BARIATRIC SURGERY- COMPLICATIONS AND SAFETY OF LAPAROSCOPIC SLEEVE GASTRECTOMY PERFORMED AT A LOWER-VOLUME TERTIARY CARE CENTER

by © Vanessa Sophie Falk submitted

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Abstract

Newfoundland and Labrador (NL) has the highest rate of obesity in Canada, prompting the establishment of a bariatric surgery program at the Health Sciences Centre in St. John's, NL. This retrospective study examined less than 30-day complication rates in over 200 consecutive patients between May 2011 and February 2014 who underwent laparoscopic sleeve gastrectomy (LSG).

A chart review was performed and data collected on less than 30-day post-operative complications. Complications were graded and reported using the Clavien-Dindo Classification. Grades I and II were defined as minor and grades III and higher were defined as major.

The first 209 LSG patients were reviewed. The mean BMI was 49.2 kg/m^2, 81% were female and the average age was 43 years. Comorbidities included: hypertension (55.0%), obstructive sleep apnea (46.4%), dyslipidemia (42.1%), diabetes (37.3%), osteoarthritis (36.4%), cardiovascular disease with previous cardiac stents (5.3%). Furthermore, 38.3% of patients reported psychiatric diagnoses such as depression and anxiety. The overall 30-day complication rate was 15.3%. The complication rate for minor complications was 13.4% and for major complications was 1.9% (i.e., two leaks, one stricture and one fistula).

Our results support the feasibility of safely performing LSG surgery at bariatric centers performing fewer than 125 procedures annually.

General Summary

The aim of this graduation thesis ‘Bariatric Surgery- Complications and safety of Laparoscopic Sleeve Gastrectomy performed at a lower-volume tertiary care center’ is to analyze the feasibility of weight loss surgery in the form of laparoscopic sleeve gastrectomy at lower volume Canadian surgical centers. Bariatric surgery is a proven treatment for obesity; but while obesity is a wide-spread disease, bariatric surgery is only offered at a limited number of tertiary care centers across Canada. For this reason, the author decided to study the feasibility and safety of bariatric surgery carried out at a smaller tertiary care center. This thesis first examines the pathophysiology of obesity, available treatment options and bariatric surgery including complications. The third chapter is dedicated to the conceptualization and design of the thesis, which is a retroactive study of the first 200 bariatric procedures performed at a new bariatric surgery center in Canada. It describes the patient selection process, services provided to patients and definitions of what is considered a Bariatric Center of Excellence as well as grading systems used for post-operative complications. In the fourth chapter, the results of the study, specifically 30-day complication rates, are reviewed. When compared to outcomes of laparoscopic sleeve gastrectomy published in the literature, the new and smaller bariatric center did not do worse. These findings are encouraging to promote wider use of bariatric programs and surgery at smaller health care centers in order to fight the rising obesity pandemic. Further research may be helpful to provide guidelines for the set-up and continued care provided by new bariatric programs in Canada.

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List of Abbreviations

%EBMIL: percent excess body mass index loss

%EWL: percent excess weight loss

%WL: percent weight loss

5-HT2C: 5-hydroxytryptamine-2cytosol

ABS: American Board of Surgery

ACS: American College of Surgeons

ASBS: American Society of Bariatric Surgery

BP: blood pressure

BSCOE: Bariatric Surgery Center of Excellence

CD: Clavien-Dindo

CME: continuing medical education

CVD: cardiovascular disease

dBP: diastolic blood pressure

DLD: dyslipidemia

DM2: diabetes mellitus type 2

DSE: Diabetes Support and Education

DVT: deep venous thrombosis

EBT: endoscopic bariatric therapies

ER: extended release

ESG: endoscopic sleeve gastroplasty

FDA: Food and Drug Administration

GERD: gastro esophageal reflux disease

GLP-1: glucagon-like peptide-1

HDL: high-density lipoprotein

HTN: Hypertension

IGB: intragastric balloon

ILI: Intensive Lifestyle Intervention

IOP: Incisionless Operation Platform

Iv: intravenous

LAGB: laparoscopic adjustable gastric band

LDL: low-density lipoprotein

LMWH: low molecular weight heparin

Look AHEAD: Action for HEAlth in Diabetes

LOS: length of stay

LRYGB: laparoscopic Roux-en Y gastric bypass

LSG: laparoscopic sleeve gastrectomy

NICE: National Institute for Health and Care Excellence

NIH: National Institutes of Health

NL: Newfoundland and Labrador

NPO: nil per os

NSQIP: National Surgery Quality Improvement Program

OA: osteoarthritis

OSA: obstructive sleep apnea

PCOS: polycystic ovarian syndrome

POSE: primary obesity surgery endoluminal

PHEN/TPM: phenterminetopiramate

QOL: quality of life

RCT: randomized controlled trial

ROSE: Revision Obesity Surgery Endoluminal

RYGB: Roux en-Y gastric bypass

SAGES: Society of American Gastrointestinal and Endoscopic Surgeons

sBP: systolic blood pressure

sc: subcutaneous

SRC: Surgical Review Corporation

SHARE: Survey of Health, Aging, and Retirement

SOS: Swedish Obese Subjects

TORe: Transoral Outlet Reduction

List of Publications

Published manuscript

Laparoscopic sleeve gastrectomy at a new bariatric surgery center in Canada: 30-day complication rates using the Clavien-Dindo classification. Falk V, Twells L, Gregory D et al. 2016. Canadian Journal of Surgery. 59(2): 93-97.

Published Abstracts/ Poster presentation

Laparoscopic sleeve gastrectomy at a small Canadian center: 30-day complication rates. Falk V, Pace D, Twells L et al. SAGES 2015 Annual Meeting. Nashville, April 2015.

Does distance to travel for follow-up assessment or presence of depression influence weight loss after laparoscopic sleeve gastrectomy? Falk V, Twells L, Pace D et al. 4th Canadian Obesity Summit. Toronto, April 2015.

Pre-operative weight change as a predictor of post-operative weight loss following laparoscopic sleeve gastrectomy. Falk V, Pace D, Tewes S et al. SAGES 2016 Annual meeting. Boston.

List of Appendices

Chapter 1: Introduction

One of the newer diseases encountered worldwide is obesity. Obesity is defined as body mass index (BMI) greater than 30kg/m^2 and considered severe when BMI is greater than 40kg/ m^2.[1] It is closely associated with organ-specific and psychosocial comorbidities shown to affect patients' quality of life and overall life expectancy[2]. These adverse health risks increase with the severity of obesity. Worldwide, the obesity epidemic is rapidly growing and Canada is not excluded from this. Data from Statistics Canada shows that the rate of obesity has more than doubled since the late 1970s when obesity was affecting 13.9% of adult Canadians[3]. In their 2014 report, Twells et al predict that by 2019 half of the Canadian provinces will have more overweight or obese adults than normal-weight adults[4]. This sadly became true in 2018, when 63.1% of adult Canadians were classified as obese or overweight; of these, 26.8% were considered obese[5]. Obesity rates vary significantly among provinces with Newfoundland and Labrador having the highest rate of adult obesity at 40.2%[5].

The impact of obesity on health has been well studied and the following conditions have been shown to be initiated or worsened through obesity: diabetes mellitus type II, hypertension, dyslipidemia, obstructive sleep apnea, osteoarthritis, cerebrovascular disease, cardiovascular disease, and biliary disease[6,7]. Other disease entities associated with obesity include female infertility, polycystic ovarian syndrome, idiopathic intracranial hypertension, as well as increased rates of pregnancy related complications and fetal loss[8,9]. Furthermore, obesity has been shown to increase the risk of certain cancers, specifically colorectal, ovarian, breast, endometrial, esophageal, renal, pancreatic, and prostate cancer. All of these certainly contribute to the lower life expectancy obese patients have[10].

Patients suffering from obesity encounter multiple socioeconomic struggles, lower self-esteem, and studies show that the rate of depression and other mood disorders is higher among overweight and obese patients[11,12].

Multiple treatment modalities exist for obesity; however, few have been proven to give long-term success. Over the years, there has been a shift from the simplistic thinking that obesity is a matter of overeating and undermoving, to realizing that this is a multifactorial disease, which requires a multidisciplinary approach to treatment[12]. The one entity, which has proven to give long-term weight loss success is bariatric surgery and as such should be considered an essential component in the management of the obesity epidemic[13]. A variety of different types of bariatric surgery exist. Like many surgeries, some of these have stood the test of time and others have fallen out of favor. Historical procedures such as vertical gastric banding and ileocolonic bypass have been abandoned due to their high failure rate and long-term complications related to malabsorption of nutrients. There has also been a shift from open to laparoscopic surgery. Today, the most commonly encountered procedures are laparoscopic adjustable gastric banding (LAGB), laparoscopic sleeve gastrectomy (LSG), laparoscopic Roux-en Y gastric bypass (LRYGB), and laparoscopic duodenal switch[14]. In Canada, LRYGB is the current gold standard for bariatric surgery; however, the number of LSG is increasing and in the United States, LSG has take over LRYGB[15]. This shift is related to recent studies showing that LSG has similar results in regards to weight loss and comorbidity resolution, while having a shorter learning curve for surgeons and overall fewer complications[16,17,18].

Chapter 2: Background and Rationale

2.1.1 Epidemiology of Obesity

Obesity is the result of excess energy intake versus energy expenditure[1,2]. The development of obesity appears to be multifactorial encompassing genetic, behavioral, environmental, social, economic, biochemical, hormonal and neural factors[2]. A widely accepted measure of obesity in adults is the body mass index (BMI) calculated by dividing weight (kg) by the square of height (m^2). This can then be used to classify obesity (Table 1.1)[1].

Table 2.1: BMI and classification of obesity

BMI (kg/m^2	Classification	BMI (kg/m^2)	Classification
<18.5	Underweight	30-34.9	Class 1 obesity
18.5-24.9	Normal	35-39.9	Class 2 obesity
25-29.9	Overweight	>40	Class 3 obesity (morbidly obese)

2.1.2 Prevalence of Obesity

The incidence and prevalence of obesity are increasing worldwide. In 2018, 63.1% of adult Canadians were classified as obese or overweight; of these 26.8% were considered obese[3]. Obesity rates vary significantly among provinces (Table 2.1) with Newfoundland and Labrador having the highest rate of adult obesity at 40.2%[3]. A similar trend is seen in Canadian children, which suggests that the rate of obesity will climb, as obese children are more likely to become obese adults. Obesity is estimated to have cost the Canadian economy approximately $4.6 billion in 2008, up $735 million or about 19% from $3.9 billion in 2000[4].

Table 2.2: The proportion of residents aged 18 years or older who were obese in each Canadian province

Province	Proportion of obese adult residents
British Columbia	23.1%
Quebec	25.0%
Ontario	26.1%
Alberta	28.8%
Manitoba	30.8%
Nova Scotia	33.7%
Saskatchewan	34.8%
New Brunswick	35.3%
Prince Edward Island	37.8%
Newfoundland and Labrador	40.2%

National Average = 26.8%

2.1.3 Pathophysiology of Obesity

White adipose tissue is the largest endocrine organ; it secretes a variety of pro-inflammatory and anti-inflammatory substances[5]. Subsequently, obesity has been linked to a variety of health problems including cardiovascular disease (CVD), dyslipidemia (DLD), diabetes mellitus type II (DM2), musculoskeletal disorders, and increased risk of certain cancers (Tables 2.2 and 2.3)[6,7]. The risk of DM2 increases with the degree and duration of obesity, as well as, the amount of adiposity[8]. The metabolic syndrome is a constellation of central abdominal obesity, DLD, hypertension (HTN), and insulin resistance[9]. This constellation leads to elevated risk of CVD and development of DM2. Furthermore, in females, obesity has been associated with depression, stress incontinence, menorrhagia, amenorrhea, polycystic ovarian syndrome (PCOS), and infertility[10]. Obese pregnant patients have higher rates of maternal complications and negative fetal outcomes[11]. Research has shown obese patients to have a decrease in quality of life (QOL) and an increased risk of

mortality at any given age. Previous studies have shown the mortality risk of a young person with a BMI>35kg/m^2 to be double compared to a normal BMI counterpart[2].

Type II Diabetes

Diabetes mellitus type II is far more common than Diabetes mellitus type I. In general, DM2 has a later onset in life and is strongly associated with obesity, poor diet, and sedentary lifestyle. While increasing BMI has been associated with an increasing risk of developing DM2, waist circumference is also important in determining patients at risk for DM2[2]. The metabolic syndrome encompasses abdominal obesity, HTN, DLD and hyperglycemia. This syndrome is linked to insulin resistance and the development of DM2[6].

Dyslipidemia

Dyslipidemia describes elevated levels of cholesterol, triglycerides and low-density lipoprotein (LDL), and low high-density lipoprotein (HDL). These changes in lipid profile are a known risk factor for CVD[2]. Multiple previous studies, including the survey of health, aging, and retirement in Europe (SHARE) have shown a higher prevalence of DLD among overweight and obese people[12].

Hypertension

Elevated blood pressure (BP) or hypertension is defined as systolic BP (sBP) greater than 130mmHg and/or diastolic BP (dBP) greater than 90mmHg. Hypertension is a significant risk factor for cardiovascular as well as cerebrovascular disease. Obesity has been established to contribute to the development and worsening of HTN[6].

Cancer

Obesity has been estimated to account for 20% of all cancer cases with 14% of cancer deaths in men and 20% of cancer deaths in women[7]. Types of malignancies, which have been

identified, to be increased among obese patients are cancer of the colon, rectum, breast (post-menopausal women), endometrium, esophagus, thyroid, pancreas, gallbladder, and kidney. This increased risk of obesity and cancer appears to be linked to higher levels of inflammation in tissues of obese patients[7].

Table 2.3: Obesity associated comorbidities[6]

Disease	**Relative Risk Male**	**Relative Risk Female**
Type II Diabetes	6.74	12.41
Dyslipidemia	N/A	N/A
Sleep apnea	N/A	N/A
Hypertension	1.84	2.42
Stroke	1.51	1.49
Osteoarthritis	4.2	1.96
Coronary artery disease	1.72	3.1
Gallbladder disease	1.43	1.49

Table 2.4: Obesity associated cancers[7]

Cancer	**Relative Risk Male**	**Relative Risk Female**
CRC	1.95	1.66
Ovarian	N/A	1.28
Endometrial	N/A	3.22
Breast (postmenopausal)	N/A	1.13
Esophageal	1.21	1.2
Kidney	1.82	2.64
Pancreatic	2.29	1.6
Prostate	1.05	N/A

2.2 Weight Loss

2.2.1 Calculating Weight Loss

Guidelines suggest that weight loss be reported using the following measures[13]:

1. Initial mean BMI
2. Change in BMI (ΔBMI):
   ΔBMI = Initial BMI – Post-operative BMI
3. Percent total weight loss (%TWL):
   %TWL = (Initial weight – Post-operative weight) / Initial weight x 100
4. Percent excess weight loss (%EWL):
   %EWL = (Initial weight – Post-operative weight) / (Initial weight – Ideal weight) x 100
   and/or
   Percent excess BMI loss (%EBMIL):
   %EBMIL = [ΔBMI / (Initial BMI – 25)] x 100

Using percent rather than absolute weight loss in pounds takes into account the fact that patients with a higher starting weight tend to lose more weight. While many medical weight loss studies use %WL, in the bariatric surgery literature %EWL is preferred[13,14]. This expresses weight loss relative to a defined goal (i.e.: ideal body weight); however, the definition of ideal body weight varies and this can lead to discrepancies among study results[14]. Furthermore, %EWL is affected by the definition of initial weight, which could be the heaviest prior to surgery or weight on the day of surgery (often after pre-operative weight loss initiative such as liquid diets)[14]. Subsequently, some have suggested using %EBMIL as alternative to %EWL. The following table shows that %WL is generally lowest and %EBMIL is much higher; hence, one has to ensure that adequate values are compared when judging weight loss outcomes[15].

TABLE 1. Data comparing weight loss calculations among six hypothetical patients.

	GENDER	HEIGHT (INCHES)	INITIAL WEIGHT (POUNDS)	FINAL WEIGHT (POUNDS)	INITIAL BMI (kg/m²)	FINAL BMI (kg/m²)	MET LIFE IDEAL (POUNDS)	WEIGHT LOSS (POUNDS)	%WEIGHT LOSS (%WL)	%EXCESS WEIGHT LOSS (%EWL)	%EXCESS BMI LOSS (%EBMIL)
PATIENT 1	Female	69.5	197.8	182.2	29	27	147.5	16	8%	31%	59%
PATIENT 2	Male	73	320	230	42	30	165	90	28%	58%	69%
PATIENT 3	Male	69	301	245	45	36	153	56	19%	38%	42%
PATIENT 4	Female	61	160.8	139	30	26	122	22	14%	56%	76%
PATIENT 5	Male	72.5	211.2	181.6	28	24	163	30	14%	61%	120%
PATIENT 6	Female	66	214.2	180	35	29	137	34	16%	44%	57%

%EBMIL = excess BMI lost using 25 as baseline BMI

Figure 2.1: Comparison of weight loss calculations

2.2.2 Approach to Weight Loss and Goals

In 2000, the National Institute for Health (NIH) guidelines were released to guide practitioners in the assessment and treatment of overweight and obese adults[16]. The assessment of the overweight/obese patient includes measurement of BMI, waist circumference, as well as, presence of obesity-related comorbidities and risk factors. Comorbidities and risk factors conferring high absolute risk include coronary heart disease, other artherosclerotic diseases, DM2, obstructive sleep apnea (OSA), HTN, cigarette-smoking, high levels of LDL and low levels of HDL, family history of early CVD, and age (male ≥45 years and female ≥55 years)[16]. Based on these parameters, they present a treatment algorithm for the overweight/obese adult with a goal of initial weight loss of 10% body weight over 6 months or two pounds per week[16]. For patients with a BMI of 25-29.9kg/m^2 and absence of high risk factors, weight maintenance is an appropriate goal[16]. In order to achieve these goals, therapies may include dietary changes (reducing daily calories by 500-1000 kcal/day), behavior therapy (self-monitoring, stress management, stimulus control, problem-solving, contingency management, cognitive restructuring, social support), physical activity (minimum 30 minutes of moderate intensity physical activity daily), pharmacotherapy (as adjunct to lifestyle changes in high risk patients), weight loss surgery (for well-informed,

motivated patients with BMI ≥40 with or without comorbidities or BMI ≥35 with at least one obesity-associated comorbidity)[16]. While these guidelines provide an approach to obesity that integrates multiple treatment modalities, which are all important components of the treatment of this disease, few people are successful at achieving weight loss goals with lifestyle changes alone. The weight loss goal of 10% is further take into question after the long-term results of the Look AHEAD study[17,18].

The Look AHEAD study is a multicenter randomized controlled trial of patients with DM2 and BMI ≥25kg/m^2. Patients were randomized to either Intensive Lifestyle Intervention (ILI) or Diabetes Support and Education (DSE) with the goal to lose and maintain 7% of initial body weight. The primary outcome of the study was to determine if long-term weight loss in patients with DM2 could reduce cardiovascular morbidity and mortality. The early results of the Look AHEAD trial (2007) demonstrated that lifestyle modifications and weight loss of 5-10% in obese patients with DM2 improves HbA1C, BP, LDL, HDL, and TG levels. This in turn led to a decrease in medication use for treatment of DM2, HTN, and DLD[17]. However, the study was terminated early in 2012 based on a futility analysis and recommendation from the data and safety monitoring board[18]. Between 2001 and 2004, a total of 5145 patients were enrolled (ILI= 2570 and DSE= 2575). The average age was 58.7 years with a mean BMI of 36kg/m^2, 14% of patients had a history of CVD. At the time of study termination, the median follow-up time was 9.6 years with fewer than 4% of patients lost to follow-up. While patients in the ILI group had significantly greater weight loss, reduction in waist circumference, and improvement in fitness level, the difference in cardiovascular risk factors diminished over time. Patients in the ILI group overall lost more weight than DSE group (mean weight loss at 1 year 8.6% versus 0.7%), the ILI patients tended to gain weight

whereas the DSE patients lost weight over time (mean weight loss at study end ILI=6.0% versus DSE=3.5%). Interestingly, LDL cholesterol levels were lower in the DSE group; however, this should be interpreted with caution, as patients in this group were also more likely to be on cholesterol-lowering medications. There was no difference in the primary study outcome of death from cardiovascular causes between groups. The authors suggest that greater sustained weight loss than was achieved in the ILI group may be necessary to reduce cardiovascular disease[18]. Overall, there were multiple confounding factors to this study such as medication use. Results also cannot be generalized to the entire obese population as this study focuses on diabetic patients. However, the results are similar to other research, which has shown that sustained long-term weight loss is only achievable through bariatric surgery. Bariatric surgery has also been shown to improve comorbidities and mortality[19]. Newer pharmacologic agents and endoscopic bariatric interventions may proof successful for sustained weight loss, but long-term data is currently not available. The NICE obesity guidelines emphasize the multivariable approach in the treatment of obesity[12].

The following paragraphs will review the pharmacologic, endoscopic, and surgical treatment options for obesity.

2.2.3 Pharmacotherapy for Weight Loss

Pharmacotherapy for obesity is Food and Drug Administration (FDA)-approved as adjunct for treatment of patients with BMI≥30kg/m^2 or when BMI ≥27kg/m^2 with obesity-associated comorbidities[20]. While multiple medications are available, fewer than 3% of qualifying individuals are being treated by prescription medication[21]. Traditionally, obesity medications worked as appetite suppressants or anorexiants and gastrointestinal fat absorption blockers[20]. The most commonly prescribed appetite-suppressant is phentermine. Common

side effects are restlessness, insomnia, dry mouth, constipation, and elevated BP and heart rate[20]. A review of six RCTs showed that patients on phentermine lost an additional 0.6 to 6.0kg of weight compared to the placebo groups[22]. Another study using phentermine continuously or intermittently over 36 weeks demonstrated that treatment groups lost 20.5% of initial body weight compared to 6% in the placebo group[23].

Orlistat® is a lipase inhibitor, which can block the digestion and absorption of up to 30% of dietary fat. It is a synthetic hydrogenated derivative of lipostatin, which inhibits the pancreatic, gastric, and carboxylester lipases and phospholipase A2. The most common side effects of Orlistat® are increased defecation, fecal urgency, oily stools, and flatus with discharge. These side effects are related to the malabsorptive effect of the drug and can be controlled by limiting dietary fat intake[20]. Multiple randomized trials have shown that Orlistat® achieves a greater mean weight loss of 2.7 to 3.2kg compared to placebo[24-26].

Lorcaserin® is not currently approved for use in Canada, but has been marketed for weight loss in the United States since 2012. It is a selective 5-HT2C receptor agonist, which decreases food intake through the pro-opiomelanocortin system of neurons[20]. The most common side effects experienced are headache, dizziness, and nausea[20]. Two randomized, placebo-controlled, double-blinded trials showed mean weight loss was 4.8 to 5.8% in the treatment groups versus 2.2 to 2.8% in the control group[27-28].

Phentermine-topiramate (PHEN/TPM) combines a catecholamine releaser (phentermine) with an anticonvulsant (topiramate). This medication is also not approved in Canada. The exact mechanism for weight loss is unknown, but PHEN/TPM reduces food intake. The most common side effects are paresthesias, dry mouth, constipation, dysgeusia, and insomnia[20]. Two 1-year randomized, controlled, double-blinded trials assessed the efficacy and safety of

PHEN/TPM. The results showed that mean weight loss for treatment groups was 10.4 to 11% compared to 1.6 to 1.8% for placebo groups[29-30].

It has to be noted that a completion rate in the aforementioned trials for Lorcaserin® and PHEN/TPM was only 55.4 to 62%. This brings into consideration the compliance aspect of pharmacotherapy. In general, a prescription effectiveness period should be set for these medications. If weight loss of 5% baseline body weight has not been achieved after 12 weeks of treatment with Lorcaserin®, the drug should be discontinued. In the case of PHEN/TPM, a dose escalation can be considered if weight loss after 12 weeks is less than 3%; however, if the patient does not lose at least 5% after another 12 weeks of treatment, the drug should be discontinued[20].

In August 2015, Canada approved liraglutide marketed as Saxenda® for weight loss therapy[31]. Saxenda® is a high dose liraglutide (3.0mg subcutaneous (sc) daily) formulation. Liraglutide is a glucagon-like peptide-1 (GLP-1) receptor agonist. Binding of the receptor leads to suppression of appetite and slowed gastric emptying[32,33]. Common side effects are nausea and vomiting, but these seem to be transient and can be mitigated by slow dose titration[31]. In multiple randomized controlled trials, Saxenda® led to a mean weight loss of 4.2 to 5.9kg greater compared to placebo[34-36]. Compared to Orlistat®, patients taking Saxenda® lost on average an extra 3kg[34]. Astrup et al compared Saxenda® to Orlistat® and placebo in a randomized, double-blind trial[37]. After 20 weeks, patients on Saxenda® had greater improvement in fasting glucose, hemoglobin A1C, and greater reduction in metabolic syndrome compared to both Orlistat® and placebo[37].

The latest medication to be approved for weight loss in Canada (February 2018) is buproprion/naltrexone, which is marketed as Contrave®. The mechanism of weight loss is

thought to be through stimulation of anorexic hormones while simultaneously inhibiting counter-acting hormones[38]. The most common side effects are nausea, dizziness, and headache[39]. In clinical trials, the naltrexone/buproprion combination led to mean 8.1% total weight loss[39,40]. Patients on Contrave® also had significant improvement in waist circumference, insulin resistance, and cholesterol levels[39].

Common to all the above medications is that they required significant patient compliance and in order to maintain weight loss have to be taken for life. Pharmacotherapy has not been able to achieve the degree of weight loss seen after bariatric surgery; however, it remains a very valuable option in overweight patients and the obese patients who do not qualify for surgery. The aforementioned medications have all been shown to achieve a minimum of 5% weight loss at 52 weeks[41]. In a meta-analysis by Khera et al, PHEN/TPM and Saxenda® had the highest odds of achieving weight loss of at least 5%[41]. Furthermore, increasing research has shown the utility of using pharmacotherapy for bariatric patients who regain weight after surgery or achieved inadequate weight loss[42,43].

2.2.4 Endoscopic Bariatric Procedures

Endoscopic bariatric therapies (EBT) are becoming more popular as they offer a less invasive and reversible treatment options for obesity. These procedures may play a role as primary therapy, bridging to bariatric surgery, or as revisional procedure after bariatric surgery[44]. EBT can be classified based on mechanism into restrictive, bypass, space-occupying, or aspiration therapy. Alternatively, they can be classified based on their anatomic location into gastric, duodenal, or intestinal[44,45]. The various types EBT will be reviewed below.

Intragastric balloons

The first FDA-approved intragastric balloon (IGB) was the Garren-Edwards Gastric Bubble in 1984. Due to complications and unsatisfactory weight loss, this device was discontinued in 1988[46]. Intragastric balloons are space-occupying devices, which induce gastric distention and delayed gastric emptying leading to satiety[47]. Both fluid-filled as well as gas-filled balloons exist. While fluid-filled IGBs have greater weight loss success, they may also be associated with higher rates of intolerance and early removal[48]. Three IGB devices are FDA-approved: Orbera® (Apollo Endosurgery, Austin, TX), ReShape Duo® (ReShape Medical, San Clemente, CA), and Obalon® (Obalon Therapeutics, Inc, Carlsbad, CA). These balloons should stay in situ for no longer than 6 months, but repeat therapy is possible. Patients who receive IGB therapy are placed on daily proton pump inhibitors to prevent gastritis and ulceration. To help with common symptoms of nausea following IGB insertion, many advocate for the use of regular antiemetics, especially in the form of scopolamine patches for the first week. Balloons are removed endoscopically after 6 months. This is generally done under general anesthesia to prevent aspiration. One should also consider use of an esophageal overtube to prevent esophageal perforation.

Orbera® (Apollo Endosurgery, Austin, TX)

The Orbera® IGB is spherical in shape, silicone based, filled with 450-700ml of saline. Some advocate adding methylene blue to the saline solution, as this will change urine color if systemically absorbed, as would be the case in balloon rupture. This can be an early warning sign for patients[45]. The balloon is attached to a catheter, which is advanced into the stomach in similar fashion to an orogastric tube. A gastroscope is then advanced into the stomach and the balloon inflated under direct endoscopic visualization. After 6 months, the balloon is

deflated and removed endoscopically. In their meta-analysis of 6645 patients, Abu Dayyeh et al showed the pooled estimated %TBWL after 6 months to be 13.2%[49]. Common adverse events were nausea and abdominal pain, occurring in up to one third of patients. The early removal rate was 7.5%. Serious adverse events such as balloon migration (1.4%) and perforation (0.1%) were rare[49].

ReShape Duo® (ReShape Medical, San Clemente, CA)

This endoscopically placed IGB device consists of two balloons attached to one another via a flexible tube. Each balloon has independent filling channels, which means that single balloon deflation or leakage does not affect the other balloon; therefore, preventing device migration. Each balloon is filled with 450ml of saline/methylene blue solution[45]. The balloon is removed endoscopically after 6 months. In a randomized sham-controlled trial of 326 patients, after 6 months, the ReShape group achieved a %TBWL of 7.6±5.5% compared to 3.6±6.3% seen in the control group[50]. Early retrieval occurred in 15% of patients. While 6% experienced spontaneous balloon deflation, none of these were complicated by migration. A common early problem was ulcer formation, which led to balloon redesign and reduction of ulceration to 10.3%[50]. Complications specific to balloon retrieval included an esophageal mucosal tear, a contained cervical esophageal perforation, and aspiration pneumonia[50].

Obalon® (Obalon Therapeutics Inc, Carlsbad, CA)

This IGB is a gas-filled device holding 250ml. It is swallowed under fluoroscopic guidance. The balloon is enclosed in a capsule and attached to a catheter allowing the balloon to be filled with gas once intragastric location is fluoroscopically confirmed[44]. Up to three balloons can be inserted immediately or sequentially[45]. The IGB is removed endoscopically by first puncturing it for deflation and then grasping it for retrieval after 12 to 26 weeks[45].

Common side effects are abdominal pain and nausea[44]. In a randomized sham controlled trial of 387 patients for 24 weeks, the Obalon® group achieved a %TBWL of 6.81±5.1% compared to 3.59±5.0% seen in the control group[51].

Other IGB systems that are not FDA-approved but used in other parts of the world include the Spatz® adjustable balloon system (Spatz Medical, Great Neck, NY) and the Ellipse® balloon (Allurion Technologies, Wellesley, MA). The Spatz® system is endoscopically placed, saline-filled, with an inflation tube allowing for intragastric volume adjustments of the balloon. Outside of North America, the Spatz® balloon is approved for use up to 12 months[45]. The Ellipse® balloon is enclosed in a capsule attached to a catheter. Once swallowed, the capsule dissolves in the stomach and the balloon is filled with 550ml of fluid. The balloon remains in the stomach for approximately 4 months, when a valve opens and allows the balloon to empty. The balloon is then excreted via the gastrointestinal system spontaneously, obviating the need for endoscopy all together[45].

Gastric Restrictive Procedures: Endoscopic Suturing and Plication

New endoscopic instruments allow remodeling of the stomach via suturing, stapling, or tissue anchor placement[44]. These procedures require advanced endoscopic skills and general anesthesia with endotracheal intubation.

Endoscopic sleeve gastroplasty (ESG)

This technique involves reduction of the gastric lumen through full-thickness sutures placed transorally with endoscopic suturing devices. The result is similar to a surgical sleeve gastrectomy. In a multicenter study of ESG performed with the Overstitch™ (Apollo Endosurgery) in 248 patients, weight loss was reported as %TBWL 15.2% (n=215) at 6 months and 18.6% (n=92) at 18 to 24 months[52]. Five patients (2%) experienced serious

adverse events including two perigastric fluid collections treated with percutaneous drainage and antibiotics, one extragastric hemorrhage that required transfusion, one pulmonary embolism, one pneumoperitoneum and pneumothorax treated with chest tube[52]. These numbers are promising but plagued by significant loss of patients to follow up. Furthermore, the longevity of the ESG has not been proven. However, in a small study (n=25) by Lopez-Nava et al, after one-year follow-up, only one patient required revision partial gastroplasty due to loosening of the plications[53]. They argue that ESG is reversible as gastric anatomy is not definitively altered, therefore, the technique is reproducible and repeatable[53].

Primary Obesity Surgery Endoluminal (POSE)

This technique involves a per-oral incisionless operating platform (USGI Medical, San Clemente, CA) with four working channels. Three transmural tissue anchor plications are placed in the gastric fundus plus three more in the distal gastric body. This reduces gastric volume and delays gastric emptying[45]. In a pivotal multicenter randomized blinded clinical trial of 221 patients, POSE was associated with 12 months %TBWL of 4.9±7% compared to 1.4±5.6% seen in the control group. Adverse events occurred in 4.7% of patients; ranging form nausea and vomiting leading to prolonged hospital stay, to extra-gastric bleeding requiring surgical exploration and control[54].

Other devices are marketed for gastric suturing and stapling. Originally named EndoCinch™ (Davol, Murray Hill, NJ), which takes superficial-thickness bites for endoscopic gastroplasty, the device was modified and renamed ReSTORe™ (Davol, Murray Hill, NJ), which is capable of fullthickness suturing[44]. Unfortunately, even after modification, follow-up endoscopy revealed partial or complete plication failure in 13 out of 18 patients[55]. The TransOral Gastroplasty™ device (TOGA; Satiety Inc, Palo Alto, CA) is a flexible

endoscopic stapler that creates a full thickness vertical gastric sleeve 8cm long and 2cm in diameter[44]. A small study of 21 patients showed gaps in the staple line in 13 patients after one year[58].

Bypass devices

Bypass of the small intestine leads to significant weight loss as well as physiologic alterations including improvement in blood glucose levels. In bariatric surgery, this is achieved through procedures such as the Roux-en Y gastric bypass (RYGB) or duodenal switch; however, various endoscopic devices have been developed to reproduce this bypass effect[44].

EndoBarrier™ duodenal-jejunal bypass liner (GI Dynamics, Lexington, MA)

This 60cm polymer sleeve contains a nickel-titanium implant, which anchors it to the duodenal bulb. The sleeve extends from the duodenum into the jejunum, preventing food from touching mucosa and being absorbed while allowing biliopancreatic secretions to pass[44]. Placement is done endoscopically under general anesthesia with fluoroscopic guidance. The sleeve can remain in situ for 12 months[45]. Removal is also done under general anesthesia endoscopically by placing a foreign body hood at the tip of the gastroscope and grasping the device anchor[44]. Small duodenal bulbs are associated with implantation failure[57]. In a multicenter randomized controlled trial of 77 diabetic patients, the 6-months %EWL was significantly higher in the EndoBarrier™ group at 32% versus 16.4% in the control group[57]. While the difference remained significant, patients did experience weight regain following device removal with %EWL decreasing to 19.8% in the treatment group at 6 months after removal, compared to 11.7% in the control group[57].

Another product under development is the gastroduodenojejunal bypass sleeve (Valen Tx Inc, Hopkins, MN).

Small Bowel Interventions in Development

The duodenal mucosal resurfacing procedure (Fractyl Laboratories, Cambridge, MA) involves ablation of the superficial duodenal mucosa via a catheter that delivers hot water after submucosal injection. It is thought that the mucosal remodeling after ablation will reset duodenal enteroendocrine cells, therefore improving diabetic control with minimal decrease in body weight[45]. Self-assembling magnets (GI Windows, Boston, MA) can be deployed endoscopically to create a dual-path enteral bypass between the proximal jejunum and ileum. This can improve diabetic control and lead to weight loss[45].

Aspiration Therapy

The AspireAssist™ (Aspire Bariatrics, King of Prussia, PA) is a large diameter gastrostomy tube with an external accessory allowing aspiration following meals[44]. The tube is inserted similar to a percutaneous endoscopic gastric tube. After consumption of a meal, tap water is flushed into the stomach and aspiration removes up to one third of ingested food[45]. In a randomized trial comparing the AspireAssist™ system with lifestyle changes alone, the 12-months %TBWL was superior in the aspiration therapy group at 14.2±9.8%, compared to 4.9±7% in the control group[59]. Complications were minimal, most common formation of stoma granulation tissue, stoma infection, peritonitis, and gastric ulcer[59].

Endoscopic Revision of Gastric Roux-en Y Bypass

Following bariatric surgery, a weight plateau usually occurs 18 months after surgery. Additionally, one third of patients regain weight two years after surgery[44]. Multiple factors are implicated in this weight regain including pre-operative patient demographics (e.g. BMI),

neuroendocrine-metabolic dysregulation resulting in a starvation-like response, and anatomic changes such as increased diameter of the gastrojejunal anastomosis or stretching of the gastric pouch[44]. While these anatomical changes can be addressed surgically, increasing interest has been developed for endoluminal revision.

Endoscopic Suturing

The EndoCinch™ (Bard Davol, Murray Hill, NJ) is a superficial-thickness suturing device used for Transoral Outlet Reduction (TORe) and/or endoscopic revision of the gastric pouch[44]. TORe involves ablation of the entire gastric margin of the gastrojejunal anastomosis with argon plasma coagulation[44]. Placing interrupted sutures along the margin until adequate outlet size is achieved reduces the diameter of the anastomosis. Creating ridges and suturing them together can reduce gastric pouch volume[44]. In a multicenter, sham-controlled double-blinded randomized controlled trial of 77 patients post RYGB surgery, the treatment group had significantly better weight loss after 6 months (%TBWL 3.8% TORe group versus 0.3% control group, $p=0.02$)[60]. Another device used for revision of the widened gastrojejunal anastomosis is the OverStich™ (Apollo, Endosurgery, Austin, TX). This device achieves full-thickness TORe as described above. It has also been used to close gastro-gastric fistulas, which can lead to weight regain after RYGB[44]. In a study of 25 RYGB patients, patients lost a mean of 11.7kg (69.5% of regained weight) after 6 months[61]. A matched cohort study comparing TORe by EndoCinch™ versus OverStitch™ device showed weight loss to be significantly higher in the OverStitch™ group (10.6±1.8 kg OverStitch versus 4.4±0.8kg EndoCinch™, $p<0.01$) and this persisted one-year after surgery (8.6±2.5kg OverStitch™ versus 2.9±1.0kg EndoCinch™, $p<0.01$)[62].

Endoscopic plication

The Incisionless Operation Platform™ (IOP) (USGI Medical, San Clemente, CA) is a full-thickness endoscopic plication device, which has been specifically optimized for Revision Obesity Surgery Endolumenal (ROSE). ROSE involves reduction of both gastrojejeunal anastomosis and gastric pouch[44]. In a prospective multicenter trial of 116 patients post RYGB; ROSE by IOP™ achieved 32% weight loss of regained weight. StomaphyX™ (EndoGastric Solutions, Redmond, Washington) achieves full-thickness endoscopic plication with the aid of a vacuum[44]. However, long-term results showed that weight loss was not sustained post StomaphyX™ revision[63].

Endoscopic Sclerotherapy

This technique involved injection of a sclerosant such as sodium morrhuate around the gastrojejunal anastomosis[44]. Injection can be done under conscious sedation, with antibiotic prophylaxis, and repeated every 3 to 6 months until the target anastomotic diameter of 12mm[44]. On average 2.3 sessions are necessary[64]. Complications include transient HTN, bleeding, and ulcerations[65]. The majority of patients experience arrest of weight reversal after one year putting the long-term feasibility of this endoscopic revision technique into question[66,67].

2.2.5 Bariatric Surgery

The NICE criteria recommend bariatric surgery in the following cases[14]:

- BMI ≥40 kg/m2, or BMI >35 kg/m2 and obesity associated comorbidities
- non-surgical measures have failed to achieve or maintain adequate, clinically beneficial weight loss for at least six months
- bariatric surgery program that encompasses all aspects of pre-op and post-op care, i.e.
- dietician, psychiatrist etc.
- patient is fit for surgery

- patient is compliant and agreeable to long-term follow up.

Previous studies have shown bariatric surgery to be the only modality to achieve significant and lasting weight loss in the morbidly obese population[19]. The Swedish Obesity Study (SOS) confirmed the effectiveness of bariatric surgery and showed a reduced cumulative overall mortality rate at 16 years for patients who underwent bariatric surgery compared to conventional treatment (hazard ratio= 0.76, p= 0.04)[68]. Bariatric surgery procedures achieve weight loss through anatomical alterations, which can be either restrictive, malabsorptive, or a combination. Most techniques are done preferably laparoscopically as this has been shown to decrease recovery time, lower complication rates, and improve patient satisfaction[69]. While various types of bariatric surgeries exist, the two most commonly performed procedures in Canada are the laparoscopic Roux-en Y gastric bypass (LRYGB) and the laparoscopic sleeve gastrectomy (LSG). The LSG has been gaining popularity, as it is a shorter and simpler procedure. In the United States, LSG has surpassed LRYGB for annual procedures performed[70]. A recent randomized, multicenter study by Peterli et al compared LSG and LRYGB in terms of weight loss, comorbidity improvement, QOL, and adverse events[71]. After 5 years, %EBMIL was not significantly different (61.1% LSG versus 68.3% LRYGB, p=0.22). Gastric reflux remission was more common after LRYGB (60.4%) versus LSG (25.0%). Furthermore, gastric reflux worsened in almost one third of LSG patients (31.8%), requiring conversion to LRYGB in 10% of patients. There was no difference with regards to amelioration of glycemic control, remission of DLD, and improvement of QOL. Both early (less than 30 days post-operative) and late complication rates did not differ significantly between LSG and LRYGB. The overall rate of reoperation/intervention did not significantly differ between LSG (15.8%) and LRYGB (22.1%, 95% CI=-0.29,0.09). Also in

2018, Salminen et al published their 5-year outcomes of a randomized control trial comparing LSG and LRYGB[72]. The estimated mean percentage excess weight loss was 49% (95% CI, 4552%) after LSG and 57% (95% CI, 53-61%) after LRYGB. The groups did not differ in remission of DM and DLD, quality of life improvement, late morbidity, and mortality. LRYGB did result in better resolution of hypertension.

However, no adequately powered study is currently available to compare these two surgeries with regards to post-operative complication rates.

Laparoscopic Sleeve Gastrectomy

The LSG was first described in 1988 as part of a more extensive bariatric surgery called duodenal switch procedure. In 1993, Johnson used it as an isolated bariatric procedure[73]. LSG is considered an irreversible restrictive procedure in which a gastric sleeve is created by firing a laparoscopic stapler along an intragastrically placed 32-60Fr bougie from approximately 5cm proximal to the pylorus to the angle of *His*. Essentially, the greater curvature of the stomach is stapled off and removed via one of the laparoscopic port sites, leaving the patient with a tubeshaped stomach (Figure 1.4). Advantages of the procedure include its shorter operative time, shorter learning curve, less post-operative malabsorption problems, and less disturbance of anatomy which allows an endoscope to still be past into the stomach and duodenum[73]. Some of the disadvantages are that it has only been used regularly in its isolated form for just over ten years, which means that long-term follow-up results are lacking and some feel it does not lead to efficient weight loss in the super-obese population ($BMI>50kg/m^2$).

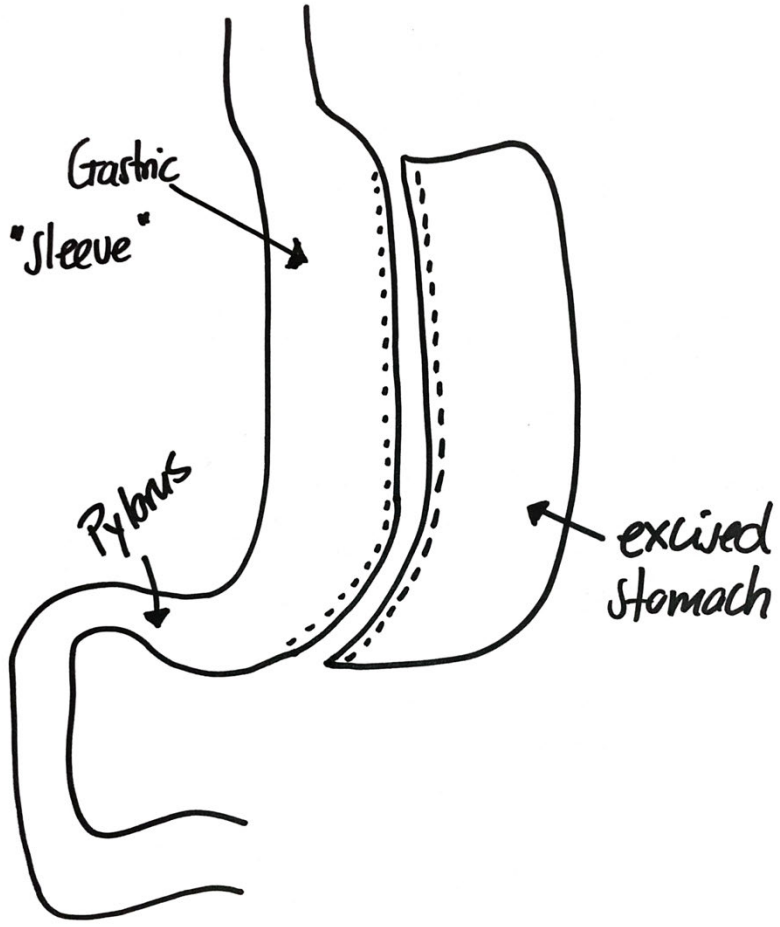

Figure 2.2: Sleeve gastrectomy

Laparoscopic Roux-en-Y Gastric Bypass

The LRYGB was first described in 1994. It is a reversible procedure, considered both restrictive and malabsorptive. It is the most commonly performed bariatric surgery in the USA and considered current standard of care in bariatric surgery in Canada[73,74]. LRYGB entails creation of a 10-30cc gastric pouch using a linear stapler. The jejunum is the divided distal to the ligament of Treitz. The distal limb is connected to the gastric pouch, thereby forming an alimentary limb. The fixed proximal or biliopancreatic limb is then connected to the alimentary limb via a jejunojejunostomy at about 100-150cm distal to the gastrojejunostomy[71]. This technique has a longer learning curve and longer operative time. As

well, the risk of complications is higher as multiple anastomoses are made. It is a preferred technique though as it has been proven very effective for weight loss in even super obese patients[19]. Some of the disadvantages include malabsorption of micronutrients, potential for post-operative internal hernias, and inability to assess the upper digestive tract by endoscopy.

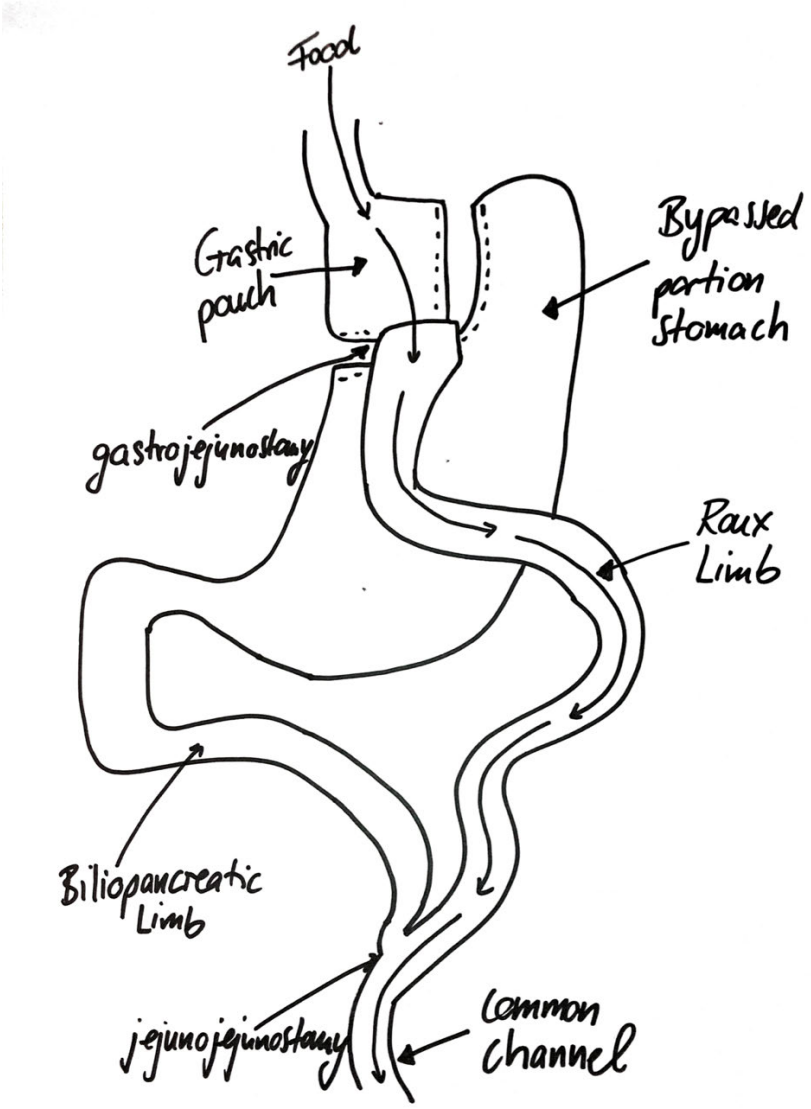

Figure 2.3: Roux-en Y gastric bypass

Recent research shows that the many benefits of bariatric surgery, including improvement of glycemic control, dyslipidemia and hepatic steatosis, can be attributed to more than just the restrictive and/or malabsorptive surgical changes. The effects of LSG and LRYGB go beyond anatomical changes. Many of the metabolic changes after bariatric surgery can be attributed to its the effects on physiology, bile acids, gut hormones, gut microbiome, exosomes, glucose metabolism and lipid metabolism[75]. LSG reduces the number of ghrelin secreting cells, accelerates gastric emptying, increases secretion of glucagon-like polypeptide 1 (GLP-1), and peptide YY (PYY)[75]. LRYGB also improves gut physiology, but by a different mechanism. While it also enhances secretion of GLP-1. PYY and cholestyramine, LRYGB additionally accelerated absorption of glucose and amino acids[75]. Bariatric surgery leads to increased systemic bile acid levels and altered bile acid composition. This change is more pronounced after LRYGB. Bile acids can alter gut microbiota and conversely, microbiota can alter bile acids via microbial enzymes[75]. More research is focusing on gut microbiota dysbiosis as potential cause of obesity. Bariatric surgery alters the gut microbiome and these changes have been seen to lead to weight loss in patients who have not undergone bariatric surgery when they have been exposed to this altered microbiome. The increase in gut hormones after bariatric surgery leads to improved appetite and glycemic control[75]. Exomes are derived from adipose tissue and help regulate gene expression in the liver which lead to insulin resistance. Through reduction in adipose tissue, these exomes are reduced by bariatric surgery and glycemic control improved[75]. While often described as restrictive and/or malabsorptive, the physiological effects of bariatric surgery are broad and subject of ongoing research.

2.3 Complications after Bariatric Surgery

The three most commonly performed bariatric procedures in North America are the laparoscopic adjustable gastric band (LAGB), LSG, and LRYGB. Birkmeyer et al reviewed a total of 15 275 patients who underwent bariatric surgery in Michigan from 2006 to 2009[76]. They report an overall complication and mortality rate of 7.3% and 0.12%, respectively[76]. Rates of serious complications were highest for LRYGB (3.1%), followed by LSG (2.2%), and lowest for LAGB (0.78%)[76]. These complication rates are lower than the data published by Carlin et al in 2013; however, they similarly show LRYGB to be associated with the highest rate of complications at 10% compared to LSG (6.3%) and LAGB (2.4%)[4]. There was no significant difference in mortality between the three bariatric procedures[77]. The largest series comes from Hutter et al in 2011. This study reviewed the complication rates of 22 365 cases (944 LSG, 14 491 LRYGB, 988 open RYGB, 12 193 LAGB)[78]. Combined 30-day mortality was 0.12%[77]. As in previous studies, LSG falls below LRYGB but above LAGB for post-operative rates of morbidity, mortality, readmission, and reoperation rates[78]. Compared to LRYGB, LSG has significantly lower rates of stricture, intestinal obstruction, and anastomotic ulcer[78].

The literature supports that LSG is associated with less overall complications than LRYGB. Nonetheless, both procedures have specific complications worth mentioning. LRYGB generally has longer operative time and hospital length of stay (LOS)[73]. The leak rate quoted varies between 0-6%[79]. Hemorrhage is also rare, occurring in 0.6-4% cases[79]. Intestinal obstruction after LRYGB can be due to post-operative adhesion; however, it is imperative to rule out internal herniation. This is more common in the retro-colic versus ante-

colic technique (3.7% versus 0.3%)[6]. A rare case of obstruction is intussusception, which generally occurs in a retrograde fashion in the jejunum[79]. Anastomotic stricture after LRYGB occurs more commonly at the gastrojejunostomy (3-9%) versus the jejunojejunostomy site (0.8-2%)[79]. Also more commonly seen at the gastrojejunostomy site are marginal ulcers[73]. These are usually treated with proton pump inhibitors, but may lead to serious complications such as strictures or perforation, requiring reoperation. Also unique to LRYGB is the development of a gastro-gastric fistula (<1%), which occurs when a fistula forms between the gastric pouch and gastric remnant. A nearby inflammatory process such as a leak or marginal ulcer often causes these[79].

The rates of bleeding and staple line leak after LSG is similar to LRYGB at 1 to 6% and 0.9 to 5%, respectively[79,80]. Staple line leaks can be classified into subclinical leaks (type I) and clinical leaks (type II), which generally present acutely and require emergency laparoscopy, washout and drainage, and insertion of a jejunostomy feeding tube[80]. Mechanical obstruction of the gastric sleeve most commonly occurs at the level of the incisura[79,80]. A late complication is gastric sleeve dilation leading to weight regain or failure to lose weight[79]. This complication is likely under represented at the present time, as long-term data for LSG is still sparse. Currently, 4.5% patients require reoperation for this reason[79]. The effect of LSG on acid reflux is still controversial and most studies suggest avoiding LSG in patients with severe preoperative gastro esophageal reflux disease (GERD)[80].

Complications associated with laparoscopic sleeve gastrectomy

Complication	Chronicity	Diagnosis	Management
Hemorrhage	Acute	Physical findings, serial CBC	Transfusion with or without laparoscopy/ laparotomy

Leak	Acute/chronic	Physical findings, UGI series	Drainage (percutaneous/laparoscopy), antibiotics and/or stenting and/or repair
Abscess	Chronic	CT scan, ultrasound	Drainage, antibiotics
Stricture	Chronic	Endoscopy, UGI series	Endoscopy (dilation), surgery (seromyotomy)
Nutrient deficiency	Chronic	Physical findings, blood work	Nutritional supplements
GERD	Chronic	History, endoscopy	Treatment with proton pump inhibitor

CBC = complete blood count; CT = computed tomography; GERD = gastroesophageal reflux disease; UGI = upper gastrointestinal.

Figure 2.4: Complications associated with laparoscopic sleeve gastrectomy

2.4 Purpose of Study

The purpose of this study is to examine the effectiveness and safety of performing LSG at a new Canadian center, which does not meet annual volume criteria to be considered a bariatric surgery center of excellence.

2.5 Significance of Study

While studies show that the overall complication rate after LSG is lower than after LRYGB, both procedures should be performed by fellowship-trained bariatric surgeons in centers where patients are treated by a multidisciplinary team both pre-and post-operatively. Guidelines specify the constellation as well as the surgeon training and annual volume in order to be considered a center of excellence. However, due to the fast-growing obesity epidemic, more and more hospitals, which do not fully comply with the guidelines for centers of excellence, have started bariatric programs. In Newfoundland, the bariatric surgery program does provide a multidisciplinary patient approach and fellowship-trained surgeons; however, annual volume does not meet criteria (minimum 125) to be considered a center of excellence. While the general consensus from surgical guidelines is to perform complex surgical procedures at dedicated tertiary car centers, no studies compare outcomes after LSG between low- and high-volume centers. This study reviews the outcomes of a new established

bariatric surgery program at a small Canadian center in order to ascertain safety even when annual volume criteria to be considered a center of excellence are not met. In order to do so, the primary outcome assessed will be post-operative complication rate within 30-days after surgery. It is important from a qualify-of-care perspective to assure that LSG can be safely performed in smaller centers. Furthermore, the results of this study may show that performance of LSG is feasible at smaller centers, which would allow more hospitals to offer this service and aid in the growing need for bariatric surgery with the increasing obesity epidemic.

2.6 Specific Research Objectives

The specific research objectives of the current study are:

1. To develop a research protocol to assess 30-day complication rates after LSG
2. To assess the rate and types of 30-day complications after LSG at a new small Bariatric Surgery Center
3. Review the literature for post-LSG complications graded according to the ClavienDindo classification and compare the results in the literature to our center's complication rates

Chapter 3: Study Conceptualization and Design

3.1 Introduction

Obesity is defined as a BMI≥30kg/m^2 and is a growing health concern in Western society[1]. In Canada, approximately 1 in 4 adults are overweight or obese[2]. While multiple treatment options exists, bariatric surgery has been the only one showing long-term success at weight loss[3]. Offering surgery to every bariatric patient who qualifies simply by BMI and WHO guidelines (BMI≥40kg/m^2 with or without obesity-associated comorbidities or BMI≥35kg/m^2 with at least one obesity-associated comorbidity) is neither effective nor safe. Many patients may have contraindications to surgery, which can be physical or mental. Some patients may also not be agreeable to surgery as this involves risks and alterations of anatomy. Bariatric surgery works best in the context of a developed bariatric surgery program, which involves multiple disciplines and provides pre-operative assessments as well as post-operative follow-up and guidance.

Definitions for center of excellence and guidelines regarding quality control of bariatric surgery programs have been established by multiple surgical societies focused on metabolic and bariatric procedures. These will be reviewed in this chapter.

Furthermore, this chapter will review the design of this study with details on grading surgical complications in order to have a more objective outcome measure.

3.1.1 Newfoundland Bariatric Surgery Program

The Provincial Bariatric Surgery Clinic was established in May 2011. It serves a population of over 300,000 people[4]. It consists of three bariatric-trained surgeons, one nurse practitioner, and one dietician with access to other allied health workers on a consultation basis. Patients are most commonly referred to the clinic by their primary care physician. All

patients are required to attend a pre-surgical education session. Prior to being seen by a bariatric surgeon, patients have to be assessed by the nurse practitioner, dietician, and undergo certain screening tests including blood work and sleep study to investigate for OSA. The focus of the original visit is to determine if the patient is an adequate candidate for bariatric surgery. If deemed adequate, they then are referred to the surgical clinic for assessment and surgical discussion.

Patients are considered eligible for bariatric surgery if they meet the following criteria[4]:

- BMI $\geq$35kg/m^2 with obesity associated comorbidities or BMI$\geq$40kg/m^2
- Maximum BMI 60kg/m^2
- Age 19 to 70 years
- Attempted non-surgical weight loss in past
- standardized referral form for the Bariatric Surgery Clinic has been completed by the primary care physician
- attended mandatory pre-surgical bariatric surgery general meeting and education session
- assessed by bariatric nurse practitioner (detailed medical history including weight history and past weight loss attempts, blood work, sleep study, and other tests based on patient health)
- assessed by bariatric dietician
- completed food journaling and 2-week liquid diet trial
- deemed medically, psychologically, and emotionally stable to consent to bariatric surgery

Exclusion Criteria[4]:

- pregnancy (or plan to become pregnant within 2 years)

Surgical Intervention:

A bariatric surgeon sees all patients for surgical consent discussion prior to their LSG procedure. This meeting involves explanation of the general risks including but not limited to

bleeding, infection, conversion to open procedure, injury to intra-peritoneal structures including small bowel, large bowel, liver, and spleen, as well as risk of incisional hernias, myocardial infarction, stroke, pneumonia, and venous thrombosis. At the time of this study, the only bariatric procedure offered is LSG. Two bariatric-trained surgeons carry out all operations.

As per protocol, patients receive pre-operative deep venous thrombosis (DVT) prophylaxis with sc heparin and a single dose of intravenous (iv) antibiotic (cefazolin 2g iv or clindamycin 600 mg iv if penicillin allergy). After administration of general anesthesia with endotracheal intubation, patients are placed in supine position. The abdomen is prepped and draped in usual fashion. The LSG is carried out using a six-port technique. Starting 5cm proximal to the pylorus, the vascular supply of the stomach is divided along the greater curve to the angle of *His* using a bipolar energy device. The gastric sleeve is then created using multiple firings of an endoscopic 60mm stapler along a 42Fr bougie. Esophagogastroduodenoscopy is carried out and an air leak test performed on the gastric sleeve. The gastric specimen is removed via the left upper quadrant port site.

Following surgery, patients are kept nil per os (NPO) and continued on DVD prophylaxis with low molecular weight heparin (LMWH). On post-operative day one, patients undergo a gastrograffin swallow to rule out staple line leak prior to commencing a small volume clear fluid diet. The bariatric nurse practitioner and dietician assess patients. Most patients are discharged home on POD #2. Surgical follow-up occurs at 6 weeks after surgery and patients have regular follow-up with the Bariatric Surgery clinic at 1, 3, 6, 12, 18, 24 months and annually thereafter.

3.1.2 Definition for Center of Excellence in Bariatric Surgery

Various organizations have provided consensus statements regarding definitions of centers of excellence in bariatric surgery. The purpose of these is to ensure patient safety, low complication rates, proper follow-up and support of the bariatric patient. The Society of American Gastrointestinal and Endoscopic Surgeons (SAGES) developed an algorithm for granting surgeons privileges to perform bariatric surgery[5].

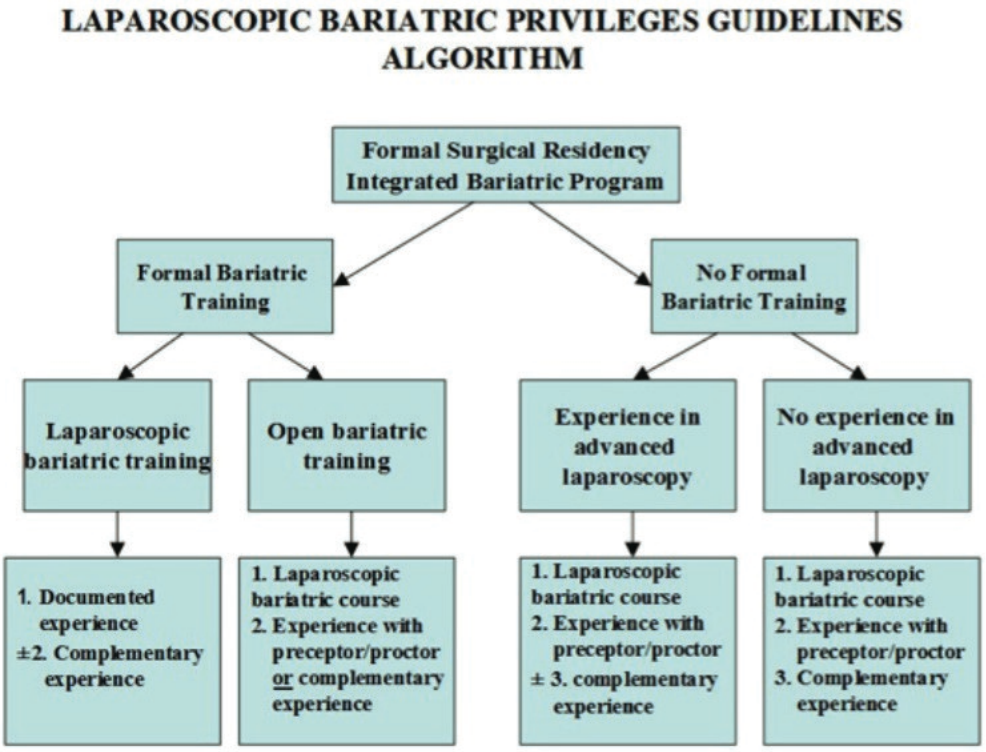

Figure 3.1: SAGES algorithm for laparoscopic bariatric privileges

The SAGES guidelines emphasize the need for an integrated program of care that provides ancillary services such as specialized nursing care, dieticians, psychological support etc. Furthermore, once privileges have been gained, the performance of the surgeon and bariatric team should be assessed regularly through outcome reviews, complication rates, and patient experiences. Continuing medical education in bariatric surgery is strongly encouraged.

In 2003, the American Society for Bariatric Surgery (ASBS) established a review committee for quality control of bariatric surgery[6]. Through the process of meta-analysis of English language published papers on bariatric surgery, followed by a consensus conference in 2005 and comment period, a final set of standards was developed. According to these standards, programs are first granted 'Provisional' status based on documentation that the required expertise and resources are available, followed by 'Full Approval' status after a site inspection verifies the provisional application and adequate outcome reporting[6]. The requirements for 'Provisional' and 'Full Status' can be found in Appendix 1 of this document. Pratt et al analyzed outcomes of 'Full Approval' centers of excellence[7]. Between August 2005 and May 2007, 235 hospitals had been granted 'Full Approval' status. Among these hospitals, 66,339 bariatric surgeries were performed, of which the majority were laparoscopic gastric bypasses. The 30-day mortality rate was 0.13% and rose to 0.36% for composite morality rate. The three main causes for mortality were pulmonary emboli, cardiac complications, and severe infection. Aggregate readmission rate was 5% with 2% re-operation rate. Ballantyne et al studied the in-hospital mortality of bariatric surgery at high volume centers in a single American State. Their mortality rate was 0.13%. They also review mortality rates from 15 bariatric surgery institutions, including both lower and high–volume centers. The mortality rates reported ranged from 0.10 to 2.00% and tended to be inversely related to operative volume. They conclude that higher volume centers can achieve lower rates of mortality[8].

The American College of Surgeons (ACS) has produced an accreditation program manual for bariatric centers to qualify as American College of Surgeons Bariatric Surgery Centers (Appendix 2)[9]. This manual emphasizes that certain patients undergoing bariatric surgery are at higher risk of complications and mortality compared to their non-obese

counterparts. Factors associated with higher risks include revision surgery, age >50 years with BMI > 50 kg/m^2, male gender, and certain comorbidities such as DM2, HTN, OSA. Those bariatric centers classified as level 1a or 1b, can manage the most challenging and complex bariatric patients, while levels 2a and 2b provide high quality of care to lower volume patients with less severe obesity and fewer obesity-related comorbidities. Level 1a centers must provide care for all patients regardless of severity of obesity, age, comorbidities, and offer revision surgery. In order to qualify as level 1a, centers must have performed bariatric procedures for two years prior to approval with outcome documentation and continue to do so for quality assurance purposes. Level 1a centers perform a minimum of 125 weight- loss operations annually, employ at least two certified bariatric surgeons lead by a bariatric surgery director, work with a multidisciplinary bariatric team, and follow patients closely at regular intervals. These centers must be able to manage any postoperative complications encountered with broad subspecialty coverage including pulmonology, cardiology, intensive care, infectious disease, nephrology, psychiatry, gastroenterology, thoracic surgery, otolaryngology, and orthopedics. While level 1b centers must comply with all the abovementioned regulations, they do not have to report outcomes on all patients undergoing weight loss surgery as part of the American College of Surgeons National Surgery Quality Improvement Program (ACS NSQIP). In contrast, level 2a centers provide weight loss surgery to obese patients under the age of 60 years in absence of cardiac or pulmonary comorbidities. Maximum BMI limits include males with a BMI ≤55 kg/m^2 and females ≤ 60 kg/m^2. Surgeons must have performed bariatric procedures for the previous 24 months with a minimum of 25 primary weight loss operations annually. The center offers a multidisciplinary bariatric program lead by a Bariatric Program Coordinator. The facility must offer a critical

care unit equipped for obese patient as well as endoscopy, laparoscopy, and radiology services suitable for obese patients. Regular follow-up appointments are scheduled at the following intervals: 2 weeks, 3 months, 6 months, 12 months, and annually thereafter. While level 2b centers must comply with all these for mentioned regulations, they do not have to report outcomes on all patients undergoing weight loss surgery as part of the ACS NSQIP.

Furthermore, ACS established credentialing criteria for bariatric surgeons. Newly trained surgeons must have completed ≥25 laparoscopic bariatric procedures and ≥10 open bariatric cases during general surgery residency and/or bariatric surgery fellowship training. Established general surgeons wanting to expand into bariatric surgery must complete a didactic course on bariatric surgery and complete 10 open cases or 25 laparoscopic cases proctored by a certified bariatric surgeon. A committee including the chief of surgery of the relevant institution will review the first 5 independent bariatric cases of the proctored surgeon. Established bariatric surgeons maintain American Board of Surgery (ABS) certification by performing a minimum of 50 primary bariatric surgeries in the previous 2 years, documenting long-term patient follow-up, having acceptable complication rates, and obtaining at least 12 weight loss surgery CME (continuing medical education) credits every 2 years from bariatric surgery meetings or accredited obesity courses. For the detailed ACS Bariatric Surgery Center Network Accreditation Program Manual refer to Appendix 2.

3.1.3 Grading of Complications

While multiple systems for post-operative complication grading and classification exist, for the purpose of this study, we aimed to collect data in an organized fashion that would allow comparison of our outcomes directly and reliably to other studies. The most commonly used grading system for post-operative complications is the Clavien-Dindo classification.

This has been applied and verified in various surgical fields, including bariatric surgery 10,11,12.

Original Clavien- Dindo classification

In 1992, Clavien et al proposed a 4 Grade classification system for surgical complications mainly focusing on outcomes after cholecystectomy[10]. This was sparked by the genuine lack of agreement among researchers and clinical staff as to what constitutes a complication and how to rank specific adverse events according to severity. In their paper, they suggest a grading system intended to be broadly applicable to various surgical procedures and respective complications. Four grades of complications were proposed based on the following three criteria: (i) whether the complication is life-threatening, (ii) whether the interventions to treat the complication carry significant risk, and (iii) whether residual disability is induced by the complication.

- Grade 1- Minor complication that if left untreated has spontaneous resolution or at most requires a bedside procedure with no or minimal analgesia. The only drugs required include analgesia, antipyretics, antiemetics, and antidiarrheal medications. No iatrogenic injures are included. The increase in LOS in hospital cannot exceed twice the median hospitalization for that procedure.
- Grade 2- A complication that is potentially life threatening and requires an intervention associated with well-described complications. These do not produce lasting or residual disability nor do they result in organ resection. This category also includes cases in which a complication leads to more than doubling of the estimated mean hospital stay. Iatrogenic injuries fall into this grade, except those causing residual disability, organ resection, or death.
    - Grade 2a- All complications requiring drug therapy other than those included for Grade 1.
    - Grade 2b- Complications requiring invasive procedures including interventional radiology (e.g. percutaneous drainage of an abscess), therapeutic

endoscopy, or reoperation. Also included are iatrogenic injuries requiring reoperation, even when performed during the same procedure.

- Grade 3- A complication with residual or lasting disability (e.g. organ resection, myocardial infarction, common bile duct stenosis compromising liver function, necrotizing infection requiring tissue loss and impairment in function).
- Grade 4- Death as result of any complication.

Modified Clavien-Dindo Classification

Following their original proposal of complication grading (described above), Clavien et al published a modified grading system for surgical complications in 2004[11]. This new grading system is in current use and was applied to this study of complications following LSG. They expanded the classification system into five grades with subcategories for grade 3 and 4. Duration of hospital stay was removed as a grading criterion.

Table 3.1: Modified Clavien-Dindo classification of surgical complications

Table 1. Classification of Surgical Complications

Grade	Definition
Grade I	Any deviation from the normal postoperative course without the need for pharmacological treatment or surgical, endoscopic, and radiological interventions Allowed therapeutic regimens are: drugs as antiemetics, antipyretics, analgetics, diuretics, electrolytes, and physiotherapy. This grade also includes wound infections opened at the bedside
Grade II	Requiring pharmacological treatment with drugs other than such allowed for grade 1 complications Blood transfusions and total parenteral nutrition are also included
Grade III	Requiring surgical, endoscopic or radiological intervention
Grade IIIa	Intervention not under general anesthesia
Grade IIIb	Intervention under general anesthesia
Grade IV	Life-threatening complication (including CNS complications)* requiring IC/ICU management
Grade IVa	Single organ dysfunction (including dialysis)
Grade IVb	Multiorgan dysfunction
Grade V	Death of a patient
Suffix “d”	If the patient suffers from a complication at the time of discharge (see examples in Table 2), the suffix “d” (for “disability”) is added to the respective grade of complication. This label indicates the need for a follow-up to fully evaluate the complication.

*Brain hemorrhage, ischemic stroke, subarrachnoidal bleeding, but excluding transient ischemic attacks. CNS, central nervous system; IC, intermediate care; ICU, intensive care unit.

They provided a list on clinical examples for each grade of complications.

Table 3.2: Clinical examples for each grade of complications

Table 2. Clinical Examples of Complication Grades

Grades	Organ System	Examples
Grade I	Cardiac	Atrial fibrillation converting after correction of K^+ -level
	Respiratory	Atelectasis requiring physiotherapy
	Neurological	Transient confusion not requiring therapy
	Gastrointestinal	Noninfectious diarrhea
	Renal	Transient elevation of serum creatinine
	Other	Wound infection treated by opening of the wound at the bedside
Grade II	Cardiac	Tachyarrhythmia requiring β-receptor antagonists for heart rate control
	Respiratory	Pneumonia treated with antibiotics on the ward
	Neurological	TIA requiring treatment with anticoagulants
	Gastrointestinal	Infectious diarrhea requiring antibiotics
	Renal	Urinary tract infection requiring antibiotics
	Other	Same as for I but followed by treatment with antibiotics because of additional phlegmonous infection
Grade IIIa	Cardiac	Bradyarrhythmia requiring pacemaker implantation in local anesthesia
	Neurological	See grade IV
	Gastrointestinal	Biloma after liver resection requiring percutaneous drainage
	Renal	Stenosis of the ureter after kidney transplantation treated by stenting
	Other	Closure of dehiscent noninfected wound in the OR under local anesthesia
Grade IIIb	Cardiac	Cardiac temponade after thoracic surgery requiring fenestration
	Respiratory	Bronchopleural fistulas after thoracic surgery requiring surgical closure
	Neurological	See grade IV
	Gastrointestinal	Anastomotic leakage after descendorectostomy requiring relaparotomy
	Renal	Stenosis of the ureter after kidney transplantation treated by surgery
	Other	Wound infection leading to eventration of small bowel
Grade IVa	Cardiac	Heart failure leading to low-output syndrome
	Respiratory	Lung failure requiring intubation
	Neurological	Ischemic stroke/brain hemorrhage
	Gastrointestinal	Necrotizing pancreatitis
	Renal	Renal insufficiency requiring dialysis
Grade IVb	Cardiac	Same as for IVa but in combination with renal failure
	Respiratory	Same as for IVa but in combination with renal failure
	Gastrointestinal	Same as for IVa but in combination with hemodynamic instability
	Neurological	Ischemic stroke/brain hemorrhage with respiratory failure
	Renal	Same as for IVa but in combination with hemodynamic instability

Suffix “d”	Cardiac	Cardiac insufficiency after myocardial infarction (IVa-d)
	Respiratory	Dyspnea after pneumonectomy for severe bleeding after chest tube placement (IIIb-d)

Table 2. Clinical Examples of Complication Grades

Grade	Organ System	Example
	Gastrointestinal	Residual fecal incontinence after abscess following descendorectostomy with surgical evacuation (IIIb-d)
	Neurological	Stroke with sensorimotor hemisyndrome (IVa-d)
	Renal	Residual renal insufficiency after sepsis with multiorgan dysfunction (IVb-d)
	Other	Hoarseness after thyroid surgery (I-d)

TIA, transient ischemic attack; OR, operating room

In 2009, Clavien et al critically appraised this complication grading system by assessing inter-observer variability for complex complication scenarios[12]. Firstly, they searched the literature for articles that used their 5-grade classification system for complications proposed in 2004. Each article was then examined as to how the classification system was applied. They observed a steady yearly increase in the use of the grading system, covering a broad field of surgical specialties including transplant surgery, hepato-biliary surgery, general surgery, colorectal surgery, urology, and gynecology. Of the studies that differentiated minor and major complications, most allocated Grade 1 and 2 complications to be minor, and Grades 3 through 5 as major. Secondly, difficult scenarios that were encountered in the previous 5 years at the University of Zurich were collected and consensus sought on grading. Thirdly, inter-observer agreement was assessed by distributing 11 difficult cases to 7 centers around the world. Most of the discussion focused on whether all complications encountered by one patient must be graded separately, or whether only the most severe complication grade should be recorded. A consensus was reached to grade the highest complication when multiple complications are clearly related to one another (e.g.: A patient who suffers an

anastomotic leak, develops sepsis, ARDS, renal failure, and death would be a grade 5 complication).

3.2 Study Design

3.2.1 Patient Selection

All patients who underwent LSG from May 2011 to January 2014 were included in this study. A minimum of 200 patients, which is approximately two years of bariatric surgery procedures at our institution were to be reviewed.

3.2.2 Study Complication Grading

Our study focuses on 30-day complications following LSG. To allow for adequate grading and comparison to other published data, each complication was graded according to the 5-Grade Clavien-Dindo classification. A system of minor and major complications was adopted to allow comparison between other centers. In agreement to previous studies, minor complications were those graded 1 and 2, while major complications were grade 3 or higher. To ensure adequate classification of complications, all complications were reviewed and scored independently by two authors.

3.2.3 Literature Review of Studies Reviewing LSG Complications

Using PubMed, a literature review of all English-language articles published between January 2000 and December 2016 was carried out. Search terms used were: “laparoscopic sleeve gastrectomy complications.” This yielded 1010 titles, which were reviewed. The following exclusion criteria were then applied: revision surgery, case reports, reviews, concurrent surgical procedures such as hiatus hernia repair or LAGB removal, single port LSG, robotic surgery, open surgery, studies limited to low ($<35 kg/m^2$) or high ($>50 kg/m^2$) BMI patients, studies looking at specific age ranges, studies including only diabetic patients, studies focused on a single specific type of complication or outcome. After applying these

exclusion criteria, 150 study abstracts were reviewed. Of these 150 abstracts, 73 full papers fit our search criteria for complications after LSG. Reasons for exclusion from full-text review included inclusion of non-primary bariatric procedures, BMI criteria not confirming to NICE guidelines, lack of reporting of complication rates altogether, reporting limited to specific types of complications such as leak or bleeding only, lack of differentiation into short-term and long-term complications, comparison of specific surgical techniques such as oversewing of staple line, and focus on effect of learning curve and/ or surgeon volume. Review of these 73 full-text articles yielded 4 studies, which specifically categorized post-LSG complications into the Clavien-Dindo classification.

Lemanu et al published the earliest of these studies in 2012[13]. This study of 400 patients who underwent primary LSG had a 1-year follow-up period. The majority of patients were female (73%) with mean age 44 years and mean pre-operative BMI of 49kg/m^2. Total 30-day postoperative complication rate was 16%. These included 20 patients with grade 1 complications, 18 grade 2 complications, 23 grade 3 complications, and 5 grade 4 complications. One mortality occurred. Any complication graded 3 or higher was defined as major; overall major complication rate was 7.2%. They also compared patients with BMI<50kg/m^2 to patients with BMI>50kg/m^2, finding no a significant difference in major complication rates between these groups (6.5% versus 8.2%, p=0.56)[13].

In 2013, Peterli et al published the early results of their prospective randomized trial comparing LSG and RYGB[14]. A total of 217 patients were enrolled at 4 bariatric surgery centers. One hundred and seven patients underwent LSG and 110 LRYGB with BMI ranging from 35 to 61kg/m^2. Both groups were similar with regards to patient characteristics. The mean operative time was shorter for LSG (87.2±52.3 minutes versus 108±42.3minutes for

LRYGB, p=0.003). The 30-day complication rate was higher among LRYGB patients at 17.2% compared to LSG (8.4%, p=0.067). Reoperation for complications was necessary in five of 110 LRYGB patients (4.5%) versus one of 107 LSG patients (0.9%, p=0.21). No significant difference was found regarding weight loss and resolution of comorbidities. While not statistically significant, LRYGB had higher complication and reoperation rates. Primary outcome was weight loss over 5 years, which means their sample size calculation is based on this outcome and not on safety. One can assume that the sample number for safety would be significantly larger and this may explain why the difference in complications between LSG and LRYGB did not reach statistical significance.

Also in 2013, Vidal et al published their observational retrospective study comparing outcomes of LSG and LRYGB[15]. Of 249 patients, 135 under LRYGB (54.2%) and 114 LSG (45.8%). The pre-operative BMI was significantly higher among LRYGB patients (45.4kg/m^2 versus 42.4kg/m^2, p<0.001). Similar to Peterli et al, operative time was significantly shorter for LSG (93 minutes versus 153 minutes, p<0.001). Minor complications were defined as ClavienDindo grade 1 or 2 with major complications being grade 3 or higher. While the rate of minor complications was significantly higher among LRYGB (21.5%) compared to LSG patients (4.4%, p=0.005), there for no significant difference in major complications (5.9% LRYGB versus 4.4% LSG, p=NS). Similarly, reoperation rates were not different between the two groups (4.4% LRYGB versus 3.5% LSG, p=0.758).

In 2015, Goitein et al retrospectively compared complications after LRYGB and LSG using the Clavien-Dindo classification[16]. The study included 2651 obese and 554 morbidly obese patients. Post-operative 30-day complication rate was 3.8% following LSG and 4.3% following LRYGB (p=0.9). They noted that the average age was higher in those patients who

had complications (47.5 years) versus those who did not (43.1 years, p=0.01). There was a trend for more bleeding and leaks after LSG, while venous thrombosis evens were more common after LRYGB; however these were not statistically significant.

Chapter 4: Laparoscopic sleeve gastrectomy at a new bariatric surgery center in Canada: 30-day complication rates using the Clavien-Dindo Classification

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4.1 Introduction

Obesity, defined as a BMI ≥ 30 kg/m^2, has been associated with significant comorbidities such as diabetes, OSA, cardiovascular disease, HTN, and DLD, as well as, an increased incidence of certain cancers[1]. While numerous treatment options exist for obesity, bariatric surgery has proven to be the only effective treatment resulting in substantial and sustainable weight loss, significant improvement in comorbid conditions, QOL, and reduction in the risk of death[2,3]. According to Canadian guidelines, surgical treatment of adult obesity is indicated

in medical refractory patients with a BMI ≥40 kg/m^2 or BMI ≥35 kg/m^2 with at least one comorbid condition[4].

Newfoundland and Labrador (NL) has the highest rate of obesity in Canada with estimated increases projected[5]. In 2011, Eastern Health established a provincial bariatric surgery program in NL at the Health Science Centre. This multidisciplinary program consists of three surgeons, a nurse practitioner, and a dietician with referral to other allied health professionals, if required. Laparoscopic sleeve gastrectomy is the primary bariatric procedure (96%) performed at this center.

LSG originated as an initial step of a two step-procedure known as the biliopancreatic bypass. It has gained popularity and is currently the second most commonly performed bariatric surgery in Canada[6]. Its relative short operative time, shorter learning curve, and lower complication rates make it an increasingly popular alternative to the LRYGB[7].

Current literature provides evidence that supports lower complication rates with LSG compared to LRYGB[8,9]. A 2010 systematic review of 15 studies comprised of 940 patients analyzed the clinical outcomes and operational impact of LSG. The authors reported a major complication rate (e.g., staple line leakage and internal bleeding) ranging from 0 to 29%. The range of leakage was 0 to 5.5% and for bleeding 0 to 15.8%. The mortality rate ranged from 0 to 3.3%. In the systematic review some studies reported all minor complications (e.g., vomiting, nausea and diarrhea) and others did not, confounding the analysis[10]. In a more recent systematic review and meta-analysis on the effectiveness and risks of bariatric surgery, Chang et al, report complication rates associated with LSG from both randomized controlled trials (RCT's) and observational studies. The meta-analytic results from the 10 observational studies (n=3647 patients) reported perioperative and postoperative mortality rates for LSG as

0.29% and 0.34%, respectively. The complication rate after LSG ranged from 8.9% (8 observational studies, n=4987 patients) to 13% (2 RCTs, n=137 patients)[2].

In response to a growing number of people living with obesity, specifically those with severe obesity (BMI ≥35kg/m^2), there has been an increase in the volume of bariatric surgeries performed in many Canadian provinces. In Canada, between 2012 and 2013, 28% of bariatric procedures performed were LSG[6]. With the increasing number of LSG procedures being performed, outcome assessment is of utmost importance.

The Surgical Review Corporation (SRC), ASBS, and Bariatric Surgery Center of Excellence (BSCOE) established guidelines to ensure patient safety and operative quality. While the NL program complies with some of the criteria for BSCOE (i.e. a dedicated multidisciplinary bariatric team and long-term patient follow-up), operative volumes are less than the minimum annual 125 bariatric procedures required to be classified as Centre of Excellence[11,12]. The purpose of this study was to assess 30-day complication and mortality rates in the first 209 consecutive patients undergoing LSG. We used the Clavien-Dindo classification system to grade and report surgical complications in a standard and comparable format to allow for valid and reliable comparisons[13].

4.2 Methods

4.2.1 Setting

The Provincial Bariatric Surgery Program was established in May 2011. This multidisciplinary team consists of three surgeons trained in bariatric surgery, a nurse practitioner, and a dietician. The three surgeons, who performed all procedures in this study (DP, DB, CS), possessed advanced laparoscopic skills. Two surgeons (DP, CS) are fellowship trained in minimally invasive and bariatric surgery.

The local health research ethics committee approved this study.

4.2.2. Patient Selection Criteria for Bariatric Surgery

The eligible population consists of all patients who (1) meet the Canadian Practice Guidelines[4] criteria for the surgical treatment of obesity (BMI ≥ 35 with risk factors, or BMI ≥ 40), (2) are referred by their primary care provider to the bariatric team using a standardized referral form submitted to a central intake system, and (3) receive preliminary eligibility screening by the nurse practitioner. Following mandatory attendance at a pre-surgical bariatric surgery general orientation and an education session provided either in-face or via webinar, patients are required to undergo extensive pre-operative work-up which includes a two-week diet trial (one week full-fluid diet and one week healthy eating), as well as a food journaling activity.

All patients meet one-on-one or via Telehealth with the nurse practitioner for further assessment and clinical review including a detailed weight history and past weight loss attempts, blood work, and sleep study to identify and treat any sleep-disordered breathing, as necessary. If any other medical concerns are identified, patients are consulted to the appropriate specialist (e.g., cardiologist, endocrinologist, respirologist) based on their comorbid condition. An appointment with one of the three bariatric surgeons in the bariatric surgery clinic is arranged to obtain formal surgical consent.

Inclusion criteria:

- Male or female patients between 19 – 70 years of age
- BMI ≥ 40 kg/m2 or ≥ 35 kg/m2 with significant obesity-related comorbidities
- Attempted nonsurgical weight loss in the past
- Deemed medically, psychologically, and emotionally stable to consent to surgery and partake in a diet and lifestyle modification regime

Exclusion Criteria:

- Pregnant or planning a pregnancy within 2 years of surgical treatment
- A medical condition that would make surgery too risky (i.e. not fit for surgery)
- BMI >60kg/m2

4.2.3 Operative Procedure

Two surgeons were present for all LSG procedures. All cases employed a five- or six-port approach. The vascular supply of the stomach is divided along the greater curve, starting 5cm proximal to the pylorus and carried to the angle of His. A gastric sleeve is created using 60mm linear staplers along a 42Fr bougie, which is advanced via the oropharynx into the stomach by the anesthesiologist. The gastric specimen is removed via the left upper quadrant port site. The staple line is leak tested with a gastroscope. On post-operative day (POD)#1, all patients undergo a gastrograffin swallow to assess for a leak from the gastric staple line and to ensure patency of the sleeve. If no problem is identified, patients are started on a clear liquid diet and generally discharged home on POD#2 with dietary instructions. Follow-up visits with the multidisciplinary team are scheduled at 1, 3, 6, 12, 18, 24 months, and annually thereafter. Patients follow up with their surgeon at 6 weeks and as needed from then on.

4.2.4 Study Design

This is a cross sectional study of all patients who underwent LSG from May 2011 to February 2014, in the NL Bariatric Surgery program. A chart review was conducted. For each chart, a single data collector (VF) reviewed pre-operative and post-operative clinic visit records, relevant laboratory investigations, and hospital discharge summaries. Data on patient demographics, post-operative complications and mortality were collected. The Clavien-Dindo (CD) Classification (Table 1: Clavien-Dindo Classification) was used to grade the complications, which were grouped into minor and major[13]. Minor complications were

defined as CD grades I and II and major complications were defined as CD grades III to V. All complications were independently reviewed by the data collector (VF) and one of the surgeons (DP) and graded according to the CD classification system. Inter-rater agreement was 100%.

Table 4.1: Clavien-Dindo Classification of Surgical Complications[14]

Grade	Description
I	Any deviation from the normal postoperative course without the need for pharmacological treatment or surgical, endoscopic and radiologic interventions. Acceptable therapeutic regimens are: drugs as antiemetics, antipyretics, analgesics, diuretics and electrolytes and physiotherapy. This grade also includes wound infections opened at the bedside.
II	Requiring pharmacological treatment with drugs other than such allowed for grade I complications. Blood transfusions, antibiotics and total parenteral nutrition are also included.
III	Requiring surgical, endoscopic or radiological intervention.
IIIa	Intervention under regional/local anesthesia
IIIb	Intervention under general anesthesia
IV	Life-threatening complication requiring intensive care/intensive care unit management
IVa	Single-organ dysfunction
IVb	Multi-organ dysfunction
V	Patient demise

4.2.5 Statistical Analysis

Categorical variables were described as frequencies and percentages. Continuous variables were described using mean and standard deviation if normally distributed and using median and range if the variables were not normally distributed. All analyses were done using IBM SPSS for Windows (Version 21; IBM, Armonk, NY).

4.3 Results

4.3.1 Patient Characteristics

Between May 2011 and February 2014, 209 patients underwent LSG at this center. The mean pre-operative BMI was 49.2 kg/m^2 (min 35.0 kg/m^2, max 67.4 kg/m^2), 82% of patients were female, and the average age was 43.4 years (min 22 years, max 70 years). The four most

common obesity- related comorbidities among the patients were: HTN (55.0%), OSA (46.4%), DLD (42.1%) and DM2 (37.8%) (Table 2: Characteristics of the first 209 patients undergoing LSG). All procedures were successfully completed laparoscopically. Operative time was available for 206 cases and ranged from 40 to 177 minutes (mean 78.63 minutes, SD 23.43min). Mean hospital LOS was 2.2 days (SD 1.26, range 1-16 days). There was no 30-day post-operative mortality.

Table 4.2: Characteristics of first 209 patients undergoing LSG

Characteristic	
Age, mean (SD) Range, years	43.4 years (9.55) 22 - 70 years
Female, n(%)	169 (80.9%)
Pre-operative weight kgs, mean (SD)	134.3kg (23.31)
Pre-operative BMI, mean (SD)	49.2 kg/m^2 (6.72)
Operative time minutes, mean (SD) Range, minutes	78.63min (23.43) 40-177 minutes
LOS in days, mean (SD) Range, days	2.2 days (1.26) 1-16 days
Comorbidity	**n(%)**
HTN	115 (55.0)
OSA	97 (46.4)
Diabetes	78 (37.3)
GERD	76 (36.4)
CVD	11 (5.3)
OA	76 (36.4)
DLD	88 (42.1)
Anxiety/Depression	80 (38.3)

4.3.2 Complications

Eight patients (3.8%) experienced CD grade I complications: 4 patients required intravenous fluid rehydration, 2 patients developed a rash requiring antihistamines, 1 patient had urinary retention, and 1 patient had a significant drop in hemoglobin leading to prolonged

LOS but not transfusion. Grade II complications occurred in 20 patients (9.6%); 6 patients experienced a post-operative drop in hemoglobin requiring blood transfusion; 2 patients suffered a pulmonary embolism (PE) and were started on anticoagulation therapy, and 12 patients developed minor infections requiring oral antibiotics. Two patients (1.0%) experienced a Grade IIIa complication: 1 patient experienced a gastric fistula treated with percutaneous drainage and another developed a stricture requiring endoscopic bougie dilation. Two leaks occurred (1.0%), requiring intervention under general anesthesia (Grade IIIB). One of these patients (0.5%) required percutaneous drainage, as well as placement of an endoscopic stent. The other patient (0.5%) experienced an almost immediate post-operative leak treated with re-operation on POD#1 (Table 3: Less than 30 day complications associated with LSG using Clavien-Dindo Classification, categorized as major and minor complications). The overall minor complication rate was 13.4% and the major complication rate was 1.9%.

4.3.3 Literature Review of Studies Assessing post-operative LSG Complications

In the study by Vidal et al. 2013, minor complications (4.4%) were reported in 5 patients that included urinary tract infection (n=2), pseudomembranous colitis (n=1), hypertensive crisis (n=1), subphrenic abscess (n=1). Major complications (4.4%) were reported in five patients and included gastric leak (n=2), post-site bleeding (n=2) and acute myocardial infarction resulting in death (n=1)[14].

In the study by Peterli et al. 2013, minor complications were reported in 7.5% of patients of which 3 were nonsurgical, one was surgical and 3 were due to dysphagia. Obstruction (n=1) and infection (n=1) were identified as major complications for a major complication rate of 0.9%[15].

Lemanu et al. 2012 reported 38 minor complications and 28 major complications. The major complications included: 23 grade III, 5 grade IV and 1 grade V. The authors report staple line leakage (2%), staple line bleeding (2.5%) and one death (0.3%)[16].

Goiten et al. 2014 also used the CD Classification and reported an overall complication rate of 3.8%. Sixty-two patients experienced minor complications (2.3%) and 48 patients developed major complications (1.8%). Absolute 30-day complication rates were reported as follows: bleeding 2.5% (n=66), leakage 0.8% (n=22), VTE 0.2% (n=4) and obstruction 0.1% (n=3)[17].

Table 4.3: Less than 30-day complications associated with LSG using the Clavien-Dindo Classification, categorized as major and minor complications[11]

	Study				
CD Grade	Falk 2015 (n=209)	Goiten18* 2015 (n=2651)	Vidal15 2013 (n=114)	Peterli[16] 2013 (n=107)	Lemanu[17] 2012 (n=400)
Minor					
I	7 (3.3%)	19 (0.7%)		5 (4.7%)	20 (5%)
II	21 (10.0%)	43 (1.6%)	5 (4.4%)	3 (2.8%)	18 (4.5%)
Minor Complications	**28 (13.4%)**		**5 (4.4%)**	**8 (7.5%)**	**38 (9.5%)**
Major					
III				1 (0.9%)	23 (5.6%)
IIIa	2 (1.0%)	18 (0.7%)			
IIIb	1 (0.5%)	22 (0.8%)	4 (3.5%)		
IV	1 (0.5%)				5 (1.3%)
IVa	-	5 (0.2%)	-		
IVb	-	2 (0.07%)	-		
V	-	1 (0.04%)	1 (0.9%)		1 (0.3%)
Major Complications	**4 (1.9%)**		**5 (4.4%)**	**1 (0.9%)**	**29 (7.3%)**
Overall Complications	32 (15.3%)	110 (3.8%)	10 (8.8%)	9 (8.4%)	67 (16.8%)

4.4 Discussion

Laparoscopic sleeve gastrectomy has been shown to be an effective stand-alone bariatric procedure[7]. It generally has a shorter operative time and easier learning curve than the current gold standard LRYGB. The increasing number of Canadians living with obesity and the growing number of LSG surgeries being performed in Canada warrant a closer look at the safety of LSG.

Our institution is a newly established bariatric surgery center comprised of three bariatric surgeons that, collectively, perform less than 125 procedures annually. Our study population demographics and comorbidity profile are similar to other bariatric surgery populations (e.g., average age 43 years, >80% female, average pre-surgery BMI 49 kg/m^2). Over a third of our patients report DM2, GERD, and DLD, while close to and over half report OSA and HTN.[6]

In our study, the major complication rate was 1.9% This finding falls in the range reported by the other comparable studies that use the CD Classification (i.e., range 0.9% to 7.3% (Table 3). The minor complication rate of 13.4% reported in our study is higher than that of the other three studies that reported minor complication rates at 4.4% to 9.5% (Table 3).

Our overall complication rate of 15.3% falls within the range of 3.8% to 16.8% reported by the four other comparable studies (Table 3). In the current study there was no 30-day mortality. Mortality rates were also low in the comparable studies and ranged from 0 to 0.9%.

This study suggests that an annual bariatric surgery procedure volume of 125 cases is not required for performing LSG safely. Although the rational for this guideline is clear, our results suggest that a lower number is acceptable. This may be explained by the fact that all cases in this study were performed by two surgeons with at least one of the surgeons involved

being fellowship-trained in bariatric surgery. Also, prior to starting the program, the first two cases were proctored by an experienced visiting surgeon who had performed several hundred LSG procedures.

Chapter 5: Summary

5.1 Overview

The results of this cross sectional study and review of the literature show that laparoscopic sleeve gastrectomy is safe and low complication rates can be achieved even in smaller centers which do not qualify as bariatric centers of excellence. This chapter reviews the strengths and limitations of this cross sectional review, implications for clinical practice, future research and overall study conclusion.

5.2 Strengths and Limitations

This study has a number of strengths. First we used a reliable and valid classification system to grade and report surgical complications following LSG. Second we had complete follow-up data on our first 209 patients. Third, all procedures were conducted by surgeons at the same academic affiliated health care institution using a two surgeon per case approach. Finally, a comprehensive chart review was conducted which is more likely to capture all minor complications (e.g., rash, dehydration) thus describing the morbidity associated with LSG more accurately.

The current study has some limitations that include its retrospective observational study design and its focus on 30-day complications rates only; therefore, we are not capturing potential delayed complications known to occur after LSG such as GERD, hernias and gastric fistula.

5.3 Clinical implications of the Current Study Findings

The findings of our study show that bariatric surgery centers performing fewer than the suggested number of procedures in order to be considered a BSCOE can achieve similar outcomes and complication rates. This study's 30-day complication rates were comparable to

those from other bariatric centers[1-4]. With the growing rate of obesity[5,6], smaller bariatric centers offering LSG as a primary weight loss surgery are a valid and safe option to accommodate the increasing number of patients seeking surgical treatment. Some patients would also prefer smaller centers as these are closer to their hometown and social support system. By supporting smaller bariatric centers, which do not perform high enough volumes to be considered centers of excellence but yet supply patients with a multidisciplinary approach to obesity management and fellowship-trained surgeons, the health care system can provide more timely and convenient access to LSG for qualifying obese patients. Furthermore, this would decrease the burden on bariatric surgery centers of excellence with high volumes, which can then focus more on complex procedures (e.g. duodenal switch) and patients (e.g. revision surgery).

5.4 Future Research

In order to standardize grading and reporting of complications following bariatric surgery, future studies should use the Clavien-Dindo Classification. In addition, future research should include an examination of long-term complications such as GERD and nutritional deficiencies after LSG. Finally, identifying predictors of complications after LSG and the potential contribution post-operative complications make to unsuccessful weight loss may help to inform clinical decision-making.

5.5 Conclusion

In summary, a new, low-volume bariatric center can safely perform laparoscopic sleeve gastrectomy if steps are taken to ensure that the surgeons are appropriately trained and patients have access to a dedicated bariatric health team. The Clavien-Dindo Classification system appears to be a useful, standardized method for comparing 30-day complication rates following LSG surgery.

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Appendices

Appendix A: Health Research Ethics Board, Full approval

NEWFOUNDLAND AND LABRADOR
HREB
HEALTH RESEARCH ETHICS BOARD

Ethics Office
Suite 200, Eastern Trust Building
95 Bonaventure Avenue
St. John's, NL
A1B 2X5

August 26, 2014

Ms Vanessa Falk
6 Days Road
Portugal Cove
St. Philips, NL

Dear Ms. Falk

Reference #14.179

Re: Complications of laparoscopic sleeve gastrectomy: a single centre's experience

Your application received an expedited review by a Sub-Committee of the Health Research Ethics Board and **full approval** was granted effective **August 25, 2014.**

This approval will lapse on August 25, 2015. **It is your responsibility to ensure that the Ethics Renewal form is forwarded to the HREB office prior to the renewal date; you may not receive a reminder, therefore the ultimate responsibility is with you as the Principle Investigator.** *The information provided in this form must be* ***current to the time of submission*** *and submitted to the HREB* ***not less than 30 nor more than 45 days*** *of the anniversary of your approval date.* The Ethics Renewal form can be downloaded from the HREB website http://www.hrea.ca.

This is to confirm that the following documents have been reviewed and approved or acknowledged (as indicated):

- Application, approved
- Chart Audit Form, approved

The Health Research Ethics Board advises THAT IF YOU DO NOT return the completed Ethics Renewal form prior to date of renewal:

- *Your ethics approval will lapse*
- *You will be required to stop research activity immediately*
- *You may not be permitted to restart the study until you reapply for and receive approval to undertake the study again*

Lapse in ethics approval may result in interruption or termination of funding

email: info@hrea.ca Phone: 777-6974 FAX: 777-8776

It is **your responsibility to seek the necessary approval from the Regional Health Authority or other organization as appropriate. You are also solely responsible for providing a copy of this letter, along with your application form, to the Office of Research Services should your research depend on funding administered through that office.**

Modifications of the protocol/consent are not permitted without prior approval from the Health Research Ethics Board. Implementing changes in the protocol/consent without HREB approval may result in the approval of your research study being revoked, necessitating cessation of all related research activity. Request for modification to the protocol/consent must be outlined on an amendment form (available on the HREB website) and submitted to the HREB for review. This research ethics board (the HREB) has reviewed and approved the research protocol and documentation as noted above for the study which is to be conducted by you as the qualified investigator named above at the specified site. This approval and the views of this Research Ethics Board have been documented in writing. In addition, please be advised that the Health Research Ethics Board currently operates according to *Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans; ICH Guidance E6: Good Clinical Practice* and applicable laws and regulations. The membership of this research ethics board is constituted in compliance with the membership requirements for research ethics boards as defined by *Health Canada Food and Drug Regulations Division 5; Part C*
Notwithstanding the approval of the HREB, the primary responsibility for the ethical conduct of the investigation remains with you.

We wish you every success with your study.

Sincerely,

[redacted]

Dr Fern Brunger, PhD (Chair Non-Clinical Trials)
Ms. Patricia Grainger, (Vice-Chair Non-Clinical Trials)
Health Research Ethics Board

For office use only: September 4, 2014

email: info@hrea.ca Phone: 777-6974 FAX: 777-8776

Appendix B: Health Research Ethics Authority, Request For Renewal

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May 2015

Health Research Ethics Authority

Request For Ethics Renewal / Study Closure

- The Tri-Council Policy Statement- Ethical Conduct for Research Involving Humans (TCPS2; 2010) (article 6.14) requires ongoing review by the approving REB at least on an annual basis. The information provided in this form must be current to the time of submission and submitted to the HREA not less than 30 days nor more than 45 days before the anniversary of your approval date.
- Ethics approval is required if there is ongoing subject contact or data collection/transfer is active.
- Ethics approval is not required and the file may be closed if the project is in analysis or the writing stage.
- Please forward a summary of findings or published abstract to the HREA Office once the study is complete.
- Incomplete forms will not be accepted and may result in delay in the review and approval process

HREB Ref Number: 14.179	Expiry Date of Current Approval ~~07/25/2015~~ 08/25/2015
Principal Investigator: Vanessa Falk	
Title of study (with Protocol Number if applicable): Complications of laparoscopic sleeve gastrectomy: a single centre's experience	
Email of PI: vsf208@mun.ca	Email of Key Contact: ethwells@mun.ca

Please chose one:

☐	I am requesting renewal of ethics approval for this file.	✓
☐	I am requesting to close this file.	

Vanessa Falk — [redacted] — 07/06/15

Name typed or printed | Signature of PI | Date (MM/DD/YYYY)

For HREB Office Use Only:

This project was reviewed on July 8, 2015 (Date) By Full Board Review [ ] By Expedited Review [✓]

Ethics approval for this project has been granted for a period of 12 months effective From July 25, 2015 to July 25, 2016

This research ethics board (the HREB) has reviewed and approved the study which is to be conducted by you as the qualified investigator/principal investigator named above. This approval and the views of this Research Ethics Board have been documented in writing. The Health Research Ethics Board operates according to *Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans, ICH Guidance E6: Good Clinical Practice: Consolidated guideline* and applicable laws and regulations. The membership of this research ethics board is constituted in compliance with the membership requirements for research ethics boards as defined by Health Canada Food and Drug Regulations Division 5; Part C.

This file has been closed as requested ☐

[redacted]

Signatu

APPROVED JUL 0 8 2015

Date

Page 1 of 3

Recruitment/Data Collection

Has the study started? Yes [✓] No [ ]

If yes, please provide the following information as it applies to your project.

	Total planned for this site	Total to date *(if applicable)*	N/A
A. Number of Participants enrolled			✓
B. Number of Health Records reviewed	250	209	
C. Number of tissue samples collected			✓
D. Number of surveys returned			✓

If more or fewer than expected, why?

Consent Form

Does this project have a consent form? Yes [ ] No [✓]

If yes, Please give the date of the most recently approved consent form MM DD YYYY

Not Applicable [✓]

For Clinical Trials Only *which are subject to ICH & Health Canada and required to report SAEs and SUSAR's to the REB*

Serious Adverse Event/s (SAE's) Or Suspected Unexpected Serious Adverse Reactions (SUSARS)

1. Since Last Approval a. Have DSMB/ QSR reports been submitted to HREB?	Yes [ ]	No [ ]
2. Since Last Approval a. Has there been amendments to this protocol as a result of safety reports ? *If yes, please provide a list amendment dates*	Yes [ ]	No [ ]
3. Since Last Approval a. Have you reported local SAE's? b. If yes, please provide number of local events: _____ c. If yes, please provide number of local SAE's related to study drug: _____	Yes [ ]	No [ ]
4. Since Last Approval a. Have you reported deviations to the sponsor? b. If yes, please provide number of Deviations: _____	Yes [ ]	No [ ]
5. Since Last Approval a. Have you requested waivers? b. If yes, please provide number of waivers: _____	Yes [ ]	No [ ]

Not Applicable [✓]

All Other Studies: Since Last Approval Have there been unexpected events or problems related to participant risk since original approval or last ethics renewal?	Yes	No
1. Have there been amendments submitted for this project?	Yes	No
If yes, please describe the events/problems/amendments : (Add an addendum to this form if necessary)		

All Studies - Status At Local Site (check all that apply)	YES	NO	N/A
1. Intervention/data collection active	✓		
2. Closed to recruitment/accrual			✓
3. Participants in follow up			✓
4. Site closed [clinical trials only]			✓
5. For secondary use of data only is Data Transfer Complete			✓

Knowledge Transfer	YES	NO	N/A
1. Have participants been informed of study findings?			✓
2. Have findings been presented/published? *Please Indicate where: (Add an addendum to this form if necessary)*	✓		

Not Applicable [✓]

For Study Closure:	
1. Sponsor close out visit	Date:
2. Participants completed the study at this site	#
3. Database to be locked	Date:
4. Reason for closure:	

Note: GCP requires a copy of the final report to be submitted to the Research Ethics Board

Additional Information:

Poster presentation @ SAGES meeting April 2015 ;
V. Talle, D. Pace, L. Twells, C. Smith, D. Boone, R. Murphy, K. Lesta,
D. Gregory. Laparoscopic Sleeve Gastrectomy at a Small
Canadian Center : 30-day Complication Rate. Surg Endosc (2015) 29: P377