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Review

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Glycaemic control strategies in people with type 2 diabetes mellitus undergoing elective surgery

Naomi M. Fearon, **Dimitri J. Pournaras**

Dept of Bariatric Surgery, Southmead Hospital, North Bristol Trust, Bristol, BS10 5NB, United Kingdom.

Correspondence to: Dr. Naomi M. Fearon, Dept of Bariatric Surgery, Southmead Hospital, North Bristol Trust, Bristol, BS10 5NB, United Kingdom. E-mail: naomifearon@rcsi.ie

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Abstract
People with diabetes mellitus (DM) undergo more elective surgery than those without DM; however, up to half of the patients are undiagnosed when referred for surgery. This is an opportunity to intervene and instigate a management plan. Preoperative strategies may vary based on coexisting medical diseases such as obesity and the availability of resources with the aim of achieving glycaemic control while also treating coexisting conditions. In the context of obesity, there is substantial overlap in some of the treatment strategies. Guidelines, such as those from the UK Centre for Perioperative Medicine, suggest target glycated haemoglobin levels, preoperative fasting blood glucose levels, and when to defer an elective operation or instigate treatment to proceed if deemed safe. Preoperatively glycaemic control is often achieved pharmacologically, and newer agents, including glucagon-like peptide one receptor agonists (GLP1-RA) and sodium-glucose co-transporter 2 (SGLT2) inhibitors, are emphasised in the preoperative management of diabetes mellitus, particularly if obesity is also present. A very low-energy diet is an underutilised but well-evidenced method of achieving both glycaemic control and weight loss with a particularly dominant effect on liver fat which is helpful for people who are due to undergo abdominal surgery. Bariatric-metabolic procedures are of growing interest as bridging interventions to surgery and are more commonly used for obesity, but they also have a well-recognized impact on the improvement and remission of DM. This review gives an overview of the necessity of preoperative identification of DM and strategies for management. Intra-operative glycaemic control is also discussed, and the role of stress hyperglycaemia perioperatively.

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Keywords: Diabetes mellitus, surgery, perioperative, calorie restriction, very-low-energy diet

INTRODUCTION

People with diabetes mellitus (DM) undergo more elective surgery due to macrovascular complications such as coronary artery disease, peripheral vascular disease and kidney disease. Up to 50% of people with DM require surgery, and patients referred for elective surgery may have a 50% higher prevalence than the general population[1]. Furthermore, as the prevalence of obesity increases, this also contributes to the predicted increase in the prevalence of both diseases. Therefore, perioperative obesity and DM care must continue to improve and be seen as an opportunity to diagnose and instigate treatment for both the perioperative and long term[2,3].

Stress hyperglycaemia encompasses hyperglycaemia, insulin resistance and glucose intolerance. Physiological changes include increased glucagon, adrenaline, cortisol, and growth hormone release leading to increased glucose levels due to increased hepatic production and insulin resistance. This induces increased oxidative stress and pro-inflammatory cytokine release[4]. These changes occur in people with and without DM, can occur after acute illness, injury, or surgery, and can be worse in those without DM. Stress hyperglycaemia is associated with increased complications, increased mortality, and a longer hospital stay. More recent data suggests this is not a causal effect and is likely an adaptive response to trauma to maintain glucose transport to vital tissues[5]. This is supported by studies demonstrating that efforts to intensively manage glycaemic control during acute stress hyperglycaemia have been associated with worse clinical outcomes[6]. Acute stress hyperglycaemia may be beneficial; however, data also shows that chronic hyperglycaemia leads to fluid shifts, renal overload, and fluid depletion[5]. A stress hyperglycaemia ratio (SHR) evaluating relative hyperglycaemia has been explored by Roberts *et al.*, who report SHR as an independent marker of critical illness. The authors found that the SHR was not different in people with glycosylated haemoglobin (HbA1c) of more or less than 6.5 mmol[7,8].

This review aims to outline interventions for T2DM to prevent stress hyperglycaemia in people with DM, particularly the use of very-low-energy diets, pharmacotherapy, and metabolic surgery as bridging interventions [Table 1]. Elective surgery usually allows time to optimise clinical status for safer surgery. Some strategies may also apply to people with type 1 diabetes (T1DM) and obesity, reducing insulin resistance and/or improving glucose control.

SURGERY

Perioperative DM care is variable and often suboptimal. Furthermore, approximately 50% of people with DM are undiagnosed; therefore, improving efforts to identify and instigate early treatment is crucial to preventing long-term complications[9]. There is global variation in criteria for diagnosis of DM and pre-DM and variations in measurements and standards used for diagnosis and remission; this has been highlighted as a particular safety issue in reporting for diabetic ketoacidosis[10]. Previous studies have shown that people with preoperatively diagnosed DM have better perioperative outcomes than those with unidentified hyperglycaemia[11,12]. This reflects an improvement in glycaemic status and optimisation of other coexistent diseases, such as cardiovascular disease. This is likely due to better control of other modifiable risk factors and optimisation of coexistent conditions leading to a lower risk of acute myocardial infarction[13].

People with DM have a longer length of stay and higher postoperative complication rates than those without DM. A comprehensive care pathway from the UK Centre for Perioperative Care (CPOC) was published in March 2021 and provides guidelines on all aspects of care, from referral to discharge planning

Table 1. Role of different preoperative strategies for type 2 diabetes mellitus

Strategy	Evidence	Relative risk	Benefits	Downsides
Medications	Moderate/high	Low	Guidelines available Can be given in combination and individualised for patients' other co-morbidities, e.g., Obesity, Cardiovascular disease Long term management	Side effects May require titration Variations in cost and accessibility
Very-low-energy diet	Low/moderate	Low	Non-invasive, non-pharmacological	Requires a high level of patient commitment Not well understood or widely supported Can be expensive Short term
Bariatric procedure Eg, IGB, SG	Low	High	Potentially long-term remission/improvement (sleeve gastrectomy)	Cost Surgical complications IGB - short term

IGB: Intragastric balloon; SG: sleeve gastrectomy.

for people with DM[14].

PREOPERATIVE

Prehabilitation before elective surgery (both for benign disease and cancer) is continuing to develop and become a tool to improve postoperative outcomes. It may involve a single focus, such as a physical exercise program, or it may be a multimodal program implementing changes in exercise, nutrition, and provision of psychological support, with the intent to improve the persons' functional capacity before surgery and prepare them for the emotional and physical stress of surgery[15].

Preoperative optimisation of people with DM (both Type 1 and Type 2) needs to be carefully considered in the context of other co-morbidities, such as obesity, cardiovascular disease and hypertension. Initiating treatment can lead to hypoglycemic episodes, and there is an ongoing debate about the optimal target range for capillary glucose levels, particularly perioperatively. The accepted preoperative HbA1c target above which complications are more likely is 43 mmol/mol, and the point at which surgery should be postponed is ≥ 69 mmol/mol (UK)[16]. The evidence is mixed for determining the impact of HbA1c on postoperative morbidity and mortality; a number of meta-analyses in cardiac and non-cardiac surgery have shown a trend toward increased complications; however, there was significant heterogeneity in the included studies making it challenging to determine any definitive conclusions[17,18]. An overview of studies of preoperative bridging interventions is provided in Table 2. A major limitation is that surgical outcomes following the intervention are not provided.

Identification

Currently, The National Institute for Health and Clinical Excellence (NICE) guidelines do not recommend screening surgical patients[19]; however, the CPOC guidelines suggest that preoperative assessment should include an HbA1c check for all everyone, thus allowing identification of people with undiagnosed T2DM and a reflection of glycaemic control for those who already had a diagnosis of T2DM. A retrospective study from Garg *et al.* demonstrated the benefits of implementing a preoperative DM program. A simple HbA1c check at a preoperative appointment followed by referral for those with HbA1c > 8% and access to a postoperative diabetes service improved identification of T2DM, led to more frequent monitoring of blood glucose levels and fewer episodes of inpatient hypoglycaemia (4.93% down to 2.48%), and reduced length of stay[20].

Table 2. Studies of preoperative interventions for patients with diabetes mellitus

Author, year	Type of study	Patients included	Intervention	Period of intervention	Outcomes
Houlden, 2017	Observational, retrospective	75 patients with T2DM and severe obesity listed for bariatric surgery Mean age 51 ± 8.3 yrs 64% F Mean weight 134.4 ± 29.2 kg Mean BMI 48.2 ± 8.3 kg Mean HbA1c 9.0% ± 1.2%	Glycaemic optimization clinic - Medication adjustment (anti-obesity medications preferentially selected) - Nutritional support - Exercise prescription Seen monthly Phonecall weekly	5 months	75% reached HbA1c < 7.5% Mean absolute decrease in HbA1c 18.2 +/- 11.6% (range 1%-41%) Mean absolutely change in wt 1.9 +/- 8 kg (range -31.6 to +12.3 kg) Post-operative outcomes not reported
Holt, 2021	Open pilot feasibility study	17 patients with suboptimally managed T2DM (HbA1c > 53 mml/mol or 7%) Listed for Cardiothoracic surgery	Nurse-led preoperative clinic - Glucose management - Lipid management - Hypertension management - Exercise program - Smoking cessation	Approximately 3 months until 2 weeks postoperatively	- Median HbA1c was 10 mmol/mol (IQR -13, -3) lower prior to surgery than at baseline 2.5 kg reduction in body weight (IQR -5, -1 kg) 4.1 cm (-5.3, -2.0) reduction in waist circumference - no change in blood pressure, lipid profile or renal function
Garg, 2018	Observational, retrospective	All patients with T2DM included (3909 patients) Patients with HbA1c > 8% referred to diabetes specialists	Clinical program for preoperative diabetes management - Increasing the frequency of bg testing - Adjusting oral medications - Adjusting insulin	Variable, not specified	LOS reduced from 4.78 ± 5.23 days to 4.62 ± 4.28 HbA1c measurement at the time of preoperative visit increased from 31% to 69% More patients were admitted to ICU after the implementation of the program (regardless of diabetic status) Mean bg on the day of surgery was 146.4 ± 51.9 mg/dL before the program and 139.9 45.6 mg/dL after the program (P = 0.0028) Fewer patients presented with bg > 200 mg/dL after the program 32.5% of patients received a diabetes consultation during their hospital stay, compared with 13.2% of patients before the program Mean bg level during the hospital stay was 166.7 ± 42.9 mg/dL before and 158.3 ± 46.6 mg/dL after the program (P < 0.0001) Number of patients with ≥ 1 hypoglycemic episode(< 50 mg/dL) was lower after the program (2.48%) than before the program (4.93%)
Lee, 2019	Meta-analysis	13 studies including 550 patients with BMI > 50 kg/m^2 (mean baseline BMI of 61.26 kg/m^2) Underwent bridging intervention prior to definitive bariatric surgery	Bridging interventions included - First-step laparoscopic sleeve gastrectomy (LSG) - Intragastric balloon (IGB) - Liquid low-calorie diet program (LLCD)	Variable, not specified	In studies that reported comorbidity prevalence, there was 48 out of 62 (68%) remission or improvement in T2DM. Details not reported Subgroup analysis LSG - significant change in BMI (pooled mean difference 15.2 kg/m^2, 95% CI 12.9 to 17.5, P < 0.0001) LLCD - significant change in BMI (pooled mean difference 9.8 kg/m^2, 95%CI 9.82 to 15.4, P = 0.0006)

					IGB – non-significant change in BMI (pooled mean difference 10.8 kg, 95%CI -1.5 to 23.1, $P = 0.08$)
Colles, 2006	Observational, prospective	32 patients (19 men and 13 women) due to undergo bariatric surgery Mean (SD) age of 47.58 years BMI 47.35 kg/m^2 13 patients with T2DM	12-week VLED Requirements outlined by a dietitian at the start of program for all subjects attended fortnightly dietetic counselling The VLED ended just prior to surgery	12 weeks	All baseline descriptive characteristics for the 32 subjects decreased significantly: Bodyweight decreased by 14.87.2 kg BMI by 5.02.4 Patients with T2DM Glycated hemoglobin A1c(%) reduced from 7.21.8 (5.6-12.7) to 6.31.1 (5-9.6)
Griffin, 2020	Observational, retrospective,	78 patients due to undergo bariatric surgery who underwent a VLED preoperatively 16 patients with T2DM	Dependent on age and ability to adhere to dietary restrictions, patients were placed on a VLED of either 800 kcals, 900 kcals or 1200 kcals - Fortnightly dietitian appointments - Monitoring of weight, dietary intake and side effects - Encouragement of structured physical activity based on physical limitations and lifestyle factors - Education on progression to general healthy eating after treatment	12 weeks	Median Hba1c (%) reduced - median (range) 7.0 (6.4-10) down to 6.4 (6.1-7.7) Mean body mass index (kg/m^2), mean (SD) 44.3 (6.2) down to 41 (6.1) $P < 0.001$*
Lips, 2006	Observational, prospective	27 patients with severe obesity and T2DM An age-matched group of lean women (n = 12) was studied as the control group lean: 47 ± 7 years obesity: 52 ± 6 years	15 patients underwent bariatric surgery (Roux-en-Y gastric bypass) 12 patients were prescribed a very-low-calorie diet (VLCD) with an average calorie intake of 600 kcal/day Systemic inflammation was assessed one month before and three months after RYGB (n = 15) or VLCD (n = 12)	3 months	At baseline, body weight, BMI, insulin, glucose, HOMA-IR and HbA1c were higher in the patients with obesity than in the lean controls Three months after the intervention - Body weight and BMI markedly reduced both by RYGB and VLCD - BMI reduction was slightly larger in the RYGB group - Insulin and glucose levels, as well as HOMA-IR and HbA1c, were reduced to the same extent by both interventions
Pournaras, 2016	RCT	Fifteen patients aged 47.9 years were included - 8 female (53%) - Mean BMI 41.34 kg/m^2	Patients were randomized to either 2 weeks of VLED before surgery (n = 7) or normal diet before surgery(n = 8) VLCD = 800 kcal, including 70 g of protein, 15 g of fat, and 100 g of carbohydrates, plus the recommended daily allowance of essential vitamins, minerals, and trace elements	2 weeks preoperatively	2 weeks after VLED -4.83 kg (range: 1.7-10.4) weight loss compared to 0.71 kg (range: +0.5 kg to -2.5 kg) in the normal diet (ND) group (P = ns) Whole body insulin sensitivity values improved by 45%, while no difference was seen in ND Antidiabetic treatment - no difference between the groups at any time point Insulin sensitivity (M) improved by 45%, while no difference was seen in ND 2 weeks after RYGB ND group reported an improvement matching the level of the VLED group, while no further increase in M was seen in the VLED group 1 year after RYGB Equal increase in M values was seen in both

groups Significant correlation between M and weight for both groups

T2DM: Type 2 diabetes mellitus; BMI: body mass index; VLED: very-low-energy diet; bg: blood glucose.

Very-low-energy diet

A very-low-energy diet (VLED) can improve glycaemic control and has been utilised as an isolated intervention or as a preoperative bridging intervention before elective surgery. A number of randomised trials have demonstrated the efficacy of a medically supervised VLED with up to 60% remission of T2DM after 12 months and 30% after 24 months. Younger people with a shorter duration of T2DM are most likely to achieve remission, and the improvement in glycaemic control seems to happen very soon after the commencement of the VLED, indicating that the initial improvement is weight loss independent. Weight loss maintenance does not directly correlate with remission of T2DM, indicating a non-linear relationship[21].

A recent sub-analysis of the multicentre Almased Concept Against Overweight and Obesity and Related Health Risk (ACOORH) trial showed that longer-term insulin reduction correlated with weight reduction, and people with obesity who undertook a phased 24 weeks high glycaemic, low-energy diet involving three meals per day reduced their insulin levels significantly more than those who received nutritional advice and monitoring only[22]. The profound impact of calorie restriction was further demonstrated by Pournaras *et al.* They randomised people with T2DM undergoing Roux-en-Y gastric bypass (RYGB) to either an 800 calorie/day preoperative diet or no preoperative diet (ND). After two weeks, the VLED group had significantly improved whole-body insulin sensitivity. Two weeks post RYGB, both groups showed similar improvements in whole-body insulin sensitivity. However, the VLED group did not demonstrate much further improvement than what had been achieved after the VLED[23].

A VLED can be used as a preoperative 'liver shrink' diet to enable liver retraction and safer exposure for upper gastrointestinal surgery. Colles *et al.* used serial imaging to demonstrate a significant reduction in liver volume (LV), visceral adipose tissue (VAT) and subcutaneous adipose tissue (SAT) at weeks 2, 4, 8 and 12 while a VLED was followed. The overall relative reduction in LV, VAT and SAT was 18.7%, 16.9% and 17.7%, respectively. This correlated with a significant decrease in fasting insulin, HbA1c and cholesterol. After two weeks, 80% of the reduction in LV occurred. The VLED was composed of shakes which amounted to 456-680 kcal/day. People who were due to undergo laparoscopic adjustable gastric band surgery were enrolled[24]. A systematic review from 2016 included 15 studies that looked at VLED before surgery (> 80% bariatric surgery) and included people with and without T2DM. There was high variation in the included studies. Still, an overall high compliance rate was tolerated. A 5%-10% total weight loss and > 10% reduction in LV were shown, reflecting an overall improvement in metabolic status, including improved insulin resistance and blood glucose levels. The impact on perioperative hyperglycaemia was not measured/reported[25]. The complex interaction between NAFLD and DM is highlighted by the frequent coexistence of the two diseases. The prevalence of NAFLD is doubled in those with T2DM, and they also have a much higher incidence of complications such as cirrhosis and the development of hepatocellular carcinoma. Stefan and Cusi outline three mechanisms for developing NAFLD, including a strong genetic component whereby specific genetic variants are associated with both severe and complicated forms of NAFLD and DM and dyslipidaemia. A second mechanism is increased hepatic de-novo lipogenesis, which may occur in hyperglycaemia, leading to increased insulin resistance and an overall worse cardiometabolic status due to hepatic inflammation and endoplasmic reticulum stress. Both mechanisms are important in the interplay of NAFLD and DM and the differences in the management approaches. The third mechanism is adipose tissue dysfunction leading to increased free fatty acids and dysfunction in adipokine and cytokine release leading to increased hepatic inflammation[26]. Both the metabolic and anthropometrical improvements associated with a VLED are beneficial for any subsequent intra-abdominal operation, particularly where liver retraction is undertaken.

Griffin *et al.* provide observational and qualitative data on their dietitian-led VLED model of care for non-bariatric elective surgery, most of which was gynaecological surgery. There was high acceptance and satisfaction from participants and surgeons. There was a mean of 7.3% weight loss ($P < 0.001$), and although HbA1c levels trended down, it was not significant. Interestingly nearly 20% of participants were excluded due to non-engagement in the program. The reasons were not specified; however, this is likely to be a typical finding in any VLED program and leads to consideration of inpatient programs that may be more attractive or more accessible for those who find it challenging to engage[27]. Ruggenenti *et al.* randomised people with overweight/obesity and T2DM to either a 25% calorie restriction (CR) or standard diet. There was a significant improvement in the glomerular filtration rate at six months compared to a regular diet. The CR group also demonstrated improved HbA1c, blood glucose, and insulin sensitivity (measured by glucose disposal rate)[28].

Despite several studies showing the feasibility and benefit of a VLED, it is not commonly used preoperatively. This is likely due to a lack of awareness from the surgical teams and under-resourcing of the dietetic and endocrinology teams, who promote and support the intervention. However, with education and clear instructions, most people can carry out a VLED for a very short period. A collaborative, interdisciplinary approach for those undergoing surgery may allow identification of T2DM and, if present, facilitate access to resources to manage the disease with a focus on preoperatively and longer-term integrated care.

Pharmacotherapy

Currently, pharmacotherapy is the mainstay in the management of T2DM. An overview of available pharmacotherapy is provided in Figure 1. Variation in preoperative management is still evident; however, several recent high-quality studies contribute to the evidence base for instigating certain oral hypoglycaemics preoperatively. A feasibility randomised controlled trial (RCT) from the OCTOPuS study group included people with DM and an HbA1c > 53 mml/mol (or ≥ 64 mmol/mol in those more than 75 years old) who were due to undergo coronary artery bypass grafting (CABG). Several preoperative interventions were implemented, including pharmacotherapy. The emphasis was on initiating a sodium-glucose cotransporter-2 (SGLT-2) inhibitor or a glucagon-like peptide 1 (GLP1) receptor agonist, which has cardiovascular benefits. The median HbA1c was 10 mmol lower than that before the intervention[29].

Insulin remains the primary treatment for T1DM, and either as monotherapy or part of combination therapy for T2DM, oral or injectable non-insulin therapies have been unable to achieve glycemic control. The CPOC guidelines outline the dosage adjustments for each type and formulation of insulin in the preoperative period[14].

Obesity is a risk factor for T2DM, and there is an overlap in pharmacotherapy to optimise both diseases preoperatively. In particular, GLP1 receptor agonists and SGLT-2 inhibitors have good efficacy, proven cardiovascular benefits, and an acceptable safety profile[30]. Houlden *et al.* showed that preoperative

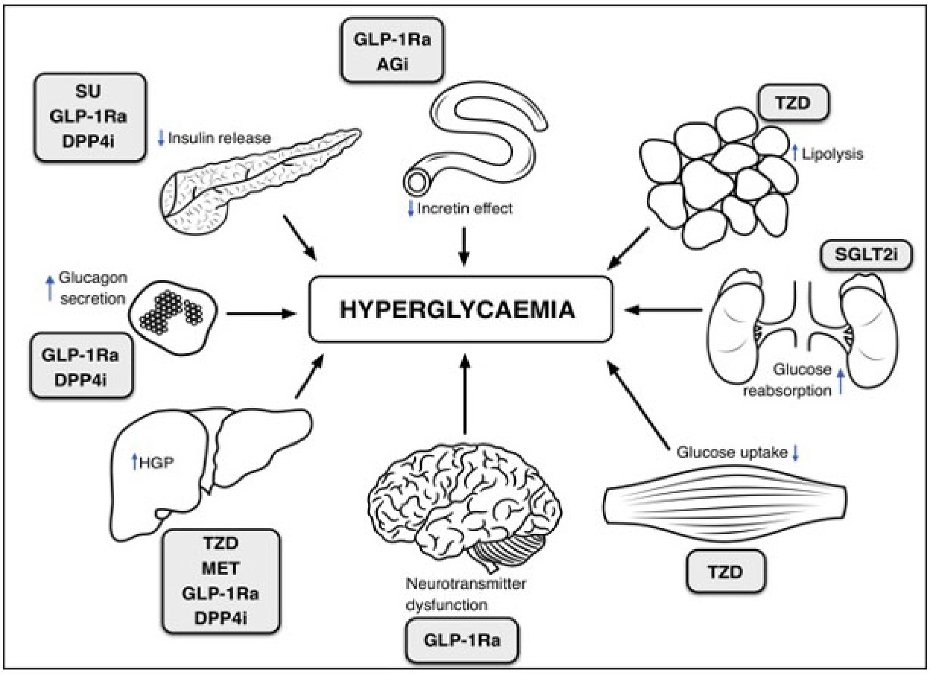

Figure 1. The ominous octet shows mechanism and site of action of medications that are used to achieve glycaemic control. GLP-1 RA: Glucagon-like peptide-1 receptor agonists; TZD: thiazolidinedione; SGLT2i: sodium-glucose co-transporter 2 inhibitor; HGP: hepatic glucose production; MET: metformin; DPP-4i: dipeptidyl peptidase-4 inhibitor.

interdisciplinary management of DM reduced HbA1c from a mean level of 9.0% ± 1.2% to ≤ 7.5% in three-quarters of people five months before bariatric surgery. The individualised treatment emphasised oral hypoglycaemics that were weight neutral or associated with weight loss, and all participants received nutritional counselling. They had weekly phone calls and monthly reviews with the interdisciplinary team, highlighting the benefit of outpatient support[31]. Newer treatments in this area include Tirzepatide, a dual glucose-dependent insulinotropic polypeptide and glucagon-like peptide-1 (GLP-1) receptor agonist, which has shown to be more efficacious in the treatment of T2DM compared to semaglutide, and in the treatment of obesity compared to placebo, in randomised studies[32,33]. Therefore, a short-term course of treatment such as a GLP1 receptor agonist, which reduces HbA1c and facilitates weight loss, will be a cost-effective intervention when balanced with the overall reduced perioperative costs.

Metabolic surgery

A meta-analysis of fifteen RCTs showed a mean reduction in HbA1c of 2% after bariatric surgery compared to 0.5% after best medical treatment[34]. Several studies are exploring the role of sleeve gastrectomy as a bridging intervention to another surgical procedure. A meta-analysis from Lee *et al.* evaluated people with a BMI > 50 kg/m^2 who underwent either sleeve gastrectomy (SG), liquid low-calorie diet (LLCD), or intragastric balloon (IGB) before RYGB. Those who underwent SG dropped their BMI significantly more than LLCD; those with an IGB did not lose significant weight (although only two studies were included). Remission or improvement in T2DM was reported in 63% of people; however, there were only 62 people with T2DM, and the criteria for remission were not outlined[35].

The IGB is placed endoscopically, under sedation or general anaesthetic, and can be left *in situ* for up to 12 months (depending on the manufacturer). Most people experience gastrointestinal side effects, and some do not tolerate it. A recent meta-analysis including 13 RCTs and 1523 people showed a significant difference in weight (4.4%, 6.1 kg) and BMI (2.13 kg/m^2) between the IGB and control groups (placement time three to eight months)[36]. A recent study from Abu Dayyeh *et al.* randomised participants to either an adjustable IGB and a lifestyle intervention program or a lifestyle intervention program alone[37]. Participants had the adjustable IGB for eight months and were followed up for six months. They underwent endoscopic adjustments during the eight months, depending on their intolerance symptoms and weight loss. The average weight loss in the IGB group was 15% compared to 3.3% in the diet and exercise group alone. A small subgroup of participants with T2DM had an improvement of 0.73% in HbA1c. Importantly, volume adjustment at the 18-week point prevented the removal of 75% of IGB in those who reported intolerance symptoms[37]. Unfortunately, it remains the case that these devices are only suitable for short-term use, and the likelihood of long-term weight regain is high; however, they remain a good option for short-term weight loss and improvement in glycaemic control and improvements in tolerability are to be welcomed. Endoscopic sleeve gastroplasty may be another option as a bridging intervention; Zorron *et al.* describe a case series whereby they include bridging to renal or liver transplant as an indication for ESG. Unfortunately, the details of subsequent procedures and outcomes are not reported[38]. The Multicentre Randomised ESG Trial (MERIT) recently reported a mean percentage of total body weight loss of 13.6% (8.0) after ESG at 52 weeks and 0.8% (5.0) for the control group (P < 0.0001). Secondary outcomes included co-morbidities, and the authors report significant improvement in fasting glucose concentrations, HOMA-IR and HbA c levels in the ESG group compared to the control group. Furthermore, 25 (93%) of 27 participants in the ESG group, compared with only four (15%) of 27 participants in the control group, reported a clinical improvement in DM[39].

There has been recent discussion about proceeding with bariatric surgery in the context of poor glycaemic control and a high HbA1c as improvement or remission in T2DM is an intrinsic benefit of metabolic surgery, and a large observational study from Albaugh *et al.* showed no difference in outcomes for people undergoing bariatric surgery who had a higher HbA1c. The mean preoperative HbA1c was 8.2 +/- 2.7% (66 +/- 29.5 mmol/mol) for the entire cohort; the outcomes of interest were a composite of major complications, a composite of infectious complications, length of stay > 5 days, re-admission within 30 days and re-operation within 30 days[40].

PERIOPERATIVE

The literature around the management of perioperative glycaemia is evolving. Several randomised control trials have been published evaluating perioperative glucose targets for cardiac surgery. This high-risk surgical group provides a setting where it is feasible to randomise fewer people due to the increased power to detect a difference. The GLUCO-CABG trial randomised people with and without T2DM to either a conservative or intensive glucose target. In participants with T2DM, there was no difference in the composite complication score; however, in those without T2DM (48% *vs.* 49%), there was a lower complication score in the intensive glucose target group (34% *vs.* 55%)[41]. A subsequent pilot RCT randomised 60 people without T2DM to preoperative (24 h beforehand) sitagliptin or placebo and found no impact on perioperative hyperglycaemia and the need for insulin therapy[42]. These outcomes appear to apply to non-cardiac surgery, where observational studies show similar findings. A retrospective study from van den Boom *et al.* has shown that HbA1c is a good predictor of perioperative glucose levels in both cardiac and non-cardiac surgery. However, it has challenged the evidence on HbA1c as a predictive marker for 30-day mortality[43]. Observational studies have shown that people with T2DM undergoing laparoscopic cholecystectomy are 17% more likely to have a more than three-day stay if preoperative glucose levels were ≥ 128 mg/dL (taken within 48 h before surgery)[44]. This has also been shown for elective laparoscopic nephrectomy for renal cancer and elective orthopaedic, colorectal and breast surgery[45-49]. Liraglutide, a GLP1 receptor agonist, has been suggested as a possible perioperative agent as an alternative to insulin in cardiac and non-cardiac surgery and can reduce the amount of insulin required on the day of surgery[50-52]. In contrast, guidelines around the use of sodium-glucose co-transporter 2 (SGLT2) inhibitors are clear that these medications should be stopped three days before surgery and should not be used in critical illness, prolonged fasting status, ketonuria, or ketonemia[53].

In general, pre-operative hyperglycaemia does not require surgery cancellation except in diabetic ketoacidosis or hyperosmolar nonketotic states, which may be confirmed with further biochemistry testing and require specific management. However, the person should be started on an insulin infusion with additional monitoring of blood glucose levels and could proceed to surgery if levels were below 16.6 mmol/mol[54].

Insulin use perioperatively is clearly outlined in CPOC guidelines, and up-to-date information can be found in the perioperative handbook provided by the Clinical Pharmacy Association[55]. In randomised studies, insulin delivery intraoperatively is of predominant interest, with options such as fully closed-loop insulin delivery showing promising outcomes for people with T2DM. Studies have shown that response to intra-operative delivery of insulin cannot be predicted based on diabetic status or previous use of insulin and does not appear to correlate with the presence of obesity or metabolic syndrome[56]. Duggan and Chen provide a comprehensive review of intra-operative glycaemic control. Epidural anaesthesia is associated with reduced intra-operative blood glucose levels, and different types of general anaesthesia, particularly total intravenous anaesthesia, are associated with better glycaemic control intra-operatively[54].

CONCLUSION

Improving perioperative glycaemic control starts with identifying, screening, and standardising criteria for safe elective surgery. Strategies for improving preoperative glycaemia and insulin resistance include calorie restriction, newer oral and injectable medications, and bariatric-metabolic surgery interventions such as intragastric balloons. The best strategy for each person should be based on other medical complications, their circumstances and wishes, and the availability of local resources and treatments. Further research could focus on the impact of these interventions on important clinical outcomes such as re-operation rates and mortality.

DECLARATIONS

Author's contributions

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Consent for publication

Not applicable.

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