Chapter 62
Chapters on Metabolic Syndrome Control and the Influence of Hormonal Changes Post-duodenal Switch (DS)

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62.1 The Hormonal Changes After a Duodenal Switch and Their Potential Mechanisms

The clinical improvements in obesity-associated complications seen after duodenal switch (DS) or biliopancreatic diversion (BPD) can be substantial. These include benefits to metabolic, cardiovascular, respiratory, reproductive and musculoskeletal health as well as improvements in renal disease and the reduction in overall and cardiovascular-associated mortality [1–3]. The mechanisms responsible that facilitates weight loss include:

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62.1.1 Reductions in Food Intake

When the first bariatric procedures were developed in the 1950s, the surgeons attempted to promote weight loss through the development of procedures that either restricted food intake or led to the malabsorption of calories. However, this hypothesis of inducing weight loss, through mechanical restriction, has been disputed in recent years, for several reasons. While on low-calorie diets, patients generally report an increase in hunger and a decrease in satiety [4, 5]. If DS/BPD's primary mechanism for weight loss was achieved through the restriction of food intake, one would expect similar symptoms in patients after surgery. However, these findings are very much in contrast with the eating behaviour seen in patients after DS. Patients report that they are generally less hungry and reach satiation faster during a meal [6, 7]. Caloric restriction through diet alone usually leads to a compensatory increase in the consumption of energy-dense food, but this occurrence is not observed in patients or animals after bariatric surgery [8, 9]. Indeed, one of the predominant reasons against the food restriction argument is seen in studies that demonstrate that patients who 'fail' bariatric surgery and have regained most of the initial weight loss can in fact consume the same amount of calories as pre-operatively, even though the size of their stomach has not increased substantially [10, 11]. Food intake can be higher after DS/BPD than after other procedures such as Roux-en-Y gastric bypass or sleeve gastrectomy alone, but it is important to note that the compensatory hyperphagia expected after DS/BPD, given the substantial weight loss, usually does not materialise even if calorie malabsorption is present [12].

62.1.2 Mechanical Factors

The research into the role of mechanical factors responsible for weight loss after DS/BPD has been conflicting, perhaps suggesting that its role is minimal or non-existent. The impact that different sizes of gastric pouches and stomas, in the case of RYGB and that of sleeve gastrectomy volumes, has on food intake and body weight is controversial. Some studies have shown that the smaller the gastric pouch and stoma diameter, the greater the weight lost [13–15], while other studies have disputed this [11, 13, 16]. Similarly, incongruent results have been found for the sleeve gastrectomy volumes [17–20]. Overall, the perceived influence of mechanical and restrictive factors on the effects seen after DS is widely accepted to have been previously overstated. It would appear that other mechanisms play a much greater role.

62.1.3 Malabsorption

According to Scopinaro, biliopancreatic diversion (BPD) is the classic malabsorptive bariatric procedure [2]. The degree of malabsorption for BPD/BPD-DS varies

according to the length of the common channel (50–125 cm), in which the digestion and absorption occur [21]. The shorter the common channel, the more effective the weight loss [22–24], but equally the more common side effects such as diarrhoea and severe vitamin A and D deficiencies become [22].

In 2015, Li et al. quantified the calorie malabsorption after DS in rats [25] and showed that BPD and DS led to significant reductions in weight gain, percentage of fat, and adipose tissue weight when compared to SG. BPD and DS produced intestinal hypertrophy, as well as higher plasma GLP-1 and PYY in both fasted and refed states [25]. However, Li concluded that the metabolic benefits seen in BPD/DS appear to be largely caused by food malabsorption. The elevation of anorectic GLP-1 and PYY are additional consequences of BPD/DS, which, together with malabsorption, however may also promote the metabolic benefits of BPD/DS [25].

62.1.4 Hypothalamic Signalling

Obesity is now considered a disease of the subcortical areas of the brain [26]. Within the subcortical areas of the brain, the hypothalamus is the control centre of hunger and satiety. It is by way of gut signals acting upon stimulatory or inhibitory neurons in the hypothalamus that determines if we are hungry or satisfied. Alterations in patients' gut hormones post-DS changes the stimulation/inhibition of the hypothalamus, thereby affecting appetite and satiety. The arcuate nucleus of the hypothalamus contains two groups of neurons with opposite effects. The first group synthesises pro-opiomelanocortin-derived peptides, among which melanocyte-stimulating hormone acts via the melanocortin receptor 4 (MC4R) on the peri-ventricular nucleus, lateral hypothalamus and the ventromedial nucleus to reduce food intake and increase energy expenditure [27]. The second group of neurons synthesise neuropeptide Y, agouti-related protein (AgRP) and γ-aminobutyric acid, which increase food intake and reduce energy expenditure by inhibiting proopiomelanocortin, but also by projecting to the peri-ventricular nucleus, lateral hypothalamus, ventromedial nucleus and dorsomedial nucleus [27]. The arcuate nucleus is also in direct contact with blood, enabling it to be responsive to nutrients and circulating gut hormones [28]. From first principles, DS surgery influencing hunger, satiety and weight loss by way of its effect on these hypothalamic neurons postoperatively makes sense. However, in practice, little evidence exists that bariatric surgery or DS reduces the weight 'set point' by altering the expression of key signalling elements in the hypothalamic nuclei.

In humans, RYGB has been shown to be effective at inducing weight loss even in patients with heterozygous mutations for MC4R [29]. This suggests that if hypothalamic signalling plays a role in the weight loss seen post bariatric surgery, it is not the solitary mechanism involved. Future studies need to examine the expression of these peptides in animal models of subjects post-DS and other bariatric surgeries, as compared to pair-fed sham animals. However, it is unclear whether these studies will lead to any viable pharmacological targets for obesity. This is because of the

failure of previously used centrally acting as weight loss drugs that were associated with substantial adverse effects (e.g. rimonabant, which has since been removed from the market) due to their action at multiple receptors and sites in the brain [30].

62.1.5 Gut Hormones and Leptin

In 1980, there was seminal work carried out that examined the hormonal changes after BPD surgery. Sarson et al. found reductions in the upper small intestinal hormones, motilin and gastric inhibitory polypeptide after both jejunoileal (JIB) and biliopancreatic (BPB) bypass surgery for morbid obesity, along with an increase in the ileal hormones, neurotensin and enteroglucagon [31]. Gianetta et al. studied insulin in these patients and found that postoperatively, there was a sharp reduction in basal and postprandial insulin values; however, this appeared to normalise after 15–20 months [32]. Finally, Civalleri et al. found that there were no significant differences in fasting and meal-stimulated peak plasma gastrin levels between patients with obesity and their control group and between any of the postoperative groups and the pre-operative group [33]. This work prompted decades of research into the hormonal changes seen after bariatric surgery and its relevance. The hormonal changes caused by these surgeries closely reflect the anatomical changes induced by each particular surgical technique. Today we know that DS changes the signalling from the gut to the hypothalamus and brainstem. The predominant hormones involved in this pathway are as follows:

62.1.5.1 Glucagon-Like Peptide-1 (GLP-1)

GLP-1 is secreted by the L-cells of the small bowel, with higher concentrations in the distal ileum and colon. The GLP-1 receptors are located in the hypothalamus, striatum, brainstem and substantia nigra, among other areas of the brain [34]. GLP-1 is produced in response to a meal and then increases satiety, reduces hunger and decreases food intake, through its effects on the hypothalamus and brainstem [35]. GLP-1 also increases insulin secretion, inhibits glucagon release and slows gastric emptying [36]. The postprandial GLP-1 levels are much higher after both RYGB and sleeve gastrectomy [37]. The altered anatomy and shorter gut seen in RYGB lead to the rapid delivery of nutrients to the distal ileum causing an increase of both GLP-1 (and PYY) levels [38]. Similar increases in gut hormones are seen after sleeve gastrectomy due to rapid gastric emptying [39]. In 2007, Borg et al. found that rats after BPD had higher levels of PYY, GLP-1 and GLP-2 when compared to the sham-operated group. They concluded that these higher levels were due to gut adaptation and hypertrophy that could be important in inducing and maintaining weight loss after bariatric surgery [40].

62.1.5.2 Oxyntomodulin (OXM)

OXM is an anorexigenic peptide co-secreted with PYY and GLP-1 in intestinal L-cells [41]. The administration of OXM reduces hunger, food intake and ghrelin levels as well as decreases gastric acid secretion, GE and duodenal motility [42]. Postprandial OXM is increased 1–2 months after RYGB [43] and may predict weight loss [40]. However, there have been very few studies looking at the change in OXM post BPD/DS.

62.1.5.3 Peptide YY (PYY)

PYY is also released from the L-cells of the distal small bowel after eating and acts at the arcuate nucleus of the hypothalamus, to decrease food intake but also via vagal afferents terminating at the nucleus of the solitary track, to signal satiety [44]. PYY also delays gastric emptying [45]. Patients with increased levels of PYY after RYGB had more weight loss [38, 46]. The postprandial release of the hormone peptide YY (PYY) is markedly higher after both RYGB and sleeve gastrectomy, but not after adjustable gastric banding or caloric restriction [4, 5, 47, 48]. The hypothesis is that PYY release is also higher in DS, although there is limited **data to support this**. Hedberg et al. found that although the pylorus is preserved in BPD/DS, stomach emptying is faster than in non-operated subjects. They observed how PYY levels are elevated in the fasting state after BPD/DS and a marked response to a test meal is seen, likely due to the rapid stimulation of intraluminal nutrients in the distal ileum [49].

62.1.5.4 Ghrelin

Ghrelin is a peptide produced by the X/A-like cells in the fundus of the stomach during fasting and acts on growth hormone secretagogue receptors [50]. Ghrelin levels are decreased after eating, with carbohydrates having more of a suppressive effect than protein and lipids [51]. Ghrelin stimulates neuropeptide Y-AgRP neurons within the arcuate nucleus [52] but also through the vagus and brainstem to increase food intake [53]. After sleeve gastrectomy, the levels of ghrelin are reduced [54]. Conversely, ghrelin levels are increased in the setting of calorie restriction and post-AGB [6]. A study on ghrelin concentration in patients with obesity prior to and 5 days and 2 months following BPD demonstrated that unlike after dieting or RYGB, only an initial reduction in ghrelin concentration was observed. However 2 months following BPD, when food intake had nearly completely resumed, ghrelin concentrations returned to the pre-operative levels [55]. This is consistent with the hypothesis that ghrelin production from the stomach is greatly influenced by the direct contact of ingested food with the gastric cells [56].

62.1.5.5 Leptin

Leptin is secreted by adipocytes and influences energy intake primarily by acting on the hypothalamus [57–59] to decrease food intake and increase energy expenditure [57]. Loss of fat mass and decreases in plasma leptin levels are seen in patients who restrict their calorie intake, either through dieting or post bariatric surgery [5, 60]. After dieting, hyperphagia is generally observed; however this is not seen in post bariatric surgery patients, suggesting that the additional physiological alterations after surgery are enough to counterbalance the reduced leptin levels [7]. de Marinis et al. studied BMI, insulin levels and leptin levels in patients post-DS. They found that leptin decreased rapidly, without correlation with BMI, indicating that body composition is not the only factor regulating leptin levels [61]. They also noted the consistent correlation between leptin levels with insulin levels suggesting an important interaction between these two hormones in post-BPD subjects [61].

62.1.6 Vagal Signalling

The contribution of the vagus nerve to weight loss after bariatric surgery and DS is an area that has not been adequately explored. However, its implication in the weight loss seen in patients post-DS is a source of great interest. The vagus nerve is a key signalling relay system between the gut and the brain and an important regulator of food intake and body weight. The presence of nutrients in the small intestine leads to the release of gut hormones, which exert part of their physiological effects through the vagus [62]. There is little data available that specifically examines the effect of DS on vagal signalling. Indeed, the limited data that does exist in the area looks at the effect of the other forms of bariatric surgery, e.g. RYGB or adjustable gastric banding and is inconclusive and often contradictory. In 2011, Seyfried et al. found that the preservation of vagal fibres during surgery was associated with greater and more sustained body weight loss in animal models of RYGB [63]. Bjorklund et al. human study supported this hypothesis by concluding that the rapid entry of food from the oesophagus, through the small gastric pouch, might trigger vagal signalling in the alimentary limb, which contributes to a reduction in food intake [64]. Conversely, Shin et al. suggested that the vagus did not play an important role after RYGB given that when they carried out a selective vagotomy to the hepatic branch of the vagus in rat models, it did not have an effect on food intake, weight loss and metabolic control [65]. Overall, the limited available data suggests that vagal signalling is the likely mechanism through which adjustable gastric banding reduces food intake and weight loss, rather than restrictive factors, and this is also likely to be the case in patients post-DS also.

62.1.7 Bile Acids

Bile acids can directly or indirectly affect food intake, energy expenditure and glycaemic control through their actions on membrane TGR5 receptors or nuclear FXR receptors and the release of fibroblast growth factors (e.g. fibroblast growth factors 19 and 21), which can exert their action on a wide range of tissues including the hypothalamus [66–68]. Bile acids also cross the blood–brain barrier, and their receptors have been identified in the brain [69, 70]. BPD/DS and other forms of bariatric surgery exert an effect on bile acid levels and type. These alterations in the levels or types of bile acids in the gut or the circulation have been implicated in the glycaemic improvements and even the reduction in food intake observed after bariatric surgery, particularly post-RYGB. Total plasma bile acids and their subfractions are higher after RYGB, but not adjustable gastric banding [71–74], and their levels negatively correlate with postprandial glucose levels [72]. Stefater et al. examined bile acids post sleeve gastrectomy and concluded that plasma bile acids are also elevated in animal models of sleeve gastrectomy [75]. This hypothesis is yet to be examined in BPD/DS. There is a need for further in-depth mechanistic analysis into the exact role that bile acids play as mediators of weight loss and glycaemic control after bariatric surgery, particularly after BPD/DS. However, by mediating the physiological effects of bile acids, fibroblast growth factors and their receptors, this represents exciting new therapeutic targets for obesity and type 2 diabetes.

62.1.8 Gut Microbiota

In recent years, there has been a focus on the potential role that alterations in gut microbiota have on obesity and weight loss. Some studies suggest that obesity is associated with unfavourable colonisation of the bowel with bacteria that are more efficient at extracting energy from nutrients and storing it as fat [76]. Indeed, part of the weight loss effect seen in patients after DS and other bariatric surgery may be achieved by a profound disturbance of this bacterial colonisation caused by the surgery. The data is limited, particularly when it comes to these bacterial changes post-DS but after RYGB that there is a reduction in the proportion of *Prevotellaceae*, *Archea*, *Firmicutes* and *Bacteroidetes* and an increase in the *Bacteroidetes*/*Prevotella* ratio and γ-proteobacteria postoperatively [77–79]. These alterations might be due to changes in dietary macronutrient composition, anatomical manipulations and pH and bile flow, among others [27]. Much like faecal transplant has proven to be very successful in the treatment of *Clostridium difficile* infections; a 2013 study by Liou et al. points towards the potential viability of a similar treatment modality for the treatment of obesity. Here, they observed how the transfer of the gut bacteria from mice post-RYGB to unoperated germ-free mice led to weight loss [80]. A rat study in 2019 found that BPD/DS caused marked alterations in faecal and small intestinal

microbiota resulting in reduced bacterial diversity and richness. It suggested that the increased abundance of *Bifidobacterium* and reduced level of two *Clostridiales* species in the gut microbiota might contribute to the positive metabolic outcomes of BPD/DS [81]. Once again, more studies and data are needed to explore the exact mechanisms through which gut bacteria contribute to weight loss. Exploiting this concept could help us explain some of the effects we see post bariatric surgery and indeed lead to more potential therapeutic targets.

62.2 The Impact of DS on the Complications of Obesity

62.2.1 What are the Metabolic Issues Caused by Obesity and How Do They Change After DS?

Obesity is defined as abnormal or excessive fat accumulation that presents a risk to health [82]. It is associated with an increased risk of all-cause mortality, with CVD and malignancy being the most common causes of death [83–86]. Excess weight can cause both anatomical and metabolic complications. Anatomical complications such as obstructive sleep apnoea (OSA), obesity hypoventilation syndrome (OHS) and osteoarthritis (OA) can occur due to increased adipose tissue placing strain at various body sites [87–89]. Indeed, increased intra-abdominal pressure is also associated with oesophageal disorders such as gastro-oesophageal reflux disease (GORD) and Barrett's oesophagus [90]. Some of the major metabolic complications of obesity include type 2 diabetes mellitus (T2DM), hypertension, cardiovascular disease, coronary heart disease, stroke and fatty liver disease among many more.

Biliopancreatic diversion with duodenal switch (BPD-DS) surgery is the most effective treatment to produce sustained weight loss with a greater improvement or resolution in obesity-related comorbidities [91, 92]. Using the King's Obesity Staging Score [93], the impact of DS on complications of obesity can be summarised as follows:

62.2.1.1 Airway

The risk of developing OSA increases 1.14-fold for every unit increase in body mass index (BMI) [94, 95]. Resolution of OSA after bariatric surgery is caused by several factors including weight-dependent [96] and weight-independent mechanisms [97]. In 2009, Greenberg et al. compiled a meta-analysis of OSA resolution post bariatric surgery. The results corroborated the previously reported improvements in AHI after bariatric surgery. The overall effect size of the pooled, weighted data showed a reduction of 38.2 events per hour in the combined study results, a

combined reduction in AHI of 71%. However, residual disease was seen in the majority of patients (62%) after bariatric surgery with a mean residual AHI of more than 15 events per hour [98]. It appears that while the more weight loss achieved post bariatric surgery, the more benefits that patients are going to see in terms of improvements in their OSA, the condition is unlikely to resolve altogether. This would favour BPD/DS, but more data are needed in relation to this.

62.2.1.2 BMI Reduction

Weight loss, the primary goal for most patients, is closely related to resolution rates of complications [99] and quality of life after bariatric surgery [100] although no exact cut-off point for these gains is established. In 2014, Hedberg et al. carried out a meta-analysis of 16 papers that compared the weight loss seen in patients post-DS vs. post-RYGB [101]. Significant weight loss was seen after both procedures, but DS led to an additional reduction of BMI. The weighted mean BMI loss after DS was 22.9 BMI units at 1 year, 25.0 BMI units at 2 years and 23.4 BMI units at more than 2 years. The corresponding results for RYGB was 17.1 BMI units at 1 year, 16.2–18.1 BMI units at 2 years and 15.8–18.3 BMI units at more than 2 years [101].

62.2.1.3 Cardiovascular Disease

Martin et al. found that weight loss after bariatric surgery can minimise and reverse obesity-associated left ventricular remodelling [102]. In a recent systematic review of studies evaluating cardiac structure and function before and after bariatric surgery using echocardiography or cardiac MRI, bariatric surgery was associated with improvements in cardiac structure (decreased left ventricular mass index, decreased left ventricular end-diastolic volume and left atrial diameter) as well as cardiac function (increased left ventricular ejection fraction and increased *E*/*A* ratio) [103].

Major adverse cardiovascular event rates in RCTs of bariatric surgery have been low, likely reflecting the relatively young age, short duration of diabetes and low prevalence of established microvascular disease among recruited individuals [102]. No significant differences in the occurrence of such events between surgically and medically treated patients have been demonstrated to date; however, cardiovascular risk factor reduction has been noted in bariatric studies:

Hypertension

Prevalence of HTN and OSA is higher in patients with severe forms of obesity in comparison to normal-weight patients [91, 104]. Prevalence of HTN can reach up to 70% in patients with obesity and OSA [105]. Hypertension is the complication for

which bariatric procedures are least successful, with a resolution rate varying between 15 and 53% [92]. Factors believed to hinder the chance of resolution of hypertension include duration of hypertension and the number of anti-hypertensive agents being used pre-operatively [96]. Conversely, the resolution rate of OSA following bariatric surgery is higher than HTN, with 79–86% of patients experiencing remission [106]. Patients with greater weight loss postoperatively have a greater chance of achieving OSA remission [96]. In a systematic review by Vest et al. which included 73 studies and 19,543 individuals undergoing a range of bariatric procedures including sleeve gastrectomy, RYGB and adjustable gastric banding, postoperative resolution or improvement of hypertension occurred in 63% of patients, with follow-up ranging from 3 months to ~15 years [107]. Other studies such as the Swedish Obese Subjects (SOS) study showed that no significant difference in the incidence of hypertension was observed between the two groups at 2 years (34% surgery vs. 21% control) and 10 years (19% surgery vs. 10% control) [108]. However, the SOS study was non-randomised, and the HTN was not the primary outcome of the trail. In summary, interpretation of the limited data on the resolution of HTN is conflicting. More RCTs in the area are required, most particularly in relation to the effects of DS on HTN.

62.2.1.4 Diabetes Mellitus

'Diabesity' describes the concurrent obesity and T2DM epidemic over the past few decades because the risk of T2DM increases with BMI. A recent population study involving 2.8 million UK adults between 2000 and 2018 showed that a BMI of 30–35 kg/m^2 was associated with a five times increased risk of T2DM, which increased to a 12 times higher risk in those with a BMI of 40–45 km/m^2 [109]. Bariatric surgery is an extremely effective way of treating diabetes.

In the ROME RCT study, Mingrone and Rubino studied DM remission in patients post bariatric surgery over a 10-year follow-up period. Individuals were randomly assigned (1:1:1) to either medical therapy, RYGB or BPD [110]. Analysis of this study showed 10-year remission rates in the intention to treat (ITT) population were 5.5% for medical therapy; 50% for BPD; and 25% for RYGB. Twenty of the 34 participants (58.8%) who were observed to be in remission at 2 years had a relapse of hyperglycaemia during the follow-up period (BPD 52.6%; RYGB 66.7%) [110]. After 10 years, patients who underwent surgery exhibited significantly greater HbA1c percentage reduction from baseline than those in the medical arm, while target HbA1c of less than 7% was met in 87.5% of patients who underwent surgery and in none in the medical therapy group [110].

Hedberg's 2014 meta-analysis again looked at the remission of T2DM in patients post-DS vs. post-RYGB and found that after DS, 88% of patients were free from treatment of diabetes at follow-up compared with 76% of RYGB patients, $P = 0.18$ [101]. HbA1c was reported in two of the included studies, and both show significantly lower levels after DS compared with RYGB [111, 112].

These findings are supported by Buchwald et al. systematic review of 132,000 patients in 2009 which showed that diabetes was resolved in 95% of patients having had DS or BPD compared to 80% after RYGB [113]. The higher T2DM remission rates after DS could be an effect of greater weight loss, but the exact mechanisms remain to be elucidated [114].

A systematic review and meta-analysis of gastric bypass and duodenal switch reported remission of type 2 diabetes mellitus in 88% of patients after duodenal switch and 76% of patients after gastric bypass [101]. Risstad et al. observed significantly lower mean values for fasting plasma glucose and haemoglobin A1c levels after duodenal switch than RYGB [115]. This could be clinically relevant because fasting plasma glucose level is associated with future incidence of type 2 diabetes mellitus, even with glucose within the normal range [116–118].

62.2.1.5 Economic

People with obesity are more than twice as likely to take sick leave and almost three times as likely to avail of disability benefits [108]. Medication prescription is reduced by bariatric surgery with resultant reductions in healthcare costs that can persist for up to 20 years [119, 120]. However, studies are needed to look at the specific economic benefits seen after DS.

62.2.1.6 Functional

Basic activities of daily living such as walking and personal hygiene can be affected by severe obesity, and this loss of autonomy can be extremely distressing for the affected individuals [121]. Bariatric surgery results in improved function status, reduced levels of back pain and greater levels of independence [122]. However, the specific functional benefits of BPD/DS over other bariatric surgeries have not been studied.

62.2.1.7 Gonadal

Moxthe et al. carried out a systematic review in 2020 on the effects of bariatric surgery on male and female reproductive health. Overall, the evidence from this review indicated that fertility parameters including sex hormones in both men and women, seminal outcomes in men, menstrual cycle and PCOS outcomes in women and sexual function in both men and women improved due to significant weight loss after various bariatric surgeries [123]. A study from Spain in 2005 examined the effects of BPD and gastric bypass surgery on women suffering from PCOS. It found that all PCOS patients recovered regular and/or ovulatory menstrual cycles after weight loss [124]. Furthermore, it found that hirsutism improved, and serum androgen concentrations returned to the reference range in all but one patient [124], thereby

curing the patients of PCOS after the bariatric surgery. Further research is also needed in assessing which type of bariatric surgery is most effective at weight loss and fertility improvements for obesity.

62.2.1.8 Health Status Perceived QoL

The fact of the negative effect of obesity and its related diseases on the quality of life is commonly known [125]. In 2020, Skogar et al. studied the differences in complications and QoL between RYGB and DS. They found that DS was associated with more early complications because of more open surgery, but long-term requirement of inpatient care was similar to RYGB [126]. They concluded that the increased risk of malnutrition/malabsorption and need for additional abdominal surgeries was contrasted with a greater improvement in QoL for DS [126]. More studies are needed to assess the effects of BPD/DS on QoL outcomes in patients.

62.2.1.9 Image

Body image dysphoria is often found in people with obesity, but this sometimes improves postoperatively [127]. A meta-analysis of both cross-sectional and longitudinal studies in 2018 suggest general improvements in body image occur following bariatric surgery [128]. However, there have been no studies specifically looking at these image changes following BPD/DS.

62.2.1.10 Junction of the Gastroesophagus

Gastroesophageal reflux disease is a common complication in bariatric patients [129]. Although weight loss and lifestyle modifications are important in reducing the symptoms of GERD, different bariatric surgeries have provided varying degrees of symptom alleviation [130]. Gastric banding has been shown to improve the symptoms of GERD in the short-term; however, a small subset of patients experience new reflux symptoms and oesophagitis in the long-term [131]. Laparoscopic sleeve gastrectomy has been associated with an increased incidence of GERD following the procedure [132]. The most effective bariatric procedure in the alleviation of GERD appears to be RYGB, which has been reported to have a similar efficiency as that of Nissen fundoplication [131, 133]. There has been a paucity of data looking at resolution of GERD following BPD/DS. Currently, significant GERD is a relative medical contraindication to BPD/DS that should prompt doctors to council the patient towards a RYGB rather than a DS, as gastric bypass achieves the greatest resolution of GERD-like symptoms. Furthermore, if a DS is performed on a patient with GERD and the symptoms persist despite maximal medical therapy, options for operative intervention are limited as the fundus of the stomach has been resected [131].

62.2.1.11 Kidney

In Mingrone et al. Rome study cohort, 16.%, 11% and 27% had albuminuria at baseline in the RYGB, BPD and IMT arms, respectively [112]. Albuminuria was present in 0% of the RYGB and BPD arms at 5-year follow-up compared with persistence of albuminuria in 27% of the IMT arm [134]. These results suggest that durable and sustained reductions in albuminuria are achieved in approximately 50% of patients at 5-year follow-up after bariatric surgery such as DS, compared with persistence or progression of albuminuria in those treated with best medical therapy alone [102]. Despite a potential beneficial impact on diabetic kidney disease, some concern exists that bariatric surgery, particularly RYGB and BPD, may be associated with adverse renal consequences such as hyperoxaluria and consequent nephrolithiasis [135, 136]. However, this has not played out in Mingrone et al. cohort where 'nephropathy' (defined as proteinuria >0.5 g/24 h) was also not significantly different between subgroups at 5-year follow-up (5%, 0% and 7% in the RYGB, BPD and IMT arms, respectively) [134]. Similar findings were seen in STAMPEDE and the Diabetes Surgery Study.

62.2.1.12 Liver: Nonalcoholic Fatty Liver Disease (NAFLD)

NAFLD is a spectrum of diseases that is associated with fatty infiltration of the liver that starts with simple fat accumulation (steatosis), which may progress into hepatic inflammation, termed as nonalcoholic steatohepatitis (NASH), with or without accompanying hepatic fibrosis/cirrhosis, with some patients eventually developing hepatocellular carcinoma [137–139]. There is a strong association of NAFLD with obesity, so weight loss has proved to have a beneficial effect on NAFLD [140]. Keshishian et al. reported the effect of DS on NAFLD. In this study, 697 patients were followed with a median of 6, 12 and 18 months and annually for 4 years. The histology results were only available in 78 out of 697 patients. These 78 patients had a second liver biopsy with a time interval ranging from 6 months to 3 years, depending on the need for a second operative procedure. Based on subjective assessment, the severity of steatosis had more than 50% reduction compared with baseline readings [141]. Similar results have been seen in studies looking at NAFLD following other bariatric procedures, e.g. Furuya et al. showed that (33%) of their patients displayed variable degrees of steatosis prior to surgery, which disappeared in 89% after 2 years ($P < 0.05$) [142]. However, once again more data from RCTs is needed to confirm this phenomenon and to better understand the underlying mechanism.

Patients with obesity and T2D have a quantity and distribution of adiposity causing pathologic levels of visceral and ectopic fat, insulin resistance, and impaired beta cell function [143]. While most bariatric surgeries are carried out electively, this variation in phenotype does present certain difficulties for the surgeon, theatre and hospital staff alike. The guidelines for pre-operative management of patients undergoing bariatric surgery are evolving, and any proposed standard of care is often based on opinion rather than level 1 evidence.

62.3 Glycaemic Control and Diet in Patients Undergoing Bariatric Surgery

Some authors suggest that patients pre-bariatric surgery should have an intensive 6-month programme of a supervised weight loss programme prior to any surgical intervention [144]. This process may aid the surgeon to be able to technically carry out the surgery, but it also provides the opportunity to intensify glycaemic management and to achieve glycaemic goals before surgery. If the patient has diabetes, then the adjustment of diabetes medications is usually required according to reductions in calorie and carbohydrate consumption and the level of glycaemic control of the patient [145]. Most bariatric centres also put patients on the 'liver shrinkage diet', i.e. a very low-calorie diet (VLCD) of <800 kcal/day for 2 weeks before surgery as a way of acutely reducing the size of the liver, making a laparoscopic technique easier and safer [145]. A VLCD can be achieved with meal replacements or a strict diet of portion-controlled lean proteins and non-starchy vegetables. Dose reduction or discontinuation of diabetes medications that can cause hypoglycaemia is required with initiation of these diets to prevent severe hypoglycaemia [146].

62.4 Pre-operative Glycaemic Management of the Patient with Diabetes Undergoing Bariatric Surgery

The AACE/TOS/ASMBS Bariatric Surgery Clinical Practice Guideline recommends that patients with T2D achieve a pre-operative HbA1c of ≤6.5–7.0%, a fasting blood glucose level of ≤110 mg/dL (6.1 mmol/L) and a 2-h postprandial blood glucose concentration of ≤140 mg/dL (7.8 mmol/L) [147], although these targets can be loosened in the cases of long-standing DM or if the clinician is happy to proceed. This guideline does not provide specific recommendations for diabetes medications to use pre-operatively but recommends discontinuation of insulin secretagogues and modification of insulin doses in the immediate postoperative period [147]. One large retrospective review of 468 patients with T2D who underwent RYGB procedures grouped them according to pre-operative A1C (<6.5, 6.5–7.9, and >8%) and found that those with the lower A1C levels experienced lower levels of postoperative hyperglycaemia, more weight loss and a greater likelihood of diabetes remission at 1 year. It remains difficult to conclude that these findings are due to patients with better glycaemic control having a less severe form of T2D. Postoperative hyperglycaemia was however independently associated with increased morbidity from wound infections and acute renal failure [148]. While there is limited similar data relating to DS, it is prudent to say that optimising the patient pre-op is most likely to lead to better postoperative outcomes. Therefore, patients should be encouraged to lose as much weight as possible, exercise regularly, eat and drink a healthy diet and keep their diabetes as well controlled as possible pre-operatively.

Patients taking oral and non-insulin injectable diabetes medications are advised to take their usual doses the day before surgery if their diet is not significantly changed [149]. Recommendations for adjustments to basal insulin are based on the patient's home regimen and generally can be in line with that for other major surgeries. All oral and non-insulin injectable diabetes medications should be discontinued on the day of admission for the bariatric surgical procedure. Patients with diabetes can have a capillary blood glucose (CBG) measured on arrival at the hospital and treated accordingly. Until more studies are performed and better data emerges, attention to glycaemic control minimises risk for adverse surgical outcomes similar to that which is observed with other surgical procedures. Poor glycaemic control as measured by HbA1c before surgery should however not be a contraindication to proceed with surgery [150–152]. This may be because the 2-week pre-operative diet is extremely effective at rapidly achieving near normoglycaemia before surgery [153], but also because the effect of surgery is so profound that even patients with poorly controlled diabetes often achieve normoglycaemia prior to discharge [154].

62.5 Psychologic Support Pre-operatively

The prevalence of psychosocial distress is high in patients seeking bariatric surgery [155, 156], and several studies have explored how psychosocial factors may predict weight loss, mental health and quality of life after surgery [157, 158]. Eating disorders are some of the most prevalent psychiatric disorders in the bariatric surgery patients [159]. Pre-operative binge-eating disorder (BED) is associated with more disturbed eating patterns after surgery and less favourable outcome, including greater weight regain [160]. There is some evidence that pre- and postoperative group counselling focusing on motivation for lifestyle changes and improving coping skills can be useful also for patients with psychiatric comorbidity and increase motivation and improve compliance with dietary and exercise guidelines [161]. Therefore, it is crucially important that psychological assessment and care is central to the pre-operative assessment and care of these patients. Not only has this been shown to improve postoperative success but also helps the medical team communicate realistic expectations for bariatric surgery for the patient. Often there is reduced capacity of psychological support pre-surgery and post-surgery. If faced with resource constraints, it may often be better to focus psychological support on the small number of patients who may benefit from it after surgery.

62.6 Dietician Support Pre-operatively

Nutritional deficiencies are commonly seen in patients presenting for bariatric surgery [162]. It is essential to screen and correct any abnormalities prior to surgery because pre-existing micronutrient deficiencies can involve poorer prognosis and postoperative complications [163].

The role of a bariatric dietician is central to the multi-disciplinary care of the bariatric patient pre-operatively for a number of reasons

1. Screen the patients: A thorough clinical nutrition evaluation that includes a micronutrient assessment should be carried out on all patients. This includes iron studies; B12; folic acid; vitamins A, C, D and E; zinc; copper; and selenium, among others [164].
2. Medical nutrition therapy (MNT): A second role of the dietitian is to prescribe to reduce weight pre-operatively, which can assist in minimising postoperative complications [165].
3. Pre-operative education: Recommended education strategies include nutritional consequences of the different bariatric surgery procedures, long-term follow-up requirements, compliance involved with adhering to a postoperative liquid diet and postoperative vitamin supplementation [147, 166].

A successful long-term outcome of bariatric surgery is dependent on the patient's commitment to a lifetime of dietary and lifestyle changes, so therefore it is essential to have a specialised dietician working with these patients throughout their journey through the bariatric service.

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