including two RCTs, and concluded that whether augmented regimens are better than standard dosing remains uncertain [28]. They also analysed five observational studies (49,797 patients) and reported uncertain effects of extended regimens.

It is key to highlight, however, that certain high-risk MBS patients could benefit from extended prophylaxis. Nimeri et al. demonstrated that using a mandatory risk assessment, such as the Caprini score, switching from UFH to LMWH, and extending prophylaxis regimens in high-risk patients reduced the VTE rate [29]. Aminian et al. then found that using their risk assessment tool, they were able to identify high-risk patient who might benefit from extended post discharge regimens [30]. They also identified key high-risk factors – such as congestive heart failure, paraplegia, reoperation, dyspnoea at rest, non-gastric band surgery, age ≥ 60 years, male sex, BMI ≥50 kg/m^2, postoperative hospital stay ≥3 days, and operative time ≥3 hours – as potential red-flags warranting the use of extended prophylaxis [30].

Anti-factor Xa is a functional assay that measures the inhibition of factor Xa by both UFH and LMWH. There is no evidence that supports using Anti-factor Xa routinely, but levels might be of value in certain high-risk patients – like those with severe renal insufficiency, an extremely-high BMI, or a hypercoagulable state – who then will need monitoring and dose adjustments [20].

Inferior vena cava (IVC) filters

Inserting an IVC filter was once considered essential for high-risk patients undergoing MBS. However, the complications associated with IVC filters seem to outweigh the potential benefits, and routine use is no longer recommended [20]. One meta-analysis of five studies failed to identify sufficient evidence to suggest that inserting IVC filters reduced the incidence of pulmonary embolism (PE) [23]. Furthermore, there was low-level evidence that IVC filters increased mortality and DVT rates. Another meta-analysis of six studies detected significantly-increased DVT risk (RR=2.81; 95% CI=1.33-5.97) with filter placement [24].

Recommendations

- Mechanical prophylaxis is low risk and potentially of benefit and, therefore, should be used in all MBS patients.
- The use of mechanical prophylaxis alone is associated with higher VTE rates than mechanical combined with pharmacological prophylaxis.
- LMWH is the most commonly used agent. However, LMWH and fondaparinux may be equally effective at reducing VTE and both are associated with lower VTE rates than UFH.
- There is little to no published evidence supporting the use of augmented doses for reducing either VTE or major bleeding.
- Very low-quality and inconclusive data exist regarding the routine use of extended prophylaxis, in terms of VTE or major bleeding.
- The importance of extended prophylaxis arises when applied selectively to high-risk patients identified using risk assessment tools.
- There is no published evidence supporting the routine use of IVC filters.

6.4. Is there any benefit of preoperative weight loss in metabolically-challenged patients? - Scott A. Shikora, MD

Introduction

Decades of experience have proven that MBS is an example of performing "complex surgery on complicated patients." The excess fat deposited into the abdominal cavity and viscera of patients with obesity complicates surgery by stiffening the abdominal wall and limiting both the workspace and visibility.

In addition to the technical difficulties of operating on an enlarged body habitus, MBS is further complicated by the metabolic comorbid conditions – such as type 2 diabetes mellitus (T2DM), sleep apnoea, liver disease, and heart disease – that are commonly associated with obesity [31, 32]. The higher the BMI, the greater the operative risk appears to be [3]. This is particularly true for the metabolically-challenged patient (BMI > 50 kg/m2). Therefore, anything that can be done to decrease risk would be welcomed. One such possibility is preoperative weight loss (PWL).

It has been estimated that 33% of patients with severe obesity have fatty livers and are at risk of having an enlarged left lobe of the liver [33]. Several publications have reported that an enlarged liver and abdominal adipose tissue will often shrink with PWL. For that reason, many surgeons require PWL before proceeding with MBS. In addition, in the U.S., several health insurance providers require PWL prior to approving a patient for MBS.

Whether PWL prior to MBS is truly beneficial is controversial. A large body of literature exists, but the results of these studies are inconclusive. While some studies are supportive, others are not. Surgeons who support the use of PWL prior to MBS believe that it dramatically reduces the operative risk and difficulty performing MBS. However, if and how PWL is beneficial has not yet been empirically established. The amount of PWL necessary to achieve the most benefit also is unknown. What is known is that only a modest weight loss is required to achieve such a benefit. Ten percent of excess weight loss is considered sufficient [31, 32]
Other surgeons feel that the complication rates are currently so low, there is no need to delay MBS for PWL. In addition, PWL is not without its own issues. For example, if anti-obesity medication (AOM) or an endoscopic procedure is necessary to achieve PWL because dietary and other lifestyle changes have been ineffective, patients may not tolerate these modalities and the cost may be prohibitive. This section will review such issues.

Does PWL result in meaningful reductions in intra-hepatic and visceral fat?

Most publications on this topic have demonstrated that patients with severe obesity can lose weight successfully in preparation for MBS. That weight loss can be achieved by several methods, including the use of low-calorie diets (LCDs), very low-calorie diets (VLCDs), commercial weight-loss programs, intragastric balloon placement, and weight-loss medications. Fris et al, reported that a 2-week VLCD resulted in a significant decrease in liver size [33]. Thirty eight of the 40 study participants lost weight (mean 4.1%). In addition, 34 patients experienced a reduction in the size of their liver (mean 5.1%) and 36 lost fat mass (mean 5.1%). However, the authors did not report post-operative outcomes. Holderbaum et al. [34] performed a systematic review of the effects of VLCDs on liver size and weight loss in patients preparing for MBS. For this, they selected nine studies (3 randomized, 6 observational) involving 849 patients. The intervention examined was VLCDs. Among patients treated with a VLCD, the mean weight loss was 2.8-14.8 kg and liver size reduced by 5%-20%. However, despite the weight loss, no significant reduction in perioperative complications was observed.

Gils Contreras et al. [35] randomized 86 patients preparing to undergo MBS to 21 days of either a VLCD or LCD and observed a significant reduction in hepatic volume in both groups. Total weight loss was 5.8% among patients on a VLCD and 4.2% in those on an LCD (p = 0.004). Both groups experienced similar reductions in serum lipids and glomerular filtration rates. In addition, the two groups had similar improvements in clinical biochemical parameters, the rate of surgical complications, and the length of hospital stay. However, the lack of a control group of patients not participating in PWL treatment was a significant study limitation. Without a control group, it is not possible to determine if any of the observed outcome effects were related to the PWL or a benefit of the MBS.

Does PWL reduce postoperative complications?

There is a large body of literature examining the perioperative effects of PWL. Using the Scandinavian Obesity Registry (SOReg), Anderin et al. investigated whether PWL would reduce the incidence of postoperative complications [36]. Data on 22,327 patients undergoing primary gastric bypass surgery were analysed. The median preoperative total weight change was -4.8%. Patients were placed into groups based on weight loss percentiles (25th, 50th, 75th). There was a 9.1% incidence of complications and the degree of risk reduction correlated with the amount of weight lost. When comparing patients in the 75th percentile group to those in the 25th percentile, the investigators found an overall 13% reduction in the risk of complications, including a 24% reduction in leaks, 37% reduction in deep infections, and 54% reduction in the incidence of minor wound complications. These reductions were present but inter-group differences less pronounced when patients in the 25th percentile group were compared to those in the 50th.

In a randomized controlled trial, Van Nivenhove et al. observed similar findings [37]. They randomized 298 patients with severe obesity preparing to undergo gastric bypass surgery to either a 14-day VLCD or no special diet (controls). The active treatment group lost significantly more weight (-4.9% vs -0.4%, $p < 0.001$), while the median visual analogue scale score of perceived difficulty encountered by the surgeon during the operation was significantly higher in controls (35 [18-50] mm vs. 26 [15-42] mm, $P = .04$) However, there were no differences in operating time, estimated blood loss, or intraoperative complications. At 30 days, the number of complications was significantly greater among controls (18 vs. 8, $p = 0.04$) [37].

On the other hand, in their systematic review of the literature, Cassie et al. found conflicting results [38]. Their review included 27 studies extracted from multiple databases. Among these 27 studies, in 17 studies with 4611 patients, the investigators deemed PWL to be beneficial, while another 10 studies (with 2075 patients) failed to detect any benefit. Operating time was only 12.5 minutes shorter for the PWL patients undergoing laparoscopic Roux-en-Y gastric bypass (RYGB). Nine studies detected a positive correlation between PWL and overall weight loss, while 15 failed to detect any benefit. Furthermore, the authors of nine studies reported no difference in perioperative complications between those patients who achieved PWL and those who did not. In two studies, PWL was associated with a significant decrease in complication rates. Cassie et al. concluded that there was insufficient evidence to support or refute the benefits of PWL [38].

Mocanu et al (10) performed a retrospective review of the Metabolic and Bariatric Surgery Accreditation and Quality Improvement Program (MBSAQIP) data registry from 2015-2018 [39]. A total of 548,597 patients were included, among whom 459,500 (83.8%) achieved PWL. There was no clinically-significant difference in operating time between those with versus without PWL (85.3 + 46.9 min vs. 83.9 + 46.2 min, respectively). However, the protective benefit was found to be most significant for patients who achieved the greatest weight loss. Those patients who lost 10% of their body weight experienced a 30% decrease in the odds of a leak (OR=0.68%; 95% CI=0.56–0.84; $p < 0001$) and a 40% decrease in the odds of death than those without PWL (OR=0.60; 0.39–0.92; $p < 0.02$).

More recently, Samaan et al. evaluated whether PWL was a predictor of weight loss success and associated with perioperative complications in 427 patients [40]. The investigators reported that PWL was associated with a significant decrease in length of stay after gastric sleeve but not after gastric bypass: the mean length of stay after sleeve was 1.3 days for PWL patients versus 1.8 days for non-PWL patients. However, though this difference was statistically significant, it might not be clinically relevant. There also was no association between PWL and either operating room time or overall complication rate.

Benotti et al. retrospectively reviewed the outcomes of 881 patients who underwent gastric bypass surgery, among whom 52.9% underwent open gastric bypass [41]. In these patients, 10% PWL was encouraged but not mandated. Overall, 67.2% of the patients lost 5% or more of their excess weight, and 48.0% lost more than 10%. Pre-operative weight loss was associated with reductions in the rates of both complications overall ($p = 0.04$) and major complications, though the latter reduction just failed to achieve statistical significance ($p = 0.06$). However, after controlling for age, sex, baseline BMI, and the type of surgery in a multiple logistic regression model, increased PWL was a predictor of reductions in both any complication ($p = 0.004$) and major ($p = 0.03$) complications. Additionally, the greater the PWL, the better the outcomes.

Wiggins et al. reviewed PWL data for 1537 patients undergoing RYGB and identified no difference in patients who achieved 5% total weight loss and those who did not lose weight preoperatively in either the complication rate (4.2% vs. 5.1%, $p= 0.29$) or reoperation rate (3.0% vs. 3.4%, $p = 0.80$) [42]. An interesting, unexpected finding was that patients who lost > 10% of their excess weight preoperatively actually had both a higher complication rate than patients not doing so (6.6% vs. 3.7%, $p = 0.017$) and higher reoperation rate (4.5% vs. 2.7%, $p < 0.001$). However, this may have been secondary to patient selection bias, since the group of patients who achieved 10% or more PWL had more older males and averaged more comorbidities [42].

Does PWL improve postoperative weight loss results?

Like most of the published studies on PWL, Alvarado et al. found that preoperative weight loss was achievable [43], with 70% of patients losing > 5% of their initial body weight prior to MBS. At the one-year post-operative assessment, after gastric bypass, every 1% loss in initial body weight preoperatively resulted in 1.8% excess weight loss ($p< 0.05$). In addition, preoperative weight loss >5% was associated with significantly-shorter operating time (mean reduction = 36 minutes). However, there was no change in the incidence of complications or improvement in co-morbidities with PWL [43].

Rodrigues et al. retrospectively investigated whether there were any preoperative factors, such as preoperative weight loss, that could predict weight loss outcomes after MBS [44]. They divided 202 patients who underwent laparoscopic gastric bypass surgery by their weight loss outcomes 24 months after surgery. They found that the patients with poor weight loss at 24 months postoperatively (< 50% excess weight loss or BMI > 30 kg/m^2) had less preoperative weight loss than patients who had significantly greater 24-month weight loss (> 80% excess weight loss). Patients who lost more weight preoperatively (% excess weight loss, EWL = 22.1 + 10.1% vs. 18.4 + 8.2%, $p < 0.006$) lost statistically more weight after MBS (%EWL = 92.0 + 10.9% vs. 44.1 + 9.38, $p < 0.001$). However, the two groups were clinically different at baseline. Patients with less weight loss at 24 months had higher baseline weight and BMI, less preoperative weight loss, a higher rate of dyslipidaemia, and a greater duration of diabetes. Linear regression identified preoperative %EWL, initial BMI (prior to any PWL), and immediate preoperative BMI (after any PWL) as independent predictors of post-operative weight loss.

Carlin et al. retrospectively reviewed the records of 295 patients who had PWL prior to RYGB [45]. In this study, PWL was mandatory for all patients and based on the patient's initial weight: for patients with a BMI < 50 kg/m^2, the PWL goal was for them to lose 5 lbs; for a BMI 50 - 59 kg/m^2, the PWL goal was to lose 5% of body weight; and for a BMI > 60 kg/m^2 to lose 10% of body weight. The weight loss goals were met or surpassed by 79% of patients. However, no correlation was found between the %EWL one year after surgery and the percentage of PWL. Preoperative weight loss, in their opinion, was not a predictor of postoperative weight loss after RYGB [45].

Solomon et al studied 100 consecutive patients preparing to undergo gastric bypass surgery, among whom 50 were randomly assigned to lose 10% or more of their excess body weight preoperatively while 50 were not obligated to lose weight [46]. One year after gastric bypass, patients in the weight loss group lost 8.2% of their excess body weight while the control group gained 1.1% of their excess weight ($p = 0.007$). However, the study was underpowered and one year after surgery, data were available for only 26 patients and there were no significant differences between the groups in weight, BMI, excess weight loss, or status of their co-morbidities. However, when the cohort was redistributed to compare patients with > 5% EWL to the patients with < 5% EWL, patients who lost 5% or more of their excess weight preoperatively lost more excess weight (85.5%, range 55 to 130 vs. 65.7%, range 55 to 125; $p = 0.002$). There still was no difference in the status of the two redefined groups' comorbid conditions [46].

Biro et al. placed 51 patents with insulin-dependent diabetes undergoing MBS on an LCD for the two weeks prior to surgery, and those patients who achieved a rapid glycaemic response while on the LCD (> 50% reduction in total insulin requirements) experienced a higher rate of early diabetes remission: 44% versus 13.6% at 6 months ($p < 0.01$) and 72.7% versus 5.9% at 12 months ($p < 0.01$) [47]. In addition, rapid responders showed greater excess weight loss at three months (40.1% vs. 28.2%, $p < 0.01$), six months (55.2% vs. 40.2%; $p < 0.01$), and 12 months (67.7% vs. 47.3%; $p < 0.01$).

Finally, Livhits et al. performed a systematic review to see if PWL immediately prior to MBS improved outcomes [48]. They analysed 15 articles (n=3404 patients). Among the 13 studies with both short-term and longer-term (≥ 12 months) data, five identified a positive effect short-term and long-term of PWL, while two further articles found a positive short-term effect that was not sustained long term. Meanwhile, five studies failed to identify any effect, and one found a negative effect (PWL predictive of less post-operative weight loss). Pooled analysis revealed a significant increase in one-year postoperative weight loss (mean difference of 5% EWL, 95% CI = 2.68–7.32) for patients who had lost weight preoperatively. Meta-analysis of other outcomes revealed decreased operating time for patients who had lost weight preoperatively (mean difference = 23.3 minutes, 13.8–32.8) [48].

In addition to the above-mentioned potential benefits of PWL – such as improved long-term weight loss, reduced postoperative complications, shorter length of hospital stay, etc. – PWL might also improve a patient's metabolic parameters like glucose metabolism; blood pressure; respiratory function; sleep apnoea; infection; and fluid status. Preoperative weight loss has also been considered a surrogate to predict a patient's compliance with MBS team instructions and postoperative performance.

Conclusions

Preoperative weight loss is thought to be beneficial for patients awaiting MBS. It is especially attractive for high-risk patients, such as those who are metabolically-challenged. Improvements in postoperative weight loss, reduced incidence of perioperative complications, reduced length of hospital stay, decreased operating time, and improvements in co-morbid medical conditions have all been reported. Pre-operative weight loss has also been touted as a means for predicting a patient's postoperative compliance While these potential benefits appear attractive, the use of PWL remains controversial as the current published literature is inconclusive regarding actual benefits. As depicted in Table 6-2, there is tremendous variability in the published studies. Study design, primary endpoints, and even patient characteristics vary greatly from one study to the next. In addition, there are no dominant characteristics, and the study results often contradict one another, making any attempts to achieve consensus impossible. Therefore, preoperative weight loss may be of benefit, but should only be used selectively at the discretion of the bariatric team and not mandatory for all MBS candidates.

Table 6-2: Summary of key findings on pre-operative weight loss

First author	Liver shrinkage	Postop weight loss	Reduced comorbidity	Reduced complications	Reduced LOHS	Reduced OR Time
Fris [33]	Yes	-	-	-	-	-
Holderbaum [34]	Yes	-	-	-	-	-
Gils Contreras [35]	Yes	-	Yes	Yes	-	-
Anderin [36]	-	-	-	Yes	-	-
Van Nieuwenhove [37]	-	-	-	Yes – 30 days	-	No
Cassie [38]	-	-	-	-	-	Yes -12.5 min
Mocanu [39]	-	-	-	-	Yes	No
Samaan [40]	-	-	-	No	Yes	No
Benotti [41]	-	-	-	Yes	-	-
Wiggins [42]	-	-	-	-	-	-
Alvarado [43]	-	Yes	No	No	-	Yes - 36 min
Rodriguez [44]	-	Yes	-	-	-	-
Carlin [45]	-	No	-	-	-	-
Solomon [46]	-	Yes	No	-	-	-
Biro [47]	-	Yes	-	-	-	-
Livhits [48]	-	Yes	-	-	-	Yes- 23 min

LOHS = length of hospital stay; OR = operating room; min = minutes

6.5. Metabolically-challenged patients – BMI ≥ 50 kg/m²

- Almino Ramos, MD, MSc, PhD

Introduction

This section discusses the challenges of and strategies for MBS in patients with a BMI ≥ 50 kg/m². Patients with such a high BMI have a more advanced stage of obesity, making them challenging to treat due to the higher risks of complications and reduced responsiveness to weight-loss treatment. Metabolic-bariatric surgery is an effective treatment for patients with a BMI ≥50, but the choice of procedure should be individualized, with laparoscopic sleeve gastrectomy (LSG) the preferred initial option for the majority of surgeons. Proper technique and follow-up are essential to achieve the best results and minimize the risk of complications. Patients with a BMI ≥50 require special attention during peri-operative follow-up and thereafter to prevent complications, some of which may occur early and others later. Despite these challenges, MBS remains a viable option for patients with a BMI ≥50, providing sustained weight loss and improvements in associated diseases that can significantly improve their quality of life.

Obesity is a worldwide epidemic that affects a significantly- and steadily-increasing number of individuals. Defined as a BMI ≥ 30 kg/m², obesity has traditionally been subdivided into three categories: initial or grade I obesity (BMI 30-34.9 kg/m²), moderate or grade II obesity (BMI 35-39.9 kg/m²) and severe or grade III obesity (BMI ≥40.0 kg/m²). As discussed elsewhere in these guidelines, however, in a Delphi survey of 43 inter-disciplinary experts from around the world, consensus was reached that at least one (grade IV), if not two (grades IV and V) further grade(s) of obesity should be created to encapsulate patients whose BMI equals or exceeds 50.0 kg/m².

In recent years, the number and percentage of patients with a BMI ≥50 has been increasing rapidly. Between 1986 and 2010, for example, the number of patients with a BMI ≥50 increased more rapidly in the United States than either class I or III obesity [8, 49, 50]. These patients present with more advanced stages of obesity, have a greater amount of fat tissue, and often suffer from associated conditions that are more severe. Patients with a BMI ≥50 also are a very a challenging group to treat with MBS, due to the higher risk of complications and reduced responsiveness to weight-loss treatment. Most of the bariatric literature concentrates on grades I-III obesity, where good results and the benefits of MBS, in terms of weight loss and control of associated diseases, have consistently been documented to be superior to those of nonsurgical treatments. However, in the BMI ≥50 cluster, numerous questions remain concerning the safety, effectiveness, and cost-benefits of MBS.

Understanding the risks

Currently, good-quality clinical studies involving patients with a BMI ≥50 are scarce, generally limited to retrospective reviews and case series. Randomized controlled trials, meta-analyses, and systematic reviews are rare and should receive priority from the international societies of obesity study.

Nonetheless, it is generally acknowledged that, relative to patients with a lower BMI, patients with a BMI ≥ 50 generally have increased surgical risk, less weight loss, and higher weight recidivism. The aetiologies behind these poorer outcomes are not well understood. However, these patients more frequently suffer from life-threatening obesity-associated health conditions, including T2DM, hypertension, congestive heart failure, sleep apnoea, and chronic obstructive pulmonary disease, among others In addition, these patients utilize more healthcare system resources, including more experienced MBS teams and more advanced equipment and devices. Furthermore, they have a higher incidence of psychological issues and eating disorders. These mental health issues can negatively affect MBS outcomes [51-59]. Based on these issues, patients with a BMI ≥50 are unanimously considered high-risk candidates for MBS. The higher risk of complications includes unplanned ICU admissions, a greater requirement for mechanical ventilation, and extended hospital lengths of stay. However, at MBS centres of excellence, patients with a BMI ≥50 do not have a higher risk of mortality than patients with lower BMIs [8, 57].

Surgical strategies and results

The goal of MBS is to achieve sustained weight loss and improvements in associated complications and co-morbidities. However, studies consistently show an association between increasing BMI and lower odds of successful weight loss and higher risk of morbidity and mortality after surgery. In patients with a BMI ≥ 50, MBS results in less weight loss and more complications relative to patients with a BMI under 50, while improvements in associated diseases are generally similar. Since the sleeve gastrectomy generally requires less operating time, is less technically challenging, and lacks an anastomosis, it is considered the preferred procedure for patients with a BMI ≥50. Some studies consider it a good option as a stand-alone procedure. Others recommend SG as the first stage of a two-stage strategy, as it often yields less weight loss when used alone. Both RYGB and duodenal switch (DS) achieve better average weight loss than SG. However, though the DS achieves better weight control and comparable diabetes remission and mortality, it has also been linked to higher risks of both hospital readmissions and reoperations related to the initial procedure [8, 60-72]. A newer option is SADI-S, which generally has results similar to the DS but less weight loss. The OAGB is increasingly becoming accepted for this group of patients. Overall, 45% of surgeons favour a staged procedure, starting with a sleeve gastrectomy as the primary procedure and a gastric bypass, DS, or SADI-S as the second. Robotic surgery for patients with severe obesity provides ergonomic advantages for the surgeon, but lacks any documented clinical advantages when compared to laparoscopic approaches.

Proper technique and follow-up

The surgical technique should be individualized for patients with a BMI ≥50 to optimize results while minimizing the risk of complications. The experience that the surgeon and surgical team has with different MBS options should be considered. The BMI decrease experienced in BMI ≥50 patients at five-year follow-up varies according to the procedure performed. The average weight loss after a SG, for example, is 10-12 kg/m^2 (= BMI units) or 25-27% total weight loss (TWL), versus 14-15 kg/m^2 (28-30%TWL) for RYGB, and 20-24 kg/m^2 (36-38%TWL) for DS. Both OAGB and SADI-S achieve weight loss that lies between that achieved with RYBG and DS, with OAGB achieving slightly better results than those achieved with SADI-S. There is no consensus concerning whether long-limb gastric bypass yields better weight loss in patients with a BMI ≥50 than shorter-limb procedures. Currently, insufficient weight loss is considered when the patient is more than two years after surgery and either still has a BMI ≥35 kg/m^2 or %EWL < 50%. Patients with a BMI ≥50 require special attention in the follow-up period, including a prevention protocol for rhabdomyolysis and DVT/PTE, both of which are particular concerns in this patient group. Nutritional counselling with vitamin, mineral, and protein supervision and alterations is mandatory, especially for surgeries involving long intestinal limbs.

Conclusions

Performing MBS in patients with a BMI ≥ 50kg/m^2 is challenging from several perspectives. From a technical standpoint, increased thickness of the abdominal wall, increased adipose limiting visualisation, excessive torque on the surgeon’s hands, and a large liver all add complexity to almost any MBS procedure. From a risk perspective, these patients generally have more numerous and more severe obesity-related complications and comorbidities. And from an outcome perspective, they generally experience more peri-operative and longer-term complications, lose less weight (as a percentage of total or excess weight), and are more likely to experience weight recurrence.

Though MBS is the most effective treatment, choosing which MBS procedure to do in which patient is crucial, meaning the MBS must be individualized, based on the patient's surgical risk, the MBS surgeon's and MBS team's experience, and the particular needs (e.g., weight loss and co-morbidity goals) of each patient. Sleeve gastrectomy continues to be the preferred option as a standalone or staged procedure to achieve adequate weight loss. Proper technique and follow-up are essential to optimize results and minimize the risk of complications. Patients with a BMI ≥50 require special attention in the follow-up period to prevent complications like rhabdomyolysis, DVT/PTE, and nutritional disorders. Despite these challenges, MBS remains a viable option in such high-BMI patients, providing sustained weight loss and improvements in associated diseases, both of which can both improve the quality and prolong the duration of a patient's life.

6.6. Should a patient who is metabolically challenged or has a BMI > 50 kg/m^2 have a sleeve gastrectomy or hypo-absorptive procedure? - Luigi Angrisani, MD

Metabolic and bariatric surgery (MBS) should be considered the preferred method to achieve clinically-significant weight loss in metabolically-challenged patients, including patients whose BMI is 50kg/m^2 and higher.

With rising experience in MBS, long-term studies have proven surgery's effectiveness in the treatment of severe obesity and its co-morbidities [14]. Studies with long-term follow-up have consistently demonstrated that MBS produces superior metabolic outcomes than both lifestyle modifications and nonoperative treatments. Also, the safety of MBS has been studied and reported extensively. The operations commonly performed have evolved as well. Older surgical operations have been replaced by technically easier, safer, and more effective operations. In the last published IFSO 2018 survey, laparoscopic sleeve gastrectomy (LSG) was the most frequently performed operation worldwide [73], a finding confirmed in the last survey performed in 2020 and 2021 (unpublished data). Moreover, in this latest survey there was a decrease in hypo-absorptive procedures possibly due to their technical difficulty. It was hypothesized that surgeons preferred a two-step approach, first performing a technically-easier procedure (LSG) and then either a RYGB, biliopancreatic diversion with duodenal switch (BPD-DS), or single-anastomosis duodeno-ileal bypass with sleeve gastrectomy (SADI-S) procedure only in patients experiencing insufficient weight loss or weight recurrence.

Since its introduction, laparoscopic BPD-DS has been considered a complex, but feasible, procedure resulting in effective weight loss with acceptable morbidity. In the first published case series, in which the safety and effectiveness of this operation was reported, a BMI > 65kg/m^2 was associated with increased morbidity and mortality [74].

To date, the optimal surgical management of patients with a BMI ≥ 60 remains controversial. Several studies suggest that patients with a BMI ≥ 60 undergoing bariatric operations have a greater risk of perioperative complications and death. As a result, for these patients a staged approach has been proposed. The first stage would include a procedure that is simple, fast, and associated with significant initial weight loss. Usually in clinical practice, such an operation would be LSG or the insertion of intragastric balloons (IGB). The second stage would involve a procedure that is a more definitive weight-loss operation, such as a gastric bypass or duodenal switch.

The effectiveness and safety of the two-step laparoscopic BPD-DS treating patients with severe obesity (BMI > 50 kg/m^2) or a BMI > 60 kg/m^2 have been reported. In a more recent original article, the authors reported no deaths and achieved acceptable morbidity, considering the high operative risk in this group [75]. Moreover, this procedure was shown to be effective for both weight loss and the resolution of co-morbidities.

The first experience with a two-stage laparoscopic RYGB (beginning with a LSG before proceeding to RYGB) was reported in 2003 [76]. The authors concluded that performing LSG with a second-stage RYGB was both feasible and effective based on short-term results. This two-stage approach represents a reasonable alternative for surgical treatment of the high-risk patient with severe obesity and a BMI > 50 kg/m^2.

More recent studies have assessed the safety of a one-step RYGB for patients with severe obesity (i.e., BMI > 60 kg/m^2). One study compared 95 patients with a BMI ≥ 60 kg/m^2 and 1,311 patients with a BMI < 60 kg/m^2 undergoing RYGB from December 2001 to May 2007 at a single centre [77]. The authors concluded that a single-stage RYGB can be performed safely for patients with BMI > 60 kg/m^2, with no overall increased risk of intraoperative complications or postoperative morbidity or mortality relative to patients with a BMI < 60 kg/m^2. These authors also compared their results against the two-staged approach reported by other colleagues [75] and found that the overall operating time was dramatically less with the single-stage approach [77]. Based on these results, a two-stage approach might not be necessary. However, it is likely that the greater experience and skills of the attending surgeons who performed the operations in more metabolically-challenged patients, compared with those of a chief resident or fellow in training, contributed to fewer intraoperative adverse events [77].

Although LSG remains the most frequently performed procedure worldwide, its efficacy in patients with severe obesity (BMI > 50 kg/m^2) remains controversial. Both RYGB and SG with duodenojejunal bypass (SG-DJB) have been reported to generate better weight loss than LSG alone in patients with severe obesity (BMI > 50 kg/m^2). One-anastomosis gastric bypass (OAGB) has also been found to yield better weight loss than LSG in short term. However, long-term data (> 5 years) comparing these different operations have been of poor quality.

In a recent study, 498 consecutive patients with a BMI from 50-59 kg/m^2 and patients with a BMI > 60 kg/m^2, who underwent LSG or RYGB or OAGB, were compared [78]. Surgical outcomes, weight loss, resolution of co-morbidities, and late complications were recorded. In this study, the RYGB group experienced greater intraoperative blood loss, and longer operating times and hospital stays than the other two groups. The RYGB patients also had a higher 30-day post-operative major complication rate (4.8%) than either LSG (0.5%) or OAGB (0.8%). At 5-year post-operative follow-up, the patients who underwent the OAGB procedure had significantly greater total weight loss (40.8%) than LSG (35.1%), but not RYGB patients (37.2%). The remission rate for T2DM was no different between the three groups. The authors concluded that LSG is an effective and durable primary bariatric procedure for the treatment of patients with severe obesity and a BMI > 50 kg/m^2 and metabolic disorders, while OAGB had similar operative risk as the LSG but resulted in better weight loss [78].

In conclusion, metabolically-challenged patients present with numerous surgical and anaesthesiology challenges. Comorbidities like T2DM, non-alcoholic steatohepatitis (NASH), nephritis, and heart failure, among others, increase their risk of operative and postoperative complications. Due to the anatomical difficulties (thicker abdominal walls, larger livers with fatty infiltration, and considerably greater amounts of perivisceral fat, poorer visualization of the operative field, and anaesthesiology problems), hypo-absorptive procedures should only be performed by experienced surgeons at high-volume centres (≥ 25 cases per year).

The first aim of MBS should be to ensure patient safety in these challenging patients, especially during the operations involving a duodeno-ileostomy. Adopting a two-step approach, by performing a technically-easier procedure first and then either a RYGB or BPD-DS or SADI-S (when necessary), may be a valuable surgical strategy.

Gastro-oesophageal reflux disease (GERD), hiatal hernias and MBS

Laparoscopic sleeve gastrectomy (LSG) remains the most commonly performed bariatric procedure worldwide. However, an important issue with the LSG is the problem of de novo or recurrent GERD. Several studies with long-term follow-up of patients undergoing LSG have identified an increased incidence of GERD [79] and Barrett's oesophagus [80]. In patients with severe GERD or a hiatal hernia, RYGB is considered the preferred procedure. An alternative to RYGB is a LSG with associated hiatal hernia repair. However, it has been argued that this procedure might be associated with hiatal hernia recurrence and the return of reflux symptoms [81]. Recently, new techniques involving the creation of anti-reflux valves in association with LSG have been proposed to overcome this issue.

The RYGB is the second most commonly performed surgical procedure for severe obesity worldwide and is usually considered the procedure of choice for patients with both severe obesity and GERD. Nevertheless, in recent studies, persistence or the development of de novo GERD after RYGB have been reported [82, 83].

For these reasons, among bariatric surgeons, great importance is afforded the complex interplay between GERD symptoms and a hiatal hernia, even in patients who undergo laparoscopic RYGB. In a recent meta-analysis on the effect of LSG and hiatal hernia repair (HHR), 18 studies totalling 937 patients were included [84]. Results of the meta-analysis demonstrated that, after LSG and HHR, patients experienced significant reductions in GERD symptoms (OR = 0.20; 95% CI: 0.10 to 0.41; $p < 0.00001$), symptoms of esophagitis (OR = 0.12, 0.05 to 0.26, $p < 0.001$), and impact of GERD on health-related quality of life (GERD-HRQL) (mean reduction = 19.13, 95% CI: 3.74 to 34.51; p=0.01). Based on these results, it appears that combining SG and HHR can positively affect weight loss, GERD resolution, esophagitis reduction, and quality of life. As such, combining these two procedures in patients with obesity and GERD seems to have a promising future.

In another study, the authors matched 1546 LSG patients with HHR to 3170 LSG patients without, and they similarly matched 457 RYGB and 1156 RYGB patients with and without HHR, respectively [85]. In these patients, those who underwent concurrent SG and HHR were more likely to have additional abdominal operations (adjusted hazard ratio [aHR] = 2.1; 95% CI = 1.5–3.1) and endoscopies (aHR = 1.5; 1.2–1.8), but not bariatric revisions/conversions (aHR = 1.7; 0.6–4.6) within one year and again within three years after surgery. On the other hand, among the RYGB patients, concurrent HHR was only associated with an increased risk of requiring an endoscopy (aHR = 1.4; 1.1–1.8)) at one year and three years of follow-up [85]. Although higher rates of endoscopy could signify GERD symptoms in the HHR group, the finding that bariatric conversions/revisions were very rare (and did not differ by HHR status) out to three years after surgery suggests that, particularly among SG patients, GERD symptoms (if present) were not leading to numerous conversions, which is reassuring.

Hence, based on the most current evidence, hiatal hernia should be repaired independent of the type of approach (1 or 2 steps) or type of operation.

6.7. Weight/metabolic disease recurrence after metabolic-bariatric surgery

- Pierre Garneau, MD

Introduction

A number of meta-analyses have been published demonstrating the effectiveness of MBS and the surgical approach and establishing it as the most effective way to both induce and maintain weight loss in patients with the disease of obesity. Surgical weight loss is also the most effective method of improving weight-related co-morbid conditions. Weight recurrence (WR) after MBS can lead to the return of weight-related co-morbidities. Despite marked weight loss following MBS, failure to sustain weight loss is seen in a sizeable proportion of patients and may occur after any MBS procedure[86, 87].

The estimated incidence of WR after primary bariatric operations varies from 9%-91%, depending on the definition. There is currently no standardized definition of WR, and therefore, its true incidence remains unknown. In addition, the ability to correlate its impact with clinical outcomes – like the resolution or recurrence of co-morbidities – is limited. An increase in BMI or having a BMI above a certain threshold has not been clearly correlated with the recurrence of co-morbidities. Likewise, research into WR and treatment algorithms are haphazard because they lack a standard definition [11, 88]

Re-operative bariatric surgery

Current evidence on re-operative bariatric surgery demonstrates improved weight loss and reduced co-morbidity post-operatively, but complication rates are generally higher after re-operative than primary surgery. This said, the outcomes of re-operative bariatric surgery are reported inconsistently in the literature [89].

Patients who present with insufficient weight loss, continued co-morbid disease, or weight regain after MBS are a challenging population. These patients may benefit from additional surgical therapy to treat their obesity, but should first be thoroughly evaluated by a multidisciplinary team to determine the potential causes for their poor response. This evaluation should include nutritional and behavioural health assessments, and an anatomic evaluation of the original procedure performed. The decision to proceed with additional medical or surgical therapy should be based on this multidisciplinary assessment and the patient's specific risk/benefit profile for a re-operative procedure [90, 91].

Surgical options...

After laparoscopic adjustable gastric band (LAGB)

Given the high failure rate observed after LAGB, repeat surgery is common. Today, the most popular stand-alone bariatric procedure, as either a primary or revisional option, has become the laparoscopic sleeve gastrectomy (LSG) [92-94]. This procedure has been shown to be efficient, safe, and technically simpler than the laparoscopic RYGB, one-anastomosis gastric bypass (OAGB), or biliopancreatic diversion with duodenal switch (BPD-DS). Current debate centres on whether a single-stage or two-stage approach is best when performing reoperation surgery following a failed LAGB [95-98]. Single-stage conversion from LAGB to LSG has been shown to be feasible and safe, albeit with a slightly higher, relative to primary LSG, leak rate of 5.5% [94]. More severe complications have been reported using RYGB after LAGB in some cases, but it is still considered an approach with merit [95, 99]. Conversion to BPD or BPD-DS results in weight loss similar to a primary malabsorptive procedure, but with published complication rates that are higher than a primary BPD-DS [100-102].

After sleeve gastrectomy

Consensus on the most effective treatment is lacking. Re-sleeve gastrectomy (re-SG), Roux-en-Y gastric bypass (RYGB), one-anastomosis gastric bypass (OAGB), single-anastomosis duodeno-ileal bypass (SADI), and duodenal switch (DS) have all been described. All procedures were feasible but differed regarding complication rates. Bypass-type revisions are preferred over re-sleeve surgery. In the absence of refractory reflux symptoms, duodenal switch-type procedures are safe and effective options, especially in patients with severe obesity before SG. Which procedure is chosen depends on both the patient's characteristics and surgeons' expertise [103, 104].

After RYGB

Reported options after a failed RYGB include placing an adjustable band around a gastric pouch to achieve additional gastric restriction, lengthening the biliopancreatic limb to increase the malabsorptive or bypass component of the operation, or converting to a duodenal switch (DS). Each of these options has demonstrated improved weight loss after salvage procedures, but the current evidence supporting these strategies is limited to case series [105-107].

After BPD-DS

Revision for insufficient weight loss after biliopancreatic diversion with duodenal switch has been reported in 0.5%-2.78% of cases. Except in situations involving inadequate channel lengths, little is to be gained by shortening the common channel. Additional gastric restriction, which results in an average 9-14 kg weight loss, is another option [108].

After vertical banded gastroplasty (VBG)

Reoperations for VBG most often include conversion to another bariatric procedure, and most frequently this is RYGB. Peri-operative complication and mortality rates among patients who have undergone conversion of VBG to RYGB have ranged from 8.9–21.0% and from 0–2%, respectively. When converting VBG to SG, a leak rate of 14% has been reported, while the leak rate is 22% among patients undergoing VBG conversion to BPD-DS. Current evidence suggests that conversion of VBG to LSG or BPD-DS should be approached with caution due to high complication rates [109-112].

After single-anastomosis duodeno-ileal bypass with sleeve gastrectomy (SADI-S)

Only a small number of studies have been published comparing SADI-S and BPD-DS. Overall, BPD-DS appears to achieve greater percentage total body weight loss (%TWL) at two years, but no superiority based on preoperative BMI has been found. The main indications for revisions after SADI-S are symptoms of bile reflex, which have been reported in 7.5% of patients post-operatively. In patients experiencing weight recurrence, BPD-DS can be implemented, with a re-sleeve procedure another option, albeit lacking clear evidence supporting efficacy in the literature [113, 114].

Table 6.3, summarizes the revision scenarios and procedures described above.

Table 6.3: Surgical options for re-operating after failed MBS procedures

LAGB • Conversion to SG • Conversion to RYGB • Conversion to OAGB • Conversion to BDP-DS or SADI-S	**SADI-S** • Conversion to BPD-DS • Re-sleeve
VBG • Conversion to RYGB • Conversion to BPD-DS or sleeve • (associated with a high complication rate)	**RYGB or OAGB** • Lengthening of the bilio-pancreatic limb • Placing a band around the gastric pouch • Conversion to BPD-DS
SLEEVE • Conversion to RYGB or OAGB • Conversion to BPD-DS or SADI-S • Re-sleeve gastrectomy	**BPD-DS** • Re-sleeve

LAGB = laparoscopic adjustable gastric band; Sleeve = sleeve gastrectomy; RYGB = Roux-en-Y gastric bypass; OAGB = one-anastomosis gastric bypass; VBG = vertical banded gastroplasty; SADI-S = single-anastomosis duodeno-ileal bypass with sleeve gastrectomy; BPD-DS = bilio-pancreatic diversion with duodenal switch

Conclusions

Reported outcomes after re-operative bariatric surgery are generally favourable and demonstrate that additional weight loss and co-morbidity reduction are typically achieved with additional therapy. However, the risks of re-operative bariatric surgery are higher than with primary bariatric surgery and the published evidence highlights the need for careful patient selection and surgeon expertise. The specific type of re-operative procedure performed should be based on the primary operation, the patient's anatomy, the patient's weight and co-morbidities, and the surgeon's experience.

6.8. NASH and metabolic-bariatric surgery

- Francois Pattou, MD, PhD

Definition of NASH

Non-alcoholic steatohepatitis (NASH) is a type of non-alcoholic fatty liver disease (NAFLD) characterized by inflammation and hepatocellular injury in addition to hepatic steatosis, with or without fibrosis [115]. The inflammation and liver damage of NASH can lead to end-stage liver disease (cirrhosis, liver failure, and cancer). The disease is also associated with an increased risk of cardiovascular disease. Patients with advanced fibrosis are at increased risk of adverse liver-related outcomes, liver transplantation, and death [116].

Diagnosis

A formal diagnosis of NASH requires a liver biopsy and histological examination demonstrating steatosis, hepatocellular injury (ballooning), and inflammation [115]. The NAFLD activity score (NAS) can be used to grade (from 0-8) the degree of steatosis (0-3), inflammation (0-3), and hepatocellular ballooning (0-2). In addition, the Fibrosis Kleiner score can be used to stage the degree of associated fibrosis (0-4). Non-invasive biomarkers and imaging tests (elastography, magnetic resonance imaging) can help to identify patients at risk of advanced liver disease when MBS is being considered [117]. In persons with severe obesity, biomarkers that are not affected by BMI – like the Fibrosis-4 score – are preferred [118].

Medical treatment

Currently, the primary treatment for NASH is weight loss obtained through lifestyle modification, diet, and exercise. In a prospective cohort study conducted in 293 patients with NASH, Vilar-Gomez et al. found that a greater amount of weight loss, induced by lifestyle changes, was associated with a greater level of improvement in the histological features of NASH [119]. In that study, the highest rates of NASH reduction, NASH resolution, and fibrosis regression occurred in patients with weight loss ≥10%. Multiple pharmacological interventions have been proposed to treat NASH in addition to lifestyle changes and currently are being tested in clinical trials. So far, none of them has yet received formal approval as a treatment for either NASH or NAFLD.

Surgical treatment

The association between surgical weight loss and both reduced liver steatosis and overall improved NAFLD has been documented in numerous retrospective observational studies [120].

The first direct evidence of the efficacy of surgery to treat NASH and liver fibrosis was provided by Lassailly et al. in a prospective cohort study of 189 patients with histologically-proven NASH [121]. Liver biopsies were repeated one and five years after surgery. Complete resolution of NASH without worsening of fibrosis was observed at one year after bariatric surgery in 84% of patients, with no significant recurrence between one and five years. Fibrosis began to decrease by one year after surgery and continued to decrease thereafter. Five years after surgery, fibrosis had decreased in 40 of 57 patients (70%) with resolution of bridging fibrosis (F3) in 15 of 22 patients (68%) [122]. Overall, these findings confirmed the importance of achieving NASH resolution and demonstrated that advanced fibrosis can be gradually reversed once the causal injury is removed.

The clinical impact of MBS in NASH was further documented by SPLENDOR, a retrospective cohort study published by Aminian et al. that investigated the long-term relationship between bariatric surgery and the incidence of major adverse liver and cardiovascular outcomes [123]. The authors analysed the electronic medical records of 650 patients with biopsy-proven fibrotic nonalcoholic steatohepatitis without cirrhosis who underwent bariatric surgery, versus 508 similar patients who did not undergo surgery. At ten years, those who had undergone MBS had a significantly-lower risk of incident major adverse liver outcomes (2.3% vs. 12.9%; adjusted absolute 10-year risk difference = 12.4%) and major adverse cardiovascular outcomes (8.5% vs. 15.7%; adjusted absolute 10-year risk difference = 13.9) when compared against patients who did not undergo MBS.

Finally, Verrastro et al. recently reported the outcome of the BRAVES study, a multicentre, open-label, randomized trial, comparing MBS (RYGB or SG) with lifestyle intervention and best medical care as treatment for NASH in 288 individuals with obesity (BMI 30-55 kg/m^2), with or without T2DM [124]. The study's primary endpoint – NASH resolution with no worsening of fibrosis – was > 3.5 times more frequent one year after surgical treatment than after lifestyle modification alone. On per-protocol analysis, this goal was achieved in 70% of patients who had had surgery, a figure that far exceeded the rate observed in controls (19%) as well as the effects of any current drug tested in randomized trials. In addition, the rate of improvement of at least one stage of fibrosis severity without worsening of NASH was almost twice as high in MBS patients as in controls. Importantly, RYGB and SG had similar efficacy treating NASH, even though RYGB was generally more effective at improving glycaemic control, lipid profile, insulin resistance, and weight loss. Subgroup analyses also demonstrated that differences between surgical and non-surgical treatment of NASH were greater among participants with more severe fibrosis (F2-F3) [124].

Safety

No death or life-threatening complications were reported in the BRAVES study [124]. The rate of severe adverse events following surgical treatment was 6%, and all resolved with medical or endoscopic management. Of note, histologically-proven cirrhosis (F4), even if clinically compensated, was an exclusion criteria in that randomized trial. Individuals with cirrhosis also were excluded from the retrospective SPLENDOR study [123]. This point is important, since advanced liver disease is classically associated with an increase in postoperative risks in general surgery patients. Following a cholecystectomy, a MELD score of 8 or above is associated with a 30-day mortality risk of 6% [125]. In the context of bariatric surgery, in a population-based study with > 1.5 million participants, cirrhosis was associated with a longer overall hospital stay and increased odds of operative complications (odds ratio, OR = 1.9) and in-hospital death (OR = 4.4) [126]. Importantly, these figures were markedly increased in cases of decompensated cirrhosis (OR = 6.2 and 11.8, respectively). As a result, patients with known or suspected cirrhosis, even if clinically compensated, should be evaluated in coordination with hepatologists prior to undertaking MBS [117].

Conclusions

In summary, available evidence shows that MBS is more effective than lifestyle changes and optimized medical therapy in the treatment of NASH in patients with obesity in the absence of cirrhosis (Level 1.b). Moreover, NASH may be considered an important indicator for prioritizing MBS in individuals with metabolic disease. Future research should evaluate safety profiles of MBS in patients with compensated cirrhosis and compare MBS with new anti-obesity drugs and other active drugs or interventions when they become available.

6.9. Cardiovascular disease and metabolic-bariatric surgery

- Dror Dicker, MD; Carmil Azran, PharmD

Obesity and cardiovascular mortality

Cardiovascular disease (CVD) and cardiovascular (CV) mortality are considered complications of obesity. Several large studies have detected a direct association between obesity and an increased risk of CV events, such as myocardial infarction, stroke, and heart failure, as well as CV mortality. For example, in a large population-based cohort of 3.6 million adults in the UK, high BMI was associated with all death categories except for transportation-related accidents [127]. In addition, there was a 27% increase in CVD risk for every 5 units increase in BMI above 25 kg/m2. This increase in CVD risk was shown to be true for any CV-related disease, but more specifically for hypertensive heart disease, ischaemic heart disease, atrial flutter and fibrillation, heart failure, and stroke [127].

The underlying mechanisms by which obesity contributes to CV morbidity and mortality are complex and multifactorial. For example, obesity is associated with several metabolic CV risk factors, including T2DM, dyslipidaemia, and hypertension, all of which are known to increase the risk of CVD. Additionally, even in the absence of CV risk factors, obesity contributes to the development and progression of CVD via the development of adipose tissue dysfunction (adiposeopathy), which in turn induces chronic low-grade inflammation, oxidative stress, and endothelial dysfunction. Adiposeopathy of the epicardial fat directly affects the myocardium and coronary arteries, inducing coronary artery disease, heart failure and arrythmias. Lastly, epicardial fat accumulation can cause organ compression that leads to hypertension and obstructive sleep apnoea [128-130].

Weight loss and its effect on CVD morbidity

Weight loss can improve multiple CV risk factors, including high blood pressure, dyslipidaemia, and insulin resistance, which can ultimately reduce the risk of adverse CV events and mortality.

The Look AHEAD trial, which compared an intensive lifestyle intervention (ILI) to diabetes support and education (DSE) in overweight and obese patients with T2DM, looked at the effects of weight reduction on CVD [131]. This RCT included over 5,000 overweight or obese patients with follow-up averaging over 9.6 years. The study did not find a significant difference in CVD incidence among ILI and DSE participants. However, on secondary analysis, persons who lost >10% body weight in the first year had a 21% lower risk of CVD events (HR=0.79, 95% CI = 0.64 to 0.98) than those with stable weight or weight gain.

When assessing residual CV risk after weight loss, Haase et al. looked at 0.5 million people in the UK and their weight patterns over four years [132]. In their study, they identified an additional benefit of weight loss (a median effect of 13%) on rates of developing T2DM, hypertension, and dyslipidaemia. In contrast, the effect of weight loss on MI/unstable angina and atrial fibrillation was not significant. Hence, the effects of weight loss on CVD morbidity may vary, based on the amount of weight loss and a previous history of T2DM [133].

Metabolic and bariatric surgery and all-cause mortality

Metabolic and bariatric surgery leads to significant durable weight loss and improvements in metabolic health. Several studies have demonstrated the positive effects of MBS on all-cause mortality. For example, a recent meta-analysis demonstrated the positive effects of MBS on CVD disease. This meta-analysis included 21 studies with over 130,000 patients after MBS and found that patients who had undergone MBS had a pooled HR of all-cause mortality of 0.55 (95% CI = 0.49-0.62, p<0.001) compared with obese subjects in the control group.

Similarly, another meta-analysis revealed that patients who underwent MBS had a reduction in the risk of death of 49.2% (95% CI 46.3-51.9, p<0.0001) and that their median life expectancy was 6.1 years longer than patients treated with usual care [134]. In addition, the reduction in mortality was similar for the different MBS procedures.

Bariatric surgery effects in patients with type 2 diabetes mellitus

It is notable that the reduction observed in mortality rate after MBS is more pronounced in patients with versus without T2DM. For example, Dicker et al. studied the survival advantage of MBS in patients with a median follow-up of 4.2 years, and found that the survival advantage was greater among individuals with T2DM than in patients without T2DM [135]. Pontiroli et al. later confirmed these findings in a study with 20 years of follow-up [136]. Likewise, Syn et al. demonstrated that the effect of MBS on mortality was greater for patients with T2DM [134]. In this last study, relative to non-surgically treated patients, the life expectancy was 9.3 years longer in MBS patients with T2DM versus just 6.1 years longer in patients without T2DM.

MBS and CVD mortality and morbidity

It has been shown that MBS improves several metabolic abnormalities associated with obesity, including dyslipidaemia, hypertension, and T2DM. Improvements in these metabolic abnormalities lead to a reduced risk of CVD and its associated morbidity. In addition, several studies have investigated the effects of MBS on CV morbidity, including myocardial infarction (MI), atrial fibrillation, heart failure and stroke. For example, the Swedish Obesity Subject (SOS), a matched prospective non-randomized study, followed more than 2,000 patients for over 14 years; and, in this study, MBS was associated with reductions in both CV mortality (HR = 0.47; 95% CI = 0.29-0.76; p = 0.002) and CV events (HR = 0.67; 0.54-0.83; p <0.001) [137].

Similarly, a meta-analysis by van Veldhuisen et al. demonstrated a reduction in all-cause CV mortality (HR = 0.55, 0.49-0.62, p < 0.001), heart failure (HR = 0.50, 0.38-0.66, p < 0.001), myocardial infarction (HR = 0.58, CI 0.43-0.76, p < 0.001), and stroke (HR = 0.64, 0.53-0.77, p < 0.001) in patients undergoing MBS [130]. In contrast, the association with atrial fibrillation was not statistically significant (HR = 0.82, 0.64-1.06, p = 0.12).

Overall, then, available evidence suggests that MBS may significantly reduce the risk of CVD and its associated morbidity in obese patients.

MBS compared to GLP-1 agonists in patients with T2DM

Obesity is a significant risk factor for the development of T2DM and its associated CV complications. Both MBS and glucagon-like peptide-1 (GLP-1) agonists are treatment modalities that have been shown to improve glycaemic control in patients with T2DM, as well as reduce the risk of CVD events. For example, GLP-1 agonists have demonstrated a reduction of major adverse cardiovascular events by 14% (HR = 0.86, 0.80-0.93, p<0.0001), all-cause mortality by 12% (HR = 0.88, 0.82-0.94, p=0.0001), and hospital admission for heart failure by 11% (HR = 0.89, 0.82-0.98, p=0.013) [138]. However, to date, there are no published head-to-head trials comparing CVD outcomes in patients treated with GLP-1 agonists versus MBS. That said, in a recent systemic review and meta-analysis, MBS demonstrated greater mean reductions in weight and BMI than GLP-1 agonists, though similar effects on glycaemic control [139].
Overall then, while both MBS and GLP-1 agonists have been shown to be effective at improving glycaemic control and reducing the risk of CVD events in patients with T2DM, the evidence suggests that MBS may be more effective at reducing weight, improving several CV risk factors, and reducing the risk of major adverse cardiac events. Nonetheless, long-term, head-to-head studies remain necessary.

Summary of evidence:

- MBS has been linked to from 35–50% reduction in all-cause mortality. (Level 1A)
- MBS has been linked to a 31% reduction of CV mortality. (Level 1A)
- MBS has been linked to from 25–58% reduction in CV events (MI, HF, Stroke). (Level 1A).

6.10. Renal outcomes after metabolic-bariatric surgery
- Ricardo V. Cohen, MD

There is mounting evidence that obesity negatively influences the risk of chronic kidney disease (CKD). Numerous epidemiologic studies have demonstrated an independent relationship between obesity or weight gain and the development of proteinuria, acute kidney injury, CKD, and end-stage renal disease (ESRD) [140].

Obesity and kidney disease

The causal link between obesity and CKD is biologically plausible and can be explained by direct and indirect effects. Presumed direct adverse effects of obesity on the kidney include adipose tissue accumulation and infiltration of the kidney, altering the haemodynamics of the kidney, leading to increased tubular sodium reabsorption, volume overload/hypertension, and glomerular hyperfiltration, all of which causes kidney injury (glomerulomegaly, glomerular hyperfiltration, podocyte dysfunction, tubule-interstitial damage, and fibrosis) [141]. Indirect effects parallel the development of associated diseases like T2DM, hypertension, and cardiopulmonary disease.

In a seminal study by Afkarian et al., patients with T2DM, albuminuria, and impaired estimated glomerular filtration (eGFR) had 10 times the mortality rate as persons with T2DM, but no albuminuria or impaired eGFR [142].

A standard strategy when treating CKD is to target each risk factor individually. However, MBS can be an appropriate reno-protective strategy for many patients, as it addresses the root causes of CKD, like obesity, T2DM, hypertension, and all other obesity-linked diseases.

How MBS improves CKD

Via various mechanisms, MBS exert kidney-protective effects. Such mechanisms include:

- Weight loss: MBS leads to significant and sustained weight loss, which reduces pressure on the kidneys and slows down or may even halt the progression of CKD [143, 144].
- Reduced blood pressure: Obesity is often associated with hypertension, a significant risk factor for CKD. Counteracting this effect, MBS appears to lower blood pressure, thereby reducing the risk of kidney damage and improving renal function [145].
- Glycaemic control: T2DM is another leading cause of CKD, and MBS has been shown to improve glycaemic control in patients with T2DM. In addition, improved blood sugar control can help slow down the progression of kidney damage in patients with T2DM [146].
- Reduced inflammation: Obesity is associated with chronic inflammation, which can contribute to kidney damage. Weight loss following MBS reduces inflammation, which may, in turn, positively impact kidney function [147].
- Lipid profile improvement: MBS has been linked to improved lipid profiles, reducing total cholesterol, low-density lipoprotein cholesterol, and triglyceride levels. This can lower the risk of atherosclerosis, a condition known to negatively impact kidney function [148].
- Reduced proteinuria: Proteinuria is a common sign of kidney damage. MBS patients with proteinuria typically experience either a reduction in or complete elimination of proteinuria, indicating improved kidney function [149].
- Hormonal changes: MBS is also associated with hormonal changes that have been demonstrated to improve kidney function. For example, MBS patients typically exhibit increased serum levels of adiponectin, a hormone with anti-inflammatory and insulin-sensitizing effects, which may be beneficial for kidney health [150].

MBS and non-diabetic kidney disease

Kidney outcomes were measured during secondary analysis of the Swedish Obese Subjects' study [151]. Over 22 years, the cumulative incidence of ESRD – defined as a composite endpoint of eGFR less than 15 ml/min/1.73 m2, dialysis, or kidney transplantation – declined by 73% in the surgical cohort, relative to controls, after adjustments were made to accommodate confounding baseline factors.

In the Longitudinal Assessment of Bariatric Surgery-2 (LABS-2) cohort, the primary renal outcome was CKD risk, measured using established criteria that combine eGFR and albuminuria, the two leading clinical indicators of CKD [152]. By year 7 of follow-up, MBS was associated with improved CKD risk, even in patients with a higher baseline risk of CKD.

In a study performed exclusively in patients with CKD, Imam et al. compared propensity-matched patients who underwent RYGB or SG with patients who were referred for but did not have MBS [153]. At baseline, 66% of individuals had T2DM and a mean eGFR of roughly 47 ml/min/1.73 m2. At three months after MBS, the mean eGFR in the surgical cohort rose significantly, while remaining unchanged in controls. Moreover, the MBS cohort's statistically- significant increase in eGFR persisted over the three-year follow-up period [153].

MBS and diabetic kidney disease (DKD)

Mounting epidemiological evidence shows that MBS has reno-protective effects that counteract DKD, including the results of a 15-study meta-analysis published in 2019 [154]. O'Brien et al., in a retrospective, matched-cohort study orchestrated to investigate the relationship between MBS and incident microvascular complications of T2DM, reported that at a median of 4.3 years for both surgical (76% of RYGB) and nonsurgical patients, those who had undergone MBS had 49% less DKD than patients in the medical treatment group [155].

Randomized controlled trials have also revealed that MBS reduces the incidence of albuminuria and slows CKD progression over extended follow-up, and therefore may have a potential complementary role to medical treatment in managing DKD. The Surgical Treatment and Medications Potentially Eradicate Diabetes Efficiently [156] trial had glycaemic control as its primary endpoint[157]. Among prespecified secondary endpoints, kidney outcomes were included. At five years, the urinary albumin-to-creatinine ratio (uACR) had decreased significantly more from baseline in the surgical group than in the medical therapy group. In the Microvascular Outcomes after Metabolic Surgery (MOMS) trial, 100 patients with T2DM, obesity, and CKD were randomized to either best medical treatment or RYGB [158]. The primary outcome was albuminuria remission (uACR < 30mg/g), while secondary outcomes included CKD remission rate and absolute change in uACR. Two-year data revealed that RYGB was more effective than the best medical treatment at achieving albuminuria remission and early-stage CKD in patients with DKD and obesity (BMI 30-35 kg/m^2). Subsequently, MOMS 5-year data revealed that albuminuria remission (uACR<30 mg/g creatinine) was not statistically different between best medical treatment and RYGB in the T2DM, early CKD, and Class 1 obesity cohort [159]. However, if albuminuria was measured as a continuous variable, the RYGB group's geometric mean for albuminuria levels was 46% lower after RYGB (Figure 6-2). Moreover, RYGB was associated with improved glycaemia, diastolic blood pressure, lipids, body weight, cardiovascular risk factors, and quality of life, all factors that, if controlled long term, could halt the progression of CKD. Furthermore, the surgical and medical groups were no different in the rate of serious adverse events [159].

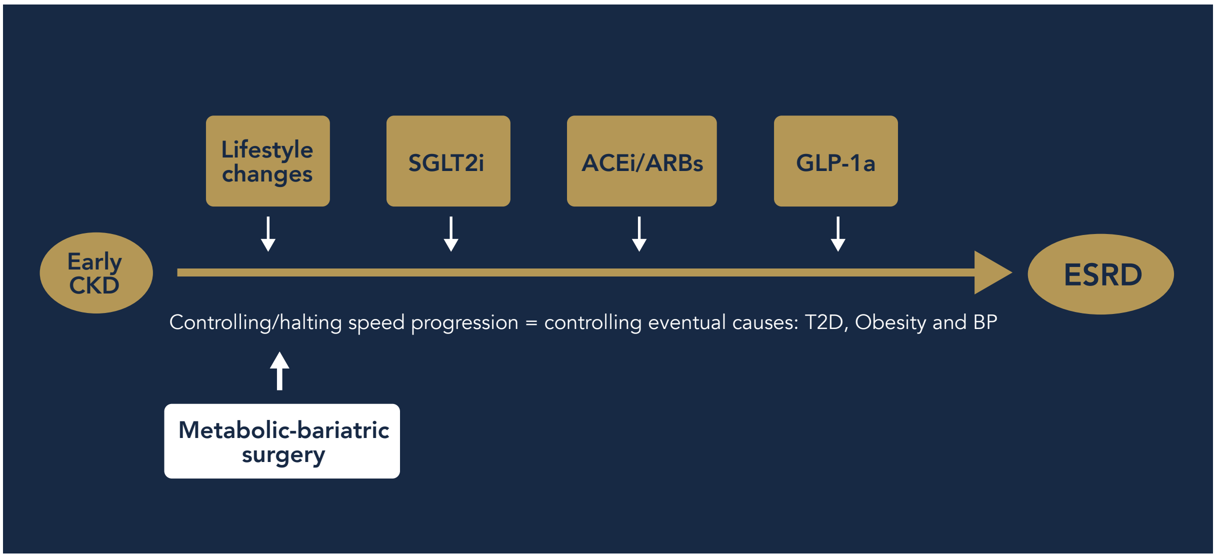
How to identify best responders for kidney outcomes after MBS

Ahlqvist et al. described five clusters of T2DM, and one of the five sub-types – severe insulin-resistant diabetes (SIRD) – is characterized by insulin resistance, hyperinsulinemia, and a high risk of DKD, but only modest hyperglycaemia [160]. Raverdy et al. have reported data that suggest that patients with SIRD submitted to MBS show markedly higher rates of T2DM remission (OR = 4.8, 2.2–12.0) and eGFR increase (mean effect size 13.1 ml/min per 1.73 m², 3.6–22.7) relative to patients classified into other subtypes, particularly severe insulin-deficient diabetes but also mild obesity-related diabetes [161]. It appears that MBS has a mechanism of action (reduced food intake and improved insulin resistance) that more clearly addresses SIRD patient dysfunction with no additional risk. Targeting the right patient to the optimal treatment strategy to achieve the best outcomes is an urgent need. Optimism regarding precision medicine has increased in recent years, and T2DM provides one of its more promising applications.

Conclusions

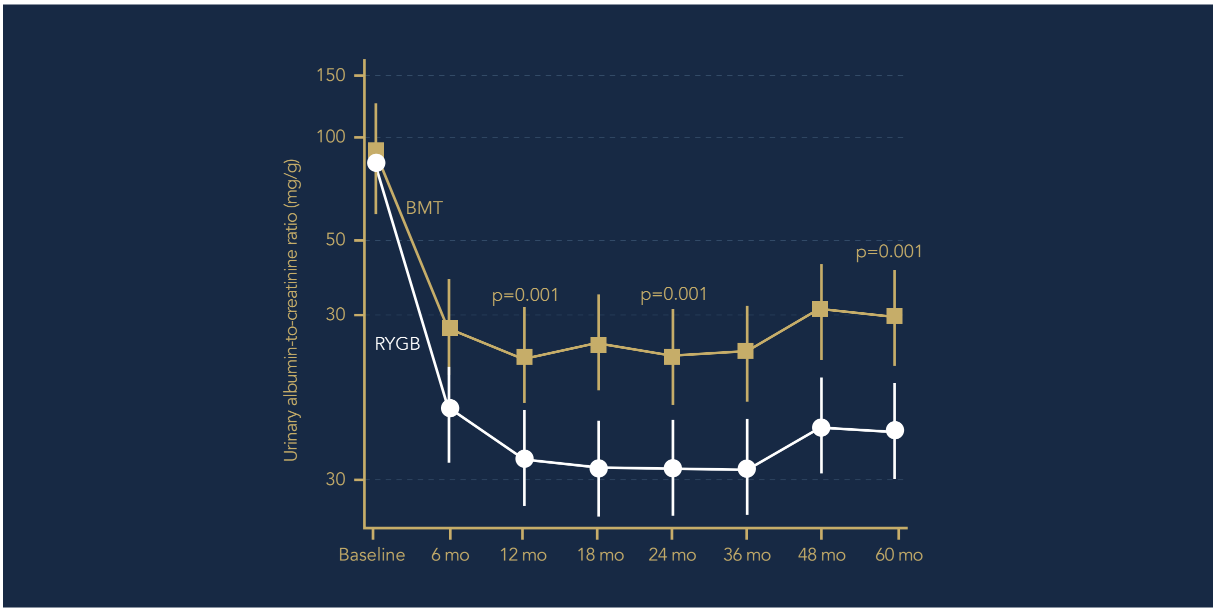
Metabolic and bariatric surgery, through its sustained weight-reducing and metabolic effects, has the potential to become a powerful tool to assist in achieving favourable renal outcomes in patients with pre-existing CKD or at high risk of developing it. It improves albuminuria and may halt or delay the progression of CKD, even compared to modern pharmacotherapy [162]. It decreases cardiovascular risk factors and is safe. As such, SIRD patients appear prime candidates for MBS to either halt or reduce DKD. Figure 6-1, below, depicts the role of MBS in preventing the progression of early chronic kidney disease to end-stage renal disease, as an alternative to standard medical management, while Figure 6-2 compares 5-year course of patients' urinary albumin/creatinine ratio in patients undergoing MBS versus medical management.

Figure 6-1: Preventing end-stage renal disease in patients with obesity-related early chronic kidney disease



CKD = chronic kidney disease; ESRD = end-stage renal disease; SGLT2i = sodium-glucose co-transporter 2 inhibitor; ACE i = angiotensin converting enzyme inhibitor; ARB = angiotensin 2 receptor blocker; GLP-1a = glucagon-like peptide 1 receptor analogues; T2D = type 2 diabetes mellitus; BP = blood pressure

Figure 6-2: Urinary albumin/creatinine ratio as a continuous variable, comparing metabolic surgery and modern pharmacotherapy at five years follow-up.



The geometric mean for albuminuria levels was 46% lower after Roux-en-Y gastric bypass (p = 0.001). (Borrowed with permission from Cohen et al., 2020) [158].

6.11. Metabolic-bariatric surgery in the elderly (>65 years of age)

- Abdelrahman Nimeri, MD, MBBCh

Initial reports in the United States (US) of MBS in the elderly (>65 years of age) are based on Medicare beneficiaries, which also includes data on non-obese patients receiving disability insurance. However, the reports still showed a higher mortality rate for older patients relative to younger patients with 30-day, 90-day, and 1-year mortality rates all in the 2.0-4.6% range [163, 164]. However, similar to how the safety of MBS improved in the general population, recent reports show that MBS – including RYGB and SG – are safe in seniors, with a 30-day mortality rate of only 0.28% [165, 166]. That said, when comparing patients >65 years old to younger patients, the former's 30-day mortality rate, while low (0.3%,), is 2-3-fold higher in seniors [165, 166]. In addition, older patients have higher incidences of respiratory, infectious, and renal complications and longer lengths of stay than younger patients [166, 167]. Furthermore, Malone et al. and Mebeza et al. both have shown that age alone is an independent risk factor for morbidity and mortality after MBS [167, 168]. In addition, two inflection points for higher morbidity and mortality with increasing age occur at 45 and 59 years of age. Nevertheless, MBS in elderly patients (>65) is as safe as hip replacement [165, 166]. 3-4 Furthermore, MBS leads to significant, durable weight loss and improvements in obesity-related medical problems [167-169]. Elderly patients undergoing MBS use less medications and have lower long-term mortality than elderly patients who do not undergo MBS [167]. Despite this, seniors remain less likely to be referred for MBS and the elderly represent only 2.7% of MBS performed at US teaching hospitals [170].

When evaluating the long-term benefits of MBS in the elderly compared to non-surgical cohorts, elderly undergoing MBS experience better post-operative weight loss; have lower risks of major adverse cardiac events, and respiratory, renal, and metabolic complications; and have lower rates of mortality [171]. The reduced mortality observed in patients over 65 after MBS is mainly related to lower rates of cardiovascular events [171, 172]. Elderly patients undergoing RYGB also lose more weight than those undergoing SG or laparoscopic adjustable gastric band (LAGB) placement and experience a higher rate of T2DM remission one year after MBS [172-174].

When choosing which type of MBS to offer patients over 65, it is important to consider the risk of SG relative to RYGB, especially because older age is a risk factor for complications [167, 168]. Recent studies have uncovered similar morality rates in seniors after SG and RYGB, but fewer complications and an overall better safety profile – in terms of complications, reinterventions, emergency department visits and readmissions – after SG [175]. In contrast, RYGB leads to reduced medication use, compared to SG, in elderly patients with T2DM, hypertension (HTN), and GERD [175, 176].

Conclusions:

- In patients over 65, MBS achieves durable weight loss and improvements in obesity-related medical conditions, including lower rates of major adverse cardiovascular events and reduced mortality, relative to medical therapy.
- Nonetheless, seniors are at higher risk of complications and mortality than younger patients and age is an independent risk factor for complications and mortality after MBS. In addition, two increased-risk inflection points for higher complications occur at earlier ages: specifically 45 and 59 years of age.
- Despite more complications in the elderly, MBS is as safe as a hip replacement.
- Both SG and RYGB are safe options for seniors.
- Though SG has a better safety profile in seniors than RYGB, in terms of peri-operative and longer-term post-operative complications, seniors with T2DM, hypertension, and GERD undergoing RYGB experience greater reductions in medication use.

6.12. Surgical treatment of children and adolescents with obesity

- Aayed Alqahtani, MD

Age and MBS

The 2019 guidelines of the American Academy of Pediatrics recommend MBS for adolescents with a BMI higher than 140% of the 95th percentile (Class III obesity) and to those with a BMI higher than 120% of the 95th percentile (Class II obesity) if they also have obesity-related medical conditions [177]. Children with severe obesity are at greater risk than children without obesity to develop hypertension, T2DM, metabolic syndrome, non-alcoholic fatty liver disease (NAFLD), atherosclerosis, and adult obesity. In addition, 50% of adolescents with T2DM on medications require insulin within one year of receiving their diagnosis [178]. Currently, MBS is the most successful strategy for significant, sustained weight loss and improvements in obesity-associated medical conditions, including T2DM, in children and adolescents. Laparoscopic SG has accounted for more than 80% of MBS procedures in adolescents over the past decade [179-182].

Laparoscopic sleeve gastrectomy

Laparoscopic SG is safe in patients ≤18 years old and produces durable weight loss and improvements in co-morbid conditions [179, 183-185]. It also has become the most widely performed and recommended procedure for children and adolescents around the world [186]. However, no RCTS assessing SG in adolescents have been published [176]. Nevertheless, in one cohort followed for up to 10 years post SG, patients lost 30% of their total weight and 70% of their excess weight, along with significant reductions in hypertension, dyslipidaemia, and hyperglycaemia. In addition, there was no significant weight loss difference comparing prepubertal children (under 14) and post-pubertal adolescents (14 and older) [180]. Furthermore, weight loss appears to be maintained safely and growth velocity is not affected [180, 187].

Retrospective analysis from the Metabolic and Bariatric Surgery Accreditation and Quality Improvement Program (MBASQIP) database show that, in youths, SG has a better safety profile than RYGB, with fewer complications and emergency department visits, and shorter lengths of hospital stay and operation times [182]. Additionally, data from Teen-LABs revealed improvements in physical function and weight-related quality of life which remained stable over three years after SG [188]. Similarly, data from TODAY and the Teen-LABs consortia found that, compared to medical therapy, SG in severely-obese adolescents with T2DM is associated with better glycaemic control and improved kidney function [181]. In yet another study, after SG, adolescents maintained higher medium-term weight loss and greater resolution of T2DM and hypertension [189].

Roux-en-Y gastric bypass

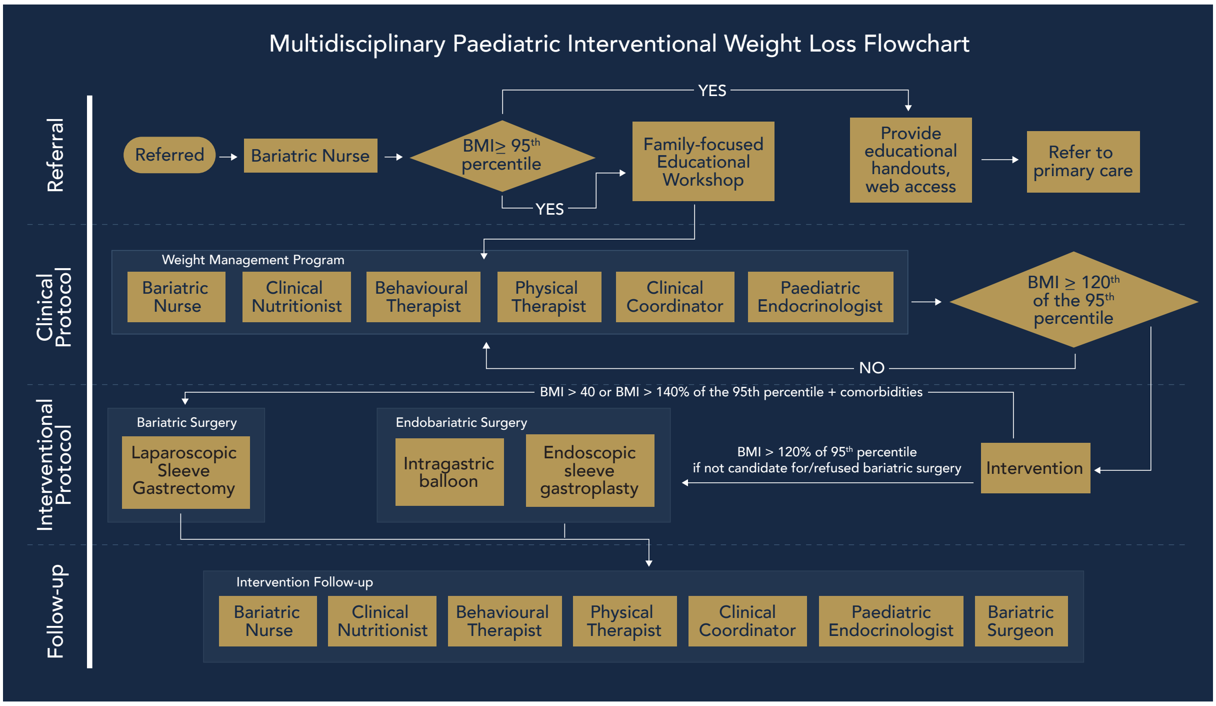
Roux-en-Y Gastric Bypass (RYGB) is also safely performed in paediatric patients. Like SG, it results in significant weight loss and improvements in obesity-related medical conditions. In addition, in randomized controlled trials including both youths and adults, RYGB has yielded similar weight loss and resolution of obesity-related medical conditions in youths as in adults, particularly in adolescents with severe obesity and obesity-related medical conditions [190]. This said, SG generally has a better safety profile than RYGB, with lower complication rates, briefer hospital stays, and shorter operation times [191]. Relative to SG, RYGB also has been documented to be generally associated with higher risks of nutritional deficiencies [192, 193]. It is absolutely essential to monitor all paediatric patients for nutritional deficiencies, pubertal development, and bone growth after RYGB [190]. The choice of MBS procedure should be individualized based on the patient's age, BMI, comorbidities, and preferences, as well as the surgeon's experience and expertise.

Endoscopic sleeve gastroplasty

Endoscopic sleeve gastroplasty (ESG) is a novel, incisionless technique whereby the effective gastric lumen is reduced by approximately 70% using lines of full thickness sutures along the greater curvature of the stomach [194, 195]. No RCTs evaluating ESG in adolescents and/or children have been published. However, the first published, single-centre study of ESG in >200 children and adolescents showed similar outcomes to those achieved among 109 adults in another study [194, 196]. In the former study, mean percentage total weight loss (%TWL) at 12 and 18 months was 14.4% and 15.4%, respectively. In addition, here were no adverse events, nor any bleeding, deaths, or unplanned admissions [196].

As such, ESG may serve as an intermediate step between non-invasive interventions and MBS. Considering the ongoing debate surrounding the appropriate timing and severity of comorbidities when deciding on interventions, ESG's reversibility and the growing body of clinical experience make it a viable consideration for patients over 10 years old. Nonetheless, further studies and long-term outcome data are needed to fully understand the potential benefits and risks of ESG in this population.

Figure 6-3: Flowchart descibing the mulidisciplinary paediatric interventional weight loss program used at our centre, which includes medical management, endo-bariatric therapy and bariatric surgery. © Alqahtani, A.R.



Biliopancreatic diversion with duodenal switch (BPD-DS) in children and adolescents

In children and adolescents, BPD-DS is a less commonly performed MBS procedure, and its use in this population remains limited due to the complexity of the surgery and potential for long-term nutritional complications [197]. Though BPD-DS has been reported to result in higher weight loss and greater resolution of comorbidities than other MBS procedures, its long-term effects on growth and development in paediatric patients are not well-established. Most practitioners recommend lifetime nutritional supplementation after BPD-DS, and this raises concerns over its potential impact upon growth and maturity among children and adolescents [198]. For this reason, it is seldom performed in this patient population.

Single-anastomosis duodeno-ileal bypass with sleeve gastrectomy (SADI-S)

A relatively-new procedure that combines a sleeve gastrectomy with single-anastomosis duodeno-ileal bypass is SADI-S. However, there is a paucity of literature on the use of SADI-S in paediatric patients and its long-term safety, efficacy, and potential complications in youths remain under investigation. As a result, SADI-S is currently not recommended for children or adolescents, and further research is needed to establish its role in the management of severe obesity in this population.

One-anastomosis gastric bypass (OAGB)

As with other complex MBS procedures, there is a paucity of literature on the use of OAGB in paediatric patients. The limited data available – primarily gleaned from small, single-centre series or case reports – have shown promising results in terms of weight loss and resolution of obesity-related comorbidities in children and adolescents [199]. However, these studies have only had short-term follow-up, and the long-term safety, efficacy, and potential complications associated with OAGB in paediatric patients remain under investigation [199-201].

Some concerns have been raised regarding the risk of bile reflux and the development of subsequent complications, such as esophagitis or gastric cancer, in patients who undergo OAGB [199]. These concerns may be particularly relevant in paediatric patients whose postoperative life expectancy should be longer than in adults. Hence, further research is needed to address these concerns and assess the long-term outcomes of OAGB in children and adolescents.

MBS in children and adolescents with syndromic obesity

Obesity is a complex, polygenic, multifactorial disease, and some children and adolescents experience genetic mutations that significantly increase their weight. The best-known genetic cause of obesity is Prader-Willi syndrome (PWS), characterized by abnormal DNA methylation in chromosome 15. Evidence regarding MBS in paediatric patients with monogenic and syndromic obesity is limited, with most data extracted from single-centre series.

One study of PWS children and adolescents, which entailed five-year follow-up, yielded positive outcomes, including resolution of obesity-related medical conditions without mortality, significant morbidity, or growth slowdown [202]. In addition, in a meta-analysis by Gunnar et al., laparoscopic SG led to a reduction of 14.9 kg/m² in BMI without mortality or revision at one-year follow-up [203]. Conversely, both Scheimann et al. and Gantz et al. reported high mortality rates following MBS and intragastric balloons in children with PWS, but this included MBS procedures like jejunoileal bypass, vertical banded gastroplasty, and BPD-DS [204, 205].

Monogenic obesity is often linked to the leptin-melanocortin pathway [206, 207], which plays a crucial role in the development of obesity. Over the past 20 years, laparoscopic SG has been offered to paediatric patients with both monogenic and syndromic forms of obesity, yielding effective and durable results with very few complications [202, 208].

It is essential to acknowledge the limited evidence, however, while continuing to study the long-term effects of MBS in this specific population. The question remains whether to choose to offer or withhold from individuals with syndromic obesity potentially life-saving treatment through MBS. This said, MBS should only be performed at highly-experienced centres that specialize in treating paediatric MBS and strict selection criteria must be employed for this unique patient population.

The next section further addresses the use of MBS specifically in adolescents.

6.13. Metabolic-bariatric surgery for adolescents: current opportunities, challenges, and limitations - Thomas H. Inge, MD, PhD

Introduction

Severe obesity affects nearly 14 million adolescents in the US [209], among whom it results in considerable deteriorations in metabolic and physical health, psychological well-being, and weight-related quality of life [181, 184, 210-212]. To date, the only intervention which has proven effective at producing significant and durable weight loss is MBS, which results in weight reduction of approximately 20-30%, an amount that is considerably more than lifestyle-based interventions for weight management. Despite the proven health benefits of significant weight loss, however, the utilization of MBS in adolescents is low, albeit increasing over the last decade.

The 2023 update of the American Academy of Pediatrics guidelines for the treatment of obesity in paediatric patients endorsed not only lifestyle interventions, but also the use of anti-obesity pharmacotherapy and MBS, thereby removing any remaining doubt that paediatric obesity should be considered a disease and should be treated aggressively and effectively. Indeed, multiple medical societies have joined the American Academy of Pediatrics, including The Endocrine Society, American Society for Metabolic and Bariatric Surgery, North American Society for Pediatric Gastroenterology, Hepatology & Nutrition, and International Federation for Surgery of Obesity and Metabolic Disorders, taking positions advocating for the surgical treatment of severe obesity in paediatric patients [177, 186, 213-215]. Indications for MBS in adolescents which have reached general consensus include:

- BMI ≥ 120% of the 95th percentile of BMI for age or BMI ≥ 35 kg/m^2 (whichever is lower), with complications of obesity that have a significant effect on health (see Table 6-4, below).
- BMI ≥ 140% of the 95th percentile of BMI for age or BMI ≥ 40 kg/m^2 (whichever is lower)

Complications of severe obesity that prompt consideration of MBS even in children and adolescents are listed in Table 6-4.

Table 6-4: Complications of severe paediatric obesity prompting consideration of metabolic-bariatric surgery

Obstructive sleep apnoea (apnoea-hypoxia index > 5)
Type 2 diabetes mellitus
Idiopathic intracranial hypertension
Nonalcoholic steatohepatitis
Blount's disease
Slipped capital femoral epiphysis
Gastroesophageal reflux disease
Hypertension
Obesity related impairment in quality of life

The largest and most comprehensive study of adolescent MBS outcomes comes from the Teen-Longitudinal Assessment of Bariatric Surgery (Teen-LABS) consortium. This multisite, prospective, NIH-funded study enrolled considerable numbers of participants who underwent either vertical sleeve gastrectomy (VSG; n=100) or RYGB (n=165) and has produced early perioperative and long-term outcome data [191, 210]. From an efficacy standpoint, these two operations have been shown to produce comparable weight loss in adolescents at 6, 12, 24, and 36 months of follow-up [210]. The 36-month percentage weight loss among those who underwent VSG and RYGB procedures was 26% and 28%, respectively. When 30-day perioperative safety results were examined, VSG and RYGB resulted in major complications in 1.5% and 7.5% of cases, respectively (inferential statistics to identify significant inter-group differences not performed). Longer-term nutritional deficiencies at five years of follow-up also were more commonly clustered in those adolescents who had undergone RYGB than VSG [216]. Indeed, the proportion of patients with ≥2 nutritional deficiencies increased over the five years after RYGB (from 12% at baseline to 59% at 5 years, $p < 0.0001$), but did not change significantly after VSG (from 6% to 27%, $p=0.09$). Similarly, the prevalence of ≥3 nutritional deficiencies increased following RYGB from 3% to 19% ($p = 0.0005$), but remained very low and unchanged after VSG (from 2% to 2.3%). From these data, it can be surmised that VSG delivers significant weight loss (comparable to RYGB) with fewer early and late adverse effects in adolescents.

We and others have also found that one of the most distinguishing and beneficial effects of MBS in adolescents has been the excellent remission of T2DM. When severely-obese adolescents with T2DM enrolled in Teen-LABS undergoing MBS were compared to a group of severely-obese participants enrolled in the TODAY study managed medically, those treated with MBS demonstrated considerably-larger metabolic improvements and resolution of T2DM. Mean HbA1c concentration decreased from 6.8% to 5.5% in Teen-LABS participants, while it increased from 6.4% to 7.8% in TODAY participants over two years of follow-up [212]. These and similar data at five years of follow-up [217] provide needed evidence to propose that the use of MBS in youths with T2DM should probably be considered even prior to them developing severe obesity and would be a reasonable treatment option in youth with class I obesity (BMI > 95th percentile for age), particularly in light of the progressive nature of the disease for so many youths when treated medically.

Conclusions

In conclusion, MBS is an effective and durable tool to treat severe obesity and notable complications of obesity in paediatric patients. Youth who meet indications for MBS should be evaluated and managed by a multidisciplinary team, regardless of their age or other complexities. Laparoscopic sleeve gastrectomy is the most common MBS procedure performed in paediatric patients, has a low rate of perioperative and longer-term nutritional complications, and yields success comparable to RYGB in terms of durable weight loss and the remission of obesity complications. Given the growing body of evidence that MBS successfully reverses complications of obesity, it is logical that the thoughtful application of MBS to treat harmful conditions like T2DM should not be restricted to those who have met an arbitrary BMI threshold defining severe obesity. Rather, similar to the adult indications, MBS should also be considered in paediatric patients with class 1 obesity and T2DM.

6.14. Results of a consensus survey

- Scott A. Shikora, MD; Abdelrahman Nimeri, MD, MBBCh

To create these IFSO Consensus Statements, Delphi analysis was performed on a number of related topics chosen by the participating experts. Consensus was reached among 43 international, interdisciplinary experts (surgeons and non-surgeons; physicians and non-physicians) on the following statements. Note that voting on statements pertaining to surgical techniques was restricted to surgeons.

- **100% consensus:**
  - Patients with weight regain require thorough multidisciplinary evaluations before being considered for modification of a previous BS procedure.
  - When performing one-anastomosis gastric bypass (OAGB), a biliopancreatic limb of 200 cm or more increases the risk of protein calorie malnutrition (PCM).
- **>95% consensus:**
  - Metabolic & bariatric surgery should be offered to individuals with class I obesity (BMI 30-35 kg/m^2) with or without T2DM if they cannot achieve substantial, durable weight loss or T2DM control (if they have T2DM) using non-surgical methods.
  - Roux-en-Y gastric bypass is preferred to SG in individuals with a large hiatal hernia and/or severe GERD.
  - All patients undergoing MBS must have both perioperative chemoprophylaxis and lower extremity compression devices to prevent venous thromboembolism (VTE). In addition, since most VTE occurs after hospital discharge, patients with known risk factors for VTE would likely benefit from extended chemoprophylaxis after hospital discharge.
  - Currently-published data do not support routine measurement of anti-factor Xa levels post-operatively.

- **>85% consensus:**
  - Suboptimal weight loss has different implications than recurrent weight gain when considering which type of intervention to select.
  - Adding anti-obesity medications and conversion to other MBS procedures are appropriate for patients with suboptimal weight loss after SG and no GERD symptoms or Barrett's esophagitis.
- **>80% consensus:**
  - The best option to treat medically-uncontrolled GERD after a SG is conversion into a RYGB.
  - To assess patients for a hiatal hernia, laparoscopic evaluation is necessary at the start of the MBS.
  - OAGB should not be considered a carcinogenic MBS procedure.
- **>75% consensus:**
  - In adult patients with obesity and T2DM, RYGB and OAGB are preferred over SG, unless contraindicated.
  - MBS should be offered to individuals with class I obesity (BMI 30-35 kg/m^2) without obesity-related complications if they cannot achieve substantial, durable weight loss with non-surgical methods.
  - For patients considering a SG, preoperative gastroscopy should be performed.
  - Revision options for patients who have had a RYGB and have suboptimal weight loss includes pouch trimming with or without band placement, gastro-jejunal anastomosis size reduction, and limb length modification.
  - At long-term follow-up, the main concerns pertaining to the risks of the SG are GERD symptoms, including heartburn and regurgitation, and endoscopic findings like esophagitis or Barrett's esophagitis.
  - The preferred treatment for persistent hypoglycemia syndrome after RYGB, despite adequate nutritional counseling, consists of anti-obesity medication (e.g., diazoxide, acarbose, octreotide, GLP-1 mimetics).
- **70% consensus:**
  - Recurrent anastomotic marginal ulcers after RYGB should be treated surgically by reducing pouch size.
  - Uncontrolled T2DM is an indication for a single-anastomosis duodeno-ileostomy with sleeve gastrectomy (SADI-S) procedure.
- **No (<70%) consensus reached:**
  - SADI-S is indicated for patients with a BMI <45kg/m^2.
  - Quality of life after duodenal switch (DS) and SADI-S is better than after RYGB.
  - For revisional surgery to achieve optimal weight loss after RYGB, revising the size of the pouch and the gastro-jejunal anastomosis should not be done during the same operation as limb length modification.
  - A SADI-S procedure with a common limb length between 250-300 results in weight loss comparable to a RYGB.
  - In the absence of GERD symptoms or Barrett's esophagitis, the most appropriate surgical option for suboptimal weight loss after a SG is conversion to a RYGB.

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CHAPTER 7

EXECUTIVE SUMMARY

7.1. Overview - Kevin P. White, MD, PhD

Obesity has become one of the world's greatest healthcare challenges, contributing to more deaths than almost any other potentially-preventable risk factor, and seriously impacts the quality of life of hundreds of millions worldwide. Fortunately, recent decades have seen the steady emergence of newer approaches for treating it that have been proven to be much more effective than all prior attempts. Leading the way has been metabolic and bariatric surgery (MBS). However, recent advances in anti-obesity medication (AOM) and endoscopic bariatric and metabolic therapy (EBMT) now provide patients with a vastly broader range of treatment options. Challenges persist, however, for several reasons. First, fewer than one percent of all persons who would otherwise be eligible for aggressive therapy to treat obesity elect to undertake it. Second, significant variability exists in how treatments are selected and administered. Third, patients differ in terms of which treatments would be safest and most effective for them, with some patient groups both at particularly high need and high risk, like patients with a body mass index (BMI) ≥50 kg/m2.

For all these reasons, early in 2022, a decision was made by the International Federation for the Surgery of Obesity and Related Disorders (IFSO) leadership to generate two updated sets of guidelines to assist in the management of patients with obesity. The first of these guidelines, which focused on non-surgical treatments and the non-surgical preparation and follow-up of patients who elect to undergo MBS, was published in 2022 [1]. It was generated from an extensive consensus survey of 94 international, inter-disciplinary experts that included bariatric surgeons, endoscopists, other physicians, nutritionists/dieticians, and psychologists. It was conducted in the spring of 2022. The results of that survey, combined with an exhaustive review of published scientific literature, were used to generate the final 300-plus page and 1000-plus reference document and two papers for publication in peer-reviewed journals.

Contrary to the 2022 guidelines, the current guidelines have primarily focused on the surgical approach to obesity management, albeit integrating non-surgical approaches that sometimes complement the surgical approach, and sometimes are used in lieu of surgery among patients who either are unsuitable or unwilling to pursue MBS. An additional critical part of the current process was coming to consensus on a core set of essential reporting definitions and reporting standards that would be acceptable not only to surgeons, but to healthcare practitioners in every other obesity-management field.

The guidelines that followed and are encapsulated here were generated using a similar process as the 2022 guidelines, including a three-round consensus survey of 43 international, interdisciplinary experts who met in person on March 9-10th, 2023 in Hamburg, Germany. Further details about the 2023 consensus survey are published elsewhere [2]. As before, these consensus results then were used to complement an exhaustive review of the scientific literature, resulting in the publication now before you.

The six chapters prior to this one, have each addressed one particular aspect of obesity management, beginning with reporting definitions and standards in Chapter 1; diet, exercise, and lifestyle in Chapter 2; medical treatment in Chapter 3; EBMT in Chapter 4; and MBS in Chapters 5 and 6. What follows below are highlights of those chapters, again focusing primarily on surgery.

7.2. Key guidelines

- Abdelrahman Nimeri, MD, MBBCh; Scott A. Shikora, MD; Kevin P. White, MD, PhD

Complications of obesity:

- Cardiovascular disease (CVD), obesity-related medical conditions like type 2 diabetes (T2DM), hypertension, dyslipidemia, chronic kidney disease (CKD), proteinuria, acute kidney injury, end-stage renal disease (ESRD), cancer, and cardiovascular mortality are among the many often life-threatening complications of obesity.
- Virtually all of these complications have been empirically-documented to improve when patients with obesity achieve appreciable weight loss.
- Virtually all of these complications also have been demonstrated to re-emerge in patients who experience appreciable recurrent weight gain after initial weight loss.

Benefits of metabolic-bariatric surgery (MBS):

- Metabolic and bariatric surgery (MBS) leads to significant and sustained weight loss, as well as improvements in metabolic health, renal outcomes, cardiovascular disease, and lower all-cause mortality.
- The effect of MBS on mortality reduction is due to reductions in major adverse cardiovascular events and is more pronounced in patients with T2DM than in patients with obesity without T2DM.
- Patients who undergo MBS experience a lower rate of mortality than those offered standard (non-surgical) care for obesity.
- Convincing evidence has been published that MBS even has reno-protective effects in patients with obesity with or without T2DM.

Preoperative weight loss

- Pre-operative weight loss (PWL) is thought to be beneficial for patients before MBS, especially those who are metabolically challenged.
- Some of the benefits of PWL include improvements in postoperative weight loss, a reduced incidence of perioperative complications, decreased operating time, a shorter hospital stay, and improvements in co-morbid medical conditions.
- However, the use of PWL remains controversial as current published literature is inconclusive.
- In general, PWL should NOT be a mandatory requirement for patients otherwise deemed suitable for MBS.

Metabolically-challenged patients

- Metabolically-challenged patients are those who have a BMI > 50 kg/m2 or a high burden of obesity-associated diseases such as T2DM, obstructive sleep apnea, hypertension, and non-alcoholic fatty liver disease (NAFLD).
- Currently, the prevalence of patients with a BMI >50 kg/m2 is increasing at a faster pace than either class I (BMI > 30 kg/m2) or severe obesity with a BMI from 40-49 kg/m2).

Patients with a BMI > 50 kg/m^2

- Patients with a BMI > 50 kg/m2 are challenging to manage intra-operatively, for reasons that include reduced operative field visibility due to excess adipose tissue and a large liver, abdominal wall thickness creating excessive torque on the surgeon's hands, and other factors.
- Patients with a BMI > 50 kg/m2 also have a higher risk of complications and generally exhibit less responsiveness with weight loss and a tendency towards weight recurrence.
- Similar to patients with stage III cancer, patients with a BMI > 50 kg/m2 must be managed differently than patients with a BMI < 50 kg/m2.
- A BMI of 50 kg/m2 is an independent risk factor for venous thromboembolism (VTE), complications, and mortality after MBS.
- Despite all these risks, in the hands of an experienced surgeon and obesity-management team, so long as a suitable procedure is selected, MBS is generally both safe and effective in patients with a BMI ≥ 50 kg/m2.

Other metabolically-challenged patients

- Patients who are metabolically challenged for reasons other than a BMI ≥ 50 kg/m2 are also at higher risk for having or acquiring the complications of obesity and may have worse short- and long-term outcomes after MBS.
- In addition, long-term adverse outcomes of MBS are also more common for metabolically-challenged patients, even when compared to patients with severe obesity (BMI 40-49 kg/m2).

Venous thromboembolism (VTE)

- Venous thromboembolism (VTE) is currently the leading cause of death after MBS.
- More than 80% of VTEs happen after the patient is discharged from the hospital.
- When considering how to prevent VTE after MBS, the use of mechanical prophylaxis alone is associated with higher VTE rates than when combined with pharmacological prophylaxis.
- In addition, when considering pharmacological prophylaxis, low molecular weight heparin (LMWH) is more effective than unfractionated heparin (UH), with no increased risk of bleeding.
- Patients considered at high risk of VTE may benefit from extended pharmacological prophylaxis after discharge from the hospital.
- There is no evidence to support the routine use of inferior vena cava (IVC) filters in high-risk patients.

Procedure selection

- Procedure selection is paramount for metabolically-challenged patients since they are, by default, a higher risk group.
- In addition, weight recurrence after sleeve gastrectomy (SG) and Roux-en-Y gastric bypass (RYGB) is generally more common in patients with a BMI > 50 kg/m2 than in patients with a BMI 40-49 kg/m2.
- Procedures considered higher risk for early and late complications, like the biliopancreatic diversion (BPD) or duodenal switch, provide more durable weight loss for metabolically- challenged patients.
- Despite all the risks, including more severe disease and worse short- and long-term complications, the health of otherwise-suitable metabolically-challenged patients should not be jeopardized by denying them MBS. Rather, MBS might be even more indicated for them, since it might literally be lifesaving.
- Biased language, and stigmatizing terms such as "superobese" should no longer be used to describe patients who have a BMI ≥ 50 kg/m2.
- Psychiatric illnesses are no longer considered contra-indications against MBS, so long as it is being adequately treated.
- Expert consensus was that not every patient being considered for MBS requires a pre-operative psychiatric assessment. However, such an assessment IS required in any patient with a known or suspected psychiatric condition, even if it is currently being treated.

Endoscopic bariatric metabolic therapy (EBMT)

- In recent years, EBMT has emerged as a viable option for treating obesity, especially in certain patient populations.
- Such populations include:
  - Patients with class I and II obesity, or even class III obesity who do not wish to have MBS.
  - Patients considered at too high risk for MBS.
  - Patients in whom EBMT might be used as a bridge to MBS or to some other surgery, like organ transplantation.
  - Pediatric patients, to avoid irreversible anatomical changes and the complications that might arise from them over the anticipated longer lifespan of children and adolescents relative to adults with obesity.
    - One notable exception is patients with syndromic causes of obesity, in whom the risk of intragastric balloon (IGB) therapy might be associated with an increased risk of complications, including severe complications (albeit only studied in one small case series).

- To date, the largest and most-convincing body of published evidence supporting the effectiveness of EBMT is for fluid-filled intragastric balloons (IGBs) and endoscopic sleeve gastroplasty (ESG).
- Relative to MBS, however, the body of evidence for the use of EBMT in children and adolescents has very few patients (74 for IGB, 109 for ESG) and no randomized clinical trials. Further research is necessary to confirm the effectiveness of EBMT in paediatric patients.

Class I obesity:

- There are three subgroups of patients with class I obesity (BMI 30-35 kg/m 2) in whom MBS may be considered:
  - Patients with T2DM.
  - Patients without T2DM, but who have some other obesity-related medical condition, like hypertension, obstructive sleep apnoea, and dyslipidaemia.
  - Patients with class I obesity but neither diabetes nor any other obesity-related medical condition.
- For the first group – class I obesity with T2DM – there is compelling evidence from several randomized clinical trials and meta-analyses on the efficacy of MBS at improving or even achieving remission of T2DM.
- For the second group – class I obesity with some obesity-related condition other than T2DM – several prospective and retrospective observational studies have shown improvements in hypertension, dyslipidemia, fatty liver disease, obstructive sleep apnoea, asthma, joint pain, urinary incontinence, reflux disease, and quality of life following MBS. In addition, both the 2022 ASMBS (American Society for Metabolic and Bariatric Surgery) and IFSO (International Federation for Surgery of Obesity) updated guidelines state that MBS should be considered in individuals with BMI = 30–34.9 kg/m2 who do not achieve substantial or durable weight loss or co-morbidity improvement using nonsurgical methods.
- For the third group of class I obesity patients who do not have any clinically-apparent obesity complications, the safety and efficacy of MBS have been less studied. Nonetheless, patients who do not achieve substantial and durable weight loss with reasonable nonsurgical methods, may be offered MBS as an option if they are otherwise deemed suitable.

Re-operative MBS:

- Currently-published evidence on re-operative MBS demonstrates improved weight loss and reduced co-morbidity, but the complication rates are higher than after primary surgery.
- The outcomes of re-operative bariatric surgery have been reported inconsistently in the literature.
- Patients who present with insufficient weight loss, continued co-morbid disease, or weight recurrence after bariatric surgery are challenging to treat.
- However, such patients may benefit from additional surgical therapy to treat their obesity and should be thoroughly evaluated by a multidisciplinary program to identify any potential reasons for their poor response.
- This evaluation may include nutritional and behavioural health assessments and an anatomical evaluation based on the original procedure performed. The decision to proceed with additional medical or surgical therapy should be based on this multidisciplinary assessment and the patient's specific risk/benefit profile for a re-operative procedure.

Adolescent obesity:

Use of anti-obesity medication (AOM)

- As with adults, the use of AOM for pediatric patients is a rapidly-evolving field. It developed to combat the poor outcomes of lifestyle therapy, particularly in adolescents, and the recognition that obesity in children and adolescents tracks strongly to adulthood.
- Only liraglutide 3mg and Semaglutide 2.4mg have been approved by both the EMA and FDA for youths ≥ 12 years old.
- More trials are needed, including those that examine the safety and efficacy of AOMs in children younger than 12 years of age.

Use of endoscopic bariatric-metabolic therapy (EMBT)

- As noted earlier, theoretical advantages of EMBT in youths include avoiding irreversible anatomical changes and the complications that might arise from them over the anticipated longer lifespan of children and adolescents relative to adults with obesity.
- The most studied and empirically supported EMBTs have been fluid-filled intragastric balloons (IGB) and endoscopic sleeve gastroplasty (ESG).
- However, relative to MBS in adolescents and EMBT in adults, the body of evidence for the use of either of these EBMTs in children and adolescents, though supportive, has very few patients – with just 74 patients for intragastric balloons (IGB) and 109 for endoscopic sleeve gastroplasty (ESG) – and there are no published randomized clinical trials.
- No convincing data have yet been published for either gas (nitrogen)-filled IGBs or duodenojejunal bypass liners (DJBL), because the few studies that have been published have far too few patients for statistical analysis.
- Further research, preferably RCTs, is therefore necessary to confirm the effectiveness and safety of EBMT in paediatric patients.
- Finally, though data are limited to a single small case series (n = 12), EMBT, notably IGB therapy, might be associated with a higher incidence of severe complications in youths with syndromic (hyperphagic) obesity and, hence, cannot be recommended in these patients. As such, testing for syndromic obesity (which accounts for roughly 5% of early-onset obesity) is necessary if EMBT is being considered in a paediatric patient.

Metabolic-bariatric surgery (MBS)

- As in adults, MBS is an effective and durable tool to treat severe obesity and the notable complications of obesity in paediatric patients.
- Outcomes in adolescents undergoing MBS are similar to those observed in adults, in terms of weight loss, improvement/remission in obesity-associated conditions, and complications.
- Youths with an indication for MBS should be evaluated and managed by a multidisciplinary team, regardless of their age or other complexities.
- Laparoscopic sleeve gastrectomy (LSG) is the most common MBS procedure performed in paediatric patients. It has a low rate of perioperative and longer-term nutritional complications, and has exhibited success comparable to other MBS procedures, such as the RYGB and the One Anastomosis Gastric Bypass (OAGB), in terms of durable weight loss and the remission of obesity complications.
- Given the growing body of evidence that MBS successfully reverses the complications of obesity, it is logical that the thoughtful application of MBS to treat harmful conditions like T2DM should not be restricted to patients who have met an arbitrary BMI threshold defining severe obesity. Rather, similar to adult indications, MBS should be considered in paediatric patients with class 1 obesity and concomitant T2DM.

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