

Expert opinion on the preoperative medical optimization of adults with diabetes undergoing metabolic surgery

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**Abstract**

Diabetes mellitus (DM) and obesity are interrelated in a complex manner, and their coexistence predisposes patients to a plethora of medical problems. Metabolic surgery has evolved as a promising therapeutic option for both conditions. It is recommended that patients, particularly those of Asian origin, maintain a lower body mass index threshold in the presence of uncontrolled DM. However, several comorbidities often accompany these chronic diseases and need to be addressed for successful surgical outcome. Laparoscopic Roux-en-Y gastric bypass (RYGB) and laparoscopic sleeve gastrectomy (LSG) are the most commonly used bariatric procedures worldwide. The bariatric benefits of RYGB and LSG are similar, but emerging evidence indicates that RYGB is more effective than LSG in improving glycemic control and induces higher rates of long-term DM remission. Several scoring systems have been formulated that are utilized to predict the chances of remission. A glycemic target of glycated hemoglobin < 7% is a reasonable goal before surgery. Cardiovascular, pulmonary, gastrointestinal, hepatic, renal, endocrine, nutritional, and psychological optimization of surgical candidates improves perioperative and long-term outcomes. Various guidelines for preoperative care of individuals with obesity have been formulated, but very few specifically focus on the concerns arising from the presence of concomitant DM. It is hoped that this statement will lead to the standardization of presurgical management of individuals with DM undergoing metabolic surgery.

Key Words: Diabetes; Obesity; Metabolic surgery; Bariatric surgery; Remission of diabetes

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Core Tip: The ambit of metabolic surgery for diabetes has increased. Individuals with inadequate glycemic control can be considered for surgery if less severely obese, and even more so if they are of Asian origin. However, both diabetes and obesity are associated with multiple comorbidities that require optimization before surgery. There are several clinical guidelines for the preoperative management of individuals with obesity; however, specific suggestions addressing these concerns in persons with diabetes have not been recommended. It is important to achieve optimal glycemic control and diagnose and manage cardiovascular, pulmonary, gastrointestinal, and renal complications before surgery. Nutritional assessment, psychological evaluation, and ruling out specific endocrine disorders are other essential adjuncts. These guidelines will help to standardize the management of preoperative comorbidities and improve postoperative outcomes in individuals with diabetes who opt for metabolic surgery.

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INTRODUCTION

The twin epidemics of diabetes mellitus (DM) and obesity have enormous medical as well as financial implications. Both are chronic and usually life-long conditions with very few definitive therapeutic choices that alter their natural course[1]. Metabolic surgery, which was commonly designated earlier as bariatric surgery, has emerged over the last three decades as a potentially disease-modifying option for both these disorders. The terms “bariatric surgery” and “metabolic surgery” have often been used interchangeably. Most societies now endorse the term “metabolic surgery” as weight-dependent and weight-independent benefits of these procedures are gradually

being recognized[2,3].

DM and uncontrolled hyperglycemia have emerged as important determinants of the need for metabolic surgery in individuals with obesity. DM is associated with multiple comorbidities that demand individualized attention around the bariatric procedure. Although there are several guidelines that address the preoperative concerns before metabolic surgery, none of them specifically focus on the issues arising in DM. This statement provides recommendations on preoperative medical management for individuals with DM who plan to undergo metabolic surgery.

DEVELOPMENT OF GUIDELINES AND GRADING OF SCIENTIFIC EVIDENCE

The expert panel met at the Society for Promotion of Education in Endocrinology and Diabetes Conference (SPEEDCON) 2020, the third annual conference of SPEED, held on 1-2, February 2020, at Gurugram, Haryana, India. The authors searched the medical literature in the PubMed related to bariatric or metabolic surgery for patients with obesity and DM. Search terms included "bariatric surgery" or "metabolic surgery", and "diabetes mellitus" in combination with the terms related to the sections that were planned to be addressed in the statement. The latter search words included "indications"; "type of surgery" and all of the common types of metabolic surgery commonly performed *e.g.*, "laparoscopic Roux-en-Y gastric bypass," "laparoscopic sleeve gastrectomy," *etc.*; "remission" and "predictors of remission," "glycemic status," "glycemic control," "glycemic management" with and without the term "perioperative"; "cardiovascular disease"; "hypertension," "blood pressure," "dyslipidemia" and "lipid profile"; "pulmonary," "respiratory," "tobacco," "smoking," "pulmonary function test," "obstructive sleep apnea," "obesity hypoventilation syndrome" and "venous thromboembolism"; "gastrointestinal," "upper gastrointestinal endoscopy," "gastroesophageal reflux disease," and "*Helicobacter pylori*"; "hepatic," "liver," "non-alcoholic fatty liver disease," and "nonalcoholic steatohepatitis"; "renal," "kidney," "creatinine," "albumin-creatinine ratio," "electrolytes," "sodium," "potassium," and "uric acid"; "nutrition," "iron," "vitamin B12," "folic acid," "anemia," "vitamin D," "vitamin A," "vitamin K," "vitamin E," "copper," "zinc," and "selenium"; "hypothyroidism," "thyroid function test," "Cushing's syndrome," "polycystic ovary syndrome," "pregnancy," "hypogonadism," "monogenic obesity" and "syndromic obesity"; "psychological" and "behavioral"; and "preoperative weight loss," "low calorie diet" and "very low calorie diet."

The authors followed the system developed by the American Diabetes Association (ADA) to grade the quality of scientific evidence supporting the recommendations (Table 1)[4]. The recommendations were allotted grades of A, B, or C based on the nature of the available evidence. Expert opinion E was ascribed to recommendations that lack evidence from clinical trials, where clinical trials may not be feasible, or the available literature is inconclusive. However, it is imperative to understand that although scientific evidence and recommendations can be crucial guiding principles, the management of every patient should ultimately be individualized for each particular case[5,6].

PROBLEM STATEMENT: PREVALENCE OF OBESITY AND DIABETES

Obesity is a common problem that has grown into a global health and economic crisis. The World Health Organization (WHO) defines overweight and obesity as 'abnormal or excessive fat accumulation that presents a health risk'[7]. According to the WHO 2016 global estimates, 39% of adults were overweight, and 13% were obese[8]. The Center for Disease Control and Prevention 2017 data suggested that 42.4% of adults in the United States of America were obese, while 9.2% were severely obese[9].

The increase in the prevalence of obesity has been accompanied by a parallel upsurge in cases of DM[10]. The International Diabetes Federation declared the current global prevalence rate of DM to be 9.3% (463 million), and predicts that it will go up to 10.2% (578 million) by 2030[11]. Both DM and obesity share a common pathogenesis, and the term "diabesity" has often been used when the two conditions coexist[12]. Obesity is recognized as a risk factor for the development of type 2 DM (T2DM)[13,14]. The coexistence of DM and obesity adversely affects the outcome of each condition and exerts an unfavorable cardiovascular impact[15].

Table 1 Evidence grading system for recommendations

Level of evidence	Description
A	Clear evidence from well-conducted, generalizable randomized controlled trials that are adequately powered, including: Evidence from a well-conducted multicenter trial; Evidence from a meta-analysis that incorporated quality ratings in the analysis. Compelling nonexperimental evidence, <i>i.e.</i> "all or none" rule developed by the Centre for Evidence-Based Medicine at the University of Oxford. Supportive evidence from well-conducted randomized controlled trials that are adequately powered, including: Evidence from a well-conducted trial at one or more institutions; Evidence from a meta-analysis that incorporated quality ratings in the analysis
B	Supportive evidence from well-conducted cohort studies: Evidence from a well-conducted prospective cohort study or registry; Evidence from a well-conducted meta-analysis of cohort studies. Supportive evidence from a well-conducted case-control study
C	Supportive evidence from poorly controlled or uncontrolled studies: Evidence from randomized clinical trials with one or more major or three or more minor methodological flaws that could invalidate the results. Evidence from observational studies with high potential for bias (such as case series with comparison with historical controls); Evidence from case series or case reports. Conflicting evidence with the weight of evidence supporting the recommendation
E	Expert consensus or clinical experience

CLASSIFICATION OF OBESITY AND DIABETES

The WHO has classified obesity based on body mass index (BMI). Obesity is conventionally defined as BMI ≥ 30 kg/m², while BMI between 25.0 and 29.9 kg/m² is defined as overweight[7]. Asians have higher body fat percentage at lower values of BMI[16, 17]; thus, more stringent criteria have been used to define obesity in the Asian population[18,19]. Table 2 depicts the classification system used to define obesity internationally and for Asia.

The ADA and WHO criteria are the established methods for diagnosing DM[20,21]. The WHO does not support the use of glycated hemoglobin (HbA1c) for diagnosing DM[21]. The ADA classifies DM into four categories: Type 1 DM (T1DM), T2DM, gestational DM, and other specific types of DM[20]. T2DM is closely inter-related to obesity and comprises the predominant subtype of DM encountered in patients undergoing metabolic surgery.

INDICATIONS FOR METABOLIC SURGERY IN DIABETES

Recommendation 1

Metabolic surgery is recommended as a therapeutic option in T2DM if the BMI is ≥ 40 kg/m² (≥ 37.5 kg/m² for Asians) irrespective of glycemic status (A). Surgery is also recommended as a treatment modality in T2DM with BMI between 35 to 39.9 kg/m² (32.5 to 37.4 kg/m² for Asians) if adequate glycemic control cannot be achieved despite standard management (B).

Recommendation 2

Metabolic surgery should be considered as a therapeutic option in T2DM with BMI between 30 to 34.9 kg/m² (27.5 to 32.4 kg/m² for Asians) if glycemic control is suboptimal despite standard management (B). However, the committee recognizes that there is limited evidence to support the long-term efficacy of metabolic surgery in Asians with T2DM and BMI < 30 kg/m², and scrutiny of risk *vs* benefit should be undertaken before performing the procedure in patients with lower BMI (E).

Recommendation 3

The associated conditions that might favor a surgical approach in T2DM with obesity are poorly controlled hypertension, non-alcoholic fatty liver disease (NAFLD), obstructive sleep apnea (OSA), obesity hypoventilation syndrome (OHS), osteoarthritis of the knee or hip, urinary stress incontinence, polycystic ovary syndrome (PCOS), gastro-esophageal reflux disease (GERD), idiopathic intracranial hypertension, severe venous stasis disease, obesity-related limited mobility and poor quality of life (E).

Discussion

The 2nd Diabetes Surgery Summit (DSS-II) defined the eligibility for metabolic surgery in T2DM with obesity, depending on the adequacy of glycemic control in conjunction with BMI[22]. Our committee broadly endorses the criteria for metabolic surgery as

Table 2 Obesity classification system for adults: International and Asian

Category	WHO International classification BMI (kg/m ²)	Asian classification BMI (kg/m ²)
Underweight	< 18.5	< 18.5
Normal weight	18.5-24.9	18.5-22.9
Overweight	25.0-29.9	23-24.9
Obesity class I	30.0-34.9	25-29.9
Obesity class II	35.0-39.9	30-34.9
Obesity class III	≥ 40	≥ 35

BMI: Body mass index.

specified in the DSS-II recommendations. The indication for metabolic surgery along with level of existing evidence is summarized in [Table 3](#).

BMI (≥ 35 kg/m²)

Long-term efficacy of metabolic surgery in improving the outcome of T2DM with BMI ≥ 35 kg/m² has been clearly demonstrated. Meta-analyses has shown that macrovascular and microvascular outcomes, and mortality are significantly better after metabolic surgery than medical therapy[23,24]. The meta-analysis by Yan *et al*[25] specifically looked into outcomes of studies with more than 5 years of follow-up. Surgery resulted in a lower incidence of macrovascular complications (relative risk [RR] = 0.43), all-cause mortality (hazard ratio [HR] = 0.65), lower weight, and better glycemic control compared to medical management. Long-term observational data from Swedish Obese Subjects registry also demonstrate the benefit of surgery in terms of DM remission (median follow-up 10 years) as well as macrovascular and microvascular complications (median follow-up 17.6 years for surgery and 18.1 years for controls) over medical therapy[26].

BMI (30-34.9 kg/m²)

Evidence also support the beneficial role of metabolic surgery in individuals with DM and BMI < 35 kg/m²[27,28]. In the meta-analysis by Müller-Stich *et al*[29] surgery resulted in a higher T2DM remission rate (odds ratio [OR] = 14.1), better rates of glycemic control (OR = 8.0) and lower HbA1c in individuals with DM and BMI < 35 kg/m² compared to standard medical management. Long-duration randomized controlled trials (RCTs) can help further substantiate this recommendation.

BMI (< 30 kg/m²)

In a meta-analysis of 12 studies done by Ji *et al*[30], 697 Asian subjects with DM and BMI < 30 kg/m² were analyzed at 6, 12, and 24 mo after metabolic surgery. After 1 year of surgery, BMI and waist circumference decreased by 2.88 kg/m² and 12.92 cm, respectively. Improvement in glycemic and lipid parameters was also observed at all three timepoints. Another meta-analysis of 26 studies assessed the remission of DM in subjects with a BMI < 30 kg/m². The follow-up duration ranged from 6 to 42.1 mo, with half of the studies having data for 12 mo only. The mixed-effect meta-analysis model estimated an overall DM remission of 43% along with an HbA1c reduction of 2.08%[31]. However, long-term outcome data to support the application of metabolic surgery in Asians with DM and BMI < 30 kg/m² is necessary before its routine clinical application.

Comorbidities

Metabolic surgery in subjects with obesity and DM demonstrated a favorable effect on hypertension[29,32]. The recent meta-analysis by Yan *et al*[25] however failed to show benefit in blood pressure after a minimum follow-up of 5 years. Various other obesity-related comorbidities improved after bariatric procedures, but specific evidence in subgroups with DM is lacking. The clinical practice guidelines by the American Association of Clinical Endocrinologists (AACE)/American College of Endocrinology, The Obesity Society (TOS), the American Society for Metabolic & Bariatric Surgery (ASMBS), the Obesity Medicine Association (OMA), and the American Society of Anesthesiologists (ASA) in 2019 suggested that bariatric procedures can be considered

Table 3 Indications for metabolic surgery in obesity along with presence of diabetes

Condition	Glycemic status	Recommendation for metabolic surgery	Evidence category
Diabetes and BMI ≥ 40 kg/m ² (≥ 37.5 kg/m ² for Asians)	Any	Strong recommendation	A
Diabetes and BMI 35-39.9 kg/m ² (32.5-37.4 kg/m ² for Asians)	Uncontrolled despite optimal treatment	Moderate recommendation	B
Diabetes and BMI 30-34.9 kg/m ² (27.5-32.4 kg/m ² for Asians)	Uncontrolled despite optimal treatment	Weak recommendation	C, E
Diabetes and obesity (BMI – not defined) with comorbidities: Poorly controlled hypertension; Non-alcoholic fatty liver disease; Obstructive sleep apnea; Obesity hypoventilation syndrome; Osteoarthritis of the knee or hip; Urinary stress incontinence; Polycystic ovary syndrome; Gastro-esophageal reflux disease; Idiopathic intracranial hypertension; Severe venous stasis disease; Obesity-related limited mobility; Obesity-related poor quality of life	Any	Weak recommendation	E

BMI: Body mass index.

in obese subjects with BMI > 35 kg/m² in the presence of comorbidities such as NAFLD, OSA, osteoarthritis of the knee or hip, and urinary stress incontinence. The guideline also recognized beneficial but weak evidence supporting the role of surgery for the amelioration of OHS, idiopathic intracranial hypertension, GERD, severe venous stasis disease, obesity-related limited mobility, and impaired quality of life [33]. Weak evidence also exists regarding improvement in fertility, menstrual irregularity, and hirsutism in women with PCOS after bariatric procedures[34]. Our expert committee advocates that metabolic surgery should be considered as a therapeutic option in obesity and DM, especially if associated with comorbidities that improve after bariatric procedures. However, the committee acknowledges that evidence in favor of such a recommendation is very weak and should be substantiated by further research.

CHOICE OF THE TYPE OF METABOLIC SURGERY IN DIABETES

Recommendation 4

Laparoscopic Roux-en-Y gastric bypass (RYGB) and laparoscopic sleeve gastrectomy (LSG) are the two most preferred bariatric procedures worldwide. RYGB and LSG result in equivalent long-term weight loss, with RYGB producing better glycemic control than LSG on prolonged follow-up and can be the preferred bariatric procedure in presence of DM (B). Other factors that might guide the choice of type of surgery are the risk of nutritional deficiencies resulting from malabsorption after RYGB and the possibility of GERD development after LSG. Institutional expertise can also guide the decision regarding the choice of the type of surgery (E).

Recommendation 5

Laparoscopic adjustable gastric banding (LAGB) is an effective procedure in inducing weight loss. The risk of complications related to the gastric band and possible need for revision surgery in the future should be taken into consideration before undertaking LAGB (B).

Recommendation 6

Biliopancreatic diversion (BPD) or BPD with duodenal switch (BPD-DS) is the most effective procedure in causing weight loss and remission of DM but has the maximum risk of immediate postoperative and long-term complications and should only be reserved for those having extremely high BMI (> 60 kg/m²) (B).

Discussion

The four standard bariatric procedures include RYGB, LSG, LAGB, BPD, or BPD-DS. There are many other variations of these procedures. Several endoscopic techniques have also emerged as means to induce weight loss in recent years. A systemic review reported the weighted means of the percentage of excess weight loss (%EWL) at 10

years or more after BPD \pm DS, RYGB, LSG, and LAGB to be 74.1%, 55.4%, 57%, and 45.9%, respectively[35].

Long-term outcome in obesity studies

A recently published meta-analysis of 18 studies (9 RCTs and 9 non-randomized interventions) comprising 2917 participants demonstrated that both RYGB and LSG had similar efficacy in causing weight reduction and remission of DM. The postoperative complication and reoperation rates were less with LSG than RYGB. However, improvement in dyslipidemia, hypertension, and GERD was better with RYGB compared to LSG[36]. Another meta-analysis of 28 studies (7 RCTs, 6 prospective observational studies, and 15 retrospective observational studies) including 9038 subjects with obesity, revealed higher remission rates of T2DM with RYGB after 3 years in comparison to the LSG group. Five-year follow-up data showed that RYGB was superior to LSG in terms of weight loss, T2DM remission, and improvement in hypertension and dyslipidemia (low-density lipoprotein [LDL])[37].

Long-term outcome in subjects with diabetes

In the meta-analysis by Madadi *et al*[38], T2DM remission rates in the LSG group were significantly (OR = 0.71, P = 0.003) less than that of the RYGB group, though the difference lost significance after 1 year. However, more DM remission was achieved with LSG compared to LAGB (OR = 2.17, P = 0.001) after 1 year[38]. Other meta-analyses have also demonstrated the superiority of RYGB over LSG in improving weight loss, and short and mid-term glycemic and lipid parameters in patients with and without T2DM[39,40]. Another meta-analysis revealed that DM resolution was highest after BPD (89%), followed by RYGB (77%), LAGB (62%), and LSG (60%)[41]. In STAMPEDE, one of the landmark trial in metabolic surgery, RYGB fared better than LSG at 5 years in achieving better glycemic control. Besides, the RYGB group required less medicine for glycemic control as compared to the LSG group[42]. Meta-analyses also revealed that immediate complication rates were higher after RYGB, and the risk of repeat surgery was higher after LAGB[35,43]. The postoperative and long-term complications were highest after BPD/BPD-DS, and the DSS-II statement suggested that these procedures should be reserved for extreme cases of obesity (BMI > 60 kg/m²)[22,44]. A comparison of the outcomes of RYGB and LSG in patients with DM and obesity is summarized in Table 4.

PREDICTORS FOR REMISSION OF DIABETES

Recommendation 7

Remission of DM can be defined as HbA1c < 6.5% and fasting plasma glucose (FPG) < 126 mg/dL (7 mmol/L) along with complete discontinuation of glucose-lowering therapy that persists for at least 6 mo (E).

Recommendation 8

We suggest that partial remission of DM can be defined as HbA1c < 5.7% and FPG < 100 mg/dL (5.6 mmol/L) persisting for at least 6 mo, when metformin is continued (E).

Recommendation 9

Preoperative fasting C-peptide level, younger age, shorter duration of DM, preoperative glycemic status, and pre-surgery requirement for insulin act as indices of pancreatic beta-cell reserve, and correlate with the chance of remission. BMI, visceral fat area (VFA), and waist circumference act as indicators of potential for reducing insulin resistance, and can also predict remission (A). Prediction models like DiaRem score, ABCD, and Individualized Metabolic Surgery (IMS) scores are validated methods to assess remission probability (B).

Discussion

Definition of remission: The most commonly applied criteria for defining DM remission was proposed by Buse *et al*[45]. Partial remission was defined as, HbA1c < 6.5%, and FPG between 100–125 mg/dL (5.6–6.9 mmol/L) lasting for 1 year or more after the procedure, in the absence of pharmacologic therapy. Complete remission was defined as HbA1c in normoglycemic range (< 5.7%) and FPG < 100 mg/dL (5.6 mmol/L) for at least 1 year. Prolonged remission or "cure" was considered as a

Table 4 Comparison between laparoscopic Roux-en-Y gastric bypass and laparoscopic sleeve gastrectomy, the two most commonly performed bariatric procedures, in patients with diabetes and obesity

	RYGB	LSG	Comments
Type of procedure	Combined malabsorptive and restrictive	Restrictive	
Effect on weight loss	+++	+++	Most studies demonstrate comparable weight loss, with slight superiority of RYGB shown in some reports
Remission of diabetes	+++	++	RYGB superior to LSG
Short term glycemic improvement	+++	++	RYGB superior to LSG
Long term glycemic improvement	+++	++	RYGB superior to LSG
Improvement in hypertension	++	+	RYGB superior to LSG
Improvement in dyslipidemia	++	+	RYGB superior to LSG
Improvement in gastroesophageal reflux disease	++	+	RYGB superior to LSG
Postoperative complications	+	+/-	Postoperative complication and reoperation rates less with LSG than RYGB
Long-term nutritional deficiencies	++	+	LSG safer than RYGB

LSG: Laparoscopic sleeve gastrectomy; RYGB: Laparoscopic Roux-en-Y gastric bypass.

complete remission lasting for 5 years or more. The stringent criteria proposed in the statement have the drawback of using different thresholds for diagnosis of DM and complete remission. Besides, many individuals who receive metformin for prophylactic purpose will not satisfy this criterion despite having HbA1c in the normoglycemic range. A definition of DM remission has also been proposed by the Association of British Clinical Diabetologists (ABCD) and the Primary Care Diabetes Society[46]. DM remission has also been defined by Kalra *et al*[47] and our panel approves the definition suggested by them. Our committee also proposes that partial remission can be defined as patients receiving metformin, and having HbA1c < 5.7% and FPG < 100 mg/dL (5.6 mmol/L) for a minimum duration of 6 mo. The HbA1c lowering effect of metformin varies between 1.12 to 0.6%. We consider that a cut-off HbA1c < 5.7% along with metformin is a reasonable approximation to the HbA1c value of 6.5% without the drug[48]. Though there is absence of outcome data in candidates receiving prophylactic metformin post-surgery, defining such a group will enable researchers to assess the usefulness of the strategy.

Predictors for remission

The rates of DM resolution after different types of metabolic surgery have already been discussed in the preceding section. DM remission results from the interplay of pancreatic beta-cell reserve and the potential for the decrement in insulin resistance [49]. The indicators of beta-cell reserve that correlate with remission include short DM duration, absence of insulin use, better glycemic control, higher serum C-peptide levels, lower age and lesser number of DM medicines[50-55]. The surrogate indices of insulin resistance with predictive value are high baseline BMI, wider waist circumference, hepatic steatosis, VFA, and inflammatory markers such as high serum C-reactive protein (CRP) and osteopontin[50,52,53,56-60].

In the meta-analysis by Wang *et al*[61], younger age, short DM duration, better glycemic control (lower HbA1c level), and absence of insulin use, correlated with remission. Asian patients were more likely to undergo remission in the presence of high baseline BMI and elevated C-peptide levels. A nationwide register-based cohort study from Sweden revealed that the chance of achieving complete remission correlated negatively with the duration of DM, insulin treatment, age, and HbA1c at baseline. Remission rates were higher among males and those having higher BMI at baseline[54]. Other reported predictors of remission in different studies are higher liver enzymes, higher white blood cell count, serum creatinine, serum LDL cholesterol and absence of long acting insulin[59,62-64].

Visceral adipose tissue is closely linked to insulin resistance and has been explored as a marker of remission[65-67]. BMI and waist circumference however might underestimate the amount of visceral adiposity in Asian population[68,69]. VFA as assessed by

magnetic resonance imaging was associated with a higher chance of remission in candidates with BMI < 35 kg/m²[57]. Visceral adiposity index (VAI) calculated from waist circumference, BMI, serum triglycerides and high-density lipoprotein is a validated marker of visceral fat content[70]. In a study from China, VAI was able to reliably predict remission in persons with BMI < 35 kg/m²[71]. The estimates of visceral adiposity might be potentially better pointers of insulin resistance than anthropometric parameters in Asians with lower BMI and hence may more reliably predict probability of remission. Further validation of this hypothesis is however needed in larger and long-term studies.

Scoring systems for remission: Several scoring systems have been proposed as predictors of DM remission following metabolic surgery. The ABCD scoring system devised by Lee *et al*[72], incorporated age at surgery (A), baseline BMI (B), C-peptide level (C), and duration of DM (D). The DiaRem score was suggested by Still *et al*[73], and includes age, insulin use, HbA1c level, and type of anti-diabetic medication. The IMS score categorizes patients into three stages of severity based on the preoperative number of DM medications, insulin use, duration of DM, and glycemic control (HbA1c < 7%). The system also provides recommendations on the type of procedure (RYGB or LSG) for each severity stage based on each procedure's efficacy and risk-benefit ratio [74]. Though one analysis suggested that the ABCD score had better predictive efficacy as compared to the IMS score and DiaRem score, the committee does not acknowledge one scoring system's superiority above the other in the absence of evidence from large multicenter studies[75,76]. ACF scoring system is another recently reported model that utilizes the three variables: age, C-peptide area under curve, and FPG to predict remission[77].

PREOPERATIVE ASSESSMENT AND OPTIMIZATION OF GLYCEMIC STATUS

Recommendation 10

The initial preoperative assessment should include a comprehensive medical, psychosocial and drug history, along with physical examination. Appropriate laboratory tests should be done to assess glycemic control. These tests should include FPG, postprandial glucose, and HbA1c in all cases and self-monitoring of blood glucose and/or continuous glucose monitoring system in selected cases. Estimation of serum C-peptide should be done to assess the scope for the remission of DM (E).

Recommendation 11

A glycemic target of HbA1c < 7% before surgery is a reasonable goal. Medical nutrition therapy, physical exercise, and pharmacotherapy should be optimally integrated to attain that goal (E). Pharmacological agents known to induce weight loss, such as sodium-glucose co-transporter-2 inhibitors and glucagon-like peptide-1 receptor agonists, should be considered as part of the treatment armamentarium whenever feasible. Drugs known to cause weight gain, such as sulfonylureas and thiazolidinediones, should be avoided as long-term therapeutic strategy if possible. The perioperative risks of deranged glycemic control *vs* benefits of early metabolic surgery have to be assessed on a case-to-case basis if glycemic control cannot be attained preoperatively despite optimal medical treatment. If a strategy of restricting calories with meal replacement therapy is employed in the preoperative weeks, the anti-diabetic medications would need to be reduced to prevent hypoglycemia (E).

Recommendation 12

After admission, most non-insulin based therapies should be stopped, and the patient should be transitioned to insulin as per institutional practice. Severe degrees of hyperglycemia will require intravenous insulin infusion. Target glucose of 100 to 180 mg/dL (5.5-10 mmol/L) is acceptable in the perioperative period (E).

Discussion

Glycemic target: Table 5 summarizes the recommended evaluation in individuals with DM before metabolic surgery. Inadequate glycemic control in the preoperative period is associated with increased 1-year mortality, wound complications, infective complications, and extended hospital stay[78-81]. Pre-surgery deranged glycemic status and medication usage, including insulin and the number of drugs required to achieve

Table 5 Preoperative evaluation before metabolic surgery in individuals with diabetes and obesity

System	Essential evaluation	Conditional evaluation	Comments
History and physical examination	Detailed evaluation along with drug history	-	-
Glycemic	FPG, PPG, HbA1c, Fasting serum C-peptide	SMBG; CGMS	HbA1c < 7% is a reasonable target, higher targets may be acceptable in long-standing diabetes; SMBG and/or CGMS in patients on insulin
Cardiovascular	BP: Fasting lipid Profile; ECG: Cardiovascular risk assessment with a validated risk prediction model ¹	Transthoracic echocardiography (in cases with unexplained dyspnea and known cases of heart failure, especially with recent changes in clinical status); If risk $\geq 1\%$, ² functional status assessment. Poor (< 4 METs) or unknown functional capacity - exercise or pharmacological stress echocardiography or radionuclide MPI	Target BP < 140/90; Abnormal results in a stress test should be managed according to current clinical practice guidelines. Patients with underlying cardiac abnormalities should undergo a formal cardiology consultation before surgery
Pulmonary	Smoking history. Screening for OSA by a clinical scoring tool ³ . Risk assessment for VTE during perioperative period by a validated method ⁴	Pulmonary function test in presence of intrinsic pulmonary disease; Overnight polysomnography if indicated from results of scoring tool. ABG for PaCO ₂ estimation and venous bicarbonate in cases of OSA to rule out OHS	Structured tobacco cessation program if applicable
Gastrointestinal	-	UGIE to be considered routinely before LSG. Conditional for other procedures; H pylori detection and eradication	
Hepatic	LFT	Abdominal USG if LFT deranged or symptomatic biliary disorder. Use of Noninvasive scoring systems ⁵ can be considered. Liver elastography; Three-dimensional magnetic resonance elastography; Intraoperative liver biopsy	The strategy to diagnose NAFLD in bariatric patients is not defined. Variations of liver elastography such as transient elastography, 2-D shear wave elastography, and ARFI can be better modalities in severely obese patients. Intraoperative liver biopsy is the gold standard, but its specific indications are not clear
Renal, electrolytes, uric acid	Serum creatinine; eGFR ⁶ ; Urinary albumin-creatinine ratio	Electrolytes in presence of CKD or drugs known to cause electrolyte imbalance. Uric acid if there is past history of gout	Serum potassium should be measured if on ACE inhibitors, ARBs, or diuretics
Nutritional	Nutritional assessment by a dietitian. Complete blood count, serum ferritin, serum iron, TIBC, and TS. Serum vitamin B12, folate. Serum calcium, 25(OH)D	Serum C-reactive protein if anemia of chronic inflammation is suspected. Serum methylmalonic acid and homocysteine in cases of low normal vitamin B12 and folate levels with high index of suspicion. Serum copper, zinc, and selenium; fat soluble vitamins such as vitamin A, E and K can be considered before malabsorptive procedures	Serum or urinary N-telopeptide, bone-specific alkaline phosphatase, and bone mineral density can be considered if osteoporosis is suspected especially in postmenopausal women
Endocrine	-	Thyroid profile if there is a past history of thyroid dysfunction, goiter or symptoms suggestive of thyroid disorder. ONDST, 24-h urinary free cortisol, or 11-pm salivary cortisol if there is suspicion of endogenous Cushing's syndrome	Evaluation of syndromic or monogenic obesity on case-by-case basis
Reproductive	-	Total and bioavailable testosterone and USG of the pelvis if PCOS is suspected. LH, FSH, and testosterone (total) if hypogonadism is suspected in males	Women should avoid pregnancy if planned for surgery. Pregnancy should be avoided for 12-18 mo after surgery
Psychological	Behavioral and psychosocial evaluation	-	-

¹e.g., Revised Cardiac Risk Index, Obesity surgery mortality risk score, Longitudinal Assessment of Bariatric Surgery consortium risk stratification system, metabolic acuity score, etc.

²Estimated perioperative mortality risk or major adverse cardiovascular risk of $\geq 1\%$.

³STOP-BANG questionnaire or Berlin questionnaire.

⁴e.g., venous thromboembolism risk assessment tool by Fink *et al* [130].

⁵Non-alcoholic steatohepatitis clinical scoring system, AST to platelet ratio index, FIB-4 index, non-alcoholic fatty liver disease fibrosis score, BARD score and Forns index.

⁶By Chronic Kidney Disease Epidemiology Collaboration formula.

25(OH)D: 25-hydroxyvitamin D; ABG: Arterial blood gas; ACE: Angiotensin converting enzyme; ARB: Angiotensin II receptor blocker; ARFI: Acoustic radiation force impulse shear wave imaging; CGMS: Continuous glucose monitoring system; eGFR: Estimated glomerular filtration rate; FPG: Fasting plasma glucose; FSH: Follicle-stimulating hormone; *H. pylori*: *Helicobacter pylori*; HbA1c: Glycated hemoglobin; LFT: Liver function test; LH: Luteinizing hormone; MET: Metabolic equivalent; MPI: Myocardial perfusion imaging; ONDST: Overnight dexamethasone suppression test; OSA: Obstructive sleep

apnea; PCOS: Polycystic ovary syndrome; PPG: Post-prandial glucose; SMBG: Self-monitoring of blood glucose; TIBC: Total iron-binding capacity; TS: Transferrin saturation; UGIE: Upper gastrointestinal endoscopy; USG: Ultrasonography; VTE: Venous thromboembolism.

euglycemia, negatively correlate with the chance of long-term remission of DM following metabolic surgery[61,73,74,76]. Only a few studies, however, have specifically assessed the role of preoperative glycemic control to short-term postoperative outcomes. The clinical practice guidelines by the AACE/TOS/ASMBS/OMA/ASA suggest an HbA1C target of 6.5% to 7.0% or less before surgery, and peri-procedure blood glucose levels of 80 to 180 mg/dL (4.4–10 mmol/L). In the presence of advanced microvascular or macrovascular complications, or comorbidities, or long duration of DM, they recommended an HbA1C target between 7% and 8% [33]. An interprofessional bariatric glycemic optimization clinic-based study analyzing 70 patients, was able to lower HbA1C from a mean level of $9.0\% \pm 1.2\%$ to $\leq 7.5\%$ in 75% of patients before surgery in 5 mo[82]. In a retrospective review of 468 patients who had undergone RYGB, higher pre-surgery HbA1c ($> 6.5\%$) was associated with an increased chance of postoperative hyperglycemia. These patients also had a greater risk of wound infection and acute renal failure[83].

A RCT of 34 patients with a mean A1C of 10% at baseline, did not show any differences in the length of stay or surgical complications in the two arms of optimized (HbA1c-8.4%) *vs* non-optimized (HbA1c-9.7%) glycemic therapy. This was the only RCT that attempted to identify the impact of two different glycemic strategies, but had shortcomings such as a narrow margin between achieved HbA1c ($> 8\%$ in both arms) and small sample size. Another drawback was both the arms were offered the same dietary and glycemic interventions for the preceding 2 wk immediately before surgery [84]. A target glucose of 100 to 180 mg/dL (5.5–10 mmol/L) should be the perioperative period goal[85]. The approach to achieve this target should be guided by institutional policy. Intravenous insulin as per protocol should be administered in cases of severe hyperglycemia[86].

Pre-operative calorie restriction for two to four weeks has been conventionally practiced in many bariatric centers. Though the methods have been very variable, these practices might warrant adjustment of anti-diabetic medications[87,88].

PREOPERATIVE ASSESSMENT AND OPTIMIZATION OF CARDIO-VASCULAR STATUS

Recommendation 13

The target blood pressure (measured by appropriately sized cuff) before surgery is $< 140/90$ mmHg. Angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARBs), thiazide diuretics, or dihydropyridine calcium channel blockers (CCBs) are the preferred agents, and multiple drug classes are usually necessary to accomplish blood pressure goals (a combination of ACE inhibitors and ARBs to be avoided) (A). Patients already on beta-blocker should be continued on the same. Initiating a beta-blocker in the preoperative phase is controversial and should be individualized after estimating risk *vs* benefit (B).

Recommendation 14

A fasting lipid profile should be done in all patients. Lipid-lowering therapy as per current recommendations should be initiated (A).

Recommendation 15

A resting 12-lead electrocardiogram (ECG) should be obtained before metabolic surgery. The ECG, other than serving as a baseline for comparison in any subsequent cardiac adverse events, can provide clues regarding left ventricular hypertrophy, possible ischemia (Q waves, ST-segment depression), and bundle branch blocks, arrhythmia, and QTc prolongation (B).

Recommendation 16

Assessment of left ventricular function by resting transthoracic echocardiography should be undertaken in patients with unexplained dyspnea, and known cases of heart failure, especially with recent changes in clinical status. Right ventricular hypertrophy in echocardiography can be indicative of pulmonary hypertension. Valvular

abnormalities and other structural lesions can also be detected by echocardiography (B).

Recommendation 17

A cardiovascular risk assessment is recommended before surgery. Several risk prediction models to assess perioperative cardiac risk have been suggested and validated in obese individuals. Individuals at an elevated risk (1% or more) of a major adverse cardiac event (MACE) during the perioperative period and having a poor (< 4 metabolic equivalents [METs]) or unknown functional capacity should undergo further risk stratification with exercise or pharmacological stress echocardiography, or radionuclide myocardial perfusion imaging to assess for myocardial ischemia. Individuals with a normal stress test can proceed to surgery, whereas those with an abnormal result should be managed according to the current clinical practice guidelines. Those with underlying cardiac abnormalities should undergo a formal cardiology consultation before surgery (E).

Discussion

Blood pressure and lipids: The target blood pressure recommended by ADA in individuals with DM is less than 140/90 mmHg. Lower targets such as 130/80 can be pursued for individuals at high risk of cardiovascular disease if that goal can be attained by reasonable therapeutic means[89]. Meta-analyses have demonstrated equivalent efficacy of ACE inhibitors or ARBs (to be avoided together), thiazide diuretics, or dihydropyridine CCBs in reducing cardiovascular outcomes, and any of these can be used as a first-line agent[90,91]. Most individuals, however, will require multiple agents for normalization of blood pressure[89]. As per the American College of Cardiology (ACC)/American Heart Association (AHA) recommendations published in 2014, beta-blockers should be continued in those who have been receiving them for long duration. The risks and benefits of initiating beta-blockers before surgery should be individualized according to the clinical situation[92]. Lipid-lowering therapy should be initiated as per the current practice guidelines[93].

12-lead ECG and echocardiography: A 12-lead ECG should be obtained before metabolic surgery. It acts as a reference against which the postoperative changes can be compared. Also, arrhythmias, pathological Q-waves, LV hypertrophy, ST depression, QTc interval prolongation, and bundle-branch blocks can provide useful clues, but the prognostic utility of an ECG to predict the perioperative cardiovascular outcome is limited[92,94]. The ACC/AHA guidelines recommend assessment of LV function by echocardiography in patients with dyspnea of unknown origin and for patients with heart failure with worsening dyspnea or recent change in clinical status [92].

Cardiac risk prediction models: Several risk prediction models have been proposed to estimate the perioperative risk of MACE in individuals undergoing non-cardiac surgery[95-98]. The most commonly used scoring system is the Revised Cardiac Risk Index, which incorporates the following variables as predictors of perioperative cardiac risk: high-risk surgery, history of ischemic heart disease, history of CHF, creatinine > 2 mg/dL, cerebrovascular disease, and DM requiring insulin. The 30 d risk of death, myocardial ischemia, or cardiac arrest is 0.4% if none of the factors are present. The presence of one predictor pertains to a risk of 0.9% for these events, two predictors carry a 6.6% risk, and three or more factors correlate with an 11% risk[99]. Bariatric surgery itself is considered as an intermediate to high-risk non-cardiac surgery, and the presence of any other additional factor will warrant further assessment[100].

Scoring systems such as obesity surgery mortality risk score (OS-MRS) for bariatric surgery have also been validated. The OS-MRS assigns one point each to the following five risk factors: age ≥ 45 years, male sex, BMI ≥ 50 kg/m², hypertension, and known risk factors for pulmonary embolism (previous thrombosis, pulmonary embolism, inferior vena cava filter *in situ*, a history of right heart failure or pulmonary hypertension and obesity-hypoventilation syndrome)[101]. The mortality rate in class A (score 0 to 1) was 0.26%, in class B (score 2 or 3) was 1.33%, and in class C (score 4 or 5) was 4.34%[102]. Other methods that have been used to stratify surgical risk in obese patients include the Longitudinal Assessment of Bariatric Surgery consortium risk stratification system, the metabolic acuity score, and a nomogram for assessing surgical complications in bariatric surgery[103-105]. Our committee recommends individualized evaluation of candidates as per recommended practices before undergoing surgery, if they have an estimated (by general or obesity specific scoring

system) perioperative mortality or MACE risk $\geq 1\%$. Further studies are required to validate the optimal prediction model to stratify perioperative risk in individuals undergoing metabolic surgery for obesity and DM.

Approach for cardiovascular evaluation and management: Our committee endorses the approach suggested in the 2014 ACC/AHA guideline of perioperative cardiovascular evaluation and management of patients undergoing non-cardiac surgery. In all cases at elevated risk (estimated perioperative mortality risk or MACE risk $\geq 1\%$), assessment of the functional status of the patient should be undertaken. In case the patient can perform ≥ 4 METs of activity (can walk up a flight of steps or a hill or walk on level ground at 3 to 4 mph), additional tests are usually not recommended. For those whose functional capacity is lower or unknown, additional stress testing may be indicated if it will influence perioperative care[92]. Assessment of functional capacity might not be possible in many patients with obesity for unrelated reasons such as osteoarthritis. Pharmacological stress testing may be warranted in such cases. Both obesity and DM are substantial risk factors for cardiovascular disease. In many situations, the strategy to assess cardiac risk has to be individualized in consultation with the cardiologist, specifically when proper assessment of the patient's functional status cannot be performed. Those with pre-existing cardiologic disease must undergo a formal cardiology consultation before metabolic surgery[33].

PREOPERATIVE EVALUATION AND OPTIMIZATION OF PULMONARY FUNCTION

Recommendation 18

A structured tobacco cessation program should be employed for patients who smoke cigarettes before undergoing surgery (E).

Recommendation 19

Pulmonary function test (PFT) or spirometry is not routinely indicated. Definitive evidence that PFT can predict postoperative pulmonary complications is lacking, and the testing should be restricted for those with an intrinsic pulmonary disease where the findings would alter the management (E).

Recommendation 20

Untreated OSA increases the risk of perioperative complications. Considering the high prevalence of undiagnosed OSA in severely obese individuals, screening for OSA by a clinical scoring tool such as the STOP-BANG questionnaire (or Berlin questionnaire) should be performed. The gold standard test to confirm the diagnosis of OSA in suspected cases is overnight polysomnography (PSG). The use of continuous positive airway pressure (CPAP) in the preoperative period for treatment of moderate to severe OSA is recommended to reduce the risk of perioperative pulmonary complications (B).

Recommendation 21

OHS often coexist with OSA in severely obese individuals, and the presence of OHS should be ruled out in all patients diagnosed to have OSA. Arterial blood gas analysis for PaCO₂ estimation along with measurement of venous HCO₃⁻ (cut off 27 mmol/L) can be used to establish the diagnosis of OHS. Institution of positive airway pressure therapy and lifestyle modification is recommended for patients diagnosed to have OHS (B).

Recommendation 22

A risk assessment for possibility of development of venous thromboembolism (VTE) in the perioperative period should be undertaken. The possible risk factors for VTE include prior VTE, higher BMI, age, gender, immobility, use of hormone therapy, OHS, pulmonary hypertension, venous stasis disease, operative time, and procedure type and approach (B). There are insufficient data to recommend a uniform strategy to prevent VTE complications. The standard recommendations are mechanical compression devices with early ambulation in addition to chemoprophylaxis (B). There is inadequate evidence to recommend prophylactic placement of inferior vena cava (IVC) filters to prevent pulmonary embolism and it should be applied under very selected circumstances (E).

Discussion

Smoking and tobacco cessation: Smoking increases the risk of postoperative morbidity following metabolic surgery. Smoking is associated with an increased risk of organ space infection, prolonged intubation, reintubation, pneumonia, sepsis, shock, and longer length of hospital stay[106]. In a recent systemic review, smoking during a year before undergoing surgery, was an independent risk factor for higher 30 d mortality and major postoperative complications, particularly wound and pulmonary complications[107]. Perioperative tobacco cessation reduces the chance of surgery-related morbidities[108]. A structured program is more effective than general advice[109].

PFT: The utility of PFT to predict postoperative complications is uncertain. In a prospective study of 485 patients who underwent laparoscopic metabolic surgery, abnormal spirometry in the preoperative period was associated with a three-fold risk of postoperative complications[110]. In a retrospective analysis of 602 patients, abnormal spirometry before surgery was shown to correlate with the risk of postoperative pulmonary complications only in those with OSA[111]. In another retrospective cohort of 146 severely obese BPD candidates, the logistic regression model suggested that the preoperative PFT could not predict respiratory complications after surgery[112].

OSA: OSA is a common comorbidity of severe obesity, with the reported prevalence of close to 80% in patients planned for metabolic surgery[113-116]. Untreated OSA increases the risk of postoperative complications[117,118]. We endorse the consensus guidelines by de Raaff *et al*[119], regarding screening and management of OSA before metabolic surgery. A clinical scoring tool to screen for OSA should be used in all patients planned for surgery. The STOP-Bang Questionnaire's sensitivity to detect mild and severe OSA was highest, while the STOP Questionnaire had the highest sensitivity to predict moderate OSA[120]. Berlin questionnaire can also be used to screen, but Epworth Sleepiness Scale is not recommended[119]. Overnight PSG is the gold standard to confirm the diagnosis of OSA. Simpler portable devices that can analyze a limited range of variables, known as type 3 portable sleep monitoring (as per definition of the American Academy of Sleep Medicine) can be used if there is a high pretest probability for moderate to severe OSA[119,121]. CPAP usage in the perioperative phase decreases the chance of pulmonary complications and is recommended for treatment of moderate to severe OSA[119,122].

OHS: OHS is defined as the triad of obesity ($\text{BMI} > 30 \text{ kg/m}^2$), daytime hypoventilation, and sleep-disordered breathing in the absence of an alternative neuromuscular, mechanical, or metabolic explanation for hypoventilation. The prevalence of OHS is 20%-30% among individuals with obesity and OSA[123]. In a recently published study, the prevalence of OHS in a bariatric cohort of 1718 patients was 68%[124]. OHS should be ruled out in patients diagnosed with OSA by measuring serum HCO_3^- or arterial blood gas analysis. Elevated serum HCO_3^- ($> 27 \text{ mmol/L}$) and/or increased PaCO_2 ($> 45 \text{ mmHg}$) are indicative of OHS[125]. Institution of positive airway pressure therapy along with lifestyle modification is recommended for patients diagnosed to have OHS[119,126].

VTE: Individuals with obesity are at an increased risk of VTE, though the overall rate following metabolic surgery has been reported to be $< 1\%$ [127-129]. A preoperative risk assessment model to stratify candidate by VTE risk was devised by Fink *et al*[130] using the following variables: procedure type, patient history of VTE, male sex, BMI, age, and operative time $> 3 \text{ h}$. By this scheme, 97% were classified into low-risk groups with a predicted VTE risk of $< 1\%$. The medium-risk group had an estimated VTE risk of 1%-4%, and the high-risk group had $> 4\%$ - 30 d VTE event rate[130]. Other tools to assess DVT risk have also been proposed[131]. Further risk factors for VTE include immobility, known hypercoagulable condition, OHS, pulmonary hypertension, venous stasis disease, hormonal therapy, and transfusion[129,130,132,133]. We endorse the ASMBS recommendations for VTE prophylaxis in those undergoing metabolic surgery. All candidates are at moderate to high risk of VTE and require mechanical prophylaxis and early ambulation. Additional chemoprophylaxis with low molecular weight heparin should be considered unless contraindications arise from bleeding tendency or other causes[134]. Placement of IVC filter is not routinely indicated[134, 135].

GASTROINTESTINAL EVALUATION

Recommendation 23

Preoperative upper gastrointestinal (GI) endoscopy can be considered before performing metabolic surgery, though conclusive evidence supporting its routine usage is lacking (C). Because of worsening of previous GERD and risk of development of new-onset GERD on long-term follow-up after LSG, it is recommended that upper GI endoscopy should be performed in candidates for LSG (B).

Recommendation 24

There is inadequate evidence to support or refute in favor of routinely performing tests to detect and treat *Helicobacter pylori* during preoperative evaluation.

Discussion

Upper gastrointestinal endoscopy: There is a lack of consensus regarding the utility of routine upper GI endoscopy before surgery[33,136]. Two meta-analyses explored the benefits of preoperative endoscopy[137,138]. In the meta-analysis by Parikh *et al*[137] ($n = 6112$), endoscopic findings were normal in the majority (92.4%), and only 7.6% had abnormalities that delayed or altered surgery[137]. In the meta-analysis by Bennett *et al*[138] ($n = 12261$), endoscopic findings necessitated a change in surgical management in 7.8% and medical management in 2.5% (after excluding *H. pylori*). The authors concluded that preoperative upper GI endoscopy in average-risk, asymptomatic individuals should be considered optional as the proportion of endoscopies with findings that resulted in alteration in management was low[138]. In two recent studies, treatment strategy was changed only in a small percentage of patients based on endoscopic findings[139,140].

GERD: GERD is increasingly recognized as a long-term complication of LSG and has been considered a relative contraindication[141]. A meta-analysis evaluating the outcome of 10718 patients after LSG found that 19% had increased symptoms and 23% developed new-onset GERD after surgery. The long-term prevalence of esophagitis was 28%, and that of Barrett's esophagus (BE) was 8%[142]. A significant percentage of patients detected to have GERD on endoscopy are asymptomatic and thus were diagnosed only on routine screening[143]. The prevalence of GERD in bariatric candidates was not different between those with or without DM[144]. Our panel recommends upper GI endoscopy in patients planned for LSG to rule out symptomatic and asymptomatic GERD. Dedicated studies to assess the evolution of GERD after LSG are required.

Gastric lesions: A recent meta-analysis scrutinized gastric lesions that requires subsequent endoscopic monitoring after surgery. Atrophic gastritis was detected in 2.64%, and intestinal metaplasia in 2.7%[145]. Lesions such as atrophic gastritis, intestinal metaplasia, or gastrointestinal stromal tumor mandate endoscopic monitoring post-surgery. LSG should be considered in preference to RYGB in the presence of these conditions. However, the prevalence of these lesions is negligible, and it is not clear whether routine preoperative endoscopy will have a significant role.

***H. pylori*:** There is a lack of consensus regarding the utility of detecting and eradicating *H. pylori* before metabolic surgery[136]. A meta-analysis of seven studies with 255435 patients revealed that rates of bleeding, leak, length of hospital stay, and weight loss were similar between *H. pylori* positive and negative groups. Marginal ulceration following RYGB was the only outcome that correlated with its presence [146]. Another meta-analysis demonstrated that eradication of *H. pylori* decreased the risk of marginal ulceration, but the rates still remained high (1.5%-18.8% following eradication *vs* 0.5%-31.2% in the non-eradicated group). The authors acknowledged the methodological limitation in many of the studies included in the meta-analysis [147]. Efficacy of *H. pylori* treatment in preventing complications (especially after RYGB) needs further assessment in well-designed trials.

HEPATIC EVALUATION

Recommendation 25

All candidates for surgery should be investigated for NAFLD. There is no consensus about the methodology for diagnosis of NAFLD. Liver function test (LFT) should be

performed routinely before surgery. Abdominal ultrasonography (USG) is recommended if LFT is deranged or symptomatic biliary disorder is suspected. Evidence to support routine imaging of the liver during preoperative evaluation is lacking (E).

Recommendation 26

Several noninvasive scoring systems have been proposed to assess the risk of fibrosis in the bariatric population. However, more evidence is required before a particular strategy can be recommended for clinical application. Liver elastography can be considered in those with suspected NAFLD, but diagnostic accuracy is limited in severe obesity. The gold standard for diagnosing NAFLD is intraoperative liver biopsy, but the clinical strategy to identify patients who will benefit from the biopsy has to be formulated through well-structured studies (E).

Discussion

NAFLD is present in up to 81% of patients undergoing metabolic surgery. The global prevalence of NAFLD and nonalcoholic steatohepatitis (NASH) in T2DM were reported to be 55.5% (95%CI: 47.3-63.7) and 37.3% (95%CI: 24.7-50.0) respectively in a meta-analysis[150]. The therapeutic options for NAFLD are limited and metabolic surgery is the only modality that has consistently demonstrated benefit[149,151-153]. However the modalities and clinical strategy to diagnose and follow these patients are not clearly defined[154-157]. Even though the sensitivity of USG to detect NAFLD is high, but its low specificity in obese individuals remains a drawback[148,158]. The noninvasive fibrosis scores that have been commonly studied in the bariatric population include NASH clinical scoring system NCS[159], aspartate aminotransferase to platelet ratio index[160], fibrosis-4 index[161], NAFLD fibrosis score[162], BARD score[163], and Forns index[164]. The scoring systems were able to predict fibrosis in some but not in all studies[155,165,166]. Their usefulness in detecting fibrosis before surgery requires validation in more extensive studies. Transient elastography, two-dimensional shear wave elastography, and acoustic radiation force impulse shear wave imaging reliably predicted advanced fibrosis in bariatric candidates in small studies[167-169]. Three-dimensional magnetic resonance elastography is a promising modality to detect NASH and has demonstrated a sensitivity of 67% and specificity of 80%[170]. Intraoperative liver biopsy remains the gold standard for the diagnosis of NASH in bariatric candidates. However, it is associated with a small increase in the rate of complications[149]. The morphology of the liver can be visualized during surgery and can provide a clue regarding necessity for biopsy[158].

Obesity and DM are associated with high prevalence of NAFLD, often with significant fibrosis[151,158]. Metabolic surgery does improve outcomes related to NAFLD in a significant proportion of patients[152-154]. Post-surgery hepatology follow-up to assess the risk of progression to cirrhosis is recommended in these groups. None of the imaging modalities and noninvasive scoring systems have convincing evidence to support their routine clinical application. Intraoperative liver biopsy provides a reliable way to diagnose and assess the severity of NAFLD, but it is currently unclear what criteria should be applied to identify patients who will benefit from biopsy.

ASSESSMENT OF RENAL FUNCTION, ELECTROLYTES, AND URIC ACID

Recommendation 27

Individuals with DM planned for metabolic surgery should undergo estimation of spot urinary albumin-creatinine ratio (ACR). Serum creatinine measurement along with the assessment of estimated glomerular filtration rate (eGFR) is also recommended (E).

Recommendation 28

In patients on diuretics, ACE inhibitors, or ARBs, serum potassium levels should be obtained. Studies to support the measurement of electrolytes on a routine basis before surgery are lacking. Clinical factors, especially the presence of chronic kidney disease (CKD) and drug history, usually indicate whether assessment of other electrolytes is necessary (E).

Recommendation 29

Serum uric acid should be measured in individuals with a history of gout, and prophylactic treatment of acute gouty arthritis should be considered in these patients (E).

Discussion

Calculation of eGFR in severe obesity: Both DM and obesity are leading causes of the development and progression of CKD[171-173]. The ADA recommends estimating urinary ACR and serum creatinine (along with eGFR) in individuals with DM annually. Serum potassium should be measured in individuals receiving ACE inhibitors, ARBs, or diuretics[174]. Calculation of eGFR is usually done using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula[175]. The CKD-EPI formula using creatinine tends to overestimate eGFR in bariatric patients both before and after surgery, while the cystatin C CKD-EPI equation tends to underestimate it[176]. The errors in using the standard equations in severely obese subjects arise from changes in the body surface area (error of indexing), alteration in serum creatinine and cystatin C levels, and obesity-induced glomerular hyperfiltration [177]. The combined equation CKD-EPIcreat-cyst using serum creatinine and cystatin C values reliably predicted eGFR in severe obesity both before and after surgery but further validation in larger cohorts is needed[176,178,179].

Reno-protective effects of metabolic surgery: Metabolic surgery is a promising reno-protective strategy in obesity, even without DM[180,181]. In a study of 737 subjects, remission of DM 5 years after surgery was associated with a lower risk of moderate or severe albuminuria but did not result in stabilization of eGFR[182]. A meta-analysis of 23 cohort studies with 3015 subjects reported a significant fall in serum creatinine level and proteinuria after surgery. The subgroup of patients with hyperfiltration and CKD also showed improvement in eGFR after 6 mo[183].

Precautions in CKD: The weight-lowering response following surgery and chances of DM remission may be diminished in CKD stages 4 and 5[182,184,185]. Decreased eGFR before metabolic surgery also correlated with a higher chance of surgical site complications, infections, cardiovascular events, and clotting disorders in the postoperative period. However, the overall number of adverse events across all stages were low[186,187].

Renal stone disease: Another renal adverse event with the potential for causing acute and chronic kidney damage is hyperoxaluria occurring after malabsorptive procedures [188-190]. A meta-analysis of 11 observational studies demonstrated that RYGB increases the risk of hyperoxaluria and renal stone formation[190]. Age, history of urinary tract infection, and renal stone disease correlate with a higher chance of new stone formation after surgery[191,192]. History of nephrolithiasis mandates close urological follow-up post-surgery.

Hyperuricemia: Obesity and hyperuricemia are closely interrelated and often coexist [193,194]. A meta-analysis of 20 studies with 5233 participants reported that the mean serum uric acid before surgery was 6.5 mg/dL. Metabolic surgery was followed by a transient elevation in serum uric acid in the first month, followed by a fall from the third month. The long-term incidence of gout was decreased[195]. There is a higher possibility of acute gout in the postoperative phase, and high-risk patients should be considered for prophylactic uric acid lowering medications before surgery[196,197].

NUTRITIONAL ASSESSMENT AND OPTIMIZATION

Recommendation 30

A preoperative nutritional assessment by a dietitian with expertise in bariatric counselling should be considered. Current macronutrient and micronutrient intake pattern should be evaluated. Medical nutrition therapy to optimize glycemic control before surgery should be reinforced. The candidate should be educated about dietary and lifestyle changes required after the surgery (E).

Recommendation 31

The low-grade chronic inflammation associated with obesity, destabilizes the iron homeostasis and predisposes to iron deficiency, and decreases iron bioavailability. A

complete blood count, serum ferritin, serum iron, total iron-binding capacity, and transferrin saturation (TS) is recommended during preoperative work-up. In presence of chronic inflammation denoted by serum CRP > 8 mg/L, serum ferritin loses specificity as an indicator of iron deficiency, and other markers like serum iron and TS should be used to define iron deficiency. Iron deficiency should be treated by oral iron supplementation. Parenteral iron should be considered if oral treatment is not tolerated or if early correction is needed (B).

Recommendation 32

Estimation of vitamin B12 and folate levels are recommended during pre-operative work up. In low-normal cases with high index of suspicion, measurement of serum methylmalonic acid and homocysteine levels can be considered. Vitamin B12 deficiency should be corrected by parenteral administration in symptomatic cases, whereas oral therapy is sufficient in asymptomatic individuals. Folic acid deficiency should be treated by oral supplements (B).

Recommendation 33

Vitamin D deficiency (VDD) is prevalent in individuals with obesity. Estimation of serum calcium and 25-hydroxyvitamin D (25(OH)D) is recommended before surgery. Serum parathyroid hormone (PTH) assessment can be considered in patients with VDD. Vitamin D should be replaced orally if VDD is present (B).

Recommendation 34

Estimation of copper, zinc, and selenium; and fat-soluble vitamins such as vitamin A, E and K can be considered before malabsorptive procedures.

Discussion

Nutritional counselling: A meta-analysis of three RCTs revealed that there was inadequate data to support or refute preoperative nutritional counselling[198]. A review on the same topic suggested that preoperative medical weight management strategies failed to achieve consistent benefits probably because of lack of dedicated trials[199]. Even then, nutritional counselling is safe, requires minimal resources, helps to create a rapport with the bariatric team and prepares the patient for necessary lifestyle modifications required around and after the surgery. It is an important adjunct to comprehensive bariatric care and is recommended by most guidelines[33, 136,200].

Anemia and iron deficiency: Micronutrient deficiency is common among candidates of metabolic surgery and worsens further during follow-up[201,202]. The prevalence of anemia and iron deficiency ranges from 6.1%-22% and 5.7%-24% respectively, in metabolic surgery candidates[203-207]. Low-grade inflammation associated with obesity can interfere with the intestinal absorption and iron utilization in the bone marrow[208,209]. Iron deficiency is characterized by serum ferritin < 30 ng/mL. CRP concentration above 8 mg/L is suggestive of overt inflammation, while levels between 3 to 8 mg/L conventionally signify subclinical inflammation[210]. In the presence of CRP > 8 mg/L, serum ferritin up to a concentration of 100 ng/mL indicates iron deficiency[211]. Serum CRP > 8 mg/L, serum ferritin > 100 ng/mL, and TS < 20% denotes anemia of chronic disease[212].

CRP > 5 mg/L, often associated with mild inflammation present in obesity, can alter iron metabolism[212,213]. Laboratory assessment of iron deficiency should be done at least 1 mo before surgery so that adequate time for replenishment of stores is available [214]. Iron supplementation is usually done through oral formulations, but parenteral preparations may be necessary if oral iron is not tolerated or if quick response is required[213,214]. Parenteral iron therapy has the advantages of rapid replenishment of iron stores before surgery and overcomes the uncertainty of absorption, compliance, and tolerability associated with oral therapy[214]. Systemic studies that investigate the benefits of parenteral iron therapy before metabolic surgery are required.

Vitamin B12 and folic acid deficiency: Vitamin B12 deficiency has been reported in up to 23% of candidates of metabolic surgery[206,215-218]. Additionally, metformin is known to cause deficiency of vitamin B12 in T2DM[219,220]. Folic acid deficiency is common among patients planned for metabolic surgery and is reported in up to 28% of cases[217,221,222]. Estimation of serum vitamin B12 and folate levels are recommended before surgery[33,223]. Low vitamin B12 should be treated by parenteral administration in megaloblastic anemia, neuropathy, or in presence of other deficiency symptoms[33,200,223-225]. A systemic review by Smelt *et al*[226] suggested

that daily oral administration of 350 µg of vitamin B12 corrects low levels in most cases. The guideline by AACE/TOS/ASMBS/OMA/ASA suggests oral vitamin B12 at a dose between 350 to 1000 µg every day. Alternatively it can be administered by nasal route[33]. Oral folic acid supplementation should be initiated to correct deficiency[33, 223]. Measurement of serum methylmalonic acid and homocysteine to assess for functional deficiency can be considered in cases with low-normal levels but high-index of suspicion, though such a strategy has not been validated[33,224,227,228].

VDD: Systematic reviews and meta-analyses have suggested that VDD is common in obese individuals and candidates of metabolic surgery[229-232]. Most guidelines recommend routine measurement of serum calcium and 25(OH)D before surgery[33, 201,223,224]. Estimation of serum PTH, serum or urinary N-telopeptide, bone-specific alkaline phosphatase, and bone mineral density can be considered if osteoporosis is suspected (especially in postmenopausal women)[224,233]. VDD should be corrected before surgery but there is no consensus on the exact dosage with guidelines recommending between 3000 IU daily to 50000 IU one to three times weekly[234].

Other trace elements: Malabsorptive procedures can cause deficiency of trace elements like zinc, copper and selenium and fat soluble vitamins (vitamins A, D, and E)[201,235-237]. Some of the guidelines suggest their preoperative measurement[33, 223,224].

ENDOCRINE AND REPRODUCTIVE FUNCTION ASSESSMENT

Recommendation 35

Case-by-case decision depending on the clinical profile should be undertaken to rule out the presence of endocrine disorders (E). Thyroid function test (TFT) should be ordered in those with past history of thyroid disorders. Medications for thyroid should be adjusted to ensure that the patient is euthyroid before surgery. In the absence of history, TFT is indicated if there is clinical suspicion of hypothyroidism or presence of goiter (E). If endogenous Cushing's syndrome is suspected, one or more of the following tests should be done: 1-mg overnight dexamethasone suppression test (ONDST), 24-h urinary free cortisol, or 11-pm salivary cortisol (E).

Recommendation 36

Women in reproductive age group scheduled to undergo metabolic surgery should avoid pregnancy. The possibility of improvement in fertility after surgery should be discussed. It is recommended to avoid pregnancy for 12-18 mo following surgery (B). Oral contraceptives or hormone replacement therapy should be discontinued 1 mo before surgery to decrease the risk of thromboembolism (E). If there is clinical suspicion of PCOS, total and bioavailable testosterone and USG of the pelvis assist in establishing the diagnosis. Hypogonadotropic hypogonadism (HH) is commonly reported in males with DM and obesity. Luteinizing hormone, follicle-stimulating hormone, and testosterone total should be measured in males if HH is suspected (E).

Recommendation 37

A decision to evaluate for monogenic or syndromic causes of obesity should be individualized (E).

Discussion

Thyroid disorders: The guideline by AACE/TOS/ASMBS/OMA/ASA recommends that patients known to have hypothyroidism should undergo TFT before surgery, and thyroxine dose should be adjusted to achieve euthyroidism[33]. A meta-analysis of 24 studies demonstrated that metabolic surgery decreased the thyroid stimulating hormone, free triiodothyronine (FT3), and total triiodothyronine levels. Additionally, thyroxine requirement was reduced in overt and subclinical hypothyroidism[238]. Preoperative FT3 above reference range and thyroid autoimmune status in euthyroid persons was shown to correlate with weight loss after metabolic surgery in small studies[239,240]. Larger studies are required to corroborate these findings. There is also a paucity of evidence to support routine preoperative evaluation of thyroid status in patients before surgery, but many insurance providers advocate it. Thyroid profile should be obtained if there are suggestive clinical features or if a goiter is present.

Cushing's syndrome: Cushing's syndrome has rarely been reported in patients undergoing metabolic surgery and should be ruled out by ONDST, 24-h urinary free cortisol, or 11-pm salivary cortisol if there is clinical suspicion[241-245]. If the screening tests are positive further evaluation is required.

Pregnancy and fertility: Most current guidelines recommend avoiding pregnancy if metabolic surgery is scheduled for a period of 12 to 18 mo after surgery[33,223,246]. A meta-analysis of 33 studies analyzing 14880 pregnancies after metabolic surgery indicated that pregnancies after restrictive surgeries tend to have a better perinatal outcome than after malabsorptive procedures[247]. In another meta-analysis, malabsorptive procedures as compared to restrictive procedures, were shown to increase the risk for small-for-gestational-age infants ($P = 0.0466$) but decreased the chance of large-for-gestational-age infants ($P < 0.0001$)[248]. Fertility rates in obese women with infertility were investigated in the meta-analysis by Milone *et al*[249]. Spontaneous pregnancy occurred in 58% of the 589 infertile women after surgery. Women in the reproductive age group should be counseled about the possibility of improvement in fertility after surgery, and contraceptive choices should be considered. The bioavailability of oral contraceptives can be decreased after malabsorptive procedures, and alternative contraception methods should figure in the conversation [250]. Estrogen preparations increase the risk of thromboembolism and should be discontinued 1 mo before surgery[33,246].

PCOS: Three meta-analyses have analyzed PCOS in relation to metabolic surgery[251-253]. PCOS was reported to be present in 36%-45.6% of women before surgery. Resolution of PCOS occurred in the majority of the cases after surgery[251,252].

Male hypogonadism: One of the meta-analysis reported the prevalence of male obesity-associated secondary hypogonadism to be 64%, with resolution occurring in 87% of patients following surgery[252]. A review demonstrated that metabolic surgery was more effective than a low-calorie diet (LCD) in improving free and total testosterone in obesity-associated HH[254]. Additionally, T2DM is also associated with low testosterone levels[255]. In the presence of suggestive clinical features, we recommend to rule out PCOS in females and HH in males during preoperative evaluation.

Monogenic or syndromic obesity: A genetic cause (monogenic or polygenic) is responsible for 5%-10% of early-onset severe obesity[256,257]. Non-syndromic monogenic obesity usually results from the affection of the leptin-melanocortin pathway[258,259]. Syndromic obesity refers to childhood-onset severe obesity associated with dysmorphism and neurodevelopmental and systemic malformations [260]. The common variants are Prader Willi, Bardet-Biedl, Cohen, and Alström syndromes[261]. There is limited evidence to support the role of metabolic surgery in genetic and syndromic obesity at present[256]. A cohort of 133 obese patients with monogenic obesity present among 8.4% of the candidates, were followed up 6 years after LSG. Subjects with monogenic obesity had less short and long-term weight loss than those who did not carry any mutation[262]. Similarly, metabolic surgery was ineffective in causing long-term weight loss in five patients with Prader Willi syndrome over a 10-year period[263]. The evidence to routinely screen for genetic causes in patients undergoing metabolic surgery is inadequate.

PSYCHOLOGICAL ASSESSMENT

Recommendation 38

Patients planned for metabolic surgery should be considered for a behavioral and psychosocial evaluation by a psychiatrist or psychologist with expertise in bariatric patients. Factors that can adversely affect the long-term outcome after metabolic surgery should be addressed (B).

Discussion

The health-related quality of life in severe obesity is worse in comparison to non-obese counterparts[264]. The psychiatric comorbidities in these patients are also high[265]. A formal psychological evaluation is suggested in the current guidelines[33,136,266]. A meta-analysis assessing preoperative mental health in 65363 patients before surgery, reported depression to be present in 19% and binge eating disorder in 17%. These

conditions, however, did not consistently affect weight loss after surgery. On the other hand, moderate-quality evidence demonstrated that the severity and prevalence of depression decreased after surgery[267]. A meta-analysis reported the overall rate of suicide after surgery was 0.3%, which was less than the general population rate of 1.4%[268]. Previous studies have documented a higher risk of suicide, especially in patients with underlying psychiatric disorders[269,270]. The possibility of higher risk of self-harm and suicide attempt after surgery was also suggested in another meta-analysis[271]. The International Federation for the Surgery of Obesity and Metabolic Disorders (IFSO) position statement considers severe and untreated psychiatric conditions like bipolar disorders, schizophrenia, active alcohol, and substance abuse, and bulimia nervosa contraindications for surgery[272]. Preoperative and postoperative psychosocial interventions, especially cognitive behavioral therapy, positively impacted eating behaviors such as binge eating and emotional eating and psychological functioning, including quality of life, depression, and anxiety[273]. The panel suggests psychological assessment to identify underlying comorbidities like depression and eating disorders and rule out alcohol and substance abuse and other frank psychiatric conditions that may interfere with surgical outcome. The patient's perception about contributors to obesity should be discussed, and the ability to cope with lifestyle changes after surgery as well as self-harm tendency should be assessed. Psychosocial interventions such as cognitive behavioral therapy might be beneficial, but structured RCTs analyzing the effect of such a strategy are few.

STRATEGIES FOR PREOPERATIVE WEIGHT LOSS

Recommendation 39

The benefits of preoperative weight loss have not been consistently proven though it has been mandated as a prerequisite by many insurance companies. Lifestyle interventions resulting in weight loss should be encouraged, however evidence demonstrating its benefit is inconsistent (E).

Recommendation 40

More aggressive strategies like very low-calorie diet (VLCD) (450-800 kcal per day) and LCD (800-1200 kcal per day) for 2 wk or more, not only induce weight loss but additionally decrease liver volume and technically assist in performing laparoscopy. There is lack of evidence to routinely recommend weight loss with VLCD and LCD before surgery although it can be considered as per institutional practice (C).

Discussion

Preoperative lifestyle changes lead to a mean weight loss of 7.42 kg in a meta-analysis but there was no effect on mortality or morbidity. The hospital stay was however reduced in the weight-loss group[274]. A meta-analysis suggested that intra-gastric balloon placement and very low-calorie diet (450-800 kcal per day) were the two most effective ways of achieving preoperative weight loss, while another meta-analysis in patients with BMI ≥ 50 kg/m² found only LSG and VLCD to be beneficial as bridging interventions[275,276]. Both LCD and VLCD induce weight loss and result in liver volume reduction[277,278]. The meta-analysis by Naseer *et al*[279] included four RCTs using VLCD and four other employing LCD. The authors inferred that the likelihood of achieving 5% weight loss was highest with a three week 700-1050 kcal diet, comprising of moderate carbohydrate, high protein and low or moderate fat. Though both LCD and VLCD cause preoperative weight loss the utility of such a strategy in improving perioperative outcome has not been validated[200]. The recommendation for preoperative weight loss to reduce liver size in order to improve the technical aspects of surgery was downgraded due to inconsistent evidence in the AACE/TOS/ASMBS/OMA/ASA guidelines published in 2019[33].

CONCLUSION

Obesity and DM are complex medical conditions and metabolic surgery is one of the few therapeutic options that alter their tendency for recidivism and progression. Individuals with diabetes are eligible for surgery at lower BMI cut-offs and emerging evidence suggests that the BMI threshold might be further decreased for Asians. Appropriate medical management of these disorders is however a critical prerequisite

for surgery. Our statement provides suggestions for systematically addressing the various conditions associated with DM and obesity that requires optimization before surgery. Dissemination and implementation of these guidelines would help to standardize the management of these comorbidities and improve the perioperative and long-term outcomes. Though these guidelines are comprehensive and up to date, more effort would be needed constantly, to update the rapidly evolving medical literature pertaining to this subject.

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