The Physiology and Pathophysiology of Laparoscopic Adjustable Gastric Bands

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SUMMARY

The laparoscopic adjustable gastric band (LAGB) has rapidly emerged as one of the most powerful medical interventions available. Originally a physically restrictive operation, evolution of the technique has resulted in what is now hypothesised to be a satiety inducing procedure.

There is limited understanding of associated physiological processes; including oesophageal motility, transit and gastric emptying. Intraluminal pressure effects of the LAGB have not been identified. Recently, a new spectrum of poorly defined intermediate term complications have arisen; presenting a major diagnostic and management challenge.

The adjustability of the LAGB offers the ideal opportunity to tailor the procedure, optimising outcomes and avoiding complications.

This thesis sought to address key areas of knowledge deficiency relating to the clinically relevant physiology and pathophysiology of the LAGB.

High resolution manometry studies showed that in successful patients the LAGB produces an intraluminal pressure of 26.9±19.8 mm Hg, immediately beneath the oesophago-gastric junction. Adding saline to the LAGB increased intraluminal pressure in a linear fashion (21.2±8.7 mm Hg/ml), after a threshold volume was reached. Lower oesophageal sphincter (LOS) basal tone was attenuated (11.2±6.9 mm Hg), although deglutitive relaxation was normal.

A mean of 4.5±2.9 oesophageal contractions were required to clear a semi-solid bolus across the LAGB. Trans LAGB flow only occurred during oesophageal peristaltic contractions; separated by reflux events that stimulated repeat peristalsis. The LOS serves a contractile function in LAGB patients, increasing intrabolus pressure in the isobaric region above the LAGB. Incorporation of assessment of LOS contractility, defined as the lower oesophageal contractile segment, improved the sensitivity of manometric diagnostic criteria.

A semi-solid stress contrast swallow protocol and high resolution manometry identified luminal dilatations above the LAGB and focal impairments in oesophageal motility where no abnormality had been seen on liquid contrast swallow. Abnormalities were classified as: Transhiatal (oesophageal) enlargement (31%), gastric enlargement (40%), pan-oesophageal dilatation with aperistalsis (6%), deficient oesophageal motility (11%) and anatomically normal (12%).

Gastric enlargements responded well to revisional LAGB surgery provided oesophageal motility was intact. Oesophageal enlargements or deficient motility were not responsive to treatment. Mild impairment of oesophageal peristalsis was not found to be clinically significant.

A new technique allowed visualisation of the LAGB during scintigraphic studies. Semi-solid transit into the infraband stomach was delayed following LAGB (11 vs. 2, *p=0.001*). Meal retention above the LAGB was not observed. Removing saline from the LAGB normalised transit. Gastric emptying was not affected by LAGB. Twelve months following LAGB satiety increased after both a standard fast (3.7±2.3 vs.4.8±2.1, *p=0.04*) and a standard semi-solid meal (5.9 vs. 7.8±1.7, *p=0.003*).

In a cross sectional study 323 of 408 patients responded (79%). Expected ranges for reflux: 8.7±9.8 (0=no reflux, 72=severe reflux), dysphagia: 19.9±8.7 (0=no dysphagia, 45=total dysphagia to water) and frequency of regurgitation (mean once per week) were established. Weight loss was the only predictor of patient reported satisfaction (r^2=0.46, p=0.01).

This thesis has described physiological processes associated with LAGB, the mechanisms of bolus transit and the intraluminal effects of adjustments. The LAGB was shown to delay transit and induce satiety, without physically restricting meal size.

New, sensitive diagnostic tests combined anatomical change with assessments of oesophageal motility; allowing the spectrum of intermediate term complications and their response to treatment to be defined.

The future challenge is to translate these data to improvements in outcomes and better understand the mechanism of weight loss.

General Declaration

I hereby declare that this thesis contains no material which has been accepted for the award of any other degree or diploma at any university or equivalent institution and that, to the best of my knowledge and belief, this thesis contains no material previously published or written by another person, except where due reference is made in the text of the thesis.

This thesis includes 6 original papers published in peer reviewed journals and 3 submitted manuscripts. The core theme of the thesis is the physiology and pathophysiology of laparoscopic adjustable gastric bands used for the treatment of obesity.

The ideas, development and writing up of all the papers in the thesis were the principal responsibility of myself, the candidate, working within the Centre for Obesity Research and Education under the supervision of Associate Professor Wendy Brown and Professor Paul O'Brien.

The inclusion of co-authors reflects the fact that the work came from active collaboration between researchers and acknowledges input into team-based research.

In the case of chapters 13 to 21 my contribution to the work involved the following:

Thesis chapter	Publication title	Publication status	Nature and extent of candidate's contribution
13	The effect of laparoscopic adjustable gastric bands on esophageal motility and the gastro-esophageal junction; analysis using high resolution video manometry	Published (*Obesity Surgery*)	Overall responsibility for all aspects of study, designing, planning, patient recruitment, conducting studies, recording and analysing data. Writing manuscript.
14	Effects of Gastric Band Adjustments on Intraluminal Pressure	Published (*Obesity Surgery*)	Overall responsibility for all aspects of study, designing, planning, patient recruitment, conducting studies, recording and analysing data. Writing manuscript.

15	Pathophysiology of laparoscopic adjustable gastric bands: Analysis and classification using high resolution video manometry and a stress barium protocol	Published (*Obesity Surgery*)	Overall responsibility for all aspects of study, designing, planning, patient recruitment, conducting studies, recording and analysing data. Writing manuscript.
16	Mechanisms of Bolus Clearance in Patients with Laparoscopic Adjustable Gastric Bands	Published (*Obesity Surgery*)	Overall responsibility for all aspects of study, designing, planning, patient recruitment, conducting studies, recording and analysing data. Writing manuscript.
17	Criteria for Assessing Esophageal Motility in Laparoscopic Adjustable Gastric Band Patients: The Importance of the Lower Esophageal Contractile Segment	Published (*Obesity Surgery*)	Overall responsibility for all aspects of study, designing, planning, patient recruitment, conducting studies, recording and analysing data. Writing manuscript.
18	Outcomes of Intermediate term complications following Laparoscopic Adjustable Gastric Banding	Submitted	Overall responsibility for all aspects of study, designing, planning, patient recruitment, conducting studies, recording and analysing data. Writing manuscript.
19	Effects of Adjustable Gastric Bands on Gastric Emptying, Supra and Infraband Transit and Satiety: A Randomised Double Blind Cross Over Trial	Submitted	Overall responsibility for all aspects of study, designing, planning, patient recruitment, conducting studies, recording and analysing data. Writing manuscript.

20	Changes in Satiety, Supra and Infra-band Transit and Gastric Emptying Following Laparoscopic Adjustable Gastric Banding: A Prospective Follow up Study	Submitted	Overall responsibility for all aspects of study, designing, planning, patient recruitment, conducting studies, recording and analysing data. Writing manuscript.
21	Outcomes, Satiety and Adverse Upper Gastrointestinal Symptoms Following Laparoscopic Adjustable Gastric Banding	Published (*Obesity Surgery*)	Overall responsibility for all aspects of study, designing, planning, patient recruitment, conducting studies, recording and analysing data. Writing manuscript.

Specific assistance was provided by Dr Ken Yap who reported the nuclear scintigraphy studies in chapters 19 and 20 and Mr Matthew O'Donnell who provided technical expertise in acquiring and reprocessing images for those same studies.

Figures 6.1, 17.4 and 18.5 were drawn by Dr Levent Efe, a commissioned professional medical artist, under my direction and from sketches I provided. They were designed to communicate specific concepts developed from research undertaken in this thesis. The copyright use of these images is exclusively licensed to me and the Centre for Obesity Research and Education.

I have renumbered sections of submitted or published papers in order to generate a consistent presentation within the thesis.

Signed: ……………………………………………………………………

Date: …………………………………................................

Publications arising from this thesis

1) **The effect of laparoscopic adjustable gastric bands on esophageal motility and the gastro-esophageal junction: analysis using high-resolution video manometry.**

Burton PR, Brown WA, Laurie C, Richards M, Afkari S, Yap K, Korin A, Hebbard G, O'Brien PE.

Obes Surg. 2009 Jul;19(7):905-14.

2) **Effects of gastric band adjustments on intraluminal pressure.**

Burton PR, Brown WA, Laurie C, Richards M, Hebbard G, O'Brien PE.

Obes Surg. 2009 Nov;19(11):1508-14.

3) **Pathophysiology of laparoscopic adjustable gastric bands: analysis and classification using high-resolution video manometry and a stress barium protocol.**

Burton PR, Brown WA, Laurie C, Korin A, Yap K, Richards M, Owens J, Crosthwaite G, Hebbard G, O'Brien PE.

Obes Surg. 2010 Jan;20(1):19-29.

4) **Criteria for Assessing Esophageal Motility in Laparoscopic Adjustable Gastric Band Patients: The Importance of the Lower Esophageal Contractile Segment.**

Burton PR, Brown WA, Laurie C, Hebbard G, O'Brien PE.

Obes Surg. 2009 Dec 12. [Epub ahead of print]

5) **Mechanisms of Bolus Clearance in Patients with Laparoscopic Adjustable Gastric Bands.**

Burton PR, Brown WA, Laurie C, Hebbard G, O'Brien PE.

Obes Surg. 2010 Jan 12. [Epub ahead of print]

6) **Outcomes, Satiety and Adverse Upper Gastrointestinal Symptoms Following Laparoscopic Adjustable Gastric Banding**

Burton PR, Brown WA, Laurie C, Lee M, Korin A, Anderson M, Hebbard G, O'Brien PE

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CHAPTER 1: *Introduction*

Laparoscopic adjustable gastric banding (LAGB) has rapidly emerged as one of the most powerful medical interventions available [1]. It safely and effectively induces and maintains a substantial weight loss [2]. Medical co-morbidities and quality of life can dramatically improve [3]. There is potentially a reduction in long term mortality and health care costs in selected patient groups [4, 5].

The overwhelming, worldwide obesity epidemic is demanding a safe and durable treatment. Non-surgical therapies or preventative measures have limited efficacy. Other bariatric procedures are more invasive and carry far higher risks of mortality and severe morbidity. The LAGB is therefore filling a critical niche.

Managing the rapidly expanding pool of patients who have undergone LAGB represents a major challenge. The adjustability of the LAGB is a unique feature that encourages ongoing follow up and allows the effects of the procedure to be finely controlled. The optimal delivery of follow up care and management of LAGB adjustments is hampered by limited understanding of the associated physiological processes.

Rapid uptake and evolution of LAGB surgical technique has simply outstripped physiological understanding. The modern procedure bears little resemblance to the original operation that was modelled on older restrictive bariatric interventions. LAGB has migrated from the creation of a small meal sized pouch to placement of the prosthesis within 1 cm of the oesophago-gastric junction (OGJ).

Improved outcomes and reduced complication rates have resulted; validating an effective procedure. The current, unique anatomical modification suggests a novel mechanism of action. There are also likely direct mechanical physiological effects.

Retention of a meal above the LAGB has traditionally been the mode of action attributed to the LAGB, although this does not fit with normal patterns of gastric emptying seen post-operatively [6]. Other data, however, suggest there is delayed emptying of the proximal stomach above the LAGB [7]. A comprehensive understanding of the characteristics of transit across the LAGB has not been established.

An alternate view is that the LAGB induces weight loss by activating the peripheral satiety mechanism without physically restricting meal size [8]. Presumably effects on the proximal stomach are important in the genesis of these sensations, although have not been precisely characterised. Whether satiety is induced through intraluminal events associated with the ingestion of food or is the result of an alternate effect remains unclear.

Classification of LAGB as either a restrictive or satiety inducing procedure remains controversial. A definitive mechanism supporting either hypothesis has not been established.

Placement of the LAGB immediately beneath the OGJ undoubtedly significantly impacts oesophageal body motility and the OGJ. It is also likely that components of oesophageal sensory and motor function are important in mediating a successful outcome following LAGB. Investigations have produced conflicting data on the

effects of LAGB on fundamental processes such as lower oesophageal sphincter function (LOS) and oesophageal motility [9]. Oesophageal manometry, whilst intrinsically appealing, has not gained acceptance as a useful investigation in LAGB patients.

Gastric prolapse was a troublesome complication early in the LAGB experience, however, has since decreased significantly in frequency with technical innovations [10]. Instead, the challenge of a more diverse spectrum of intermediate term complications has arisen. Patients are at times presenting with either adverse symptoms or unsatisfactory weight loss. These often represent variable patterns of luminal dilatation above the LAGB and are not always amenable to surgical intervention. Sometimes no abnormality is detected using a liquid contrast swallow or upper gastrointestinal endoscopy.

These problems remain poorly described in the literature both pathophysiologically and epidemiologically. Disparate reports on the incidence and management of LAGB complications are frequent. Without objective characterisation of these complications, meaningful comparative studies are difficult to undertake and interpretation of published outcome data subject to limitations. The management of these patients is difficult without an accurate description of the problems or sensitive diagnostic tests.

A major future challenge with LAGB lies in better understanding its mechanisms of action and the nature of post-operative complications. Ideally, the follow up and adjustment process would be linked by integrated physiological understanding. This could be leveraged to optimise weight loss, whilst avoiding adverse symptoms

or longer term complications. Alternatively, if complications were to arise, the availability of robust investigational techniques and clear management pathways would significantly enhance patient care. Furthermore, comparative studies with more objective outcomes and end points could be undertaken.

To achieve these goals an improved understanding of the physiological effects of LAGB adjustments, the associated follow up process and the anatomy and pathophysiology of post-operative problems is required.

The underlying premise of this thesis is that the LAGB is a highly effective and widely used treatment, yet we simply do not know enough about the associated physiological and pathophysiological processes. These are primarily clinically questions, however, may also provide insights into how the LAGB circumvents lipostatic drive, thereby achieving and sustaining weight loss.

The overall goal is to establish a better understanding of the peripheral physiological processes associated with the LAGB. The spectrum of physiological and anatomical changes associated with adverse symptoms or unsatisfactory progress will also be investigated. This should lead to the development of improved diagnostic tests and treatment pathways.

This thesis consists of a literature review and justification of research questions followed by 9 research chapters; each representing a published or submitted research paper in manuscript format. Finally, a conclusion and discussion synthesise research findings.

CHAPTER 2: *Overview of Literature Review*

The background literature review is divided into 3 themes over 7 chapters.

1) *The background problem of obesity and treatment options*

2) *The laparoscopic adjustable gastric band*

3) *Physiology relevant to the laparoscopic adjustable gastric band*

Chapter 3 introduces the background problem of obesity; its prevalence, consequences, genetic and physiological basis. The rationale for ascribing a high priority to the global health problem of obesity is established and currently available non surgical treatments and preventative measures considered in chapter 4.

In the second theme area, commencing in chapter 5, the worldwide rise of bariatric surgery in response to the obesity epidemic and the lack of effective treatments is reported. The development of bariatric surgery is detailed and its strengths and weaknesses objectively appraised. The rapid uptake of LAGB is justified as a response to the inherent problems associated with other more invasive surgical procedures; that are nonetheless highly successful.

Chapter 6 develops the surgical theme further, critically reviewing the published literature relating to LAGB. The evolution of LAGB surgical technique as a series of innovations over the past 15 years is described. Current outcomes, strengths, weaknesses and complications of LAGB are analysed.

Several key areas of knowledge deficiency relating to the LAGB are identified. These include the limited evidence base surrounding the follow up and adjustment process and the rise of a new spectrum of complex intermediate term complications that remain poorly defined. The opportunity to leverage the follow up process as a means of optimising outcomes is emphasised, yet shown to be an area in which there has been little investigation and physiological understanding is lacking.

The third section of the literature review assesses the physiological mechanisms potentially relevant to the LAGB, including previous work involving LAGB.

Chapter 7 focuses on the hypothesis that the LAGB procedure is satiety inducing; leading to a consideration of mechanisms potentially activating the peripheral satiety mechanism. The satiety hypothesis is balanced against traditional understanding and recent data that suggest the LAGB is a physically restrictive procedure; delaying emptying of the stomach above the LAGB and limiting meal size.

Physiological processes of gastric of emptying, motility and the generation of sensations due to intraluminal stimulation as well as hormonal feedback are considered in general and in previous work relating to bariatric surgery and the LAGB.

Weaknesses of studies documenting the physiology of LAGB are highlighted, showing there is a need to clarify the mechanisms of transit through the LAGB.

Chapter 9 and 10 detail the controversial area of oesophageal motility in LAGB patients. Conflicting data that has lead to confusion is presented, along with related animal data. The research methodologies of these studies are critically evaluated leading to a more detailed analysis of the key components of oesophageal physiology in general. Recent advances in the understanding of oesophageal physiology and means of investigating oesophageal function (high resolution video manometry) are presented, with the clear corollary that they may prove most useful in LAGB patients.

Chapter 11 is a synthesis of the background data identified in the literature review. Current knowledge about the LAGB process, problem areas and key knowledge deficits are matched with identified techniques that will best advance knowledge. This section demonstrates how the goals of the thesis were established by identifying clinical problems and matching these with means of answering critical questions.

CHAPTER 3: *Obesity – The Problem*

Definition and the background problem

Obesity and overweight represent one of the most significant global health care challenges [11]. Increasing prevalence of the disease and recognition of its consequences has focused medical, community and media attention on the problem.

Obesity is defined as a disease in which fat has accumulated to an extent that health is impaired. This may be due to an increased number of fat cells or the presence of larger fat cells [12]. Excess adipose tissue directly leads to significant social stigmata, discrimination, decreased employment opportunities, decreased quality of life and physical limitations [13-18].

The medical significance of obesity lies in the multiplicity of severe secondary adverse effects. These vary between patterns of obesity and are affected by genetic and environmental influences. There is a causative link between obesity and many diseases; most importantly type 2 diabetes, metabolic syndrome and increased cardiovascular risk [19, 20]. There is an increased mortality rate [21-25].

The body mass index (BMI) is the most widely used means of estimating adiposity and classifying obesity. It has the advantages of simplicity and reproducibility. BMI is a simple calculation that divides weight in kilograms by height in metres squared. Usually there are significant differences in body composition between an individual with a normal BMI and one considered obese. In a healthy adult male with a body mass index (BMI) of 22 kg/m^2, approximately 20% of total tissue mass is fat. In

contrast, in an obese individual with a BMI of 30 kg/m^2, approximately 50% of total body mass will be adipose tissue [26].

The World Health Organisation (WHO) classifies underweight as: BMI < 18.5 kg/m^2, healthy weight: BMI > 18.5 kg/m^2 to BMI < 25 kg/m^2, overweight: BMI> 25 kg/m^2 to < 30 kg/m^2 and obese: BMI > 30 kg/m^2. Obesity can be further classified into severe obesity: BMI >35 kg/m^2, morbid obesity: BMI >40 kg/m^2 and super obesity: BMI >50 kg/m^2. Whilst there are situations where the BMI can be erroneous, such as in muscular athletes and it is not suited for use in children; it has proven adequate in the vast majority of patients, particularly those seeking surgical treatment [27]. Adaption of BMI categories may also be required to account for racial differences [28].

Patterns of obesity can also be stratified based on the anatomical distribution of fat depots [29]. The use of more specific measures, such as waist circumference, may be better at defining specific syndromes and determining cardiovascular risk [30]. Dual X-ray absorptiometry and isotopic dilution techniques are able to give more precise quantification of total body adiposity, however, are not practically useful outside research [31]. Other simpler methods including bio-electrical impedance or skin fold testing can also be used.

Central obesity, typically associated with the metabolic syndrome and increased cardiovascular risk, is associated with enlarged visceral fat depots. Waist circumference and waist to hip ratio are frequently advocated as measurements better able to predict cardiovascular risk [32].

Epidemiology

There are ample, worldwide data on the prevalence of obesity and the severity of consequences. The WHO, in 2006, estimated there were 400 million obese people and a further 1.6 billion who were overweight [33]. This is projected, by 2015, to increase to 2.3 billion overweight and 700 million obese adults. Globally, at least 20 million children under the age of 5 years were overweight in 2005.

Australian data, derived from the most recent National Health Survey (NHS) data in 2007-2008, measured Body Mass Index (BMI) in representative population samples [34]. Twenty five percent of persons aged 18 years and over were found to be obese, 37% overweight, 37% normal weight and 2% underweight. The highest rate of overweight/obesity was in the 65–74 year old age group, at 75%. More adult males (68%) were overweight or obese than females (55%) [34]. Other estimates suggest the current prevalence of overweight and obesity is 62% of males and 45% of females [35].

This pattern is repeated throughout the Western world where obesity rates have at least doubled over the past 25 years [36]. In Britain, 24% of the adult population are obese along with 10% of children. A further 20–25% of children are overweight. The prevalence of morbid obesity is 2.1%. A United Kingdom government report estimated that 40% of Britons would be obese by 2025 and by 2050 Britain could be a mainly obese society [37]. In the United States 5.1% of adults are morbidly obese [38].

Originally concentrated in Western countries, obesity has become a global problem. Previously underdeveloped nations are seeing over nutrition surpass under nutrition as a problem for the first time [39, 40]. Low and middle income countries are increasingly afflicted, particularly in inner urban areas [33].

Worldwide obesity rates have been increasing since the 1950s. The current rate of increase is estimated to be 1% per year [41]. In Australia, levels of overweight increased from 29.5% reported in the 1995 NHS to 32.6% in 2004-05 [35]. Obesity rose from 11.1% in 1995 to an estimated 25% today. Not only is the prevalence of overweight and obesity increasing but the prevalence of the more severe forms (morbid obesity, BMI >40 kg/m^2) is also increasing [42]. It can be argued that the rate of increase may have possibly stopped or slowed [43]. However, with such a prevalent disease, increases cannot continue indefinitely.

Obesity is now a major problem in childhood, affecting 6-8% of Australian Children [44]. This represents a quarter of a million obese school aged children in Australia. The rate of overweight and obesity combined has increased from approximately 10-12% in 1985 to 25% in 2004. An increase of 1.8% in the incidence of childhood obesity in the past 5 years represents an additional 65,000 obese children [44].

The natural history of obesity is for one third of overweight individuals to become overweight before they are twenty with others becoming overweight in adulthood. Obese adolescents are 5 to 20 times (depending on age and family situation) more likely to become obese adults [45, 46]. Having an obese parent at least doubles the risk of obesity in adult life [45]. More concerning are the projected life long associated medical, physical and psychological problems [47]. Overweight and

obese children were at significantly increased risk of mortality and a range of medical problems over a 55 year follow up period [46].

Consequences of obesity

Overall, 7.5% of Australia's total disease burden in 2003 was attributable to obesity, making it the third most important risk factor after cigarette smoking (7.8%) and hypertension (7.6%) [48]. It may well have already surpassed these other risk factors, or will do so in the near future. Obesity is possibly the most significant problem currently facing our health care system [36].

Compared to other similarly developed countries, Australia has greater obesity rates, whilst other significant health risk factors, such as cigarette smoking, are relatively better controlled. Access Economics estimated that in 2005 the total financial cost of obesity in Australia was $4 billion [48].

Diseases such as type 2 diabetes, osteoarthritis, hypertension, obstructive sleep apnoea and depression are more common and annual health care costs higher in patients who have a BMI greater than $35kg/m^2$ compared to patients with a BMI in the healthy range [36]. These patients also have an increased risk of death [49]. Excess weight and obesity have most significantly been associated with excess mortality due to cardiovascular diseases [21]. It remains unknown how exactly obesity drives a diverse spectrum of health problems [50].

A recent Australian prospective follow up study reported 15 year data on determinants of cardiovascular disease mortality amongst 8,862 Australian adults. Central obesity and cigarette smoking were the most powerful predictors. It was

concluded that the management of central obesity was at least as important as the management of lipid levels and hypertension [51].

Population data from the US suggest that obesity is associated with significantly increased cardiovascular mortality, resulting in 112,159 excess deaths annually [21]. Overweight and obesity combined were associated with increased mortality from diabetes and kidney disease. Mortality was also increased from cancers considered obesity related; being responsible for an annual 13,839 deaths [21].

A recent systematic review evaluated the evidence base supporting the strength of association of obesity and overweight with 20 significant diseases commonly associated [52]. This study identified the extreme risk of diabetes with obese females having an increased risk of 12 times and males 6 times. Obesity has recently been suggested to represent the greatest risk factor for venous thromboembolism [53].

The WHO, in 2000, classified the relative risks of particular disease in obese people into three broad categories: greatly increased risk (relative risk much greater than 3), including type 2 diabetes, dyslipidaemia, insulin resistance, breathlessness, sleep apnoea and gall bladder diseases; moderately increased risk (relative risk 2 to 3), including cardiovascular disease, hypertension, osteoarthritis of the knees and gout; and slightly increased risk (relative risk 1 to 2), including colon cancer, breast cancer in postmenopausal women, endometrial cancer, reproductive hormone abnormalities, polycystic ovary syndrome, impaired fertility, foetal defects, low back pain and risk of anaesthetic complications.

There is convincing evidence of a positive association between overweight/obesity and risk for adenocarcinoma of the oesophagus and the gastric cardia, colorectal cancer, postmenopausal breast cancer and several other malignancies [54-56]. There may be an increased risk of cancers of the liver, gallbladder, pancreas, thyroid gland and in lymphoid and haematopoietic tissue [57, 58]. In some cancers obesity confers an increased risk at a younger age, with decreased survival following diagnosis [59].

The aetiology of the increased risk of cancer is unknown [60]. Insulin resistance may be significant; however, there are several other candidate systems. With such a diversity of obesity related cancers there are likely to be multiple mechanisms [61]. Overlapping associations and environmental exposures may increase both the risk of obesity and cancer.

Causation of obesity

There are multiple theories concerning the aetiology of obesity with most focusing on genetic predisposition combining with environmental triggers [36, 62-64]. Obesity is the end result of excess caloric intake in relation to expenditure [26, 65-68]. This positive energy balance is favoured in modern society, with easy access to palatable, high energy foods including caloric containing beverages [69]. Over the past two decades the total amount of food purchased and presumably consumed per person has increased [70].

Increased caloric intake, rather than decreased expenditure is considered most responsible for the modern obesity epidemic [41]. Supporting this theory are data

that suggest the majority of energy expenditure is not necessarily modifiable and humans struggle to match excess intake with an equivalent expenditure [41].

On an individual basis, energy expenditure is often less than total caloric intake – promoting the storage of excess energy as adipose tissue [41, 71]. Laboratory animals, when offered a modern diet become obese [26]. Sustained over time, excess energy is stored as adipose tissue supportive of the observation that obesity often develops over a period of years.

Obese individuals do not appear to intake a greater caloric load than normal weight people (per kg of lean body mass) and have an equivalent resting energy expenditure (per kg of lean body mass) [72]. One prospective study did not identify any association between obesity and   overall energy intake in children followed longitudinally [73].

Rising obesity rates have also correlated with an apparent decrease in mean sleep duration over the second half of the twentieth century [74]. Several proposed mechanisms associate decreased sleep with obesity [75, 76]. Appetite stimulation, with decreases in leptin and increases in ghrelin, as well as a reduction in insulin sensitivity has been proposed as a mechanism [74].

Genetics and hereditary factors in obesity

Hereditary factors appear to significantly influence BMI, with an effect estimated at between 64 and 84% [62]. Adopted twins have a body weight comparable to their biological rather than adoptive parents [77]. Similarly, twins reared apart demonstrate a close concordance in body weight [78, 79].

Multiple individual genes have been implicated in the causation of obesity, with several hundred potential loci identified [80]. The most common form of obesity appears to be polygenetic. Genetic predisposition interacts with the environment to determine phenotypic expression [81]. Genetically predisposed individuals are likely to become obese with minimal environmental exposure. Alternatively, those strongly or slightly predisposed demonstrate an increased BMI in response to increased environmental exposure. Another group of individuals can be considered resistant to the development of obesity, despite strong environmental exposure.

A variety of rare, syndromic genetic disorders associated with obesity have been well characterised [82, 83]. Prader-Willi and Bardet-Biedl syndrome are inherited in a Mendelian pattern and exhibit a range of associated anomalies [84]. The obesity expressed in these diseases appears the end result of hypothalamic dysfunction [62, 64]. Satiety and food intake is altered, without strong evidence of an effect on metabolism and energy balance. On this basis O'Rahilly and Farroqi concluded that "from an aetiological/genetic standpoint, human obesity appears less a metabolic than a neuro-behavioural disease" [62].

Recent discoveries have identified several monogenic obesity syndromes thought to be responsible for a small, but measurable, proportion of the obese within the population [85]. These include mutations in the melanocortin 4 receptor and brain-derived neurotrophic factor [86]. Potentially this area will be far better understood in the near future, with improved characterisation of other monogenetic and polygenetic mutations that drive obesity.

Regulation of appetite, body weight and energy balance

The control of energy balance, appetite and body weight appear to be closely interrelated [70]. This system precisely controls overall body weight and fat stores despite significant variations in energy expenditure and intake that occur on a day to day basis [87] .

Unfortunately, changes in body weight are difficult to achieve and harder to sustain. The physiology of the human body is set to vigorously defend what it perceives as an optimal weight [88, 89]. Subjects who are either under or overfed rapidly return to their previous weight once an unrestricted diet is reinstituted [65].

A reduction in caloric intake initiates an immediate compensatory decrease in energy expenditure [90, 91]. A series of physiological adaptations aim to reduce energy expenditure [92]. These metabolic changes seek to match the reduction in caloric intake with an equivalent reduction in energy expenditure [65].

Central regulation of body weight

Several brain locations are considered particularly important in the integrated control of body weight, energy balance and appetite. The nucleus of the tractus solitarius in the hindbrain is deemed a centrally important node [93]. A variety of peripheral and central signals converge on this region either via neural projections, directly via the blood stream or indirectly via receptors on the vagus nerve [94].

Satiety and hunger centres, located in the hypothalamus, are also deemed important, communicating with the nucleus tractus solitarius, forebrain, paraventricular nucleus and receiving direct inputs from circulating factors [93].

The medio-basal hypothalamus is considered a critical intersection as it is able to receive inputs from satiety and adiposity signals as well as sense other mediators; identifying the availability of circulating and stored fuels. Via its projections it can subsequently influence a range of body processes and initiate adaptive homeostatic responses through recruitment of behavioural, autonomic and endocrine circuits [95].

Together, this integrated signalling system represents a complicated communication network with inbuilt redundancies. The presence of multiple, sophisticated mechanisms appear able to overcome temporary alterations in one or more inputs. When stimulated by minor physiological changes, counter-regulatory processes are activated that vigorously resist change and seek to rapidly restore pre-existing parameters.

More complex understanding of the control of body weight, appetite and energy balance has replaced theories that attributed intake to depletion/repletion effects, related, for example, to blood glucose levels [96].

Lipostatic model of body weight control

The lipostatic model is a simplified representation of the regulation of body weight that summarises current understanding [70]. The model postulates that there are three important categories of signal: satiety signals, adiposity signals and central effectors mechanisms that collectively control hunger, food intake and total body energy stores.

Satiety signals are generally considered to be those that arise from the gastrointestinal tract and promote meal termination. These signals are thought to influence eating behaviour by activating neurons in the nucleus of the solitary tract in the hindbrain. The effects of satiety signals are modified by the effects of adiposity signals. Hypothalamic catabolic and anabolic signals also project to the hindbrain to further modify the interpretation of satiety signals [97].

Adiposity signals rise and fall relative to changes in total body fat stores. Leptin and insulin are the best characterised adiposity signals [97]. Leptin levels are proportional to body fat stores [98-100]. Fasting and post-prandial insulin levels have also been identified as being proportional to total body fat stores [101, 102]. Both these hormones directly enter the brain and activate receptors in the hypothalamus [96]. Collectively, these and other adiposity signals appear to affect the interpretation of satiety signals thereby modifying the size and timing of meals. For example, when signals of meal termination are administered to animals each time they feed a compensatory increase in feeding frequency is observed to maintain body weight and energy stores [103].

Central effector signals integrate multiple inputs, satiety, adiposity and other brain signalling to influence food intake. These can be divided into catabolic and anabolic responses, that either decrease or increase food intake [104]. These can be described as mechanisms by which social inputs such as learned behaviour, habits and personality intersect and influence food intake. An example would be decreased hunger during periods of extreme stress.

The lipostatic model is qualified by the capacity of conscious stimuli to override generated signalling. Various visual, olfactory and gustatory stimuli can stimulate or hinder intake. The social setting or other environmental modifiers can substantially alter food intake [97].

Food intake in a real world situation

For humans living freely, the dominant determinant of overall total food intake is the amount of food taken in once a meal commences rather than when the meal commences or the frequency of eating [105]. Humans ingest food episodically, consuming discrete meals. It appears there are a wide range of reasons for initiating or terminating a meal [96].

It is currently accepted that in humans the timing of meals is a learned behaviour relating to the social situation, convenience and routine rather than a response to falling energy levels [104]. Reported feelings of hunger often do not correlate with actual food intake, complicating assessments of satiety and hunger [106]. Portion size appears to be important in the regulation of total intake, with larger portions resulting in increased total energy intake without affecting perceived levels of hunger or satiety [107, 108].

Some authors have separated the concept of satiety from satiation [109]. With satiety representing an intermeal absence of hunger, compared to satiation which is the signalling that leads to termination of an individual meal. Undoubtedly, they are at least partially overlapping physiological processes.

Gastrointestinal hormones regulating satiety and food intake

There has been considerable interest in gastrointestinal hormones involved in regulation of food intake, appetite and energy balance [104, 110-112]. This has particular been the case in the setting of bariatric surgery where efforts have (unsuccessfully so far) aimed to uncover a mediator responsible for weight loss [113].

These chemical messengers are usually elaborated in response to the gastrointestinal delivery of various nutrients. Peripherally they modulate a range of gastrointestinal processes such as gastric emptying and affect the vagus nerve. Centrally they can have direct effects, particularly on the hind brain, although the hypothalamus is also receptive [114, 115].

Cholecystokinin (CKK), Peptide YY (PYY) and Glucagon like peptide 1 (GLP-1) are the most characterised gastrointestinal satiety hormones in the context of bariatric surgery. Ghrelin has also received much focus based on its unique attribute of stimulating eating.

Cholecystokinin is a powerful satiating hormone that has both central and peripheral effects [115]. It is one of the most studied gastrointestinal satiety signals. It is released from the proximal small intestine in response to caloric delivery (particularly fat). There are feedback effects both centrally to the CNS, inducing satiety sensations and peripherally, modulating vagal receptors and resulting in gastric wall relaxation [116, 117]. CCK is able to decrease meal size in a dose dependent fashion when administered exogenously [94].

Glucagon like Peptide 1 (GLP-1) is produced in the I cells of the small bowel and secretion is stimulated by the presence of nutrients within the bowel wall [104]. GLP-1 feeds back and interacts with the vagus nerve to affect the ileal break mechanism, whereby distally delivered calories slow gastric emptying [118-120].

Other hormones, such as PYY, may also be involved in this process [121]. PYY is also produced in the distal small intestine. It is proposed to have a satiety inducing effect and decreases hunger, with levels reported to be lower in the obese than in lean controls [122].

Ghrelin is a recently discovered mediator that has the unique property of stimulating appetite and increasing intake [123, 124]. It has since been defined as a gut-brain hormone, although was first recognised due to its growth hormone releasing effects [124]. Whilst animal and human data have suggested the exogenous administration of ghrelin can stimulate feeding, whether this is a true physiological function remains unclear. Ghrelin currently has no role as a therapy for overweight or obesity.

Produced in the gastric fundus, ghrelin levels appear to increase after LAGB and diet induced weight loss [125], although they may fall following Roux-en-Y gastric bypass (RYGB) [126]. In RYGB the absence of a compensatory increase in ghrelin may partially explain the ability of the procedure to circumvent normal control processes that seek to restore body weight [127]. Alternatively, this illustrates the capacity of the LAGB to maintain long term suppression of appetite, overcoming compensatory hormonal changes.

Each of these hormones has multiple physiological functions. It remains critical to establish a true physiological role for peripheral satiety and hunger signals [128].

CHAPTER 4: *Weight Loss*

Benefits of weight loss

The known adverse effects and associations of obesity have driven the development of many weight loss strategies [129]. Most obese or overweight people have attempted self directed or supported weight loss programs [130]. Not surprisingly, obesity has been declared a major health problem or priority by many agencies, including the WHO, who have called for significant action [131].

In a prospective study of over 40,000 overweight US females, in obese women with obesity-related health conditions (n = 15,069), achieving intentional weight loss of any amount was associated with a 20% reduction in all-cause mortality [132]. This was primarily due to a 40-50% reduction in mortality from obesity related cancers. Diabetes associated mortality was also reduced by 30-40%. In those with no pre-existing illness, intentional weight loss was associated with a 25% reduction in all-cause, cardiovascular and cancer mortality [132].

A recent review suggested that achieving and maintaining weight loss could result in a significant reduction in the overall cancer burden [133].

Some mortality studies evaluating weight loss have been confounded by not separating intentional from unintentional weight loss, thereby suggesting a correlation between weight loss and morbidity/mortality [134]. Cigarette smoking is at times another confounder [135].

A recent multicentre randomised controlled trial compared intensive lifestyle intervention involving behavioural modification, dietary intervention and physical

activity with a conventional program in overweight and obese diabetic patients [136]. There were over 5,000 participants, with the intensive therapy group achieving weight loss of 8.6% of their initial weight vs. 0.7% in the control group at one year follow up. In the weight loss group diabetes control improved significantly as did the cardiovascular risk profile. The major questions raised were whether weight loss could be maintained and a genuine impact on mortality achieved.

Treatment of obesity

Changes in lifestyle over the past 50 years have been associated with the emergence of obesity as a population wide problem. Logically, interventions targeting lifestyle have been proposed as a means of combating obesity and overweight. Once obesity or overweight develops it is very difficult to treat, even if this occurs in childhood [45]. Therefore, prevention has been seen as of paramount importance. Certain epidemiological predictors have been identified, suggesting means of reducing overweight and obesity, for example breast fed infants appear to have lower rates of obesity and overweight in adolescence [137]. Various programs aiming to promote healthier lifestyle choices, particularly in children, have been trialled or implemented [138].

The WHO Global Strategy on Diet, Physical Activity and Health describes the actions needed to support the adoption of healthy diets and regular physical activity. The strategy calls upon all stakeholders to take action at global, regional and local levels and aims to lead to a significant reduction in the prevalence of chronic diseases and their common risk factors, primarily unhealthy diet and physical inactivity [33]. The food industry has been called upon to reduce the fat, sugar and salt content of

processed foods and portion sizes, to increase the introduction of innovative, healthy, and nutritious choices and to review current marketing practices [33].

Unfortunately, on a population basis, effective lifestyle interventions have not been established [139].

Non-surgical treatment of obesity

With the obvious health benefits and social appeal of ideal body weight, numerous weight loss strategies are available [140]. Self directed lifestyle interventions, commercial dietary programs, behavioural therapy, medications and various combinations are commonly used. Up to 40% of the population may be on some form of caloric restrictive diet at any one time [70].

In a meta-analyses of 80 clinical trials evaluating non-surgical methods of weight loss, with a minimum of 1 year follow up (up to 4 years), the ability of interventions to achieve only a modest weight loss was highlighted [141]. Very low energy diets affected a far greater weight loss than other treatments, of up to 18 kg at 6 months. This could not be sustained, with weight loss only 6 kg at 36 months. Significantly, of the 18,000 participants included in these analyses, only 69% completed the studies [141]. Is the attrition rate due to non-compliance from patients or as a result of drop out due to ineffective methods?

A range of non-surgical therapeutic approaches are available for the treatment of obesity or overweight.

Dietary Interventions

Despite billions of dollars spent on commercial and medical diet programs [142] there is little evidence they are able to induce sustained weight loss [143]. Modifications of dietary content generally focus on reducing the intake of high energy fats and refined sugars. Manipulations of carbohydrate and other dietary components are also common. In the short term a weight loss of 5-6kg appears achievable, with many studies not demonstrating any effect [144].

Behavioural therapy

Behavioural therapy programs are intensive, requiring therapy sessions once per week for variable periods, generally six months or more [145]. They aim to reduce caloric intake to 1,000-1,500 kcal daily by altering key behaviours. Generally, therapy programs are combined with exercise and lifestyle interventions and expectations that the patient monitors and records their own activities (intake and exercise). An intensive induction phase is usually followed by fortnightly or monthly sessions for a further 6 to 12 months.

Considered at their best, these treatments have demonstrated modest success, achieving up to 10 kg weight loss over a six month period. However, continued in the longer term, at a less intense level, weight appears to be regained, with a mean of only 6 kg weight loss observed after two years [145].

Pharmacological treatment

The development of an effective weight loss drug is a most attractive prize for a pharmaceutical company, although has proven challenging so far. A range of

medications are available or have previously been used. Sibutramine (Reductil) and orlistat (Xenical) are the most commonly used medications in Australia [146]. Sibutramine inhibits serotonin and noradrenaline re-uptake centrally and is moderately effective, resulting in loss of 5% of total body weight [147]. Orlistat inhibits lipase in the gastrointestinal tract, thereby preventing fat absorption [147]. Diarrhoea is a significant side effect [148]. This medication results in the loss of approximately 3% of total body weight [140].

Targeting cannabinoid receptors was previously considered promising, however, due to unacceptable side effects, efforts have moved away from this area [149]. Various other medications and combinations of pre-existing drugs are currently under evaluation [149].

A systematic review of pharmacological treatments for weight loss showed that compared to placebo, orlistat reduced weight by 2.9 kg (95% Confidence Interval (CI) 2.5 to 3.2 kg) and sibutramine by 4.2 kg (95% CI 3.6 to 4.7 kg) [150]. Medications were found to be less effective in patients with type 2 diabetes. A major problem with medication trials was the attrition rate of 30-40%, with patients withdrawing due to side effects. The Cochrane review in 2004 attributed a modest effect to medications, although noted considerable drop out in clinical trials [151].

A major limitation of current pharmacotherapy is that affected pathways are not specific to weight or energy balance. Therefore, side effects are common [152]. Medications have not proven vastly superior to alternative means of reducing weight [147].

Summary of non-surgical treatments

Even if initial success is achieved with weight loss programs, much of the lost weight has been regained within one year and invariably almost all after 5 years [153]. Medical and pharmaceutical treatments have simply not proven effective in the management of obesity [154]. Low energy diets, exercise programs and medications can achieve modest weight loss at best [141].

In a systematic review of dietary interventions, behavioural therapies and exercise programs, Söderlund found that combining therapies was the most effective means of inducing weight loss [155]. To be effective in inducing weight loss considerable multi-disciplinary resources are required. This systematic review highlighted that studies usually involved individuals with a BMI of 30 kg/m^2 and often less. They also considered preventing further weight gain a success.

CHAPTER 5: *Bariatric Surgery*

Overview of bariatric surgery

Surgical treatment of obesity was first reported in the 1950's and seeks to reduce body weight by decreasing intake, reducing caloric absorption, or combining these measures [156]. Different anatomical modifications to the gastrointestinal tract achieve these aims with variable risk, efficacy and durability.

The 2009 Cochrane review of surgery for obesity concluded that surgical procedures were more effective than conventional management at achieving weight loss [157]. As a result of the worldwide obesity epidemic, bariatric surgery has emerged as a prominent specialty.

A recent systematic review of the treatment of obesity found that over a 2-4 year period surgical therapies provide an average of 25-75 kg of weight loss compared to less than 5kg for dietary interventions [158]. In addition to inducing and sustaining a substantial weight loss there is increasing evidence that obesity related co-morbidities are improved.

Several groups have reported that intermediate to longer term mortality is decreased in bariatric surgical cohorts (LAGB, Roux-en-Y gastric bypass and gastroplasty) compared to medical or community controls [4, 159-161].

A range of significant medical co-morbidities improve with bariatric surgery, particularly those associated with diabetes, the metabolic syndrome and cardiovascular risk [162]. Quality of life is better and psychiatric illnesses such as depression improve [163, 164].

The Cochrane review of bariatric surgery concluded that improvements in a range of health-related quality of life indices occur within two years, but effects at ten years are less clear [157]. In a prospective study, hyperlipidaemia (up to ten times reduction), diabetes and hypertension were all been found to improve in those undergoing bariatric surgery compared with little change in controls [165].

Synthesis of available studies suggests that bariatric surgery is cost effective for moderately or severely obese people [166]. In diabetic patients, with a BMI 30-40 kg/m^2, data derived from a randomised trial supports LAGB as a cost effective intervention [5, 167].

The Swedish Obese Subjects (SOS) study is a major and in many ways unique source of bariatric surgical outcome data [168]. Initiated in 1987, 2,010 patients and 2,037 matched controls were prospectively enrolled in a non-randomised cohort follow up study. Some have now been followed for up to twenty years, although recruitment continued until 2001 [168].

The study primarily aimed to determine if weight loss induced by bariatric surgery affected mortality in comparison to matched controls. Effects on diabetes, other co-morbidities, quality of life and economics were also evaluated. Comprehensive national registries greatly simplified follow up.

Gastroplasty was the predominant procedure (n=1,369), gastric banding (n=376) and gastric bypass (n=265) were also performed [169]. The gastric banding group predominantly consisted of fixed gastric bands.

The unadjusted overall mortality was reduced by 23.7% in the surgery group (relative to controls), whereas the gender, age and risk factor adjusted mortality reduction was 30.7% [170]. The authors concluded that bariatric surgery for severe obesity is associated with long-term weight loss, improved risk factors and decreased overall mortality.

An average weight loss of 25.3±9.7% was seen after one year, at 6 years it was 16.9±11.6%, which was maintained until 10 years. Comparatively, the mean weight change of the control group was less than 2%. This strongly validates the ability of surgery to achieve and maintain a substantial weight loss.

Three distinct phases following surgical treatment were observed. An initial rapid weight loss phase, lasting one year, was followed by a weight regain phase of 1-6 years and then a stability phase of 6-10 years [161, 165, 170-172].

Since the SOS commenced, bariatric surgery has evolved towards a minimally invasive (laparoscopic) approach and adjustable gastric banding has emerged as a popular procedure. Gastroplasty is no longer commonly performed and has essentially been abandoned in Australia.

Currently LAGB and Laparoscopic Roux-en-Y gastric bypass (LRYGBP) are the most commonly performed bariatric procedures worldwide. Bilio-pancreatic diversion (BPD) or its derivations are performed in a few centres as the first choice, although has limited acceptance as a primary procedure elsewhere. Sleeve gastrectomy has emerged as the most recent procedure to be popularised, although outcome data remain limited [173].

Bariatric surgical options past and present

A number of bariatric procedures are currently performed. Operations have been classified as either restrictive or malabsorptive, based on the presumed mechanism of action. Some are attributed mixed restrictive/malabsorptive effects. These terms have been incorporated into the bariatric surgical vernacular, however, lack specificity. There is not a robust and accepted definition of what constitutes either a restrictive or malabsorptive procedure. The confusion likely relates to limited mechanistic understanding and the classification of procedures is largely based on historical deductions of how weight loss was presumed to be induced. All current procedures reduce or partition gastric volume in some way and could therefore be classified as somewhat restrictive.

A definition of a restrictive procedure would be along the lines of: A procedure that restricts eating by reducing gastric volume either focally or by division, such that a patient is physically unable to consume a volume of food greater than a small meal. Continued eating is therefore inhibited and the feeling of fullness remains as the food slowly empties.

A malabsorptive procedure can be considered one where: Caloric absorption is reduced due to either limitation of contact of nutrients with absorptive small bowel or diversion of digestive enzymes away from the nutrient stream. The intrinsic adaptability of small bowel absorptive capacity suggests that it would be difficult to ideally tailor such a procedure to selectively produce weight loss.

Enteric bypass

Enteric bypass as a means of reducing weight was first performed in the 1950's [156]. This procedure was truly malabsorptive. This represented the first widespread use of a surgical procedure that induced weight loss. An estimated 100,000 people underwent enteric bypass. After dividing the small bowel, proximal jejunum was anastomosed to distal ileum, limiting absorptive capacity to a short common channel. Consequently, a long blind loop remained. Effective weight loss was achieved with improvements seen in co-morbidities, particularly hyperlipidaemia.

The procedure resulted in a range of peri-operative and late post-operative complications. Insurmountable problems included deficiencies in fat soluble vitamins, renal stones, gall stones and liver failure. These and mortalities led to the procedure being abandoned in the 1960's [174].

Roux-en-Y gastric bypass

Laparoscopic Roux-en-Y gastric bypass has proven a highly successful bariatric procedure, particularly in North America where its status as the gold standard is only now being challenged by LAGB. The open procedure has been efficiently translated to a laparoscopic equivalent [175]. Effective weight loss is achieved and many co-morbidities improve [176]. Longer term mortality is thought to be reduced in gastric bypass patients; in one study it was 40% less than age and BMI matched controls [160]. A disproportionate effect on diabetes has been attributed to hormonal effects, although not yet substantiated [176].

RYGB involves gastric partitioning by stapling, or more commonly, division of the upper stomach. This creates an isolated gastric pouch above the main body of stomach. Despite multiple technical variations, particularly in the creation of the gastroenterostomy, uniformly, a small volume (30 ml) lesser curve based vertical gastric pouch is now advocated [177]. The gastric pouch empties via a Roux limb. Intestinal continuity is restored by an entero-enterostomy.

Gastric bypass was first introduced in 1967 [178]. It most likely arose out of observations that weight loss followed gastrectomy for ulcer disease. There was also the need for an effective operation with a safer profile than intestinal bypass. The subsequent introduction of stapling devices made the procedure more efficient [156].

An uncalibrated gastric pouch was rapidly reduced to a minimal volume gastric pouch, measuring 30 ml. This was due to early failures associated with increased volume of the gastric pouch identified at revisional surgery [156]. Certainly, when there is dilatation of the gastric pouch, weight regain is invariable [179]. A range of technical modifications have emerged since. Advocates have proposed use of a banded bypass or applied mini-gastric bypass that uses a loop gastroenterostomy, rather than a Roux limb [180, 181].

The small proximal gastric pouch is thought to restrict the patient to a small meal. Rapid delivery of calories to the distal small bowel may stimulate the release of gastrointestinal hormones that contribute to weight loss or release incretins that control diabetes [182]. Suggestions that a malabsorptive effect of RYGB contributes to weight loss are common, although definitive evidence is lacking [183].

Disadvantages of RYGB include early risks of severe morbidity and mortality and robust data is lacking on longer term durability [2]. The lack of prospective studies or randomised trials limits knowledge on the true incidence of short to intermediate term complications such as anastomotic stenosis, intestinal obstruction and nutrient deficiencies [184-186]. A recent randomised trial reported a 45% incidence of post-operative complications over 4 years [187].

The international bariatric surgery registry reported only a 10.9% follow up rate 8 years post-operatively, despite having enrolled nearly 2,000 RYGB patients [188]. When specifically evaluated, RYGB patients have been found to infrequently attend follow up, with those attending having significantly better weight loss than non-attenders [189]. Although follow up is desirable, there is no intrinsic necessity with generally 40-50% of patients lost to follow up within one year [190].

Early morbidity and mortality is a major concern following RYGB. In a United States based population study of 16,155 public patients undergoing bariatric surgery (predominantly RYGB), the rates of 30-day, 90-day, and 1-year mortality were 2.0%, 2.8%, and 4.6%, respectively [191]. No deaths were reported in 1,198 LAGBs. In another RYGB study, over a 15 year period, the thirty-day mortality was 1.9% and was most associated with surgical inexperience [192]. Two further studies from the United States have reported peri-operative mortality in large cohorts of RYGB patients: 0.3% in 16,232 patients from California and 0.6% in 4,685 patients from Pennsylvania [193, 194].

DeMaria recently defined a 3 tiered score predictive of RYGB mortality risk, based on 5 patient related factors [195]. The classification system was subsequently validated against outcomes from 4 other dedicated bariatric programs [196]. An overall mortality of 0.7% was identified. Class A patients had a mortality of 0.2% (n= 2,164), class B patients 1.1% (n=2,142), and the 125 high risk class C patients had a mortality risk of 2.4%.

Bilio-pancreatic diversion "Scopinaro" procedure and duodenal switch

Scopinaro developed bilio-pancreatic diversion (BPD) in the 1970's, after performing initial experiments in animals [197-199]. A distal gastrectomy, leaving a 200 ml calibrated gastric residual, is performed. The small bowel is divided and an alimentary limb, bilio-pancreatic limb and short (50-100 cm) common channel created. Diversion of the nutrient stream from the biliary and pancreatic enzymes, except in the common channel, is deemed critical to the procedure. The ability to produce selective malabsorption of fats and starches is viewed as a major advantage over traditional enteric bypass. A blind loop is also avoided. Scopinaro advocates the procedure as one of controlled, selective malabsorption, largely free from major complications [197, 200].

Data quality for BPD is limited, with no randomised trials identified. Weight loss appears to be superior; however, there is a high risk of severe early complications coupled with significant ongoing adverse effects. The early mortality rate is around 1% and Scopinaro reported a 30% incidence of incisional hernia development [197].

Marceau's group have advocated the most widely used modification to BPD, the duodenal switch (DS) [201]. Distal gastrectomy is replaced with a pylorus preserving sleeve gastrectomy and the alimentary limb directly anastomosed to the proximal duodenum. This preserves the important aspects of the physiology of the original procedure whilst reducing adverse effects such as dumping and ulceration by preserving the pylorus [202]. It has the disadvantage of technical complexity.

Laparoscopic BPD and DS can be performed. Early reports had very high complication and mortality rates [203]. As the major complications associated with BPD are not necessarily associated with the incision, benefits of the laparoscopic approach are less clear.

Gastroplasty

Gastroplasty was first performed in the early 1970's, aiming to avoid the significant complications associated with gastric bypass [204]. It was hypothesised that gastric bypass induced weight loss primarily by reducing intake as a result of the small volume gastric pouch. Therefore, it was aimed to reproduce a small meal sized pouch that would slowly empty into the distal stomach, avoiding the need for an anastomosis.

The initial procedures were relatively unsuccessful, consisting of a horizontal staple line with a stoma based on the greater curve. Subsequently the stoma was moved to the lesser curve. These procedures were initially highly effective. In Victoria, Michael Long at the Royal Melbourne Hospital pioneered a widely used vertical gastroplasty (Long gastroplasty) [205].

Disadvantages of gastroplasty relate to high failure fates as a result of staple line dehiscence or stomal dilatation; stomal stenosis results in severe stasis and reflux [206].

The Adelaide study, a randomised trial comparing three techniques of bariatric surgery, presented 91% follow up at three years and concluded that gastric bypass was superior to gastroplasty [207]. Another randomised trial by Sugerman also favoured RYGB [208].

Gastroplasties can be performed laparoscopically [209]. Despite this, the popularity of gastroplasty has rapidly diminished and it will likely become a historical procedure within the next decade.

Sleeve gastrectomy

First used as part of the duodenal switch, sleeve gastrectomy has recently emerged as an independent operation. Sleeve gastrectomy, however, is fundamentally similar to other previously used procedures; the Magenstrasse and Mill procedure and gastroplasty [210, 211]. Sleeve gastrectomy involves removing the bulk of the greater curve. Generally, the lesser curve based tube is created over an approximately 1 cm diameter bougie or a gastroscope.

A number of groups have reported promising early results with sleeve gastrectomy as a primary procedure [212, 213]. Longer term data remains to be reported and prospective studies or randomised trials are not available. Adequate follow up will likely be challenging in these patients and potentially limit true understanding of the outcomes.

Advocates argue that sleeve gastrectomy has the advantages of hormonal effects, controlling appetite by removing the ghrelin producing part of the stomach [214]. Whether sleeve gastrectomy provides advantages over LAGB or RYGB remains to be determined. It does carry the inherent risks associated with a significant gastric resection, although an anastomosis is avoided.

Summary of the status of bariatric surgery

Despite the widespread popularisation and clear benefits of bariatric surgery, only a tiny proportion of those eligible undergo surgery. In Australia an estimated 15,000 of 4.8 million obese patients undergo bariatric surgery annually, representative of 0.3% of those potentially eligible [215]. The use of LAGB has increased eight fold in the past nine years and appears to be increasing by 20% annually. The procedure remains largely excluded from the public system [216].

United States data is similar, only 0.6% of those eligible undergo surgery, with 175,000 procedures performed annually [217, 218]. A nationwide inpatient sample determined that bariatric procedures increased from 13,365 in 1998 to 72,177 in 2002 [217]. Another similar study also showed that the population incidence of gastric bypass increased from 0.7 to 10.6 per 100,000 from 1987 to 2001 [192].

There is much debate concerning the optimal or preferred bariatric procedure; this is unlikely to be definitively resolved. LAGB appears to offer significant, unique advantages over other procedures and provides an acceptable option to many patients who would not consider more invasive operations. For a variety of reasons

LAGB is an attractive bariatric procedure to patients, surgeons and referring clinicians.

Worldwide, LAGB and RYGB are the two most commonly performed bariatric procedures. LAGB is used almost exclusively in Australia (96%), predominantly in Europe (approximately 75% of procedures) and increasingly (25%) in the United States [1]. Up to 250,000 procedures will be performed in 2010 [218]. An estimated 500,000 to 1 million people, including 50,000 Australians, have undergone LAGB.

The success and popularity of the LAGB is attributed to its safety, efficacy and adjustability; characteristics intrinsically attractive to patients. The technical simplicity and low complication rate are appealing to surgeons. Adjustability and easy reversibility are unique advantages [1]. Whilst debate continues over the relative efficacy and durability of different bariatric operations, the positive attributes of LAGB guarantee ongoing use [219].

CHAPTER 6: *Laparoscopic Adjustable Gastric Banding*

Evolution and history of adjustable gastric banding

The concept of an adjustable gastric band (AGB) as a bariatric procedure is widely attributed to Kuzmak, who presented his idea over 20 years ago [220]. Possibly Austrian researchers were the first to use an AGB in an animal model and Swedish surgeons developed a similar device parallel to Kuzmak [221].

Currently several manufacturers produce LAGBs, all remain very similar in principle to the original. An outer silicone shell surrounds an inner inflatable balloon. Tubing connects the balloon to a subcutaneous reservoir, via which adjustments to LAGB volume can be easily made in consulting rooms, without complicated equipment. Adjustments alter the stoma size and effect of the LAGB. This allows the procedure to be individualised or controlled in certain circumstances; such as intercurrent illness or pregnancy [222, 223].

Differing physical properties, locking mechanisms and intraballoon pressure-volume profiles differentiate devices [224, 225]. None of these has been convincingly shown to be superior. The LAP-BAND (Allergan, Santa Barbara, CA) and Swedish band (Ethicon EndoSurgery, Cincinnati, OH) are the most widely used and appear to produce comparable results [226]. Limited outcome data is available for other prosthesis [227]. The literature, particularly randomised controlled trials, is more extensive for the LAP-BAND than the Swedish band [228].

Originally, AGBs were placed via laparotomy, they encircled the upper stomach, several centimetres below the OGJ [229, 230]. The aim was to create a gastric

pouch only large enough to accommodate a small meal. This likely intended to reproduce the anatomical modification common to gastroplasty and gastric bypass - a restricted, small volume, proximal gastric pouch.

Fixed gastric banding with the creation of a definite supra-band pouch was the immediate predecessor of AGB [231]. It was hoped that creation of a small gastric pouch would cause the patient to feel satisfied after consuming a very small volume of food. Subsequent gradual emptying of the pouch was hypothesised to maintain a prolonged sense of fullness. The advantage of AGB was the ability to individualise effects.

Kuzmak reported his experience in 1991. Excess weight loss was an impressive 64% at 3 years, with few complications and superior outcomes to fixed gastric banding [229]. Prior to the laparoscopic era AGB was used successfully by others but not widely [232]. One randomised trial reported good short term outcomes [233].

Laparoscopic era

Mitiku Belachew was the first to report placement of a LAGB, in 1993 [234]. The device used and subsequently popularised was a close derivation of the original Kuzmak band. The laparoscopic approach mirrored the open technique [235]. A peri-gastric dissection was performed, identifying the lesser curve of the stomach. A pathway was created from the lesser curve, across the lesser sack, with the LAGB emerging laterally at the level of the first short gastric vessel. This resulted in a small volume gastric pouch being created above the LAGB.

Whilst the ability to perform the procedure laparoscopically was important in heralding later widespread uptake, it was an inevitable rather than innovative step [236]. At this time other technically complex laparoscopic procedures, such as hiatus hernia repair, various fundoplications and Roux-en-Y gastric bypass were either well established or becoming so [175].

The early experience with LAGB was most encouraging, effective weight loss with acceptable complication rates were reported from several centres [237-239]. Critically, there were very low (or absent) mortality and serious morbidity rates [240-242]. These significant advantages drove ongoing use. Despite such promising results, prolapse of the stomach through the LAGB was proving troublesome [243, 244].

Prolapse (also termed slippage) can be classified as anterior or posterior, based on the lead point of the stomach herniating up through the LAGB. Usually diagnosed with a liquid contrast swallow, prolapse is manifested by a large volume of stomach and stasis above the LAGB [245]. Not surprisingly, volume reflux and unpredictable regurgitation result. Of variable chronicity, these problems can present acutely with intolerance to food or even water, or may take a more indolent course. Characteristically the lie of the LAGB, which is normally 45°, is altered in prolapse. A vertical lie is seen with posterior prolapse whereas a horizontal lie is indicative of anterior prolapse.

Morino, in 1997, reported 9 of 15 patients developing early gastric prolapse after Kuzmak's open technique was faithfully reproduced laparoscopically [246]. Other reports documenting this problem rapidly followed [247-249]. A small Australian

series, published in 2004, documented a 25% prolapse rate within two years early in the experience, although a moderate weight loss was achieved [250]. Other reports identified incidences of up to 32 of 90 (35%) patients requiring re-operation [243].

Kuzmak argued, with the open procedure, although a small degree of pouch dilatation was inevitable, this was not common and did not compromise outcomes [251]. A randomised trial comparing open with laparoscopic adjustable gastric banding, conducted between 1995 and 1997, identified no prolapses in the open group after 1 year of follow up. Open surgery, involving more extensive dissection may have resulted in scarring posteriorly, fixing the LAGB [252].

O'Brien published data on 302 LAGB patients in 1999, with a prolapse rate of 9% [253]. Data in this study, however, included only 120 patients with 12 months follow up, where an excess weight loss of 51% had been achieved. A similar early prolapse rate of 7% was also reported by Belachew [253, 254].

Reducing prolapse, initially predominantly posterior, was a major focus in the first five years of LAGB use and drove important modifications to the technique [172, 255, 256]. Varying methods of posterior fixation, including the use of mesh pledgets, were advocated [253]. Placement of the LAGB migrated closer to the oesophago-gastric junction (OGJ) [256]. The apex of a 25 ml oro-gastric calibration balloon, engaged at the OGJ, was used to calibrate a virtual pouch above the LAGB; a major reduction from the small meal sized pouches originally advocated [257, 258]. More gastro-gastric sutures were used, extensively fixing the LAGB anteriorly [256, 259, 260]. Collectively, these measures contributed to decreasing prolapse

rates in the first five years of use. Figure 6.1 schematically contrasts the anatomical modifications created with early gastric banding procedures and the modern technique.

Improved, more extensive anterior fixation of the stomach, along with a reduction in supra-band gastric volume, can be considered to have reduced the incidence of anterior prolapse. Progressive popularisation of the pars flaccida approach from around 1999 has since largely eliminated posterior prolapse [230]. The pars flaccida innovation involved tunnelling the LAGB above the lesser sack posteriorly and also avoided the need for a lesser curve perigastric dissection; making it technically simpler [261]. Posteriorly, the pathway overlaps the OGJ and the prosthesis is laid within 1 cm of the OGJ anteriorly, aiming to minimise the volume of supraband stomach [262].

The modern pars flaccida era can be considered to have occurred since 2003, with 1994-1999 representing the development phase and 1999-2003 being the transition to the modern technique. Analysis of any LAGB data must consider the era from which it was reported and account for the surgical technique used. The current procedure is a different operation to that performed in earlier years.

FIGURE 6.1 Evolution of LAGB technique

Fixed Gastric Band   **Modern placement**
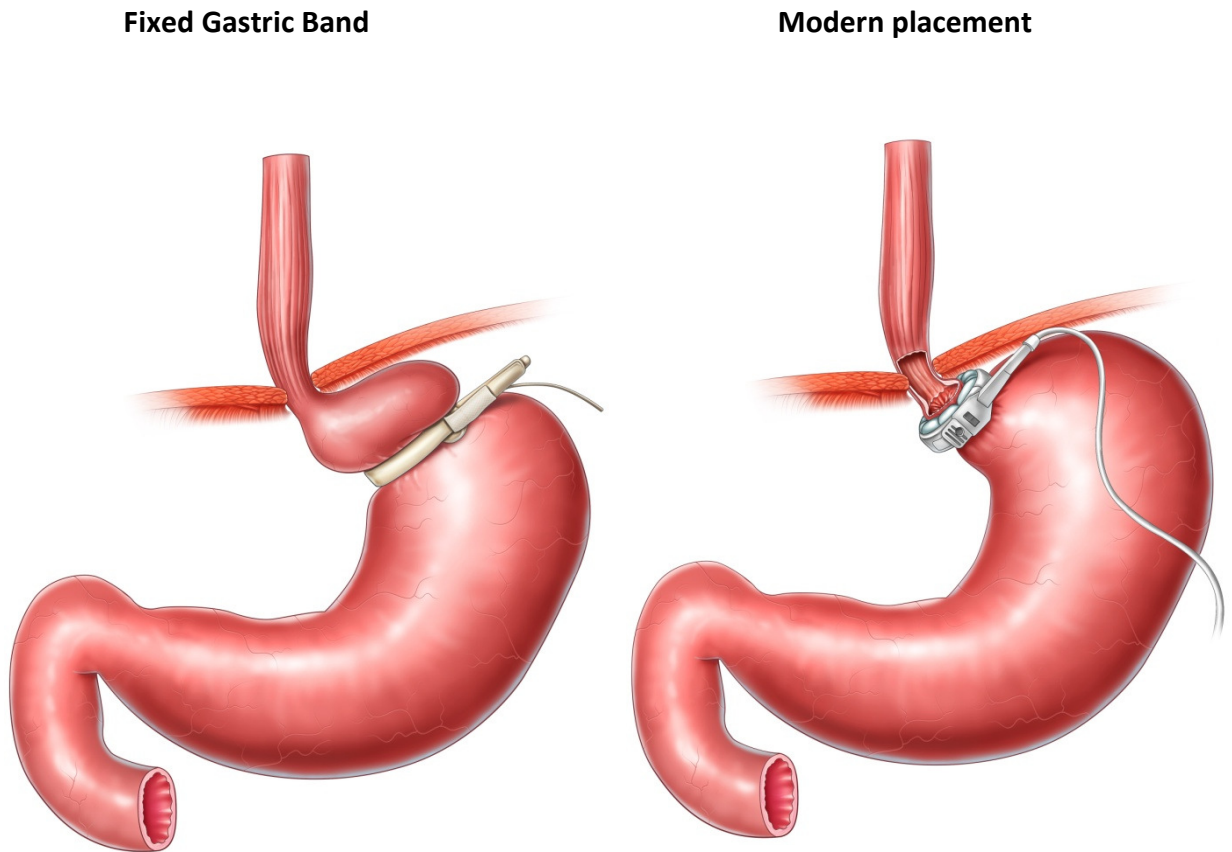
Figure 6.1 Legend: *Schematic of placement of fixed gastric band, creating a small meal sized pouch above the band – a restrictive procedure. This was the basis of initial open and early laparoscopic adjustable gastric band procedures. The modern surgical technique mandates secure fixation of the LAGB immediately beneath the oesophago-gastric junction.*

Health benefits of laparoscopic adjustable gastric banding

Data from several randomised trials, reported since 2004, have highlighted the positive effect of LAGB induced weight loss on obesity related co-morbidities. In a trial designed to test the effect of LAGB on recent onset (< 2 years) Type 2 diabetes, in those with a BMI 30 – 40 kg/m^2, the disease was found to remit completely in 73% of patients treated surgically [263]. Triglycerides and total cholesterol also reduced significantly. Two other randomised control trials documented significant reductions in the incidence of metabolic syndrome following LAGB [10, 264]. The superiority of LAGB in comparison to optimal medical management of obesity was also established [264]. These trials appear to have validated LAGB in the eyes of the wider medical community as a safe and effective mainstream treatment.

Prospective studies have noted that hypertension, sleep apnoea and hyperlipidaemia improved following LAGB, although were not primarily aimed or powered sufficiently to address these questions [265]. In one randomised trial gastro-oesophageal reflux improved in 83.3% of patients, however, developed in another 8.8% of patients. Quality of life, using the medical outcomes short form (SF-36) instrument, has been shown to variably improve across the eight domain scores, tending to closely approach or reach community norms from a significantly lower baseline [10, 187, 264].

Multiple case series have attributed a broader spectrum of benefits to LAGB induced weight loss. Hypertension [266], hypercholesterolaemia, reflux oesophagitis [267-269], asthma [270], depression [164], non-alcoholic steatohepatitis [271], polycystic ovarian syndrome [272], sleep apnoea [273] and

overall quality of life [266, 274] have all been noted to improve following LAGB. The range of obesity related disease and logistics associated with randomised trials makes it unlikely each co-morbidity will be formally evaluated.

The relative risk of death following LAGB, compared to matched controls, was found to be 0.38 in comparison to a medical cohort and 0.28 compared to community controls [4, 275].

Weight loss following LAGB appears to be a favourable pattern, with a significant reduction in central adiposity, concomitantly reducing insulin resistance [276-278]. This is an advantage over other bariatric procedures where comparatively a greater loss of fat free mass is observed [279].

The positive health effects of LAGB induced weight loss appear substantial and indisputable. Rather, it is questions relating to patient selection, long term efficacy and cost effectiveness of the procedure that remain unanswered [166, 280, 281]

Laparoscopic adjustable gastric banding evidence base

With LAGB now well established, evaluations frequently focus on comparisons with other bariatric procedures. The safety of LAGB is a key difference. The LAGB appears to be at least 5-10 times safer than RYGB [282]. Without extensive dissection, visceral division, resection or anastomosis the potential spectrum of intra-abdominal complications is significantly reduced [283]. The rare post LAGB deaths that have occurred have usually been as a result of pulmonary embolism or myocardial infarction, although occasionally gastrointestinal perforations or major vascular injuries due to surgical misadventure have been recorded [284].

An extensive LAGB literature has developed, paralleling the massive increase in bariatric surgery. There are only twelve relevant randomised trials along with numerous case series, reviews and 6 systematic reviews. Truly prospective controlled or uncontrolled cohort studies, particularly documenting longer term outcomes, are lacking. A significant number of retrospective cohort studies are of modest quality and primarily report short term or incomplete data [285].

The observational bariatric surgical data, in general, is confounded by two consistently observed deficiencies. The first was highlighted by O'Brien in 2004. The recurrent failure to systematically report loss to follow up rates was noted as a major weakness that could lead easily lead to systematic bias [2, 286]. Maggard, in another systematic review, noted that adverse events and complications were consistently reported at lower rates in retrospective, compared to prospective studies. Potentially introducing significant bias into any analysis [287]. Both of these problems favour gastric bypass when comparisons are made with LAGB. This is because RYGB has a much higher intrinsic risk of major complications such as death or anastomotic leak and follow up is generally poor. Additionally, those attending RYGB follow up have significantly better weight loss than those that do not [189].

Systematic reviews

The six groups reporting systematic reviews addressing aspects of bariatric surgery have tended to focus on comparisons of different bariatric procedures. High quality comparative trials of different bariatric procedures are sparse. In some cases this has resulted in the pooled analysis of large volumes of retrospective data. The rapid

evolution of the LAGB procedure also does not lend itself well to non-selective meta-analysis. Consequently, conclusions reached based on these calculations are not necessarily reliable.

Stated aims, inclusion criteria and outcome measurements in each systematic review varied considerably – explaining contrasting conclusions. On each of the three occasions the Cochrane collaboration has addressed bariatric surgery they have deemed data to be of insufficient quality to permit meta-analysis [157, 288, 289]. In 2009 they concluded that bariatric surgery overall is effective at inducing weight loss, however, outcome data was significantly limited as were comparisons of different procedures [157].

Chapman analysed 64 studies, seeking to compare the safety and efficacy of different bariatric procedures. His group concluded that after 2-4 years, weight loss was comparable between RYGB and LAGB, although RYGB induces faster weight loss in the initial two post-operative years [282]. This review also concluded that short term mortality (0.05% vs. 0.50%) and morbidity (11.3% vs. 23.6%) was far less for LAGB than RYGB.

 O'Brien aimed to assess the medium term outcomes of different bariatric procedures. Strict criteria were applied; only studies with >100 subjects and a minimum of 3 years follow up were considered. A total of 43 suitable studies were identified. This review concluded that more rapid weight loss was initially observed with gastric bypass than LAGB, however, after 2-4 years weight loss was similar at between 50-60% excess weight loss (EWL) [2]. This was largely accounted for by weight regain in the RYGB groups.

Maggard evaluated 147 studies, focusing on comparisons of surgical vs. non surgical management of obesity [287]. It was concluded that surgical therapy was more efficacious for BMI > 40 kg/m^2, although more data was required for those with a BMI < 40 kg/m^2 [287]. Case series strongly supported the use of bariatric surgery in BMI 35-40 kg/m^2. The authors did not consider this conclusive and were concerned about the heterogeneity of studies. Only five comparative trials of different surgical treatments were identified.

Tice aimed to perform a meta analysis of studies that compared gastric bypass with LAGB directly [290]. In the weakest of the systematic reviews, only 14 relevant studies that directly compared LAGB with LRYGB were identified. The quality of these studies was generally poor, consisting of retrospective and unmatched comparative cohorts. One randomised control trial was identified [265]. This review concluded that mortality rates were statistically similar, although still three times higher in the RYGB group. This difference was accounted for by a lower than expected mortality rate in the RYGB (0.17%) rather than a difference in LAGB mortality (0.06%). Short term re-operations were more common with RYGB (9% vs. 5%). The authors acknowledged the significant weakness of these data. The poor quality of included studies largely invalidates this review as a worthwhile contribution.

Buchwald analysed 136 studies aiming to evaluate bariatric surgery overall [162]. His group concluded that bariatric surgery was effective, although different procedures produced varying levels of excess weight loss: RYGB 61.6% (56.7-66.5) vs. gastric banding 47.5% (40.7-54.2) vs. gastroplasty 68.2(61.5-74.8) vs. bilio-

pancreatic diversion 70.1% (66.3- 73.9). The duration at which this weight loss was recorded was not stated. Procedure specific mortality rates were not reported for LAGB, although the restrictive procedures (including gastroplasty) had a mortality rate (0.1%) 5 times less than gastric bypass (0.5%) and eleven times less than bilio-pancreatic diversion (1.1%). This systematic review did not assess short or long term complications (other than early mortality), justifying this by describing the available data as heterogeneous and not amenable to meta-analysis.

Overall, the systematic reviews agreed that LAGB induces substantial weight loss, improves co-morbidities and is far safer in the peri-operative period than other procedures. Maximal weight loss, durability, complication rates and the optimal procedure remain sources of controversy. None of the studies were equipped to definitively answer the questions they posed due to the lack of high quality prospective studies.

Numerous other reviews also cloud this area [226, 228, 291, 292]. Guller, for instance, produced a report entitled "Safety and effectiveness of bariatric surgery: Roux-en-Y gastric bypass is superior to gastric banding in the management of morbidly obese patients". This study demonstrated selective use of data to argue that RYGB was superior to LAGB [293]. This report drew significant criticism from a group who reanalysed much of the data and described Guller's paper as "biased, unsubstantiated, not supported by the current literature and represents a disservice to the scientific and health care community" [294].

Randomised trials

Only 12 randomised trials relevant to the LAGB (one involved open AGB placement), either in comparison to non surgical treatments or comparisons of different surgical techniques were identified. Table 6.1 summarises these. Data from a total of 858 LAGB patients were available. There were no peri-operative deaths or severe early morbidity. Weight loss was generally excellent (range 44% to 87% EWL) at short term follow up (2-3 years), with only one study reporting 5 year data and none beyond this. There have been no follow up reports of outcomes of these trials, despite a number having reached 5 and in one case 10 year maturity. Weight loss was reported in different formats (%EWL, Kg weight loss and change in BMI).

Whilst LAGB was found to be extremely safe, life threatening events were observed in studies involving comparisons with alternate bariatric procedures, with a death due to gastroplasty and severe, life threatening complications following LRYGB and sleeve gastrectomy, despite small numbers. In a trial comparing LAGB and RYGB, 3 of 24 LRYGB patients suffered early, life threatening complications [265]. Similarly, in the trial comparing sleeve gastrectomy with LAGB, 2 of the 40 sleeve gastrectomy patients suffered a severe early complication (one required a total gastrectomy and another return to theatre for bleeding). A recent large trial (n=200) comparing LAGB and RYGB identified a much higher complication rate of 45% in the RYGB group compared to 17% over 4 years of follow up [187].

TABLE 6.1: Summary Data on LAGB Outcomes in Randomised Control Trials

Study/Arm	Subjects	Complication Rate	% Excess weight loss	Follow up (years)
O'Brien[264] 2006 LAGB vs. intensive medical program (BMI 30-35)				
Medical	40	-	21.8%	2
Surgical	40	10%	87%	2
O'Brien[10] 2005 Pars flaccida vs. peri-gastric				
Perigastric	101	16%	53%	2
Pars flaccid	101	4%	46%	2
Dixon[263] 2008 LAGB vs. medical treatment in diabetics				
Medical	30	-	4.3%	2
Surgical	30	10%	62.5%	2
de Wit[233] 1999 Open versus laparoscopic adjustable gastric banding				
Open	25	12%	34.4 kg	1
Laparoscopic	25	0%	35 kg	1
Himpens[295] Sleeve Gastrectomy vs. LAGB				
Sleeve	40	5%	66%	3
LAGB	40	10%	48%	3
van Dielen[206] LAGB vs. Open Gastroplasty				
LAGB	50	40%	54.9%	2
Gastroplasty	50	36%	70%	2
Morino[296] 2003 LAGB vs. laparoscopic vertical banded gastroplasty				
LAGB	49	24.5%	41.4%	2
Laparoscopic Gastroplasty	51	14.7%	63.5%	2
Angrisani[265] LRYGB vs. LAGB 2007				
LRYGB	24	12.5%	66.6%	5
LAGB	27	14.8%	47.5%	5
Angrisani[297] 2009 LAGB vs. LAGB and vagotomy				
LAGB	25	0	46.6	1.5
LAGB + vagotomy	25	0	44.1	1.5
Nilsell[252]† 2001 Adjustable gastric banding and vertical banded gastroplasty				
LAGB	29	10.3%	43 kg	
Gastroplasty	29	38%	35 kg	
Suter[298] LAP-BAND vs. Swedish Band				
LAP-BAND	90	12.2%	50%†	3‡
Swedish Band	90	8.8%	50%†	3
Thorne[299] LAGB vs. LAGB + omentectomy				
LAGB	25	*	27kg	2
LAGB + omentectomy	25	*	36kg	2
Nguyen[187] LAGB vs. RYGB				
LAGB	86	17.4%	45%	4
RYGB	111	45.0%	68%	4

*†Data were presented categorically, means not presented ‡ Variable follow up, * 3 complications in the entire study, not separated by group*

The LAGB re-operation rate was variable, ranging from 0 to 36%. This is largely accounted for by significant differences in surgical technique and evolution of the procedure. O'Brien's randomised trial illustrated the efficacy of the pars flaccida approach, with the 2 year re-operation rate due to prolapse being 16% in the peri-gastric group compared to 4% in the pars flaccida group [10]. Variable definitions of complications make comparisons difficult.

The Cochrane review criticised several of the RCTs for being poorly constructed, not demonstrating adequate randomisation and lacking pre-defined outcome measures [157]. Despite these limitations the data validate the short term safety and efficacy of the LAGB. They have illustrated the ability of the LAGB to safely and effectively induce weight loss and improve a range of medical co-morbidities and quality of life. Robust longer term data is urgently needed as are controlled trials relating to specific patient populations and disease states.

Case series

Without long term follow up from randomised control trials or prospective cohort studies, case series represent the best available intermediate to longer term data. Favretti highlighted two distinct patterns of case series in the literature: either strongly favouring or opposing the LAGB [1]. The reason for this division can partly be explained by the evolution of LAGB surgical technique. Early series reported variable, although frequently high, prolapse rates. These are no way reflective of outcomes of the current procedure; in effect a different operation. Significantly contrasting perspectives, however, are presented in studies of similar nature. Table

6.2 summarises data from case series with a focus on Australian studies and those with > 500 patients.

The majority of these studies have presented good intermediate term results, with modest complication rates. Mortality has remained very low, with only 5 deaths out of more than 12,000 cases (0.03%), from the series presented in Table 6.2. There are few quality true long term data. The most recent large Australian study, presented in 2008, included 1,000 patients and noted a EWL of 51% at 8 years, although less than 5% of the total cohort had achieved this follow up [300]. The prolapse rate was only 3%. O'Brien's report from 2002 was of 98.6% follow up in 709 patients [301]. Only 112 of these had 4 year data, where a EWL of 52% was observed.

Complication rates varied between groups (0.26% to 20.5%) as larger series reported an experience that straddled the transition from the peri-gastric to pars flaccida era and follow up was highly variable.

In the most comprehensive publication of long term data, Favretti reported on 1,791 patients from Italy [275]. This included 4 patients out to 12 years and 210 with nine year follow up. At each time point, follow up was greater than 85%. Excess weight loss was between 35 and 40% for each of the years 5 to 10. The re-operation rate was very low; 6% in the entire cohort. Weiner reported on 100 patients out to 8 years, with nearly complete follow up. EWL was 59.3%, although there was a 17% re-operation rate [302].

TABLE 6.2: Summary of Large LAGB Case Series

Author	Year	Number	Follow up time (years)	Complication rate	% Excess Weight loss	30 day mortality (number)
O'Brien[303]	2002	709	6	12.5%	54%	0
Toouli[300]	2008	1,000	8	3.0%	52%	1
Brancastiano[304]	2008	838	3	-	54%	0
Parikh[305]	2005	749	2	6.7%	52%	0
Watkins[306]	2008	2,412	1	10%	41%	1
Singhal[307]	2008	1,140	1	0.26%	59%	0
Dargent[308]	2003	973	7	10.9%	54%	2
Favretti[275]	2007	1,791	12	9%	38%	0
Ponce[309]	2005	1,014	4	20.5% /1.4%†	64%	0
Belachew[285]	2002	763	4	11.1%	50-60%	1
Brown[310]	2008	425	4	4.4%	55%	0
Weiner[302]	2003	984	8	17%	59%	0

†complication rates in pars flaccida vs. perigastric approach were separated.

Several groups have recently reported early data (2-3 years), suggesting that problems of proximal gastric dilatation following LAGB have largely been eliminated by minor technical modifications [254, 307, 311-313]. The reduction in complication rates has been attributed to searching for and repairing hiatus hernias or variable methods of securely fixing the gastric wall. More likely the pars flaccida technique combined with a meticulous and broad fixation of the LAGB can be achieved in several equivalent ways. Adhering to these basic principles largely removes the issue of early gastric prolapse. These reports emphasise the necessity for robust definitions of complications and failure as well as for the provision of accurate data on the duration and completeness of follow up.

Reflective of Favretti's observation relating to the dichotomous nature of the literature, several studies have presented high complication and failure rates in the intermediate to longer term. Guller, in 2009, argued that the ongoing use of LAGB cannot be justified as the rate of long-term complications and band removal is high and failure to lose weight after laparoscopic gastric banding is prevalent [293]. This echoed similar reports from 2002 which predicted that LAGB would not stand the test of time [314]. In this series, after a median follow-up of 7 years, 58% of the patients had been reoperated on, almost always by conversion to Roux-en-Y gastric bypass. Mittermair reported on up to ten year data from 785 patients, 396 (50.4%) who experienced complications [315]. Additionally, 43% of patients had been lost to follow up within five years

Two other studies with good longer term follow up reported high late failure rates. Suter reported on 84 patients at 7 years with 82% follow up [316]. Good weight loss was observed in those who maintained the LAGB; 58% EWL. Although a failure rate of 37% was noted. Tolonen similarly followed up 123 consecutive patients who were at least 5 years post-LAGB. Mean EWL was 56% at 7 years, although this decreased to 46% if patients who no longer had the LAGB were also analysed. The failure rate was 15% over the first 3 years, although increased to nearly 40% by year 9 [317].

A possible explanation for the difference in longer term outcomes, most strikingly the complication and failure rates, could relate to the adjustment schedule. Favretti had a very low re-operation rate, although weight loss was modest. Suter and Tolonen had better weight loss, however, were disappointed with the high failure and complication rates.

Management of gastric prolapse and revisional surgery

When it does occur, gastric prolapse can be effectively dealt with by performing revisional LAGB surgery [230, 318, 319]. This is not surprising as prolapse is a mechanical problem that disrupts function. Correcting the anatomical problem should therefore be successful. This has been illustrated where moderately high revision rates (16%) were not found to compromise longer term weight loss [320].

Data supports the management of prolapse with revisional LAGB surgery. Kediar, in 2002, reported the largest series on gastric prolapse of 125 patients [321]. Seventy patients had the LAGB removed and in 55 revisional LAGB surgery was performed.

This was a highly successful strategy and only 10% of those who had a revision had further problems. More recently, prolapse of a LAGB placed via the peri-gastric approach has routinely been converted to a pars flaccida LAGB procedure, with good weight loss and few failures [322, 323].

High failure rates following revisional LAGB surgery have been reported, with patients gaining weight and nearly 45% undergoing a further revisional procedure in one series [324]. This has lead to calls for routine conversion of LAGB complications to RYGB or other procedures [325, 326]. Others have reported extreme rates of generalised oesophageal dilatation [327]. These negative reports possibly arise from the approach taken to follow up or the selection of patients for revisional surgery.

Other LAGB specific complications – infection and erosion

LAGB specific problems relate to migration of the prosthesis into the lumen, infection and mechanical problems with the port, tubing or LAGB itself. Luminal erosion of prosthesis placed adjacent to viscera has long been acknowledged as a problem [328-330]. With LAGB, this appears to occur in approximately 1% of patients. It can be managed with re-operation and staged re-insertion, alternatively, endoscopic techniques for removal are available [328].

Mechanical problems with the LAGB itself are rare. Movement or leakage of the port is relatively common, occurring in 10-15% of patients [331, 332]. Leakage is normally due to a needlestick injury to the hub or proximal tubing [333]. Both of these problems frequently require re-operation, although this is usually as a day

case. The morbidity of these problems is of a troublesome nature and should be overcome with attention to adequate fixation of the port and improved prosthesis design.

Early infection of the subcutaneous port appears to occur in approximately 1% of patients and requires removal of the port, leaving the LAGB in situ [334]. Staged port re-insertion with placement at an alternate site appears to be an effective strategy [335]. Infection of the LAGB itself is rare and requires the application of sound surgical principles.

The modern challenge - Intermediate term complications in the pars flaccida era

With controlled trials consistently presenting good early results and reduced prolapse rates, the major challenges following LAGB have shifted to a later stage [172, 303, 309]. These intermediate term problems lack definition and detailed analyses in the peer reviewed literature, however, are a significant issue.

Intermediate term post LAGB problems can present symptomatically; with reflux or regurgitation, or with weight regain. Liquid contrast swallow and upper gastrointestinal endoscopy are the available modes of investigation. Using these investigations luminal dilatation above the LAGB is frequently identified. A normal lie of the band differentiates these from gastric prolapse. Sometimes no anatomical abnormality is identified.

Luminal dilatations can be classified temporally as acute or chronic. Anatomically they could be gastric, OGJ or oesophageal, or variable combinations. The utility of

functional assessments, such as oesophageal manometry, have not been established.

Acute luminal dilatation has been recognised as a difficult problem from early in the pars flaccida era [336]. Initially gastric pouch dilatation was described as an early phase of prolapse for which removal of fluid from the LAGB and attention to eating patterns was advocated [336]. More recently, acute dilatations have been termed pouch dilatations; likely recognising uncertainty over the anatomical nature of the enlargement. In the acute setting, removal of saline from the LAGB has been reported as successful in 77% of patients [337]. Most likely many clinicians simply remove saline from the LAGB without performing a contrast swallow; saline is subsequently reintroduced after a variable period of time.

The chronic situation where removal and reintroduction of saline is unsuccessful or luminal dilatation is persistent or extensive presents a far more complex problem. Re-operation or conversion to another bariatric procedure may be considered.

Ponce attempted to sub-classify gastric pouch dilatations of a more chronic nature. These were divided into isolated pouch dilatation and those associated with hiatus hernia or oesophageal dilatation [338]. This initial classification was limited and exploratory, involving only 11 patients and has not been validated anatomically nor has there been a correlation with outcomes.

Dargent used his personal experience of over 1,000 LAGBs to differentiate problems amenable to revisional LAGB surgery [254, 308]. Revisional LAGB surgery for an obvious mechanical problem was often successful. A moderate incidence of

revisional surgery was accepted as a reality of LAGB. If an obvious mechanical problem is not present optimal management is less clear [254, 308]. There was also an acceptance that the system could fail, without there being a recourse to further LAGB surgery. Failure of the system was defined as poor weight loss (defined as the loss of less than 25% excess weight) or gross oesophageal dilatation. An incidence of 13.7% was identified after 5 years [308]. The physiological and anatomical basis for failure remained poorly defined.

Moving further into the pars flaccida era there has been a reducing incidence of gastric prolapse, meaning that mechanical problems potentially requiring revisional surgery are now of a different nature.

Brown defined the clinical nature and management of one pattern of intermediate term luminal dilatation [310]. Symmetrical gastric pouch dilatation (SPD) was shown to have replaced prolapse as the most common indication for revisional surgery. This series, reported in 2008, encompassed the author's personal experience of 425 consecutive primary LAGBs in all of whom the modern pars flaccida technique had been used.

Up to 4 year follow up (98.5% complete) was available. A 4.4% re-operation rate was noted. Only 2 of these were for prolapse, with 17 being for SPD. Re-operated patients achieved a weight loss following revision equivalent to the background cohort.

The clinical presentation of SPD resulted in adverse symptoms of reflux and regurgitation. The LAGB maintained a normal lie in SPD, although there was excess

volume of supraband stomach visualised on liquid contrast swallow. Whilst the clinical presentation was similar to prolapse, pathophysiologically SPD appeared more representative of stretching of the luminal wall, rather than migration of part of the stomach.

It was hypothesised that SPD is a result of excess intraluminal pressure transmitted to the proximal pouch, over time, resulting in dilatation. Episodes of obstruction and poor eating behaviour were postulated as the events leading to over pressurisation.

This study was limited, being relatively short term. Consequently, significant numbers of patients would not have mature (> 2 year) follow up data. It did suggest that like gastric prolapse other mechanical problems above the LAGB are amenable to surgical correction. Comprehensive longer term outcome data on this cohort of patients would be of great interest.

The alternate spectrum of luminal dilatation; oesophageal or OGJ dilatation, is not well defined. Post LAGB oesophageal dilatation has been described as ranging from acute and resolvable to generalised, gross and irreversible [327, 339]. A prevalence of 14% was reported; with dilatation defined as a luminal diameter greater than 35 mm when measured at liquid contrast swallow [340]. A clinical significance of this finding was not identified. Definitions of oesophageal dilatation overlap anatomical appearance with assessments of motility, of which contrast swallow is not a satisfactory modality.

A group of patients do present with adverse symptoms or poor weight loss despite an anatomically normal liquid contrast swallow or upper gastrointestinal endoscopy. Without a diagnosis or treatment pathway, there is little LAGB can offer these patients presently. It is likely they are frequently lost to follow up or in some series conversion to another bariatric procedure undertaken. A logical strategy for assessing and managing these patients is required, particularly if they have previously had good weight loss. Outcome data also needs to define an incidence of these problems.

Without detailed understanding, the spectrum of intermediate term complications remains difficult to manage clinically and impossible to accurately characterise epidemiologically – limiting the progression of the clinical science of LAGB. There appears to be variable indications and outcomes reported for revisional surgery. Most importantly, the ability to diagnose or intervene earlier to avoid their development is significantly hampered.

The LAGB follow up process is an ideal opportunity to intervene and the adjustability of the LAGB provides a unique means of altering the effects of the procedure; if this could be guided objectively. To do this a true physiological understanding of the effects of LAGB adjustments needs to be integrated with better knowledge of the follow up process and the nature of post-operative problems.

The follow up process

Life-long follow up after bariatric surgery has long been advocated for all procedures, although with the exception of LAGB is not often practiced [341]. The importance of patient education, generalising the necessary key behavioural changes has been widely emphasised [342]. Slow consumption of nutritious foods is considered critical, as is small portion size and adequate chewing prior to swallowing. Patients are advised to stop eating once they feel full. Adverse symptoms are not expected and if present should be reported to the treating team [342].

The follow up process is deemed critical to the success of LAGB, emphasised by surgeons and to patients in educational material [3, 343-345]. Protocols vary, however, clinical contact is commonly recommended every 4-6 weeks in the first year and as a minimum, annually for life [346]. Saline is known to passively escape from the system over a period of months [347, 348]. This encourages attendance at follow up with small adjustments required to maintain efficacy. Intrinsically, the adjustability of the LAGB ties patients to a follow up program; provided the program is accessible.

LAGB follow up can be divided into the clinical consultation and the adjustment. These can be performed synchronously, as is typical in Australia, with an adjustment performed, if required, following a consultation. Alternatively, more regimented follow up and adjustment schedules are used, with less frequent clinical contact [187]. Sometimes the components are separated, with adjustments

performed under image guidance by radiologists the mainstay of post-operative care [337].

During follow up consultations eating advice involving a reduction in the speed of eating, eating smaller portions and eliminating foods of different texture such as bread or red meat is usually advocated [301]. This is coupled with adjustments, where fluid is progressively added to the LAGB or removed if there are adverse symptoms.

Clinical zones: the yellow, green and red zones are used and communicated to patients in one follow up strategy [343]. These zones represent collections of sensations associated with the desired outcomes and the simple schema facilitates communication of key concepts to patients. The green or optimal zone is where small meals satisfy, hunger is not prominent and weight loss is usually good. The yellow zone represents a LAGB that is ineffectual or too loose. Once in the red zone, the LAGB is too tight and obstructive symptoms supervene. Patients may lose weight due to obstruction; however, maladaptive eating may compromise weight loss. Patients are encouraged to present for frequent clinical review and to seek urgent attention if they develop red zone symptoms.

Few studies have specifically addressed the follow up process or separately, its two components. Several randomised trials have used follow up visits every 4-6 weeks. During these visits adjustments to LAGB volume were made if indicated [187, 263]. In one trial patients were seen up to 20 times over the two year period [167]. Another randomised trial used a limited follow up regime of 3 monthly clinical contact [296]. This trial reported modest weight loss (40% EWL), possibly

attributable to the abbreviated follow up schedule. Other strategies involve seeing patients frequently in the first year, focusing on rapidly optimising the adjustment [349, 350]. After this, the frequency of clinical follow up is greatly reduced [351].

Busetto evaluated patients following surgery and determined that more aggressive filling of the LAGB increased complication rates, although an increased LAGB volume was associated with more weight loss [352]. It was found that pouch dilatation requiring removal of fluid occurred in 23% of patients when fluid was added aggressively. A pouch dilatation rate of 9.3% was documented in patients where saline was not added to the LAGB at the time of surgery and 19% in patients where it was. Similarly, the rate of oesophageal dilatation was increased: 2.9% vs. 9.2%.

The use of radiography to optimise adjustments is a strategy where fewer adjustments are performed and clinical follow up is not as frequent [353, 354]. A definitive protocol has not been defined, however, frequently a liquid contrast swallow is used to calibrate the adjustment [354]. Whether this strategy achieves different outcomes to more intensive approaches has not been tested. Kuzmak, in his original description, calibrated the stoma over the LAGB at the time of operation, aiming for a diameter of 13 mm [231]. Although used very early in the laparoscopic era, stomal calibration has long since been discarded.

Susmallian performed a randomised trial of different approaches to adjustments [355]. Fluoroscopy was compared to dynamic radioisotope scintigraphy for band adjustment. It was found that performing adjustments using radioisotope scintigraphy guidance rather than fluoroscopy achieved better total weight loss

(20.3% vs. 12.3%) and required fewer adjustments (0.3 vs. 1.9) in the initial six months. The number of adjustments, however, seems very low in both groups and not reflective of practices elsewhere. Moreover, the follow up time was very short.

Favouring the use of a regular follow up program are several reports that have correlated worse early outcomes with limited attendance at follow up. Poor attendance, particularly in men, has been associated with poor weight loss [356]. Follow up frequency in the first post-operative year has also been found to be a significant determinant of weight loss [357]. When an intensive follow up regime was undertaken, adherence to scheduled visits and compliance to recommended rules predicted the success of LAGB [358]. The addition of a more intensive lifestyle program appears to provide better weight loss than standard post-operative care [359]. The more intensive program also affected greater changes in eating behaviour, with more restrained eating developing.

The importance of follow up has been highlighted with other bariatric procedures. Harper reported a loss to follow up in the first year following RYGB of 48% [189]. When specifically followed up, non-attenders were found to have significantly worse weight loss by around 20%. Another 6% were totally lost to follow up.

Baseline independent predictors of outcome following LAGB have been investigated, although only small effects identified. Insulin resistance, advanced age, pain and physical disability predict a lesser weight loss [360]. Effects, however, were statistically but not clinically significant.

Naslund and Kral argued that in the search for predictors of outcome after obesity surgery, preoperative eating behaviour is important [342]. In one study sweet eaters fared less well after gastric restrictive surgery than non-sweet eaters [361]. Several others studies found that sweet eaters and non-sweet eaters are equally successful in terms of weight loss after gastric restrictive procedures and LAGB [362-364].

Colles found that uncontrolled eating and grazing after LAGB showed high overlap and were associated with poorer weight loss [365]. Although follow up time was short and differences were small [366].

After any bariatric procedure those attending follow up appear to have better weight loss. Whether lack of attendance at follow up causes poor weight loss or those that do not achieve initial success simply don't attend follow up remains unclear. A totally independent effect of the clinical follow up program has not been demonstrated. Undoubtedly, regularly seeing patients offers the opportunity to identify and intervene if progress is unsatisfactory or a complication suspected. Available evidence suggests maintaining this may well improve outcomes. The adjustability of the LAGB offers a unique opportunity to tailor the effects of the procedure; however, understanding of the physiological effects of the LAGB or alterations induced by adjustments remains limited.

CHAPTER 7: *LAGB Mechanisms of Action, Gastric Emptying and Hormonal Factors*

Reduction of caloric intake and change in eating patterns

The LAGB is hypothesised to be satiety inducing, suppressing appetite thereby reducing total food intake [8]. Adding or removing saline from the system appears to be able to fine tune these sensations or return them to normal if the LAGB is completely emptied [8]. Others classify the LAGB as a restrictive procedure that works primarily by mechanically limiting intake and conditioning behaviour [292, 362]. Which mechanism is dominant and how the LAGB circumvents sophisticated longer term control processes that rigidly guard body weight is unknown.

The mode of weight loss with LAGB is reduction of caloric intake, due to significantly modified eating behaviour [362]. A shift to softer foods, with a reduction in the consumption of solids is also noted [352]. Longitudinal studies have reported a more restrained eating pattern and decreased susceptibility to hunger following LAGB [367-369].

Colles evaluated eating patterns prior to LAGB and 12 months post-operatively in 129 LAGB patients [365, 366]. The marked behaviour changes observed led to the recommendation that management of LAGB patients should focus on combining use of the LAGB to control physical hunger with conventional approaches to increase physical activity and reduce total energy intake [365, 366].

The reason for this behavioural adaption does not appear to be pure mechanical restriction. O'Brien observed that LAGB patients consistently reported early and

prolonged satiety [3, 253, 264, 283]. This was proposed as the likely principle mechanism of action and achieving satiety deemed crucial and a major aim of the follow up and adjustment process.

Induction of satiety following LAGB

In the only specific physiological investigation of the mechanism of action of LAGB in humans, monitored breakfast tests were performed on a cohort of successful LAGB patients. Hormonal changes and reported satiety were measured over a six hour period under standardised conditions [8].

The study was designed as a blinded, cross over trial with the LAGB at optimal and a reduced volume and incorporated a group of obese controls. The alteration in LAGB volume, however, was performed 48 hours prior to the test. It is highly likely subjects would have become aware of the volume status of the LAGB by the morning of the study. The authors asserted that patients were blinded to the volume status and were actually unable to correctly guess the volume status. Clinical experience suggests that patients detect a reduction in LAGB volume almost immediately when they eat solid food.

It appears as though patients were asked to guess the volume status immediately after the adjustment rather than on the morning of the test. Whether knowledge of the volume status is of practical importance remains unclear – it appears to have been deemed so by the authors.

After a 14 hour fast, subjective feelings of hunger were recorded over a 6 hour period (3 hours before and 3 hours after a standard LAGB breakfast). Both fasting

and postprandial feelings of satiety were significantly increased at optimal LAGB volume compared to 2 days of reduced volume. A marked satiating effect following the meal was observed at optimal volume. BMI matched controls (non-LAGB patients) were also less hungry than LAGB patients at reduced volume, suggestive of a rebound phenomenon.

A rebound increase in hunger would fit with suppression of satiety signals by low levels of adiposity signals, leading to increased feeding upon removal of the LAGB effect. These data suggest the optimally adjusted LAGB is able to overcome homeostatic process that increase hunger in response to a reduction in body weight. Removal of saline from the LAGB appears to allow the resumption of normal control mechanisms that facilitate energy intake until body weight is restored.

This study identified no hormonal or biochemical changes to account for the differences observed, although several mediators (PYY, ghrelin, insulin, glucose and leptin) were measured.

Gastric emptying in LAGB patients

Two recent studies have suggested there is a prolonged emptying of the supraband stomach following LAGB [370, 371]. Retention of food in the pouch of stomach above the LAGB, with gradual emptying, could result in sustained vagal stimulation due to ongoing distension of the cardia. This could plausibly explain the induced satiety and early satiation [8]. These data support the hypothesis that the LAGB functions primarily as a restrictive procedure.

One study measured gastric emptying in LAGB patients and controls following a yoghurt meal. Post LAGB patients had a prolonged gastric emptying half time (36.6 ±9.8 min) compared to obese controls (23.8±4.7 min) and healthy volunteers (22.8±6.8 min) [370]. It was concluded that retention in the supraband compartment was responsible for the delay in emptying observed. The use of a near liquid meal (yoghurt) may have identified a brief delay in transit, as this meal consistently emptied rapidly in both the pre-operative patients and the volunteers. Most laboratories use standardised semi-solid meals that demonstrate a normal emptying half time of 40-60 minutes [372].

Another study used supine magnetic resonance imaging (MRI) to evaluate emptying of the supraband compartment [371]. Prolonged retention of the meal within the oesophagus was identified in the 5 patients studied. An average of 16.9 ml was retained within the oesophagus following consumption of a standard meal (mean volume 79 ml). This study included a representative image that was an obvious gastric prolapse, with a large volume of meal accumulated above the LAGB and within the oesophagus - not the expected LAGB situation.

In a 6 month follow up study, gastric emptying half times did not change following LAGB when assessed with standard techniques [6]. In another study that used concurrent manometry and nuclear scintigraphy, a pouch emptying half time of 3 minutes was estimated [7]. However, a 90% emptying time of 40 minutes was also documented [7]. This observation is consistent with a biphasic pattern of emptying of the supraband stomach. Potentially separate mechanisms mediate initial rapid

transit, after which there is retention of a small volume of the meal that subsequently empties more slowly.

A major limitation of three of these studies has been the poor spatial resolution of nuclear scintigraphy [373]. This is a particular problem in patients with a LAGB, where a primary aim is to determine if the proximal pouch is restricting meal size or affecting transit.

Any residual meal within the tiny gastric pouch above the LAGB needs to be separated from expected accumulation in the gastric fundus; immediately beneath the LAGB. Retention within a small gastric pouch above the LAGB may not necessarily be measurable as a change in gastric emptying half time. MRI has improved anatomical resolution, although not widely used, appears a valid means of assessing gastric function [374, 375]. It was, however, only used in 5 patients including one not representative of the normal post LAGB state.

The four evaluations of gastric emptying following LAGB appear to agree that overall semi-solid gastric emptying and function of the stomach below the band is not affected by LAGB. Events in the region of the LAGB and oesophago-gastric junction are less well defined. Three of the four studies favour a restricted proximal pouch, with meal retention.

Gastric emptying in restrictive bariatric procedures

Over the past twenty years investigations of gastric emptying in various other forms of restrictive bariatric surgery have not proven insightful in deciphering their mechanisms of action.

Van Dielen studied 40 obese patients before and after vertical banded gastroplasty and identified no difference in gastric myoelectric activity using electrogastrography [376]. Others reported no effects on gastric emptying [377]. A slight decrease in solid emptying, without an effect on liquids has been documented following gastroplasty [378]. Naslund studied patients after both gastric bypass and gastroplasty and found no difference in the rate of gastric emptying at 12 months [379]. Recently, sleeve gastrectomy with preservation of the gastric antrum was not found to alter gastric emptying [380].

Balloon distension of the proximal pouch in gastroplasty patients was found to accelerate gastric emptying initially but did not affect overall emptying [381]. This study was unable to identify a relationship between weight loss and stomal diameter, pouch volume or gastric emptying. It did, however, illustrate the potentially complex effects of bariatric surgery, well beyond the simple effects envisaged as a result of the gross anatomical modifications.

Despite studies not defining a significant effect of bariatric surgery on gastric emptying, it remains likely the effects are mediated via the stomach. The stomach is a complex and highly sensate organ, involved in multiple regulatory and feedback processes [382]. Its volume status and emptying patterns are important mediators of satiety and food intake as well as being associated with related visceral sensations such as discomfort and nausea [382].

Gastric emptying in obesity

It has been hypothesised that obese patients have a higher gastric capacity than non-obese subjects, both proximally and distally, facilitating overconsumption [383]. Tosetti argued that gastric emptying is accelerated in obesity and decreased following weight loss, suggesting that increased gastric emptying is part of the aetiology of obesity [384]. Others have found that fasting gastric volume, gastric accommodation and perception in response to gastric distension were not altered in obese patients [385-387]. Verdich found no difference in overall gastric emptying between obese and lean males; obese patients were restudied after a mean diet induced 18.8 kg weight loss and no change in gastric emptying identified [388].

Current consensus suggests that altered gastric emptying is not central to the causation of obesity [383, 388]. It is therefore not surprising that bariatric procedures do not significantly alter overall gastric emptying. Severe adverse symptoms can be induced, with only minor changes to gastric emptying or accommodation [389-391]. Moreover, if delayed gastric emptying was observed in obesity, this would possibly be attributable to an effect of obesity rather than the underlying cause.

Normal gastric physiology and emptying

When food first enters the stomach there is immediate, vagally mediated, receptive relaxation of the fundus to accommodate the increase in volume, without an increase in pressure [373, 392]. As a meal is progressively consumed adaptive relaxation supervenes due to stimulation of gastric mechanoreceptors [375, 393].

Gastric distension and associated relaxation is involved in feedback processes that subsequently reduce food intake [394].

If there is impaired proximal gastric accommodation a meal may be rapidly forced into the distal stomach, likely inducing adverse symptoms [395-398]. Normally, progressive contraction of the stomach commences soon after gastric delivery of a bolus [375]. This results in mechanical and chemical digestion of food that is progressively delivered to the distal stomach. Intrinsic gastric motor activity regulates this process, with co-ordinated relaxation of the pylorus facilitating intermittent transit of chyme to the duodenum.

Gastric emptying is subject to numerous inputs and control processes, including whether the meal is liquid or solid, particulate size and caloric density [399, 400]. Higher energy density meals tend to empty at a reduced rate in comparison to lower energy density meals [401, 402]. In general, for liquid meals, 50% of gastric emptying can be achieved within 20 to 30 minutes and the emptying takes place in an exponential fashion without lag [383]. Solid emptying frequently demonstrates a significant lag phase, followed by linear emptying [403]. The lag phase is thought to be a result of the requirement for mechanical and chemical breakdown of ingested food into small segments (chyme) 1-2 mm in diameter prior to duodenal delivery [404, 405]. Elevated blood glucose levels, within the physiological range, also slow gastric emptying [403].

The vagus nerve innervates the stomach and receives feedback from gastric mechanoreceptors. Two types of vagal afferent receptors are present within the gastric muscularis externa, intramuscular arrays (IMA) and intraganglionic laminar

endings (IGLE) [406]. Receptors within the gastric wall are low threshold and importantly individually respond to a differing range of wall tension [407]. They appear to be slowly adapting, particularly those in the cardia [393]. These receptors respond either to tension or elongation [408]. Based on data derived from microscopy studies, it has been proposed that IMAs are tension receptors whereas IGLEs have a chemo-sensory role [409]. Others have argued that both respond to changes in tension [410].

Gastric wall tension and stretch (volume) generate perceptions of gastric fullness [395]. It remains controversial which stimulus is dominant. Changes in wall tension may be more important in mediating immediate sensations of fullness [411]. Others have suggested that volume rather than wall tension is the most significant mediator [412, 413].

In animals, it has been demonstrated that gastric distension rather than nutrient delivery to the stomach determines meal termination or satiation [414]. In rats, inducing gastric distension by occluding the pylorus and infusing caloric containing liquids into the stomach suppresses eating [414]. This is a purely volumetric effect and requires an intact vagus nerve [394]. Continued eating is observed if the pylorus is occluded and the stomach aspirated via a gastrotomy.

Similar human experiments have also established that intragastric volume, independent of caloric density, is important in generating satiation [415-417]. These studies have shown sensations can be generated without distal caloric delivery [416, 417], although caloric delivery, in particular fats that stimulate

cholecystokinin release, combine with gastric distension to augment satiation [116, 418].

Sustained gastric stretch, delivered alone, is a temporary satiation stimulus. Performed prior to a test meal, distensions of up to 800ml for ten minutes did not affect food intake when the distension was relieved prior to the meal [419]. The site of the distension seems likely to have some effect on the sensations induced. In health, gastric satiation signals may be mediated via antral distension rather than distension of the fundus or cardia [420-422]. The mechanical stimulus required to generate gastric mediated sensation differs from the proximal to the distal stomach with the proximal stomach demonstrating increased compliance, accommodating a larger volume [395]. If there is low grade antral distension the relaxation or accommodation response of the proximal stomach is decreased [395].

These data illustrate the capacity of the stomach to powerfully modulate food intake. Effects of the LAGB appear largely localised to the proximal stomach, without measurable effects on distal gastric emptying.

Specific intraluminal events above the LAGB may be stimulating the small supra-band stomach. This could be via retention of food and delivery of a sustained cardial stretch. Alternatively, episodic stimulation of the supra-band stomach may occur as a result of rapid transit of food into the infra-band stomach. Overall, the mechanics of transit through this region are poorly characterised.

CHAPTER 9: *Oesophageal Anatomy and Function*

Oesophageal motility and LAGB

Oesophageal motility in LAGB patients has been a focus of considerable investigation and controversy. Placement of the LAGB immediately beneath the OGJ undoubtedly directly impacts this region and oesophageal motility. Potentially, just as important is the role oesophageal motility and sensory feedback plays in mediating weight loss. The longer term effects of the LAGB on oesophageal motor and sensory function are not known.

DeMaria drew excessive attention to the potential adverse effects of the LAGB on the oesophagus. Gross oesophageal dilatation, requiring LAGB removal, occurred within two years in 18 of 37 patients [327]. Whilst degrees of oesophageal dilatation can occur following LAGB, results akin to DeMaria's have not been replicated [339, 340, 423-425]. The placement of a LAGB with tailored adjustments must be differentiated from obstruction induced by a non-calibrated resistance placed immediately beneath the OGJ [426].

The extreme nature of DeMaria's report has tarnished the LAGB as a procedure that induces oesophageal motility disorders and exacerbates any underlying peristaltic deficiency. This is reflected in Klaus's authoritatively toned review of the role of oesophageal manometry in LAGB patients where it was concluded that LAGB should not be performed in those with weak oesophageal motility [427]. It was also argued that those with a weak LOS were predisposed to reflux, as the angle of His was dissected. Data that supported either of these assertions was not presented.

A recent systematic review and meta analysis synthesised available literature concerning LAGB, gastro-oesophageal reflux disease (GORD) and oesophageal motility [9]. It was concluded that LAGB increased lower oesophageal sphincter (LOS) tone, although impaired deglutitive relaxation. Oesophageal body dysmotility was reported to increase from 3.5% to 12.6%. Whilst this paper is a careful and objective meta-analysis, the true physiology of the LAGB needs to be better defined before pooled statistical analysis is of value.

A pre-operatively dysmotility rate of 3.5% is extremely low in an obese population; it could be considered low in any random sample of the community. Varying degrees of dysmotility are observed in the obese, generally of the order of 40-50%, depending on the criteria used [428-431]. Some actually consider the most common disorder of oesophageal motility; non-specific oesophageal motility disorder, a consequence of GORD [432]. GORD is undoubtedly significantly increased in obesity [433]. This is most likely due to altered physiology, with increased transient LOS relaxations [434, 435]. Direct mechanical effects, increasing intra-abdominal pressure, appear to have a lesser role [436].

Eight studies have specifically evaluated oesophageal motility in LAGB patients. These are summarised in Table 9.1. Conflicting results were obtained concerning the effect of the LAGB on oesophageal motility and LOS function. This was despite the use of similar conventional manometric techniques, study designs and patient populations. None of the studies were genuinely prospective and drop out was a significant problem. These limitations, however, do not account for the disparate

results recorded. The dichotomous nature of the data, with 180° opposing conclusions, raises concerns about performing pooled statistical analysis.

The studies in Table 9.1 reached varying conclusions. It has been suggested that the LAGB induces oesophageal motility disorders [269, 437-440]. Others observed no effect of the LAGB on oesophageal motility or LOS tone [268]. Impaired LOS relaxation without an effect on basal tone has been documented [440]. Augmentation of LOS tone with or without impairment of oesophageal motility has been recorded [269, 441].

Conventional manometric techniques were used in all studies, with LOS assessment via station pull through. Surprisingly, the LAGB itself was not documented as a physiological presence or intraluminal pressure. Possibly because the LOS is within 1 cm of the LAGB, conventional manometric techniques are not sensitive enough to separate these close structures. If the LAGB does produce an intraluminal pressure, measuring this, rather than the true LOS, may account for increases in basal tone and impaired relaxation.

TABLE 9.1: Summary of Studies Addressing Oesophageal Motility Following LAGB

Author	Year	Manometric technique	LOS tone	LOS relaxation	Oesophageal motility	Subjects	Follow up time
Korenkov [442]	2002	Pull back	Increased	No effect	No effect	32	22 months
Gamgaris [437]	2008	Solid state (conventional)	Increased	Decreased	Impaired	33	6/12 months
Tolonen [268]	2006	Not stated	None	Decreased	No effect	31	19 months
Weiss [438]	2000	Pull Back	Increased	Decreased	Impaired	43	6 months
De Jong [441]	2006	Pull back	Increased	Decreased.	No Effect	29	6wks/6 months
Suter [439]	2005	Pull back	No effect	Not reported	Impaired	43	6-18 months
Iovino, [269]	2002	Pull back	Increased	None	Impaired	11	18 months
Klaus [440]	2006	Stationary	No change	Decreased	Impaired	164	unclear

Animal models of LAGB effects

Attempts have been made to model the effects of   LAGB on the oesophagus in animals. O'Rourke performed gastric banding, calibrated to a luminal diameter of 6.7 mm, in opossums [443]. Manometry was serially performed for up to 14 weeks, including 4 weeks following band removal. In a number of cases the band was removed early due to rapid weight loss precipitated by oesophageal obstruction.

This study found that basal LOS pressure decreased significantly immediately after removal of the band, although returned to normal after a short recovery period. LOS relaxation was significantly decreased when a band was in situ, also returning to normal after band removal. Distal peristaltic amplitude decreased significantly. Recovery was observed after 2 weeks, however, was incomplete. This study illustrated that obstruction of the oesophagus can induce proximal dilatation and impair oesophageal function. However, once the obstruction is relieved there is rapid, although incomplete, recovery of oesophageal function.

Schneider performed a similar study in cats that aimed to simulate achalasia and determine if motility abnormalities were recoverable [426]. The oesophagus was subjected to a moderate obstruction for up to six weeks. Oesophageal dilatation with a consequent impairment in peristalsis was induced. Rapid recovery of peristaltic function occurred after the obstruction was relieved.

These animal data, not surprisingly, show that distal obstruction results in proximal dilatation and consequently adversely effects oesophageal motility. Increases in LOS tone and decreased relaxation were observed, similar to several human LAGB

studies. The LOS effects, however, where only observed when the prosthesis was in situ, with the LOS being hypotensive immediately the obstruction was relieved. This suggests that pressures measurements were of the prosthesis rather than the true LOS.

The animal studies are significantly limited as they modelled high grade obstruction over a very short period of time; not representative of the human LAGB situation.

Normal oesophageal and oesophago-gastric junction anatomy and function

The oesophagus is an approximately 25 cm long muscular tube that runs from the upper oesophageal sphincter, passing through the thoracic cavity, then via the oesophageal hiatus in the diaphragm to intersect the gastric cardia [444]. Typically, the thoracic oesophagus is anatomically divided into upper, middle and lower thirds, separate from the cervical part.

A feature of the oesophagus is the mixed distribution of skeletal and smooth muscle within the wall. Only around 4% of oesophageal length is purely skeletal muscle [445]. A mixture of striated and smooth muscle fibres are found over the proximal third of the oesophagus [444, 446, 447]. The transition point, where smooth muscle predominates (manometrically defined as the transition zone), occurs at approximately 20% of the length, a mean of 4.7 cm below the upper oesophageal sphincter [445]. The distal oesophageal muscularis is entirely smooth muscle.

The muscularis of the smooth muscle oesophagus is considered to consist of separate circular and longitudinal layers. The arrangement may be better appreciated as an overlapping spiral pattern [444].

The function of the oesophagus is to transfer a swallowed bolus to the stomach. The upper skeletal muscle sphincter, predominantly cricopharyngeus, remains tonically closed, opening to facilitate deglutition [448]. Distally, the lower oesophageal sphincter complex separates the oesophagus from the stomach, guarding against the reflux of gastric contents, whilst relaxing appropriately to allow passage of a swallowed bolus or venting excess gas.

The LOS complex, normally located immediately above the OGJ, includes the diaphragmatic crura and hiatal canal, phreno-oesophageal ligament as well as the intrinsic (smooth muscle) sphincter.

Passage of the oesophagus into the abdominal cavity occurs via the oesophageal hiatus in the right crus, normally located at the level of the T10 vertebrae [449]. The hiatus is a complex structure, originally described as a channel, not an orifice. Superior and inferior components were described. The superior aspect is a complete muscular channel of approximately 2.5 cm in length, inferior to this is a semi-circular gutter, supporting the posterior aspect of the oesophagus [449]. Others have since described this manometrically as the hiatal canal, within which lies the smooth muscle LOS. The hiatal canal contributes to the antireflux barrier, complementing the intrinsic LOS [450]. If this relationship is disrupted the differing components that collectively form the lower oesophageal high pressure zone are separated, significantly degrading its barrier function [451].

During deep inspirations, where intra-abdominal pressure is elevated, the gastro-oesophageal pressure gradient favours reflux. Diaphragmatic contraction onto the LOS (the pinchcock effect), focally increases intraluminal pressure at this point, preserving the barrier at the OGJ [452].

The junction between the oesophagus and the stomach is a deep cardiac notch that forms an acute angle (appreciated by surgeons as the angle of His). This angulation, lined with a mucosal valve, has been regarded as one of the mechanisms essential to gastro-oesophageal continence [453]. Likely of importance in animals such as the pig, a clear role has not been definitively established in humans [454, 455].

The phreno-oesophageal ligament is a bi-leaved condensation of thickened sub-peritoneal fascia that surrounds the oesophageal hiatus and attaches to the oesophagus [456]. A possible function is to limit intra-thoracic excursion of the oesophagus [457]. An autopsy study suggested that high insertion of the ligament into the oesophagus, permitting excess mobility of the OGJ, favoured reflux [456].

The intrinsic (smooth muscle) lower oesophageal sphincter

First identified as a high pressure zone, the smooth muscle LOS is macroscopically indistinguishable from more proximal oesophageal muscle [458]. Normally, measuring 2-4 cm longitudinally, it consists of two opposite, incomplete fibre bundles arising from the proximal stomach. Semicircular clasps arise at the lesser curve and gastric sling fibres from the greater curve [459, 460]. This arrangement results in radial asymmetry of the pressure profile of the LOS region [461].

The peak LOS intraluminal pressure correlates with the corresponding regional muscle thickness [458, 460, 462]. Overall, the circular muscle layer that constitutes the LOS is thicker than more proximal oesophageal muscle [459].

Individual LOS muscle cells demonstrate a significantly higher resting tone than more proximal oesophageal smooth muscle [463].They exist in a depolarised state (-41 mV compared to -50 mV) this is theorised to lead to spontaneous action potentials, which maintain basal tone [464]. Descending innervations may also contribute to this [465]. Innervating vagal fibres, however, appear to primarily mediate relaxation, with the majority of basal tone being myogenic [458].

As a propagated peristaltic wave reaches the distal oesophagus, the LOS must relax in a co-ordinated fashion [466]. Most likely to facilitate this the myenteric plexus lies in several muscle planes, in contrast to the body of the oesophagus, where the plexus lies between the layers of longitudinal and circular muscle [467].

Deglutitive LOS relaxation is regulated centrally through the dorsal motor nucleus of the vagus [458]. Sectioning the vagus at the base of skull in animals induces achalasia with failure of relaxation of the LOS [468-470]. Neurally mediated relaxations of the lower oesophageal sphincter, termed transient LOS relaxations, are the common mechanism of reflux [471]. They are physiological events, likely induced by stimulation of proximal gastric mechanoreceptors and serve the purpose of venting swallowed air from the stomach [472]. During transient lower oesophageal sphincter relaxations the intrinsic LOS muscle and diaphragmatic crura are both observed to relax [473].

Muscles cells from the LOS demonstrate differing mechanical and contractile properties to more proximal circular oesophageal smooth muscle, with the LOS zone thought to be relatively non-compliant [474]. Animal studies have shown that in response to stretch, the more proximal oesophageal muscle is able to develop greater tension than LOS fibres [475]. LOS fibres also develop optimal contractility at a lower preload [463, 476].

Clouse documented the in-vivo capacity of the LOS to contract and defined this as the lower oesophageal sphincter aftercontraction [477]. It has been shown both in patients and on the bench top that the LOS has similar contractile properties to proximal oesophageal muscle [463, 475-477]. However, the clinical significance of this property has not been investigated.

Understandably, efforts have focused on LOS relaxation in response to a peristaltic wave as impairment in LOS relaxation is the basis of many dysphagia syndromes [478].

Oesophageal innervation

Spinal nerves and the vagus nerve supply dense innervation to all layers of the oesophagus [479]. Spinal and sympathetic afferents most likely mediate pain with descending vagal signalling influencing motility that appears primarily coordinated peripherally. Mucosal afferents also respond to stretch, light touch and a variety of chemical stimuli including altered pH [480-482].

The enteric nervous system is highly developed between the oesophageal muscle layers as the myenteric plexus [444]. The primary role of this plexus is to exercise

neural control over motor activity. There are also important functional overlaps with respiratory and cardiovascular reflexes [444].

Vagal afferents are very sensitive to distension, important in the peripheral regulation of peristalsis [479]. To graded intensities of balloon distension (10 to 120 mmHg) most vagal afferent fibres exhibit a steep increase in activity within a narrow range of distending pressure. Responses reach a plateau at noxious intensities of distending pressure; around 60 mmHg. Splanchnic afferent fibres can have either low (5mmHg) or high (40mmHg) thresholds for response, exhibiting a linear increase in response to distension [483].

This differing response profile supports the hypothesis that vagally related peripheral neurons co-ordinate the reflex functions of the oesophagus. Vagal innervation is both excitatory and inhibitory [484]. Specific splanchnic nerves may also contribute. During situations of acute stimulation, such as acute obstruction or reflux, high threshold splanchnic nerves are dominant [479].

An important function of the sensory innervation of the oesophagus is to protect against aspiration. The intrinsic sensory innervation and reflex contractility aids in the clearance of any refluxate that enters the oesophagus [485].

The dorsal horn neurons innervating the oesophagus also receive converging input from somatic neurons covering the chest and forearm regions, meaning referred oesophageal noxious stimuli may be interpreted in these regions [479].

The oesophagus is not known to directly mediate sensations of satiety or satiation, although there is undoubtedly an overlapping innervation with the proximal stomach [467].

Oesophageal peristalsis

Oesophageal peristalsis is a complex, finely co-ordinated process which can be classified as primary or secondary. The initiation of swallowing, leading to a primary peristaltic contraction, is mediated via the swallowing centre and neurons from the nucleus ambiguus regulate pharyngeal initiation of swallowing [466]. Neuromuscular control of oesophageal skeletal muscle is via the vagus nerve [486].

Normally a swallowed bolus initiates centrally mediated primary peristalsis [486]. The regulation of a propagating peristaltic wave within the smooth muscle oesophagus occurs largely peripherally. The myenteric plexus coordinates sequential, focal muscular contraction and relaxation [487]. Descending central inputs appear to contribute, however, play a lesser role [485].

Secondary peristalsis is a locally mediated response to wall distension [485, 488]. In patients with a healthy oesophagus, acute focal distension results in secondary contractions proximal to the stimulus and an inhibition of distal contraction [489]. The oesophageal response to distension is consistent, with the upper oesophageal sphincter closing and the induction of secondary peristalsis [484].

Low volume reflux events can also stimulate secondary peristalsis. Presumably, sensitive neurons innervating the mucosa detect chemical changes or respond to slight distension. Following reflux events salivation is stimulated, generally leading

to a pharyngeal contraction and a primary peristaltic contraction [484]. Up to 90%

of the reflux volume is cleared by one or two peristaltic contractions [490].

Secondary peristalsis may be a more important protective mechanism during

episodes of nocturnal reflux [485].

Peristalsis involves the generation of tension and closing pressures above a

swallowed bolus, resulting in an intrabolus pressure. A pressure gradient is

established that propels the bolus towards the stomach [491]. The efficient

peristaltic mechanism is able to overcome gravity if required.

During peristalsis there is simultaneous and coordinated contraction of

oesophageal circular and longitudinal smooth muscle [492]. The purpose of these

layers is thought to be complementary; decreasing energy expenditure and

allowing the development of variable levels of propulsive forces. Contraction of

longitudinal muscle concentrates the contracting circular muscle where maximal

pressure is required. The circular muscle is three times thicker where an occluding

pressure is generated due to actions of the longitudinal muscle layer. The

longitudinal muscle reduces the total number of muscle fibres required by up to

two thirds. It also reduces the level of pressure that is needed to maintain luminal

closure above the bolus [491].

Oesophageal contraction zones

Clouse, in the early 1990's, challenged assumptions relating to the temporal

progression of a peristaltic wave [493]. It had long been considered that a

peristaltic wave represented the regulated progression of a homogeneous pressure

domain. Clouse hypothesised that the oesophagus was composed of separate contractile segments. If traditional views were valid, sampling intraluminal pressure from only a few different sites would give a reliable overview of oesophageal function, accurately characterising the peristaltic wave. However, the clinical yield from oesophageal manometry using few pressure sensors had remained relatively low.

Topographical analysis was used to document segmental variations in oesophageal peristalsis and most importantly identify focal low pressure areas deemed to represent transitions between segments [477]. Three amplitude troughs divided the oesophagus into four functional segments: the skeletal muscle segment, two different parts of the smooth muscle body and the lower oesophageal sphincter region. The proposed aetiology of these differing contractions zone is the neurotransmitters within the oesophageal wall or in the case of the upper zone, transition to differing neural control. This work challenged established paradigms and suggested a peristaltic wave was more dynamic and regionally variable than previously appreciated.

Oesophageal bolus transit

The key components of oesophageal function are coordinated peristalsis and LOS relaxation. Disruption of either of these can impair bolus transit, resulting in dysphagia. Localised oesophageal contractile deficiencies or regional hypotonia may allow a swallowed bolus to escape [494]. Inadequate LOS relaxation may obstruct the delivery of a swallowed bolus to the stomach. The frequency and

intensity of symptoms of dysphagia will also be subject to considerable variability, influenced by eating patterns and behaviour.

During water swallows the intrabolus pressure required to generate flow across the OGJ is generally only 5 mmHg [495]. This is easily achieved when the LOS relaxes in response to a propagating peristaltic contraction. Even in the presence of impaired deglutitive LOS relaxation successful bolus transit occurs if intrabolus pressure exceeds the presented resistance [496]. The success of bolus transit is also dependent on bolus size and consistency, although, regardless of changes in these variables a positive pressure gradient between the intrabolus pressure and OGJ is required [497].

When measuring intraluminal pressure it is important to distinguish the oesophageal intraluminal pressures during swallowing due to luminal occlusion from those that occur within the swallowed bolus. Intrabolus pressure has previously been termed the ramp pressure when observed on chart recordings, although conventionally diagnostic techniques have not paid significant attention to the ramp pressure [498].

Luminal occluding pressures 20 mmHg or greater than the pressure within the swallowed bolus are required to prevent retrograde bolus escape [497]. Effectively, this means maintenance of at least a 30 mmHg wavefront minimises the chance of a liquid bolus escaping the peristaltic wave [494, 499]. Therefore, a contiguous 30 mmHg propagating pressure domain is deemed representative of a normal peristaltic contraction [500]

To clear a bolus across the OGJ, a pressure gradient needs to be maintained for a sufficient time [495]. To ensure complete oesophageal clearance it appears this gradient must be maintained for at least 2.5 seconds [496].

These findings relating to bolus transit have served as the basis for classifying swallows as normal or abnormal when topographical manometric analysis is performed. The aim is to identify whether an individual peristaltic contraction will deliver a swallowed bolus to the stomach [501].

CHAPTER 10: *Measuring Oesophageal Function*

Development of oesophageal manometry

Oesophageal manometry is widely used as a diagnostic test in the assessment of deglutitive disorders and as a research tool [502]. Its clinical purpose has been described as being: to accurately define oesophageal motor function, define abnormal motor function and delineate a treatment plan based on abnormalities [503]. Until recently, its ability to fulfil these criteria, particularly the third, was limited.

Passage of a nasogastric tube able to transmit information concerning intraluminal pressure remains the basis of oesophageal manometry. Initial experiments in the 1800's used swallowed, intraluminal balloons connected to external recording devices. There were few advances in manometric technique from this baseline until the 1950's [504]. In the 1950's-60's, non perfused water filled catheters were used with the water column connected to an external pressure transducer. Perfusion based techniques were then developed where a few microlitres per minutes were perfused through the lumina of catheters [505-507]. The basic data output of manometric studies was of single or multiple line tracings representing pressure change versus time at several discrete oesophageal loci [508]. For the next 50 years this method of displaying data was maintained and is still widely used.

The development of perfused catheter innovations permitted more accurate assessments of lower oesophageal sphincter pressure that were deemed clinically relevant [461]. Pope, however, demonstrated that low flow rates through perfused

luminal catheters were inaccurate at assessing peristaltic pressures [509]. Alterations to the perfusion rates and design of specific apparatus allowed more accurate assessments of peristaltic amplitude [510].

In the 1970's and 80's improved water perfusion technology allowed more accurate measurement of basal LOS pressure and oesophageal peristaltic pressures [511, 512]. Dent also replaced syringe based perfusion systems with a pneumatically driven perfusion pump connected to a manifold [513]. This utilised a high driving pressure (in a low compliance system), far exceeding intraluminal pressure and allowed for a reduction in the perfusion rate. The process of acquiring pressure data was simplified and better adapted for clinical use.

The sleeve sensor was also developed in the late 1970's. This innovation allowed the measurement of maximal pressure over a 5 cm (later increased up to 8 cm) length [512]. This overcame the problem of movement artefact that made measurements of LOS function from a single side hole unreliable [514, 515]. The sleeve sensor permitted accurate characterisation of LOS pressure over time and facilitated the assessment of LOS relaxation during swallowing. Sleeve technology also allowed correlation of reflux events with transient LOS relaxations; which were subsequently shown to be the pathophysiological basis for gastro-oesophageal reflux disease [516].

Current manometry technology can be divided into water perfused systems where intraluminal pressure is relayed through water perfused channels to pressure transducers outside the patient. Solid state technology uses within catheter pressure transducers that signal proximally.

Water perfused manometry has the advantage that the catheters are relatively robust and the location of side holes can be customised at relatively low expense. However, artefacts can occur if the capillaries are obstructed by debris or air bubbles. Solid-state sensors are better able to record motor activity in the pharynx and upper oesophageal sphincter because they have a more rapid response time. However, this equipment is more expensive, fragile and subject to thermal drift [517].

Clinical use of conventional manometric techniques

An ongoing limitation from 1980 until the high resolution era was lack of uniform standards for performing and interpreting oesophageal manometry. Variable techniques and methods were used. There was significant debate concerning the use of wet or dry swallows [518].

Assessments of oesophageal motility have used defined normal ranges of intraluminal pressures from volunteers as the basis for reporting abnormalities of motility [519].

Conventional criteria classify motility abnormalities into patterns of inadequate LOS relaxation, hypocontraction, hypercontraction or uncoordinated contraction [520]. Unfortunately, the range of normal is very wide [519, 521]. This has limited the specificity of manometric reports, unless there is a major abnormality of peristaltic function such as achalasia [432].

High resolution manometry and topographical presentation of data

Use of multiple pressure sensors, generally 16 or more, is defined as high resolution manometry [522]. This technique was first proposed approximately 10 years ago and despite initial scepticism has gained wide spread acceptance [523, 524]. Increasing evidence has highlighted the usefulness of more pressure sensors, providing higher spatial resolution. An ongoing worldwide collaboration seeks to improve the clinical utility, standardise methods across laboratories and improve diagnostic algorithms [525].

Topographical plots have allowed increased volumes of data to be displayed and analysed, frequently with the assistance of automated computer algorithms [508]. Clinical data on the superiority of the technique is accruing [526].

Solid state systems and water perfused technology have both been adapted for high resolution use [508]. High resolution manometry has been facilitated by parallel improvements in computers that are now able to easily synthesise and present large volumes of data as detailed colour spatiotemporal plots [527]. Furthermore, improved fidelity of recording systems that are more responsive to rapid changes in intraluminal pressure have become increasingly available [528].

The first report of high resolution manometry used only a three channel manometry catheter moved repeatedly [493]. An accurate profile of the pressure topography throughout the oesophagus was established by deriving mean values over a series of swallows from the same individual. The aggregated data set allowed the interpolated mapping of the pressure profile of the entire oesophagus.

Usefulness of recording from multiple pressure sensors was previously limited by the techniques of data recording, display and analysis. Chart recorders had been used since the 1950's to record and display manometric data; interpretation of multiple tracings can be time consuming and confusing. This limited the appeal of multi channel recordings which had become available in the 1990's with the application of extrusion technology that allowed the creation of 32 channel silicone rubber manometry catheters.

Initial reports of topographical analysis used spatio-temporal displays of data to accommodate the third dimension - pressure amplitude. Initially, in black and white format, these were presented in a similar manner to topographical displays of geographical data that incorporate longitude, latitude and elevation.

Use of spatio-temporal displays made the analysis of large volumes of data possible in a realistic timeframe and preserved the ability to focus on fine detail if required. This made the routine use of multi-channel oesophageal manometry a potentially worthwhile exercise. Current techniques use different colours to represent these data. Evidence suggests colour plots are easier to interpret than line tracings [527]. Figure 10.1 is a comparison of a line plot and a colour spatio-temporal plot.

FIGURE 10.1: High Resolution Manometry Data Presented as Multiple Line Tracings and a Spatio-temporal Plot
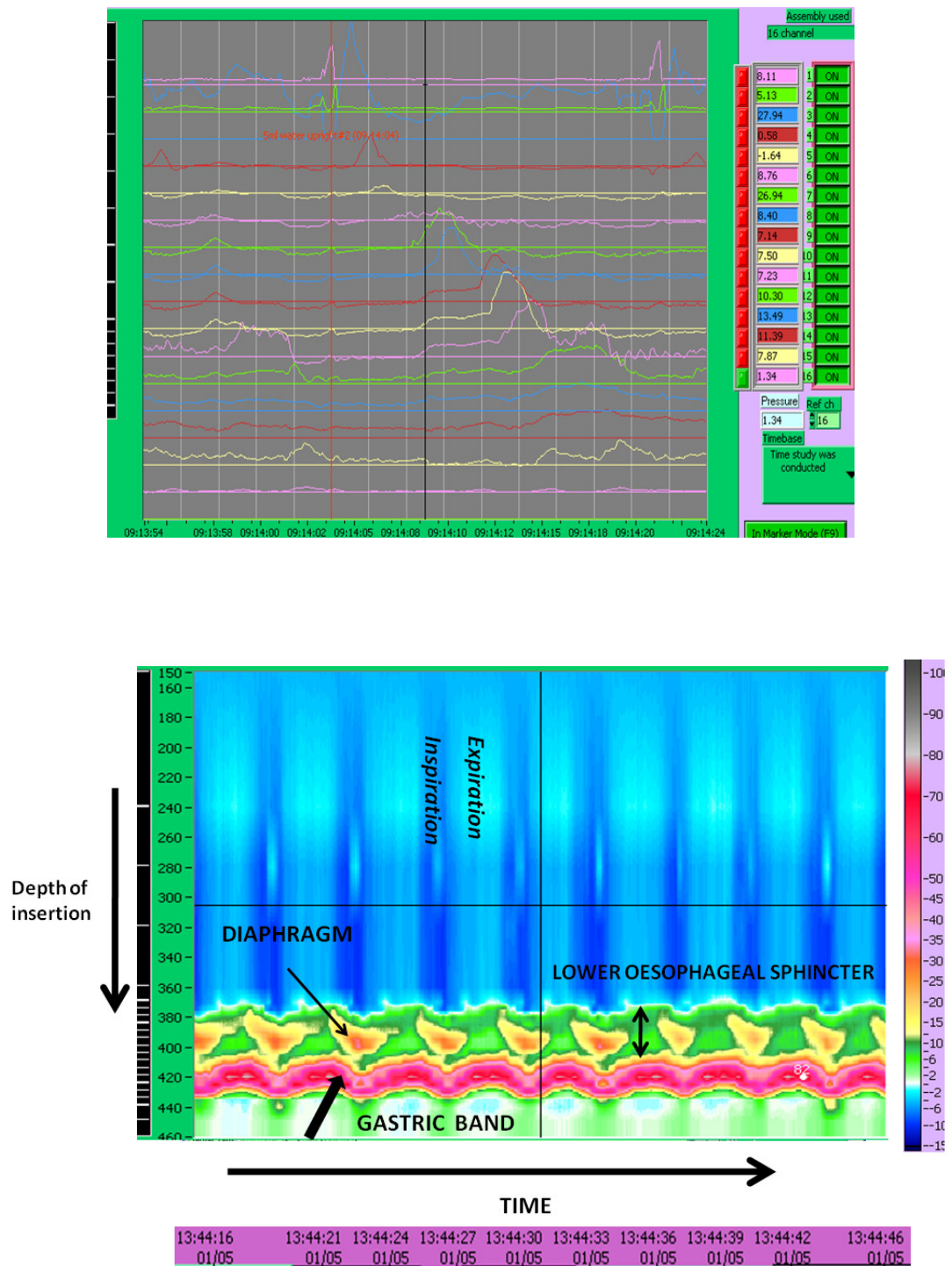
Figure 10.1 legend: *In the top image multiple line traces convey intraluminal pressure data. Alternatively, data can be presented as a spatiotemporal plot*

(bottom image), where the y axis is distance from the nares (spatial) and the x axis is time. A third dimension, pressure, is represented by different colours (scale shown). This presentation of data allows an overview of different events in space and time to be appreciated at a glance, with high spatial fidelity. The colour plot is a basal tracing of a LAGB patient during quiet respirations.

Clinical Use of High Resolution Manometry

Importantly, valid high resolution manometry criteria for assessing motility have been developed by integrating new understanding of the role of oesophageal motility in bolus transit and the likely mediators of dysphagia symptoms [501, 508]. High resolution manometry has proved at least as sensitive in the assessment of transient LOS relaxations as a sleeve sensor [529]. Deglutitive LOS relaxation is well assessed and there is the advantage of a quicker response time. Diagnostic algorithms have been established based on improved understanding of oesophageal function and measurements performed in asymptomatic subjects [478, 501, 530].

The basis for established high resolution manometry diagnostic algorithms has been the analysis of the success of peristaltic contractions in achieving oesophageal clearance [494]. Receiver operator characteristic curves have suggested the use of a 30 mmHg intact isobaric pressure wave front is the appropriate cut off for differentiating normal from abnormal swallows. These, along with profiles of

peristaltic waves and deglutitive relaxation of the LOS, have been the basis of diagnostic criteria [478, 530].

High resolution manometry has involved the translation of research concerning oesophageal function to clinical use. This has facilitated the development of reproducible algorithms capable of accurately and reproducibly assessing oesophageal function [522].

An additional complementary aspect of high resolution manometry has been the design of computer programs that have the capacity to synchronously display and record video fluoroscopy. This allows visualisation of bolus transit and correlation of anatomical information with intraluminal pressure. The use of concurrent recordings of impedance also provides information concerning bolus transit without the requirement for fluoroscopy [500]. These are useful features in research and may become more so in the clinical environment.

High resolution manometry has not been applied to LAGB patients. These techniques may prove powerful means of assessing LAGB patients, providing functional, anatomical and transit data.

Chapter 11: *Synthesis of Background Data and Rationale for Research Directions*

The prevalence and severity of the ongoing obesity epidemic is indisputable. Without effective lifestyle or pharmaceutical interventions there will be increasing use of LAGB.

Data strongly supports LAGB as a safe and effective procedure, justifiably the first choice in many centres. Whilst longer term outcome data is somewhat limited, high quality research highlighting the benefits of the procedure continues to accrue.

The attributes of the LAGB encourage follow up, likely enhancing overall patient care and facilitating data collection. This has created a rapidly expanding pool of patients requiring indefinite care. Optimising the follow up and adjustment process, together with recognising, better treating or avoiding complex intermediate term complications represent major future challenges.

Key areas of knowledge deficiency relate to the peripheral physiological processes associated with the LAGB in terms of oesophageal motility, transit and gastric emptying. The effect of adjustments on these processes is not known.

There is a critical need for a comprehensive understanding of the spectrum of intermediate term complications that can be used to guide treatment. Anatomically, luminal dilatation appears to be significant, however, remains poorly characterised with likely several patterns mandating different management. There has been no overlap of anatomical change with impairments in function, bolus

transit or oesophageal motility. Furthermore, clinicians lack sensitive diagnostic tests where conventional means such as liquid contrast swallow or endoscopy are equivocal or revisional surgery has not resolved the problem.

Limited understanding is hampering the care of individual patients. It is also leading to variations in the reporting of outcomes of LAGB and revisional surgery. This situation is unlikely to be remedied until the spectrum of intermediate term complications is objectively characterised.

A key feature of the LAGB; adjustability, has not been fully leveraged to optimise outcomes. The importance of follow up and tailored adjustments are emphasised, yet accumulated clinical experience rather than objective data guides this process.

With luminal dilatations above the LAGB appearing to underpin many chronic, significant post LAGB problems the opportunity to avoid or reduce their incidence or severity exists. Adjustments provide an avenue for intervening at an earlier stage or adapting the effects of the procedure to individuals or particular circumstances. Without understanding the key physiological effects of adjustments this capacity is limited.

Researching the physiology and pathophysiology of LAGB is of considerable practical importance to clinicians caring for these patients. There is the opportunity to rapidly translate new knowledge to clinical practice.

Three research themes are presented based on the modalities deemed most able to extend existing knowledge in key areas:

Research theme 1: High resolution video manometry

Research theme 2: Nuclear scintigraphy: Gastric emptying, transit and satiety

Research theme 3: Assessing outcomes, satiety and adverse symptoms using cross sectional research design

Research Theme 1: High resolution manometry

The interaction of oesophageal motility the OGJ and LAGB appears important on a variety of levels. This, however, is a poorly defined area. Previous investigations have utilised established, although now superseded, investigational techniques.

The literature in this area consists of contradictory data concerning oesophageal motility and LOS function. A concerning omission from physiological evaluations has been the absence of intraluminal effects of the LAGB.

High resolution manometry allows detailed topographical mapping of intraluminal pressure. This is particularly useful around the OGJ where multiple, closely spaced structures including the LAGB are located. These techniques appear ideally placed to progress physiological knowledge relating to the LAGB. Topographical data analysis should facilitate identification of the direct effects of LAGB adjustments on intraluminal pressure.

Technical innovations now allow the co-display of anatomical and pressure data during manometry studies. Described as video manometry, this provides the

opportunity to correlate intraluminal pressures with anatomical change and transit data.

High resolution video manometry also offers the potential to be adapted as a diagnostic test; if the expected physiology can be determined and suitable diagnostic criteria defined.

Research Theme 2: Gastric emptying, transit and satiety following LAGB

Induction of satiety is thought to be a key mechanism of action of the LAGB. Recent data, however, is supportive of the hypothesis that there is retention of a meal above the LAGB, with progressive emptying – in keeping with the mode of action of a physically restrictive procedure.

Overall gastric emptying does not appear to change substantially following LAGB. This suggests that regional effects on the stomach are important but the details have not been identified. Arguments that the LAGB is a satiety inducing procedure are supported by the anatomical modifications produced by LAGB, which appear to preclude significant supraband retention of food.

It is of critical importance that a sound understanding of the intraluminal events that occur when a patient eats are established. This will provide significant insights into the mode of action of the LAGB. Previous studies have lacked anatomical resolution or patient numbers to definitively answer these questions. The effect of altering LAGB volume also has not been considered.

The small volume supraband stomach is the likely site of important actions of the LAGB. If superior anatomical resolution can be achieved the opportunity to better characterise intraluminal events is presented.

Research theme 3: Assessing outcomes, satiety and adverse symptoms using cross sectional research design

This research theme seeks to provide insights into the realities of providing follow up care to LAGB patients. It aims to collect practical, clinically relevant data. This is a necessary step to ensure findings from studies in theme 1 and 2 can be practically translated to changes in patient outcomes.

There is very little objective data to guide the post LAGB follow up processes. Few studies have specifically addressed this area. Strategies to reduce complications are hampered by limited knowledge linking adjustments and follow up to outcomes or complications.

Data on outcomes following LAGB have focused on positive health outcomes, quality of life and changes in eating patterns. Little is known about the expected prevalence of upper gastrointestinal symptoms and sensations.

Sophisticated physiological investigations will be not available during routine clinical follow up. Changes in physiology will be interpreted by patients as altered sensations, symptoms or weight loss. Understanding what is normal following LAGB will aid greatly in the clinical follow up of these patients as well as potentially flagging symptoms or behaviours that are either a risk for or suggestive of a problem.

Summary

Increasing physiological knowledge and better understanding the nature of complications require urgent attention. However, without better understanding the details of the follow up process, later translating that knowledge to improved outcomes will be difficult. Ultimately any direct interventions have to be integrated into clinical practice and accepted by patients.

CHAPTER 12: *Aims*

The central goal of this thesis was to improve understanding of the clinically relevant physiology and pathophysiology of the laparoscopic adjustable gastric band, aiming also to facilitate the translation of new knowledge into clinical practice.

Specific research aims

1. Define the physiology associated with a successful outcome following LAGB in terms of: oesophageal motility, intraluminal pressure topography and bolus transit

2. Determine the physiological effects on the above parameters of adjusting the volume within the LAGB

3. Define the anatomical and pathophysiological features associated with inadequate weight loss and adverse symptoms following LAGB, relating to the spectrum of intermediate term complications

4. Develop and validate high resolution video manometry as a clinically useful diagnostic test for LAGB patients, particularly in patients where there is no explanation for unsatisfactory progress identified with conventional investigations

5. Determine the effect of altering LAGB volume on overall, supra and infraband gastric emptying, bolus transit and satiety

6. Identify changes in total, supra and infraband gastric emptying and bolus transit following LAGB placement and correlate these with weight loss and changes in satiety

7. Determine if the LAGB should be classified as a restrictive procedure that physically limits the size of meal able to be consumed

8. Establish expected ranges for different outcomes, satiety and adverse upper gastrointestinal symptoms following LAGB

9. Determine how upper gastrointestinal symptoms, satiety and weight loss affect different outcome measurements following LAGB

Declaration for Thesis Chapter 13

This Chapter represents a manuscript that has been published in *Obesity Surgery,* (*Obes Surg. 2009 Jul;19(7):905-14*)

Declaration by candidate

In the case of Chapter 13, the nature and extent of my contribution to the work was the following:

Nature of contribution	Extent of contribution (%)
Overall responsibility for all aspects of the study, conception, planning, patient recruitment, conducting experiments and recording data. Data analysis and interpretation. Statistical analysis. Crafting and revising manuscript, submission to journal.	>90%

The following co-authors contributed to the work:

Name	Nature of contribution
Wendy A Brown	Designing study and recruiting patients, manuscript review
Cheryl Laurie	Recruiting patients and conducting studies
Melissa Richards	Conducting studies, data analysis
Sohail Afkari	Technical expertise, data collection and analysis
Kenneth Yap	Intellectual contribution, data analysis and drafting of manuscript
Anna Korin	Patient recruitment, intellectual input
Geoff Hebbard	Experiment design, data acquisition and analysis, review of manuscript
Paul O'Brien	Experiment design, data analysis, review of manuscript

Candidate's Signature		Date

Declaration by co-authors

The undersigned hereby certify that:

(1) the above declaration correctly reflects the nature and extent of the candidate's contribution to this work, and the nature of the contribution of each of the co-authors.
(2) they meet the criteria for authorship in that they have participated in the conception, execution, or interpretation, of at least that part of the publication in their field of expertise;
(3) they take public responsibility for their part of the publication, except for the responsible author who accepts overall responsibility for the publication;
(4) there are no other authors of the publication according to these criteria;
(5) potential conflicts of interest have been disclosed to (a) granting bodies, (b) the editor or publisher of journals or other publications, and (c) the head of the responsible academic unit; and
(6) the original data are stored at the following location(s) and will be held for at least five years from the date indicated below:

Location(s)	Monash University, Alfred Hospital

[Please note that the location(s) must be institutional in nature, and should be indicated here as a department, centre or institute, with specific campus identification where relevant.]

		Date
Wendy A Brown		27/10/09
Cheryl Laurie		4/11/09
Melissa Richards		02.11.09.
Sohail Afkari		1/11/09
Anna Korin		5/11/9.
Geoff Hebbard		1/11/09
Paul E O'Brien		27.10.09
KENNETH YAP		2/11/09.

CHAPTER 13: *The Effect of Laparoscopic Adjustable Gastric Bands on Oesophageal Motility and the Gastro-oesophageal Junction; Analysis Using High Resolution Video Manometry*

Abstract

Background: Laparoscopic adjustable gastric bands (LAGB) are a safe and effective treatment for obesity. Conflicting data exists concerning their effect on the oesophagus, oesophago-gastric junction and mechanism of action. These patients will increasingly require accurate assessment of their oesophageal function.

Methods: Twenty LAGB patients underwent high resolution video manometry with the LAGB empty, 20% under, 20% over and at their optimal volume. Twenty obese controls were also studied. Effects on oesophageal motility, the lower oesophageal sphincter (LOS) and the oesophago-gastric junction were measured. Transit during liquid and semi-solid swallows was assessed.

Results: The intraluminal pressure at the level of LAGB was a mean of 26.9±19.8 mmHg. This pressure varied depending on the volume within the LAGB and was separate to and distal to the lower oesophageal sphincter (LOS). The LOS was attenuated compared to controls (11.2±6.9 mmHg vs. 20.2±9.6 mmHg, *p<0.01*), although relaxed normally. Oesophageal motility was well preserved at optimal volume compared to 20% overfilled, with 77% normal swallows vs. 51%, (*p=0.008*). Repetitive oesophageal contractions were observed in 40% of swallows at optimal volume compared to 16% in controls, (*p=0.02*). In comparison to controls, the

transit of liquid, 21 seconds vs. 8 seconds (*p<0.001*) and semisolids, 50 seconds vs. 16 seconds (*p<0.001*) was delayed.

Conclusions: In LAGB patients the LOS is attenuated, although relaxes normally. Oesophageal motility is preserved, although disrupted by overfilling the band. In the optimally adjusted LAGB a delay in transit of liquids and semi-solids through the oesophagus and band is produced, along with an increase in repeated oesophageal contractions.

Introduction

Surgery has proven to be the most effective treatment for obesity and its related co-morbidities [162, 263, 264, 270, 271, 282]. Laparoscopic adjustable gastric banding (LAGB) is one of the most commonly performed bariatric surgical procedures. It has advantages in terms of safety, adjustability, reversibility and ease of insertion [2]. LAGB has been used for over 14 years internationally. In the United States, although the procedure has only been approved since 2001, a projected 100,000 procedures will be performed in the next 12 months, with this expected to rapidly increase in the future. LAGB patients require ongoing follow up and management for life [253]. Symptoms such as reflux, regurgitation or poor weight loss are likely to mandate investigation. It would be expected that during the follow up years many LAGB patients will develop symptoms that require physiological assessment. Currently there is a lack of understanding of the normal physiology of the LAGB and the interpretation of investigations such as oesophageal manometry remains unclear in these patients.

A LAGB is an adjustable silicone band that is placed laparoscopically around the cardia of the stomach. Secure placement 1-2 cm beneath the oesophago-gastric junction (OGJ) appears critical to its success [8]. It is unknown exactly how the LAGB induces and sustains weight loss. Whilst it is hypothesised to be a satiety inducing procedure [8], the exact mechanism of action has not been clearly defined. It is important to understand the physiological changes around the OGJ induced by the LAGB. This will allow for better interpretation of investigations such as oesophageal manometry.

There are limited and conflicting data concerning the impact of the LAGB on oesophageal motility and the lower oesophageal sphincter (LOS). It has been suggested that the LAGB can induce oesophageal motility disorders [439], with reports of significant oesophageal dilatation [327]. Others have suggested no effect on oesophageal motility or the LOS [437, 442]. Impaired relaxation of the LOS without an effect on tone [268, 438] has been a finding documented in two studies. Others have documented an augmentation in LOS tone and length with [438] or without an impairment in oesophageal motility [441]. The effect of altering the volume within the LAGB has not previously been studied. These confusing data and the lack of a "normal" standard to assess patients against have prevented manometry from being used in situations where it clearly has the potential to be invaluable.

Video manometry is a technique that combines high resolution manometry with concurrent fluoroscopy. This allows for real time analysis and recording of physiological, anatomical and transit data. A specifically designed computer program records and displays high resolution manometry recordings as a colour spatio-temporal pressure plot alongside simultaneously recorded video images and allows for subsequent detailed analysis [522, 527].

This study was designed to define the high resolution video manometric profile of the LAGB in patients with a successful outcome. We also aimed to analyse the effect of changing the volume of fluid within the LAGB on the LOS, oesophageal motility, the pressure profile around the OGJ and transit of liquids and semi solids through this region. It is hoped that improving the understanding of the physiology

of the LAGB will allow the identification of a normal standard for video manometry, against which patients with poor weight loss or adverse symptoms can be evaluated.

Methods

This study was approved by the Melbourne Health and Monash University Human Research ethics committees. Informed consent was obtained from all participants.

Subjects

LAGB patients whose surgery was considered to be successful, as defined below, volunteered to participate in the study after being given information during consultations with bariatric physicians. They were subsequently screened for suitability. Patients were recruited from a range of different time points following surgery (minimum 4 months). A control group of 20 patients prior to LAGB surgery was recruited.

Criteria for inclusion in the study (successful patients): loss of >50% of excess weight (unless within 12 months of surgery); normal barium swallow within 12 months of enrolment in the study (performed as a part of routine care); absence of adverse symptoms such as reflux or vomiting; confirmation that the volume of fluid within the LAGB was optimal by a) absence of significant symptoms of reflux and b) no requirement for change in the volume within the LAGB in the past 2 months. Exclusion criteria included: current pregnancy, previous gastric surgery prior to LAGB placement, age under 18 years or over 70 years.

Manometry Technique

A 21 channel water perfused manometry system with a custom made 21 channel silicone rubber manometry catheter (Dentsleeve, Ontario, Canada) was used to record pressures from the pharynx to the gastric body below the LAGB. The catheters were designed specifically to assess the region of the OGJ and to differentiate the pressure signals generated by the LAGB from those produced by the LOS. Side holes in the catheter were spaced 0.5 cm apart over a 9 cm high resolution zone. Radiopaque markers were placed on the catheter to allow identification at fluoroscopy. The manometry system was connected to a personal computer via a data acquisition card and video input card (National Instruments, Austin, Texas). Simultaneous high resolution manometry and video fluoroscopy information was recorded using TRACE! 1.2 (written by G Hebbard using LabVIEW, National Instruments, Austin, Texas).

All subjects underwent a standardised protocol.

1) Nasogastric intubation with manometry catheter

2) Identification of the LAGB (confirmation with image intensification if required)

3) Adjustment of the manometry catheter such that the most distal side hole was positioned 1 cm beneath the inferior aspect of the LAGB

4) Supine basal recording for 30 seconds (preceded by a 5 minute accommodation period)

5) 10 wet swallows of 5 ml of water in the right lateral position

6) Oesophageal video manometry see below (preceded by 5 minutes accommodation)

7) Rest for 10 minutes

8) Access the LAGB port with a 23 Gauge non coring needle attached to a three way stopcock and syringe to allow repeated adjustment of the volume within the LAGB

9) Basal recordings altering the volume within the LAGB sequentially from an optimal level of restriction

10) 5 further wet swallows with the band empty, at 20% below optimal and 20% above optimal volume

Video Manometry Protocol

1) 5 ml barium swallow anterior view – 2 swallows

2) 5 ml barium swallow lateral view - 2 swallows

3) 1 spoon of barium soaked porridge anterior view – 2 swallows

All pressures were referenced to end expiratory intragastric pressure, measured by the side hole placed distal to the LAGB. The catheter was placed such that the area of the LAGB and the LOS were contained within the high resolution zone.

The LOS basal pressure was recorded as the median peak end expiratory pressure over 5 consecutive respiratory cycles, following a minimum 15 second period in which no peristaltic activity was observed. The LOS was differentiated from the LAGB (Figure 13.1). If clarification of the position of the LOS in relation to the LAGB was required, fluoroscopy was used to confirm the position of the structures by referencing the LAGB to radio-opaque markers on the manometry catheter. Alternatively, the LAGB port was accessed and fluid injected to identify a rise in pressure at the site of the LAGB (Figure 13.2). A virtual sleeve was constructed by taking the highest pressure across the range of sensors designated as being within the sleeve zone.

The LOS pressure was measured with the band at its optimal volume and then again emptied of all saline. At each volume the virtual sleeve was placed selectively over the LOS region. This incorporated the area of lower oesophagus up to the upper part of the stomach above the band. An additional measurement was taken with the virtual sleeve placed over the entire region determined to represent the LOS and band complex

LOS relaxation was defined as the nadir pressure recorded in the region of the LOS following pharyngeal initiation of swallowing until the LOS reformed. The median relaxation over three to five swallows was used for analysis.

The Length of the LOS was measured as the contiguous length of the LOS high pressure zone greater than 5 mmHg at end expiration.

The basal intra-luminal pressure at the level of the band was measured by locating

the sleeve at the level of the band and recording the median end expiratory

pressure over 5 respiratory cycles.

FIGURE 13.1: Basal High Resolution Manometry Trace in a LAGB Patient
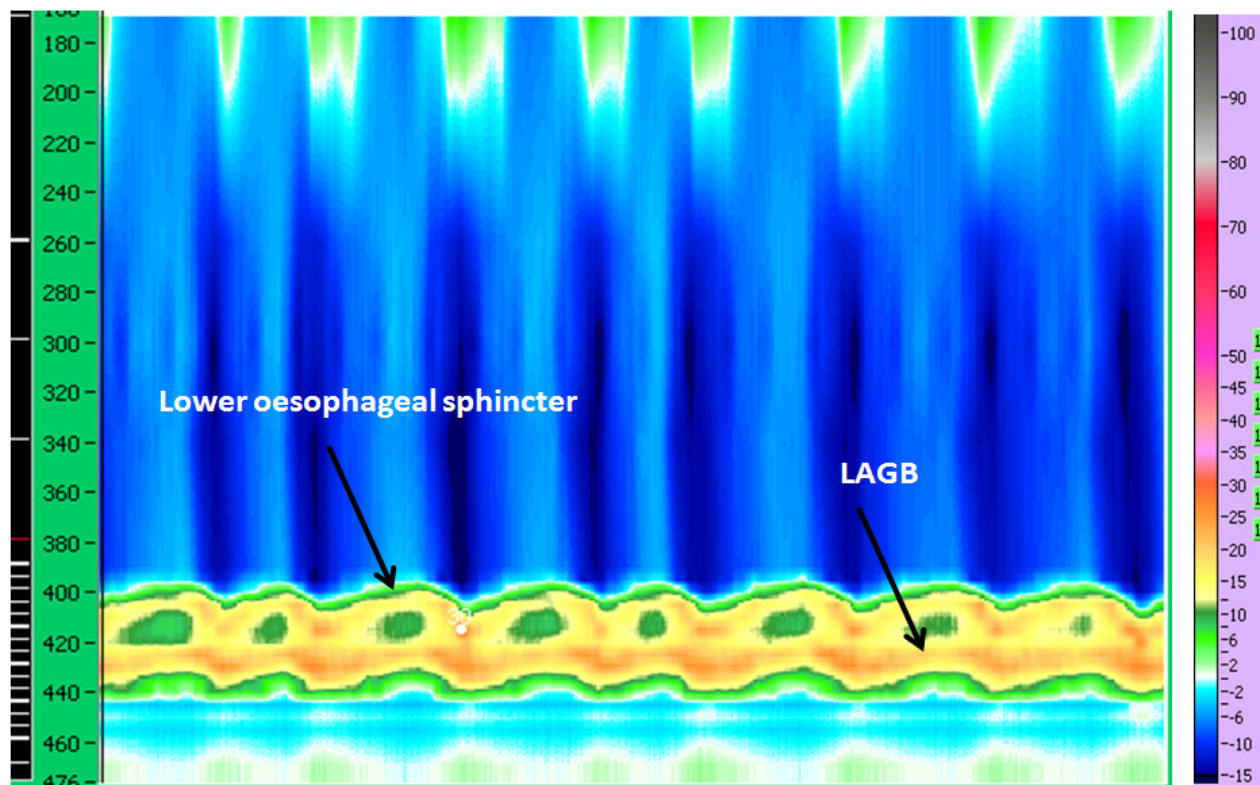
Figure 13.1 Legend: *A basal high resolution manometry recording of a successful*

LAGB patient. The pressure signatures produced by the LAGB and the LOS can be

clearly differentiated and their anatomical separation appreciated. The legend for

interpretation of the colour plot is shown at the right of the figure.

FIGURE 13.2: High Resolution Manometry Recording Co-Displayed as a Line Trace and a Spatio-Temporal Plot During Rapid Saline Injection into the LAGB

Spatio-Temporal Plot

Line Trace
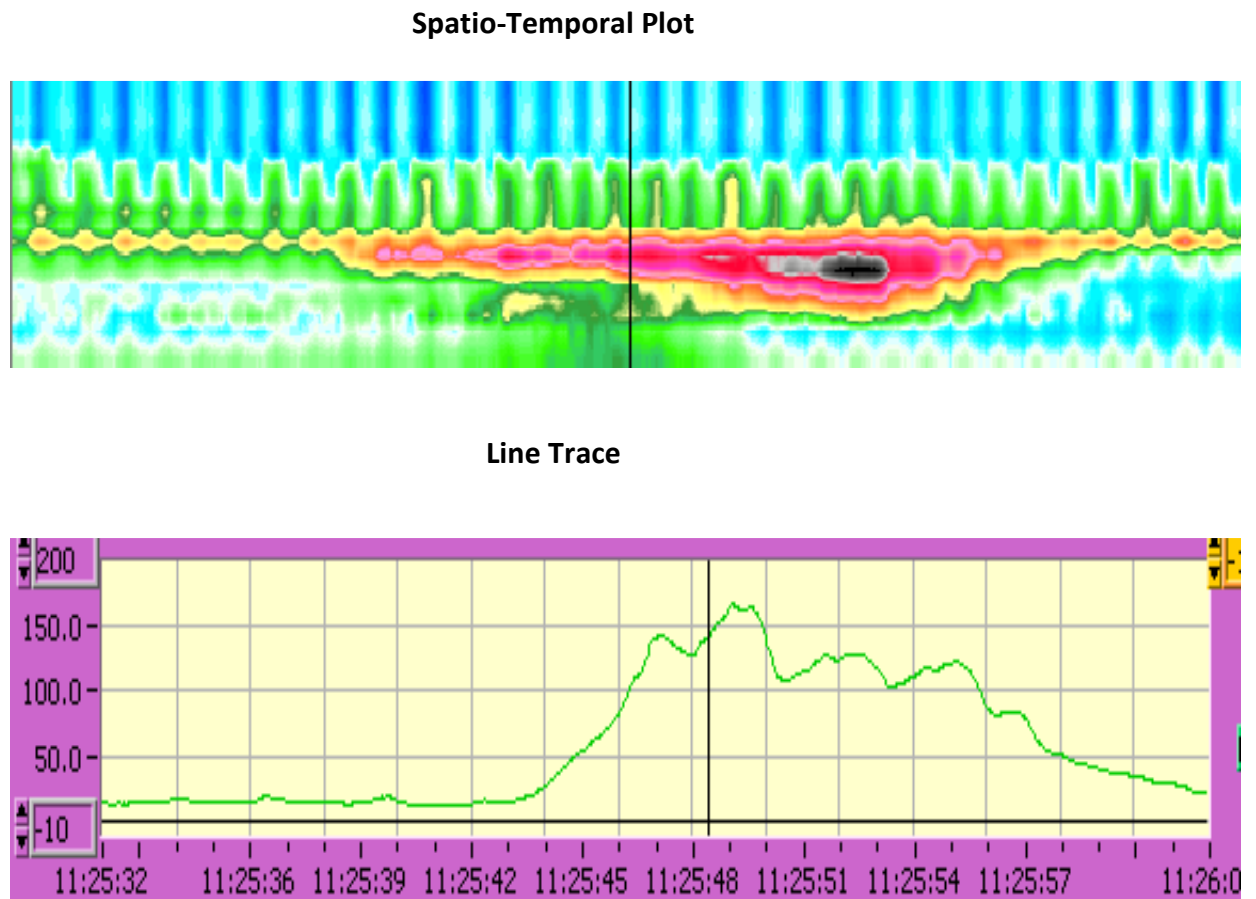
Figure 13.2 Legend: *Changes in intraluminal pressure at the level of the LAGB during rapid injection of saline into the LAGB, followed by complete re-aspiration. Simultaneous display of focused colour spatiotemporal plot and virtual sleeve line plot of pressure change at the level of the LAGB over 25 seconds. These show a rapid rise and fall in pressure as saline is injected and re-aspirated from the band. Scale shown on line plot is in mmHg. See figure 13.1 for colour plot scale.*

Oesophageal Motility

Oesophageal body motility was analysed on the results of 10 right lateral swallows of 5 ml of water. Each swallow and the overall motility pattern for each individual was classified based on published guidelines [501]. Each swallow was additionally categorised as normal or abnormal. An assessment was made of the presence of repetitive oesophageal contractions following each swallow. Any pressurisation in the oesophageal body of 30 mmHg or greater, initiated within ten seconds of the oesophageal contraction wave reaching the level of the lower oesophageal sphincter was classified as repetitive. This included situations when the patient swallowed again. This measurement was designed to identify the requirement for repeat oesophageal contractions or pressurisations to propel a liquid bolus through the resistance produced by the LAGB.

Pressure Profile in the Region of the Oesophago-gastric Junction

For each normal or hypertensive swallow at each of the volumes within the LAGB, a further detailed analysis was undertaken. Figure 13.3 illustrates the parameters analysed. The following data were collected: peak distal oesophageal pressure, peak intraluminal pressure at the level of the LAGB, peak pressure at the level of the lower oesophageal sphincter, length of the high pressure zone (defined as the contiguous area of pressure greater than 5 mmHg between the lower oesophagus and the LAGB) and peak pouch pressure. Pouch pressure was defined as the peak pressure generated in the middle of the high pressure zone (representative of the isobaric region of stomach between the lower oesophageal sphincter and the LAGB).

The velocity of contraction was defined as the rate of movement of the 30 mmHg isobaric pressure wave, over the lower 4 cm of the oesophagus, between side holes. The location of the lower oesophageal sphincter and the LAGB was taken into account to ensure that the velocity of the oesophageal contraction was measured only over the lower 4 cm of oesophagus.

Proportions were used for analysis. For each individual with three acceptable measurements, the median result for each parameter was recorded and used for pooled analysis.

Oesophageal and Pouch Bolus Transit

Clearance of the bolus from the pouch and oesophagus was measured during video manometry. Timing commenced from when the pharyngeal swallow was observed on manometry. The time taken for the bolus to pass completely from the gastro-oesophageal region above the LAGB into the stomach below the LAGB was recorded. Continuous fluoroscopy was used for a period of up to 1 minute or until the bolus had passed into the gastric body below the band. If the bolus had not passed through the LAGB after 1 minute, repeated screening was used at 30 second intervals until the bolus had moved into the stomach below the LAGB.

Statistical analysis

Comparative values for continuous variables were analysed using students t tests or paired t tests when measurements were taken on the same individual under different conditions, specifically when data was recorded with the LAGB at different volumes. A two sided *p* value of 0.05 was considered statistically significant. Values

were reported as means and standard deviation unless otherwise stated. SPSS version 11 (SPSS Inc, Chicago, Illinois) was used for statistical computations.

Results

Twenty successful LAGB patients (5 males) and 20 obese controls (6 males), recruited from preoperative LAGB patients participated in the study. Patient details are displayed in Table 13.1. All bands were LAP-BANDS (Allergan, Ca). Ten 10 cm, 3 VG and 7 APS bands were used. The longest duration since surgery for the APS bands was 18 months as these have only been in use by our group since 2006.

All patients tolerated the procedure well and were compliant with the study protocol.

Figure 13.2 shows a focused high resolution manometry tracing from the region of the oesophago-gastric junction co-displayed as spatiotemporal and virtual sleeve plots of pressure at this level. This demonstrates the rise and fall in pressure at the level of the LAGB produced by rapid injection and aspiration of fluid from the LAGB. When fluid is removed from the LAGB this pressure signature disappears. Figure 13.1 is a basal high resolution manometry recording of a LAGB patient with the LAGB at its optimal volume. This shows that the LAGB produces an intraluminal pressure that is separate to and located below the lower oesophageal sphincter.

The mean basal intraluminal pressure at the level of the LAGB was 26.9±19.8 mmHg with the optimal volume in the band. There were only 4 patients in whom this pressure was greater than 30 mmHg, and only one patient with a pressure less than 10 mmHg. Changing the volume in the band and comparing this with the values

obtained at the optimal volume, it was found that when: empty this pressure was 2.7±3.2 mmHg, (*p=0.04*), reduced to 20% under optimal volume the pressure was 15.0±7.5 mmHg, (*p=0.003*) and when the volume was 20% over optimal the pressure was 68.0±38.1 mmHg, (*p<0.005*).

TABLE 13.1: Patient Weight and Demographic Details

	Successful patients	Pre-operative patients
Age (years)	46 ±11.5	45 ±11.6
Start weight (kg)	117 ± 23.2	112 ± 25.6
Start BMI (kg/m^2)	42.2 ± 6.5	41.3 ± 7.5
Weight loss (kg)	34 ±14	-
Current weight (kg)	83 ±15	-
Current BMI (kg/m^2)	29.8 ± 4.0	-
Duration from surgery (days)	1212 ±1076	-
Percent excess weight loss	70 ±17	-

Data presented as mean and standard deviation

Lower Oesophageal Sphincter

In LAGB patients the LOS was found to be significantly attenuated in terms of length and basal tone, although it relaxed normally. In LAGB patients the mean LOS pressure was 11.2±6.9 mmHg. Nine patients had a hypotensive LOS (less than 10 mmHg). Only two patients had an LOS >15 mmHg. Table 13.2 summarises the LOS data obtained using different methods at optimal volume and empty. With the band empty, identical measurements were obtained using the two methods; therefore only one value is displayed. Data from pre-operative patients are also shown.

These data show that when using a selective sleeve placed across the LOS with the band at its optimal volume, the same value is obtained as with the band empty. Although when the sleeve was placed across the entire LOS/Band complex, an artificially elevated LOS tone and length are reported in conjunction with impaired relaxation. The LOS/Band complex reports LOS tone and length as being not significantly different from pre-operative patients, however impaired relaxation was observed.

TABLE 13.2: Lower Oesophageal Sphincter Measurements in LAGB and Pre-operative Patients

	LAGB optimal volume (sleeve only over LOS region)	LAGB empty	LAGB optimal volume (sleeve over entire LOS/Band complex)	Pre-operative patients
LOS tone (mmHg)	11.2 ±6.9	12.1 ±7.6 (0.49)	26.7±18.6 (0.004)	20.2±9.7 (0.002)
LOS length (cm)	1.6 ±0.6	1.9 ±1.0 (0.09)	3.7 ±1.3 (<0.005)	1.9 ±1.0 (0.13)
% LOS relaxation	84.2 ±16.4	86.1±12.5 (0.50)	0.5±0.3 (<0.005)	78.0±20.8 (0.31)

Values are mean and standard deviation with p value in italics comparative to optimal LAGB volume measured with a selective sleeve placed over the LOS region

During swallows a common cavity (isobaric) high pressure zone was noted to develop between the advancing peristaltic pressure wave and the LAGB. This was found to represent the pressure within the fluid contained in a high pressure zone of stomach between the LAGB and the lower oesophageal contraction. This area was defined as the "high pressure zone". Figure 13.3 illustrates a liquid swallow in a LAGB patient and demonstrates this. The high pressure zone consisted of three components; the lower oesophageal sphincter, the isobaric zone representing the "pouch of stomach" above the LAGB and the intraluminal pressure within the stomach at the level of the LAGB.

FIGURE 13.3: Liquid Swallow in a LAGB Patient with the Optimal Volume in the Band
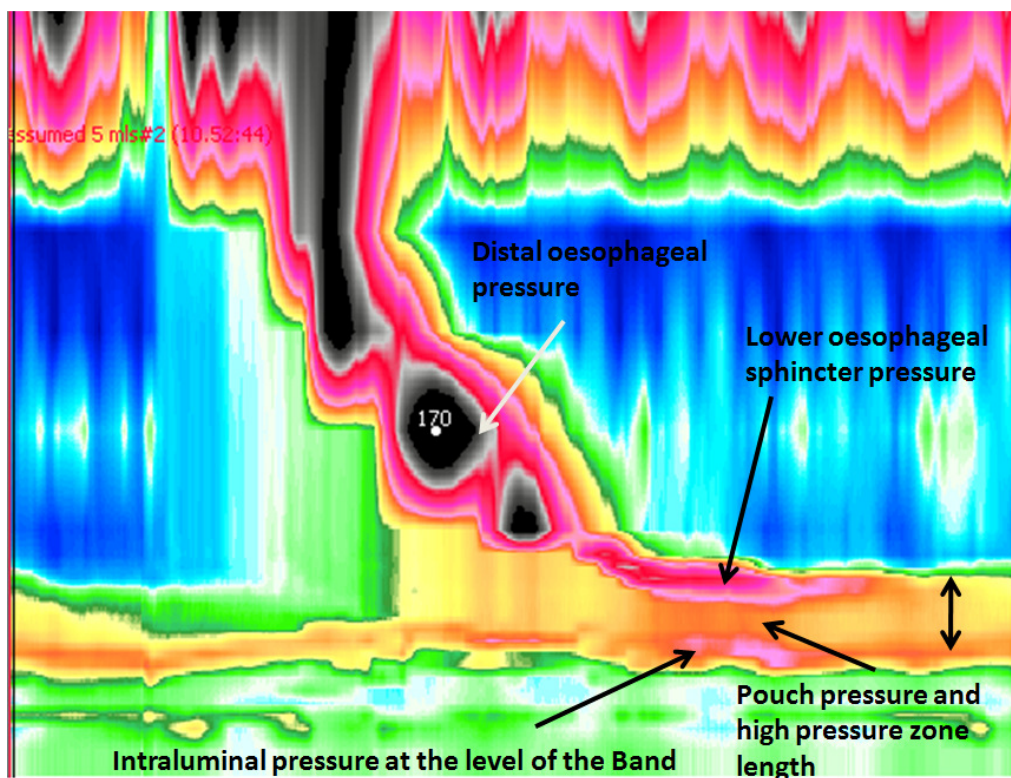
Figure 13.3 Legend: *Relaxation of the LOS is observed; however, the LAGB pressure signature remains intact. The oesophageal peristaltic wave progresses normally, followed by which a high pressure zone develops above the LAGB. This high pressure zone consists of three zones; the lower oesophageal contraction, the isobaric region above the LAGB representing the gastric pouch and the intraluminal pressure at the level of the LAGB. See figure 13.1 for colour plot scale.*

At optimal volume the mean length of the high pressure zone was 4.1±1.2 cm and in all patients it was less than 6 cm. In all patients this zone could be identified with the LOS being a minimum of 2 cm above the band. This compared to the high pressure zone in pre-operative patients, i.e. the zone of high pressure induced by contraction of the lower oesophagus of 2.9±0.7 cm. Altering the volume within the LAGB produced significant changes in the length of this zone. Reducing the volume by 20% resulted in a significant decrease in the length of the high pressure zone ($p=0.006$) to 4.2±1.0 cm. Similarly, emptying the LAGB of all fluid resulted in a significantly decreased ($p <0.001$) length of this zone to 3.3±0.9 cm. Increasing the volume by 20% significantly ($p=0.001$) increased the length of the high pressure zone to 6.1±1.1 cm.

The velocity of oesophageal peristalsis was found to be more rapid in the pre-operative patients (3.1±1.3 cm/sec) compared to patients with the optimal volume in the LAGB (1.8±0.8 cm/sec, $p=0.001$). Increasing the volume in the LAGB by 20% did not significantly affect the velocity of oesophageal peristalsis (1.9±0.9 cm/sec $p = 0.62$). When the volume in the LAGB was reduced by 20% (2.5±1.4 cm/sec, $p=$

0.06) or emptied of all fluid (2.6±1.7 cm/sec, *p=0.07*) the velocity was not

significantly changed.

Figure 13.4 summarises the data on altering the volume in the LAGB on the

pressure profile in the distal oesophagus and the region of the LAGB with different

volumes in the LAGB. Lower oesophageal pressure did not change with altering the

volume in the LAGB, or in comparison to preoperative patients. Increasing the

volume to 20% above optimal resulted in significantly increased distal oesophageal

pressure. The pouch pressure was not significantly changed by reducing the volume

by 20%, although emptying significantly reduced these pressures, and increasing

the volume by 20% significantly increased these pressures. The intraluminal

pressure at the level of the LAGB progressively and significantly increased as the

volume was increased from empty, 20% under optimal, optimal and 20% over the

optimal volume.

FIGURE 13.4: Effect of LAGB Volume on Oesophago-gastric Junction Pressure

Topography during Water Swallows
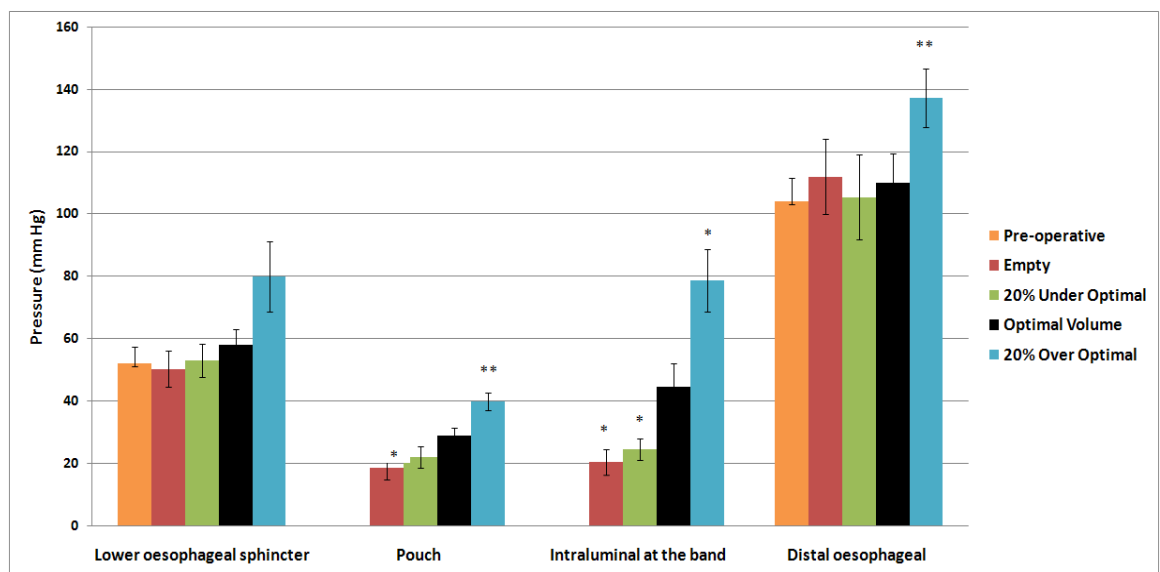
Figure 13.4 Legend: *For each separate anatomical structure in the region of the oesophago-gastric junction, pressure data during water swallows is displayed. Figure 13.3 illustrates the separation of these anatomical components during a liquid swallow. Data is displayed comparing the pressure recorded at each of the 4 locations stratified by LAGB volume. Data from pre-operative patients is shown as a baseline comparison. The pressures generated at the level of the lower oesophageal sphincter were not affected by the volume in the LAGB. The pouch pressure and intraluminal pressure at the level of the LAGB increased with addition of fluid to the band. Distal oesophageal pressure increased significantly when the LAGB was overfilled. Error Bars represent SEM. p values are in comparison to optimal LAGB volume. Significantly different values are represented by an * on the top of the column for p<0.05, or ** for p<0.005*

Oesophageal Motility

In the pre-operative patients there were two patients with oesophageal motility disorders. These were both mild oesophageal peristaltic dysfunction. In the post-operative patients with the optimal volume within the LAGB, 1 patient fitted the criteria for an oesophageal motility disorder, that of hypertensive peristalsis, although this was asymptomatic.

Figure 13.5 summarises the results of the assessment of oesophageal motility at different levels of restriction in comparison to the optimal volume. At optimal volume, 20% under and empty, the LAGB patients had similar oesophageal motility to the pre-operative patients. There was no significant difference in terms of the number of abnormal swallows or when this was analysed according to the subtypes

of abnormal swallows. The only significant difference was the finding that the proportion of repetitive contractions (40%) was increased when the LAGB was at optimal volume, in comparison to the pre-operative patients (16%, *p = 0.02*). Reducing the volume within the LAGB reduced the proportion of repetitive contractions although this did not reach statistical significance.

Overfilling the LAGB by 20% resulted in a disruption of oesophageal peristalsis. The proportion of normal swallows decreased to 50%. The majority of these were hypertensive contractions. The proportion of repetitive contractions also increased significantly to 58%, (*p =0.02*).

Transit in the Region of the LAGB

Oesophageal transit during liquid (barium) swallows in the LAGB patients was 21 seconds vs. 8 seconds in the control group (*p<0.001*). Transit of semi-solids was 50 seconds vs. 16 seconds (*p<0.001*). In only three of the LAGB patients was there retention of semi-solid or liquid in the oesophagus or gastric pouch above the LAGB for greater than 5 minutes. Compared to the control group, there was an increased duration of liquid and more prominently, solid swallows. Transit of solids (porridge) took significantly longer in the LAGB patients than did the transit of barium (*p<0.001*).

FIGURE 13.5: Effect of LAGB Volume on Oesophageal Motility
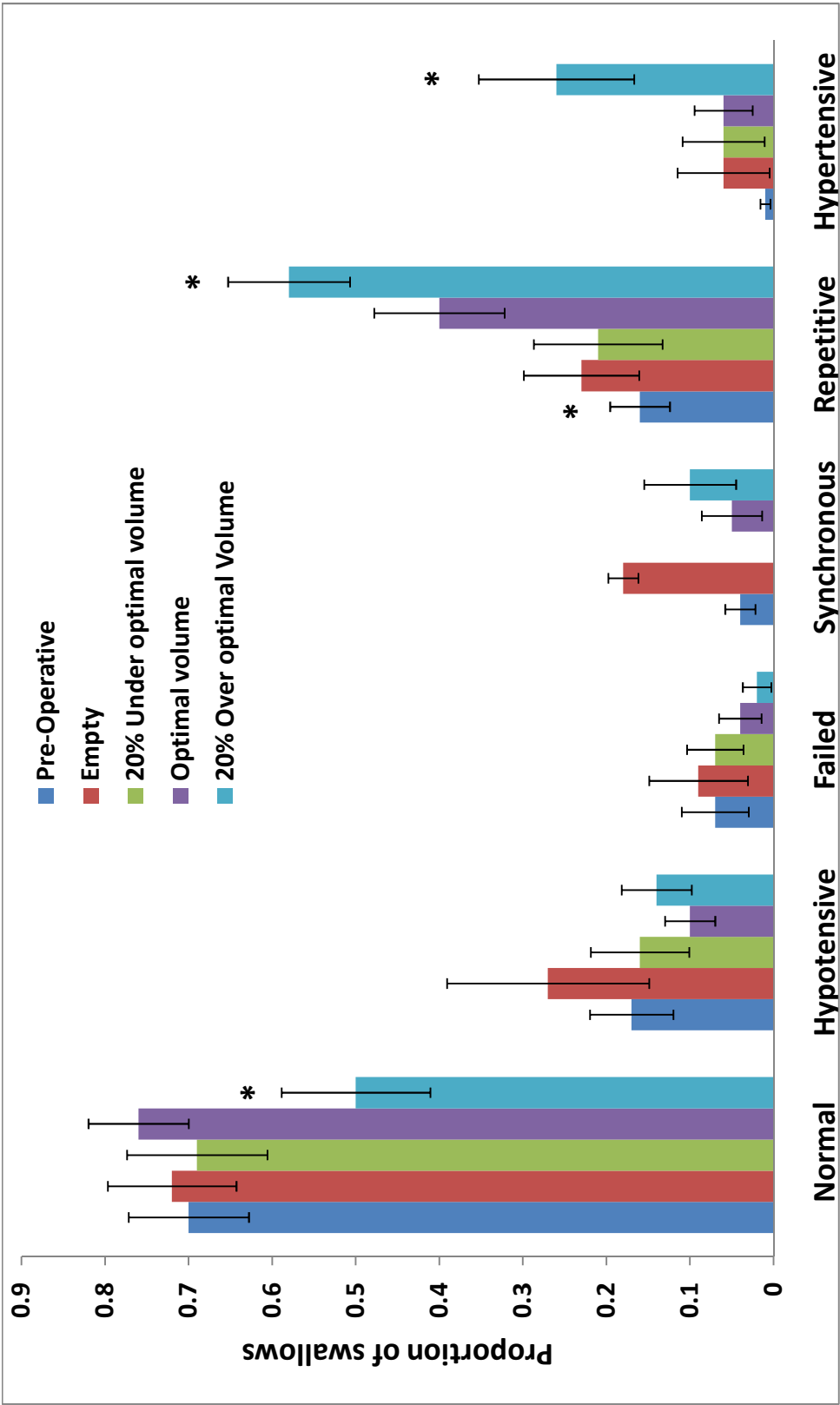
Figure 13.5 Legend: *The proportion of swallows classified in each category according to high resolution manometry criteria are shown stratified by LAGB volume. Data from pre-operative patients is shown as a baseline comparison. More abnormal swallows and hypertensive swallows were observed when the volume in the LAGB was increased by 20%. Otherwise no differences were observed between the preoperative patients and other LAGB volumes. Error bars represent SEM. p values are in comparison to optimal fill and are represented by an * on the top of the column, *p<0.05 **p<0.005*

During swallowing, the response to pressurisation of the pouch was flow across the LAGB and reflux into the oesophagus of any remaining bolus once the oesophageal contraction was completed. Reflux was followed by another primary or secondary oesophageal contraction that resulted in bolus being pushed back into the pouch above the band and further flow being generated. Semi-solids and liquids did not "sit" in the pouch above the LAGB.

Discussion

This study has used high resolution video manometry to describe the physiological profile of LAGBs in patients with a successful outcome. In these patients the presence of a LAGB has been shown to have consistent effects on the lower oesophageal sphincter, oesophageal contractility and the transit of liquids and solids. Altering the volume of fluid within the LAGB also had predictable effects on

the pressure profile of the distal oesophagus and the region of the oesophago-gastric junction at rest and during swallowing.

In this study comparisons were made between successful patients, primarily acting as their own controls, with adjustments made to the volume of fluid in the LAGB. We chose to perform measurements at their "optimal" volume and compare these results with those obtained when the volume was varied to empty, 20% under optimal volume, and 20% over the optimal volume. These volumes were chosen based on our clinical observation that a change in volume of 20% has a clinically significant effect on weight loss and sensations reported by patients.

The LOS was found to be significantly attenuated in LAGB patients in both tone and length, although relaxation was normal. This finding differs from previous reports of manometry in LAGB patients. Others have suggested that the LAGB has no effect on LOS tone, enhances LOS tone or that impaired LOS relaxation is observed [268, 438]. Our results are likely to be more accurate due to the high resolution video manometry technique used and our ability to clearly separate the LOS and LAGB pressure signals. The finding of a decreased LOS basal pressure is not surprising, as placing a high pressure obstruction immediately beneath this can be expected to result in a degree of dilatation and likely attenuation of the LOS. It is hypothesised that this attenuation of the basal LOS pressure occurs progressively over time. Animal studies on the effect of placement of non-adjustable gastric bands, whilst not necessarily precisely reproducing the physiology of the LAGB, have documented similar effects on the LOS to our findings [443].

At rest, the optimally adjusted LAGB produces a distinct intraluminal high pressure signature just beneath the oesophago-gastric junction, which is separate to the LOS. This is of significance when performing manometry on a LAGB patient. If the LAGB is not accounted for, particularly if a sleeve sensor or a pull through technique is used, the LAGB may be mistaken for the LOS. Reporting the LOS/Band complex pressure rather than the true LOS will produce an erroneously elevated value for the LOS, as well as inaccurate information on the relaxation and length of the LOS. These findings account for the variable results obtained by others when assessing LOS function and tone following LAGB.

The basal intraluminal pressure at the level of LAGB is likely to be an important measurement, as this is representative of the level of restriction produced by the LAGB. Without restriction patients do not lose weight, alternatively too much restriction results in adverse symptoms such as reflux. Sixteen of the 20 patients demonstrated a pressure between 10-30 mmHg at their optimal volume. It may be that this represents the level of restriction that promotes weight loss without causing adverse symptoms or resulting in complications [531]. Varying the volume in the LAGB by amounts known to produce clinically significant effects resulted in measurable changes in the intraluminal pressure at the level of the LAGB. Emptying the band resulted in a near absence of a measurable intraluminal pressure, which correlates with patients reporting an absence of restriction and increased hunger [8]. Increasing the volume in the LAGB by only 20% above the optimal level resulted in a threefold increase in the pressure and disrupted oesophageal function. Three patients had intra-luminal pressures at the level of the LAGB greater than 40 mmHg

and up to 70 mmHg at their optimal volume. Patients with a very "tight" LAGB, manifested by a high intraluminal pressure at the level of LAGB, may be at risk of developing the complication of symmetrical pouch dilatation [531]. It is assumed that the stretching of the stomach wall above the LAGB is a result of chronic, excessive, pressurisation of this region. This is likely to be due to a combination of poor eating behaviour and an excessively tight LAGB [531].

During swallowing, an isobaric pressure zone consistently developed between the LAGB and the advancing pressure wave in the oesophagus. This was the pressure within the gastric pouch above the LAGB. Once the peristaltic wave had reached the level of the lower oesophageal sphincter the high pressure zone was measured. A measurement of the high pressure zone (HPZ) was defined (Figure 13.3). It is important to note that this vertical length included: the lower oesophageal contraction, the isobaric zone representing the gastric pouch and the intraluminal pressure at the level of the LAGB. The length of this zone remained less than 6 cm in all patients, with a median length of 4 cm and a minimum of 2 cm. The peak pressure generated in the pouch was found to progressively increase with the addition of fluid, as did the intraluminal pressure at the level of the LAGB. The peak distal oesophageal pressure increased when the band was overfilled, most likely as a result of obstruction. This adds weight to the hypothesis that over-pressurisation of this region by over-tightening the LAGB may contribute to complications following LAGB placement [531]. Our data illustrates the mechanisms by which this increased pressurisation occurs.

Oesophageal motility was found to be well preserved in LAGB patients with a successful outcome. Only one LAGB patient had a diagnosis of an oesophageal motility disorder. In the control group, two patients were diagnosed with an oesophageal motility disorder. Varying the volume, between optimal, 20% under and empty produced few changes in oesophageal motility. A detailed analysis of the effect of altering the volume in the LAGB on oesophageal motility identified two key effects. Firstly repetitive oesophageal contractions were observed in 40% of swallows in LAGB patients with the optimal volume in the LAGB, compared to only 16% of swallows in pre-operative patients. Repetitive contractions appear to be of importance in the functioning of the LAGB as they appear to represent the response of the oesophagus to a hold up in bolus transport across the LAGB; requiring a repeat oesophageal contraction to generate flow across the LAGB. Secondly increasing the volume in the LAGB to 20% over optimal induced a significantly increased proportion of abnormal swallows (50%): these were primarily hypertensive. Over-tightening the LAGB also increased the proportion of repetitive contractions, as the oesophagus tried to propel the liquid across the increased resistance of the LAGB.

Transit during liquid and semi-solid swallows was relatively rapid in LAGB patients. During each swallow there was a hold up of the liquid or semisolid bolus in the gastric pouch for a matter of additional seconds. This was more apparent during the semi-solid swallows than the liquid. If the bolus did not completely pass through the LAGB prior to relaxation of the lower oesophageal contraction, it was observed to actively reflux back into the oesophagus and a repeat oesophageal contraction

was observed, re-pressurising the area above the LAGB and generating further flow across the LAGB. These findings are suggestive of a consistent pattern of oesophageal and pouch emptying in successful patients.

This study provides a reference point for clinicians investigating symptomatic LAGB patients using high resolution manometry, with or without concurrent fluoroscopy. The importance of differentiating the LOS from the band is emphasised. There was a consistent basal intraluminal pressure at the level of the LAGB representing the restriction produced by the band. An enlarged high pressure zone (greater than 6 centimetres) or disruptions of oesophageal peristalsis were not seen in a cohort of 20 successful LAGB patients. However, increasing the volume within the LAGB did significantly affect oesophageal motility. In the majority of patients transit of the semi-solid bolus was delayed only temporarily by the LAGB. Repetitive oesophageal contractions appear to be a normal finding in LAGB patients with the optimal volume within the LAGB. These parameters can be assessed using high resolution video manometry, however, they require an understanding of the expected anatomical and manometric profile in LAGB patients.

Our findings lead us to hypothesise that in successful LAGB patients, the food bolus impacts the gastric pouch due to ordered oesophageal peristalsis, after which there is a slight but noticeable delay, followed by pouch emptying. These events are associated with the generation of signals that mediate weight loss. Variations from this physiology may be an explanation for adverse symptoms or poor weight loss.

Declaration for Thesis Chapter 14

This Chapter represents a manuscript published in *Obesity Surgery (Obes Surg. 2009 Nov;19(11):1508-14).*

Declaration by candidate

In the case of Chapter 14 the nature and extent of my contribution to the work was the following:

Nature of contribution	Extent of contribution (%)
Overall responsibility for all aspects of the study, conception, planning, patient recruitment, conducting experiments and recording data. Data analysis and interpretation. Statistical analysis. Crafting and revising manuscript, submission to journal.	>90%

The following co-authors contributed to the work:

Name	Nature of contribution
Wendy A Brown	Designing study, and recruiting patients, manuscript review
Cheryl Laurie	Recruiting and conducting studies
Melissa Richards	Conducting studies, data analysis
Geoff Hebbard	Experiment design, data acquisition and analysis, review of manuscript
Paul O'Brien	Experiment design, data acquisition and analysis, review of manuscript

Candidate's Signature		Date

Declaration by co-authors

The undersigned hereby certify that:

(1) the above declaration correctly reflects the nature and extent of the candidate's contribution to this work, and the nature of the contribution of each of the co-authors.
(2) they meet the criteria for authorship in that they have participated in the conception, execution, or interpretation, of at least that part of the publication in their field of expertise;
(3) they take public responsibility for their part of the publication, except for the responsible author who accepts overall responsibility for the publication;
(4) there are no other authors of the publication according to these criteria;
(5) potential conflicts of interest have been disclosed to (a) granting bodies, (b) the editor or publisher of journals or other publications, and (c) the head of the responsible academic unit; and
(6) the original data are stored at the following location(s) and will be held for at least five years from the date indicated below:

Location(s) | Centre for Obesity Research and Education, Monash University, Alfred Hospital

[Please note that the location(s) must be institutional in nature, and should be indicated here as a department, centre or institute, with specific campus identification where relevant.]

		Date
Wendy A Brown		27/10/04
Cheryl Laurie		4-11.09
Melissa Richards		02.11.09.
Geoff Hebbard		2/11/09
Paul E O'Brien		27.10.09

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CHAPTER 14: *Effects of Gastric Band Adjustments on Intraluminal Pressure*

Abstract

Background: Understanding of the effects of adjustments to laparoscopic adjustable gastric band (LAGB) volume is limited. Changes in intraluminal pressure may be important and explain patients reporting a tighter LAGB after saline is removed and an identical volume replaced.

Methods: Using high resolution manometry, changes in the basal intraluminal pressure at the level of the LAGB, in response to sequential, small alterations in LAGB volume were recorded. All fluid was removed from the LAGB and replaced; pressures and motility were reassessed.

Results: Sixteen patients (4 male, mean age 45.4±13.2 years) participated. A linear increase (r^2 = 0.87±0.12) in intraluminal pressure was observed after a threshold volume was reached. The threshold volume varied considerably (1.0 to 5.8 ml). The gradient of the linear increase was 21.2±8.7 mmHg/ml. The mean basal intraluminal pressure at the level of the LAGB was initially 19.1±8.9 mmHg and increased to 37.0±20.4 mmHg (*p=0.001*), after removing and replacing the same volume of saline. There was an increase in distal oesophageal peristaltic pressure (123.5±34.7 mmHg vs. 157.4±52.6 mmHg, *p=0.003*) and a decrease in the proportion of normal swallows (0.85±0.22 vs. 0.53±0.47, *p=0.02*). Nine patients also developed adverse symptoms.

Conclusions: Intraluminal pressure at the level of the LAGB is an objective measure of the restriction produced by LAGBs. The addition of fluid to the LAGB results in a linear increase in intraluminal pressure, once a threshold volume is reached. The removal and replacement of the same volume of saline from the LAGB may temporarily increase intraluminal pressure.

Introduction

Laparoscopic adjustable gastric banding (LAGB) is a highly effective treatment for obesity [253, 264]. Its advantages of safety, ease of insertion, reversibility and adjustability have lead to increasing popularity [2, 283, 532]. Adjustments to LAGB volume are a major feature and integral to the follow up process. Despite widespread use, the physiological effects of adjustments are not well understood. Changes in intraluminal pressure, both at the level of the LAGB and above, may be affected significantly by adjustments. If these were better understood improvements to post-operative care could be made and insights potentially gained into preventing complications.

There is much variation, between patients, in the total volume of saline required within the LAGB, yet similar clinical effects and near identical outcomes can be observed. Anecdotally, patients often report the LAGB being tight for the initial 24 to 48 hours following an adjustment, however, this effect has not been defined physiologically.

High resolution manometry utilises multiple, closely spaced pressure sensors [522]. This allows pressurisations around the oesophago-gastric (OGJ) produced by the crural diaphragm, lower oesophageal sphincter (LOS), LAGB and proximal stomach to be separated [533]. This technique has clarified the physiological effect the LAGB has on oesophageal motility and pressure topography [533]. It has shown that successful patients have a similar intraluminal pressure at the level of the LAGB, regardless of band type or volume [533].

Our goal was to establish a better understanding of changes in intraluminal pressure at the level of the LAGB when adjustments are made to LAGB volume. We hypothesised that the intraluminal pressure at the level of the LAGB was the critical variable, mediating effects on oesophageal motility, pressure topography and symptoms. We also aimed to determine why sometimes patients report different sensations and a tighter LAGB when saline is removed from the LAGB and an identical volume replaced.

Methods

Participants

LAGB patients, whose surgery was considered to be successful, were invited to participate. Criteria for inclusion in the study were: loss of >50% of excess weight (unless within 12 months of surgery), normal contrast swallow within 12 months of enrolment in the study (performed as a part of routine care), absence of adverse symptoms such as reflux or vomiting, confirmation that the volume of fluid within the LAGB was optimal by: absence of significant symptoms of reflux and maintenance of a stable, optimal volume of saline within the LAGB with no requirement for change in volume in the preceding 2 months. Exclusion criteria included: current pregnancy, previous gastric surgery prior to LAGB placement, age under 18 years or over 70 years

The Melbourne Health and Monash University Human ethics committees approved this research and all participants gave informed consent.

All patients underwent a standardised high resolution manometry protocol, described in detail elsewhere [533]. Briefly, high resolution manometry with a custom designed 21 channel silicone rubber catheter (Dentsleeve, Ontario, Canada) and a water perfused manometry system was performed. Manometry data was recorded and analysed using TRACE! 1.2 (written by G Hebbard using LabVIEW, National Instruments, Austin, Texas).

Mapping of Changes in Intraluminal Pressure at the Level of the LAGB

After completion of the standard manometry study, the LAGB port was accessed using a 23 gauge Huber tipped needle and a 3 way stopcock, with a saline filled syringe on the other arm. Care was taken not to remove fluid from the LAGB when accessing the port. Saline was incrementally added in a bolus fashion (0.2 ml for APS^{TM}, APL^{TM} and VG^{TM} bands and 0.1 ml for 10cm bands) to the LAGB. This continued until a basal intraluminal pressure of 80 mmHg was observed at the level of the LAGB or the patient developed discomfort. Saline was then removed in the same increments, until the intraluminal pressure at the level of the LAGB was zero. Following each change in LAGB volume there was a minimum 30 second accommodation period. Once the intraluminal pressure had stabilised, it was measured using a virtual sleeve, selectively placed over the region of interest. The median, peak end expiratory pressure over 5 respiratory cycles was recorded. As this was a basal measurement, it was only recorded if no pharyngeal or oesophageal body swallow had been observed for a minimum of 15 seconds.

Following the detailed measurements of intraluminal pressure, all saline was removed from the LAGB for a period of 5 minutes. The needle was maintained within the access port. The system was not disconnected, ensuring no air was inadvertently added. The volume of saline within the LAGB was then restored to its original, starting volume and the needle removed. After a 5 minute accommodation period, the basal intraluminal pressure at the level of the LAGB was measured. The manometry protocol was repeated with 5 ml right lateral water swallows.

Oesophageal motility was assessed using standardised criteria for the assessment of oesophageal motility using high resolution manometry [501]. Individual swallows were categorised as normal or abnormal. Abnormal swallows were further defined as: hypotensive, failed, hypertensive or synchronous. An assessment was made of the presence of repetitive oesophageal contractions following each swallow. Any pressurisation in the oesophageal body of 30 mmHg or greater, initiated within ten seconds of the oesophageal contraction wave reaching the level of the lower oesophageal sphincter, was classified as repetitive. This included situations when the patient swallowed again. This measurement was designed to identify the requirement for repeat oesophageal contractions or pressurisations to propel a liquid bolus through the resistance produced by the LAGB.

Each swallow categorised as normal or hypertensive was subjected to detailed analysis of pressure topography. For these swallows, data were collected on the peak pressure generated at the level of each of: the lower oesophageal sphincter, within the distal oesophagus (smooth muscle oesophagus), isobaric pouch high pressure zone (HPZ) above the LAGB and at the level of the LAGB. Peristaltic velocity was recorded as the movement of the 30 mmHg pressure wavefront over the lower 4 cm of oesophagus; this was measured between catheter side holes. The length of the high pressure zone that developed above the LAGB was measured. This was measured at end expiration once the peristaltic wave had stopped travelling distally. The technique for this measurement has been previously described [533].

During studies, adverse symptoms or discomfort experienced by patients was recorded. These were correlated with individual swallows. However, for the purposes of analysis, adverse symptoms were recorded as a binary outcome.

Comparisons of oesophageal motility, basal intraluminal pressure, pressure topography and symptoms were made between swallows performed prior to accessing the LAGB port and with data obtained after removing and replacing the same volume of saline.

The same sequence for performing manometry was used in each patient.

Statistical analysis

All statistical analysis was performed using SPSS version 11 (SPSS, Inc, Chicago, Illinois). Correlations were performed using Pearson's correlation. Regression

analysis was linear, and the r^2 change reported. For analysis of proportions, Chi square tests were used. For comparison of means, paired t tests were used for normally distributed continuous data. Data are presented as mean and standard deviation. A two sided p value of 0.05 was considered statistically significant.

Results

Sixteen patients participated in the study. Patient details are shown in Table 14.1. All bands were LAP-BANDS[TM] (Allergan, CA), although different models were used.

Changes in intraluminal pressure at the level of the LAGB

The intraluminal pressure at the level of the LAGB was dependent on LAGB volume. Figure 14.1 illustrates changes in intraluminal pressure with band volume for 3 patients and is representative of the consistent pattern observed. With the band empty, as the intraband volume was increased there was no initial change in intraluminal pressure, until a threshold volume was reached. Once this threshold volume was reached there was then a linear increase in intraluminal pressure.

FIGURE 14.1: Examples of Changes in Intraluminal Pressure with LAGB Volume in 3 Patients
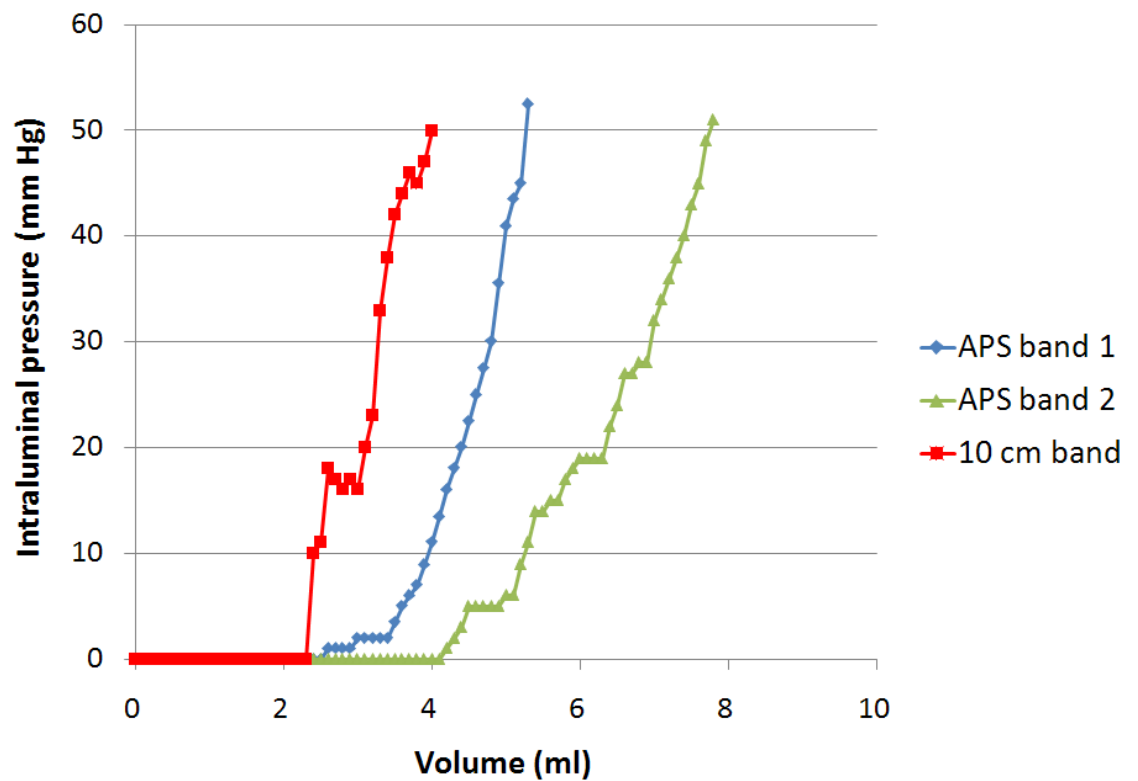
Figure 14.1 Legend: *Intraluminal pressure at the level of the LAGB plotted against intra-band volume in three patients, 2 with APS^{TM} bands and 1 with a 10 cm band. In each case there is a linear increase in pressure once a threshold volume is reached. There is a different threshold volume for each patient, although the gradient of the increase is not as variable. A similar pattern was seen for each patient in this study.*

TABLE 14.1: Patient Details (n=16)

Age (years)	45.4 ±13.2
Start weight (kg)	114.9±16.19
Males/Females	4/12
10 cm bands	4
VG^{TM} bands	2
APS^{TM} bands	9
APL^{TM} bands	1
% excess weight loss	66.1±17.2
Current weight (kg)	84.1±13.4
Weight loss (kg)	30.9±11.3
Duration from surgery (days)	722±703
Start weight (kg)	118.4±22.3
Start BMI (kg/m^2)	42.2±5.6
Current BMI(kg/m^2)	30.4±3.8

†Data are mean and standard deviation

The mean correlation coefficient was 0.89±0.17 during the linear increase in intraluminal pressure beyond the threshold volume. This was statistically significant in each case *(p<0.05)*. The linear nature of this relationship was confirmed with regression analysis (mean r^2=0.87±0.12). Table 14.2 summarises these data.

TABLE 14.2: Threshold Volume and Gradient of the Linear Section of Pressure Volume Curve for Individual Patients

Patient Number	Type of LAGB	Optimal volume (ml)	Threshold volume	Gradient mmHg / ml†	Regression coefficient (r^2)	*p* value
1	APS	4.5	4	29.3	0.97	<0.005
2	APS	5	3.6	16.9	0.68	0.001
3	10cm	3.4	2.4	25	0.92	<0.005
4	10 cm	2.8	1.5	29.3	0.78	<0.005
5	APS	6	5.8	21	0.92	0.002
6	APL	6	4	24.1	0.89	<0.005
7	APS	4.5	2.5	13	0.62	0.04
8	APS	6.2	5.4	15.4	0.92	<0.005
9	APS	5	2	11	0.93	0.04
10	VG	9	6	24	0.95	0.004
11	APS	5.3	3.5	25	0.80	0.04
12	VG	6.2	2.5	7.3	0.97	0.001
13	10cm	2.5	1.8	43	0.85	0.001
14	APS	4.0	2.7	15.58	0.99	<0.005
15	10 cm	2.3	1.0	16	0.69	0.006
16	APS	3.5	4.5	23.4	0.98	0.001

† Gradient of the curve for the range of intraluminal pressures of 10 – 50 mmHg, expressed in terms of mmHg/ ml

The gradient of the linear increase in intraluminal pressure, beyond the threshold volume, was a mean of 21.2±8.7 mmHg. This gradient was not significantly different between patients regardless of the type of band. The gradient for those with APS[TM] bands was 19.0 ±6.1 mmHg/ml (range 11.3-28.4 mmHg/ml) compared to a mean of 28.3 ±11.2 mmHg/ml for those with 10 cm bands (range 16.6 to 43.8 mmHg/ml) (*p=0.20*).   Two VG[TM] bands were tested and the gradients were 7 and 24 mmHg/ml respectively. The gradient for the single APL[TM] band tested was 24 mmHg/ml.

The optimal LAGB volume (the volume within the LAGB when they presented for the study) was significantly higher in the APS^{TM} than the 10 cm bands (4.9±0.8 ml vs. 2.8±0.5 ml, *p=0.001*). Similarly, the threshold volume was higher in the APS^{TM} compared to the 10 cm bands (3.8±1.3 ml vs. 1.7±0.6 ml, *p=0.002*).

Effect of Removing and Replacing Saline into the LAGB: Changes in Pressure

Topography

The mean intraluminal pressure at the level of the LAGB increased from 19.1±8.9 mmHg to 37.0±20.4 mmHg (*p=0.001*). Eleven of the 16 patients (69%) demonstrated an increase in the basal intraluminal pressure at the level of the LAGB of greater than 10 mmHg.

Table 14.3 summarises pressure topography and oesophageal motility data at baseline and following removal and replacement of saline. During 5 ml right lateral water swallows, the pressure increased significantly in the distal oesophagus, although not at the level of the lower oesophageal sphincter. The pouch pressure and the intraluminal pressure at the level of the LAGB also increased significantly. Peristaltic velocity did not increase significantly, nor did the length of the high pressure zone. Figure 14.2 illustrates this effect, with increased pressurisations and high pressure zone length evolving in response to the increase in basal intraluminal pressure at the level of the LAGB. In patients where there was no significant increase in the basal intraluminal pressure at the level of the LAGB, there was no change in pressure topography.

TABLE 14.3: Oesophageal Motility and Pressure Topography During 5 ml Water Swallows: Initially and After Removal and Reinsertion of an Identical Volume of Saline

	Initially	After replacement of saline	*p* value
Distal oesophageal pressure (mmHg)	123.5±34.7	157.4±52.6	0.003
Lower oesophageal sphincter pressure (mmHg)	58.7±20.7	80.5±46.1	0.08
Intrabolus pressure (mmHg)	27.1±8.1	41.6±8.8	<0.005
Intraluminal pressure at the level of band (mmHg)	33.1±11.1	58.6±18.9	0.001
Length of high pressure zone (cm)	4.6±0.8	5.1±1.0	0.20
Peristaltic velocity (cm/sec)	2.1±0.9	1.8±0.6	0.31
Proportion of normal swallows	0.85±0.22	0.53±0.47	0.02
Proportion of hypotensive swallows	0.07±0.16	0	0.09
Proportion of failed swallows	0.03±0.07	0	0.12
Proportion of repetitive swallows	0.28±0.31	0.38±0.38	0.46
Proportion of hypertensive swallows	0.05±0.17	0.33±0.44	0.01
Adverse symptoms during water swallows (number)	1	9	0.003

Data are mean and standard deviation

FIGURE 14.2: 5 ml Right Lateral Water Swallows in a LAGB Patient, at Baseline and After Removing and Replacing the Same Volume of Saline
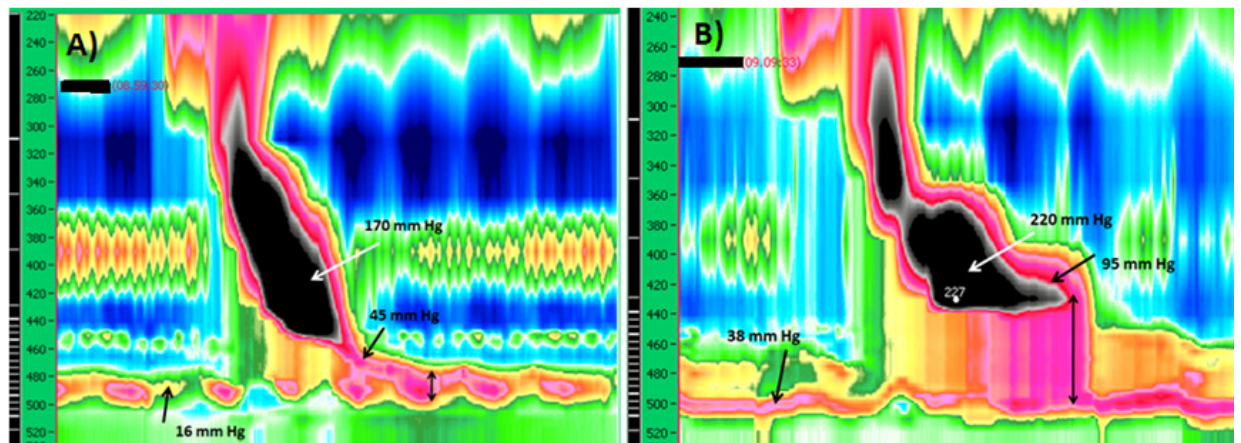
Figure 14.2 Legend: *5 ml right lateral water swallows, 10 minutes apart, from the same patient, with an identical volume within the LAGB. Panel A is an initial water swallow, panel B is an identical water swallow after removing and then replacing the same volume of fluid into the LAGB. In panel A the basal intraluminal pressure at the level of the LAGB is 16 mmHg (black arrow). A regulated peristaltic contraction, with moderate pressurisation in the high pressure zone above the LAGB is observed. In panel B, after removal and replacement of the same volume of saline, there is an increase in the basal intraluminal pressure at the level of the LAGB to 38 mmHg (black arrow). This induces a significant elevation of the peristaltic amplitude, from 170 to 220 mmHg, with a more vigorous, sustained contraction. The length of the high pressure zone has increased from 3 cm to 7.5 cm (double headed arrow). The patient also, not surprisingly, developed discomfort.*

Oesophageal Motility

Oesophageal motility was notably affected (Table 14.3) with a significant decrease in the proportion of normal swallows, accounted for by a significant increase in the proportion of hypertensive swallows. No other significant change in oesophageal motility was observed. Only patients who had an increase in the basal intraluminal pressure at the level of the LAGB, on replacing the saline, were found to have changes in oesophageal motility.

Adverse Symptoms

One patient complained of dysphagia during the initial manometry study. Following removal and replacement of saline 9 patients developed symptoms of either dysphagia, retrosternal or epigastric comfort or excessive fullness. In each of these patients an increase in the basal intraluminal pressure at the level of the LAGB of greater than 10 mmHg was observed. There were associated increases in distal oesophageal pressures in these patients.

Discussion

We have illustrated the importance of the basal intraluminal pressure at the level of the LAGB to the adjustment process. This pressure varied with LAGB volume. The relationship was linear, once a threshold volume had been instilled into the LAGB. The threshold volume varied between patients, the gradient of the increase in intraluminal pressure beyond this volume, however, was more consistent.

When saline was removed from the LAGB and an identical volume replaced, a higher intraluminal pressure at the level of the LAGB was observed in more than

half the patients. As a result of this increased pressure, changes in oesophageal motility and pressure topography were observed. These changes correlated with adverse symptoms typically associated with an overly tight LAGB.

The basal intraluminal pressure at the level of the LAGB has been shown to be consistent between successful patients [533]. This is despite patients having different types of LAGBs with varying volumes of saline within them. This pressure represents the degree of restriction produced by the LAGB. Oesophageal peristalsis must overcome this to generate flow across the LAGB.

For an individual patient, there is a narrow range of intraband volumes which produce a basal intraluminal pressure of 15-35 mmHg, usually of the order of 1 ml. It is this section of the pressure volume curve that is critical. It represents the relatively narrow range of volumes able to induce satiety and weight loss, without causing obstructive symptoms. It demonstrates how over or under adjusting by 0.5ml or less, can cause obstructive symptoms or the loss of restriction.

The major difference with the larger capacity LAGBs is the higher threshold volume. Only one APL^{TM}, the largest capacity LAP-BAND^{TM} available, was included. This band also demonstrated a rapid increase in intraluminal pressure (24 mmHg/ml), once the threshold volume had been reached. These findings suggest that even with the larger capacity LAGBs, small volume adjustments should be used to optimise restriction without causing obstruction.

The yellow, green and red zones are clinical states which partially overlap and can be associated with ranges of intraluminal pressures at the level of the LAGB. A

schema of this interaction, using data from the APS[TM] bands, is represented in

Figure 14.3. When in the yellow zone, patients are able to eat freely. There is no

delay in the transit of food through the LAGB into the distal stomach, consequently

weight loss is unsatisfactory. This represents, in most patients, an intraluminal

pressure at the level of the LAGB of less than 15 mmHg.   When in the green zone,

the increased resistance produced by the LAGB slows eating behaviour and is

associated with prolonged satiety; there is usually good weight loss. The green zone

represents an intraluminal pressure of 15-35 mmHg. The red zone appears to

transition at around 35 mmHg. The obstruction produced results in dysphagia and

reflux. Often, solid food is simply unable to transit through the LAGB. Maladaptive

eating may then supervene, compromising weight loss. We believe that an

excessively tight LAGB, in combination with poor eating behaviour, including

frequent regurgitation, may be significant factors in the development of

symmetrical pouch dilatation [310].

Previous work has shown that a gradient across the OGJ of at least 30 mmHg is

optimal, in order to clear a liquid bolus into the stomach, in patients without a

LAGB [496]. This is the likely reason that few LAGB patients exceed a basal

intraluminal pressure of 35 mmHg – it is simply beyond the capacity of the

oesophagus to transit solid food across the LAGB

FIGURE 14.3: Schematic Illustration of the Effect of LAGB Volume on Intraluminal Pressure and Correlation with Different Clinical States: Pooled Data from 9 patients With APS™ Bands
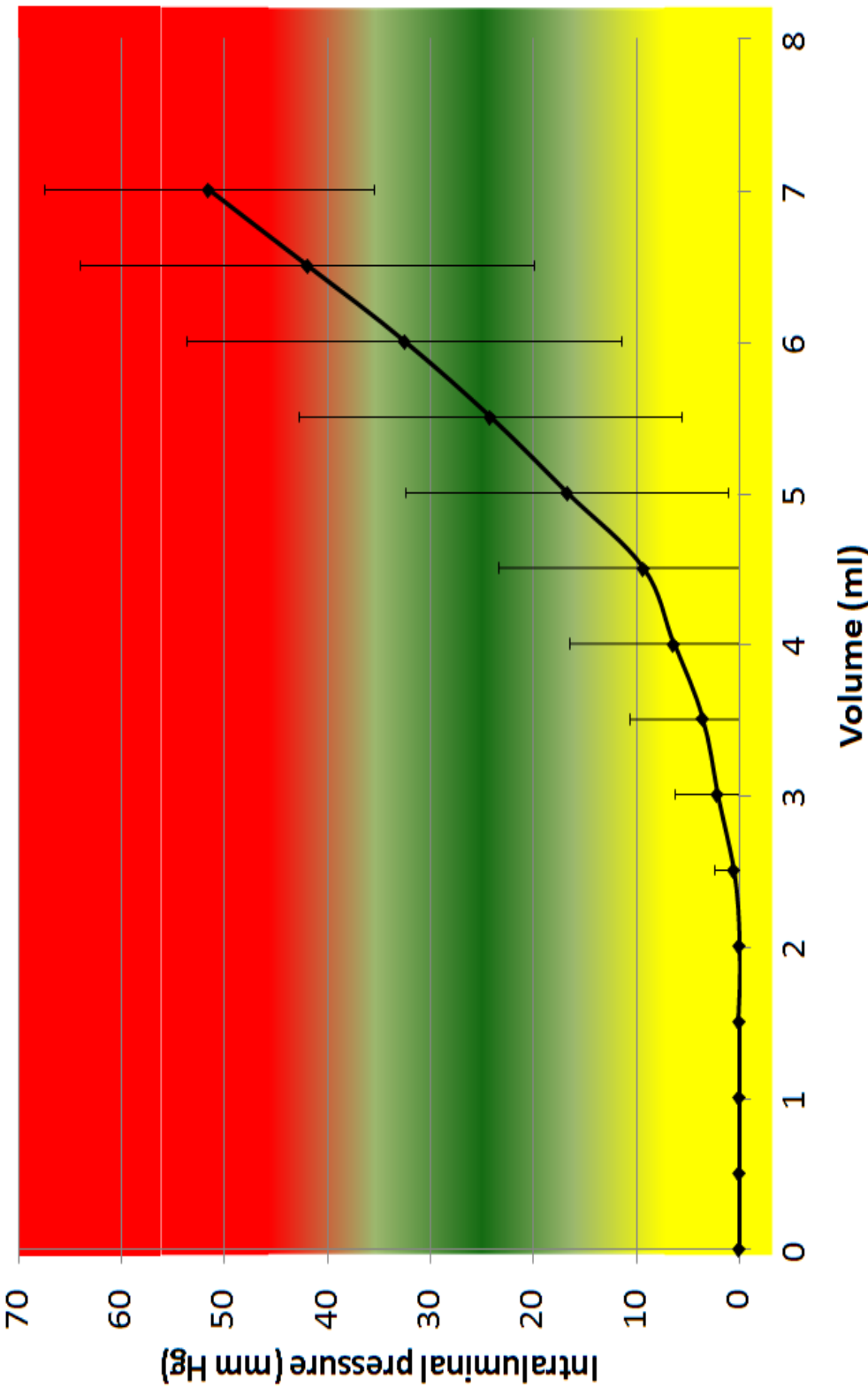
Figure 14.3 Legend: *Schematic illustration of changes in intraluminal pressure (mean and standard deviation) with volume, for the nine APS^{TM} bands tested, along with a schema representing different clinical states. The threshold volume, at which an increase in intraluminal pressure is first observed, varies considerably between patients. The gradient of the linear section of the curve, however, can be expected to be relatively consistent. These findings can be correlated with different clinical states. The yellow zone may be representative of a large range of volumes. The green zone is represented by a narrow range of volume, around 1 ml in most patients, before there is a transition into the red zone, where obstructive symptoms supervene. See text for discussion of these different clinical states.*

The physiological effect of removing saline from the LAGB and then replacing it has been puzzling. Some longstanding patients request removal and replacement of fluid, rather than have additional fluid added to the LAGB. We have shown that this can cause a dramatic increase in intraluminal pressure at the level of the LAGB, mimicking the addition of saline to the LAGB. The rise in pressure at this level has predictable effects on oesophageal motility, with hypertensive peristalsis and increased pressures observed in the distal oesophagus. Adverse symptoms may also occur. These changes are all a response to the increased resistance at the level of the LAGB, measured as an intraluminal pressure.

A possible explanation for this effect is that when fluid is replaced, the LAGB recompresses the tissues in a different configuration, resulting in an increased

intraluminal pressure at the level of the LAGB. However, over time, the tissue likely mould better into the shape of the LAGB, reducing the intraluminal pressure back to a stable level. This is supported by our observation that performing small adjustments, without removing all the saline, did not cause unexpected changes in the intraluminal pressure. It was an effect only observed when the LAGB was emptied and then refilled.

Conclusions

This study has added to the understanding of the physiology of LAGB adjustments. The intraluminal pressure at the level of the LAGB affects the pressure generated within the oesophagus and stomach above the LAGB, as well as oesophageal motility. Whilst intraluminal pressure is governed by LAGB volume, the effect of changing this volume varies considerably between patients. Removing and replacing the entire volume of saline during an adjustment may result in a transient elevation in intraluminal pressure, accounting for the discomfort experienced by some patients. This may be obviated by performing fine adjustments only. Future efforts need to further evaluate the physiology associated with LAGB adjustments, as well as translating this knowledge into patient management, determining if there is an impact on satiety and weight loss.

Declaration for Thesis Chapter 15

This chapter represents a manuscript published in *Obesity Surgery*, 2009 (*Obes Surg. 2010 Jan;20(1):19-29*).

Declaration by candidate

In the case of Chapter 15, the nature and extent of my contribution to the work was the following:

Nature of contribution	Extent of contribution (%)
Overall responsibility for all aspects of the study, conception, planning, patient recruitment, conducting experiments and recording data. Data analysis and interpretation. Statistical analysis. Crafting and revising manuscript, submission to journal.	>90%

The following co-authors contributed to the work:

Name	Nature of contribution
Wendy A Brown	Designing study, and recruiting patients, manuscript review
Cheryl Laurie	Recruiting and conducting studies
Anna Korin	Patient recruitment, data analysis, intellectual contribution
Kenneth Yap	Intellectual contribution, data analysis and drafting of manuscript
Melissa Richards	Conducting studies, data analysis
John Owens	Intellectual contribution, radiographic expertise, assistance with development of the stress barium
Gary Crosthwaite	Patient recruitment, data analysis, revision of manuscript
Geoff Hebbard	Experiment design, data acquisition and analysis, review of manuscript
Paul O'Brien	Experiment design, data acquisition and analysis, review of manuscript

Candidate's Signature		Date

Declaration by co-authors

The undersigned hereby certify that:

(1) the above declaration correctly reflects the nature and extent of the candidate's contribution to this work, and the nature of the contribution of each of the co-authors.
(2) they meet the criteria for authorship in that they have participated in the conception, execution, or interpretation, of at least that part of the publication in their field of expertise;
(3) they take public responsibility for their part of the publication, except for the responsible author who accepts overall responsibility for the publication;
(4) there are no other authors of the publication according to these criteria;

(5) potential conflicts of interest have been disclosed to (a) granting bodies, (b) the editor or publisher of journals or other publications, and (c) the head of the responsible academic unit; and

(6) the original data are stored at the following location(s) and will be held for at least five years from the date indicated below:

Location(s)	Centre for Obesity Research and Education, Monash University, Alfred Hospital

[Please note that the location(s) must be institutional in nature, and should be indicated here as a department, centre or institute, with specific campus identification where relevant.]

		Date
Wendy A Brown		27/10/09
Cheryl Laurie		4/11/09
Anna Korin		5/11/9
Kenneth Yap		2/11/09
Melissa Richards		02.11.09
John Owens		30/10/09.
Gary Crosthwaite		27/10/09
Geoff Hebbard		2/11/09
Paul E O'Brien		27.10.09

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CHAPTER 15: *Pathophysiology of Laparoscopic Adjustable Gastric Bands: Analysis and Classification Using High Resolution Video Manometry and a Stress Barium Protocol*

Abstract

Background: Symmetrical pouch dilatation has become the most common problem following laparoscopic adjustable gastric banding (LAGB). Although, in a significant number of symptomatic patients, no explanation for the underlying problem is identified with a contrast swallow. There is a need for a better understanding of the pathophysiology of LAGBs and more sensitive diagnostic tests.

Methods: LAGB patients with adverse symptoms or poor weight loss (symptomatic patients), in whom a contrast swallow had not shown an abnormality, underwent high resolution video manometry. This incorporated a semi-solid, stress barium, swallow protocol. Outcomes were categorised based on anatomical appearance, transit through the LAGB and oesophageal motility. Cohorts of successful (>50% excess weight loss with no adverse symptoms) and pre-operative patients were used as controls.

Results: 123 symptomatic patients participated along with 30 successful and 56 preoperative patients. Five pathophysiological patterns were defined: transhiatal enlargement (n=40), sub-diaphragmatic enlargement (n=39), no abnormality (n=30), aperistaltic oesophagus (n=7) and intermittent gastric prolapse (n=3). Oesophageal motility disorders were more common in symptomatic and pre-operative patients than in successful patients (*p=0.01*). Differences between successful and symptomatic patients were identified in terms of the length of the

high pressure zone above the LAGB ($p<0.005$), peristaltic velocity ($p<0.005$), frequency of previous surgery ($p=0.01$) and lower oesophageal sphincter tone ($p=0.05$).

Conclusions: Video manometry identified abnormalities in three quarters of symptomatic patients where conventional contrast swallow had not been diagnostic. Five primary patterns of pathophysiology were defined. These were used to develop a 7 category, clinical, classification system based on the anatomical appearance at stress barium. This system stratifies the spectrum of symmetrical pouch dilatation and can be used to logically guide treatment.

Introduction

Laparoscopic adjustable gastric banding (LAGB) has become one of the most commonly performed bariatric procedures [283]. Whilst its success in safely achieving and maintaining weight loss and controlling co-morbidities guarantees ongoing use, patients require lifelong follow up [253, 264, 303]. During this time some patients will present with symptoms such as reflux or unpredictable regurgitation; alternatively lost weight may be regained. Understanding of the anatomy and pathophysiology that leads to these clinical syndromes is lacking. Defining this area better has the potential to facilitate specific treatments, promote recognition and intervention at an earlier stage, or optimally, prevent problems from developing.

Symmetrical pouch dilatation (SPD) is now the most common problem following LAGB [310]. This has occurred with changes in surgical technique that have dramatically decreased the early incidence of gastric prolapse [10]. SPD tends to occur at an intermediate or later stage. It likely constitutes a spectrum of problems, representative of different anatomy, pathophysiology and clinical significance.

Contrast radiography and upper gastrointestinal endoscopy are commonly used to assess symptomatic LAGB patients. These investigations do not model the physiological and anatomical changes that occur when a LAGB patient eats. This may explain why patients who are clearly symptomatic may not have demonstrable abnormalities. Conventional oesophageal manometry, using a pull back or sleeve technique, has not gained acceptance as a routine means of assessing LAGB

patients. This is largely due to a lack of sensitivity and the varying conclusions reached by different investigators [269, 437, 442].

Video manometry combines high resolution manometry with concurrent fluoroscopy [522]. This technique, in combination with a semi-solid contrast swallow protocol, has clarified the effect of the LAGB on oesophageal physiology and bolus transit [533]. It allows for the separation of pressures produced by close anatomical structures such as the lower oesophageal sphincter (LOS), diaphragm and LAGB. Additionally, synchronous anatomical and transit data is provided.

We hypothesised that high resolution video manometry, incorporating a semi-solid stress barium protocol, could identify patterns of anatomical and associated pathophysiological change in symptomatic LAGB patients. We aimed to determine if this technique could be used as a diagnostic test where conventional investigations had not identified an abnormality. Finally, our goal was to use this understanding to develop a system of classifying pathophysiology following LAGB. This was intended to be easily reproducible without requiring additional equipment or special expertise.

Methods

Participants

Symptomatic patients following LAGB, for the purposes of this study, were defined as patients aged between 18 and 65 years, who experienced either poor weight loss (<25% of excess weight loss 12 months post-operatively) and/or had adverse symptoms (volume reflux, dysphagia, regurgitation/vomiting or the inability to tolerate fluid in the LAGB due to these symptoms) despite a normal or near normal contrast swallow. Patients were excluded from the study if they were pregnant; due to the risk of radiation. "Successful" LAGB patients for this study were defined as those patients who had lost >50% excess weight after 12 months, who had had no previous bariatric or oesophago-gastric surgery prior to LAGB placement and who were experiencing no adverse symptoms. The "control" patients were consecutive pre-operative LAGB patients.

The study was approved by the Melbourne Health and Monash University Human Ethics Committees and all patients gave informed consent.

Manometry Protocol

All patients underwent a standardised video manometry protocol. This technique, in LAGB patients, has been described previously [533]. In brief,   a 21-channel water perfused manometry system with a custom made 21 channel silicone rubber manometry catheter (Dentsleeve, Ontario, Canada) was used. The catheters were designed specifically to assess the region of the oesophago-gastric junction (OGJ) and to differentiate the pressure signals generated by the LAGB and LOS. The manometry system was connected to a personal computer via data acquisition and

video input cards (National Instruments). Simultaneous high resolution manometry and video fluoroscopy information was recorded using TRACE! 1.2 (written by G Hebbard using LabVIEW, National Instruments, Austin, Texas).

Supine basal recording was performed for 30 seconds without swallowing. Ten wet swallows of 5 ml of water were then performed with the patient in the right lateral position. Oesophageal video manometry was performed after a 5 minute accommodation period by having the upright patient take two swallows of 5 ml of barium in both the anterior-posterior (AP) and lateral position. This was followed by two swallows of one spoonful of barium soaked porridge, again in the AP and lateral position.

For the interpretation of high resolution oesophageal manometry traces, presented as colour spatio-temporal plots, we refer the reader, for general information, to publications from Kahrilas [501] and Grubel [527] or our previous work in LAGB patients [533].

Stress barium protocol

The patients ingested two consecutive spoonfuls of barium soaked porridge. These were   followed immediately by drinking of up to 80 ml of liquid barium via a straw. Patients were instructed to continue drinking until either symptoms of dysphagia, discomfort or nausea developed or they felt excessively full. The aim was to maximally distend any pouch above the LAGB. Fluoroscopy was used to ensure patients had drunk barium to the point of either developing reflux from the pouch or a significant enlargement, with stasis, was observed above the LAGB. We aimed

to generate an intraluminal pressure immediately above the LAGB of at least 30 mmHg. Delayed images were taken intermittently for a period of up to 5 minutes, to document transit and emptying of the oesophago-gastric compartment above the LAGB. Figure 15.1 is a description of the stress barium protocol and its interpretation.

If it was not possible on the barium study to accurately define the OGJ, patients underwent upper gastrointestinal endoscopy and radio-opaque marking clips were placed on the Z-line, marking the transition from oesophageal to gastric mucosa. The stress barium was then repeated, the diaphragm was identified during deep inspiration and expiration, and the position of the clips in relation to the diaphragm and any enlargement were noted.

Lower Oesophageal Sphincter Assessment

The basal LOS pressure was recorded as the median peak end expiratory pressure over the LOS region, recorded over 5 respiratory cycles. It was ensured that the LOS pressure rather than the intra-luminal pressure at the level of the LAGB was recorded. This technique and the importance of differentiating the LOS from the LAGB has been described previously [533].

FIGURE 15.1: Stress Barium Protocol and Features Used to Separate Normal from Abnormal Appearance

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Protocol

I. 2 consecutive standard teaspoons porridge soaked in barium
II. After consumption of porridge, immediate drinking of liquid barium from a straw (80 ml), with the patient instructed to cease drinking if they develop dysphagia, discomfort or nausea or feel completely full
III. Continuous fluoroscopic screening
IV. Observation of oesophageal pattern of trans LAGB flow and observation for gross oesophageal dilatation
V. If an enlargement with stasis develops above the LAGB then: Deep inspiration with visualisation of the crural indentation used to identify the relationship of the enlargement to the diaphragm
VI. Intermittent fluoroscopic screening for up to 5 minutes to determine if there is successful clearance of the semi-solid bolus

Normal

Complete clearance of semi-solid bolus through the LAGB within 3 minutes

Capacity of the patient to identify whether the semi-solid bolus has transited across the LAGB

Pattern of episodic bolus transit across the LAGB during oesophageal contractions followed by gastro-oesophageal reflux, and then repeated oesophageal contractions driving flow across the LAGB – a pattern repeated until complete clearance is observed.

Abnormal

Failure to clear semi-solid bolus within three minutes

A focal enlargement developing above the LAGB in which there is *stasis* and an *air fluid level*

Inability of the patient to determine if the semi-solid bolus has cleared into the distal stomach, particularly if there is stasis above the LAGB and manifested by patient continuing to drink or able to consume additional spoons of porridge

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Oesophageal Motility

Oesophageal motility was assessed on the basis of 10 right lateral water swallows of 5 ml of water. Each swallow was classified as: normal, hypotensive, failed, hypertensive or synchronous. An overall assessment of motility was determined, based on standardised criteria for the reporting of oesophageal motility disorders, using high resolution manometry [501].

Analysis of OGJ Pressure and Distal Oesophageal Pressure Topography

Detailed analysis of pressure topography was undertaken for each 5ml water right lateral swallow classified as normal or hypertensive. The following data were collected: peak distal oesophageal pressure, peak intra-luminal pressure at the level of the LAGB, peak pressure at the level of the LOS, and peak pressure generated in the middle of the high pressure zone (HPZ). The method of separating the intraluminal pressure at the level of these close anatomical structures has been described previously [533].

The HPZ was defined, during water swallows, as the contiguous area of pressure greater than 5 mmHg between the lower oesophagus and the LAGB that occurred at end expiration. This was only assessed once the oesophageal peristaltic wave had stopped travelling distally. The HPZ has three components: the distal end of the lower oesophageal contraction, the isobaric zone representing an intra-luminal zone passively transmitting the bolus pressure, and the intra-luminal pressure at the level of the LAGB. The isobaric zone, in the normal state, can be considered to be the gastric pouch above the LAGB [533]. It is important to note that the length of

the HPZ was the sum of these three components and so extends from the upper margin of the contracting lower oesophagus (usually the LOS) to the inferior border of the LAGB.

Peristaltic velocity was defined as the rate of movement of the 30 mmHg isobaric pressure wave over the lower 4 cm of the oesophagus, between side holes. The location of the LOS and the LAGB were taken into account to ensure that the velocity was measured only over the lower 4 cm of oesophagus.

For pooled analysis, the median value of a minimum of 3 swallows, from any individual was used.

Statistical analysis

Statistical analysis was performed using SPSS version 11 (SPSS Inc, Chicago, Ill). For normally distributed continuous data, when comparing multiple groups, one way ANOVA was used. Post hoc analysis, using the Bonferroni transformation was performed on pre-defined sub groups of interest. To compare multiple groups, with non-normally distributed continuous data, Kruskal-Wallis tests were used. When comparing categorical data, Chi square tests were used.

A two sided *p*-value of 0.05 was considered to be statistically significant. Data are presented as means and standard deviation unless otherwise stated.

Results

There were 209 patients enrolled in the study - 123 symptomatic patients, 30 successful and 56 preoperative LAGB patients. Four symptomatic patients were

excluded from analysis, one was unable to tolerate the manometry catheter, one had broken tubing connecting the LAGB to the subcutaneous port, one had a leaking port and another mechanical failure of the LAGB. One successful patient was unable to tolerate the manometry catheter.

The normal appearance of the stress barium was defined from results obtained from the successful patients (Figure 15.2). Normal appearance consisted of rapid transit of the semi-solid bolus across the LAGB. Trans LAGB flow was generated during oesophageal contractions. Following completion of the oesophageal contraction, if there was residual bolus above the LAGB, this refluxed back into the oesophagus. Repeated oesophageal contraction then drove further flow. Complete clearance of the bolus into the distal stomach was expected within 3 minutes. Successful patients were able to determine whether the semi-solid bolus had transited across the LAGB.

FIGURE 15.2: Normal Appearance of Liquid Contrast Swallow, Stress Barium and Manometry.
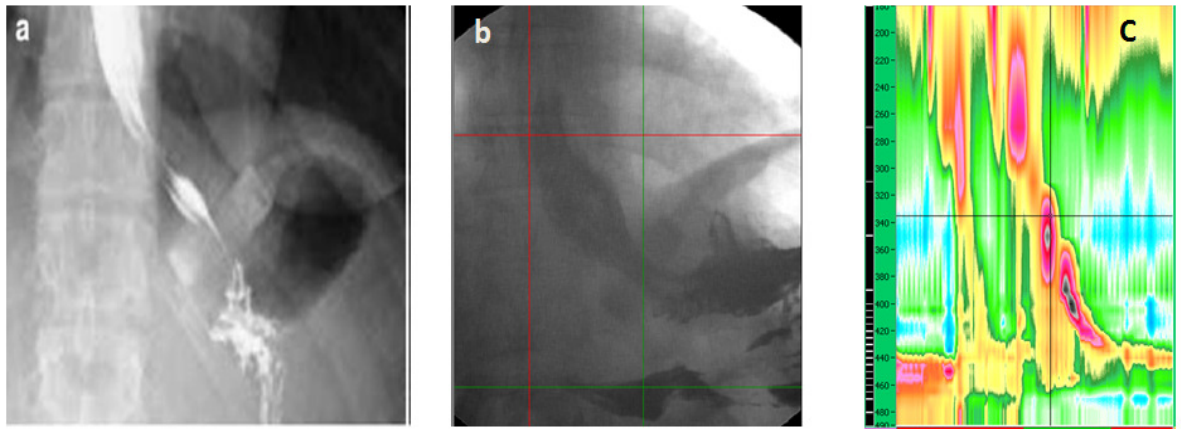
Figure 15.2 Legend: *Panel a: Liquid contrast swallow confirms the location of the LAGB immediately beneath the OGJ junction. There is flow through the LAGB without enlargement. Panel b: Appearance using the stress barium protocol – regulated transit across the LAGB is observed. There is no enlargement or stasis above the LAGB. The concurrent high resolution manometry recording; panel c, shows 2 co-ordinated oesophageal contractions driving flow across the LAGB, with a narrow vertical high pressure zone between the distal oesophagus and LAGB.*

In the abnormal state, stasis developed above the LAGB and persisted for greater than 3 minutes. Incomplete bolus transit and stasis was the critical difference between the normal and abnormal state. Three distinct abnormal anatomical appearances were identified: transhiatal enlargement, sub-diaphragmatic enlargement and gastric prolapse. A fourth category; aperistaltic oesophagus, due to pan oesophageal dilatation, was defined, primarily on manometric data.

Additionally, the symptomatic patients were frequently unable to identify whether the bolus had transited through the LAGB, into the distal stomach. Examples illustrating the physiological and anatomical features of each of these categories are displayed in Figure 15.3.

Using these criteria, an abnormality was identified in 79 (66%) symptomatic patients. In 23 cases, doubt existed as to whether the enlargement was transhiatal or sub-diaphragmatic. Endoscopic marking of the Z-line was performed in each of these patients, after which 14 were classified as transhiatal oesophageal, 3 as transhiatal gastric or hiatal hernia and 6 as sub-diaphragmatic gastric. In each of these, the repeat stress barium study confirmed the provisional diagnosis made at video manometry.

Table 15.1 shows patient detail pre-operatively and at the time of manometry. Symptomatic patients were divided into groups, for further analysis, based on the category defined by the stress barium. There were no significant pre-operative baseline differences between the groups. Symptomatic patients underwent manometry at a significantly later time following LAGB placement than did the successful patients ($p <0.005$). The successful patients had greater excess weight loss (EWL) following LAGB placement than the symptomatic patients ($p<0.005$).

FIGURE 15.3: Anatomical and Pathophysiological Patterns in Symptomatic LAGB Patients
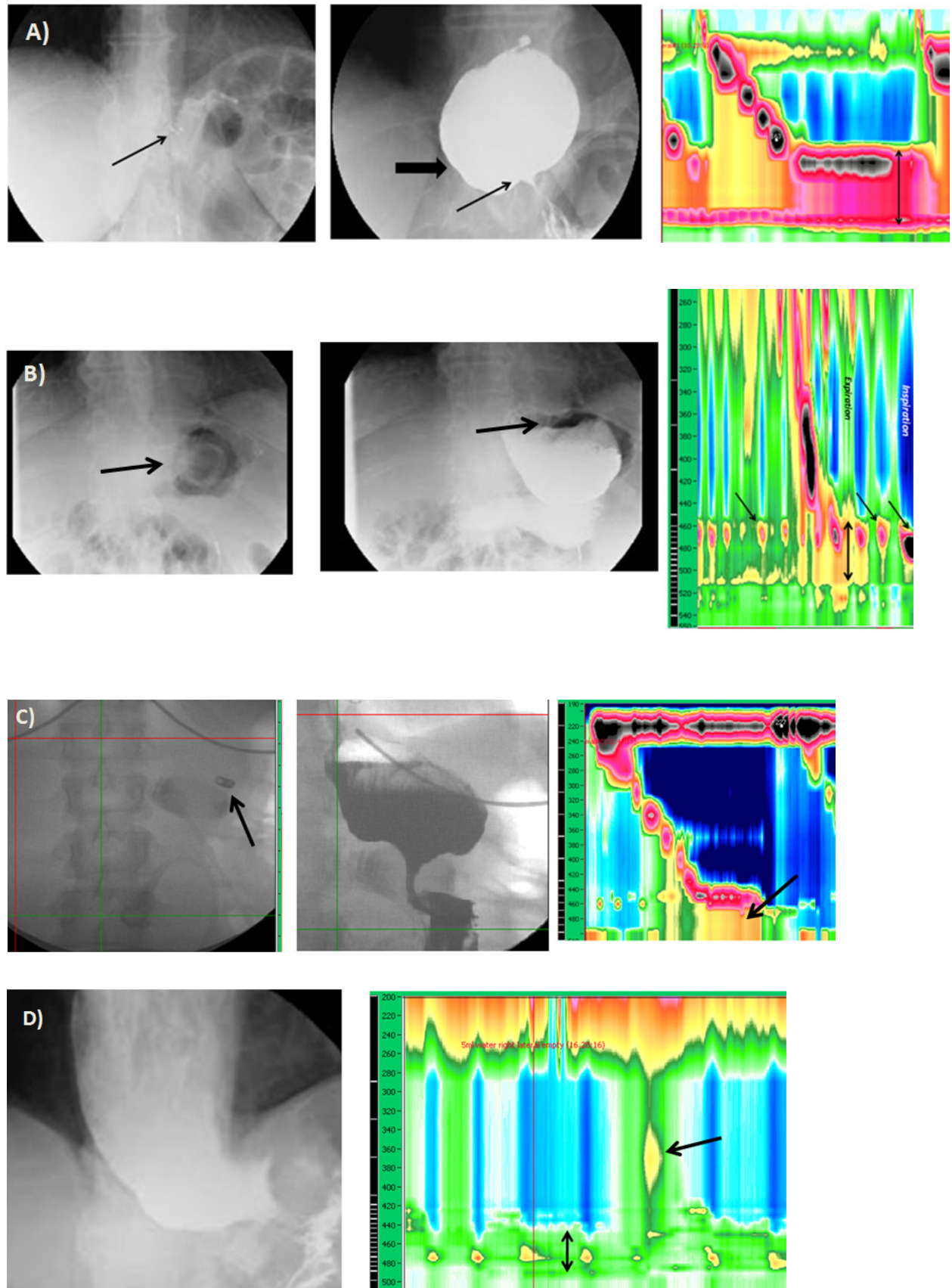
Figure 15.3 Legend: *Anatomical and pathophysiological abnormalities following*

LAGB: Appearance during liquid contrast swallow, stress barium and synchronous

manometric changes

A) Transhiatal enlargement*: First image, radiopaque marking clips have been placed*

on the Z-line at endoscopy (thin arrow). In the second image, following the semi-

solid swallow protocol, a significant enlargement with stasis has developed above

the LAGB. This is a transhiatal oesophageal enlargement; the level of the

diaphragm, during a deep inspiration is illustrated by the crural imprint (large

arrow) – with the enlargement well above this level. An elongated high pressure

zone above the LAGB is shown (double headed arrow) in the manometry trace.

B) Sub-diaphragmatic enlargement*: In the first panel the black arrows illustrate*

endoscopic marking clips on the Z-line. In the Second panel, after administration of

the semi-solid swallow protocol, a sub-diaphragmatic enlargement has developed

with stasis and an air fluid level – the arrow shows the position of the clips at the Z-

line. The manometry plot illustrates an increased high pressure zone (double headed

arrow) of 6 cm. The single arrows show diaphragmatic contractions, confirming the

sub-diaphragmatic location of the enlargement.

C) Gastric prolapse: *First panel - there is an abnormal lie of the band, in this case*

horizontal; indicative of an anterior gastric prolapse. The radiopaque tip of the

manometry catheter (arrow) is unable to transit through the LAGB into the distal

stomach. The stress barium (second panel) produces a significant enlargement, with

stasis, above the LAGB. As the manometry catheter has not passed through the

LAGB, pressure and motility data is unreliable. In the third panel the arrow indicates

the high pressure zone on the manometry plot, although this is incompletely

measured and the lower extent is not identified.

 D) Aperistaltic oesophagus*: The oesophagus is dilated in the stress barium with no*

regulated transport of liquids or semi-solids across the LAGB. In the manometry plot,

there is no identifiable lower oesophageal sphincter and no peristaltic activity is

seen. The double headed arrow is the region of the LOS and the single headed arrow

indicates a degree of compartmental oesophageal pressurisation due to an

uncoordinated, ineffective, oesophageal contraction.

There was no difference in the EWL (Table 15.1) between the transhiatal group and the group with no abnormality ($p=1.0$). The sub-diaphragmatic group had greater EWL than the transhiatal group ($p<0.005$), as well as the group with no abnormality ($p<0.005$).   The group with no abnormality was more likely to have had a previous LAGB (65%) compared to the sub-diaphragmatic (3%) and transhiatal (46%) groups ($p = 0.01$).

The prolapse group was excluded from all manometric analysis as the abnormal lie of the LAGB impaired passage of the manometry catheter through the LAGB, potentially invalidating manometry data. There was no value in comparing the oesophageal function of the aperistalsis group, as by definition, they had none.

TABLE 15.1: Patient Details

	Successful	Pre-operative	Transhiatal	Sub-diaphragmatic	Prolapse	Aperistalsis	No abnormality identified	p value
Number	30	56	40	39	3	7	30	
Age (years)	45.6±12.2	47.7±15.0	49.9±13.4	48.2±17.5	39.7±10.8	50.9±8.1	48.6±14.7	0.78
Males (proportion)	0.26	0.20	0.13	0.13	0.33	0.57	0.17	0.17
Start weight (kg)	118.4±22.2	117.2±22.3	118.1±22.9	124.4±23.5	123.7	148.2±26.2	120.0±22.1	0.13
Start BMI	42.7±6.7	42.4±7.3	43.3±7.4	44.3±7.1	40.4±5.3	48.6±7.0	44.03	0.57
Duration from Surgery (days)	1039±968	-	1669±929	1592±775	2029±1046	2585±1074	1822±948	0.001
Weight loss (kg)	32.4±14.0	-	11.6±13.6	25.2±17.8	16.8±1.5	39.1±13.78	12.2±12.4	<0.005
% Excess weight loss	66.6±18.7	-	27.3±25.3	48.5±32.8	41.8±26.2	51.8±16.30	25.6±21.8	<0.005
Current weight (kg)	86.0±15.5	-	107.3±21.3	99.2±24.0	106.8±29.9	109.1±20.5	107.9±18.6	<0.005
Current BMI (kg/m²)	30.6±4.6	-	41.0±13.6	35.1±7.6	34.7±6.4	36.1±5.1	39.0±7.2	<0.005
Previous LAGB (proportion)	0	—	0.46	0.14	0	0.57	0.65	0.01

†Comparison between multiple groups performed using one way ANOVA. Post hoc analysis between predefined subgroups of interest using the Bonferroni transformation are detailed in the text. Proportions compared using Chi square test. Values are mean and standard deviation

The LOS was attenuated in all LAGB patients in both basal tone and length in comparison to pre-operative patients ($p<0.005$).   Table 15.2 outlines the LOS data in detail.   There was no difference between the normal and sub-diaphragmatic group in terms of LOS tone (*p=0.50*). The LOS tone of both the transhiatal group (*p<0.005*) and the no abnormality group (*p=0.05*) were significantly less in comparison to the successful patients. The LOS tone of the transhiatal group, in comparison to the sub-diaphragmatic group, was significantly less (*p=0.002*). Although there was no significant difference noted between the transhiatal and the no abnormality group (*p=0.19*). LOS relaxation was normal in all groups. The aperistalsis group had no identifiable LOS.

TABLE 15.2: Lower Oesophageal Sphincter Characteristics According to Patient Group

	SUCCESSFUL	PRE-OPERATIVE	SYMPTOMATIC			
			Transhiatal	*Sub-diaphragmatic*	*No abnormality*	*p* value
Basal tone (mmHg)	12.4±7.1	20.3±9.6	4.7±5.3	10.3±8.0	7.6±6.3	<0.005
Length (cm	2.0±1.0	2.1±1.0	0.8±0.1	1.4±1.3	11.6±10.7	0.007
Relaxation (proportion)	0.8±1.0	0.8±0.2	1.0 ±0.1	0.9±0.16	0.9 ±0.2	<0.005
Normal LOS † (proportion of patients)	0.66	0.89	0.17	0.58	0.36	<0.005

Data are mean and standard deviation†, Normal LOS is defined as LOS >10 mmHg, < 45 mmHg, LOS – Lower oesophageal sphincter

The prevalence of oesophageal motility disorders in the successful patients was 10%. This was significantly lower than the prevalence in all other groups (*p = 0.01*). The prevalence of an oesophageal motility disorder in the transhiatal group was 50%, sub-diaphragmatic group 36%, no abnormality group 40% and the preoperative group 34%. The incidence was not different when comparing the symptomatic groups and the pre-operative patients (*p=0.43*). Most of the difference between the symptomatic and successful patients was due to mild peristaltic dysfunction. When analysed based on individual swallows (Figure 15.4), the successful patients had less hypotensive swallows (*p= 0.05*), however, the proportion of normal (*p=0.13*), failed (*p=0.10*), synchronous (*p=0.95*) and hypertensive (*p=0.82*) swallows was not different.

FIGURE 15.4: Classification of Water Swallows
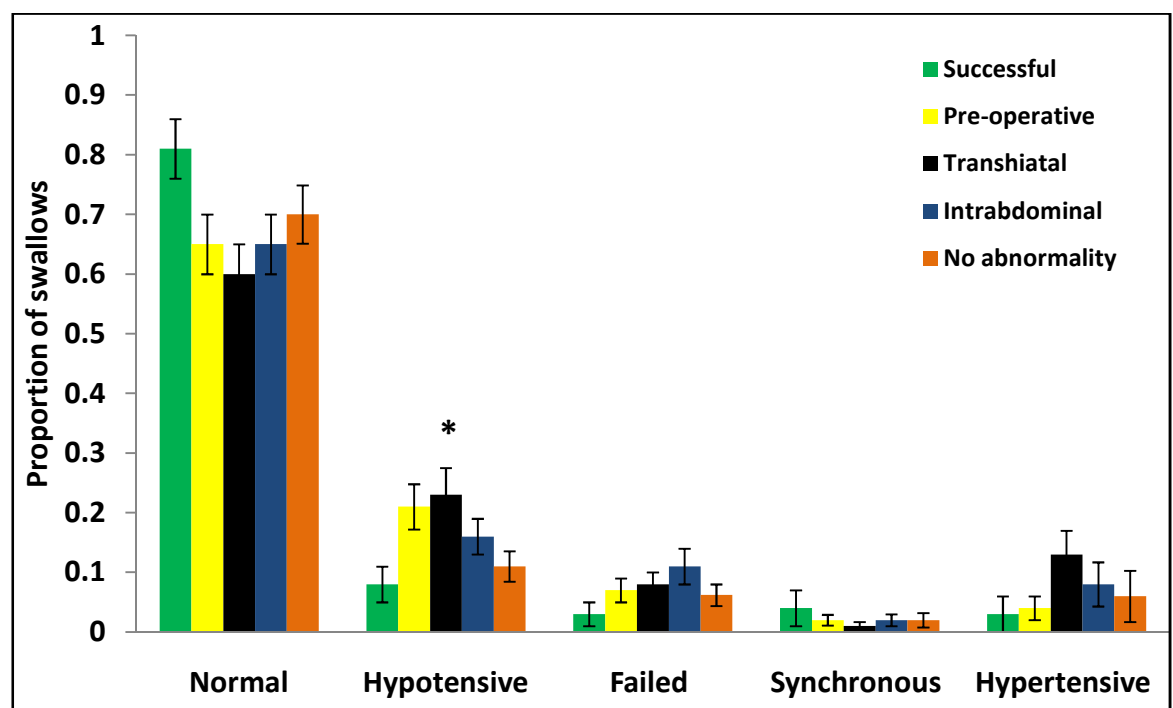
Statistically significant difference between groups, p<0.05. Data are mean and standard error

The basal intraluminal pressure at the level of the LAGB was similar in all groups (*p=0.07*), measuring 25.7±18.7 mmHg in successful patients, 20.4±14.0 mmHg in the group with transhiatal enlargement, 17.3±9.9 in the group with sub-diaphragmatic enlargement, 16.1±16.3 mmHg with no abnormality and 32.4±31.8 mmHg in the group with aperistalsis.

There was no significant difference between groups in the pressures generated during right lateral water swallows in the distal oesophagus (*p=0.39*), at the lower oesophageal sphincter (*p=0.26*), in middle of the high pressure zone (*p=0.51*) or at the level of the LAGB (*p=0.83*).

The length of the HPZ during swallowing was significantly different between groups (*p<0.005*). This length was 4.8±0.9 cm in successful patients, 6.8±1.8 cm in the transhiatal group, 5.8±1.4 cm in the sub-diaphragmatic group and 4.8±1.3 cm in the group with no abnormality. The HPZ length was significantly longer in the transhiatal group (*p<0.005*) and the sub-diaphragmatic group (*p=0.002*) than in the successful patients. There was no difference in this length when the successful patients were compared to the group with no abnormality (*p = 0.91*). The HPZ was significantly longer in the sub-diaphragmatic group compared to the transhiatal group (*p = 0.018*). The HPZ was significantly longer in the transhiatal (*p<0.005*) group and the sub-diaphragmatic group (*p=0.01*), than the group with no abnormality.

Peristaltic velocity was found to be significantly different (*p<0.005*) between groups. Successful patients recorded a velocity of 1.8±0.7 cm/sec, pre-operative patients 3.3 ±1.1 cm/sec, transhiatal group 2.9±4.7 cm/sec, sub-diaphragmatic

group 2.3±1.2 cm/sec, no abnormality group 3.4±2.1 cm/sec. The successful patients had a significantly reduced velocity in comparison to the pre-operative ($p<0.005$) and no abnormality ($p=0.002$) groups. The successful patients were not different to the sub-diaphragmatic ($p=0.18$) or transhiatal ($p=0.18$) groups. Within the symptomatic patients, the no abnormality group had significantly more rapid peristalsis than did those with sub-diaphragmatic ($p=0.04$) or transhiatal ($p=0.03$) enlargements.

The 5 categories defined, were translated into a clinical classification, detailed in Table 15.3. For practical use, the 5 defined categories defined have been extended to 7. Transhiatal enlargements and aperistaltic oesophagus have been each been sub classified into two, giving a total of 7 different diagnosis. Aperistaltic oesophagus is described by the category pan-oesophageal dilatation, reflective of the nature of the clinical classification; based on anatomical appearance rather than manometric criteria.

This classification shown in table 15.3 is based on the appearance induced using the stress barium protocol. There are 5 primary abnormalities. The transhiatal enlargements and pan oesophageal dilatation consist of two different subtypes. The classification can be enhanced with high resolution manometry, performed either synchronously (video manometry) or as a separate test. In cases of pan oesophageal dilatation, manometry can confirm the absence of peristaltic contractions.

TABLE 15.3: Clinical Classification of Abnormalities Following LAGB Based on Stress Barium Appearance

Abnormality	Key features
Transhiatal oesophageal enlargement	Focal enlargement of the lower oesophagus at the level of the lower oesophageal sphincter, presenting intrathoracically - potentially mimicking a hiatus hernia
Transhiatal gastric enlargement	True hiatus hernia, with excess stomach above the LAGB, herniating into the chest
Sub-diaphragmatic gastric enlargement	Symmetrical enlargement of stomach below the diaphragm
Gastric prolapse	Herniation of the stomach through the LAGB, with an abnormal lie of the band – this pathology may be intermittent, identifiable only with the stress protocol and/or addition of saline to the LAGB
Pan oesophageal dilatation (primary)	Pan oesophageal dilatation, with a normally placed LAGB.
Pan oesophageal dilatation (secondary)	Pan oesophageal dilatation, due to obstruction, as a result of a focal enlargement above the LAGB
Functional abnormality	Anatomically normally sited LAGB with no inducible abnormality or apparent pathophysiology

Discussion

Video manometry was able to delineate an abnormality in three quarters of symptomatic LAGB patients, where conventional contrast swallow was not diagnostic. A persistent, focal enlargement above the LAGB was the most common. This was demonstrated using a standardised, semi-solid and liquid swallow protocol that we have described as a stress barium. The hallmark was stasis, manifested by the persistence of an air fluid level above the LAGB for greater than 3 minutes. Five patterns of abnormality were defined by combining physiological, anatomical and functional data.

These 5 pathophysiological patterns were the basis of a classification system with 7 categories, designed to be used clinically. This clinical classification represented only a slight expansion of the pathophysiological patterns, to make it more practical. The transhiatal enlargements were subdivided into focal oesophageal enlargements and true hiatus hernias. Aperistalsis of the oesophagus was described as pan-oesophageal dilatation seen on the stress barium, as manometry is required to demonstrate aperistalsis. This category was also divided into situations where the LAGB was normally sited (primary) or where there was an excess of stomach above the LAGB (secondary). The 7 categories were defined to reflect the requirement for different management for each.

Transhiatal enlargements usually represent focal dilatation of the lower oesophagus. The enlargement presents intra-thoracically, mimicking a hiatus hernia. Only 3 true hiatus hernias were identified in our series. Transhiatal oesophageal and gastric enlargements were differentiated based on the

appearance of the stress barium. The ability of this method to differentiate these two abnormalities was confirmed by applying endoscopic marking clips to the Z-line. We suspect these focal oesophageal enlargements are, at revisional operation, sometimes described as a hiatus hernia [311].

Sub-diaphragmatic enlargements represent lateral spread of an increased volume of stomach below the diaphragm. These patients tended to have reasonable weight loss (47% EWL), but suffer adverse symptoms. A relatively intact LOS was observed in these patients, similar to that observed in successful patients. It is possible that the intact LOS has aided in confining dilatation to the stomach, keeping it within the abdominal cavity.

We observed a small number (n=3) of patients with intermittent gastric prolapse. These patients initially had what appeared to be normal positioning of the LAGB, with no excess of stomach above the band. The stress barium, however, induced an enlargement, in conjunction with an abnormal lie of the LAGB. In these patients it was difficult to pass the manometry catheter through the LAGB. An aperistaltic oesophagus was seen in only 7 patients. The small numbers precluded more detailed statistical analysis.

In 25% of symptomatic patients no abnormality was identified. These patients had poor weight loss, decreased LOS tone and more rapid peristaltic velocity, in comparison to successful patients. However, no anatomical abnormality or increase in the HPZ length was identified. The significance of the decreased LOS tone is unclear. Another major difference between these and other symptomatic patients was the higher prevalence (60%) of previous, revisional, LAGB surgery. Whether this

represents an initial failure unable to be corrected by revisional surgery or a subsequent failure that has followed the revision, is not known.

We hypothesise that sub-diaphragmatic gastric enlargements and gastric prolapse are readily amenable to revisional surgery. Revisional surgery can ensure that the LAGB is correctly placed in relation to the oesophago-gastric junction. In patients with transhiatal oesophageal enlargements, revisional LAGB surgery cannot help. In patients with an anatomical correctly sited LAGB and no focal enlargement, confirmed by the stress barium; symptoms, loss of satiety or increased weight may be observed. The physiological basis for this may be more subtle, with focal impairment in distal oesophageal function, manifested by the inability to generate effective trans LAGB bolus clearance. Alternatively, there may have been a reduction in sensitivity of the cardia to the LAGB and a sense of satiety is just not achieved. Future efforts need to examine these areas in more detail.

The successful patients had a lower prevalence of oesophageal motility disorders than the other groups. We found no difference in the prevalence of oesophageal motility disorders in the symptomatic compared to the pre-operative patients. One explanation for this is that patients with good oesophageal motility are those who are successful following LAGB placement. This seems unlikely, given the high prevalence of oesophageal motility disorders in the obese [428, 429]. Alternatively, with optimal placement of the LAGB an improvement in overall oesophageal motility may occur, similar to that seen post fundoplication [534], possibly as a result of weight loss or control of gastro-oesophageal reflux.

The symptomatic and successful patients developed similar pressurisation in the distal oesophagus and all locations analysed in the region of the LAGB. Patients with anatomical abnormalities, however, were unable to clear the region above the LAGB of the semi-solid bolus, instead stasis developed. This indicates that absolute pressures are not the mediators of success post LAGB. Rather, the generation of appropriate sensations in response to these stimuli and efficient bolus transit into the distal stomach are the important mediators. We believe that stasis above the LAGB is exacerbated when patients are unable to determine whether the bolus has transited through the LAGB into the distal stomach. This may explain why patients report loss of satiety, leading to weight gain and unpredictable reflux or regurgitation. If there is stasis above the LAGB, in the presence of an attenuated LOS, reflux and regurgitation is favoured.

The HPZ was frequently longer in symptomatic than in successful patients. We believe this is an important physiological difference that correlates with the presence of stasis above the LAGB. In successful patients, oesophageal peristalsis mediates relatively rapid transit across the LAGB [533]. To generate flow across the LAGB, the intrabolus pressure must exceed the resistance of the LAGB, which is measured as an intraluminal pressure. Increased HPZ length is a marker of increased luminal volume above the LAGB that is not contributing effective peristalsis. As this volume increases, the probability of complete bolus transit decreases. It is in this region that stasis develops, be it stomach or oesophagus. Once a critical volume is exceeded, even normal oesophageal contractions are unable to completely clear this region, resulting in stasis. The HPZ length can

therefore be seen as a marker of the capacity of the oesophagus to successfully clear the bolus across the LAGB into the distal stomach.

The first step in managing symptomatic patients is generally to remove fluid from the band, then to gradually re-instil fluid until a good balance between weight loss and adverse symptoms is achieved [310]. If this balance is not able to be achieved, revisional surgery is sometimes performed – limited outcome data suggests that this approach is often successful [322]. In this study, no patient had been able to find a satisfactory balance between weight loss and adverse symptoms. Longer term studies of outcomes in this cohort of patients, treated conservatively or with further LAGB surgery will provide additional information.

Focal dilatation, gastric or oesophageal, underlies the vast majority of post LAGB problems. The likely cause is chronic over pressurisation, resulting in expansion of the weakest point of the luminal wall. This has been hypothesised to be the result of poor eating behaviour, with frequent episodes of obstruction and regurgitation recurrently over pressurising the lumen above the LAGB [310]. Reducing the transmission of force to the luminal wall is a logical preventative strategy. Firstly, adjustments should target satiety [8] rather than restriction; ensuring only a modest level of restriction is produced by the LAGB. Increasing the volume within the LAGB by only 20% has been shown to significantly increase the pressures in the oesophagus and stomach above the LAGB [533]. A second important preventative strategy is to ensure patients are well educated about appropriate eating behaviour. The avoidance of blockages, consumption of small meals slowly with

each limited bolus chewed well prior to swallowing should be emphasised. Foods of inappropriate texture must be avoided.

All bariatric procedures have an incidence of failure and conversion of one procedure to another has been documented, often with success [535, 536]. Increasing knowledge of LAGB physiology indicates that oesophageal transit is delayed, without prolonged stasis. In contrast, alternate procedures have differing mechanisms of action [342]; none of which are likely to be compromised following LAGB. This should allow their use if required. At this stage, we advocate focusing further research on the outcomes of these different pathophysiological patterns prior to evaluating alternate revisional procedures.

If alternate procedures are to be considered, those with transhiatal enlargements or an aperistaltic oesophagus are the likely candidates. In the future, we may be able to identify sub-groups of those with a gastric prolapse or sub-diaphragmatic enlargement that will not succeed with further LAGB surgery. We don't see a definitive advantage of any of the alternative bariatric procedure. Data concerning their strengths and weakness are available [157]. We suggest that the LAGB be removed several months prior to sleeve gastrectomy or gastric bypass to make the procedure technically easier and reduce the risk of anastomotic leak. Alternatively, a bilio-pancreatic diversion avoids the proximal stomach and should not be affected by a previous LAGB.

Conclusions

High resolution video manometry and a stress barium protocol have now been validated as diagnostic tests in symptomatic LAGB patients. They have allowed the description of pathophysiological patterns of failure following LAGB and significantly extended knowledge concerning symmetrical pouch dilatation as well as the normal physiology of the LAGB. A clinically useful classification, requiring only the stress barium has been developed. Complementary information can be provided by high resolution manometry – although this is not mandatory. Future research should validate this classification system against outcome and examine therapies and preventative methods. We advocate an objective, physiological approach to symptomatic LAGB patients. Utilising the stress barium classification system will allow logical stratification of the management of symptomatic LAGB patients; particularly those with symmetrical pouch dilatation or a normal appearance on standard contrast swallow

Declaration for Thesis Chapter 16

This Chapter represents a manuscript published in *Obesity Surgery (Obes Surg. 2010 Jan 12. [Epub ahead of print])*.

Declaration by candidate

In the case of Chapter 16, the nature and extent of my contribution to the work was the following:

Nature of contribution	Extent of contribution (%)
Overall responsibility for all aspects of the study, conception, planning, patient recruitment, conducting experiments and recording data. Data analysis and interpretation. Statistical analysis. Crafting and revising manuscript, submission to journal.	>90%

The following co-authors contributed to the work:

Name	Nature of contribution
Wendy A Brown	Designing study, and recruiting patients, data analysis, manuscript review
Cheryl Laurie	Recruiting and conducting studies, manuscript review
Geoff Hebbard	Experiment design, data acquisition and analysis, review of manuscript
Paul O'Brien	Experiment design, data acquisition and analysis, review of manuscript

Candidate's Signature		**Date**

Declaration by co-authors

The undersigned hereby certify that:

(1) the above declaration correctly reflects the nature and extent of the candidate's contribution to this work, and the nature of the contribution of each of the co-authors.
(2) they meet the criteria for authorship in that they have participated in the conception, execution, or interpretation, of at least that part of the publication in their field of expertise;
(3) they take public responsibility for their part of the publication, except for the responsible author who accepts overall responsibility for the publication;
(4) there are no other authors of the publication according to these criteria;
(5) potential conflicts of interest have been disclosed to (a) granting bodies, (b) the editor or publisher of journals or other publications, and (c) the head of the responsible academic unit; and
(6) the original data are stored at the following location(s) and will be held for at least five years from the date indicated below:

Location(s)	**Centre for Obesity Research and Education, Monash University, Alfred Hospital**

		Date
Wendy A Brown	████████████	27/10/09
Cheryl Laurie	████████████	4/11/09
Geoff Hebbard	████████████	2/11/09
Paul E O'Brien	████████████	27.10.09

Chapter 16: *Mechanisms of Bolus Clearance in Patients with Laparoscopic Adjustable Gastric Bands*

Abstract

Background: The components of oesophageal function important to success with laparoscopic adjustable gastric banding (LAGB) are not well understood. A pattern of delayed, however, successful bolus transit across the LAGB is observed.

Methods: Successful LAGB patients underwent a high resolution video manometry study in which bolus clearance, flow and intraluminal pressures were recorded. Liquid and semi-solid swallows and a stress barium (a combination of semi-solid and liquid barium swallows) were performed. A new measurement; the lower oesophageal contractile segment (LECS) was defined and evaluated.

Results: Twenty patients participated (mean age 48.3 ± 12.0 years, 4 males, %excess weight loss 65.6 ± 18.0). During semi-solid swallows two patterns of oesophageal clearance were observed. Firstly, a native pattern (n=10) similar to that which is expected in non LAGB patients. Secondly, a lower oesophageal sphincter dependent pattern (n=7), where flow only occurred when the intrabolus pressure increased during the LOS aftercontraction. In both patterns, if there was incomplete bolus clearance, reflux was observed and was usually followed by another swallow. A mean of 4.5 ± 2.9 contractions were required to clear the semi-solid bolus. Contractions with an intact LECS demonstrated longer flow duration: 7.1 ± 3.8 sec. vs.1.6 ± 3.2 sec., *(p<0.005)*. During the stress barium an intrabolus pressure of 44.5 ± 16.0 mmHg lead to cessation of intake.

Conclusions: In LAGB patients, normal oesophageal peristaltic contractions transition to a LOS aftercontraction producing trans-LAGB flow. Repeated contractions are required to clear a semi-solid bolus. Incorporating measurements of the LECS into assessments of oesophageal motility in LAGB patients may improve the usefulness of this investigation.

Introduction

Laparoscopic adjustable gastric banding (LAGB) is established as a safe and effective bariatric procedure [1, 283, 301]. There has been much focus on the importance of oesophageal function following LAGB [9], however, a lack of understanding of the expected post LAGB physiology has limited the usefulness of tests such as oesophageal manometry. New data have suggested that in successful patients the LAGB limits flow, thereby delaying bolus transit into the stomach [533, 537]. Repeated oesophageal contractions appear to mediate episodes of flow across the LAGB. This indicates that specific aspects of oesophageal function, probably those associated with overcoming the resistance of the LAGB, are important. If these mechanisms were better defined the assessment of oesophageal motility could be established as a diagnostic test in LAGB patients.

Normally, the key components of oesophageal function are coordinated peristalsis and lower oesophageal sphincter (LOS) relaxation [466]. In subjects without a LAGB, the intrabolus pressure required to generate flow across the oesophago-gastric junction (OGJ) during water swallows is generally only 5 mmHg [495]. This is easily achieved when the lower oesophageal sphincter relaxes in response to a propagating peristaltic contraction [496]. Even if there is impaired deglutitive LOS relaxation, successful bolus transit can occur provided adequate pressures are generated in the distal oesophagus [500]. An uninterrupted, propagating oesophageal pressure wavefront of 30 mmHg has been defined as necessary to prevent bolus escape [499] and is the basis for classifying swallows as normal or

abnormal [501]. Disturbance of these processes results in impaired bolus transit; the likely basis of many symptoms of dysphagia [522].

When a LAGB is optimally adjusted it produces an intraluminal pressure of approximately 20-30 mmHg, 1-2 cm distal to the caudal end of the LOS [533, 538]. This creates a situation akin to impaired deglutitive LOS relaxation where the oesophagus must overcome a resistance at the OGJ. To generate flow this resistance must be exceeded by the intrabolus pressure. In a LAGB patient it is likely that a coordinated contraction of the LOS is significant in maintaining the intrabolus pressure above the LAGB, thereby facilitating flow. It has been shown, both in patients and in-vitro, that the LOS has similar contractile properties to proximal oesophageal muscle [463, 475-477]. In-vivo this property has been defined as a LOS aftercontraction [477]. However, its contribution to bolus transit has not been investigated.

We aimed to evaluate the mechanism by which liquid and semi-solid boluses were transited across the LAGB; thereby defining the facets of oesophageal function important to LAGB patients. It was hypothesised that coordinated oesophageal peristalsis and an effectively contracting lower oesophageal sphincter were required to generate flow across the LAGB. We also aimed to determine the intraluminal pressures associated with the generation of basic visceral sensations that appear to be important in slowing eating behaviour and mediating meal termination.

Methods

The Monash University and Melbourne Health human ethics committees approved this research and all patients gave informed consent.

Subjects

Patients who had undergone LAGB and achieved a successful outcome were invited to participate. Inclusion criteria were: loss of >50% excess weight after 12 months, no previous bariatric or oesophago-gastric surgery prior to LAGB placement and no adverse symptoms. Pregnant patients were excluded.

Study Protocol

A 21-channel water perfused manometry system with a custom made silicone rubber manometry catheter (Dentsleeve, Ontario, Canada) was used. The intraluminal pressure at the level of the LAGB was measured, with the patient standing, after a 15 second period of not swallowing.

Video manometry involved recording synchronous manometry and transit data with the patient standing. Data was captured by TRACE! 1.2 (written by G Hebbard using LabVIEW, National Instruments, Austin, Texas). Two 5 ml barium (liquid) swallows were performed, followed by 2 swallows of 10 ml of barium soaked porridge (semi-solid). After each bolus was swallowed, continuous screening was performed for 30 seconds or until the bolus had passed through the LAGB. When clearance was not immediate, intermittent screening was used when any oesophageal pressure indicative of a contraction was observed. There was at least a

one minute rest period between clearance of a bolus through the LAGB and administration of the next bolus.

Finally, a stress barium was performed. This involved two consecutive spoonfuls of porridge followed immediately by drinking rapidly from a cup of 80 ml of barium, via a straw. Patients were instructed to cease drinking when they felt excessively full, nauseated or developed discomfort. The aim was to induce a transient obstruction above the LAGB and determine the intraluminal pressure that lead to cessation of intake.

Interpretation and Analysis of Video Manometry

Analysis was based on each swallowed bolus. The total number of oesophageal contractions required to generate complete clearance was recorded. Swallows were classified as normal or hypotensive according to standardised criteria [501]. Contractions were classified as secondary if no pharyngeal initiation was observed. The duration of flow across the LAGB was recorded for each contraction.

Detailed Pressure Topography and Video Manometry Analysis

For each oesophageal contraction detailed topographical analysis was undertaken. Data were collected on: peak pressure at the level of the LOS, peak intrabolus pressure (defined as the intraluminal pressure in the isobaric zone above the LAGB) and peak pressure in the distal oesophagus. The method of separating the intraluminal pressure at the level of these close anatomical structures has been described previously [533]. The duration a pressure greater than 30 mmHg was maintained at the level of the LOS, once the peristaltic wave had reached this level,

was recorded. The lower oesophageal contractile segment (LECS) was assessed for each contraction as being intact or deficient, as defined below.

The intraluminal pressure at the level of the LAGB was measured using a virtual sleeve placed over the high pressure zone representative of the LAGB. The mean peak end expiratory pressure, observed over 5 respiratory cycles, was recorded.

The Lower Oesophageal Contractile Segment

We defined a new measurement: The lower oesophageal contractile segment (LECS). It aimed to measure the coordination of the transition of the oesophageal peristaltic wave from the distal oesophagus to the lower oesophageal sphincter and the ability of the LOS to generate and maintain an aftercontraction. This segment was defined anatomically as the lower 2 cm of oesophagus and the lower oesophageal sphincter. For the LECS to be intact it needed to demonstrate all of:

1) A pressure greater than 30 mmHg at the lower oesophageal sphincter, measured at end expiration

2) Maintenance of that pressure for greater than 0.5 seconds

3) A lower oesophageal sphincter closing pressure, exceeding the pressure within the isobaric zone by > 5 mmHg.

4) Coordinated transition of the peristaltic wave from the lower oesophagus to the lower oesophageal sphincter, with no (vertical) defect in the 30 mmHg isobaric contour greater than 0.5 cm.

Figure 16.1 shows 2 swallows categorised as normal, however, demonstrating an intact and deficient LECS.

FIGURE 16.1: Lower Oesophageal Contractile Segment in Swallows Classified as
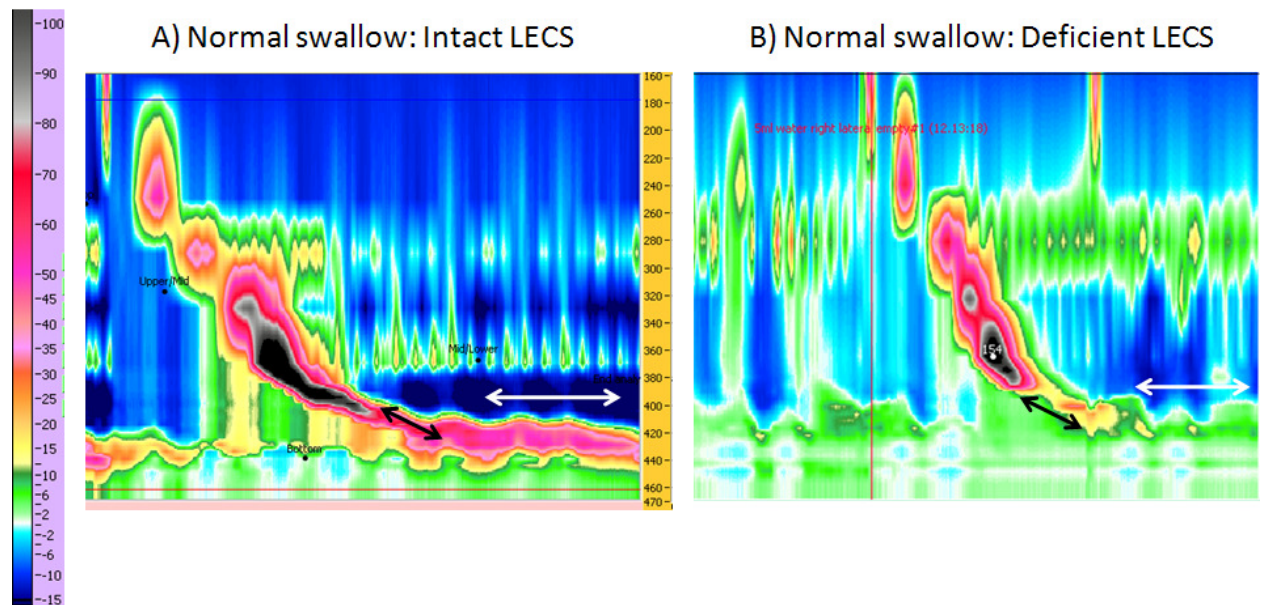
Normal

Figure 16.1 Legend: *Two 5 ml right lateral water swallows from LAGB patients, both*

classified as normal according to standardised criteria. In panel A, there is normal

oesophageal body peristalsis that transitions (black double headed arrow) to a

sustained lower oesophageal sphincter aftercontraction (white doubled headed

arrow). The LECS is intact. In contrast, in panel B, whilst oesophageal body

peristalsis is intact, there is poor transition of the peristaltic wave to the lower

oesophageal sphincter and there is no LOS aftercontraction. The LECS is deficient.

Statistical analysis

All statistical computations were performed using SPSS V 16.0 (SPSS Inc, Chi, Ill). For

comparisons of means derived from repeated measurements, paired t tests were

used. For comparison of multiple measures derived from the same subject a

repeated measures ANOVA was used. Step wise (multiple) linear regression was used to establish predictors of continuous outcome measures. A two sided *p* value of 0.05 was considered statistically significant. Data are presented as means and standard deviation.

Results

Twenty patients participated in the study; details are shown in Table 16.1. All had achieved and maintained a substantial weight loss. All LAGBs were LAP-BANDS[TM] (Allergan, CA). There were seven 10 cm bands, 3 VG[TM], and 10 APS[TM] bands.

All patients successfully cleared the liquid swallows. Three patients developed an immediate obstruction when ingesting the semi-solid, complaining of dysphagia and discomfort. Therefore they did not undergo the stress barium and analysis of the semi-solid swallow was not possible.

Age (years)	48.3±12.0
Male/Female (number)	4/16
Current weight (kg)	84.9±15.9
Current BMI (kg/m^2)	30.9±4.9
Pre-operative weight (kg)	115.8±23.4
Pre-operative BMI (kg/m^2)	42.3±7.3
Excess Weight Loss (%)	65.6±18.0
Weight loss (kg)	30.9±14.2
Duration post surgery (years)	2.4±2.2
Intraluminal pressure at the level of the LAGB (standing) (mmHg)	19.2±9.9
Lower oesophageal sphincter basal tone (mmHg)	12.8±7.3

Data are mean and standard deviation

General Characteristics of Oesophageal Clearance During Semi-Solid Swallows

After swallowing, flow across the LAGB commenced only when the intrabolus

pressure exceeded the intraluminal pressure at the level of the LAGB. Two patterns

of flow were observed, these are shown in Figure 16.2. In type 1, defined as *native*

clearance, flow is generated in a similar manner to patients without a LAGB. Flow

commenced well before the peristaltic contraction reached the level of the LOS and

was largely complete by the time it reached the LOS. Ten patients demonstrated this pattern of clearance. Type 2 was defined as *LOS dependent clearance*; 7 patients demonstrated this pattern. The intrabolus pressure, generated ahead of the advancing peristaltic wavefront, was inadequate to generate flow. Once the peristaltic wave reached the level of the LOS, there was an LOS aftercontraction that increased the intrabolus pressure above the LAGB and resulted in flow. Flow only occurred whilst the intrabolus pressure was maintained by the LOS aftercontraction. In both patterns once the contraction completed there was reflux of the remaining bolus (if any) back into the oesophagus before a further peristaltic contraction was initiated (usually another swallow). This cycle continued until clearance was complete.

Patients were able to accurately determine whether the semi-solid bolus had passed through the LAGB. This was more apparent during the stress barium, where once the pouch was fully distended and a peak pressure observed within the isobaric region, reflux was observed and patients ceased drinking and reported sensations of fullness. In the 3 patients, where an acute obstruction developed during a semi-solid swallow, there were symptoms of dysphagia and discomfort and these patients were aware of the obstruction. Multiple swallows with vigorous peristalsis were observed. Part of the bolus, above the obstruction, refluxed after each peristaltic contraction.

Figure 16.2: Patterns of Oesophageal Clearance

LOS Dependent Clearance
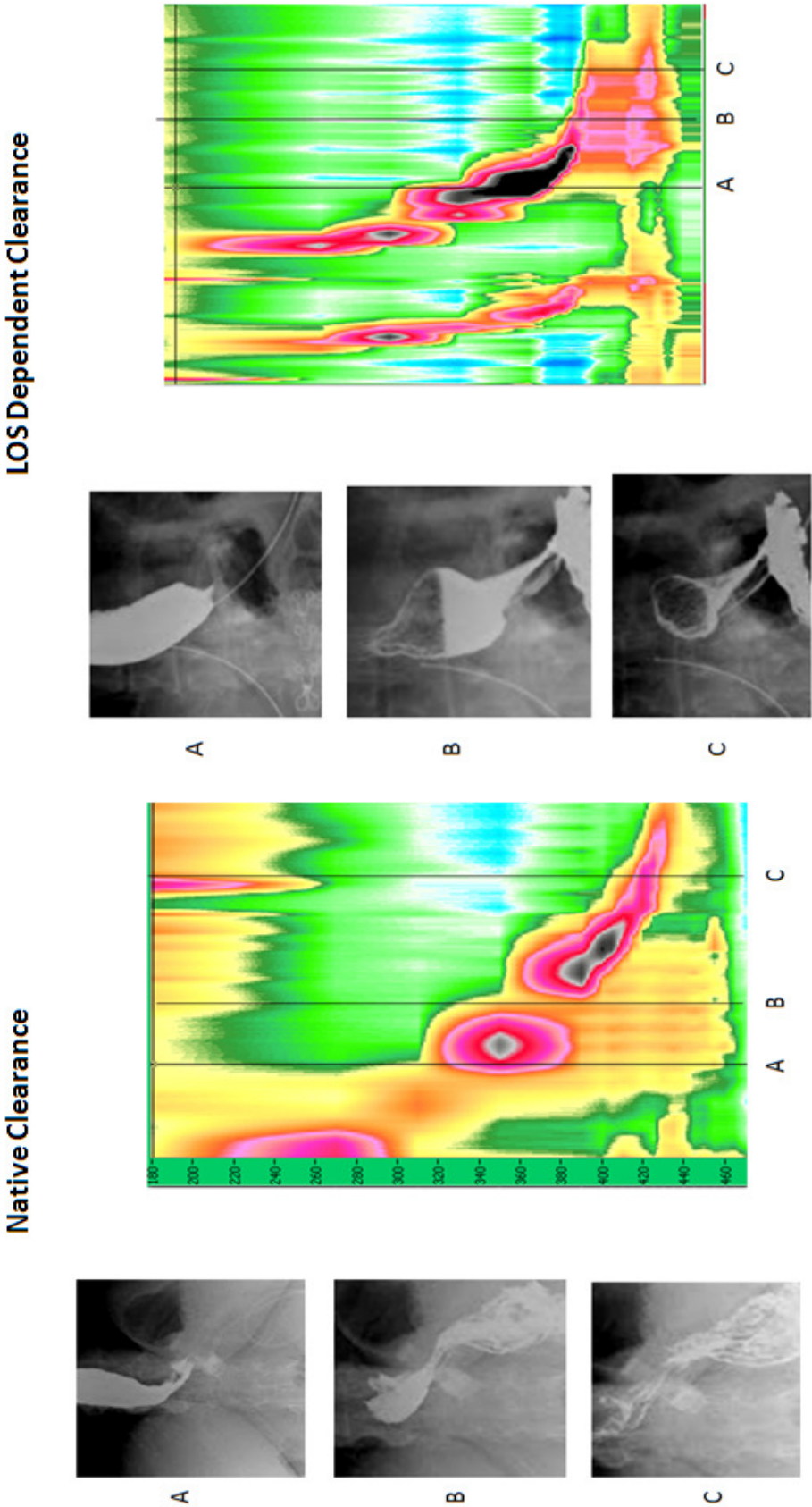
Native Clearance

Figure 16.2 Legend: *In the native oesophageal clearance pattern flow commences at A, well before the peristaltic wave has reached the lower oesophageal sphincter. The intrabolus pressure has exceeded the resistance of the LAGB, allowing flow. This continues at B, although by the time the peristaltic contraction reaches the lower oesophageal sphincter the bolus has been cleared. In the LOS dependent pattern, at A, whilst there is intrabolus pressurisation, flow has not commenced. Once the peristaltic wave reaches the level of the LOS there is an increase in intrabolus pressure and flow is observed. The LOS contraction is maintained out to C with ongoing flow whilst this positive gradient exists.*

Comparison of native vs. LOS dependent oesophageal clearance

The LOS dependent group required more contractions to clear the liquid 1.6±1.0 vs. 3.5±2.4, (*p=0.04*) and the semi-solid 3.6±2.8 vs. 6.7±2.1, (*p=0.04*). There were no differences in %excess weight loss (EWL) between these two groups 65.3±20.4% vs. 68.5±19.2%, (*p=0.74*). The intraluminal pressure at the LAGB was not statistically significantly different, 22.6±7.7 mmHg vs. 16.6±5.1 mmHg, (*p=0.13*).

Figure 16.3 compares the differences in intraluminal pressure during liquid and semi-solid swallows stratified by the pattern of oesophageal clearance. The intrabolus pressure was elevated in the LOS dependent group during liquid swallows. During semi-solid swallows the LOS pressure and intrabolus pressure were significantly higher in the LOS dependent group.

Figure 16.3: Intraluminal Pressure During LOS Dependent and Native Oesophageal Clearance
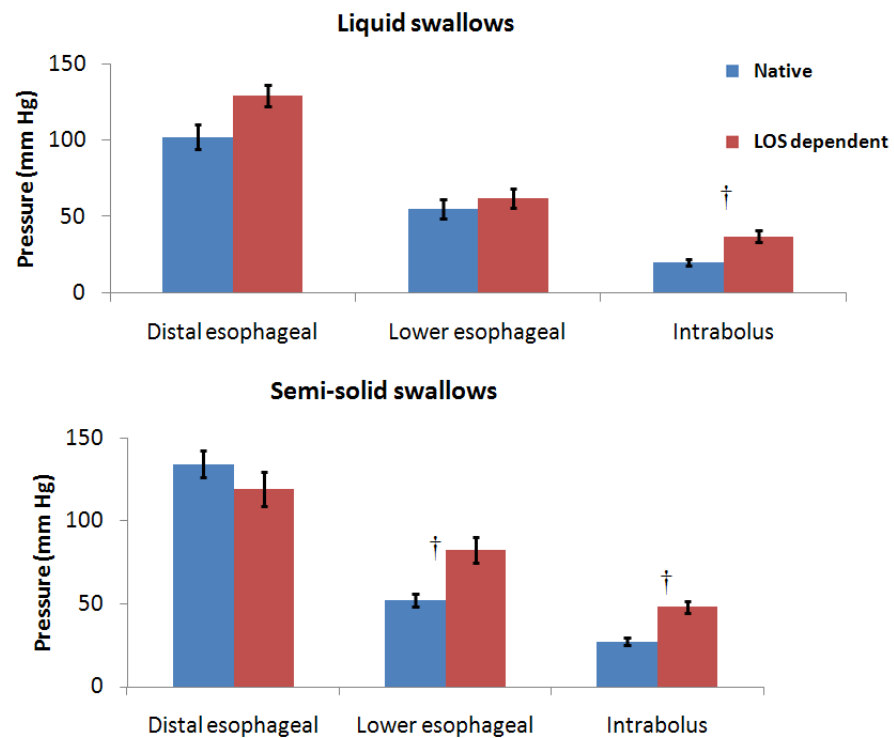
Figure 16.3 Legend: *During liquid swallows, the LOS dependent group demonstrates a significantly elevated intrabolus pressure, however no other differences were observed. During semi-solid swallows, the LOS dependent group develop higher intraluminal pressure at the level of the LOS and a higher intrabolus pressure, although distal oesophageal pressure was not different.*

† p<0.05

Data are mean and standard error

Overall, more contractions were required to clear semi-solids than liquid: 4.6±2.9 vs. 2.2±1.8, (*p=0.002)*. More normal swallows: 3.4±2.8 vs. 1.2±1.0 (*p=0.002)* were observed with semi-solid than liquid swallows*;* no difference in the number of hypotensive swallows: 0.8±1.1 vs. 0.5±0.7, (*p=0.36)* or secondary contractions; 0.9±1.1 vs. 0.5±0.8 (*p=0.09)* was observed.

For liquid swallows, categorised as normal, the mean duration of flow was: 8.4±4.2 sec. vs. 3.1±2.9 sec. for hypotensive swallows (*p=0.14*) and 0.6±0.9 sec. for secondary contractions (*p=0.007)*. For semi-solids: normal swallows 7.0±4.0 sec. vs. 2.1±3.6 sec. for hypotensive swallows (*p=0.02),* vs. 0.6±1.1 sec. for secondary contractions (*p=0.005)*.

The intrabolus pressure was higher in liquid swallows classified as normal: 31.7±17.6 mmHg compared to hypotensive: 22.7±13.9 mmHg, (*p=0.05)* or secondary contractions: 12.3±5.0 mmHg, (*p=0.05)*. During semi-solid swallows, the intrabolus pressure was higher in swallows classified as normal: 41.2±15.9 mmHg compared to hypotensive swallows: 19.2±3.5 mmHg, (*p=0.007)*. No significant difference was observed between normal swallows and secondary contractions: 27.8±17.3 mmHg, (*p=0.13)*.

Multiple linear regression showed predictors of an increased duration of flow with liquid swallows classified as normal were: Increased distal oesophageal pressure, increased intrabolus pressure and a longer duration of the lower oesophageal contraction (*r^2=0.63, p<0.005)*. For semi-solid swallows classified as normal, only an

increased distal oesophageal pressure predicted an increased duration of flow ($r^2=$0.37, $p=0.005$). Standardised Beta coefficients are shown in Table 16.2.

TABLE 16.2: Predictors of Increased Duration of Flow (Standardised Beta Coefficients)

	Semi-solid	Liquid
Distal oesophageal pressure (mmHg)	0.49†	0.38‡
Lower oesophageal pressure (mmHg)	-0.13	0.07
Intrabolus pressure (mmHg)	-0.19	-0.37†
Duration of contraction (seconds)	0.39	0.65‡
Intraluminal pressure at the level of the LAGB (mmHg)	-0.19	0.18

Semi-solid: r^2 = 0.37, p=0.005, Liquid: r^2 =0.63, p<0.005

†p<0.05, ‡p<0.005

More liquid swallows categorised as normal demonstrated an intact LECS than did hypotensive swallows: 90% vs. 38%, (*p<0.005*). Too few secondary contractions were observed to allow statistical analysis. During semi-solid swallows, an intact LECS was observed in 81% of normal swallows, 29% of hypotensive swallows and none of the secondary contractions, (*p < 0.005*).

The duration of flow was significantly longer for contractions where the LECS was intact: Liquid swallows: 7.6±4.4 sec. vs. 1.9±2.6 sec., (*p<0.005*). Semi-solid swallows: 7.1±3.8 sec. vs. 1.6±3.2 sec., (p<*0.005*).

Pressure Topography

During normal swallows, significant differences in the intraluminal pressures were observed during liquid and semi-solid swallows and during the stress barium. At each location assessed there was a step wise increase in pressure from liquid to semi-solid to stress barium. Figure 16.4 illustrates these differences

The mean peak intrabolus pressure was 44.5±16.0 mmHg (range 25-77 mmHg) during the stress barium. This was the pressure at which patients ceased intake and reported sensations of fullness.

Predictors of intrabolus pressure

There were no predictors of intrabolus pressure during liquid swallows (r^2=0.33, *p=0.13*). During semi-solid swallows, predictors of intrabolus pressure (r^2=0.77, *p<0.005*) were the intraluminal pressure at the level of the LAGB and the amplitude of the lower oesophageal contraction. During the stress barium, distal oesophageal pressure was the only predictor of intrabolus pressure (r^2=0.75, *p<0.005*). Standardised Beta coefficients are shown in Table 16.3.

Figure 16.4: Intraluminal Pressure During Liquid Swallows, Semi-solid Swallows and Stress barium
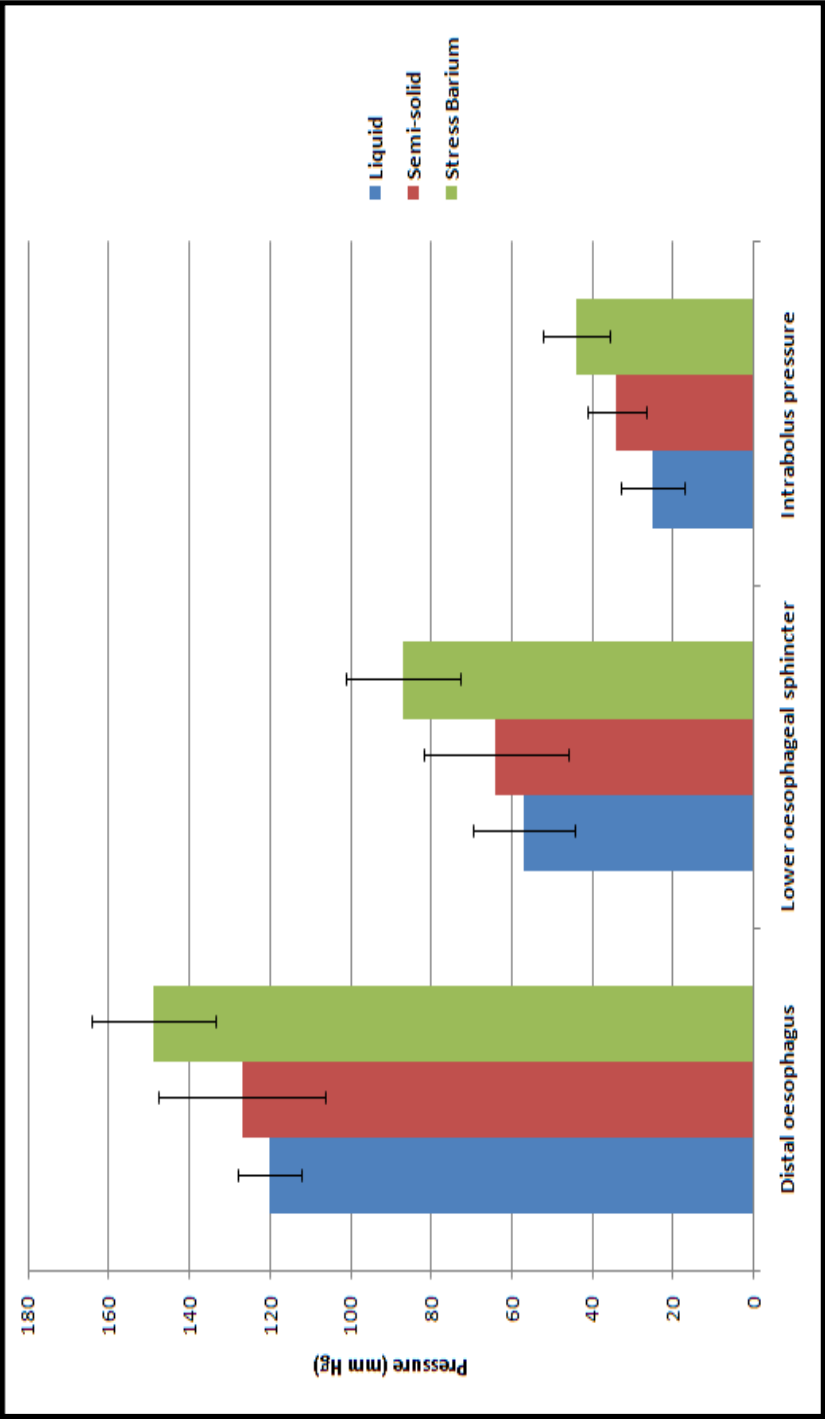
Figure 16.4 Legend: *At each site there was a significant, step wise, increase in intraluminal pressure when comparing liquid to semi-solid to the stress barium. This illustrates the changes in distending pressure transmitted to the luminal wall with alterations in eating behaviour.*

Data are mean and standard error.

TABLE 16.3: Predictors of Intrabolus Pressure During Semi Solid Swallows and Stress Barium (Standardised Beta Coefficients)

	Stress barium	Semi-solid
Intraluminal pressure at the level of the LAGB (mmHg)	-0.12	0.55‡
Distal oesophageal pressure (mmHg)	0.63‡	0.24
Lower oesophageal pressure (mmHg)	0.52‡	0.62‡

Semi-solid swallows: r^2=0.77, *p<0.005.* Stress barium: r^2=0.75, *p<0.005.*

‡p<0.005

Discussion

We have shown that the optimally adjusted LAGB briefly delays the passage of liquid and semi-solid boluses through the LAGB. Episodes of flow, mediated by repeated oesophageal peristalsis, clear the bolus. Two patterns were observed: A native type, where flow commenced once the intrabolus pressure exceeded the

resistance of the LAGB, occurring well before the peristaltic contraction reached the LOS and a LOS dependent type where flow only occurred during a LOS aftercontraction. More contractions and higher intra-bolus pressures were required to generate flow and complete clearance in the LOS dependent type. Primary swallows, categorised as normal, initiated flow, whereas hypotensive or secondary contractions were not as effective. An intact LECS was found to be a major difference between contractions generating flow and those that did not.

During semi-solid swallows, the intrabolus pressure was determined by the intraluminal pressure at the level of the LAGB and the amplitude of the LOS aftercontraction. The amplitude of the distal oesophageal contraction determined this pressure during the stress barium. This is not surprising, as the stoma of the LAGB had been transiently obstructed. A mean, peak, intrabolus pressure of 44.5 mmHg, was observed during the stress barium. This was associated with sensations that lead to cessation of intake.

Standardised criteria define normal swallows as possessing an intact, propagating 30 mmHg pressure domain [501]. This decreases the likelihood a swallowed bolus will escape the peristaltic contraction [499]. In LAGB patients, normal oesophageal body motility is required to deliver the bolus to the LOS and small volume of stomach above the LAGB. Hypotensive or secondary contractions were not effective at achieving this. Once positioned immediately above the LAGB, the intrabolus pressure needs to exceed the intraluminal pressure at the level of the LAGB to generate flow. Regulated transition of the peristaltic wave to a LOS

aftercontraction can contribute to initiating and maintaining flow; this can be assessed using the LECS.

LAGB patients are advised to take small mouthfuls of appropriate foods and chew them thoroughly. This affects the viscosity of the swallowed bolus significantly, a property known to alter oesophageal transit [539]. Our data show that if a bolus can be transited across the LAGB in stages, successful clearance generally occurs. This is representative of most semi-solid or softer foods that are chewed well, provided a modest sized bolus is swallowed. In contrast, more congruent foods such as white bread or red meat, or more viscous semi-solids, will not transit across the LAGB as they remain an intact bolus.

We have defined a unique pattern of oesophageal clearance. In LAGB patients, primary peristalsis drives flow. However, the time limited nature of each contraction means that complete clearance is not always achieved. In subjects without a LAGB, a flow permissive time, where the intrabolus pressure exceeds the OGJ resistance, of 2.5 seconds is generally adequate to clear the bolus [496]. In LAGB patients, when a positive pressure gradient is achieved, the rate of flow is limited by the LAGB and the duration of the contraction. Therefore repeated peristaltic contractions are required to clear the bolus.

After a peristaltic contraction has completed, any residual pressurised bolus refluxes back into the oesophagus. The oesophagus is innervated by a complex neural network that responds to distension induced by reflux by contracting [474]. We observed predominantly primary, rather than secondary peristalsis in response to these reflux events. This is usual, even following low volume reflux events [485].

Although pharyngeal skeletal muscle contractions were observed on the manometry trace, patients were not consciously initiating these. Pharyngeal swallowing, without oral initiation, is well documented as a protective reflex when minimal amounts of fluid contact the luminal wall in this region [484]. This staged clearance, with repeated reflux events is a novel pattern of oesophageal clearance. It is different to the repeated swallows observed in normal subjects who ingest a large bread bolus, where transit stops at specific points within the oesophageal body [539].

These patients were able to interpret visceral sensations generated by pressurisation of the lumen immediately above the LAGB. During the stress barium, a mean intrabolus pressure of 44.5 mmHg was observed. This resulted in patients stopping drinking prior to the oesophagus becoming overfilled. The patients who developed obstruction were aware that the bolus had impacted at the LAGB stoma. The generation and interpretation of sensations generated by luminal distension appear important for success with the LAGB. Without these, appropriate modification of eating behaviour cannot occur.

Luminal dilatation above the LAGB has emerged as the most significant post LAGB problem [310]. The aetiology is unclear, although transmitted force to the luminal wall must be a factor. We have shown that a tighter LAGB, when resistance is measured as an intraluminal pressure, results in a higher distending pressure during semi-solid swallows. This will occur with each eating episode. Alternatively, during episodes of obstruction, the intrabolus pressure is increased further, being mediated by distal oesophageal contractions responding to the obstruction. We

suspect even higher pressures occur when a larger bolus of inappropriately textured food is swallowed and becomes impacted.

Whether chronic exposure to increased pressure due to a tighter LAGB, or intermittent episodes of obstruction inducing very high pressures, are greater risks for symmetrical pouch dilatation is unknown. Regardless, good eating behaviour should be emphasised, with adjustments aiming to produce satiety rather than mechanical restriction.

Video manometry has helped establish a paradigm of oesophageal function in LAGB patients. Repeated oesophageal contractions and a lower oesophageal sphincter aftercontraction are not expected, or assessed, when motility is evaluated using conventional criteria. These significant differences in oesophageal function post LAGB may explain why standardised criteria have not proven useful in these patients. The technique of video manometry is complex, time consuming and only allows the assessment of a small number of swallows. The next logical step is to apply this knowledge to supine water swallows. This will allow us to establish criteria for objectively assessing oesophageal motility in LAGB patients. We would aim to integrate current high resolution manometry diagnostic criteria regarding oesophageal body motility with an assessment of the LECS.

Declaration for Thesis Chapter 17

This Chapter represents a manuscript that has been published in *Obesity Surgery* (*Obes Surg. 2009 Dec 12. [Epub ahead of print]*).

Declaration by candidate

In the case of Chapter 17 the nature and extent of my contribution to the work was the following:

Nature of contribution	Extent of contribution (%)
Overall responsibility for all aspects of the study, conception, planning, patient recruitment, conducting experiments and recording data. Data analysis and interpretation. Statistical analysis. Crafting and revising manuscript, submission to journal.	>90%

The following co-authors contributed to the work:

Name	Nature of contribution
Wendy A Brown	Designing study, and recruiting patients, data analysis, manuscript review
Cheryl Laurie	Recruiting and conducting studies
Geoff Hebbard	Experiment design, data acquisition and analysis, review of manuscript
Paul O'Brien	Experiment design, data acquisition and analysis, review of manuscript

Candidate's Signature		Date

Declaration by co-authors

The undersigned hereby certify that:

(1) the above declaration correctly reflects the nature and extent of the candidate's contribution to this work, and the nature of the contribution of each of the co-authors.
(2) they meet the criteria for authorship in that they have participated in the conception, execution, or interpretation, of at least that part of the publication in their field of expertise;
(3) they take public responsibility for their part of the publication, except for the responsible author who accepts overall responsibility for the publication;
(4) there are no other authors of the publication according to these criteria;
(5) potential conflicts of interest have been disclosed to (a) granting bodies, (b) the editor or publisher of journals or other publications, and (c) the head of the responsible academic unit; and
(6) the original data are stored at the following location(s) and will be held for at least five years from the date indicated below:

Location(s)	Monash University, Alfred Hospital

		Date
Wendy A Brown		27/10/09
Cheryl Laurie		4/11/09
Geoff Hebbard		2/11/09
Paul E O'Brien		27.10.09

Chapter 17: *Criteria for Assessing Oesophageal Motility in Laparoscopic Adjustable Gastric Band Patients: The Importance of the Lower Oesophageal Contractile Segment*

Abstract

Background: Oesophageal function appears critical in laparoscopic adjustable gastric band (LAGB) patients, however, conventional motility assessments have not proven clinically useful. Recent combined video fluoroscopic and high resolution manometric studies have identified important components of oesophageal function in LAGB patients.

Methods: Successful and symptomatic LAGB patients, with normal or mildly impaired oesophageal peristalsis, underwent a standardised, water swallow high resolution manometry protocol. The lower oesophageal contractile segment (LECS) was specifically assessed and combined with conventional measures of oesophageal motility. Differences in response to changes in LAGB volume were assessed.

Results: There were 101 symptomatic and 29 successful patients. More symptomatic patients had a mild impairment in oesophageal motility (39.6% vs. 3.4%, *p<0.005*). Successful patients demonstrated an intact LECS during normal swallows more frequently than symptomatic patients (95% vs. 43%, *p<0.005*). Absolute intraluminal pressures were not different between the groups. Removing all fluid from the LAGB revealed more hypotensive swallows in the symptomatic patients (30% vs. 17%, *p=0.002*), an effect not observed when the LAGB volume was increased (8% vs. 5%, *p=0.21*). Receiver operator characteristic analysis determined

that an intact LECS in 70% of normal swallows defined normal motility in LAGB patients.

Conclusions: The LECS is a valuable measure of oesophageal function in LAGB patients and complements conventional manometric criteria. Symptomatic patients have less normal swallows; however, these also frequently demonstrate a deficient LECS. Further information can be elucidated by performing swallows at differing LAGB volumes. High resolution manometry, using these adapted criteria, is now a useful investigation in symptomatic LAGB patients.

Introduction

Laparoscopic adjustable gastric banding (LAGB) is an increasingly popular treatment for obesity [1, 2]. Whilst normal oesophageal function appears to be important for the success of the procedure [9], manometry has not proven useful in the assessment of symptomatic patients [441, 442]. This may be because the components of oesophageal function relevant to LAGB patients are not specifically assessed and until recently, were not well defined [533].

New data, derived using concurrent video fluoroscopy and high resolution manometry, have determined that successful LAGB patients demonstrate delayed but effective transit of liquid and semi-solid boluses across the LAGB [533]. This is mediated by repeated swallows that produce a pattern of episodic flow, until clearance is complete. Individual peristaltic contractions efficiently transition to a lower oesophageal sphincter aftercontraction, driving flow against the resistance of the LAGB [540]. This new understanding offers the opportunity to adapt conventional manometric techniques and modify diagnostic criteria, making them applicable to LAGB patients.

High resolution manometry has clarified some of the effects of the LAGB on oesophageal motility [533, 538]. Normal contractility, with an attenuated lower oesophageal sphincter (LOS) that relaxes appropriately, is observed in successful patients [533]. Disappointingly, new standardised high resolution manometry diagnostic criteria [501] have not proven clinically useful when applied to LAGB patients [537]. Whilst symptomatic patients do have worse overall motility, almost all of this is accounted for by mild peristaltic impairment [537]. This is not

considered a significant disturbance in oesophageal function. When analysed on the basis of total swallows, differences are even more difficult to appreciate with symptomatic patients having only 10% less normal swallows than successful patients [537]. These statistical differences do not account for the completely different outcomes observed.

Standardised criteria for the reporting of oesophageal motility were developed primarily to assess the capacity of individual oesophageal peristaltic contractions to completely transit a bolus across the oesophago-gastric junction (OGJ) [508]. They also, quite correctly, focus on relaxation rather than aftercontraction of the lower oesophageal sphincter [501]. Staged bolus clearance is not considered; as any peristaltic contraction during which oesophageal clearance is not achieved is considered abnormal and was the basis for these criteria [494]. Complete clearance of a swallowed semi-solid or liquid bolus is not expected in a LAGB patient after one peristaltic wave, generally 3-5 contractions are required [540].

In LAGB patients the generation of trans-LAGB flow requires a positive pressure gradient across the band, a well established mechanical necessity observed in non-LAGB patients generating flow across the OGJ [495, 496]. A coordinated lower oesophageal sphincter aftercontraction, occurring in series with the oesophageal peristaltic wave, is the most effective way of maximising flow [540]. The reliance on the LOS contraction is not surprising given the resistance of the LAGB is 1-2 cm distal to the caudal end of the oesophagus. Experiments, both in patients and on the bench top, have illustrated that the LOS has similar contractile properties to the more proximal oesophageal muscle [463, 475-477].

We have developed a means of assessing the contractile function of the lower oesophagus, defining this measurement as the lower oesophageal contractile segment (LECS). The LECS assesses the transition of the peristaltic wave to a sustained LOS aftercontraction. If this can be combined with an accurate assessment of the ability of the oesophageal body to deliver a bolus to the LOS, a means of comprehensively assessing oesophageal motility in LAGB patients could be established.

We hypothesised that measurements of the ability of the oesophagus to generate bolus transit across the resistance of the LAGB would be important in assessing oesophageal motility in LAGB patients. Our aim was to validate the assessment of oesophageal motility in LAGB patients using a modified conventional high resolution manometry protocol, performed with water swallows.

Methods

The Monash University and Melbourne Health human ethics committees approved this research and all patients gave informed consent.

Subjects

Symptomatic patients following LAGB, for the purposes of this study, were defined as patients aged between 18 and 65 years, who experienced either poor weight loss (<25% of excess weight loss >12 months post-operatively) and/or had adverse symptoms (volume reflux, dysphagia, regurgitation or the inability to tolerate fluid in the LAGB due to these symptoms), despite a normal or near normal liquid contrast swallow. A control group of successful patients were recruited. These were

defined as: patients who had lost >50% excess weight after 12 months, who had had no previous bariatric or oesophago-gastric surgery prior to LAGB placement and who were experiencing no adverse symptoms.

Experimental Protocol

All patients underwent a standardised manometry study. This technique, when performed in LAGB patients, has been described [533]. In brief, a 21-channel water perfused manometry system with a custom made 21 channel silicone rubber manometry catheter (Dentsleeve, Ontario, Canada) was used. The catheters were designed specifically to assess the region of the OGJ, incorporating and differentiating pressures generated by the lower oesophagus, LAGB and crural diaphragm. The manometry system was connected to a personal computer via data acquisition and video input cards (National Instruments, Austin, Texas). Manometry data was recorded and analysed with TRACE! 1.2 (written by G Hebbard using LabVIEW, National Instruments, Austin, Texas).

After performing 10 supine, 5 ml water swallows the LAGB port was accessed using a 21 gauge Huber tipped needle. Basal measurements and 5 further right lateral swallows were performed with the LAGB empty and following a 20% increase from the starting volume.

Oesophageal Motility Analysis

Oesophageal motility was analysed according to standardised criteria [501]. Only those patients with a diagnosis of either normal or mildly impaired oesophageal motility were included in this study. This was because the profound nature of more

severe oesophageal body peristaltic dysfunction (<30% normal swallows) was deemed an adequate explanation for patients demonstrating impaired bolus transit.

Only swallows classified as normal or hypotensive, according to published criteria [501], were analysed in more detail (see below). Failed swallows were not considered as we have shown that hypotensive swallows are not effective at generating flow against the resistance of the LAGB. Therefore, grossly abnormal (failed or synchronous contractions) swallows cannot be expected to create flow. For the purposes of this study hypertensive swallows were also considered normal, as there is nothing to suggest that bolus transit is impaired by increased peristaltic amplitude.

Each swallow was assessed to determine if the LECS was intact or deficient. The criteria we defined for assessing the LECS have been previously described [540]. In brief, this consisted of measuring the transition of an intact pressure domain from the distal oesophagus to a sustained lower oesophageal sphincter aftercontraction. The way these data are extracted from a high resolution manometry topographical plot is illustrated in Figure 17.1.

FIGURE 17.1: Assessing the Lower Oesophageal Contractile Segment
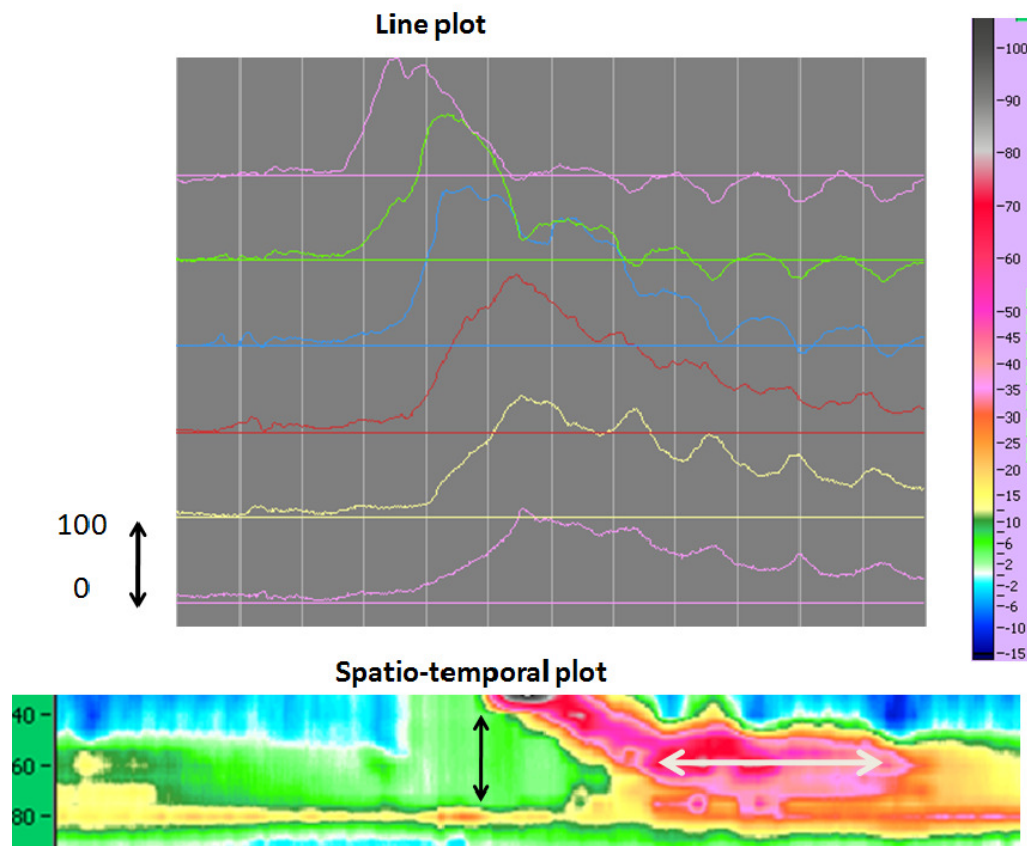
Figure 17.1 Legend: *A focused (over lower 4 cm of oesophagus) high resolution manometry plot of the lower oesophageal contractile segment displayed as a line plot and a spatiotemporal plot. It shows coordinated transition of the oesophageal peristaltic wave to a lower oesophageal sphincter after contraction. The pressure at each of the line plot sites is represented by the height above its own baseline (in mmHg). The scale for the spatiotemporal plot is shown. In the spatio-temporal plot, the vertical extent of the transition zone between the oesophageal peristaltic wave and the lower oesophageal sphincter is designated by the black double headed arrow. The white double headed arrow demonstrates the duration of pressurisation >30 mmHg, by the lower oesophageal sphincter aftercontraction. The LECS assesses the ability of a bolus to be efficiently delivered from the distal oesophagus to the LOS region and the ability of the LOS aftercontraction to drive flow across the LAGB.*

For each swallow data were collected on: peak pressure at the level of the LOS,

peak intrabolus pressure (defined as the intraluminal pressure in the isobaric zone

above the LAGB) and peak pressure in the distal oesophagus. The method of

separating the intraluminal pressure at the level of these close anatomical

structures has been described previously [533]. The duration a pressure of greater

than 30 mmHg was maintained at the level of the LOS, once the peristaltic wave

had reached this level, was recorded. The pressure at the level of the lower

oesophageal sphincter was defined anatomically; in some cases this was contiguous

with the isobaric zone.

For pooled analysis, the median value of a minimum of 2 swallows was used.

Statistical analysis and data management

All weight loss data were obtained from a prospectively maintained online bariatric

database, LAPBASE[TM] *(www.lapbase.net).* All statistical analysis was performed

using SPSS, version 16.0 (SPSS Inc, Chi, Ill). Normally distributed continuous data are

presented as means and standard deviation. For the comparison of continuous,

normally distributed data, t tests were used. For paired comparisons of continuous,

normally distributed data paired t tests were used. For comparison of proportions,

Chi square tests were used. Pearson's correlation coefficient was used for

correlations. A two sided *p* value of 0.05 was considered statistically significant.

Results

One hundred and one symptomatic post operative LAGB patients and 29 successful

patients were studied. Patient details are shown in Table 17.1. Demographic and

baseline characteristics were similar. The unsuccessful patients had lost less weight

and underwent manometry significantly longer after surgery.

TABLE 17.1: Patient Details

	Successful (n=29)	Symptomatic (n=101)	*p* value
Age (years)	49.3±16.0	45.6±12.2	0.19
Males/Females	9/20	13/88	0.09
Current weight (kg)	86.0±15.5	104.6±20.4	<0.005
Current BMI (kg/m^2)	30.6±4.7	38.6±10.3	<0.005
Pre-operative weight (kg)	118.4±22.3	120.3±20.9	0.69
%Excess weight loss	66.6±18.7	31.6±26.9	0.42
Weight loss (kg)	32.4±14.0	16.4±15.5	<0.005
Duration since surgery (years)	2.8±2.7	4.6±2.4	0.004

Data are mean and standard deviation

There were 2020 swallows (in symptomatic patients) and 580 swallows (in

successful patients) available for analysis. More symptomatic patients had a

diagnosis of mild impairment in peristalsis 40 (39.6%) vs. 1 (3.4%), *p<0.005*. On

presentation for the study, successful patients had a significantly tighter LAGB when

resistance was measured as intraluminal pressure at the level of the LAGB (successful patients: 25.7±18.7 mmHg vs. symptomatic patients: 17.5±13.3 mmHg, *p=0.02*).   When fluid was removed from the LAGB there was a significantly greater proportion of hypotensive swallows in the symptomatic than in the successful patients (see Table 17.2). When the LAGB volume was increased, no difference was observed between the groups. Figure 17.2 highlights the differences observed between successful and symptomatic patients when LAGB volume was varied.

In the successful patients, the majority of swallows classified as normal demonstrated an intact LECS. This proportion was higher in the successful than in the symptomatic patients at each of the LAGB volumes tested: start volume (95% vs. 43%, *p<0.005*), empty (84% vs. 43%, *p=0.001*) and when the volume was increased (85% vs. 45%, *p=0.005*).   No difference in the proportion of hypotensive swallows with an intact LECS was identified between the two groups. Start volume (20% vs. 9%, *p<0.16*), empty (0% vs. 16%, *p =0.65*) or when the volume was increased (20% vs. 50%, *p=0.52*).

When all patients were included, there was no correlation between the basal lower oesophageal sphincter tone and the pressure amplitude measured at the lower oesophageal sphincter during normal swallows, *C=0.18, (p=0.07)*. There was no difference when the groups were analysed separately. Successful patients, *C= 0.23, (p = 0.31)* and symptomatic patients, *C= 0.13, (p = 0.25)*.

TABLE 17.2: Classification of Swallows at Different LAGB Volumes

Type of Swallow	Start Volume		
	Successful	Symptomatic	*p* value
Normal	87% (252)	69% (697)	<0.005
Hypotensive	7% (20)	16% (162)	0.02
	Increased Volume		
	Successful	Symptomatic	*p* value
Normal	89% (129)	89% (454)	0.74
Hypotensive	5% (7)	8% (40)	0.21
	Empty		
	Successful	Symptomatic	*p* value
Normal	74% (107)	58% (293)	0.001
Hypotensive	17% (25)	30% (152)	0.002

†All swallows in which there was an intact 30 mmHg isobaric contour with a peristaltic velocity < 8 cm/sec were considered normal

Values shown are percentage of total swallows available for analysis – only swallows categorised as normal or hypotensive were analysed. Bracketed numbers represent total number of swallows in that category.

FIGURE 17.2: Differing Oesophageal Responses to Changes in LAGB Volume
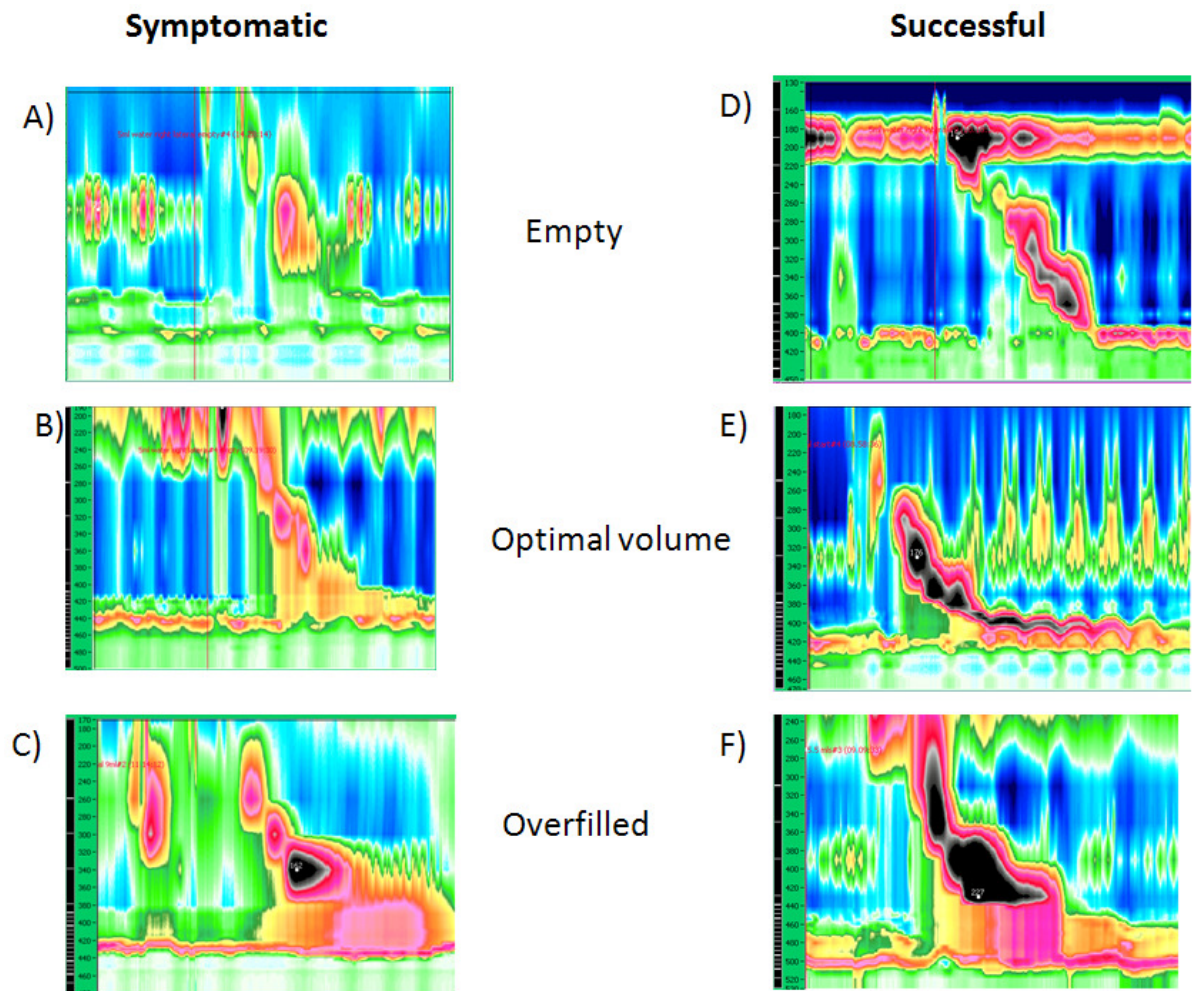
Figure 17.2 Legend: *In the symptomatic patient, in panel A) empty, whilst there is pressurisation of the mid oesophagus, this is a hypotensive swallow as there is a break in the 30 mmHg isobaric contour. Also there is no lower oesophageal sphincter contraction – the LECS is deficient. Comparatively in D) the successful patient demonstrates regulated peristaltic activity to the level of the LOS, with a lower oesophageal sphincter aftercontraction. With fluid in the LAGB, representative of an intraluminal pressure of approximately 20 mmHg at the level of*

the LAGB (B and E), the symptomatic patient demonstrates compartmental pressurisation up to the level of the LOS, whereas a contraction of the LOS is observed in the successful patient. In C), when the LAGB is overfilled, in the symptomatic patient, compartmental pressures are present at the LOS, although a stronger contraction of the distal oesophagus is observed in response to the obstruction. In F), the increased LAGB resistance has lengthened the isobaric zone above the LAGB, inducing hypertensive peristalsis and a vigorous contraction above the obstruction at the level of the LAGB.

Validation of Lower Oesophageal Contractile Segment Measurement

To identify an appropriate cut-off value for the proportion of normal swallows that demonstrate an intact LECS, a receiver operator characteristic (ROC) curve was generated (Figure 17.3). The area under the curve was 0.84 (95% Confidence Interval 0.75 – 0.92), *p < 0.005*. A cut off of 70% normal swallows demonstrating an intact LECS provided a sensitivity of 67% with a specificity of 93%. Alternatively, a cut off value of 30% was 97% specific, however, only 46% sensitive. We therefore defined greater than 70% intact LECS as normal, 30-70% mildly impaired LECS and <30% intact LECS as severely impaired.

On this basis: twenty seven of the successful patients had an intact LECS, one a mild impairment and one a severe impairment. Of the symptomatic patients 34 had normal, 18 mild and 49 severely impaired LECS. These differences were significant (*p<0.005*). The presence of a mild impairment in oesophageal body peristalsis did

not influence whether the LECS was categorised as normal, mildly or severely

impaired (*p=0.15*).

There was a significant correlation between the proportion of swallows

demonstrating an intact LECS and the basal LOS tone, *C=0.23, p=0.01*.

FIGURE 17.3: Receiver Operator Characteristic Curve for the Lower Oesophageal

Contractile Segment
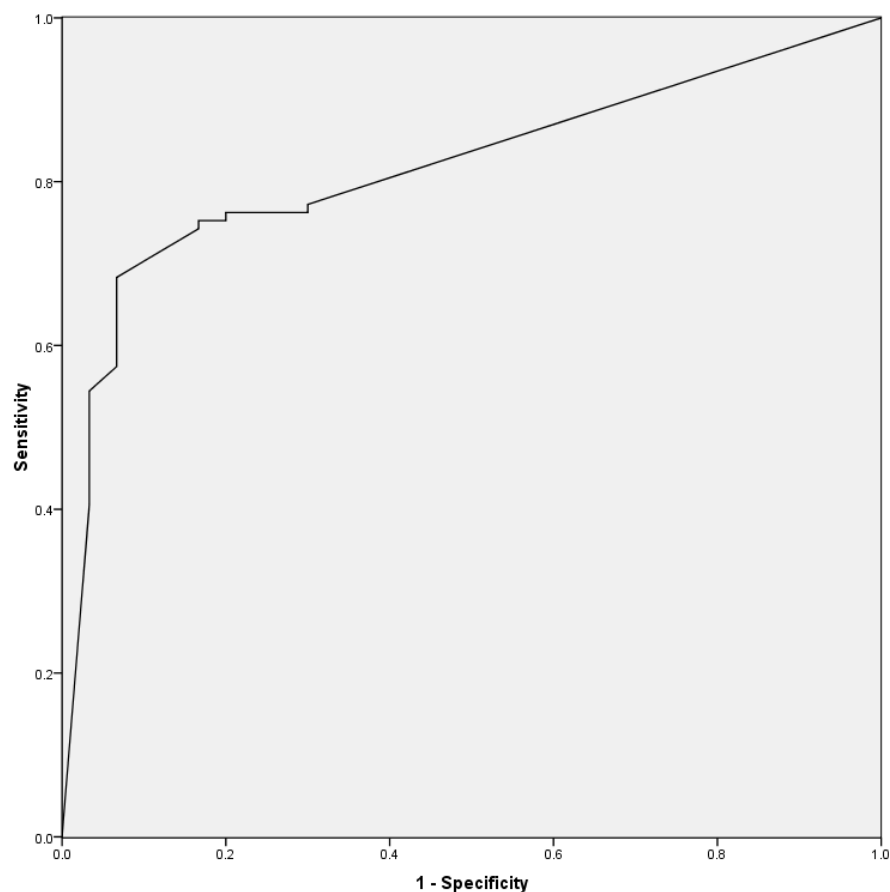
Figure 17.3 Legend: *The receiver operator characteristic curve plots sensitivity*

versus 1- specificity for the proportion of 5 ml water swallows categorised as normal

that demonstrate an intact LECS. A sensitivity of 67% can be obtained whilst

maintaining a specificity of 93%, if a cut off of 70% of swallows is used.

Alternatively, if a cut off of 30% is used, this is 97% specific although only 46%

sensitive. Total area under the curve = 0.84. It is important to note that this curve

only considered patients where motility was considered either normal or mildly

impaired. It is not representative of the overall sensitivity of oesophageal motility as

a diagnostic test.

Figure 17.4 is a schematic representation of the hypothesised role of the LECS in

LAGB patients, illustrating how this region appears to be important in generating

bolus transit.

Analysis of Pressure Topography

During swallows classified as normal, the peak pressures at different sites were not

different in the successful and symptomatic patients. This was not affected by

varying LAGB volume. These data are shown in Table 17.3. The isobaric (intrabolus)

high pressure zone was significantly longer in the symptomatic patients at optimal

volume, although not when the volume was increased or the LAGB emptied.

Similarly, the duration for which a pressure domain more than 30 mmHg was

observed, at the LOS, was greater for the successful than the symptomatic patients

at the start LAGB volume. No difference was observed when the LAGB was emptied

or its volume increased.

On the basis of these results, a protocol for performing and interpreting high

resolution manometry in LAGB patients was developed; this is shown in Tables 17.4

and 17.5. The basis for the classification was that both an intact LECS and a normal

oesophageal body peristaltic contraction are required in LAGB patients.

FIGURE 17.4: Schematic Representation of the Role of the Lower Oesophageal Contractile Segment in Bolus Transit

NORMAL LECS
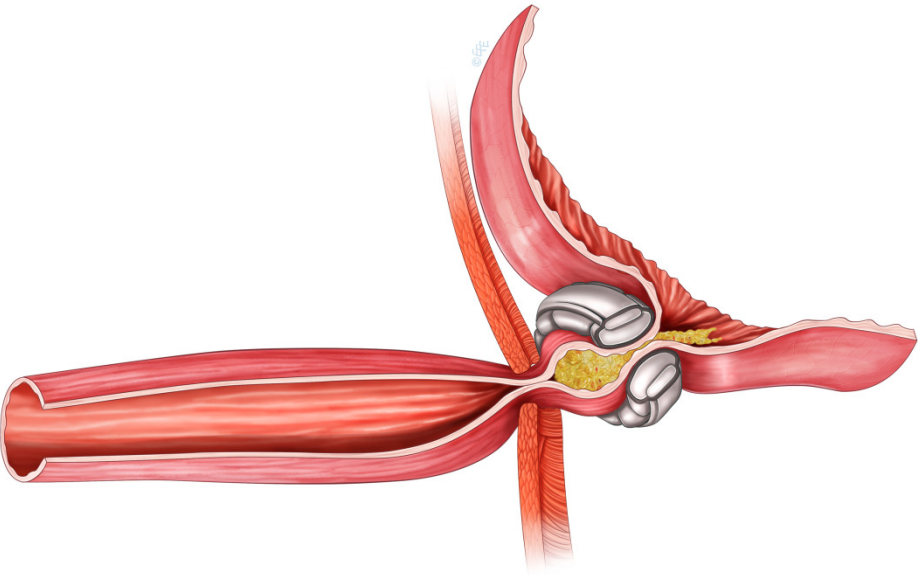
DEFICIENT LECS
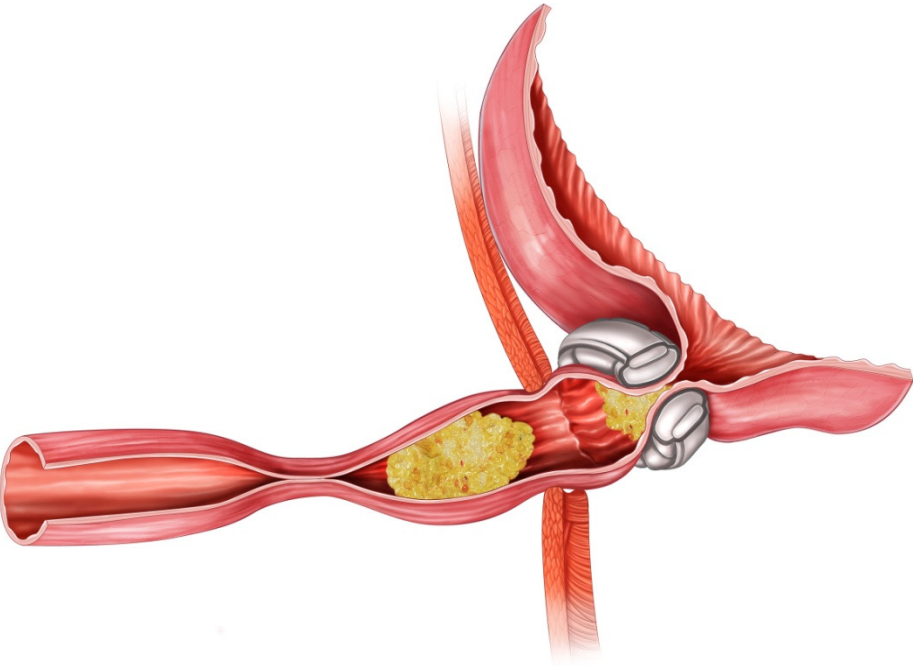
Figure 17.4 Legend:

A) Normal intact lower oesophageal contractile segment: Coordinated oesophageal peristalsis pushes a bolus into the small gastric pouch above the band. The intrabolus driving pressure is contributed to by contraction of the lower oesophageal sphincter, generating flow across the band. Several peristaltic contractions may be required to achieve complete bolus clearance as the rate of flow is limited by the stoma size of the LAGB.

B) Impaired contractility of lower oesophageal segment: The LAGB is positioned appropriately, just beneath the oesophago-gastric junction. The oesophageal body functions normally and delivers the bolus to the region of the LOS. However, the lower oesophageal sphincter does not contract effectively. Therefore bolus transit is impaired, reliant on drive from the more proximal oesophagus.

TABLE 17.3: Analysis of Pressure Topography at Different LAGB Volumes During Normal Swallows

Start (Optimal) Volume			
	Successful	Symptomatic	*p* value
Distal oesophageal (mmHg)	113.2±39.9	112.1±47.1	0.91
Lower oesophageal sphincter (mmHg)	57.1±22.0	48.3±26.3	0.13
Isobaric zone (mmHg)	28.7±10.9	25.7±14.3	0.35
Isobaric zone length (cm)	4.8±0.89	5.8±1.7	0.005
Duration of LOS contraction (seconds)	7.05±3.7	2.7±4.5	0.002
Empty			
	Successful	Symptomatic	*p* value
Distal oesophageal (mmHg)	114.3±46.7	117.1±25.2	0.87
Lower oesophageal sphincter (mmHg)	54.0±19.4	38.0±21.5	0.17
Isobaric zone (mmHg)	16.6±7.0	13.6±8.3	0.34
Isobaric zone length (cm)	3.6±0.7	4.1±1.4	0.32
Duration of LOS contraction (seconds)	7.07±5.1	4.2±11.1	0.27
Increased Volume			
	Successful	Symptomatic	*p* value
Distal oesophageal (mmHg)	145.8±46.3	125.8±58.1	0.35
Lower oesophageal sphincter (mmHg)	68.8±37.7	50.6±26.3	0.09
Isobaric zone (mmHg)	37.8±16.7	30.6±10.0	0.09
Isobaric zone length (cm)	5.4±1.2	5.9±1.2	0.27
Duration of LOS contraction (seconds)	8.9±6.5	7.8±19.1	0.80

Values are mean and standard deviation

Only swallows categorised as normal according to standardised criteria were included in this analysis

TABLE 17.4: Protocol for Performing and Interpreting Oesophageal Manometry in LAGB Patients

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<u>Manometry protocol</u>

Ensure catheter has been passed through the LAGB, positioning reference side hole in the distal stomach. The LAGB/LOS region needs to be within the high resolution zone of the manometry catheter.

Measure lower oesophageal sphincter basal tone

Measure basal intraluminal pressure at the level of the LAGB

10 supine 5 ml water swallows

Repeat basal measurements and 5 further right lateral swallows with LAGB empty

Repeat basal measurements and further 5 right lateral swallows with >25 mmHg basal intraluminal pressure at the LAGB

<u>Guidelines for manometry reports</u>

Each swallow is classified and overall motility assessed according to standard criteria.
LOS basal tone and relaxation are reported
Classification of swallows are stratified by LAGB resistance (intraluminal pressure)
The proportion of swallows demonstrating a lower oesophageal contractile segment are reported
The length of the isobaric high pressure zone above the LAGB during swallows is reported (< 6 cm is normal)

Summary: Should describe the essential components of motility, but also characterise the response of the oesophagus to the resistance of the LAGB. This should particularly highlight the efficacy of the LECS.

Table 17.5: Criteria for Classifying Oesophageal Motility in LAGB Patients

	Proportion of normal oesophageal body peristaltic contractions	*Proportion of normal swallows with an intact lower oesophageal contractile segment*	
Normal motility	*>70%*	*AND*	*>70%*
Mild impairment in motility	*>70%*	*AND*	*<70%*
		OR	
	30 - 70%	*AND*	*30-70%*
Severe impairment in motility	*>70%*	*AND*	*<30%*
		OR	
	30 - 70%	*AND*	*<30%*
		OR	
	<30%	*AND*	*ANY*

The diagnostic categories are identical to those used in conventional assessments of high resolution manometry, although the criteria differ. This modified classification recognizes that for contractions to be effective in LAGB patients, both oesophageal body peristalsis and the LECS must be adequate. Functionally, those with a severe impairment in oesophageal motility could be expected to demonstrate a significant impairment in bolus transit across the LAGB.

Discussion

We identified significant differences in oesophageal motility between successful and symptomatic LAGB patients. This was based on a new measurement; the LECS. This complements an overall assessment of oesophageal motility and was derived from mechanisms of oesophageal function defined as important in LAGB patients [540]. Significantly, the LECS was frequently deficient in symptomatic patients, even in swallows categorised as normal according to conventional criteria. Hypotensive swallows rarely had an intact LECS. Successful patients were able to sustain a >30 mmHg contraction at the level of the lower oesophageal sphincter for significantly longer than symptomatic patients. Symptomatic patients did have worse overall oesophageal motility, although this was almost always described as a mild impairment in peristalsis. However, when combined with the differences in the LECS, a profound difference in oesophageal motility was identified between the two groups. This, in many cases, accounts for the disparate outcomes observed.

Assessing the oesophageal response to changes in LAGB volume provides complimentary information about motility. The variability of the outflow resistance (when measured as an intraluminal pressure) presented by the LAGB is an important and unique aspect of the LAGB that needs to be considered when performing any diagnostic test. Removing fluid allows an assessment of the underlying native oesophageal function. This removes artificial inflations in pressure induced by the resistance of the LAGB. These inflations occur if there is mechanical obstruction and failed bolus transit. The resulting compartmental pressurisation makes interpretation of pressure topography difficult. Alternatively,

increasing the fluid in the LAGB allows an assessment of the oesophageal response to increased outflow resistance. In successful patients, the intraluminal pressure at the LAGB is almost always in the order of 20-30 mmHg and appears to be necessary to induce weight loss. The oesophagus must be able to clear a swallowed bolus against this resistance. If it cannot, there is likely to be dysphagia and regurgitation in combination or alternating with, unsatisfactory weight loss.

There was no correlation between basal LOS tone and pressure amplitude measured at the level of the LOS during water swallows. This does not surprise us, as absolute intraluminal pressures are not the critical factor in mediating bolus transit [540]. It is more important to measure the ability of the oesophagus to generate ordered peristaltic contractions and a sustained positive pressure gradient across the LAGB to generate flow. There was, however, a weak correlation between LOS basal tone and the proportion of swallows with an intact LECS. This is likely indicative that a weak LOS tends to demonstrates poor contractility, although this is not invariable

Basal tone, contractility and distensibility of the LOS represent different, related, physiological properties of the region. Basal LOS tone has not been demonstrated to be important in LAGB patients. LOS contractility is very important in generating bolus transit in LAGB patients. Contractility will vary with muscle fibre length [463]. Alternatively, increased distensibility of the region results in transhiatal oesophageal enlargements and stasis, now one of the most significant intermediate term problems following LAGB [537]. The relative significance and relationship of

these properties, particularly compliance and contractility need to be better defined.

We have previously shown that an intact LECS is important in mediating bolus transit in LAGB patients [540]. For this to occur there must be delivery of the bolus to the lower oesophagus; which requires a normal oesophageal body peristaltic contraction [499]. This needs to be followed, in a coordinated fashion, by a contraction of the lower oesophageal sphincter that drives the bolus across the resistance of the LAGB. A hypotensive swallow is at risk of not delivering the bolus to the lower oesophageal sphincter and an inadequate LECS will not effectively propel a bolus across the resistance of the LAGB.

The aetiology of the impaired LECS observed in symptomatic patients is an important question. We believe it is secondary to a chronic distension of the LOS, resulting in a focal impairment in contractility. This is not necessarily a change that can be identified anatomically.   It is also unclear why some patients develop dilatation of the stomach above the LAGB and others an impairment in lower oesophageal function or even identifiable focal lower oesophageal dilatation [537]. In the future, anatomical and functional changes seen after LAGB need to be integrated to establish a comprehensive method of assessing LAGB patients.

We have proposed new criteria for the assessment of oesophageal motility in LAGB patients. A standardised evaluation according to established guidelines is worthwhile, however, is not sensitive enough to be useful in LAGB patients. Whilst severe peristaltic impairment will result in poor bolus transit, it is unusual in LAGB patients [537].

We found that it was not uncommon for normal contractions to demonstrate a deficient LECS. In LAGB patients a contraction with a deficient LECS is ineffective in the same way a hypotensive swallow is. In this cohort of patients we also identified that they tended to either demonstrate a predominantly intact or deficient LECS. This led us to set cut offs for normal (>70% intact LECS) and severely impaired (<30% intact LECS). Reassuringly, less than 20% of patients fitted into the middle group, described as mildly impaired. The middle group does still represent a grey zone, the significance of which is unclear.

It is unknown whether these problems developed following LAGB or are more associated with pre-operative oesophageal motility. These problems were observed a mean of 4.5 years following LAGB. This suggests to us that the motility changes developed post-operatively. Non-specific or mild impairments in oesophageal peristalsis, are very common in the obese [428, 429] and cannot be considered a contraindication to LAGB. In the short term these do not affect the outcome of LAGB [541], during which time the complication rate is low [310].

Outcomes following revisional LAGB surgery are variable [310, 322, 324]. We suspect the status of the LECS is an important mediator of this. A gastric enlargement above the LAGB may have impaired the function of the LECS. If the impairment is significant and does not recover, bolus transit may still be poor, reducing the chance of a good outcome.

Conclusion

The importance of oesophageal function in LAGB patients relates to the ability of the oesophagus to clear a bolus against the resistance of the LAGB. This requires both coordinated oesophageal body peristalsis and a functional LECS. These can be accurately assessed by adapting conventional high resolution manometry protocols and using the validated assessment of the LECS we have developed. Isolated deficiencies of the LECS can occur and may be the basis for inadequate bolus transit. Measuring the oesophageal response to changes in LAGB volume provides complimentary information. High resolution manometry can now be advocated as a clinical tool for the assessment of symptomatic LAGB patients.

Declaration for Thesis Chapter 18

This chapter represents a submitted manuscript.

Declaration by candidate

In the case of Chapter 18, the nature and extent of my contribution to the work was the following:

Nature of contribution	Extent of contribution (%)
Overall responsibility for all aspects of the study, conception, planning, patient recruitment, conducting experiments and recording data. Data analysis and interpretation. Statistical analysis. Crafting and revising manuscript.	>90%

The following co-authors contributed to the work:

Name	Nature of contribution
Wendy A Brown	Designing study, and recruiting patients, manuscript review
Cheryl Laurie	Recruiting patients and conducting studies
Geoff Hebbard	Experiment design, data acquisition and analysis, review of manuscript
Paul O'Brien	Experiment design, data analysis, review of manuscript

Candidate's Signature		Date

Declaration by co-authors

The undersigned hereby certify that:

(1) the above declaration correctly reflects the nature and extent of the candidate's contribution to this work, and the nature of the contribution of each of the co-authors.
(2) they meet the criteria for authorship in that they have participated in the conception, execution, or interpretation, of at least that part of the publication in their field of expertise;
(3) they take public responsibility for their part of the publication, except for the responsible author who accepts overall responsibility for the publication;
(4) there are no other authors of the publication according to these criteria;
(5) potential conflicts of interest have been disclosed to (a) granting bodies, (b) the editor or publisher of journals or other publications, and (c) the head of the responsible academic unit; and
(6) the original data are stored at the following location(s) and will be held for at least five years from the date indicated below:

Location(s)	Monash University, Alfred Hospital

[Please note that the location(s) must be institutional in nature, and should be indicated here as a department, centre or institute, with specific campus identification where relevant.]

		Date
Wendy A Brown	███████████	27/10/09
Cheryl Laurie	███████████	4/11/09
Geoff Hebbard	███████████	2/11/09
Paul E O'Brien	███████████	27.10.09

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CHAPTER 18: *Outcomes of Intermediate Term Complications Following Laparoscopic Adjustable Gastric Banding*

Abstract

Background: Patients with laparoscopic adjustable gastric bands (LAGB) present at times with adverse symptoms or unsatisfactory weight loss, where a liquid contrast swallow or upper gastrointestinal endoscopy is not diagnostic. Stress barium and high resolution manometry are promising investigations, however, have not yet been established as clinically useful.

Methods: Patients with an unsatisfactory outcome following LAGB, where liquid contrast swallow and endoscopy were not diagnostic, were evaluated using high resolution video manometry and a stress barium. Pre-operative and follow up clinical data were collected. Oesophageal motility was classified as intact or deficient using new criteria, the "Melbourne criteria".

Results: There were 143 patients. Stress barium identified the following appearances: gastric enlargement (n=57), transhiatal enlargement (n=44), pan oesophageal dilatation (n=9) and anatomically normal (n=33). Twenty four (72%) of the anatomically normal patients had deficient oesophageal motility. Patients with gastric enlargements presented primarily with reflux (75%), whereas dysphagia (45%) and reflux (45%) occurred equally in transhiatal enlargements, with dysphagia predominating if the stress barium was anatomically normal (68%). All patients with pan oesophageal dilatation presented with loss of satiety. Revisional LAGB surgery was performed in 56 patients. This was successful in gastric enlargements when motility was intact: %Excess weight loss (EWL) 58.3±16.2 vs.

35.4±19.7, *p=0.002*). Revisional surgery for transhiatal enlargements improved symptoms but did not improve poor weight loss (%EWL 20.6±24.9 vs. 17.2±25, *p=0.1*).

Conclusions: A clinically useful classification, "The CORE Classification", combines anatomical change with oesophageal motility and has been defined for intermediate term complications following LAGB where conventional investigations have not been diagnostic. Revisional LAGB surgery is helpful for patients with a gastric enlargement above the LAGB if oesophageal motility is intact. If motility is deficient or there is an oesophageal anatomical abnormality, intervention is not likely to remedy poor weight loss.

Introduction

The laparoscopic adjustable gastric band is well established as a safe, effective and durable bariatric procedure [1]. Modification of the original surgical technique has largely overcome the problem of early gastric prolapse [10]. Data, out to 8 and 12 years, with high follow up rates have demonstrated maintenance of weight loss [275, 302].

Others, however, have reported higher complication and failure rates in the intermediate term [317, 542]. Differences in reported outcomes are possibly accounted for by differing definitions and management of post-operative complications. Controversy in this area is not surprising as the complex spectrum of pathophysiology that can occur after LAGB has, until recently, been poorly defined [537]. With ongoing use and an estimated 500,000 LAGBs placed worldwide, sensitive diagnostic tests able to objectively stratify treatment are urgently required. Robust definitions of complications are also required to facilitate comparative outcome studies.

The two most common intermediate term complications in the pars flaccid era are acute luminal dilatations above the LAGB or chronic symmetrical dilatation of the gastric pouch [537]. Acute dilatation is usually well managed with the removal of saline from the LAGB and attention to eating behaviour [308, 337]. A regular, ongoing follow up program should identify these problems and facilitate intervention at an early stage; although, if left untreated a more significant problem may evolve [327].

Symmetrical gastric pouch dilatation, where there is focal luminal dilatation above the LAGB is now the most common indication for revisional LAGB surgery, which is generally a successful strategy [254, 310]. There are, however, a group of patients who present with significant adverse symptoms or increasing weight despite a normal or equivocal liquid contrast swallow or endoscopy. Alternatively, revisional LAGB surgery may resolve an anatomical problem, however, fail to correct the clinical situation; suggestive of a functional problem.

Use of a semi-solid stress barium and high resolution manometry has shown that patients with no clear explanation for unsatisfactory progress frequently have inducible anatomical abnormalities above the LAGB or specific patterns of oesophageal dysmotility [537, 543]. These new data have provided insights into the pathophysiology associated with LAGB, however, have not yet been translated to clinical use.

We hypothesised that gastric dilatations would be amenable to surgical correction providing the critical aspects of oesophageal motility remained intact. Oesophageal dilatation, focal or pan-oesophageal, or deficient motility was not expected to be amenable to surgery or improve substantially with conservative management. We aimed to integrate recently described criteria for assessing oesophageal motility with patterns of anatomical change induced with a stress barium. By doing this we aimed to develop a clinically useful classification of complications following LAGB predictive of the response to different treatment strategies.

Methods

The Melbourne health, Monash University and Avenue hospital human ethics committees approved this research and all patients gave informed consent. A prospective observational study was conducted on consecutive LAGB patients who presented with unsatisfactory progress.

Subjects

Patients with unsatisfactory progress following LAGB, for the purposes of this study, were defined as aged between 18 and 65 years, who experienced either poor weight loss (<25% of excess weight loss 12 months post-operatively) and/or had adverse symptoms (volume reflux, dysphagia, regurgitation/vomiting or the inability to tolerate fluid in the LAGB due to these symptoms) despite a normal or near normal liquid contrast swallow or upper gastrointestinal endoscopy. Confirmation that the patient had attended regular follow up over at least three months, with attempts to optimise the LAGB adjustment, was also required. Therefore, this study was of a select group of patients in whom there was no obvious anatomical abnormality and routine management had proven unsuccessful.

Pre-operative Clinical Assessment

Prior to video manometry each patient completed a standardised questionnaire that constituted validated reflux (0 no reflux, 72 severe reflux) and dysphagia (0 no dysphagia to 45 total dysphagia to water) scores [544, 545]. A standardised clinical interview was conducted prior to the study. The most significant or primary presenting symptom was categorised as one of: reflux, dysphagia or loss of satiety.

Video Manometry

All patients underwent a standardised high resolution video manometry study, incorporating a semi-solid stress barium. Video manometry was performed as has been previously described [533]. In brief,   a water perfused manometry system with a custom made 21 channel silicone rubber manometry catheter (Dentsleeve, Ontario, Canada) was used. The catheters were designed specifically to assess the region of the oesophago-gastric junction (OGJ) and to differentiate the pressure signals generated by the LAGB and lower oesophageal sphincter (LOS). The manometry system was connected to a personal computer via data acquisition and video input cards (National Instruments, Austin, Texas). Simultaneous high resolution manometry and video fluoroscopy information was recorded using TRACE! 1.2 (written by G Hebbard using LabVIEW, National Instruments, Austin, Texas).

Supine basal recording was performed for 30 seconds without swallowing. Ten wet swallows of 5 ml of water were then performed with the patient in the right lateral position**.**

Analysis of Oesophageal Motility

Oesophageal motility was assessed using adapted criteria specific to LAGB patients, defined as the Melbourne criteria [543]. This was a modified version of the Chicago criteria, the current standard for reporting high resolution manometry [501]. Detailed analysis of the lower oesophageal contractile segment (LECS) was undertaken to make these specific to LAGB patients [501, 543]. For purposes of

analysis, oesophageal motility was classified as intact or deficient. Intact motility included patients who had normal or mild impairment in peristalsis whereas a severe peristaltic impairment constituted deficient motility.

Stress Barium Protocol

Patients ingested two consecutive spoonfuls of barium soaked porridge. These were   followed immediately by drinking of up to 80 ml of liquid barium via a straw. Patients were instructed to continue drinking until either symptoms of dysphagia, discomfort or nausea developed or they felt excessively full. The aim was to maximally distend the lumen above the LAGB. Fluoroscopy was used to ensure patients had drunk barium to the point of either developing reflux from the pouch or a significant enlargement (with stasis) was observed above the LAGB. We aimed to generate an intraluminal pressure immediately above the LAGB of at least 30 mmHg. Delayed images were taken intermittently for a period of up to 5 minutes, to document transit and emptying of the lumen above the LAGB.

Analysis of Stress Barium

The anatomical appearance observed at stress barium was central to the analysis of data, with patients primarily categorised on this appearance. An enlargement was defined as a focal or generalised luminal dilatation above the LAGB in which there was stasis. The appearance was classified as: gastric enlargement (either symmetrical gastric dilatation or gastric prolapse), transhiatal enlargement, generalised (pan) oesophageal dilatation or anatomically normal.

Management Following Video Manometry

The pathophysiological change was documented as was motility and a report provided. Post manometry management was at the discretion of the referring clinician.

Revisional surgery was performed using a standard technique where the old LAGB was removed and the crural pillars mobilised and repaired anteriorly. A new posterior pathway for the LAGB was created with a broad anterior gastro-gastric fixation. A liquid contrast swallow was performed post-operatively to confirm accurate placement of the LAGB.

Patient Follow Up

All patients were followed up for a minimum of 6 months following video manometry. Weight loss data were recorded six months following video manometry if operative intervention had not occurred and was not planned. If a re-operation was performed, weight loss data was recorded six months following this. All patients who underwent re-operation were contacted by phone and a matched follow up questionnaire completed.

Statistical analysis and data management

All statistical analysis was performed using SPSS V. 16.0 (SPSS Inc., Chi, Ill). Data are displayed as mean and standard deviation if normally distributed or median and interquartile range if not normally distributed. Paired t tests were used for analysis of repeat measurements of normally distributed continuous data. Student's t tests were used for comparisons of normally distributed continuous independent data.

Mann-Whitney tests were used for analysis of non-normally distributed continuous data. One way ANOVA was used for comparison of multiple normally distributed continuous variables. Kruskal-Wallis tests were used for comparison of multiple non-normally distributed continuous variables. A two sided p value of 0.05 was considered statistically significant.

All weight loss and demographic data was sourced from a prospectively maintained online database (*www.lapbase.net*).

Results

Data from 143 patients were available for analysis. Patient details are shown in Table 18.1, based on the anatomical appearance at stress barium. Significant baseline differences existed between the groups in terms of %excess weight loss (%EWL) at follow up, %EWL at presentation, and peak %EWL. Peak %EWL was the maximal weight loss the patient had achieved following LAGB. Notably the mean peak weight loss was over 50% EWL.

The gastric enlargements included 3 gastric prolapses that were not seen on liquid contrast swallow, although were induced by the addition of saline to the LAGB and the stress barium. The method for differentiating transhiatal oesophageal from gastric enlargements herniating through the hiatus has previously been described [537].

	Transhiatal oesophageal enlargement	Gastric enlargement	Anatomically normal	Pan oesophageal dilatation	*p* value
Number	44 (31%)	57 (40%)	33 (23%)	9 (6%)	-
Age (years)	48±9.3	45.7±13.2	46.5±9.4	50.2±7.4	0.45
% EWL at presentation	26.3±3.6	52.8±30.2	24.1±21.8	46.1±15.0	<0.005
Peak %EWL	56.5±25.4	68.3±26.8	51.1±24.3	67.4±9.1	0.03
%EWL at follow up	24.1±23.1	49.6±26.4	22.4±23.4	41.1±19.5	<0.005
Start BMI (kg/m^2)	43.5±7.3	44.5±7.7	44.2±7.9	48.6±7.0	0.61
Start weight (kg)	120.0±23.3	121.6±22.9	120.3±21.3	148.2±26.2	0.10
Duration from initial surgery (days)	1655±950	1545±784	1893±933	2367±976	0.20
Revision LAGB since manometry	14 (32%)	34 (61%)	8 (24%)	0	0.005

Symptoms at presentation

The gastric enlargement group most commonly identified reflux as the primary symptom. The pan oesophageal dilatation patients all presented primarily with loss of satiety. The transhiatal enlargement group presented equally with reflux and dysphagia, whereas the anatomically normal group presented more commonly with dysphagia. These differences between the primary presenting symptoms in the groups was significant (*p<0.005*). Figure 18.1 summarises these data.

Oesophageal Motility

Using conventional (Chicago) criteria for the assessment of oesophageal motility, there was no difference, between groups, in the proportion of patients with intact motility (*p=0.43*). The Melbourne criteria demonstrated a statistically significant changes in the proportion classified as having intact motility within each group *(p<0.05)* compared to use of the Chicago criteria. These data are shown in figure 18.2. Application of the Melbourne criteria showed that motility was significantly better in the gastric enlargement group compared to the anatomically normal and transhiatal groups, (*p=0.02)*. The pan oesophageal dilatation group was excluded from motility analysis, as they had no peristaltic function. Within the anatomically normal group 24 (72%) patients had a significant abnormality of oesophageal peristalsis. This allowed the division of this group into those with severe peristaltic impairment (deficient motility) and a functional group, with no anatomical or physiological explanation for the symptoms or outcome.

Management and Outcome

Fifty six patients underwent revisional LAGB surgery following video manometry. More patients with gastric enlargements underwent revisional LAGB surgery (Table 18.1), compared to patients with transhiatal enlargements or no anatomical abnormality. Revisional LAGB surgery had no effect on excess weight loss in any group. In the gastric enlargement group mean %EWL was 52.8±30.2 at presentation for video manometry and this was maintained at follow up post-operatively. In the transhiatal and anatomically normal groups, mean %EWL was <25 at presentation and did not improve following revisional surgery.

FIGURE 18.1: Primary Presenting Symptom
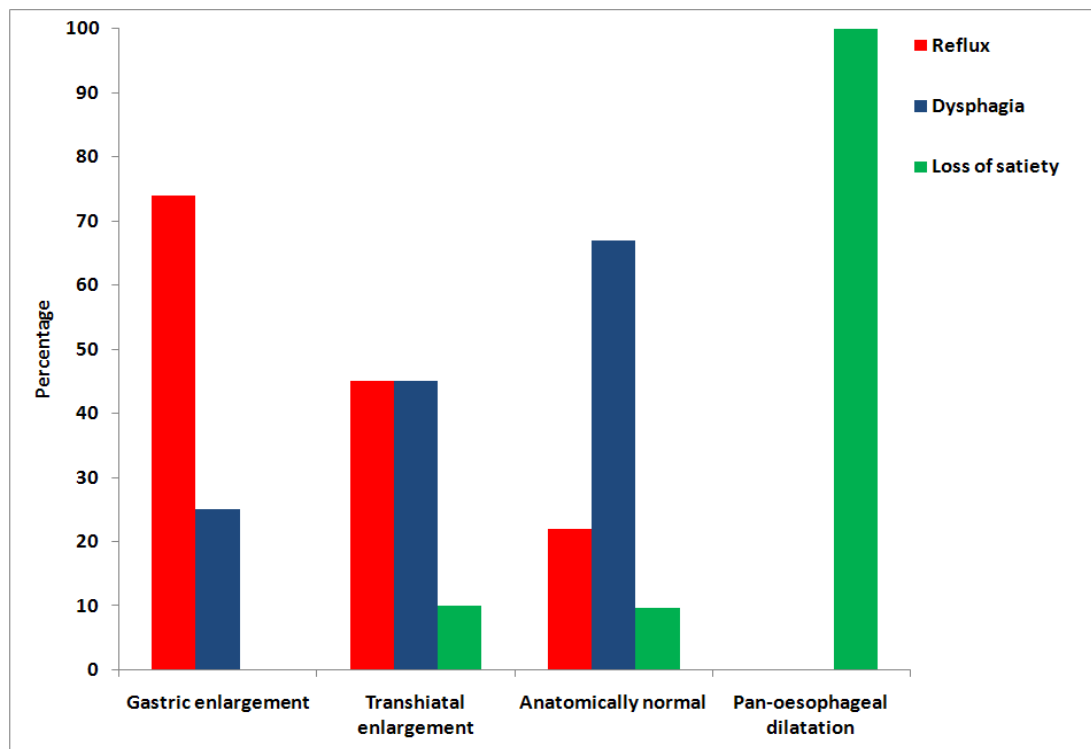
FIGURE 18.2: Percentage of Patients with Intact Oesophageal Motility Using Specific (Melbourne) vs. Conventional (Chicago) High Resolution Manometry Criteria
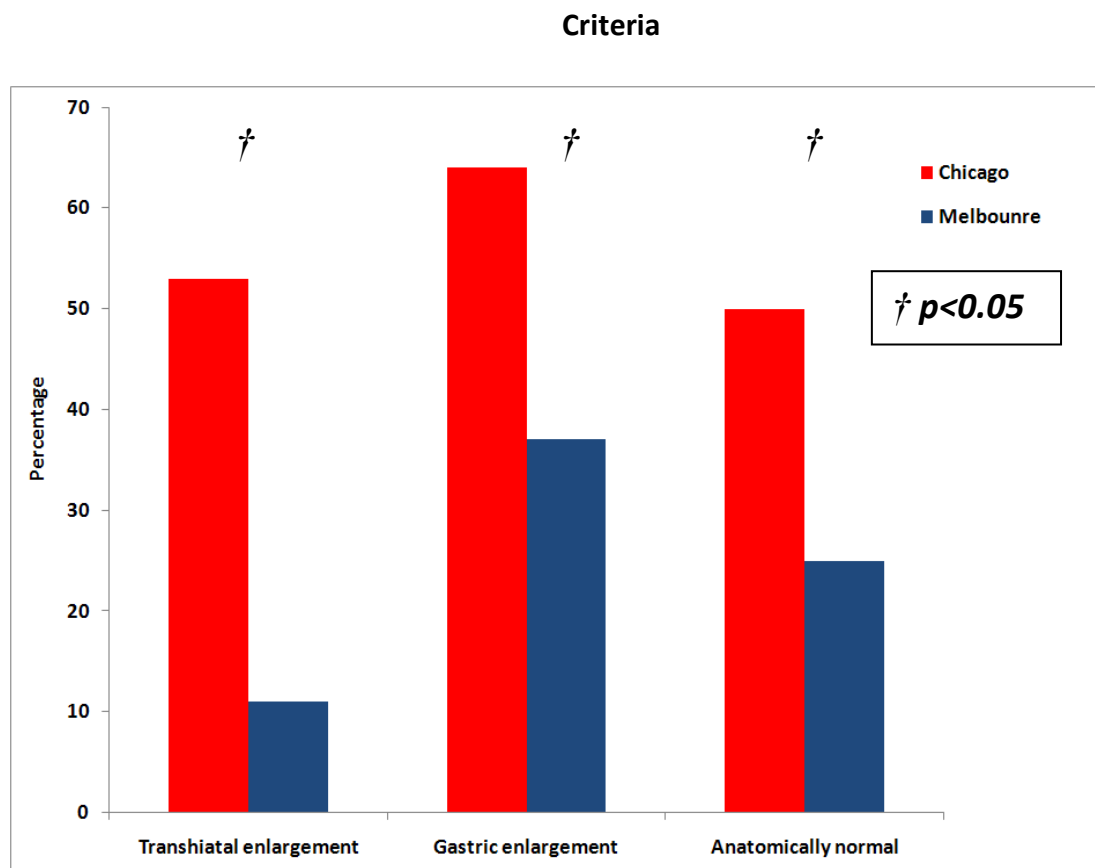
Figure 18.3 summarises these data. Reflux and dysphagia scores improved

significantly in both the transhiatal (*p< 0.005*, *p<0.007*) and gastric enlargement

groups (*p=<0.005, p<0.007*) but were unchanged in the anatomically normal group

(*p=0.16, p=0.19*). These data are summarised in figure 18.4.

FIGURE 18.3: Weight loss following Revisional LAGB surgery
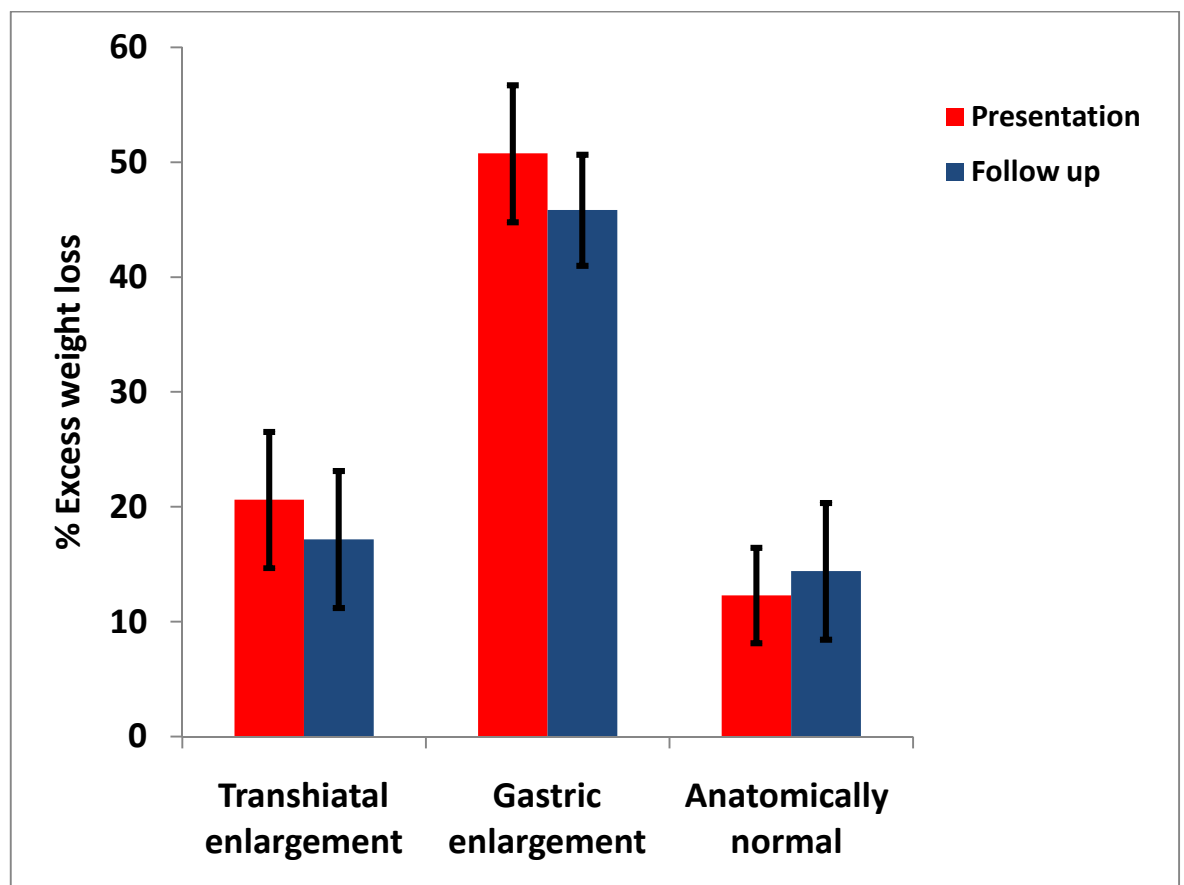
Figure 18.3 Legend*: There was no statistically significant change in %EWL following

revisional surgery in any group.*

Data are mean and standard error

Patients with gastric enlargements who had intact oesophageal motility maintained good weight loss following revisional surgery. Patients with deficient oesophageal motility were found to have increased their weight at follow up, such that the difference between the two groups was statistically significant (*p=0.002*). Data are shown in table 18.2.

The CORE Classification

As a result of these collective data we defined the CORE classification of intermediate term complications following LAGB. This classification combined anatomical appearance with an assessment of oesophageal motility. Three general anatomical appearances at stress barium were identified:

1) Gastric enlargements

2) Oesophageal enlargements

3) Anatomically normal.

The nature of the anatomical appearance can be made more specific within each category and these data supplemented with high resolution manometric data. Table 18.3 summarises the key features of each category. Figure 18.5 illustrates the anatomical abnormalities.

FIGURE 18.4: Change in Dysphagia and Reflux Symptoms Following Revisional LAGB Surgery

A: Dysphagia Score
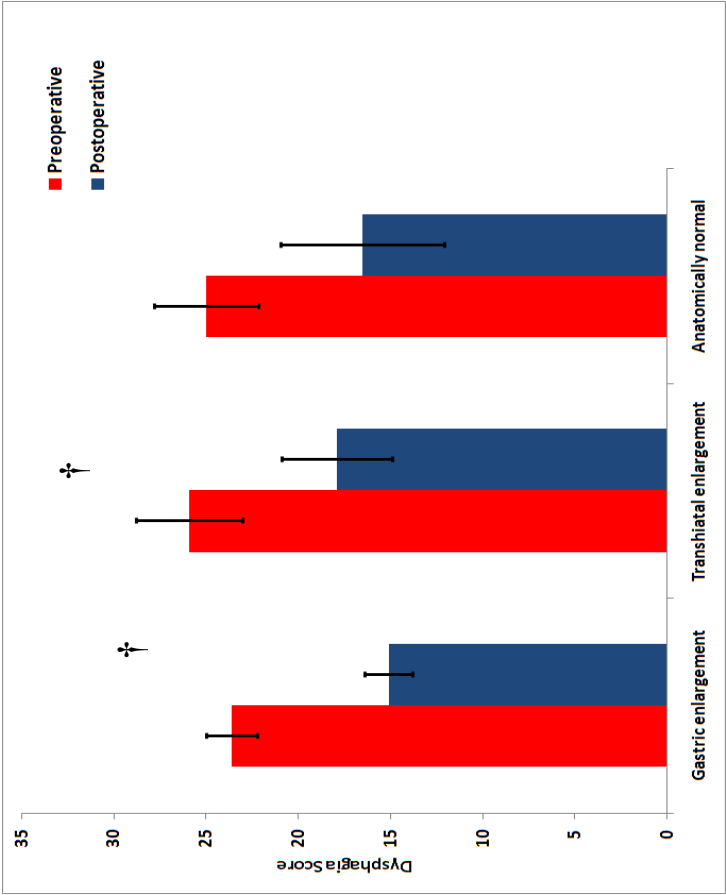
B: Reflux Score
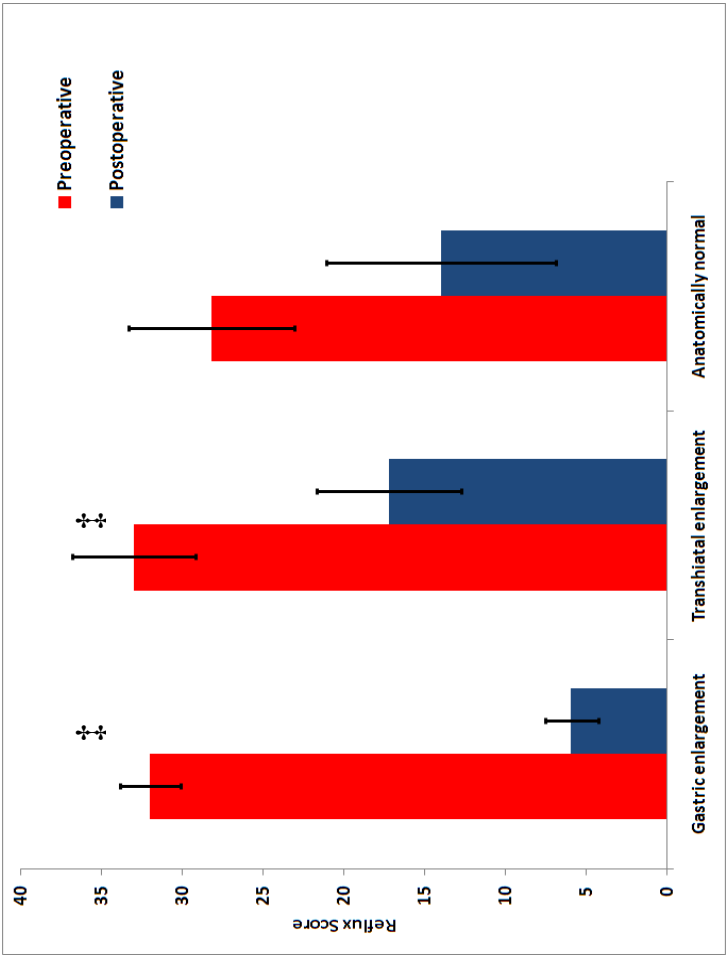
Data are mean and standard error

† *p<0.05*   ‡ *p<0.05*

TABLE 18.2: Outcomes of Revisional Surgery in Patients with Gastric Enlargements

	Intact motility (n= 13)	Deficient motility (n= 21)	*p* value
Age (years)	42±11	43±9	0.82
Pre operative reflux score (0-72)‡	35.3±11.7	31.1±10.5	0.30
Pre operative dysphagia score (0-45)†	21.4±8.3	23.7±7.7	0.43
Post operative reflux score (0-72)‡	2.5±2.5	8.6±11.6	0.05
Post operative dysphagia score (0-45)†	14.0±4.9	15.2±8.5	0.66
Excess weight loss at follow up (%)	58.3±16.2	35.4±19.7	0.002
Excess weight loss at manometry (%)	59.9±30.1	44.1±30.1	0.18

‡0 is no reflux, 72 severe reflux

†0 is no dysphagia, 45 total dysphagia to liquids

FIGURE 18.5: Schematic Representation of the CORE Classification

Gastric enlargement
(symmetrical sub-diaphragmatic)
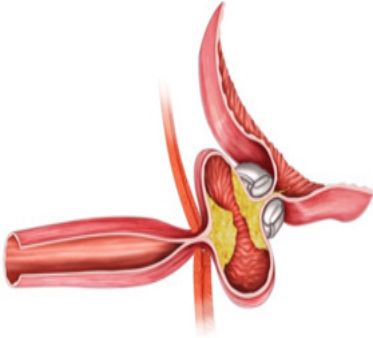
Gastric prolapse (anterior)
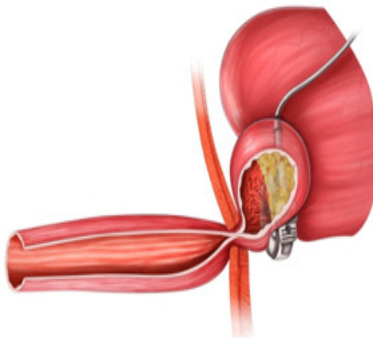
Transhiatal gastric
enlargement
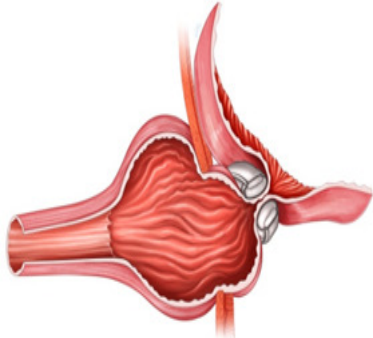
Transhiatal oesophageal enlargement
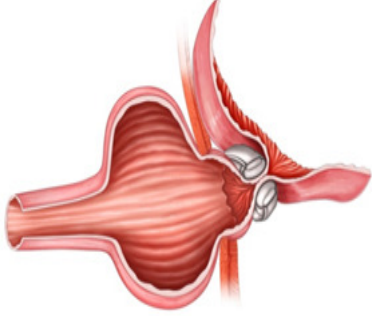
Aperistaltic oesophagus
(pan oesophageal dilatation)
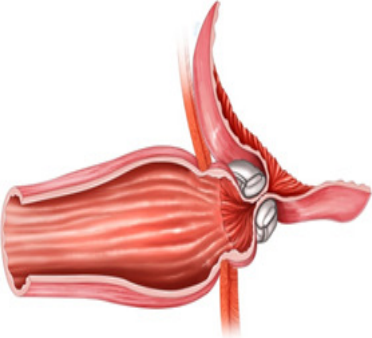
Deficient Motility

TABLE 18.3: Key Features of the CORE Classification: Based on Appearance at Stress Barium

Abnormality	Proportion*	Key features
GASTRIC ENLARGEMENTS (40%)		
Symmetrical sub-diaphragmatic	34%	Symmetrical enlargement of stomach arising below the diaphragm, although may impinge on the hiatus as it expands. Patients frequently present with significant reflux symptoms. Intact motility predicts a good outcome following revisional LAGB surgery
Transhiatal	2%	True hiatus hernia, with excess stomach above the LAGB transiting up into the thoracic cavity
Prolapse	4%	Prolapse can be considered a (asymmetrical) gastric enlargement. Can be anterior or posterior.
OESOPHAGEAL ENLARGEMENTS (37%)		
Transhiatal	31%	Focal oesophageal enlargement, transiting the hiatus. Have mixed symptoms of dysphagia and reflux. Oesophageal motility is frequently significantly impaired.
Pan-Oesophageal	6%	Pan-oesophageal dilatation, with a normally placed LAGB, the oesophagus demonstrates no ordered peristaltic contractions. Patients do not have satiety, but may also report reflux or regurgitation
ANATOMICALLY NORMAL (23%)		
Deficient motility	17%	Severe impairment in oesophageal motility with anatomically normal stress barium. The impairment in motility is often only identified at high resolution manometry using the Melbourne criteria; specifically a significant impairment in the lower oesophageal contractile segment. Dysphagia symptoms are common.
Intact motility	6%	Anatomically normal stress barium with intact oesophageal motility including lower oesophageal contractile segment. No specific cause for unsatisfactory progress identified.

Proportions are of the number of patients included in this series.

Discussion

We evaluated the outcomes of LAGB patients where no explanation for unsatisfactory progress had been identified with a liquid contrast swallow or upper gastrointestinal endoscopy. Use of a stress barium contrast swallow allowed the anatomy above the LAGB to be determined; illustrating various luminal enlargements. Application of the Melbourne criteria, high resolution manometry criteria adapted to LAGB patients, made the assessment of oesophageal motility highly clinically relevant. Combining the anatomical appearance with assessment of specific aspects of oesophageal motility allowed the CORE classification of intermediate term complications following LAGB to be defined. This classification was found to be clinically relevant; able to guide treatment.

Our data show that patients with gastric enlargements above the LAGB respond well to revisional LAGB surgery, provided oesophageal motility is intact. Other problems associated with oesophageal dilatation or deficient oesophageal motility generally present with poor weight loss and are not responsive to further LAGB treatment.

We emphasise this was a study of a specific patient group, representative of only a small proportion of the total post LAGB population. Only those patients where conventional investigations and treatment had been unhelpful were included. These patients, however, are a major challenge in optimising the intermediate term outcomes after LAGB surgery. Significantly, the majority of these patients had achieved a good weight loss initially with a mean EWL of >50% in each group.

If initial investigations are not diagnostic or conventional treatment unsuccessful, more detailed assessment with a stress barium and/or high resolution manometry has now been shown to be useful in managing these patients.

Patients with different anatomical or motility problems presented with different symptoms. Although symptoms were not always specific, gastric enlargements were primarily associated with reflux. Patients with transhiatal oesophageal enlargements had a range of symptoms. Alternatively, patients with no anatomical abnormality tended to present with dysphagia, likely reflective of impaired bolus transit. Pan-oesophageal dilatation was always primarily associated with the loss of satiety; suggestive of a loss of visceral sensitivity.

Initial adjustments to LAGB volume or revisional surgery to correct a mechanical problem such as prolapse or symmetrical gastric pouch dilatation resolve most post LAGB problems [308, 310]. Our data now support this approach in cases where the gastric enlargement is more subtle, being identified only by a stress barium. We have also extended knowledge by showing that regardless of anatomy, intact motility is important in mediating a successful outcome after revisional surgery.

Re-operating on patients with transhiatal enlargements appeared to improve symptoms, however, did not impact on unacceptable weight loss (25% EWL). We therefore cannot see that revisional LAGB surgery is worthwhile in this situation.

Transmission of excess force to the luminal wall is suspected of underpinning luminal dilatations and impairments in the contractile function of the lower oesophageal sphincter. Possibly these problems represent aspects of the same

spectrum of pathophysiology, with anatomical change occurring at a later stage. During normal swallows, transmission of force to the luminal wall has been shown to be mediated by how tight the LAGB is when measured as an intraluminal pressure [540]. Also, episodes of acute obstruction result in very elevated intraluminal pressures and are mediated by the amplitude of proximal oesophageal peristalsis [540].

To avoid the transmission of force to the luminal wall, adjusting the LAGB to target satiety not mechanical restriction is advocated. Good eating behaviour is emphasised, ensuring that portion sizes are small. Each mouthful must be chewed well before being swallowed. If the LAGB is inducing adverse symptoms we should seek to relieve any obstruction by removing saline promptly.

The question of how best to manage patients with an established problem that is not amenable to further LAGB treatment remains difficult. There is much discussion amongst surgeons about converting one bariatric procedure to another. High quality prospective studies will be needed to answer these questions.

A limitation of this study was its observational nature. We did not randomise treatment arms. Therefore, definitive conclusions about treatment need to be treated with some caution. Our data, however, strongly proffered messages that we are comfortable in adopting in our practice. In the future, this classification facilitates prospective, objective evaluations of different treatments or preferably preventative strategies.

Unsatisfactory progress in LAGB patients with either adverse symptoms or poor weight loss can usually be explained by pathophysiology or anatomical change. A stress barium and high resolution manometry are now sensitive, validated diagnostic tests. This facilitates selection of treatment with an accurate means of predicting outcome. The future challenge is to develop strategies that prevent these problems from developing as well as better understanding how and why they occur.

Declaration for Thesis Chapter 19

This Chapter represents a submitted manuscript.

Declaration by candidate

In the case of Chapter 19   the nature and extent of my contribution to the work was the following:

Nature of contribution	Extent of contribution (%)
Overall responsibility for all aspects of the study, conception, planning, patient recruitment, conducting experiments and recording data. Data analysis and interpretation. Statistical analysis. Crafting and revising manuscript.	>90%

The following co-authors contributed to the work:

Name	Nature of contribution
Kenneth Yap	Experimental design, development of technique, reporting of scintigraphic scans, manuscript review
Wendy A Brown	Designing study and recruiting patients, manuscript review
Cheryl Laurie	Recruiting and conducting studies
Matthew O'Donnell	Development of technique, performing and reconstructing studies
Geoff Hebbard	Experiment design, review of manuscript
Victor Kalff	Experiment design, development of technique, data acquisition and analysis, review of manuscript
Paul O'Brien	Experiment design, review of manuscript

Candidate's Signature		Date

Declaration by co-authors

The undersigned hereby certify that:

(1) the above declaration correctly reflects the nature and extent of the candidate's contribution to this work, and the nature of the contribution of each of the co-authors.
(2) they meet the criteria for authorship in that they have participated in the conception, execution, or interpretation, of at least that part of the publication in their field of expertise;
(3) they take public responsibility for their part of the publication, except for the responsible author who accepts overall responsibility for the publication;
(4) there are no other authors of the publication according to these criteria;
(5) potential conflicts of interest have been disclosed to (a) granting bodies, (b) the editor or publisher of journals or other publications, and (c) the head of the responsible academic unit; and
(6) the original data are stored at the following location(s) and will be held for at least five years from the date indicated below:

Location(s)	Centre for Obesity Research and Education, Monash University, Alfred Hospital

[Please note that the location(s) must be institutional in nature, and should be indicated here as a department, centre or institute, with specific campus identification where relevant.]

			Date
Kenneth Yap	███████████		2/11/9.
Wendy A Brown	███████████		27/10/09
Cheryl Laurie	███████████		4/11/09
Matthew O'Donnell	███████████		2/11/09
Geoff Hebbard	███████████		2/11/09
Victor Kalff	███████████		2/10/9
Paul E O'Brien	███████████		27.10.09

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CHAPTER 19: Effects of Adjustable Gastric Bands on Gastric Emptying, Supra and Infraband Transit and Satiety: A Randomised Double Blind Cross Over Trial

Abstract

Background: The laparoscopic adjustable gastric band (LAGB) has previously been classified as a restrictive procedure; inducing weight loss by physically limiting meal size. Recently, the key mechanism has been hypothesised to be the induction of early and prolonged satiety. These sensations can be controlled by modifying LAGB volume, possibly as a result of effects on gastric emptying or transit through the LAGB.

Methods: Successful LAGB patients underwent paired, double blinded, oesophageal transit and gastric emptying scintigraphic studies; performed with the LAGB at optimal volume and near empty. A new technique was developed that allowed reliable assessment of emptying and transit through the infra and supra band compartments.

Results: Fourteen of 17 patients completed both scans (6 males, mean age 48.9 ± 11.3 years, % excess weight loss 69.0 ± 15.2). At optimal volume a delay in transit of semi-solids into the infraband compartment was observed in 10 patients vs. 3 when the LAGB was empty, ($p=0.01$). Liquid transit was not affected. The median percentage retention of a meal in the supraband compartment immediately after cessation of intake was: empty 2.8% (2.3-7.9) vs. optimal 3.6% (1.7-4.5), ($p=0.57$). Overall gastric emptying half time (minutes) was normal at both volumes:

optimal 64.2±29.8 vs. empty 95.2±64.1, (*p=0.14*). LAGB volume did not affect

satiety before the scan: optimal 4.3±1.9 vs. empty 4.0±2.2, (*p=0.49*), or 90 minutes

later: optimal 6.1±1.9 vs. empty 5.9±1.4, (*p=0.68*).

Conclusions: The optimally adjusted LAGB briefly delays semi-solid transit into the

infra-band stomach. Overall gastric emptying is not affected. The supraband

compartment is usually empty of an ingested meal 1-2 minutes after intake ceases.

There was no evidence of physical restriction of meal size, although no change in

satiety was identified either.

Introduction

The laparoscopic adjustable gastric band (LAGB) has emerged as a safe and effective treatment for obesity [1, 2, 162, 282]. Traditionally the LAGB has been described as restrictive procedure; physically limiting meal size. More recently the key mechanism has been hypothesised to be the induction of early and prolonged satiety which can fine-tuned by adding or removing saline from the system [8].

How the LAGB circumvents control processes that vigorously defend body weight remains unknown. Although gastric emptying half times do not appear to change following LAGB [6], localised alterations in the transit and distribution of an ingested meal may be specific to the optimally adjusted LAGB. It is also possible that other effects of the LAGB around the gastric cardia are activating the peripheral satiety mechanism.

The stomach is a powerful and complex mediator of food intake [382]. Intragastric volume, independent of caloric density, is important in generating satiation; the immediate feeling of fullness [415-417]. Gastric distension needs to be maintained to inhibit intake in the absence of distal caloric delivery [419]. Gastric distension, both proximally and distally, is augmented by duodenal caloric delivery which releases satiety hormones that feedback peripherally and act centrally [116, 418]. Subtle changes in gastric emptying; even alterations in the fundal accommodation reflex can activate sensations of satiety and modulate appetite [396, 397].

Several studies have not identified alterations in gastric emptying half times following LAGB   or other bariatric procedures [6, 377, 379, 380]. Two recent studies

have, however, suggested there is prolonged emptying of the pouch of stomach above the LAGB [370, 371]. Sustained focal distension of the cardia with linear pouch emptying over minutes to hours could be expected to generate signals of satiety. This would also suggest that the LAGB is acting as a restrictive procedure; physically limiting food intake by filling the small pouch of stomach above the LAGB and thereby causing the patient to feel full.

Video fluoroscopic studies, in contrast, have shown that the transit of individual semi-solid boluses through the LAGB is delayed only by seconds to 1-2 minutes [533]. A basal intraluminal pressure of approximately 20-30 mmHg, at the LAGB, is consistently observed in successful patients and limits trans LAGB flow [533, 538].

Repeated peristaltic contractions are stimulated by luminal distension above the LAGB, a pattern that continues until the supraband compartment is cleared [540]. Transit across the LAGB is only observed during peristaltic contractions. More prolonged stasis above the LAGB is strongly associated with adverse symptoms such as reflux, dysphagia and regurgitation [537].

This question of how a meal is distributed and transited through the oesophago-gastric compartment in a LAGB patient remains unanswered.

Assessments of gastric emptying using nuclear scintigraphy are limited by poor anatomical resolution [373]. This is a particular problem with the LAGB as a meal within the tiny gastric pouch above the LAGB needs to be separated from the expected accumulation in the gastric fundus; immediately beneath the LAGB.

We aimed to identify the effects on gastric emptying and transit through the supraband compartment of changing LAGB volume in patients with good weight loss. We hypothesised that alterations in transit, localised to the region above the LAGB, would be identifiable if a means for accurately anatomically localising the LAGB during scintigraphic studies could be developed.

Methods

This research was approved by the Monash University and Alfred hospital human ethics committees. All participants gave informed consent.

Subjects

Patients whose surgery was considered successful were invited to participate during consultations with bariatric physicians. Criteria for inclusion were: age 18-65 years, % excess weight loss (EWL) >50, > 12 months following surgery, normal contrast swallow or endoscopy performed within 12 months as part of routine care, no significant adverse symptoms of regurgitation or reflux and a stable volume of saline maintained within the LAGB for the past 3 months.

Exclusion criteria were: diabetes (including a past history), use of medications considered to affect gastric emptying, known abnormality of gastric motility or emptying, pregnancy or breast feeding. Patients with less than 2 ml in their band could not participate for technical reasons (see below). Patients who had undergone revisional LAGB surgery, previous gastric or bariatric surgery were also excluded.

Each patient underwent 2 nuclear scintigraphic oesophageal transit and gastric emptying studies. One was performed with the LAGB at its optimal volume and another with 1 ml within the LAGB (to allow visualisation of the LAGB – see below). Scans were performed 7-14 days apart, commencing at 0830 following a complete fast from midnight.

Satiety was assessed before commencing and after completing each scan. A 25 cm visual analogue scale was used; with 0 representing starving hungry and 10 being absolutely full, to the point of bursting.

The sequence of scans was randomised and patients, the physician reporting the scans and technicians were at no stage informed of the volume status of the LAGB. At the conclusion of each scan the LAGB volume was returned to its original level or a sham adjustment performed.

Gastric Emptying and Oesophageal Transit Scintigraphy Protocol

A new technique was developed that allowed LAGB visualisation during scintigraphic studies. Figure 19.1 highlights the difficulties in assessing transit in the region of the LAGB using conventional techniques. The new technique involved accessing the LAGB port with a 21 gauge Huber needle, attached to a syringe with a three way stopcock. A syringe containing 10 MBq of Technetium (Tc)-99m Pertechnetate in 0.5 ml of saline was attached to the sidearm. After accessing the LAGB port it was either emptied or 1 ml of saline removed; depending on the randomised condition of the scan. The Technetium was then injected into the band

followed by a 0.5 ml saline flush. A static 2 min image was acquired with the patient supine in the left anterior oblique (LAO) 30° projection to obtain a baseline image of the LAGB. Consequently, different regions of interest (ROI) above and below the LAGB were able to be identified. This allowed division and separate analysis of transit through and emptying of the supra and infraband compartments. Importantly, the appearance of the LAGB was checked prior to the ingestion of any labelled meal. This allowed accurate characterisation of the appearance of the region immediately above the LAGB for comparison during the study. Figure 19.2 illustrates the use of this technique.

Subjects presented following an overnight fast. A modified version of a previously described radiolabelled semi-solid porridge meal was prepared as follows: 30g of quick oatmeal and 100 ml of full cream milk were microwaved and mixed well with 1 teaspoon of cane sugar and 30 MBq of Tc-99m Calcium Phytate (Austin Health, Melb, Aus) [372].

Scintigraphy was performed using a General Electric Millenium MPS single detector head Gamma Camera (Milwaukee, WI) with low energy high resolution collimation, 64 x 64 pixel matrix and without zoom. Images were processed on a General Electric Xeleris 1.1 Functional Imaging Workstation.

FIGURE 19.1: Poor Anatomical Resolution of Nuclear Scintigraphy

Scintigraphic image   **Liquid contrast swallow**

Figure 19.1 Legend: *Scintigraphic image and liquid contrast swallow from the same patient. It is impossible to identify the site of the LAGB in the scinitgraphic image. The contrast swallow provides good anatomical detail, however, only limited functional information.*

FIGURE 19.2: Visualisation of LAGB and Supraband Region of Interest

Prior to Eating   **After Eating**
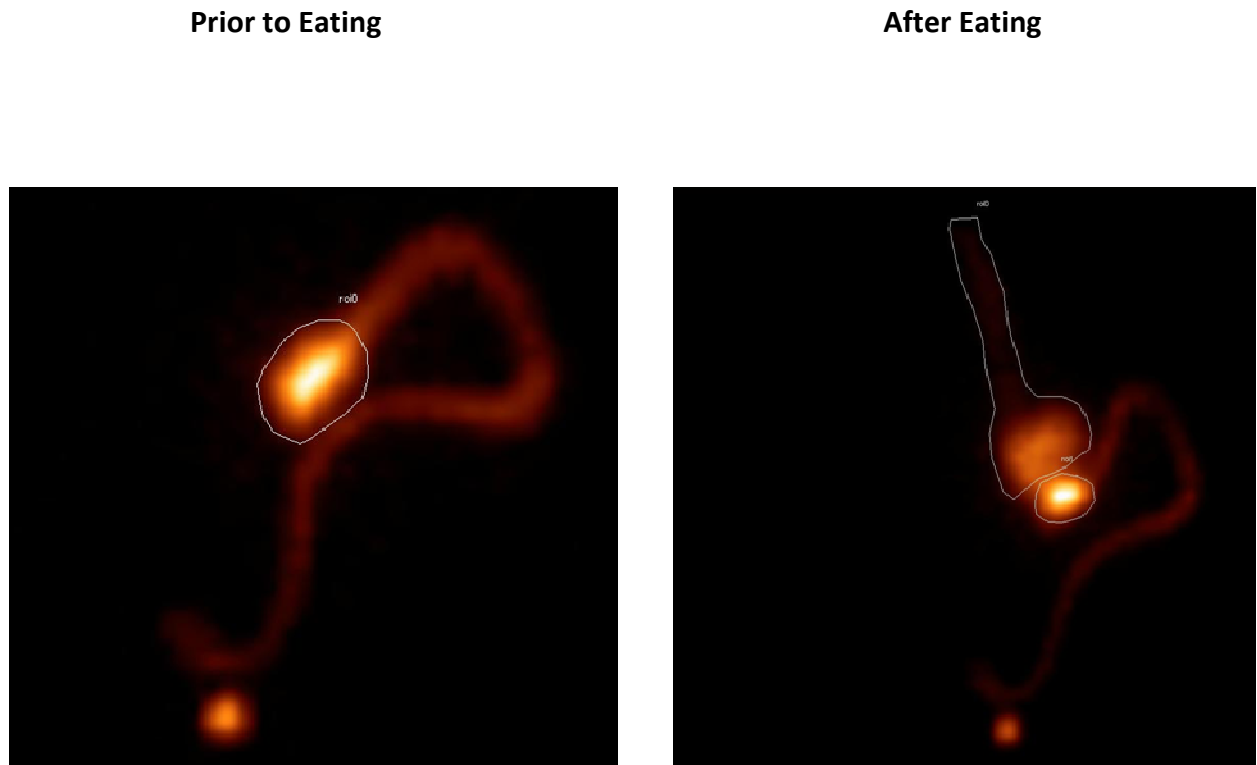
Figure 19.2 Legend: *Prior to eating, the LAGB, port and connecting tubing are clearly seen following injection of 4 MBq of Technetium diluted in 0.5 ml of saline. In the second panel, after eating has commenced, regions of interest have been drawn above and around the LAGB. The location of the ingested bolus can be seen clearly; in this case it is above the LAGB.*

Semi-solid transit through the oesophagus and supraband compartment into the infraband compartment was imaged in the erect position by performing duplicate studies of a single swallow of a tablespoon full of porridge on command. Images were acquired in the posterior projection, one second per frame for 60 seconds. Following this, the patient was instructed to consume as much of the remainder of the meal as tolerable over up to 15 minutes. The amount of the meal consumed and any symptoms precipitated over the duration of the study were recorded.

The gastric emptying study was performed by acquiring images with the patient supine in the left anterior oblique 30° projection. Sequential 2 minute acquisitions were performed over 90 minutes. Standardised room conditions were maintained and the patient was required to lie still and not sleep.

Liquid oesophageal transit was performed after completion of the gastric emptying study. Images were acquired in the supine position by performing duplicate, supine studies of a single swallow of 5 MBq of Tc-99m Calcium Phytate in 10 ml of water administered by a syringe. Images were acquired from a posterior projection on a radiolucent imaging table, one second per frame for 60 seconds.

The semi-solid and liquid transit images were processed in the same way. For each swallow the activity counts in a ROI drawn around the oesophagus and supraband compartment, without encompassing the LAGB, were recorded. These were subsequently represented as a function of time in a time-activity curve (TAC) over 60 seconds (1 image per second). Each semi-solid and liquid transit study was graded as delayed or normal and the nature of any delay noted. Normal transit was defined as complete clearance across the oesophago-gastric junction and LAGB by

progressive antegrade transit, without reflux. Delayed transit was defined as any appreciable hold up of the bolus above the LAGB or evidence of reflux back into the oesophagus from the region above the LAGB. If a delay was observed the nature and pattern and any associated symptoms were recorded.

Immediately after completing the standard meal, residual semi-solid retained above the LAGB was quantified using the first 2 min acquisition frame of the gastric emptying study. Counts within the supraband ROI were expressed as a percentage of the total counts within the ROI encompassing the entire gastro-oesophageal region, excluding counts within the LAGB.

Gastric emptying images were processed by determining the counts and TAC in a ROI encompassing the entire gastro-oesophageal region and LAGB with an emptying halftime derived from the TAC.

Statistical analysis

All statistical analysis was performed using SPSS V 16.0 (SPSS inc., Chi, Ill). For comparisons of paired, normally distributed, continuous data paired t tests were used. For non-normally distributed data Mann-Whitney Rank Sum tests were used. Chi square tests or Fisher's exact test, as appropriate, were used to compare proportions. A two sided *p* value of 0.05 was considered statistically significant. Normally distributed data are presented as means and standard deviation and non-normally distributed data as median and interquartile range.

Weight and demographic data was sourced from a prospectively maintained online bariatric database (*www.lapbase.net*).

Results

Seventeen patients participated, 3 were excluded as they were unable to complete the study; two during the initial scan and another was unable to tolerate the second scan after successfully completing the initial scan. Patient details are shown in Table 19.1. All patients had achieved and maintained a substantial weight loss.

TABLE 19.1: Patient Details (n=14)

Age (years)	48.9±11.3
Start weight (kg)	143.3±25.5
Start BMI (kg/m^2)	48.1±5.9
Current Weight (kg)	96.3±18.2
Current BMI (kg/m^2)	32.2±4.1
Excess Weight loss (%)	69.0±15.2
Duration from surgery (years)	2.6±1.4
Male/Female	6/8
APS band	7
APL band	3
VG band	3
10 cm band	1

Transit into the infraband stomach

Semi-Solid: When the LAGB was at optimal volume 10 patients demonstrated delayed   transit into the infraband compartment compared to only 3 when the

LAGB was empty (*p=0.01*). Two general patterns of delay were observed. In both the hold up was at the LAGB. The first pattern consisted of a brief delay at the level of the LAGB, after which the bolus fully transited into the infraband stomach. The second pattern consisted of an oscillating pattern where the bolus (or a part thereof) refluxed back into the oesophagus, before being pushed down into the supraband stomach again. There was progressive delivery of the bolus into the infraband stomach with a decline in activity in the supraband compartment corresponding to an increase in counts in the infraband compartment. Anatomical resolution was not considered adequate to reliably classify transit further than normal or delayed. Figure 19.3 shows semi-solid transit with the LAGB at optimal volume and empty.

The three patients that were unable to complete the study developed obstruction during the semi-solid swallow, with the bolus becoming impacted above the LAGB. These patients were immediately aware of the obstruction and developed significant symptoms of discomfort.

Liquid: The same 3 patients in each group demonstrated a delay in transit with the LAGB empty and at optimal volume.

FIGURE 19.3: Semisolid Swallows with LAGB Empty (A) and Optimal Volume (B)

A) Empty – Immediate transit

B) Optimal volume – Delayed transit
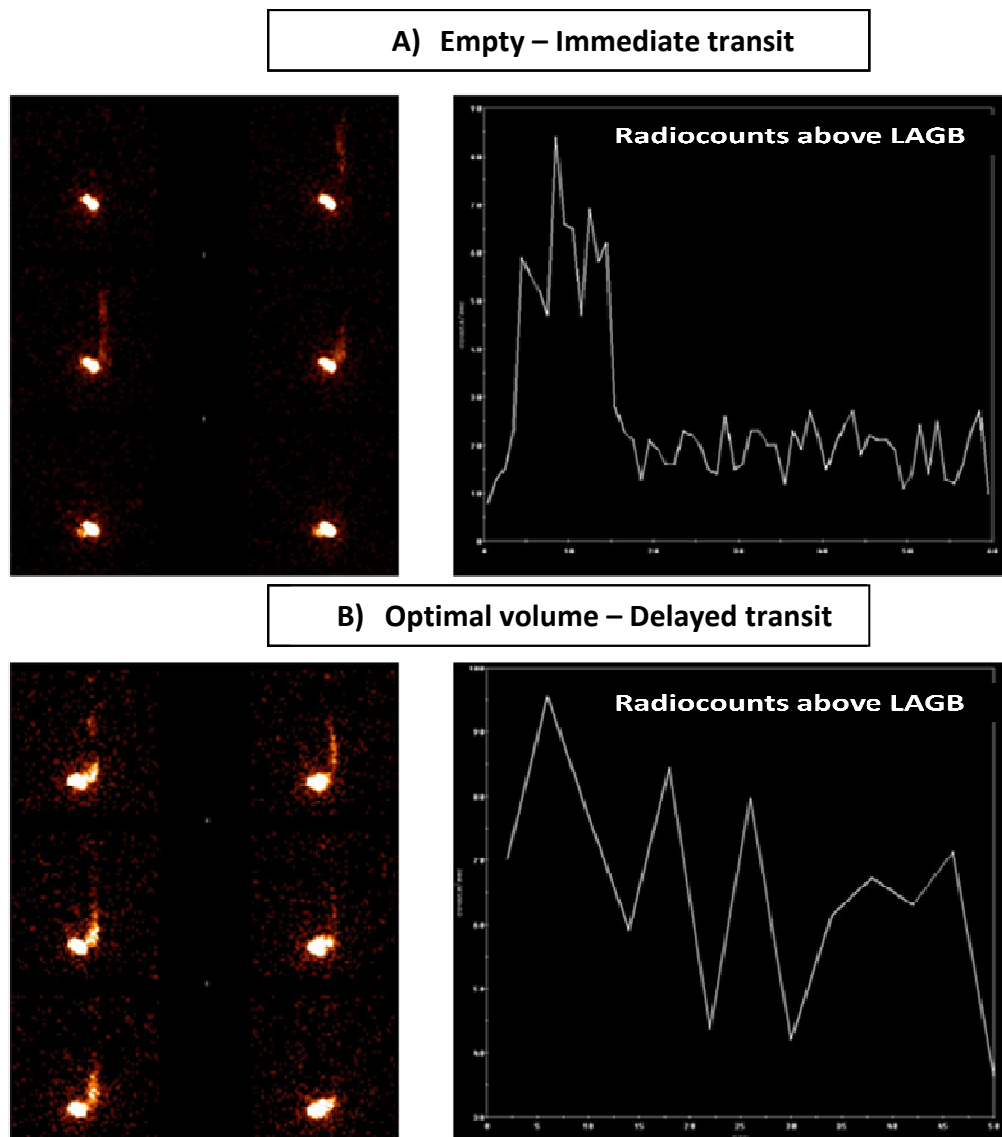
Figure 19.3 Legend: *Images of transit over 60 seconds co-displayed with the radiocounts measured above the LAGB. In panel A, with the LAGB empty, there is rapid transit of semi-solid into the infraband compartment. There is no appreciable hold up. The images show the bolus rapidly passing through the oesophagus and supraband compartment, the bolus becomes clearly visible beneath the LAGB within*

the infraband compartment. In Panel B an oscillating pattern of counts within the supraband compartment is observed. Episodes of reflux are observed, however, there is progressive transit of the bolus into the infraband compartment.

Gastric emptying

No difference in overall gastric emptying half time was identified: at optimal volume 64.2±29.8 min. vs. 95.2±64.1 min. empty, (*p=0.14*).

There was minimal residual activity above the LAGB at either volume immediately after consumption of the semi-solid meal in the majority of patients. The median proportion (IQR) empty was 2.8% (2.3 – 7.9) vs. 3.6% (1.7 – 14.5), (*p=0.57*) at optimal volume. Data for individual patients are displayed in Figure 19.4. Calculation of supra and infraband emptying half times was not deemed useful because virtually the entire meal had passed into the infraband stomach by the time the initial 2 minute frame had been acquired.

Satiety

There was no significant difference in satiety before the scan (optimal 4.3±1.9 vs. empty 4.0±2.2, *p=0.49*). There was no difference in satiety after the scan (optimal 6.11±1.9 vs. empty 5.9±1.4, *p=0.68*). Under both conditions patients were significantly less hungry at the completion of the scan (optimal, *p=0.02*, empty, *p=0.10*).

No difference was detected in the volume of the porridge meal consumed between the LAGB at optimal volume compared to empty: 95±12% vs. 91±16%, (*p=0.44)*; nor was there a difference in the time taken to consume the meal: 6.0±4.2 min. vs. 7.1±4.2 min., (*p=0.22)*.

**FIGURE 19.4: Percentage of Semi-Solid Meal Retained Above LAGB 2 Minutes after Meal Completion**
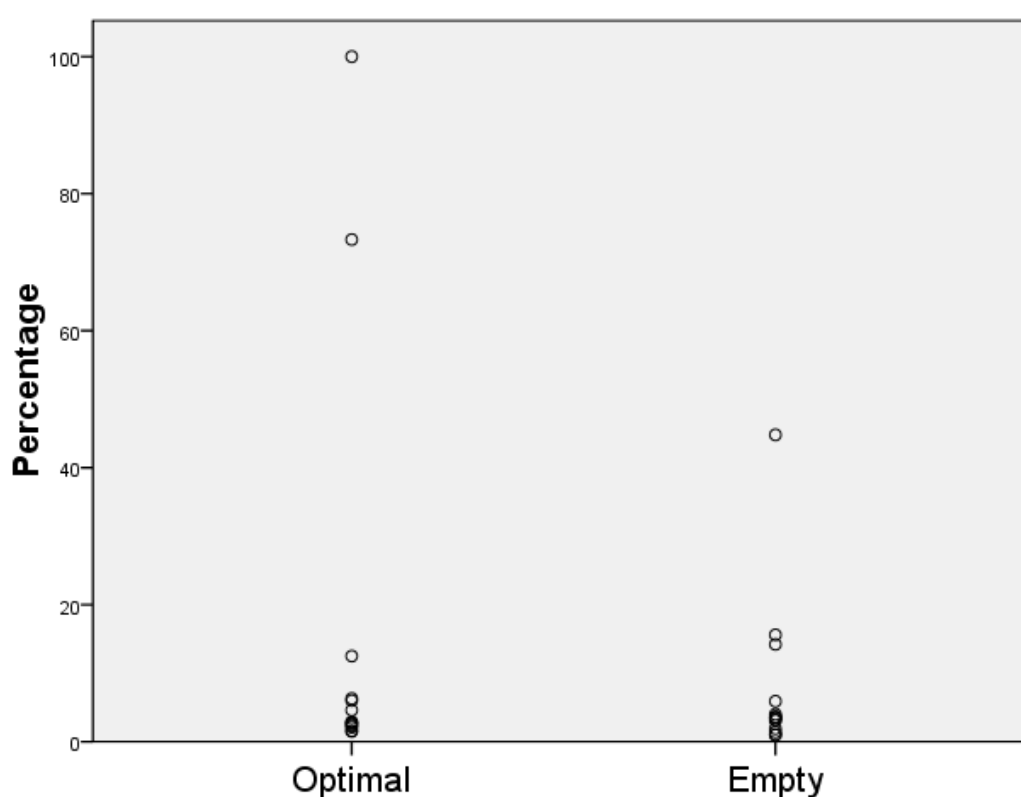
Figure 19.4 Legend: *The proportion of the semi-solid meal (expressed as percentage of total radiocounts) above the LAGB determined by the initial 2 minute acquisition frame. A data point is displayed for each individual stratified by LAGB volume.*

Discussion

We have shown that in successful LAGB patients there is a brief delay in the passage of semi-solids but not liquids, into the infraband stomach. This only occurred when the LAGB was at optimal volume. Bolus transit was delayed at the level of the LAGB. If complete clearance was not immediately achieved, at times, residual bolus was observed to reflux back into the oesophagus; presumably stimulating repeat peristalsis driving the bolus back to the LAGB.

Meal retention above the LAGB was not observed at either LAGB volume. The initial 2 minute acquisition frame generally demonstrated virtually no radiocounts above the LAGB. Measuring an emptying half time of the supraband compartment was not considered practical as by this time virtually all radiocounts were in the infraband compartment. The optimally adjusted LAGB does not appear to act as a restrictive procedure, transit is briefly delayed but total meal size is not physically limited.

We developed a specific, novel technique that allowed us to confidently visualise the LAGB and thereby definitively evaluate the regions above and below it. In contrast to previous studies we did not identify any evidence of retention within the supraband stomach [7, 370, 371]. It is most difficult to accurately determine the location of the LAGB without this anatomical resolution and this may explain different results obtained by others.

Overall gastric emptying was not affected by alterations to LAGB volume. We were not surprised that the gastric emptying half time was not affected by altering LAGB volume; it was within the normal range under both conditions. Other investigators

have made similar observations using paired pre and post-operative gastric emptying studies [6].

Early descriptions of the technique for placement of an adjustable gastric band involved creating a pouch of stomach, the size of a small meal, above the LAGB. It was hypothesised that distension, followed by progressive emptying of this small pouch would sustain the activation of gastric sensory receptors; ensuring that early satiation and prolonged satiety occurred after only a small meal [229]. The current LAGB surgical technique, however, involves placement of the LAGB immediately beneath the oesophago-gastric junction, meaning that the supraband pouch of stomach is unable to accommodate even the smallest of meals.

In successful patients the LAGB produces an intraluminal pressure of 20-30 mmHg, 1-2 cm beneath the oesophago-gastric junction [533, 538]. This consistent finding is associated with weight loss. Due to the significant resistance presented by the LAGB, oesophageal peristalsis is required to mediate episodes of liquid or semi-solid flow across the LAGB [533]. We suspect that the normal situation following LAGB is for a meal to be cleared episodically. Boluses are swallowed in a slow interspersed manner, with the patient dependent on oesophageal and proximal gastric sensory feedback to determine when it is appropriate to take the next mouthful. If even a small bolus is impacted above the LAGB, unpleasant sensory feedback as a result of high intraluminal pressure and luminal wall distension, alerts the patient. Further intake is delayed until the bolus has transited across the LAGB.

In this study LAGB volume did not appear to significantly affect satiety, although few patients reported significant hunger at any stage. All patients presented on the

morning of each scan with a stable, optimal volume within the LAGB. After consumption of the semi-solid meal they were all significantly less hungry. However, no difference in satiety was observed with alterations in LAGB volume to which they were blinded.

This is in contrast to a previous study where a powerful immediate and prolonged satiating effect was observed when patients were given a standard meal at their optimal volume compared to a reduced volume [8]. There are three possible explanations for this. Firstly, the current study truly blinded patients, whereas in the previous study alterations to LAGB volume were made 48 hours prior to the assessment of satiety. Undoubtedly, over two days, patients would have become aware that the LAGB volume had been reduced. This knowledge could easily influence perceptions of such a subjective and complex sensation as satiety. Secondly, we removed saline immediately prior to the study starting and assessed hunger only over a 90 minute period. On the morning of the study the LAGB was active and this effect may not have waned over this relatively brief period of time. Thirdly, a homogeneous, bland semi-solid meal was given. This may not have been of an appropriate texture or volume to adequately activate the satiety response. Assessing satiety and hunger is also complicated by the poor correlation of reported hunger and observed food intake [106].

This study suggests that the LABG functions differently to restrictive procedures that reduce or compartmentalise gastric volume: gastroplasty, sleeve gastrectomy or gastric bypass (excluding additional hormonal effects). With these procedures the reduced stomach volume is distended as it accommodates a small meal; this is

followed by normal gastric emptying. Not surprisingly, these patients feel completely full after a small meal.

Alterations in transit following LAGB have been demonstrated, however, were not associated with changes in satiety. These patterns appear to be the expected norm following LAGB. However, it has not been conclusively shown that the LAGB should be classified as satiety inducing.

We have shown that the optimally adjusted LAGB briefly delays transit into the infraband stomach. A semi-solid meal was not retained in the supra band stomach. Therefore, the LAGB should not be considered to act as a restrictive procedure; it does not physically limit the size of a meal that can be consumed. The delay in transit was reversed by removing saline from the LAGB. As the next step it will be important to correlate changes in transit and emptying patterns with weight loss and changes in satiety that develop following LAGB.

Declaration for Thesis Chapter 20

This chapter represents a submitted manuscript.

Declaration by candidate

In the case of Chapter 21 the nature and extent of my contribution to the work was the following:

Nature of contribution	Extent of contribution (%)
Overall responsibility for all aspects of the study, conception, planning, patient recruitment, conducting experiments and recording data. Data analysis and interpretation. Statistical analysis. Crafting and revising manuscript.	>90%

The following co-authors contributed to the work:

Name	Nature of contribution
Kenneth Yap	Experimental design, development of technique, reporting of scintigraphic scans
Wendy A Brown	Designing study and recruiting patients, manuscript review
Cheryl Laurie	Recruiting patients and conducting studies, manuscript review
Matthew O'Donnell	Development of technique, performing and reconstructing studies
Geoff Hebbard	Experiment design, review of manuscript
Victor Kalff	Experiment design, development of technique, data acquisition and analysis, review of manuscript
Paul O'Brien	Experiment design, review of manuscript

Candidate's Signature		Date	

Declaration by co-authors

The undersigned hereby certify that:

(1) the above declaration correctly reflects the nature and extent of the candidate's contribution to this work, and the nature of the contribution of each of the co-authors.
(2) they meet the criteria for authorship in that they have participated in the conception, execution, or interpretation, of at least that part of the publication in their field of expertise;
(3) they take public responsibility for their part of the publication, except for the responsible author who accepts overall responsibility for the publication;
(4) there are no other authors of the publication according to these criteria;
(5) potential conflicts of interest have been disclosed to (a) granting bodies, (b) the editor or publisher of journals or other publications, and (c) the head of the responsible academic unit; and
(6) the original data are stored at the following location(s) and will be held for at least five years from the date indicated below:

| Location(s) | Centre for Obesity Research and Education, Monash University, Alfred Hospital |

[Please note that the location(s) must be institutional in nature, and should be indicated here as a department, centre or institute, with specific campus identification where relevant.]

		Date
Kenneth Yap	████████████	2/11/9.
Wendy A Brown	████████████	27/10/09
Cheryl Laurie	████████████	4/11/09
Matthew O'Donnell	████████████	2/11/09
Geoff Hebbard	████████████	2/11/09
Victor Kalff	████████████	2/11/09
Paul E O'Brien	████████████	27.10.09

CHAPTER 20: *Changes in Satiety, Supra and Infra-band Transit and Gastric Emptying Following Laparoscopic Adjustable Gastric Banding: A Prospective Follow up Study*

Abstract

Background: Laparoscopic adjustable gastric banding (LAGB) induces and sustains weight loss, likely by activating the peripheral satiety mechanism. Recent data suggests that food is not retained above the optimally adjusted LAGB; suggesting that an alternate mechanism is inducing satiety. How transit and gastric emptying change following LAGB and correlate with satiety and weight loss have not been adequately defined.

Methods: LAGB patients underwent pre-operative and 12 month follow up nuclear scintigraphic assessments of oesophageal transit and gastric emptying. A new technique that allowed the calculation of emptying times and transit through the supra and infraband compartments was used to assess emptying and transit patterns post-operatively.

Results: Post-operatively, patients reported increased satiety both after a standard fast (3.7±2.3 vs.4.8±2.1, *p=0.04*) and following a standard semi-solid meal (5.9 vs. 7.8±1.7, *p=0.003*). The mean %excess weight loss was 48.5±23.2%. The gastric emptying half time (minutes) did not change significantly (63.5±41.1 vs. 73.3±26.8, *p=0.64*). Semi-solid transit into the infraband stomach was delayed briefly post-operatively in more patients (11 vs. 2, *p=0.001*). There was minimal retention of the meal above the LAGB 2 minutes after commencing the gastric emptying study

(median 3%, interquartile range: 1.75-10); therefore an emptying half time of the supraband region could not be defined.

Conclusions: Weight loss, satiety and early satiation following LAGB were associated with briefly delayed bolus transit into the infraband stomach. Retention of the semi-solid meal above the LAGB was not observed. This is further evidence that suggests satiety develops following LAGB without physical restriction of meal size.

Introduction

Despite worldwide use of the laparoscopic adjustable gastric band (LAGB), much remains unknown about the physiological changes that occur following placement [1]. Data from chapter 19 supports the hypothesis that the LAGB does not physically restrict meal size. At optimal volume a brief delay brief delay in semi-solid transit into the infraband stomach was observed. This effect was removed when LAGB volume was reduced. That study, however, did not identify an effect of altering LAGB volume on satiety.

A possible explanation for satiety not changing was that there were ongoing effects that had not yet waned; as LAGB volume was altered immediately before the meal. If alterations in satiety can be demonstrated without meal retention above the LAGB, this would strongly suggest that the LAGB is activating the peripheral satiety mechanism without physically limiting meal size.

It is likely that any effect is mediated via the stomach. Therefore, characterising changes in transit and gastric emptying that occur after LAGB placement will provide important information. This will also allow changes in these physiological measurements to be correlated with weight loss and reported satiety.

Whilst the stomach and its volume status is an important mediator of satiety and food intake [382], changes in overall gastric emptying are not seen following LAGB or other bariatric procedures [6, 377, 379, 380]. Accelerated gastric emptying has been proposed as a mechanism of obesity [384]. Current consensus suggests that altered gastric emptying is not central to the causation of obesity [383, 388]. If

bariatric procedures significantly delayed gastric emptying, weight loss would not necessarily occur, although severe symptoms could be induced [389]. It seems more likely the placement of the LAGB immediately beneath the oesophago-gastric junction (OGJ) has specific extra or intraluminal effects that induce early and prolonged satiety.

Combined high resolution manometry and video fluoroscopic studies have shown the optimally adjusted LAGB produces an intraluminal pressure of 20-30 mmHg, just distal to the OGJ [533, 538]. This delays semi-solid bolus transit into the infraband stomach. A limitation of the fluoroscopic studies is that they have not modelled the intake of an entire meal, evaluating only the transit of individual boluses. Importantly, they have not assessed patients pre and post-operatively; therefore prospective correlations of alterations in physiology with reported satiety and weight loss have been limited.

We hypothesised that following LAGB, specific focal physiological changes developed in the region of the LAGB without altering the gastric emptying half time. We also hypothesised that these changes would be associated with increased fasting satiety and post meal satiation. We aimed to characterise changes in transit and emptying of the supra and infraband stomach and determine how these physiological changes correlated with weight loss and satiety following LAGB.

Methods

The Monash University and Alfred Hospital human ethics committees approved this research. All participants gave informed consent.

Subjects

Patients undergoing primary LAGB were given information during pre-operative consultations with surgeons and invited to participate. Inclusion criteria were: age 18-65 yrs and undergoing LAGB. Exclusion criteria were: diabetes, use of medication known to modify gastric motility or known abnormality of gastric motility, previous gastric, oesophageal or bariatric surgery, pregnancy or breast feeding.

Study

Patients underwent a nuclear scintigraphic gastric emptying and oesophageal transit study pre-operatively and 12 months post-operatively. All pre-operative scans were performed prior to patients commencing a pre-operative, very low calorie diet which we frequently use to reduce liver size [546].

Immediately prior to the scan patients were asked to mark on a 25 cm visual analogue scale how satisfied or hungry they felt. Possible scores ranged from 0 ravenously hungry, to 10 completely full to the point of bursting. Immediately after completing the scan patients were asked to complete the same score.

Surgical technique

A standardised, pars flaccida surgical technique was used with secure placement of the LAGB immediately beneath the OGJ. The location of the LAGB in relation to the OGJ was checked using the calibration balloon containing 25 ml of air, with the anterior aspect of the LAGB circling the apex of distension produced by the balloon. A broad anterior fixation, with 3 sequential gastro-gastric seromuscular sutures was used to create a wrap over the top of the band, to within 1 cm of the buckle. An additional lesser curve plicating stitch was performed to imbricate the gastric wall just beneath the LAGB, reducing its capacity to prolapse medially. Post-operatively, the initial 4 week follow up appointment was with the surgeon. Subsequent follow up occurred at a large, dedicated LAGB follow up centre. Patients were then managed by bariatric physicians who were not aware these patients had participated in the study. Follow up was in a routine manner, with adjustments made to LAGB volume based on weight loss and satiety evaluated against the presence of adverse symptoms (if any) [3].

Technique of nuclear scintigraphy

A standard oesophageal transit and gastric emptying study was performed pre-operatively, using the method described in chapter 19. Twelve months post-operatively patients presented for the second scan. To facilitate identification of the LAGB a new technique was developed that allowed the LAGB to be visualised during nuclear scintigraphic studies. This allowed regions of interest (ROI) to be accurately defined above and below the LAGB. This technique and the method used

to calculate overall and compartmental gastric emptying were described in chapter 19.

Semi-solid transit through the oesophagus and supraband compartment (or the oesophagus and OGJ pre-operatively) into the infraband compartment (or stomach pre-operatively) was imaged in the erect position by performing duplicate studies of a single swallow of a tablespoon full of porridge on command.

Statistical analysis

All statistical analysis was performed using SPSS v 16.0 (SPSS, Chi, Ill). Normally distributed data are presented as means and standard deviation; non-normally distributed data are presented as median and interquartile range. Comparisons of normally distributed continuous data were made using paired t tests. For non-normally distributed data, Mann Whitney Ranked Sum tests were used. For the analysis of categorical data Chi square or Fisher's exact tests were used as appropriate. A two sided *p* value of 0.05 was considered statistically significant. All weight loss and demographic data was sourced from a prospectively maintained, online dedicated bariatric surgical database (*www.lapbase.net)*.

Results

Eighteen patients participated; details are shown in Table 20.1. Fourteen returned for the 12 month follow up scan. Of the 4 that did not return, 3 had moved interstate or overseas as a result of their employment and 1 patient withdrew from the study. At the follow up scan two patients developed obstruction and

regurgitation, therefore transit and gastric emptying data was not available for the post-operative scan; they were excluded from analysis.

TABLE 20.1: Patient Details

Number	12
Male /Female	2/10
Age (years)	40.4±12.7
Start weight (kg)	121.8±15.8
Start BMI (kg/m^2)	45.3±6.5
Weight (kg) at follow up	96.7
BMI at follow up (kg/m^2)	36.0±6.8
% Excess weight loss	48.5±23.2

Satiety and Consumption of Standard Meal

Post-operatively, patients reported significantly less hunger, both before and following the scan. Satiety before the scan increased from 3.7±2.3 to 4.8±2.1, (*p=0.04*). Satiety after the scan increased from 5.9±1.2 to 7.8±1.7, (*p=0.003*). Patients reported significantly less hunger following the scan both pre (*p=0.009*) and post-operatively (*p=0.001*). The increase in satiety, when comparing reported satiety before the meal and after the scan was greater post-operatively; (1.9±2.1 vs. 3.0±2.3*, p=0.04*). Figure 20.1 illustrates changes in satiety.

Significantly less of the standard meal was consumed post-operatively, 65±29%vs. 100%, (*p=0.005*). No difference in the time taken to consume the meal was identified 6.5±3.1 min. vs. 5.7±2.6 min. (*p=0.58*).

FIGURE 20.1: Change in Reported Satiety Following LAGB: Before and 90 Minutes After a Standard Semi-Solid Meal
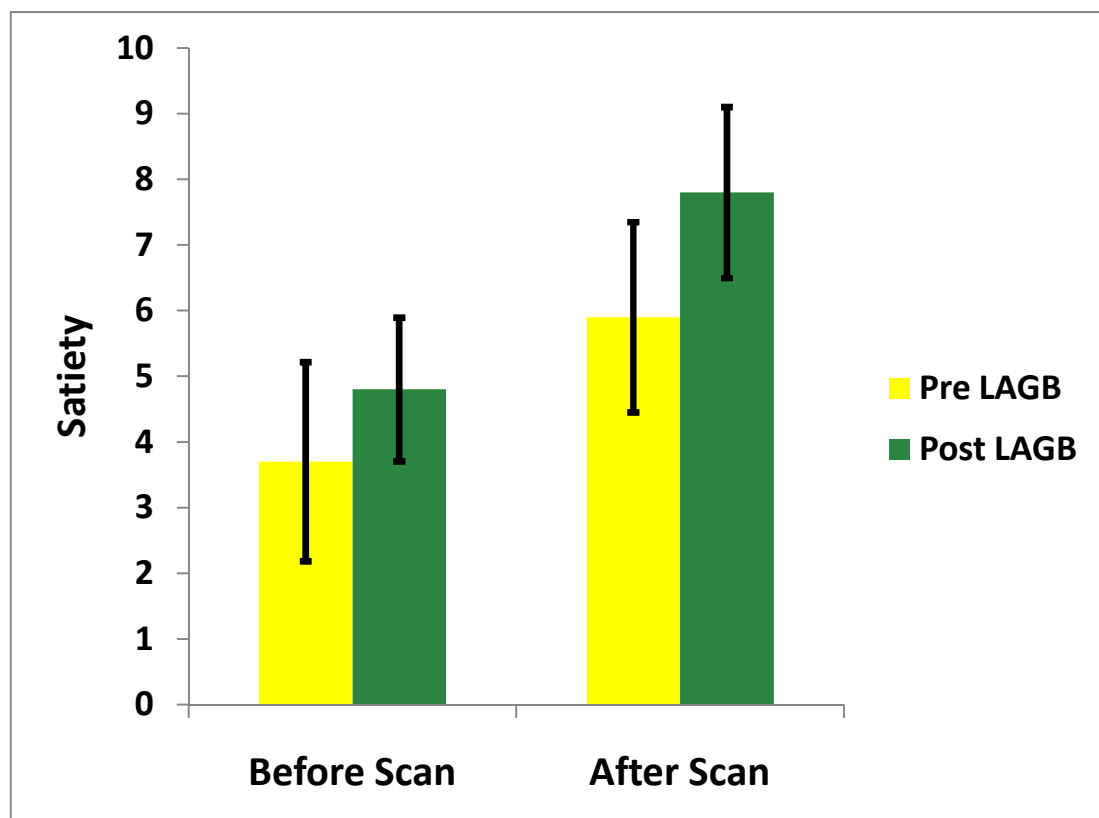
Figure 20.1 Legend: *Following LAGB fasting satiety increased significantly as did satiety 90 minutes following a standard semi-solid meal (p<0.05).*

Pre-operatively, only one patient demonstrated evidence of a delay in semi-solid oesophageal transit, whilst post-operatively 11 patients demonstrated delayed transit into the infraband stomach (*p=0.001*). Figure 20.2 illustrates the delay in transit observed. Post-operatively, prolonged retention or stasis in the supra-band stomach with progressive emptying was not observed. In contrast, the patients who developed severe symptoms of obstruction had the semi-solid bolus impacted in the region immediately above the LAGB.

FIGURE 20.2: Delay in Semi-Solid Transit into the Infraband Compartment
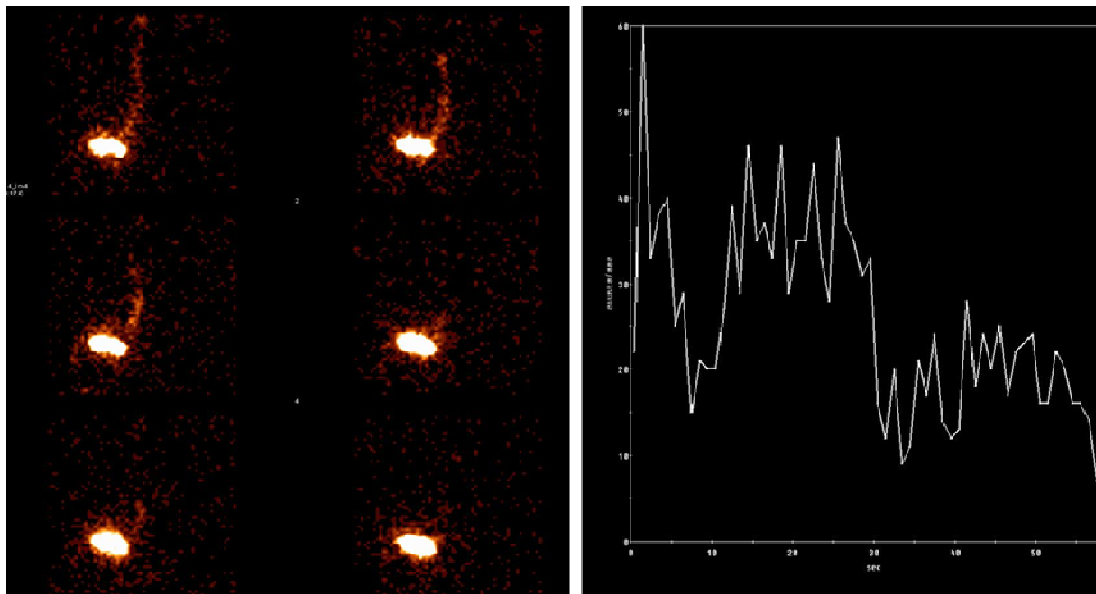
Figure 20.2 Legend: *Post-operative scan of semi-solid transit through the supraband compartment. The images demonstrate progressive transit through the oesophagus, with a delay in passage of the bolus into the infraband stomach. The*

corresponding graph shows the decline in radiocounts detected in the supraband

region of interest over 60 seconds. Transit of the bolus, whilst delayed, is complete.

The patient demonstrating a delay in semi-solid transit through the supraband

compartment pre-operatively underwent high resolution video manometry, which

diagnosed a severe impairment in oesophageal motility. At follow up, this patient

had lost 23kg (34% EWL); although semi-solid transit was again significantly

delayed.

No patient demonstrated a delay in liquid transit pre-operatively and only one did

post-operatively, (*p=0.37*).

Changes in Gastric Emptying

Post-operatively, the median percentage of total counts in the supraband

compartment at the start of the scan was 3% (interquartile range: 1.75-10). There

was no definable emptying half time able to be calculated from this region. Figure

20.3 illustrates an initial 2 minute supraband acquisition frame from the gastric

emptying study. One patient demonstrated significant stasis above the LAGB with

72% of the meal remaining above the band at the start of the study, although this

patient was significantly symptomatic, having to get up and walk around until the

bolus cleared into the infraband stomach. The initial image from this patient is

shown in figure 20.4.

FIGURE 20.3: Emptying of the Supraband Compartment
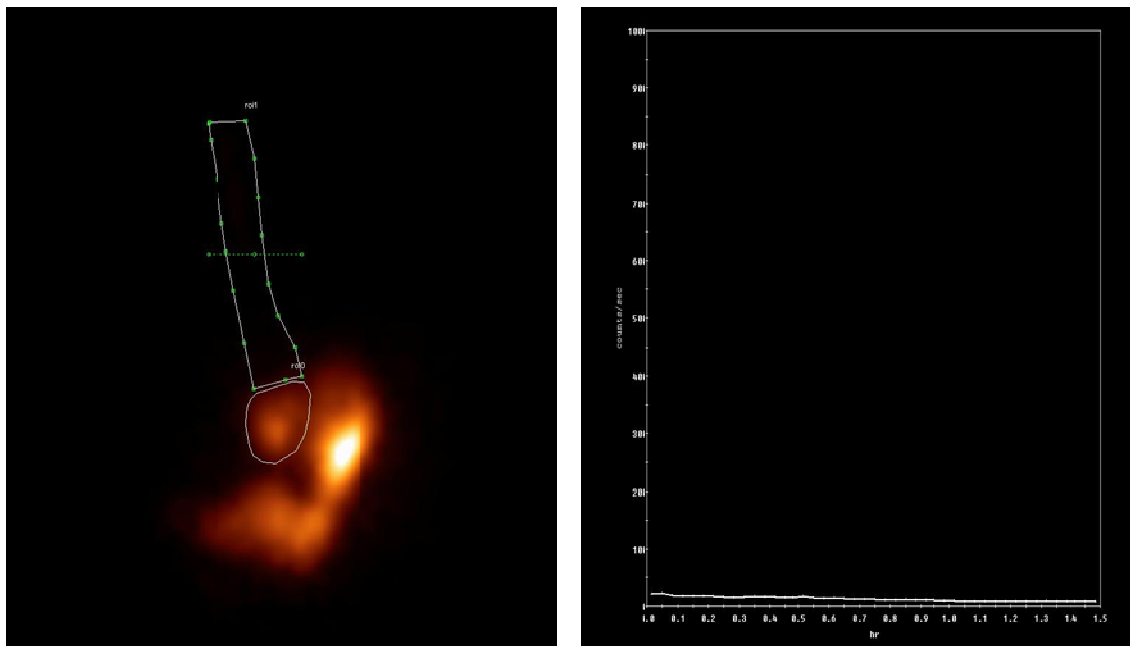
Figure 20.3 Legend: *Regions of interest have been drawn around the LAGB and the supraband compartment. The image displayed is the initial 2 minute acquisition frame following completion of the standardised meal. The corresponding graph illustrates observed counts in the supraband region of interest over 90 minutes. Virtually the entire meal has passed into the infraband stomach on acquisition of the initial 2 minute frame. There is no definable emptying half time of this region.*

FIGURE 20.4: Retention of Semi-Solid Above the LAGB Resulting in Severe Symptoms
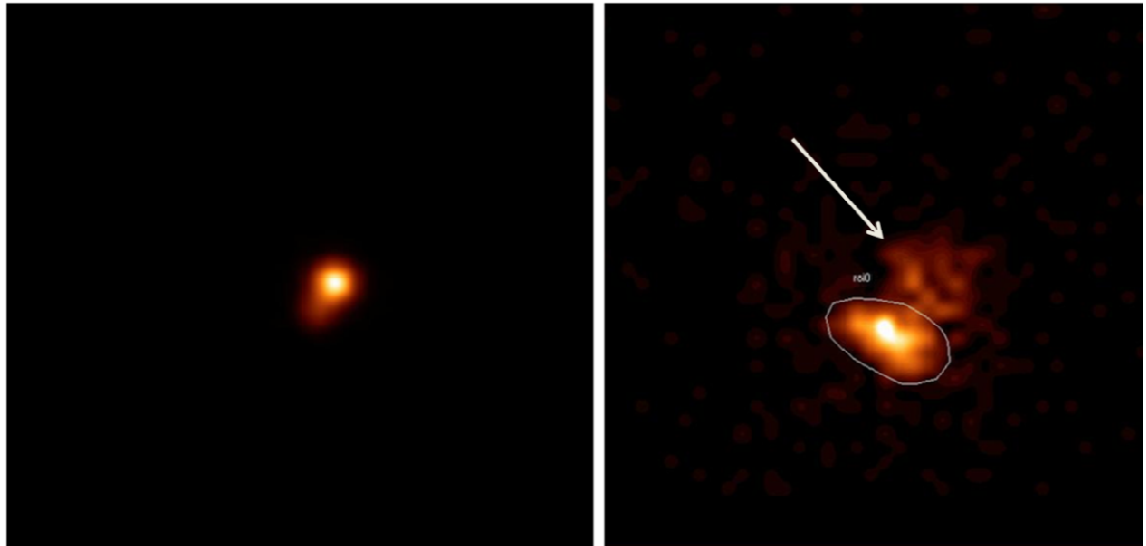
Figure 20.4 Legend: *This patient developed severe symptoms upon ingesting the semi-solid. The first image is the LAGB prior to ingestion of the meal. In the second image a region of interest has been drawn around the LAGB. The ingested meal (arrowed) has impacted above the LAGB. This is representative of when a LAGB patient develops an obstruction due to inappropriate eating. It may be cleared into the distal stomach or become dislodged and regurgitated. This patient subsequently cleared the bolus into the infraband stomach and was able to complete the study.*

The gastric emptying half time did not change following LAGB. Preoperatively the emptying half time was 63.5±34.1 min. vs. 73.3±26.8 min. post-operatively, (*p=0.64*). One patient had severe gastrostasis pre-operatively, with no gastric

emptying during the 90 minute scan. Twelve months post-operatively, following a weight loss of 49 kg (63% of excess weight) gastric emptying was normal.

 Discussion

We have shown that following LAGB a pattern of delayed bolus transit into the infraband stomach developed. Weight loss, increased satiety and early satiation were also observed post-operatively. As expected, the overall gastric emptying half time did not change.

Post-operatively, consumption of a smaller volume of a standard meal resulted in greater suppression of hunger. Retention of the meal within the supraband compartment was not identified. Therefore a mechanism other than physical restriction of the patient to a small meal is responsible for the observed satiety.

In chapter 19, changes in transit without an effect on gastric emptying were established when LAGB volume was varied. Satiety and satiation, however, did not change when alterations were made to LAGB volume; possibly because of ongoing effects of the LAGB.

Our data and other evidence suggest that following LAGB satiety is a significant factor [8]. A critical question remains as to the mechanism that mediates this.   One possible pathway is repeated pressurisation of the cardia above the LAGB, probably activating gastric mechanoreceptors that relay via the vagus nerve. Another possible mechanism is direct pressure or contact of the LAGB against the gastric wall. This effect, if it resulted in neruomodulation, could have ongoing effects after

saline was removed from the LAGB. Further investigation will be critical to better understanding this poorly defined area.

The LAGB appears to be inducing prolonged intermeal satiety as well as signalling early satiation; terminating meals at an earlier stage. Possibly the early satiation is more important as total caloric intake is governed more by the volume consumed at an individual meal rather than the frequency of feeding [104, 105].

Much emphasis is placed on patients changing their eating habits following LAGB, selecting foods of appropriate textures, reducing meal volume, slowing intake and chewing food well [346]. This behaviour change is necessary to support the altered nature of transit that appears associated with a successful outcome.

Other data suggest that oesophageal motor and sensory function are both important following LAGB [533, 537]. The intraluminal pressure produced by the LAGB, of 20-30 mmHg, means that flow across the LAGB only occurs during oesophageal peristaltic contractions [533]. This is because an intrabolus pressure that exceeds the intraluminal pressure at the level of the LAGB must develop for flow to occur. Oesophageal and proximal gastric sensory feedback is also required. The patient needs to interpret visceral sensations and determine when a bolus has transited into the infraband stomach. Dense oesophageal and gastric innervation that responds to distension likely alerts the patient to the presence of the bolus above the LAGB [474, 479, 489]. Without accurate sensory feedback, patients will find it difficult to control their eating and dysphagia with unpredictable regurgitation can be expected.

Rapid and complete delivery of a semi-solid meal to the infraband stomach refutes other data that propose supraband retention with a definable emptying half time as the mechanism of satiety following LAGB [370, 371]. Whilst liquids may be able to passively trickle past the resistance of the LAGB, how could solids or semi-solids pass across the LAGB over a 30 minute period?

A further complexity that urgently needs to be clarified is whether satiety or satiation is actually critical to the weight loss seen following LAGB. The LAGB modifies transit and the range of foods able to be consumed. It also conditions behaviour. The most important mediator of weight loss has not been definitively identified. Much further research is required to fully appreciate the mechanism of action of LAGB.

Retention of semi-solid in the supraband compartment was found to represent bolus impaction at the level of the LAGB. This produced severe symptoms of dysphagia and patients were unable to complete the study or the bolus acutely passed into the infraband stomach – relieving symptoms. Patients who swallow an inappropriately sized or textured bolus report immediate obstructive symptoms. Unrecognised, prolonged stasis in a focal enlargement above the LAGB is associated with severe adverse symptoms such as reflux [537]. This suggests that the supraband stomach should be empty within one to two minutes of a patient swallowing a bolus.

These data are complementary to findings from chapter 19 that showed altering LAGB volume affected transit. The development of a consistent pattern of delayed transit has now been shown to be associated with satiety and weight loss in a

prospective follow up study. There are several candidate processes that may be important in generating satiation and prolonged satiety, delayed transit is not necessarily the key physiological change. This area requires much further delineation and is an attractive area for future research. Key understanding of intraluminal processes refutes suggestions the LAGB should be classified as a restrictive procedure.

Declaration for Thesis Chapter 21

This chapter represents a manuscript that has been published in *Obesity Surgery*: (*Obes Surg. 2010 Feb 9. [Epub ahead of print]*).

Declaration by candidate

In the case of Chapter 21, the nature and extent of my contribution to the work was the following:

Nature of contribution	Extent of contribution (%)
Overall responsibility for all aspects of the study, conception, planning, patient recruitment, conducting experiments and recording data. Data analysis and interpretation. Statistical analysis. Crafting and revising manuscript.	>90%

The following co-authors contributed to the work:

Name	Nature of contribution
Wendy A Brown	Designing study, and recruiting patients, manuscript review
Cheryl Laurie	Recruiting and conducting studies
Minaje Lee	Recruiting and collating studies, data entry
Anna Korin	Recruiting and collating studies, review of manuscript
Margaret Anderson	Access to database, retrieval of demographic data
Geoff Hebbard	Experiment design, review of manuscript
Paul O'Brien	Experiment design, review of manuscript

Candidate's Signature		Date

Declaration by co-authors

The undersigned hereby certify that:

(1) the above declaration correctly reflects the nature and extent of the candidate's contribution to this work, and the nature of the contribution of each of the co-authors.
(2) they meet the criteria for authorship in that they have participated in the conception, execution, or interpretation, of at least that part of the publication in their field of expertise;
(3) they take public responsibility for their part of the publication, except for the responsible author who accepts overall responsibility for the publication;
(4) there are no other authors of the publication according to these criteria;
(5) potential conflicts of interest have been disclosed to (a) granting bodies, (b) the editor or publisher of journals or other publications, and (c) the head of the responsible academic unit; and
(6) the original data are stored at the following location(s) and will be held for at least five years from the date indicated below:

Location(s) | Monash University, Alfred Hospital |

[Please note that the location(s) must be institutional in nature, and should be indicated here as a department, centre or institute, with specific campus identification where relevant.]

Name		Date
Wendy A Brown		27/10/09
Cheryl Laurie		4/11/09
Minaje Lee		2/11/09
Anna Korin		5/11/9
Margaret Anderson		5/11/09.
Geoff Hebbard		2/11/09
Paul O'Brien		27/10/09

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Chapter 21: *Outcomes, Satiety and Adverse Upper Gastrointestinal Symptoms Following Laparoscopic Adjustable Gastric Banding*

Abstract

Background: Follow up is critical to the success of laparoscopic adjustable gastric banding (LAGB). There are few data to guide this and expected norms of satiety, adverse symptoms and outcomes have not been defined.

Methods: Consecutive patients, who underwent LAGB, were evaluated using a newly developed instrument that assessed: Satiety, adverse upper gastrointestinal symptoms (dysphagia, reflux and epigastric pain) and outcomes (overall satisfaction, weight loss and quality of life (SF-36)).

Results: 323 of 408 patients responded (79%), mean age 44.4±11.8 years, 56 males. Excess weight loss was 52%, 3 years post-operatively. Satiety was greater at breakfast compared to lunch (5.3±1.9 vs. 4.1±1.7, *p<0.005*) or dinner (3.8±1.8, *p<0.005*). The mean satisfaction score was 8.3±2.1 out of 10 and 91% would have the surgery again if given the choice. Quality of life was less than community norms, except in physical functioning (83.4±20.4 vs. 84.7±22.0, *p=0.25*) and bodily pain (78.4±15.2 vs. 75.9±25.3, *p=0.004*). The inability to consume certain foods was cited as the biggest problem following surgery by 66% of respondents. The dysphagia score was 19.9±8.7; softer foods were tolerated, although difficulty was noted with firmer foods. The reflux score was 8.7±9.8 and regurgitation occurred a mean of once per week. Weight loss and the mental component summary score were the only predictors of overall satisfaction (*r² = 0.46, p=0.01*).

Conclusions: Patients are highly satisfied with the outcome of LAGB and achieve a substantial weight loss. Expected ranges of: satiety, adverse upper gastrointestinal symptoms and outcomes have been defined. The most troublesome symptom is the inability to consume certain foods. Weight loss predicted overall satisfaction, regardless of the severity of adverse symptoms.

Introduction

Laparoscopic adjustable gastric banding (LAGB) safely induces and sustains weight loss [2, 253]. It leads to improvements in obesity related co-morbidities [263]. Importantly, quality of life is improved [163]. A regular, life long, follow up program is critical to the success of the procedure. Despite widespread use over the past 15 years there are few objective data available to guide follow up. If normal ranges for different outcomes, satiety and adverse symptoms were available, the follow up process could be improved. Variations from normal could be recognised more easily, potentially facilitating intervention prior to complications developing. Additionally, more specific pre-operative information could be provided to patients concerning the likely post-operative course.

LAGB patients must eat small volumes of appropriate foods slowly; otherwise they are at risk of regurgitating a swallowed bolus. Therefore, patients variably eliminate foods of different texture from their diet in concert with modifying eating behaviour. Adjustments to LAGB volume target satiety [8], whilst avoiding obstruction. Expected norms, in terms of patient's reported satiety, their ability to consume different food types and frequency of regurgitation have not been defined. The expected prevalence and severity of gastro-oesophageal reflux disease (GORD) following LAGB remains controversial. GORD has been reported to improve post-operatively [437], with others arguing that the LAGB induces reflux [547].

A range of different outcomes can be defined following LAGB, [2, 532, 548]. We hypothesised that patients base their overall satisfaction with the procedure almost solely on weight loss; potentially accepting significant adverse symptoms provided

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this goal is achieved. Adverse symptoms, such as recurrent regurgitation, are likely

significant risk factors for the development of symmetrical pouch dilatation [310,

533, 549], now the most significant post LAGB problem.

We performed a cross sectional study of a cohort of LAGB patients, aiming to

establish expected ranges for different outcomes, satiety and adverse upper

gastrointestinal symptoms, thereby providing a reference point for clinicians

following up individual patients. We also sought to establish how adverse upper

gastrointestinal symptoms, satiety and weight loss affected different outcome

measurements.

Methods

The Monash University Human ethics committee approved this research.

Patients

Consecutive patients, who underwent primary LAGB surgery performed by one

surgeon (WB), between 1st of July 2003 and 14th August 2007, were invited to

participate. Inclusion criteria were: age 16-65 years and having undergone primary

LAGB surgery. Exclusion criteria were previous bariatric or upper gastrointestinal

surgery prior to LAGB.

Study

A self reported questionnaire was developed, designed to measure satiety, adverse

symptoms and different outcomes following LAGB surgery (appendix 1).

All patients were initially mailed the questionnaire or it was handed to them during follow up consultations. Those who did not return the questionnaire were sent an additional reminder.

Questionnaire Design

Items within the questionnaire addressed:

1) Satiety

2) Outcomes following surgery

3) Adverse symptoms

Previously validated scores were used where available. Where these did not exist, specific, additional questions with visual analogue scales were used or a categorical range of responses provided if this was more appropriate.

1) SATIETY

Satiety was reported prior to breakfast, lunch and dinner time. A 25 cm visual analogue scale was used. This ranged from 0 to 10, with 0 being ravenously hungry and 10 being completely full, unable to eat any more.

2) OUTCOMES

Outcomes defined were:

- Percentage of excess weight loss (%EWL)

- Quality of life: Measured using the Medical Outcome Study Short Form-36 (SF-36) health survey. Scores derived for the 8 health concepts were

reported. For multi-variate analysis the mental and physical component summary scores were used.

- The patient's overall satisfaction with the results of surgery: Reported on a ten point visual analogue scale (with 0 being totally unsatisfied, worst outcome imaginable and 10 being totally satisfied, couldn't imagine a better outcome).

3) ADVERSE SYMPTOMS

Adverse symptoms consisted of categorical measurements of the worst symptom or biggest problem experienced following LAGB, with patients given the option of recording other problems not included. Symptoms of GORD, dysphagia and epigastric discomfort were individually assessed. GORD was assessed using a validated score [544]. This consisted of 6 separate domains, each graded in frequency and severity, resulting in a scaled score ranging from 0 to 72. The use of antireflux or acid suppressing medications was recorded.

Dysphagia was assessed using a validated score [545]. This graded dysphagia based on the ability to consume 9 different types of food, each progressively more difficult to swallow. Food textures ranged from liquids and semi-solids through to red meat and bread. A score of between 0 (no dysphagia to any food) and 45 (total dysphagia to all liquids and solids) was produced. The subjective severity of the dysphagia (0-10) and the extent to which the patients modified their diet as a result of the inability to consume different foods was also assessed.

The frequency of post prandial epigastric pain was assessed categorically.

The frequency of regurgitation was recorded categorically as was the extent of dietary modification required to avoid regurgitation. How bothered patients were by regurgitation was assessed on a visual analogue scale of 0 to 10 (0 not bothered at all, 10 severely bothered).

Weight Loss, Demographic and Complication Data

The prospectively maintained online bariatric database LAPBASE[TM] (*www.lapbase.net*) was used to extract information concerning: Demographic data, baseline and follow up weight data and complications.

A complication was defined as a repeat operative intervention. These were coded as port and tubing related problems and revision of the LAGB (divided into gastric prolapse, symmetrical pouch dilatation or other). Erosions were also recorded.

Group comparisons were made between those who returned the surveys and those who did not, in terms of: Demographic and weight loss details, attendance at follow up and complication rates.

Statistical analysis and data management

Data were compiled and entered into a specifically designed database using Microsoft Access (Microsoft Corp, Redmond, WA). Continuous data were presented as means and standard deviation; categorical data were presented as frequencies. SPSS V 11 (SPPS inc., Chicago, Ill) was used for statistical computations. Correlations were performed using Pearson's correlation. For continuous outcome measurements a standard, step wise, linear regression model was used to identify

predictors of different outcomes. Results were presented as r^2 values, with standardised beta coefficients.

When comparing groups, normally distributed continuous data was analysed using t-tests. Chi square tests were used to compare categorical data. A two sided p value of 0.05 was considered statistically significant.

Results

Three hundred and twenty three responses were received from 408 eligible patients (79%). The mean age was 44.4±11.8 years. There were 56 males (17.5%). The mean pre-operative weight was 120.7±25.2kg and the BMI was 43.8±7.8kg/m^2. At a mean follow up of 1214±440 days (range 544-2044 days), BMI was 35.2 ±6.9 kg/m^2 and total weight loss 23.7±14.8 kg. Figure 21.1 illustrates excess weight loss versus time. Ongoing weight loss is observed until 24 months, after which weight loss is sustained at approximately 52% EWL. Only 37 patients had been followed up to 60 months.

Fifty four (17%) patients had a complication, 31 (10%) had a port or tubing related problem, including 2 port infections. Twenty six (8%) revisional procedures were performed on the LAGB. Five (1.5%) were for gastric prolapse and 18 (5.6%) for symmetrical pouch dilatation. Three other revisions were performed: one was for band intolerance, one was for a broken band and in another the band had spontaneously opened. There were 2 erosions of the LAGB into the stomach, both successfully managed by laparoscopic removal and staged reinsertion of another LAGB.

There were no peri-operative deaths or major morbidity. Two patients were

deceased, one at 260 weeks of metastatic colon cancer and one at 120 weeks due

to chronic obstructive airways disease.

All bands were LAP-BANDS (Allergan, Ca).   One hundred and sixty nine were 10 cm,

54 were Advanced Platform Small (APS^{TM}), 30 were Advanced Platform Large

(APL^{TM}) and 70 were VG^{TM}.

FIGURE 21.1: Excess Weight Loss Following LAGB Surgery
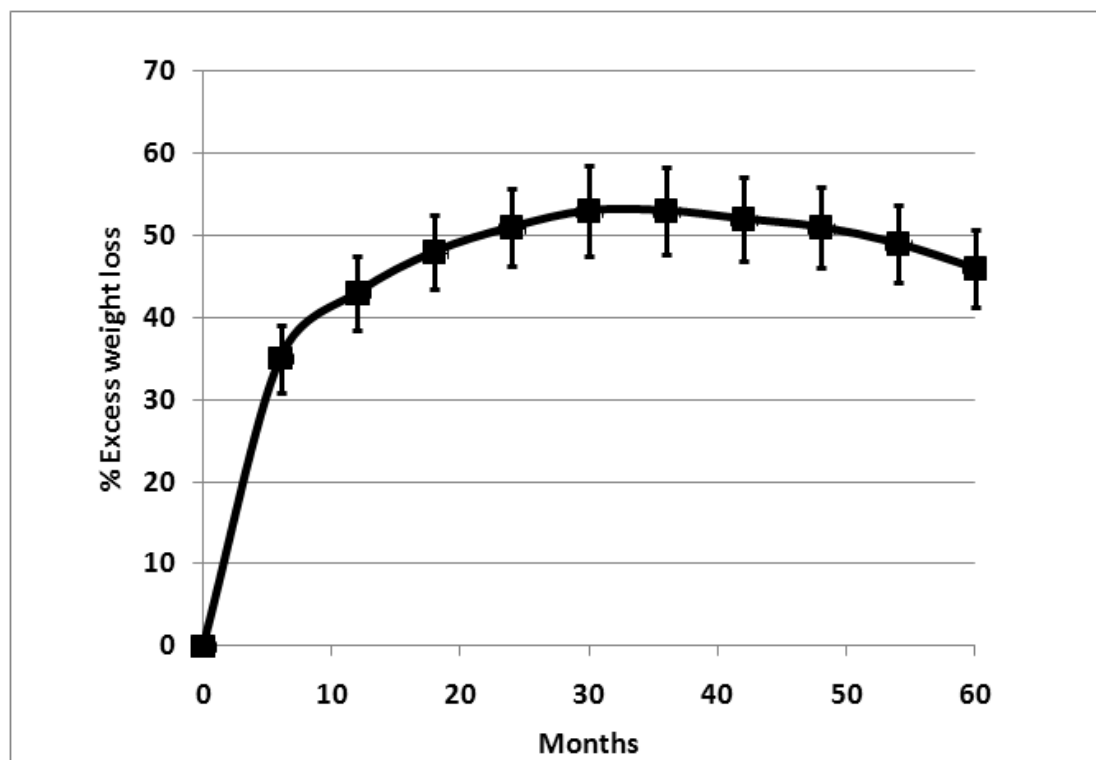
Figure 21.1 Legend: *There is ongoing weight loss until approximately 24 months.*

After which there is stabilisation at approximately 52% EWL. This decreased to 45%

EWL between 50 and 60 months, although there were only 37 patients followed up

for this duration. Data are mean and standard error.

Satiety

The majority of patients reported only moderate hunger prior to meals. The mean satiety scores were: Breakfast 5.3±1.9, lunch 4.1±1.7 and dinner 3.8±1.8. There were significant differences in hunger at these times (*p<0.005*). Patients were more hungry at dinner than at either lunch (*p=0.008*) or breakfast (*p<0.005*). They were more hungry at lunch than at breakfast (*p<0.005*).

There were statistically significant (*p<0.01*) correlations between increased satiety in patients at breakfast and lunch (*C=0.39*), breakfast and dinner (*C=0.25*) and lunch and dinner (*C=0.54*).

Satisfaction with the Procedure

Patients were highly satisfied with the outcome of LAGB. The mean satisfaction score was 8.3±2.1, with 261 (82%) patients rating it as 10 out of 10. Two hundred and eighty nine (91%) patients would have the surgery again if given the choice, 13 were unsure (4.1%) and 16 (5%) would probably not have the surgery again.

Quality of Life

Quality of life measurements approached, although were significantly less (*p<0.005*), than defined community norms [550] in six of the 8 health concepts measured by the SF-36 instrument. These comparisons are shown in Figure 21.2. No difference was identified in the physical functioning concept (*p=0.25*). LAGB patients reported less bodily pain (*p=0.004*). Two hundred and thirty five patients (73%) described their health as better than 12 months previously, 56 said it was the same and only 27 (8%) stated it was worse.

FIGURE 21.2: Quality of Life Compared to Australian Community Norms
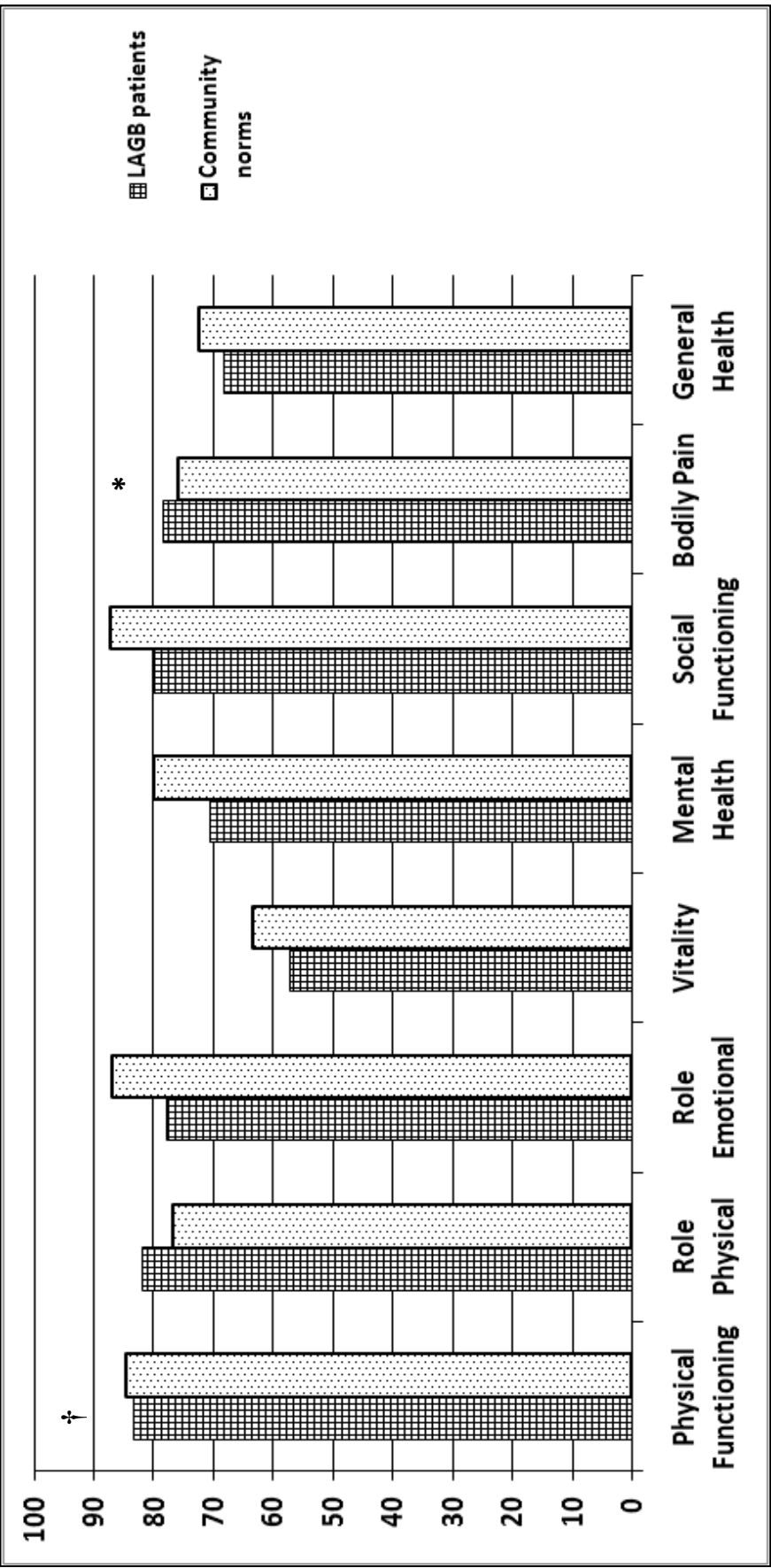
Figure 21.2 Legend: *In 6 of the 8 SF-36 concepts, LAGB scores approached community norms although were statistically significantly less. There was no difference identified in the physical functioning concept domain (†) and LAGB patients reported less bodily pain (*) than the community norm. Community norms were derived from a survey of 3012 Australian adults, performed in 2002* [550]*.*

Adverse Symptoms

The inability to consume foods of different textures was cited as the most troublesome symptom or problem following LAGB surgery by the majority of respondents. Figure 21.3 summarises these. Thirty one (9.7%) patients cited reasons other than those listed. These, however, were predominantly related to the mechanical constraints imposed by the LAGB. For instance: "having to watch others consume a larger quantity and range of food than I am able to". Fifty two (16.2%) patients stated that they had not experienced any troublesome symptoms or problems following surgery.

FIGURE 21.3: Most Significant Problem or Troublesome Symptom Following LAGB
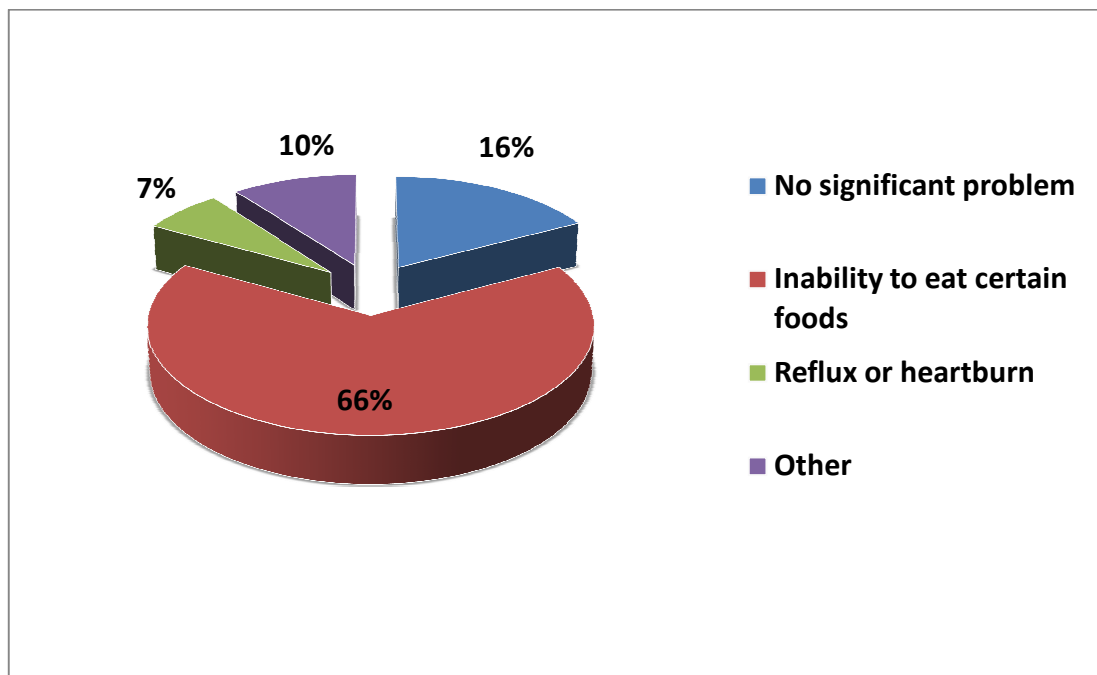
Figure 21.3 Legend: *Two thirds of patients cited regurgitation of food, or the inability to consume a range of foods due to regurgitation, as the most troublesome symptom or problem following surgery. Only 23 (7.3%) cited heartburn or reflux and 16.2% reported no problem at all.*

Sixty seven percent of patients reported regurgitation of food at times, whereas only 9% regurgitated daily or more frequently. Figure 21.4 summarises these data. One hundred and twenty (37.9%) patients reported not being bothered by regurgitation at all. One hundred and twenty six (39.7%) were mildly bothered, 45 (14.2%) were moderately bothered and 25 (7.8%) were severely bothered.

FIGURE 21.4: Frequency of Regurgitation Episodes Following LAGB Surgery
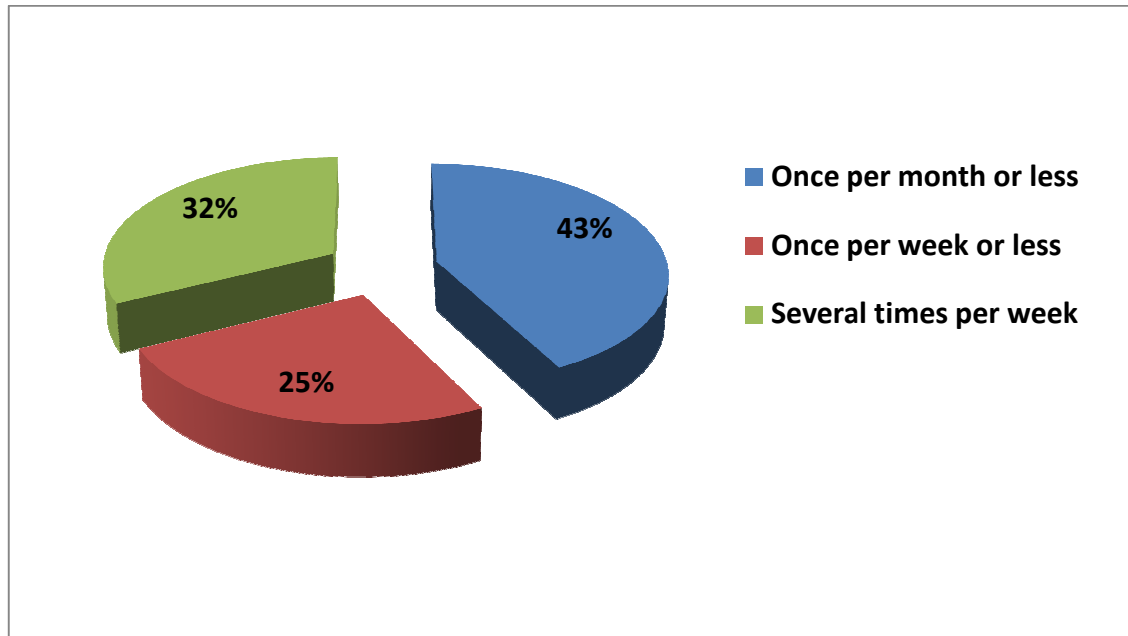
Figure 21.4 Legend: *The majority (67%) of patients reported regurgitation of food at times. This was generally between once per week and once per month. One third of patients (32%) reported regurgitation more frequently than once per week.*

The mean dysphagia score was moderately high; 19.9±8.7 out of 45 (with 0 representing no dysphagia to any food and 45 being total dysphagia, unable to swallow water). A score of 19 represents an ability to consume most soft foods, however, not foods of thicker texture such as red meat or white bread. Patients rated the extent to which they were bothered by dysphagia as 4.03±2.17 out of ten, with 0 being not bothered at all and 10 being extremely bothered. Figure 21.5 gives an overview of the capacity of patients to tolerate different foods.

One hundred and ninety nine (60%) patients never experienced heartburn, with 67 (20%) experiencing it around once per month and another 66 (20%) experiencing it weekly or more frequently. Nineteen (5%) patients reported daily heartburn. The reflux score was low, a mean of 8.7±9.8 out of 72. Two hundred and forty four (76%) patients reported an improvement in reflux symptoms following surgery, 58 (18%) described these as having deteriorated and 19 (6%) reported no change. Eighty (25%) patients were taking some form of acid suppressive or anti-reflux medication (at least once per month): 58 (18%) were taking proton pump inhibitors, 5 (1.6%) H2 Blockers and 19 (6%) over the counter antacids.

One hundred and thirty nine patients (43.3%) never experienced post prandial epigastric pain, 90 (28.2%) had pain once per month or less, 49 (15.4%) had pain once per week, 35 (11.0%) had pain two to four times per week, 6 patients (1.9%) had pain most days.

Predictors of outcome measures

Excess weight loss and an increased (SF-36) mental component summary score were predictors of increased overall satisfaction ($r^2=0.46$, $p=0.01$). Table 21.1 illustrates the standardised Beta coefficients for different variables. Satiety, adverse symptoms or other outcome measures did not affect the mental ($r^2=0.14$, $p=0.43$) or physical component summary scores ($r^2=0.16$, $p=0.34$). There were no predictors of increased excess weight loss identified ($r^2=0.08$, $p=0.48$).

FIGURE 21.5: Patient's Ability to Consume Foods of Different Textures

(Frequency of regurgitation of different foods)
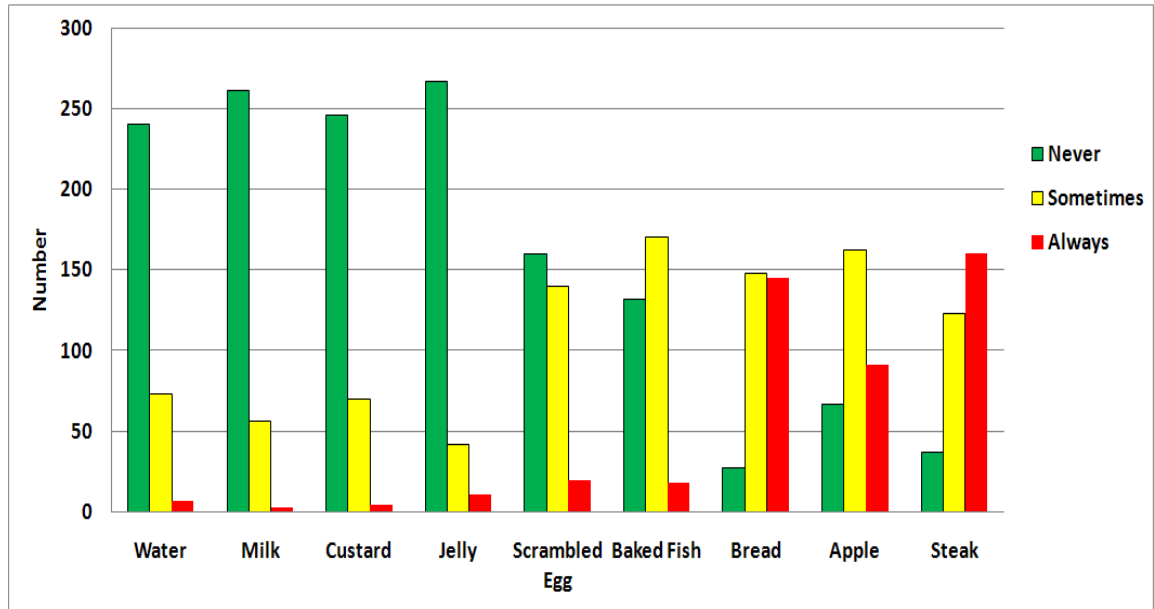
Figure 21.5 Legend: *For each food type listed, patients were asked if, when they consumed these foods: they never regurgitated, sometimes regurgitated or always regurgitated. For each of the nine categories several alternate foods of equivalent texture where also listed, to account for patients who may never consume the specific foods listed. The overall dysphagia score was derived from these data. Foods were weighed in terms of points, from 1 (water) to 9 (steak), half points were given for the response "sometimes", which did not specify a frequency. A moderately high overall score is expected in patients who are unable to consume only the more difficult foods, such as steak, bread etc.*

	Standardised Beta coefficient	*p* value
%Excess weight loss	0.39	0.001
Dysphagia score	-0.09	0.44
Breakfast satiety	-0.18	0.13
Lunch satiety	-0.08	0.55
Dinner satiety	0.24	0.07
Reflux score	0.09	0.56
Start weight	-1.07	0.13
Start BMI	-3.32	0.07
Current BMI	3.29	0.07
Mental score	0.32	0.02
Physical score	0.12	0.35
Weight loss	3.12	0.09
Difficulty swallowing	-0.01	0.94
Follow up duration	0.07	0.53
Change in reflux symptoms	-0.03	0.81
Epigastric discomfort	-0.11	0.13

Effect of complications on outcomes and adverse symptoms

The presence of a complication did not affect any outcome measurement, overall satisfaction (8.3±2.2 vs. 8.3±1.96, *p=0.98*), %EWL (46.3±23.6 vs. 47.7±24.9*, p=0.69*), quality of life (mental component score: 45.7±7.17 vs. 47.3±6.9, *p*=0.13 and physical component score: 49.8±7.1 vs. 49.3±6.1, *p*=0.60) or adverse symptoms: Dysphagia (21.6±8.6 vs. 19.6±8.7, *p=0.11*) or reflux (9.6±9.3 vs. 8.6±9.9, *p=0.53*).

A revision of the LAGB did not affect overall satisfaction (8.73±1.61 vs. 8.35±2.20, *p=0.39*). Although the mental component summary score (43.9±7.5 vs. 47.3±6.9, *p* =0.016) was lower in those who had undergone a revision. There was no difference in the physical component score (49.2±7.9 vs. 49.4±6.1, *p* =0.83), %EWL

(47.1±22.8vs 47.5±24.9, *p*=0.93) or the reflux score, (9.4±8.5 vs. 8.8±10.0, *p*=0.77). Those that had a revision had a significantly greater dysphagia score compared to those that had not (23.6±8.1 vs19.6±8.6, *p*= 0.02).

Responders vs. Non-responders

There were no differences identified between those who completed the questionnaire and those that did not in terms of: %EWL (47.6±24.7 vs. 45.1±25.1, *p*=0.43) or BMI (35.2±6.9 kg/m^2 vs. 36.1±8.3 kg/m^2, *p*=0.85) at the last clinic visit. There was no difference in the number of attendances at follow up between the two groups (23.4±14.5 vs. 22.9±14.6, *p=0.77*).

Discussion

We have shown that following LAGB substantial weight loss is maintained for at least 3-5 years. Patients are highly satisfied with the outcome of surgery. We have defined expected norms following LAGB in terms of satiety, expected weight loss, the ability to consume different food types and a range of adverse symptoms, including the expected frequency of regurgitation. Adverse symptoms relate primarily to the inability to consume foods of different textures. These data can serve as a reference point at follow up.

A 17% re-operation rate within 5 years could be considered high. More than half of these were port and tubing related and can readily be resolved as a day case. Symmetrical pouch dilatation or gastric prolapse can be successfully managed with operative revision, securing the LAGB closer to the oesophago-gastric junction. These problems affected only 8% of patients. Weight loss and overall satisfaction

were not affected by these complications. Although substantial reductions in revisional surgery rates have occurred in the pars flaccid era [10], reducing these rates further should be a major focus.

The constraint imposed on the range of foods able to be consumed was the most troublesome symptom or problem reported by patients. As a result of this constraint, regurgitation of food was reported on average once per week. Whilst patients were bothered by being unable to consume desirable foods, only 1 in 5 were more than mildly bothered by regurgitation. These data indicate that regurgitation is expected at times following LAGB. However, this can be minimised by eating appropriate foods slowly and in small volumes. That the patients were not markedly bothered by regurgitation suggests that many had made the adaption required following surgery, changing eating patterns and avoiding inappropriate foods. Undoubtedly patients would prefer to be able to eat completely freely in terms of range and volume of foods and achieve weight loss!

Few patients reported significant hunger and this should be emphasised, aiming to modify eating behaviour, harnessing the satiating effects of the LAGB rather than challenging its mechanical properties.   Patients should be informed of these realities pre-operatively.

Weight loss and the mental component summary score were the only parameters found to influence overall satisfaction, regardless of the severity of adverse symptoms. This indicates that patients are, in some cases at least, prepared to accept adverse symptoms as the price to pay for weight loss. At each follow up visit clinicians need to specifically enquire about the presence, severity and frequency of

regurgitation, reflux and other adverse symptoms. Frequent regurgitation recurrently overpressurises the region above the LAGB. This is likely to be the most important risk factor in the development of symmetrical pouch dilatation [533].

A mean reflux score of 8 out of 72 indicates that severe reflux is relatively uncommon, with three quarters of patients reporting an improvement in reflux following LAGB. This highlights that, in general, the LAGB is an effective antireflux procedure [267, 268]. If reflux does develop following LAGB it can be considered abnormal and is likely representative of a LAGB that is simply too tight.

Alternatively, persistent or more severe reflux, particularly with volume or nocturnal symptoms, is indicative of a complication. Whilst a moderate number of patients were taking proton pump inhibitors, a much higher prevalence of this has been observed in similar community surveys on patients following fundoplication [551]. It does not surprise us that many of these patients were prescribed acid suppressive medication by their primary care providers. The LAGB undoubtedly affects the upper gastrointestinal tract and therefore different sensations and symptoms, possibly interpreted as reflux, develop.

We feel that the response rate achieved, 80%, is acceptably high. It is unusual for large cross sectional studies to achieve such a high response rate. A 20% non-response does still leave the potential for significant bias. There are likely some patients whom are lost to follow up, although this is rare in our practice where non attendance for greater than 12 months triggers us to contact that patient. There was not a significant difference in the number of clinic visits, complications or weight loss in the group who did not respond compared to those that completed

the questionnaire. We therefore believe that we have provided an accurate cross sectional overview of a large cohort of LAGB patients.

Conclusion

These data can be used as an objective reference for clinicians following up LAGB patients. Pre-operatively, patients should be counselled to expect a significant reduction in the range and speed with which they can consume food. The follow up process should promote good eating behaviour and emphasise satiety; it should also aim to identify any adverse symptoms at an early stage. Occasional regurgitation is expected and is invariable if there is inappropriate eating behaviour, however, with appropriate advice and eating practices this can be minimised. We emphasise that good weight loss can be achieved without frequent regurgitation or the development of GORD. Patients, however, prioritise weight loss over other outcomes and may tolerate significant adverse symptoms in order to achieve this; potentially increasing the risk of complications.

CHAPTER 22*: Discussion and Conclusions*

This thesis has demonstrated that the LAGB has consistent physiological effects in successful patients. The optimally adjusted LAGB briefly delayed semi-solid transit into the infraband stomach without retention above the LAGB. The LAGB therefore should not be classified as a restrictive procedure; it appears to induce early satiation and prolonged satiety. Establishing important aspects of the peripheral physiology in successful patients allowed the spectrum of intermediate term complications to be defined and correlated with outcomes.

High resolution manometry studies led to the central discovery that successful LAGB patients consistently demonstrated a mean intraluminal pressure of approximately 27 mmHg at the level of the LAGB. This pressure directly varied with changes in LAGB volume, once a threshold volume had been reached.

Alterations to oesophageal function in successful patients were a predictable response to the resistance presented by the LAGB. Trans LAGB flow only occurred during peristaltic contractions. Episodes of flow were observed, after which residual bolus refluxed into the oesophagus; stimulating further primary peristalsis. Staged clearance of a bolus was the norm, explaining why LAGB patients are limited in the range of food textures they can consume. Only a tiny bolus or one which can be transited across the LAGB in portions, such as a semi-solid, is able to be consumed.

The basal tone of the lower oesophageal sphincter (LOS) was significantly attenuated in successful LAGB patients compared to obese controls. The LOS serves

a novel role in LAGB patients, contracting and contributing to bolus transit across the LABG. The barrier function of the LOS in LAGB patients is less clear.

The importance of the contractile function of the LOS was established in more detailed evaluations of the mechanics of bolus transit across the LAGB. This served as the basis for criteria designed specifically to assess oesophageal motility in LAGB patients. This included establishing a novel, objective measurement; the lower oesophageal contractile segment (LECS).

Data concerning oesophageal function and motility in LAGB patients is vastly different to previous reports and represents a paradigm shift in the understanding of oesophageal function in LAGB patients. The technical superiority of the equipment used and systematic nature of investigations performed ensures reliability. High resolution manometry was able to separate the intraluminal pressures produced by close structures in the region of the oesophago-gastric junction.

A novel technique that allowed visualisation of the LAGB during nuclear scintigraphic studies was developed. This overcame the limited anatomical resolution of previous studies which supported the classification of the LAGB as a restrictive procedure, where the proximal pouch retained food; physically limiting total meal size.

Two very closely related scintigraphic studies were performed, although two distinct questions were asked. One study was in a group of successful patients, assessed at optimal and a reduced LAGB volume. A second prospective follow up study evaluated patients pre and post-operatively.

Both studies confirmed that the LAGB delayed transit into the infraband stomach, although this was a brief, dynamic delay, quite different to static retention with linear emptying. These data confirmed video fluoroscopic data that had shown repeated peristaltic contractions were required to mediate bolus transit across the LAGB.

Overall gastric emptying was normal and there was no definable emptying half time from the supra-band stomach. This importantly showed that a proximal pouch restricting patients to a small meal was not the mode of action of the LAGB.

Satiety and satiation did not differ when LAGB volume was altered, however, in the prospective study a profound change in these parameters was observed 12 months post-operatively. This suggests there is a specific mechanism activating satiety following LAGB.

Acute retention of semi-solids above the LAGB caused significant symptoms of obstruction in successful patients. Chronic retention of liquids and semi-solids in an enlarged lumen above the LAGB was a hallmark of unsuccessful patients; closely correlated with symptoms of reflux and dysphagia.

These data have collectively shown the physiological changes that develop following LAGB are consistent, however, a precise understanding of physiological signalling or the mechanism of weight loss has not yet been established.

Understanding and managing the spectrum of intermediate term complications following LAGB is a major challenge. These complications are of significance to individual patients and troublesome in clinical practice, however, have not been

well described in the literature. Importantly, these problems appeared to be affecting many patients who had previously achieved good weight loss.

Luminal dilatation above the LAGB or deficient oesophageal motility that impaired bolus transit was found to underpin the majority of intermediate term problems. These were identified with a semi-solid stress barium protocol that was validated in successful patients. Specific high resolution manometry criteria, the Melbourne criteria, were also adapted to LAGB patients. These were found to be far more sensitive diagnostic tests than liquid contrast swallows, upper gastrointestinal endoscopy or the application of conventional high resolution manometry diagnostic criteria.

Combining anatomical, motility and transit data allowed a comprehensive classification of the spectrum of intermediate term complications to be defined: The CORE classification. This classification should now allow patients to be better investigated and treated. More objective comparisons of the response to treatment or the incidence of complications will also be easier to undertake; with objective endpoints.

Of the identified intermediate term complications, gastric enlargements were found to be amenable to further LAGB intervention, provided oesophageal motility was intact. If motility was deficient or there was oesophageal dilatation, revisional surgery was unlikely to be helpful. This reaffirms previous work that suggests mechanical problems with the stomach above the LAGB can generally be remedied surgically [310].

Only severely impaired oesophageal motility, deemed deficient, was found to alter the outcome following LAGB. This is important as there is much confusion surrounding oesophageal motility in LAGB patients. This data does not support selecting patients to undergo LAGB on the basis of oesophageal motility; unless there is a profound deficiency in peristaltic function.

The aetiology of intermediate term complications requires attention. Transmission of excess force to the luminal wall appears the likely mechanism leading to dilatation above the LAGB or impairments in lower oesophageal motility.

The intraluminal pressure at the level of the LAGB was found to mediate the intraluminal pressure above the LAGB during semi-solid swallows, however, during episodes of transient obstruction this pressure was further increased, mediated by distal oesophageal peristaltic amplitude.

The two mechanisms of reducing intraluminal pressure above the LAGB are therefore: minimising the intraluminal pressure at the level of the LAGB and ensuring that episodes of obstruction are avoided. For practical purposes this means adjustments should target satiety, avoiding adding excess saline to the LAGB. Eating behaviour should also be a focus with patients educated to avoid episodes of obstruction, select appropriate foods and ensure small portions are chewed well.

Whilst these are logical strategies; it remains unknown whether they can be successfully implemented or will change outcomes.

The cross sectional study, of outcomes, satiety and adverse symptoms, provided important insights into patients' perspectives of the follow up process and hopefully allows the recognition of variations from the expected norm. LAGB patients were significantly limited in the texture of foods able to be consumed. A relatively high dysphagia score of 20 out 45 was reflective of this. Understanding of the oesophageal physiology illustrates that congruent food simply will not pass across the LAGB; staged clearance is required to generate transit across the resistance of the LAGB.

The majority of patients reported low reflux scores (mean of 8.7 out of 72), although significant numbers were on anti-reflux medication. Regurgitation does occur in most LAGB patients at least once a month. This is reflective of the necessity for patients to change their eating behaviour and accept the mechanical imposition of the LAGB. These data provide clinicians with a baseline of expected symptoms and sensations to use when following up individual patients. Variations from these are suspicious of a physiological or anatomical problem and intervention is advocated.

Not surprisingly, LAGB patients appeared to prioritise weight loss and were prepared to accept a range of adverse effects if this was achieved. This is concerning as patients may not accept removal of saline from the LABG if this in any way compromises weight loss, despites its intention being to reduce the risk of a future complication. This will be a major hurdle in integrating these research findings into clinical practice.

This links to a major future hypothesis, that luminal dilatations above the LAGB transition an acute, reversible phase. Human observations studies in LAGB patients, although weak methodologically, suggest that acute dilatations above the LAGB can often be alleviated by removal of saline [337]. Animal studies, modelling the effects of more acute obstruction show that there is recovery after short periods of obstruction [426, 443]. If this early stage could be identified and saline removed from the LAGB, potentially a future, more significant chronic problem could be alleviated.

Possibly regular contrast swallows or the use of more sophisticated devices able to assess luminal compliance and supraband volume may be able to be developed as clinical tools for identifying early stage luminal dilatation. Ultimately, patients need to actively participate in the follow up program and accept goals that prioritise avoiding intermediate term complications.

Limitations

These studies have been observational, predominantly interventional physiological research where the aim was to identify mechanisms. This thesis has established consistent physiological effects of the LAGB. Yet these are not necessarily those responsible for the desired effect – weight loss. The induction of satiety, circumventing processes that control body weight, appears a likely mechanism, although the pathways that mediate this remain unknown.

In patients with unsatisfactory progress, close associations between patterns of anatomical and physiological change and responses to different treatments were

found. These findings were logical, as oesophageal dilatation or deficient motility could not be expected to respond to further surgery.

Ideally the response of intermediate term complications would have been assessed in a randomised trial of different treatments. This is unlikely to occur due to the complexity of conducting such trials. The developed classification correlated outcomes of observed treatment with different pathophysiological patterns. In the future at least validating these criteria in other centres will be of significant benefit.

A critical question is how do these intermediate term problems develop and are there pre-operative predictors? Manometry studies were cross sectional, correlating outcomes with physiology, function and anatomy. At this stage longitudinal follow up studies have not been performed. This means that longer term effects of LAGB on oesophageal motility have not been definitively established. It is strongly suspected that these problems develop progressively as a result of the chronic transmission of force to the luminal wall. To definitively answer these questions prospective follow up studies over 4-5 years with repeat manometry would be necessary - a challenging undertaking.

It is a significant leap to suggest that the incidence or severity of intermediate term complications will be altered by providing these data to clinicians undertaking follow up. Firstly, it is unknown whether more intensive follow up with attention to adjustments and avoiding over adjustments will have any impact on longer term outcomes. The Second area of concern is how alterations to the follow up and adjustment schedule will be accepted by patients. This is particularly significant if a strategy involves reducing saline within the LAGB, potentially impeding weight loss.

Future Research directions

These data have provided significant momentum for research into several areas.

Linking the peripheral physiological changes that occur with LAGB with mechanism of weight loss is an obvious avenue. The details of this are unlikely to be elucidated in a single step and will be investigated over several years.

Satiety, early satiation, mechanical restriction and enforced changes in eating behaviour are all observed following LAGB. Whether there is a dominant or common mode of weight loss remains a perplexing and important question.

Gut brain communication has been investigated in bariatric surgery; however, studies have been designed to identify single mediators responsible for overall effects. The inbuilt redundancies of homeostatic processes suggest that altering a signal mediator will be overcome by compensatory changes.

Data from this thesis have led to the hypothesis that stimulation of the proximal cardia with hormonal feedback results in meal termination or satiation. This fits with obesity theories that propose habitual caloric overconsumption during individual meals, rather than a neuro-hormonal drive to eat, mediates obesity [62].

Future studies will investigate sensory thresholds when the supra band cardia is stimulated via an intraluminal balloon, as well as the response of LAGB patients to the administration of satiety hormones under different conditions.

Other studies will further investigate the mechanical properties around the oesophago-gastric junction (OGJ). These particularly relate to measuring the compliance of the supraband stomach, OGJ and lower oesophagus. Compliance or

distensibility appears to be a related concept to the anatomical change observed, however, could well be adapted as a clinically relevant investigation. The hysteresis characteristics of the region will also be considered and may relate to the signalling of meal termination.

Whilst intermediate term complications are challenging clinically, they remain poorly documented longitudinally. The next step is to establish the true incidences of these complications and promote the use of these standardised terms as a means of communicating in the literature. This should facilitate comparative research studies. Cohorts of patients operated on in the pars flaccid era have already been reported on and future outcomes will be assessed vigorously against defined standards and lost to follow up accounted for.

More in depth physiological analysis of patients with obvious gastric prolapse or symmetrical pouch dilatation may allow patients to be better selected for revisional surgery. High resolution manometry using the Melbourne criteria could be applied prior to revisional LAGB surgery to determine whether this prooves useful when applied routinely in clinical practice.

More objective data relating to different adjustment and follow up strategies are urgently needed. This is a sorely neglected area of clinical research with most efforts focusing on the technical aspects of the operation.

Initial efforts should involve straightforward comparisons of modified adjustment schedules that aim to reduce the transmission of force to the supraband lumen. These protocols need to be defined and evaluated for patient acceptance and practicality. Finally, they will need to be performed as double armed appropriately

constructed and powered trials. With the large numbers of LAGB procedures performed every day these are feasible undertakings.

Conclusions

A successful outcome following LAGB is associated with a series of physiological changes. The intraluminal pressure at the level of the LAGB is central to these.

The LAGB is not a restrictive procedure; it does not physically limit the size of a meal. Transit into the infraband stomach is delayed. This is associated with early satiation and prolonged satiety. Anatomical or physiological disruption of these functions results in an unsatisfactory outcome. Outcomes of complications vary predictably depending on the nature of the problem.

Luminal dilatation and focal impairments in oesophageal motility represent the majority of intermediate term complications. These can be identified with a stress barium and high resolution manometry. Revisional LAGB surgery is advocated for gastric enlargements where oesophageal motility is intact.

Focusing on adjusting to satiety not mechanical restriction, avoiding episodes of obstruction and removing saline from the LAGB if adverse symptoms develop are the logical translations to clinical practice. Whether these can be successfully integrated into the follow up schedule and accepted by patients is not clear.

The LAGB remains an excellent bariatric option. Significant strides have been made in understanding the physiology, pathophysiology and follow up process. There is the opportunity to directly harness the adjustability of the LAGB to further improve patient outcomes. This will only occur with endeavours that further increase basic

physiological understanding and aim to objectively evaluate means of translating current findings into clinical practice.

The LAGB provides an excellent model for increasing the understanding of the physiology of obesity and the regulation of appetite and food intake. The LAGB is able to successfully induce weight loss and uniquely its effects can be switched on and off. Better defining these mechanisms provides an exceptional opportunity to link to urgently needed future treatments.

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APPENDIX 1 - *Lap-Band Questionnaire*

SECTION A

The following questions are regarding symptoms you may or may not be experiencing.

For each question please tick the box which most applies to you. Only tick one box for each question.

If you are taking medications for the treatment of reflux, heartburn or indigestion *please tick the box which describes your symptoms if you stop taking your medications for several days, or how your symptoms were before you began taking medications.*

1) Do you ever experience "heartburn"? By this we mean a feeling of discomfort behind your breastbone rising up towards your throat, often associated with large or spicey meals.

   Never have heartburn or it happens less than once per month
   Have heartburn once per month
   Have heartburn once per week
   Have heartburn two to four times per week
   Have heartburn most days

2) Overall how much does heartburn bother you?

   Not at all, doesn't bother me at all or never experience heartburn
   Mildly bothered
   Moderately bothered
   Severely bothered

3) Do you ever experience effortless regurgitation of undigested or partially digested food spontaneously after eating? This may especially happen when lying down after eating. *This is not vomiting.*

   Never have regurgitation or it happens less than once per month
   Have regurgitation about once per month
   Have regurgitation once per week
   Have regurgitation two to four times per week
   Have regurgitation most days

4) Overall how much does the problem of regurgitation bother you?

   Not at all, doesn't bother me at all or never experience regurgitation
   Mildly bothered
   Moderately bothered
   Severely bothered

5) Do you ever experience discomfort or pain in the upper abdomen or the lower chest after large or spicy meals?

    Never have or it happens less than once per month
    Once per month
    Once per week
    Two to four times per week
    Most days

6) Overall how much does the problem of upper abdominal or lower chest pain or discomfort bother you?

    Not at all, doesn't bother me at all or never experience upper abdominal or lower chest pain
    Mildly bothered
    Moderately bothered
    Severely bothered

7) Do you ever experience a sensation of upper abdominal fullness or bloating?

    Never have or it happens less than once per month
    Once per month
    Once per week
    Two to four times per week
    Most days

8) Overall how much are you bothered by upper abdominal bloating or fullness?

    Not at all, doesn't bother me at all or never experience heartburn
    Mildly bothered
    Moderately bothered
    Severely bothered

9) Do you ever experience difficulty swallowing or foods "stick" going down, particularly with foods such as bread or chicken?

    Never have or it happens less than once per month
    Once per month
    Once per week
    Two to four times per week if symptoms
    Most days

10) Overall how bothered are you by difficulty swallowing?

    Not at all, doesn't bother me at all or never experience difficulty swallowing
    Mildly bothered
    Moderately bothered

Severely bothered

11) Do you ever experience a cough associated with lying down or following meals? *(This does not mean a cough at other times)*

    Never experience coughing at these times or it happens less than once per month
    Once per month
    Once per week
    Two to four times per week
    Most days

12) How bothered by cough are you? This only means cough associated with lying down or occurring after spicy meals *NOT COUGH OCCURING AT OTHER TIMES*

    Not at all, doesn't bother me at all or rarely have a cough
    Mildly bothered
    Moderately bothered
    Severely bothered

13) Are you taking any medications for reflux, heartburn or indigestion? These might include drugs such as Losec, Nexium, Pariet, Zantac, Tagamet or antacids such as quickeze or Mylanta.

Please write down medications you are taking for the treatment of reflux, heartburn or indigestion. Please also write down the dose of medication, how frequently you take the medication and for how long you have been taking the medication for.

_____
_____
_____
_____

14) When you eat the following foods do you experience difficulty swallowing? (eg food sticks in your throat, causes pain or you avoid that particular type of food because it is difficult for you to swallow)

Please rate how frequently you find it difficult to swallow these different types of food

Please tick the box next to each type of food which best represents what happens to you
Always – every time you eat that food
Sometimes – occasionally or half the time
Never – rarely if ever

Severity (choose one for each food class)

	Always	Never	Sometimes
Water			
Milk or thin soup			
Custard or yoghurt or pureed fruit			
Scrambled eggs or baked beans or mashed potato			
Baked fish or steamed potato or cooked carrot			
Bread or pastries			
Apple or raw carrot			
Steak or lamb chop			

15) Do you experience difficulty swallowing some foods or a sensation of certain food sticking in the throat?

Please place a mark on the line which you feel represents overall how much difficulty you have with swallowing foods.

No difficulty   Moderate difficulty   Severe difficulty

0   1   2   3   4   5   6   7   8   9   10

16) Overall how satisfied with the Lap-Band surgery are you?

Please place a mark on the line which you feel represents overall how much satisfied with your Lap-Band surgery.

Unsatisfied   Moderately satisfied   Very
satisfied

    0   1   2   3   4   5   6   7   8   9   10
_____

17) Following your Lap-Band surgery do you feel that your symptoms of reflux   or heartburn have changed in any way?

(On a scale of -5 to 0 to +5 please put a mark on the line where you believe the outcome of the surgery for you lies, -5 being terrible, the worst thing that could have happened; reflux symptoms are much worse, 0 being in the middle – no change in reflux symptoms, +5 being fantastic, a great outcome for you, reflux symptoms remarkably improved).

Worse   No change
Better

    -5   -4   -3   -2   -1   0   +1   +2   +3   +4   +5
_____

18) Have you noticed that you suffer from upper abdominal bloating or swelling, particularly after meals. If so does this bother you?
(On a scale of 0 to 10 please put a mark on the line where you believe the outcome of the fundoplication for you lies, 0 being not bothered at all or don't have this problem, , 10 being bothered a lot, a real problem couldn't think of anything worse.)

Not bothered at all   Moderately bothered   Bothered a lot

    0   1   2   3   4   5   6   7   8   9   10
_____

19) Based on what your experience following Lap-Band surgery have been and what the outcome of surgery has been for you, if you could go back in time would you have chosen to have the surgery done again?

(Please tick one box only)

    Definitely would have the surgery again
    Would probably have the surgery again
    Unsure if would have the surgery again
    Would probably not have the surgery again
    Definitely wouldn't have the surgery again

20) What has been the biggest problem or troublesome symptom for you following your Lap-Band surgery?

    No significant problem or symptom
    Vomiting or regurgitation of food or food getting stuck
    Reflux or heartburn
    Being unable to eat certain food types
    Other symptom or problem – please detail below?

21) Do you ever experience pain in the upper abdomen after eating? Particularly after you have eaten a large meal

    Never have pain in the upper abdomen or it happens less than once per month
    Have pain in the upper abdomen once per month
    Have pain in the upper abdomen once per week
    Have pain in the upper abdomen two to four times per week
    Have pain in the upper abdomen most days

22) Overall how much does this pain in the upper abdomen after you eat bother you?

    Not at all, doesn't bother me at all or rarely if ever experience upper abdominal pain
    Mildly bothered
    Moderately bothered
    Severely bothered

23) Do you modify your diet by avoiding certain foods or adjust the amount of food you eat to avoid abdominal pain after eating?

    Not at all
    A little bit (only modify diet slightly or eat slightly differently)
    Moderate (modify several foods in diet, noticeably change diet to avoid pain after eating)

A lot (Modify a lot of items in diet to avoid pain associated with eating)

The following questions relate to VOMITING OR REGURGITATION. It means food coming back up out of the mouth after you have chewed and swallowed it. This includes food that you have swallowed gets stuck and then comes back up again out of your mouth.

24) How often do you vomit or regurgitate? (please tick the one most appropriate box)

less than once per month
once per month
once per week
two to four times per week
daily
more than once per day

25) How much does the vomiting or regurgitation bother you? (please tick the one most appropriate box)

Not bothered at all, or don't vomit frequently
Mildly bothered
Moderately bothered
Severely bothered

26) Do you modify your diet and the foods you eat to prevent vomiting or regurgitation, specifically are there some types of foods you avoid to prevent vomiting or regurgitation? (please tick the one most appropriate box)

Don't modify diet or foods at all,
Modify diet slightly and avoid small number of foods
Modify diet moderately and avoid quite a few different types of food
Modify diet a lot avoid many different types of food

27) Do you avoid certain foods because you know they will make you vomit or regurgitate? (please tick the most appropriate answer)

Do not avoid any types of food
Avoid some types of food   (a few not many)
Avoid a moderate number of types of food (but still have a number of foods you can eat)
Avoid a lot of types of food. Difficult to find foods I can eat without vomiting or regurgitating

HUNGER SCORE

Please rate how hungry you feel on a normal day. This is when you have a normal nights sleep and don't snack excessively between meals. Place a mark on the number or between the numbers which you think most represents how you feel. The numbers and statements are a guide only. With 0 being starving and 10 being as full as you could possibly imagine.

BEFORE BREAKFAST (when you first wake up)

	Very hungry			A little bit hungry				Full		Bursting, feeling sick
0	1	2	3	4	5	6	7	8	9	10
Starving		Moderately hungry					Satisfied		Completely full	

BEFORE LUNCH (around midday)

	Very hungry			A little bit hungry				Full		Bursting, feeling sick
0	1	2	3	4	5	6	7	8	9	10
Starving		Moderately hungry					Satisfied		Completely full	

BEFORE MAIN EVENING MEAL

	Very hungry			A little bit hungry				Full		Bursting, feeling sick
0	1	2	3	4	5	6	7	8	9	10
Starving		Moderately hungry					Satisfied		Completely full	

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