Turun yliopisto
University of Turku

LAPAROSCOPIC ROUX-EN-Y GASTRIC BYPASS FOR MORBID OBESITY

Impact of Preoperative Endoscopy, Enhanced Recovery Protocol, and on the Prevalence of Obstructive Sleep Apnoea

Pipsa Peromaa-Haavisto

TURUN YLIOPISTON JULKAISUJA – ANNALES UNIVERSITATIS TURKUENSIS
Sarja - ser. D osa - tom. 1252 | Medica - Odontologica | Turku 2016

University of Turku

Faculty of Medicine

Department of Surgery

Turku Doctoral Programme of Clinical Investigation

Department of Surgery, Hatanpää City Hospital, Tampere and Vaasa Central Hospital, Vaasa

In association with Departments of Surgery in Kuopio University Hospital, Kuopio and Lahti Region Central Hospital, Lahti

Supervised by

Professor Mikael Victorzon
Department of Surgery
Vaasa Central Hospital, Vaasa, Finland
University of Turku, Finland

Docent Henri Tuomilehto
Oivauni Sleep Clinic,
Kuopio and Tampere, Finland
Department of Clinical Nutrition,
Institute of Public Health and
Clinical Nutrition
University of Eastern Finland

Reviewed by

Docent Timo Heikkinen
Terveystalo Helsinki and Oulu, Finland

Docent Tom Scheinin
Department of Surgery
Helsinki University Hospital, Finland

Opponent

Associate Professor Torsten Olbers
Department of Surgery,
Sahlgrenska University Hospital
Gothenburg, Sweden

The originality of this dissertation has been checked in accordance with the University of Turku quality assurance system using the Turnitin Originality Check service.

ISBN 978-951-29-6616-5 (PRINT)
ISBN 978-951-29-6617-2 (PDF)
ISSN 0355-9483 (Print)
ISSN 2343-3213 (Online)
Hämeen Kirjapaino Oy - Tampere, Finland 2016

To Hermanni

Abstract

Pipsa Peromaa-Haavisto: LAPAROSCOPIC ROUX-EN-Y GASTRIC BYPASS FOR MORBID OBESITY. Impact of preoperative endoscopy, enhanced recovery protocol, and on the prevalence of obstructive sleep apnoea. University of Turku, Faculty of Medicine, Department of Surgery, University of Turku Doctoral Programme of Clinical Investigation, Turku, Finland. Department of Surgery, Hatanpää City Hospital (Tampere) and Vaasa Central Hospital (Vaasa). In association with Departments of Surgery in Kuopio University Hospital (Kuopio) and Lahti Region Central Hospital (Lahti).

Obesity has become one of the greatest public health concerns in the world. Obesity increases morbidity and mortality, and causes costs to society. Conventional therapy is ineffective, and the long-term results are poor. Bariatric surgery is proven to be effective and safe.

The aim of this thesis was to identify the findings in upper gastrointestinal endoscopy (UGI) prior to laparoscopic Roux-en-Y Gastric Bypass (LRYGB) and to investigate the safety of enhanced recovery after surgery (ERAS) protocol in a general hospital. In addition, this study aimed at evaluating the prevalence of obstructive sleep apnoea (OSA) in bariatric surgery candidates and to investigate the effect of LRYGB on OSA at 12 months postoperatively.

The most common findings in UGI were hiatal hernia and gastro-oesophageal reflux, which are relative contraindications for sleeve gastrectomy (SG), but not for LRYGB. According to this study, a routine UGI is not needed prior LRYGB, but may be indicated prior to SG.

A systematic use of ERAS protocol reduced the length of hospital stay from two days to one day. At the same time overall morbidity and major complications decreased.

The prevalence of OSA in bariatric patients was 71%, which decreased to 44% after surgery. OSA was resolved in 54% and resolved or improved in 90% of the patients. LRYGB is an effective treatment for OSA, but postoperative cardiorespiratory recordings are recommended in order to identify the approximately 20% of patients with persistent OSA.

Keywords: LRYGB, OSA, ERAS, UGI, prevalence of OSA, bariatric surgery

Tiivistelmä

Pipsa Peromaa-Haavisto: MAHALAUKUN OHITUSLEIKKAUS VAIKEAN LIHAVUUDEN HOIDOSSA. Mahalaukun tähystyksen ja nopean toipumisen mallin vaikutus leikkaushoitoon ja leikkauksen vaikutus uniapnean esiintyvyyteen. Turun Yliopisto, Lääketieteellinen tiedekunta, Turun Yliopiston Kliininen Tohtoriohjelma, Turku ja Kirurgian klinikka, Hatanpään sairaala, Tampere sekä Vaasan keskussairaala, Vaasa. Yhteistyössä Kuopion Yliopistollisen sairaalan (Kuopio) ja Päijät-Hämeen keskussairaalan (Lahti) kirurgian klinikoiden kanssa.

Lihavuus on yksi maailman suurimmista kansanterveyden ongelmista. Lihavuuden liitännäissairaudet lisäävät väestön sairastavuutta ja kuolleisuutta, mikä aiheuttaa yhteiskunnalle kuluja. Lihavuuden konservatiivinen hoito on tehotonta ja pitkäaikaistulokset huonoja. Lihavuuskirurgia on todistetusti tehokas ja turvallinen hoito vaikeassa lihavuudessa.

Tutkimuksen tarkoitus oli arvioida mahalaukun tähystyslöydöksiä lihavuuskirurgisilla potilailla ennen leikkausta ja tutkia nopean toipumisen mallin käytön turvallisuutta pienemmissä bariatrisissa yksiköissä. Lisäksi tutkimuksen tarkoitus oli arvioida uniapnean esiintyvyyttä lihavuuskirurgisilla potilailla ja tutkia mahalaukun ohitusleikkauksen tehoa uniapneaan 12 kk kuluttua leikkauksesta.

Yleisimmät löydökset mahalaukun tähystyksessä olivat palleatyrä ja refluksitauti, jotka ovat relatiivisia vasta-aiheita mahalaukun kavennuksessa, mutta eivät mahalaukun ohitusleikkauksessa. Tutkimuksen perusteella tähystys ei ole tarpeen ennen mahalaukun ohitusleikkausta, mutta voisi olla aiheellinen ennen kavennusleikkausta.

Nopean toipumisen mallin käyttö vähensi sairaalassaoloa leikkauksen jälkeen kahdesta päivästä yhteen. Samaan aikaan morbiditeetti ja vakavat komplikaatiot vähenivät.

Uniapnean prevalenssi lihavuusleikkaukseen tulevilla oli 71 %, mikä laski 44 %:iin leikkauksen jälkeen. Uniapnea parani 45 %:lla ja parani tai helpottui 90 %:lla. Mahalaukun ohitusleikkaus on tehokas hoito uniapneaan, mutta seurantamittaukset tulisi tehdä kaikille, jotta noin 20 %:lle jäävä uniapnea todetaan.

Avainsanat: mahalaukun ohitusleikkaus, uniapnea, nopean toipumisen malli, mahalaukun tähystys

Table of contents

Abbreviations

AGB	Adjustable gastric banding
AHI	Apnoea-hypopnea index
ASGE	The American Society of Gastrointestinal and Endoscopic Surgeons
BMI	Body mass index
BNSQ	Basic Nordic Sleep Questionnaire
BPD	Biliopancreatic diversion
BPD-DS	Biliopancreatic diversion with duodenal switch
CPAP	Continuous positive airway pressure
%EBMIL	Per cent of excess BMI loss
EMA	European Medicines Agency
ERAS	Enhanced recovery after surgery
ESS	Epworth sleepiness scale
%EWL	Excess weight loss
GBP	Gastric bypass
GER	Gastro-oesophageal reflux
GJ	Gastro-jejunal
GLP-1	Glucagon-like peptide 1
HbA1C	Glycosylated haemoglobin
HDL	High-density lipoprotein
HP	Helicobacter pylori
ILI	Intensive lifestyle intervention
JIB	Jejuno-ileal bypass
LA	Los Angeles Classification of esophagitis A, B, C and D
LDL	Low-density lipoprotein
LOS	Length of stay
LRYGB	Laparoscopic Roux-en-Y gastric bypass
MGB	Mini gastric bypass
NASH	Nonalcoholic steatohepatitis

NIH	National Institute of Health
NSAID	Nonsteroidal anti-inflammatory drugs
OR	Odds ratio
OSA	Obstructive sleep apnoea
PCOS	Polycystic ovarian syndrome
PYY	Peptide YY
QoL	Quality of life
RCT	Randomised clinical trial
SADI	Single-anastomosis duodeno-ileal bypass
SADI-S	Single-anastomosis duodeno-ileal bypass with SG
SAGB	Single-anastomosis gastric bypass
SD	Standard deviation
SG	Sleeve gastrectomy
SIPS	Stomach intestinal pylorus sparing surgery
SOS	Snore outcome survey
SOS study	Swedish Obesity Subjects study
SpO_2	Arterial oxygen saturation (pulse oximetry)
T2DM	Type 2 diabetes mellitus
%TWL	Per cent of total weight loss
UGI	Upper gastrointestinal endoscopy
VBG	Vertical banded gastroplasty
VLCD	Very low calorie diet
WHO	World Health Organization

List of original publications

I. Peromaa-Haavisto P, Victorzon M. Is routine preoperative upper GI endoscopy needed prior to gastric bypass? Obes Surg. 2013 Jun;23(6):736-9.

II. Hahl T, Peromaa-Haavisto P, Tarkiainen P, Knutar O, Victorzon M. Outcome of Laparoscopic Gastric Bypass (LRYGB) with a Program for Enhanced Recovery After Surgery (ERAS). Obes Surg. 2016 Mar;26(3):505-11

III. Peromaa-Haavisto P, Tuomilehto H, Kössi J, Virtanen J, Luostarinen M, Pihlajamäki J, Käkelä P, Victorzon M. Prevalence of Obstructive Sleep Apnoea Among Patients Admitted for Bariatric Surgery. A Prospective Multicentre Trial. Obes Surg. 2016 Jul;26(7):1384-90

IV. Peromaa-Haavisto P, Tuomilehto H, Kössi J, Virtanen J, Luostarinen M, Pihlajamäki J, Käkelä P, Victorzon M. Obstructive sleep apnea: The effect of bariatric surgery after 12 months. A Prospective Multicentre Trial. Submitted

1 Introduction

Obesity has become one of the major public health concerns worldwide. According to the estimation made by the World Health Organization (WHO), there are more than 500 million obese adults in the world. Between 1980 and 2014 the prevalence of obesity worldwide has nearly doubled [WHO 2014]. In recent data the increase in the prevalence of obesity has stabilised in the USA [Nguyen et al 2010, Ogden et al 2015]. The same trend is shown in Finland according to the National Institute for Health and Welfare report FINRISKI 2012 National Survey [THL report 22/2013]. However, the prevalence of obesity remains high, and an effective treatment with sustainable long-term results is needed.

Weight loss by healthy lifestyle is recommended for all obesity related chronic diseases, but weight loss programmes are successful only for a fraction of obese, and the long-term results are modest after conventional therapy. Bariatric surgery, lately also referred to as metabolic surgery, has demonstrated a well-documented, greater, and more permanent weight reduction in obesity treatment than conventional therapy [Ribaric et al 2014]. Particularly laparoscopic Roux-en-Y gastric bypass (LRYGB) has proven effective in treating obesity related diseases, such as type 2 diabetes, hypertension, hyperlipidaemia, and obstructive sleep apnoea (OSA) [Buchwald et al 2004]. Despite these well-documented good results, the obesity problem is still stigmatised, and the general public may be afraid of the harmful effects of possible surgical complications.

Upper gastrointestinal endoscopy (UGI) is an excellent diagnostic tool for oesophageal and gastric diseases. After LRYGB the normal UGI is no longer possible. The role of routine UGI prior to the LRYGB operation has been argued, but there is no consensus about this matter. Patients often experience the UGI investigation unpleasant without sedation. In Finland sedation is rarely used during UGI, but Küper et al. (2010) showed that it was safe, even though they observed severe hypoxemia after sedative use in UGI in two patients (2.9%), both of them suffering from OSA. Routine UGI demands resources even when performed without sedation. In Finland no gastric diseases, such as gastric cancer or Barret's oesophagus, are screened systematically in the general population.

Traditionally, surgical patients were hospitalised for a longer period after operation in order to be observed for possible postoperative complications. Sometimes hospitalisation started days before the operation. The improvements in anaesthetic and surgical techniques, especially the introduction of laparoscopic techniques,

have decreased the postoperative length of stay in hospital. The standardised pathway for enhanced recovery was first introduced by Henrik Kehlet and co-workers (2002). Enhanced recovery after surgery (ERAS) protocols consist of preoperative counselling, optimisation of nutrition, standardisation of perioperative care, multi-modal analgesia and early mobilisation aiming at a reduction of the patient's stress response. It was first used in colorectal surgery, but was rapidly adopted to other fields of surgery, including bariatric surgery.

Obstructive sleep apnoea (OSA) is a highly prevalent breathing disorder observed during sleep. The underlying mechanisms predisposing to OSA are most likely multifactorial and still not very well understood, but obesity is the most important single cause. OSA causes daytime symptoms, such as tiredness and impaired quality of life due to fragmentation of sleep, but is also tightly linked to metabolic abnormalities and increased morbidity and mortality due to cardiovascular diseases, especially in more severe stages of OSA [Tuomilehto et al 2008, Muraja-Murro et al 2013]. Approximately 70% of patients with diagnosed OSA are obese [Vgontzas et al 1994]. The diagnosis of OSA should always be based on a cardiorespiratory recording, and from this perspective the prevalence of OSA ranges from 17% to 24% among men and 5% to 9% among women. In the obese population the prevalence is even higher; in metabolic surgery candidates it ranged from 60% to 83% [Ashrafian et al 2012].

In this doctoral thesis the aim of the first study was to investigate the findings in preoperative UGI in order to evaluate whether or not to recommend it as a routine investigation before surgery. In the second study the safety of an ERAS programme in bariatric patients was investigated. The aim of the third and fourth studies was to investigate OSA in bariatric surgery candidates. OSA is considered highly underdiagnosed, and in the third study the true prevalence of OSA was evaluated with cardiorespiratory recordings prior to bariatric surgery. In the fourth study, a second cardiorespiratory recording was conducted 12 months after the operation to investigate the effect of bariatric surgery on OSA.

2 Review of literature

2.1 Epidemiology of obesity

Obesity is defined as an excess of body fat. It is not easy to measure in routine examinations, and that is why the body mass index (BMI) was introduced in the 1980s for practical use as an indicator of the degree of obesity. BMI is calculated as body mass divided by the square of body height. In the 1990s WHO defined that BMI 25 kg/m^2 to 30 kg/m^2 should be considered overweight and BMI more than 30 kg/m^2 obese. Obesity is categorised in three classes: BMI 30 kg/m^2 to 35 kg/m^2 as class I, moderately obese, BMI 35 kg/m^2 to 40 kg/m^2 as class II, severely obese, and more than 40 kg/m^2 class III, very severely obese or morbidly obese.

Already in the 1960s an alarming trend in the increase of obesity was noticed in the regular, national surveys in the USA [Harlan et al 1988]. The prevalence of obesity continued to rise the next 40 years. The year 2000 was historical; that is when the number of overweight adults surpassed the number of underweight adults in the world [Caballero 2007]. Fortunately, in recent studies it seems that the prevalence of obesity has reached a plateau, and the number of obese people is not increasing [Nguyen et al 2010, Ogden et al 2015]. Even though the prevalence is generally lower in low-income and middle-income countries, it is increasing faster in those countries than in high-income countries [Seidell et Halberstadt 2015]. In 2014, 39% of adults were overweight worldwide, and 11% of men and 15% of women were obese. There are great regional differences; 61% of Americans are overweight and 27% are obese, whereas in South-East Asia 22% are overweight and only 5% are obese [WHO 2014]. In European countries the prevalence of obesity ranged from 4% to 28% in men and from 6% to 37% in women. The regional variance was also strong in Europe, Western and Northern Europe being leaner [Berghöfer et al 2008].

In Finland obesity has been studied in national epidemiological surveys since the mid-1960s. At that time 8% of men and 17% of women were obese. Since then the increase in the prevalence of obesity has been strong in both sexes and in all age and educational groups. The most striking increase has been among well-educated men. By 2002 the prevalence of obesity was 21% in men and 20% in women [Lahti-Koski et al 2010]. According to the latest FINRISKI 2012 national survey, the prevalence of obesity in men is 20%, and overweight and obesity combined is 66%. In women the numbers are 19% and 46%, respectively. Central obesity, i.e. waist circumference over 100 cm in men and over 90 cm in women, is found in 30% of Finns. It is well

established that central obesity is strongly connected to the obesity related metabolic disorders [THL report 22/2013].

Previously Finnish men have been the heaviest in the Nordic countries, but according to the WHO 2006 interactive statistical charts, 21.6% of Finnish men are obese, which is the lowest percentage among Nordic men (Denmark 21.7%, Sweden 22.5%, Iceland 24.1%, Norway 24.6%). Finnish women are in the third place with 19.6% after Danish (17.0%) and Swedish (18.6%) women, and followed by Iceland (21.5%) and Norway (21.7%) [WHO 2006].

2.2 Obesity related morbidity and mortality

Obesity associated health risks start to increase already when BMI exceeds 25 kg/m^2. Obesity strongly influences the global incidence of type II diabetes mellitus (T2DM), obstructive sleep apnoea, cardiovascular diseases, cancer, stroke, and osteoarthritis, not to mention work disability and reduced quality of life [Seidell et Halberstadt 2015]. Other diseases associated with obesity are metabolic syndrome, gallstones, liver disease [most commonly nonalcoholic steatohepatitis (NASH)], asthma, gout, polycystic ovary disease, infertility, urinary incontinence, depression, and gastro-oesophageal reflux disease [Nguyen et al 2010, Bächler et al 2014, Martin-Rodriguez et al 2015].

Obesity is an independent risk factor for increased morbidity and mortality. Globally, overweight and obesity are estimated to be the fifth leading cause of death and account for 3.4 million deaths per year [Smith et Smith 2016, WHO 2014]. In one study, obesity decreased the life expectancy by seven years in obese women and six years in obese men, findings similar to smokers [Peeters et al 2003]. Still, obesity has a stronger effect on morbidity than on mortality. Especially in industrialised countries the disability of obesity related diseases will grow when patients survive for example cardiovascular events due to a good health care more often than in developing countries [Vissher et Seidell 2001].

Overweight and obesity are associated with an increased risk for multiple morbidities, but one of the strongest associations is with T2DM. More than 80% of T2DM is attributable to overweight and obesity, and obese subjects have a seven-fold risk to develop T2DM compared to normal weight subjects [Smith et Smith 2016]. The global prevalence of T2DM (defined as a fasting plasma glucose more

than 7.0 mmol/l or being on medication for raised blood glucose) was 9% in 2014 according to the WHO [WHO 2014].

In Finland T2DM is one of the greatest and the most fast-growing public health concerns. In 2007 more than 245 000 patients had T2DM. The number is constantly growing; in one decade, between 1997 and 2007, the growth was 77%. According to the national health survey, only half of T2DM patients are diagnosed. It is estimated that the real number of T2DM patients in Finland is closer to 500 000 or 600 000 [Koski 2011].

Obesity also has a strong relationship with cardiovascular diseases. An increased risk of stroke, heart failure, atrial fibrillation, hyperlipidaemias, hypertension, and coronary disease are associated with obesity. In 2010 the first two leading causes of death worldwide were ischemic heart disease and stroke [Lozano et al 2012].

An increased risk of ten different cancer types are linked to obesity; cancer of the oesophagus (adenocarcinoma), colorectum, breast (in post-menopausal women), pancreas, liver, gallbladder, ovary, endometrium, kidney, and prostate. Sixty-seven per cent of these cancers are diagnosed in highly developed countries, and they comprise 27% of the total global burden of cancer [Arnold et al 2016]. In addition, not only were obese subjects more likely to develop an obesity related cancer, but being obese prior the diagnosis of colorectal, breast, and pancreatic cancer increased the risk of cancer-specific and all-cause mortality [Lee et al 2015, Arnold et al 2016].

OSA and its relation to obesity are discussed in chapter 2.8.

2.3 Economic impact of obesity

Calculating the exact total costs of obesity is difficult. The direct costs of obesity, i.e. increased medical expenses, are easier to estimate than indirect costs, such as reduced productivity at work, increased sick leaves, and premature retirement. In the USA direct medical costs were calculated to be 42% higher among obese adults compared with healthy-weight individuals in 2006 [Finkelstein et al 2009]. The United States leads the world in obesity-related spending; the total annual costs were estimated to exceed 275 billion dollars [Spieker et Pyzocha 2016]. According to the estimation of WHO, obesity is responsible for 2% to 8% of health costs in the European region.

In Finland the annual costs of obesity were estimated to be more than 260 million euros in 2005. The direct costs, i.e. health care costs, were nearly 190 million euros, half of it being hospital costs and 40% medical expenses. Indirect costs, approximately 70 million euros, are mostly due to premature pensions. Two thirds of the costs were related to T2DM, stroke, and osteoarthritis [Pekurinen 2006]. In a large Finnish survey of more than 31 000 subjects between 1966 and 1972, the risk of work disability was linearly increased with the increasing BMI. At that time, 22% of all premature pensions in women and 9% in men were attributable to overweight and obesity. Disability pensions were granted 2.0 times more often to obese women and 1.5 times more often to obese men than to normal weight women and men [Rissanen et al 1990]. In the more recent study by Pekurinen et al. (2006), 5200 persons were on premature pension because of obesity, and sick leave days due to obesity exceeded 340 000 days annually. The cost-utility of bariatric surgery in Finland was shown in the study by Mäklin et al. (2011). In ten years the expected health-care costs of patients having ordinary treatment were fairly constant and about 1.5 times higher than the costs of bariatric surgery patients. Surgical patients' reduced annual healthcare costs, mainly due to loss of weight and co-morbidities, compensated for the costs of LRYGB and sleeve gastrectomy (SG) in five years.

2.4 Conservative treatment of obesity

2.4.1. Nutrition and physical activity

To maintain a healthy weight should be easy; a balance between energy consumed and energy expended. In 2014 WHO published The Global Status report on non-communicable diseases with nine targets to attain. The target number seven was: Halt the rise in diabetes and obesity. The tools to attain this target are population-wide policies, i.e. changes in agricultural subsidies to encourage the production of healthier food, taxation schemes to produce changes in price to change purchasing habits to healthier direction, setting-based interventions, i.e. promoting healthy diets and physical activities at school and workplaces, and individual interventions, i.e. counselling through primary health care [WHO 2014].

Conservative treatment of obesity consists of life-style interventions including nutritional counselling (individual or in groups) and dietary therapy [very low calorie diet (VLCD) or other reduction diet] combined with physical activity counselling, behavioural therapy, and/or pharmacological treatment. It is important to set realistic goals. When BMI is between 25 kg/m^2 and 35 kg/m^2, a weight loss more than 5% in

long-term is considered successful. With BMI more than 35 kg/m^2, 10% weight loss can be considered successful [Wirth et al 2014]. In five meta-analyses and two randomised clinical studies (RCT) analysing the effect of various forms of dietary therapy the reduction in weight was around four kilograms in one to two years [Wirth et al 2014]. In a review of conservative treatment of obese children and adolescents, the mean weight loss after one year was from 0.05 to 0.39 BMI units, which implies that other methods to influence children's obesity are needed [Mühlig et al 2014]. In one older study, a significant weight reduction of 12.9 kg at one year was achieved with VLCD (400–500 kcal/day) and behavioural therapy combined. With VLCD alone, the weight loss was 4.6 kg, which is closer to the average in other studies [Wadden et Stunkard 1986]. In a Finnish study of VLCD and behavioural therapy, morbidly obese patients were divided in two groups: the other had VLCD and behavioural treatment and the other only behavioural treatment. At the end of the five-year follow-up, the weight reduction in the VLCD and behavioural therapy group was 16.9 kg compared to 4.9 kg in the behavioural treatment only group [Pekkarinen et Mustajoki 1997]. In a Finnish randomised trial VLCD was combined with walking training in obese women. In the 12-week weight reduction phase the mean weight loss was 13.1 kg. In the 40-week weight maintenance phase a control group had nutritional counselling only, while walking groups had counselling and in addition 2 to 3 or 4 to 6 hours per week walking exercise. In the two-year follow-up all the groups gained weight 5.9 kg to 9.6 kg, but the best result was seen in the 2 to 3 hours per week walking exercise group. The programme of physical activity recommended after weight reduction improved the maintenance of weight reduction [Fogelholm et al 2000]. In another Finnish study of middle-aged men, walking exercise and muscle exercise did not improve long-term weight maintenance due to a poor adherence to the recommended physical activity [Borg et al 2002]. Even though increased physical activity is often included in the weight maintenance programme, beneficial effects of exercise on long-term weight maintenance have not been demonstrated unequivocally [Fogelholm et Kukkonen-Harjula 2000]. In a unique study of obese patients, the Swedish Obese Subjects (SOS) study, with a follow-up of ten years, weight had increased 1.6% in the control subjects with conventional therapy alone [Sjöström et al 2004].

2.4.2. Pharmacotherapy

Pharmacological treatment is never a first choice treatment for obesity, but can be combined to conventional therapy to increase weight loss. Unfortunately only one drug is available on the Finnish market at the moment: orlistat.

Orlistat is an inhibitor of gastrointestinal lipases, which means that dietary triglycerides cannot be broken into absorbable free fatty acids. This leads to a 30% decrease in absorption of ingested triglycerides. Orlistat should always be combined with low-fat diet to reduce the side effects, such as oily stools, faecal urgency, and increased defecation [Wharton 2015]. In a meta-analysis investigating long-term pharmacotherapy for obesity, orlistat reduced weight by 2.9 kg or 2.9% more than placebo. Both orlistat and placebo arms showed similar weight regain during the second year of follow up [Rucker et al 2007]. Orlistat was shown to lower total cholesterol and low-density lipoprotein (LDL) cholesterol significantly compared to a placebo group, and risk for cardiovascular events was also reduced [Sjöström et al 1998].

Previously two different medical products for obesity treatment have been on the market in Finland: sibutramine and rimonabant. Sibutramine is an oral anorexiant. By inhibiting reuptake of serotonin and norepinephrine in brain, it helps to enhance satiety. It reduces weight 4.2 kg or 4.3% more than placebo [Rucker et al 2007]. Because of an association to an increased risk of cardiovascular events and strokes, it was withdrawn from the market in Finland and many other countries in 2010. Rimonabant is a selective cannabinoid-1 receptor agonist with an anorectic affect. Patients receiving rimonabant lost 4.7 kg more weight than those in the placebo group. A significant reduction in waist circumference, blood pressure, and lipid profiles was also seen [Rucker et al 2007]. Unfortunately, severe adverse effects were reported, i.e. suicidality, depression, anxiety, and aggression. The product was withdrawn from the market in Finland in 2008.

In the near future it is possible to have two new products for the treatment of obesity in Finland. European Medicines Agency (EMA) has already approved liraglutide and bupropion combined with naltrexone for the treatment of obesity in Europe, but it is still unknown when these products will be available on the Finnish market. Liraglutide is a glucagon-like peptide 1 receptor agonist, which enhances satiety and reduces caloric intake. It is an injectable drug, and is already in use in Finland for T2DM. After one year of therapy with liraglutide, the weight reduction was 5.6 kg to 5.9 kg or 4.0% to 6% more than achieved by placebo [Wharton 2015]. Bupropion/naltrexone combination is the only antidepressant-containing product approved for obesity treatment at the moment. Bupropion increases dopamine activity in the brain, reduces appetite, and increases energy expenditure, while naltrexone blocks opioid receptors and reduces food cravings. An extra 5% to 9% weight loss due to bupropion/naltrexone was shown in four studies compared with placebo [Rodriguez et Campbell 2016].

It is important to have a wider spectrum of drugs for obesity treatment in Finland, even though the effect of drugs is modest and adverse effects of drugs cause many users to discontinue the therapy. For comparison, in United States there are eight different products for obesity currently available. Beside orlistat, liraglutide and bupropion/naltrexone, there are five stimulants that can be used for treatment of obesity. New medications targeting different mechanisms of action are already under development. Conventional therapy of obesity is difficult, and if a combined drug therapy improves weight reduction, it should be added to the treatment regimen.

2.5. Operative treatment of obesity

2.5.1. Indications for bariatric surgery

Bariatric surgery is a good choice of treatment for carefully selected patients with severe or morbid obesity. It can be considered if conservative treatment for obesity has failed. In 1991 the National Institute of Health (NIH) Consensus Development Panel gave a recommendation for a gastrointestinal surgery for severe obesity [NIH conference 1991]. These guidelines are still in use in Finland and worldwide. Indications for surgery are BMI over 40 kg/m^2 or BMI over 35 kg/m^2 if the patient has obesity related diseases such as T2DM, hypertension, OSA, osteoarthritis, or polycystic ovary syndrome (PCOS). Age limits in Finland are set between 18 and 65 years, but in both ends an individual evaluation is possible [Current Care Guidelines, Käypä hoito –suositus, 2013]. KELA (Social Insurance Institution) has set the BMI criteria for bariatric surgery even higher; BMI over 45 kg/m^2 or 40 kg/m^2 if patient has co-morbidities. A surgery candidate has to have undergone conservative treatment for obesity and has to be motivated for the life style change. Alcohol or drug abuse and severe psychiatric disorders are strict contraindications for surgery. The current guidelines have been criticised lately, while new results show the benefit of operating T2DM patients with BMI less than 35kg/m^2. In the recent review of the key results of the Swedish Obesity Subjects trial, high insulin and/or high glucose at baseline predicted favourable effect after bariatric surgery, whereas high BMI at baseline did not. Re-evaluation and redefinition of the selection criteria for metabolic surgery will be needed in the near future [Sjöström 2013].

2.5.2. History of bariatric surgery

The very first operation aiming at the reduction of weight was performed in 1952 by the Swedish surgeon Viktor Henriksson, who resected 105 cm of small bowel

[Henriksson 1952]. Jejuno-ileal bypass (JIB) was reported in 1954 by Kremen (1954). This operation was shown to produce permanent weight reduction, and it became the most performed bariatric operation from late 1960s to early 1970s. Because of a significant fatty diarrhoea, liver problems, and other adverse effects, JIB was abandoned. Safer procedures were developed, including the biliopancreatic diversion (BPD) by Scopinaro in 1976. BPD was further developed by Hess into a BPD with duodenal switch. These are highly malabsorptive operations and contain a risk for malnutrition [Buchwald 2014, Salameh 2006].

Already in 1966, the first version of gastric bypass (GBP) was introduced by Edward Mason, "the father of bariatric surgery". This operation was less malabsorptive and more restrictive than BPD [Mason et Ito 1967]. It has been modified since, and when Wittgrove et al. (1994) introduced their technique with laparoscopic approach in 1994, it rapidly became one of the most commonly performed bariatric procedures worldwide.

Mason also introduced a purely restrictive procedure, the vertical banded gastroplasty (VBG) [Mason 1982]. Weight reduction was less permanent due to enlargements of the pouches and to the development of gastro-gastric fistulas. Because of these long-term complications, VBG was abandoned.

Another purely restrictive procedure that became very popular in the 1990s and early 2000s is the adjustable gastric banding (AGB). Like in VBG, the mid-term results up to five years were good, but the long-term results beyond ten years were disappointing, and with time the number of complications increased (i.e. band slippages and band erosions). The advantages and disadvantages of the AGB have been extensively studied in a former Finnish doctoral thesis [Tolonen 2008]. The use of laparoscopic AGB is decreasing, and many of the AGB patients have now been converted to other bariatric procedures, such as GBP or sleeve gastrectomy (SG). The free-standing SG is a restrictive procedure and previously used only as a first stage operation in BPD-DS. It was shown to be effective as a free-standing operation, and in 2013–2014 it became the most rapidly growing bariatric procedure in the world [Buchwald 2014, Salameh 2006].

In Finland a few bariatric procedures were performed already in the 1970s. In Helsinki university hospital, 47 JIBs were performed between 1972 and 1980, and 33 VBGs between 1983 and 1990. AGB operations were initiated in Helsinki, Kuopio and Vaasa in mid-1990s. The first GBP was performed in Lahti in the end of 1990s [THL report 16/2009]. The LRYGB operations were started in a larger scale

at several Finnish hospitals in 2006, and the first laparoscopic sleeve gastrectomy was performed at Vaasa central hospital in December 2006.

2.5.3. The most common bariatric procedures

Laparoscopic Roux-en-Y gastric bypass (LRYGB)

LRYGB is the dominant bariatric procedure in the world at the moment. In 2013 of nearly 469 000 bariatric operations performed worldwide, 45% were LRYGBs. Of all bariatric procedures 96% are carried out laparoscopically [Angrisani et al 2015]. In LRYGB a small pouch of 15 to 30 ml is divided from the upper part of stomach. The remnant stomach and duodenum is then bypassed by anastomosing jejunum up to the stomach pouch. An alimentary limb starting from the pouch is usually approximately 100 cm to 150 cm to the second anastomosis, where a biliary limb of 50 cm to 150 cm is connected to the jejunum (Fig 1). The length of both limbs can vary depending on the different techniques introduced by several surgeons. In a distal LRYGB the second anastomosis is moved towards the end of the small intestine, usually 100 cm to 150 cm from the ileo-caecal angle, which makes the procedure more malabsorptive and thus more effective in terms of weight loss. In an effort to make the restrictive component of the LRYGB more permanent, Fobi added a silastic ring above the gastro-jejunostomy [Fobi 1991].

The mini gastric bypass (MGB) or single-anastomosis gastric bypass (SAGB) is a modification of the LRYGB developed by Robert Rutledge in 1997. A long narrow pouch is created along the lesser curvature down to the incisura, and a 200 cm or longer loop of small intestine is attached to this narrow tube through a single gastro-jejunostomy (Fig 2) [Lee et Lin 2014].

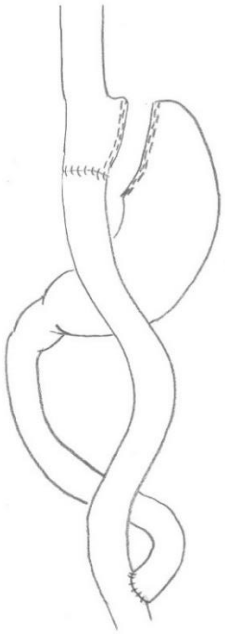


Figure 1. Gastric bypass

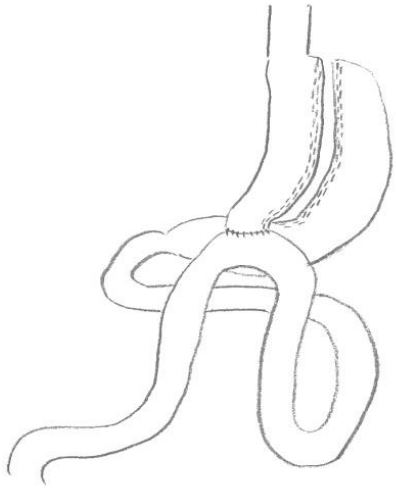


Figure 2. Mini gastric bypass

Gastric bypass is considered both restrictive and malabsorptive, but the exact mechanisms leading to its well documented, good long-term weight loss effects are still mostly unclear. The small pouch restricts the portion size and induces satiety leading to a smaller energy intake, and the bypassed small bowel decreases fat absorption. In addition, the more rapid delivery of nutrients to the distal small intestine is inducing changes in gut hormone profiles, such as glucagon-like peptide 1 (GLP-1) and peptide YY (PYY), which can lead to a loss of hunger and increase in satiety [le Roux et al 2007]. Exclusion of the proximal small intestine reduces the secretion of upper gastrointestinal factors, anti-incretins, which are assumed to suppress insulin secretion and/or promote insulin resistance [Rubino 2010]. The changes in gut microbiota observed after gastric bypass may also have influence on weight by reduction of low-grade inflammation associated with obesity [Abdeen et le Roux 2016].

Sleeve gastrectomy (SG)

SG is the most rapidly increasing bariatric procedure. The proportion of SG of all bariatric operations increased from 0% in 2003 to 37% in 2013, when it was already the most frequently performed procedure in the USA, Canada, and in the Asia-

Pacific region, even though the data of long-term outcome is lacking [Angrisani et al 2015].

In SG a narrow tube along the lesser curvature is created with stapling device, starting from the antrum 4 cm to 6 cm proximal from the pylorus. Approximately two thirds of stomach is removed (Fig. 3).

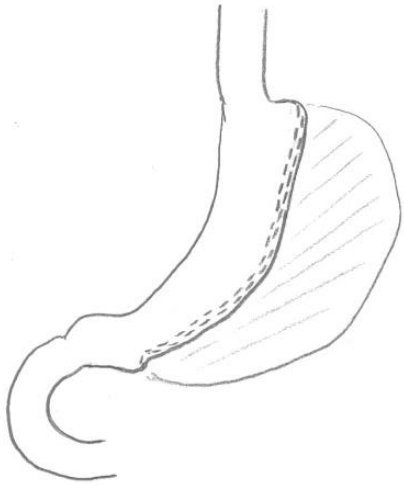


Figure 3. Sleeve gastrectomy

There are hormonal components involved in the mechanism of losing weight after SG similar to those seen after LRYGB. Rapid passage of undigested food arriving in the small intestine may increase the secretion of gut hormones such as GLP-1. Removal of the fundus and a decrease in the secretion of ghrelin has been thought to reduce appetite after SG. However, ghrelin may not be as important as previously thought, because the procedure has been equally effective in ghrelin-deficient and ghrelin-intact mice. In addition, ghrelin levels increase after AGB and increase, decrease, or remain unaltered after LRYGB, which may imply that ghrelin needs to be further studied [Miras et le Roux 2013].

Biliopancreatic diversion (BPD) and biliopancreatic diversion with duodenal switch (BPD-DS)

In the BPD a part of stomach is removed, but the remaining part is still large enough to allow normal meal portions. The small bowel is transected approximately halfway between the ligament of Treitz and the ileo-coecal valve. The distal part of small bowel is anastomosed to the gastric pouch and biliopancreatic limb is anastomosed to the distal ileum 50 cm prior to the ileo-coecal valve. The common channel is only 50 cm long causing malabsorption (Fig. 4).

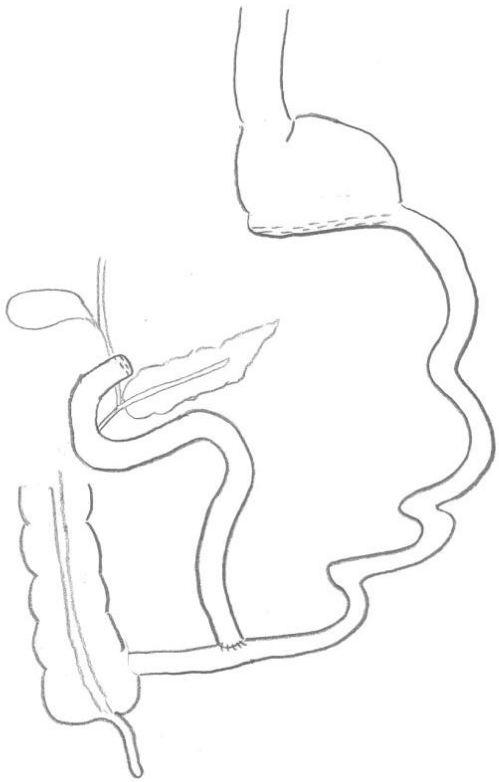


Figure 4. Biliopancreatic diversion

BPD-DS is a modification of BPD, in which SG is usually performed as a first-step operation in high risk, super-obese patients. A second-step operation is usually performed safely one year later, if needed (Fig. 5). In the second operation the duodenum is transected below the pylorus and the alimentary limb is measured 250

cm from the ileo-coecal valve and anastomosed to the proximal part of duodenum. The biliary limb is then anastomosed 100 cm from the ileo-coecal valve, creating 100 cm of common channel.

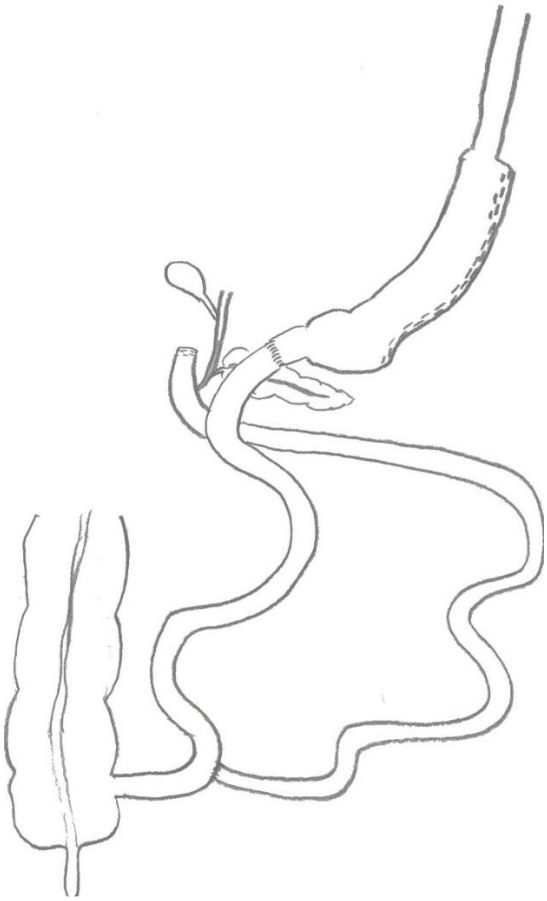


Figure 5. Biliopancreatic diversion with duodenal switch

2.5.4. New methods

Two review articles listing new methods for interventional obesity treatment were published last year. The authors strongly believed that both obesity and T2DM treatment with surgical and endoscopic procedures will increase. New minimally invasive, endoscopic procedures are needed for those who fear the complications of bariatric surgery [Roslin et al 2015, Kumar 2015].

Endoscopic procedures

All the endoscopic methods are not new, like intra-gastric balloon, but new improved designs are expected on the market. A silicone balloon is usually implanted in the stomach for six months and induces satiety by filling the stomach. The future devices might be swallowed without endoscopy or anaesthesia and even possibly be self-excreted with stool [Roslin et al 2015, Kumar 2015, Dargent 2016].

The EndoBarrier® is a plastic sheath attached to the first portion of duodenum and jejunum aiming at bypassing these intestinal parts and thus mimicking the effect of a gastric bypass. This device is put in place endoscopically and can be used for one year. In a multicentre randomised controlled trial, 77 obese patients with T2DM were randomised into an EndoBarrier® group or to a dietary intervention group. Thirty-four devices were successfully implanted, and 31 patients completed a six-month follow-up. In the EndoBarrier® group excess weight loss percentage (%EWL) was 32% versus 16% in the control group. At one year the %EWL was still 20%, when in the control group it was 12%. Glycosylated haemoglobin (HbA1c) was also significantly lower ($p<0.05$) in the EndoBarrier® group [Koehestanie et al 2014, Kumar 2015].

New generations of endoscopic suturing and stapling devices allow the gastric partition transorally. There are four competing devices available for gastric plication: USGI-POSE®, Apollo OverStitch®, ACE stapler® and EndoCinch®. Equivalent outcome to that seen after AGB has been reported one year after POSE®. Long-term outcome is still lacking. At one year after EndoCinch® %EWL was 58% in adult patients with average baseline BMI 40 kg/m^2 and 67% in adolescent patients with average BMI 36 kg/m^2 [Roslin et al 2015, Kumar 2015, Dargent 2016].

Surgical procedures

Single-anastomosis duodeno-ileal bypass (SADI) with or without SG (SADI-S), sometimes called stomach intestinal pylorus sparing surgery (SIPS), has shown promising results in weight reduction and metabolic effects. This is a simplified one-loop DS without enteroanastomosis. In SADI-S a SG is performed and a small bowel loop is anastomosed to the duodenum 200 cm to 300 cm from the ileo-caecal angle leaving the pylorus intact (Fig. 6). EWL percentage at 12 months was 97%, at 18 months 118%, and remained over 100% during the third postoperative year [Sanchez-Pernaute et al. 2010]. In a study of obese diabetic patients undergoing SADI-S, 70% to 84% had obtained control of their T2DM at five-year follow-up with HbA1c values below 6% [Sanchez-Pernaute et al. 2010].

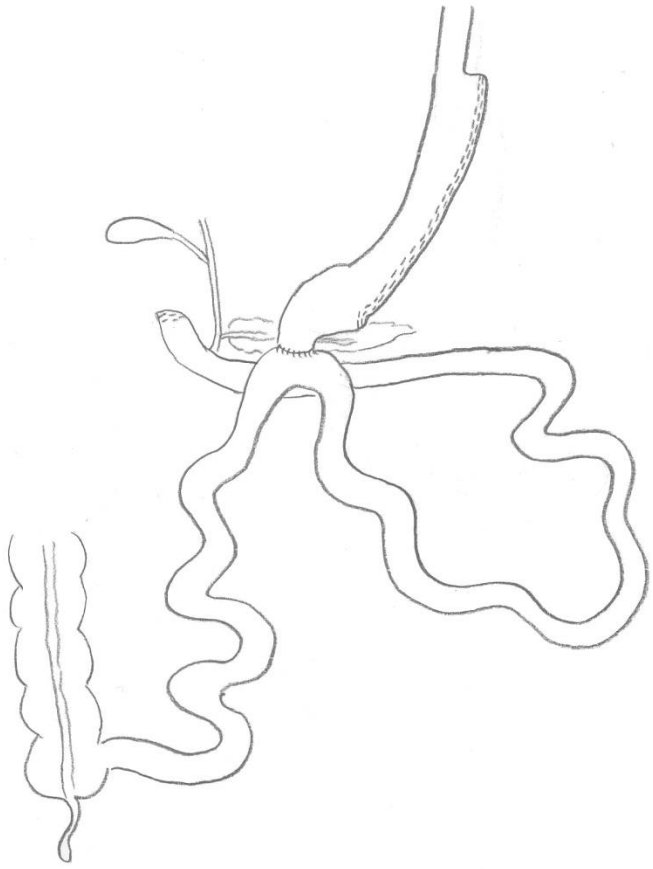


Figure 6. Single-anastomosis duodeno-ileal bypass with sleeve gastrectomy

2.5.5. ERAS –protocols

In 2002 Henrik Kehlet and Douglas Wilmore published an article "Multimodal strategies to improve surgical outcome". In this paper they evaluated the effect of modifying perioperative care in order to reduce the stress of an operation, accelerate the rehabilitation, and decrease the hospitalisation. This started the development of ERAS-protocols, which were first introduced in colorectal surgery but rapidly adopted to other fields of surgery, including bariatric surgery. ERAS-protocols consist of preoperative counselling, optimisation of nutrition, standardisation of perioperative care, multi-modal analgesia, and early mobilisation aiming at a reduction of the patient's stress response.

In a prospective study of 226 bariatric patients ERAS was used safely. The length of stay (LOS) after LRYGB was 1.9 days and 30-day re-admission rate was low (2.7%)

[Awad et al 2014]. In a retrospective study 1967 patients were evaluated after bariatric operation, 1313 of them treated with ERAS protocol. The use of an ERAS protocol resulted in shorter procedural times and decreased LOS from 3.2 to 2.0 nights. After introducing the ERAS protocol, an increase in minor complications was seen, which the authors considered was a result of better registration of complications [Mannaerts et al 2016].

2.6. Effect of bariatric surgery

2.6.1. Effect on weight loss

The superiority of bariatric surgery in terms of weight loss and maintenance of weight loss compared to conventional therapy has been well documented in many studies. The weight loss after bariatric surgery is usually reported as per cent of total weight loss (%TWL), per cent of excess BMI loss (%EBMIL) and/or per cent of excess weight loss (%EWL).

In Buchwald's meta-analysis from 2004 the %EWL following LRYGB was 61.6%, and 70.1% after BPD. At that time data from SG was not available. In a later systematic review of long-term outcomes, the %EWL following LRYGB was 54.0%, while BPD was associated with a similar 71.7% EWL. In this review all the data was beyond ten years [O'Brien et al 2013]. The long-term follow-up data of both LRYGB and SG was reported in a systematic review in 2014, which had the sample-size-weighted mean %EWL 65.7% after LRYGB at three to five years and 64.5% after SG at three years [Puzziferri et al 2014]. In the SOS study only a small portion of the patients were treated by LRYGB, but those who were had a maximal weight loss of 32% after one to two years and 27% after 15 years of follow-up [Sjöström et al 2007]. The same kind of slow increase in weight with time was seen in a 10-year outcome study after LRYGB, which showed a significant reduction in %EBMIL with time; from 74.7% at two years to 52.5% at ten years [Mehaffey et al 2015].

Several studies have compared LRYGB and SG. In a Finnish on-going prospective randomised controlled SLEEVEPASS study the outcome of both procedures has been very similar at six months; the %EWL was 53% after LRYGB and 49% after SG [Helmiö et al 2014]. An article reporting the data from one Finnish centre, comparing these two procedures, showed a better maintenance of weight loss after LRYGB at long-term. TWL percentage was 24.1% after one year and 23.0% after a

median of five years following LRYGB while the numbers were 23.7% and 20.2% after SG, respectively [Pekkarinen et al 2016]. In a retrospective matched cohort study comparing LRYGB and SG, the %EWL was 65.1% following LRYGB and 62.5% following SG at five years [Dogan et al 2015].

A study of 3003 patients operated in a high volume centre showed the %EWL after SG was as good as 72% at one year [Sakran et al 2016], while a German study of 746 SG patients reported 36% EWL at eight years [O'Brien 2016]. Himpens et al. (2010) documented similar results in their long-term SG study; 72.8% EWL at a three-year follow-up, which dropped to 57.3% after six years. They concluded that SG appears to be subjected to weight regain after three years. A review of weight loss results eight years or more after SG showed 54.8% EWL [Diamantis et al 2014].

Current outcomes of BPD from 2011 to 2015 showed excellent %EWL of 81% at one year and 83% at three years [Biertho et al 2016].

2.6.2. Effect on morbidity

In a large meta-analysis bariatric surgery had a laudable effect on all obesity related diseases [Buchwald et al 2004]. In one single-centre study with a ten-year follow up of LRYGB patients, co-morbidity prevalence was significantly lower in the end of the follow-up than at baseline in all eight co-morbidities recorded; gastro-oesophageal reflux, cardiovascular disease, degenerative joint disease, T2DM, OSA, hypertension, pulmonary co-morbidity, and psychiatric co-morbidity [Mehaffey et al 2016].

T2DM

After LRYGB T2DM was resolved in 83.7% and after BPD in 98.9% of patients in a large meta-analysis [Buchwald et al 2004]. In a systematic review of long-term follow-up after LRYGB, sample-size-weighted remission rate for T2DM was 66.7% [Puzziferri et al 2014]. In four RCTs bariatric surgery (AGB, LRYGB, BPD and SG) was compared to conventional treatments of T2DM. Surgery was superior to lifestyle intervention and the best available medical treatment in achieving glycaemic control in all studies. In all but one studies also diabetic patients with BMI from 27 kg/m^2 to 35 kg/m^2 were included. These studies support the growing consensus of using bariatric surgery as a treatment method for non-obese diabetic patients. Dixon et al. (2008) and Mingrone et al. (2012) reported remission of T2DM at two years in 73% to 95% of the patients, respectively. In the other two RCTs glycaemic control (HbA1c < 6%) was achieved in 42% to 44% of the patients after LRYGB and 37% after SG at one year [Ikramuddin et al 2013, Schauer et al 2015]. In a prospective

study concentrating on the resolution of T2DM after LRYGB and BPD-DS at one and two years of follow-up, oral diabetic medication was still in use in 22% and 13% of LRYGB patients and in 11% and 13% of BPD-DS patients, respectively [Parikh et al 2007]. In the SLEEVEPASS study 93% of T2DM had resolved or improved after LRYGB and 84% after SG at six months [Helmiö et al 2014]. A long-term remission or improvement of T2DM was reported after LRYGB compared with obese controls in a retrospective study. Among patients in the surgery group 74.4% had complete or partial remission of their T2DM, even though 15.4% had diabetes recurrence after initial remission during 11 years' follow-up [Chen et al 2015]. In the SOS study similar remission rate of T2DM at two years was shown (72%), and at ten years it was still 36%. It is noteworthy that bariatric surgery reduced the risk of developing T2DM by 84% at ten years and 78% at 15 years compared to conventional care [Sjöström 2013].

OSA

In a large meta-analysis of bariatric surgery, OSA was resolved after surgery in 85.7% of patients [Buchwald et al 2004]. In another meta-analysis, surgical weight loss from pooled BMI 55.6 kg/m^2 to 37.7 kg/m^2 reduced the pooled apnoea-hypopnea index (AHI) from 54.0 events/hour to 15.8 events/hour, which equals to moderate OSA [Greenburg et al 2009]. One SG study reported the resolution of OSA as high as 98% [Sakran et al 2016]. Also contrary findings have been reported. A study of 58 moderate to severe OSA patients undergoing gastric bypass did not report a single total resolution of OSA after bariatric surgery [Rasheid et al 2003]. In another study of 24 patients with OSA at baseline and significant weight loss after gastric banding, only one (4%) patient experienced a resolution of OSA, and 71% still had moderate to severe OSA one year after the bariatric operation [Lettieri et al 2008].

Hypertension

Buchwald's meta-analysis reported resolved or improved hypertension in 78.5% of patients after bariatric surgery [Buchwald et al 2004]. At six months after LRYGB hypertension was resolved or improved in 82% and after SG in 77% [Helmiö et al 2014]. Mingrone et al. (2012) reported reduced or discontinued antihypertensive therapy in 80% of patients after LRYGB, and in 85% after BPD. In a recent SG study resolution of hypertension at one year was observed in 44% of patients and improvement in 41.5% [Sakran et al 2016]. In another SG study the resolution rate of hypertension at two years was 31% [Abelson et al 2015]. In a long-term follow-up hypertension was in remission in 46% of the patients at ten years after LRYGB [Obeid et al 2016].

Hyperlipidaemia

Both hypercholesterolemia and hypertriglyceridemia are significantly improved after bariatric surgery. According to Buchwald's meta-analysis, hyperlipidaemia improved in 70% or more of the patients, and the best improvement was shown after LRYGB (96.9%) and BPD (99.1%) [Buchwald et al 2004]. In a RCT of diabetic patients randomised in bariatric surgery or medical therapy, at two years after LRYGB and BPD total cholesterol levels had normalized in 100% of those operated compared to 27.3% in the medical-therapy group. High-density lipoprotein (HDL) levels had normalised in 100% of patients after LRYGB and 72.7% after BPD compared to 11.1% in medical-therapy group [Mingrone et al 2012]. In the SOS study, a significant decrease in serum triglycerides and a significant increase in HDL were shown in bariatric surgery group compared to usual care, but no significant difference was found in total cholesterol between groups [Romeo et al 2012].

Cardiovascular disease

The SOS study was the first prospective study to show that bariatric surgery is associated with a reduced number of cardiovascular deaths and first-time events (myocardial infarction or stroke) [Sjöström et al 2012]. This trial also demonstrated a significant 44% reduction in the incidence of myocardial infarction at 13 years in patients with T2DM at baseline [Romeo et al 2012]. In a study with a long-term follow-up of LRYGB patients and controls with T2DM, the surgery group had significant reduction in micro- and macrovascular complications compared with controls during an 11-year follow-up [Chen et al 2015].

Asthma

Obese patients with asthma suffer from more severe symptoms and poor symptom control with high risk of exacerbations. They are less responsive to asthma therapy compared with non-obese asthma patients. Weight reduction has a positive impact on symptoms, lung function, and medication requirements. Weight loss also reduces hyper responsiveness and inflammation in airways reducing the need for emergency department visits and hospital admissions for asthma [Ulrik 2016]. In a trial of bariatric surgery patients with asthma compared with non-asthma bariatric candidates, a significant improvement was seen in small airway function and systemic inflammation in both groups after surgery. In the asthma group airway hyper responsiveness as well as asthma control improved, but the weight loss did not influence the obstruction of larger airways in asthma patients [van Huisstede et al 2015].

Non-alcoholic fatty liver disease

Non-alcoholic fatty liver disease is the most common liver disorder in the Western countries and non-alcoholic steatohepatitis (NASH) is its inflammatory form. In the Finnish population aged 47 to 75 years the prevalence of NASH is approximately 5% [Hyysalo et al 2014]. Bariatric surgery was reported to induce the disappearance of NASH in nearly 85% of patients after one year. In addition to significant reductions in BMI and insulin resistance, mean levels of alanine aminotransferase and γ-glutamyltransferase were significantly reduced after surgery [Lassailly et al 2015].

Polycystic ovarian syndrome (PCOS) and infertility

PCOS is the most common endocrine disorder in women and strongly associated with obesity and metabolic syndrome. Very few studies have specifically investigated bariatric surgery targeted for PCOS patients, and no RCTs were found. In a recent systematic review and meta-analysis of the impact of bariatric surgery on PCOS, the preoperative incidence of PCOS was 45.6%, which significantly decreased to 6.8% at one year after surgery. Over half of the patients had irregular menstruation, which was significantly improved at one year. The preoperative infertility was 18.2%, which also was significantly improved to 4.3% [Skubleny et al 2016]. The effect of bariatric surgery on obesity-related infertility was investigated in a systematic review and meta-analysis pooling together the data from 589 infertile obese women. An impressive 58% of infertile women became spontaneously pregnant after bariatric surgery [Milone et al 2016].

Urinary incontinence

Urinary incontinence is very common in the obese female population with a prevalence of 45% to 70%. In a large study of urinary incontinence before and after bariatric surgery, urinary incontinence was prevalent in 49.3% of women and 21.8% of men before surgery. At one year the prevalence was significantly lower in both sexes (18.3% in women and 9.8% in men). At three years the prevalence was higher than at one year but still significantly lower than before surgery in both sexes. Weight loss, younger age, and absence of severe walking limitations were independently related to urinary incontinence remission [Subak et al 2015].

2.6.3. Effect on mortality

The SOS study has shown that bariatric surgery reduces the number of cardiovascular deaths and lowers the incidence of cardiovascular events in an obese

population [Sjöström et al 2012]. During a 16-year follow-up 6.3% in the control group and 5.0% in the surgery group died. The unadjusted overall hazard ratio in the surgery group was 0.76 compared to controls, and the hazard ratio adjusted for sex, age, and risk factors was 0.71 [Sjöström et al 2007]. In a study comparing the general population in New York State to the bariatric population, the mean bariatric mortality rate was 2.5% with 8 to 14 years of follow-up, while the actuarial mortality predictions for the general population was 3.1% (p=0.01). Long-term mortality rates of bariatric patients were significantly improved regardless of the bariatric operation type performed. Perioperative complications did not increase long-term mortality risk [Telem et al 2015]. Also a large meta-analysis of 44 022 patients from eight trials reported a reduced risk of overall mortality [odds ratio (OR)=0.55], cardiovascular mortality (OR=0.58), and of all-cause mortality (OR=0.70) associated with bariatric surgery [Pontiroli et Morabito 2011]. In a study calculating life expectancy, 6.7 years were gained with bariatric surgery – as an example – for a 45-year old diabetic woman with a BMI of 45 kg/m^2. The results were similar for both sexes and in all age groups [Schauer et al 2015].

2.6.4. Effect on quality of life (QoL)

Obesity is associated with impairments in physical, psychological, and social well-being. Impact of excess weight on physical health is mostly due to co-morbidities but also to decreased physical activity. Psychological effects may be low self-esteem and self-motivation, depression, and eating disorders. Obesity also affects social relations by weight-related stigmatisation and shame. In a systematic review, bariatric surgery was reported to result in greater improvement in QoL than other obesity treatments, mostly due to a greater and more sustained weight reduction. QoL was more likely to improve during the first two years after surgery with greater improvements in physical than mental QoL [Hachem et Brennan 2015]. In a meta-analysis of long-term QoL after bariatric surgery, a significant improvement in physical and mental health was found in the surgical group compared to controls with a follow-up from 5 to 25 years after surgery [Driscoll et al 2016]. A prospective matched control study of T2DM patients undergoing LRYGB demonstrated a significant improvement in health-related QoL in the surgery group, but not in the control group receiving standard medical therapy combined with a diabetes support and education programme [Omotosho et al 2016].

2.7. Complications of bariatric surgery

There is a risk of mortality involved in any kind of surgery. When comparing LRYGB with open RYGB, mortality is significantly lower after LRYGB (0.11% vs. 0.25%) [Weller et Rosati 2008]. The data from the Agency for Healthcare Quality and Research of United States revealed that from 1998 to 2004 the national inpatient mortality associated with bariatric surgery decreased nearly 80%, from 0.89% to 0.19%. At the same time the number of bariatric operations increased nine-fold [Zhao et Encinosa 2006]. In a recent study with more than 2500 LRYGB patients, 30-day total mortality was 0.04% as it was in a large Scandinavian study from 2014, whereas in a large meta-analysis from 2004 the 30-day mortality for LRYGB was 0.16% [Stenberg et al 2016, Stenberg et al 2014, Buchwald et al 2004]. In three large studies of SG, the 30-day mortality varied from 0.03% to 0.24% [Stroch et al 2016, Young et al 2015, Sakran et al 2016]. After more malabsorptive operations the mortality has always been higher. In Buchwald's large meta-analysis in 2007, the 30-day mortality after BPD and BPD-DS was 1.1%. However, current data from patients operated between 2011 and 2015 with modern technology and perioperative care showed no 90-day mortality, and major and minor 30-day complication rates were 3.0% and 2.5%, respectively. These rates were similar to those seen after other mixed bariatric procedures [Biertho et al 2016].

In a large prospective multicentre study of nearly 5000 bariatric patients, a total of 4.3% had at least one serious complication, including 0.3% death rate, within 30 days after LRYGB and AGB [Flum et al 2009]. Concerning early postoperative complications LRYGB and SG have been comparable. In one study SG showed lower overall 30-day morbidity compared to LRYGB [Young et al 2015], and in another study fewer major early complications were associated with SG compared to LRYGB [Osland et al 2016]. Dogan et al (2015) found that SG and LRYGB were comparable in 30-day complication rates (7.6% after SG and 5.7% after LRYGB). However, 9% of SG patients needed revisional surgery later and were converted to LRYGB mostly due to a poor weight loss. The most common post-operative complications after SG were leakage (1.6%), bleeding/hematoma (2.9%), and intra-abdominal abscess (1.6%), and after LRYGB bleeding/hematoma (2.0%), and wound infection (0.8%) [Dogan et al 2015]. Readmission rates were higher after SG in two studies [Helmiö et al 2014, Dogan et al 2015] and lower in one study [Young et al 2015].

Long-term complication rates have been higher after LRYGB than after SG in many studies (9.0% to 9.9% vs. 2.9% to 5%) [Dogan et al 2015, Sakran et al 2016]. The most common complications after LRYGB were symptomatic gallstones (4.9%), unexplained abdominal pain (3.3%), internal hernia (1.6%), and pancreatitis (0.8%), while after SG they were symptomatic gallstones (3.7%), passage complaint (0.8%), and incisional hernias (0.8%) [Dogan et al 2015, Sakran et al 2016].

The incidence of small bowel obstruction after LRYGB, which mostly occurs due to an internal hernia, ranges from 0.6% to 11% in different studies. The incidence of internal hernias after LRYGB is strongly dependent on the surgical technique. The lowest internal hernia incidence (1%) was reported using the antecoelic technique with closure of all defects [Geubbels et al 2015]. In a recent Swedish randomised trial comparing closure of mesenteric defects to non-closure, a significant reduction of reoperations caused by internal hernias was seen in the closure group at three years after surgery. However, an increase in severe postoperative complications, mainly due to kinking of the jejuno-jejunostomy was seen in the closure group [Stenberg et al 2016]. One limitation in this study is the fact that the technique for closure of the mesenteric defects was not standardised. Intermittent internal hernia should be kept in mind in case of chronic abdominal pain, and especially in LRYGB operated pregnant women, as pregnancy increases the risk of internal hernia by increasing the abdominal cavity pressure [Maggard et al 2008].

2.8. Epidemiology of obstructive sleep apnoea

OSA is defined as a reduction (hypopnea) or cessation (apnoea) of breathing during sleep, which is caused by a collapse of the upper airway and leads to sleep fragmentation and intermittent hypoxia during sleep. Owing to this fragmented sleep, OSA patients may suffer from daytime sleepiness, slow reaction time, poor memory and concentration, irritability, and reduction in QoL.

Hypopnea is defined as a reduction (more than 30%) of airflow for more than 10 seconds with an oxygen desaturation of 4% or more. Apnoea is defined as a cessation (more than 90%) of airflow for more than 10 seconds. Apnoea-hypopnea index (AHI) is defined as the number of apnoea and hypopnea events per hour (AHI less than 5 events/h is considered normal, AHI 5 - 15 events/h as mild OSA, AHI 15 - 30 events/h as moderate OSA, and AHI more than 30 events/h as severe OSA). The diagnosis of OSA is always based on overnight cardiorespiratory recording demonstrating at least five apnoea or hypopnea events per hour [Qaseem et al 2014].

Obesity is the most important single risk factor for OSA. The prevalence of OSA is 17% to 24% in men and 5% to 9% in women [Ashrafian et al 2012]. In the obese population the incidence of OSA is 12 to 30 times higher than in the general population. In bariatric surgery patients the prevalence ranges from 60% to 83% [Ashrafian et al 2012].

OSA affects mostly middle-aged workforce, causing a major burden to public health. Besides causing daytime somnolence and low quality of life, OSA has also been found to be tightly linked to metabolic abnormalities, particularly T2DM [Tuomilehto et al 2008, Tasali et al 2008], but also pre-diabetes was reported to be associated with OSA in extremely obese subjects. In this study the prevalence of OSA was 33% in patients with normal glucose tolerance, but in pre-diabetic patients the prevalence increased to 67%, and in diabetic patients the prevalence was 78% [Fredheim et al 2011].

Based on the current scientific evidence OSA is a major factor for an increased risk for cardiovascular disease. Patients with OSA have higher cardiovascular mortality, and the risk of cardiovascular disease is increased even in mild OSA. Hypertension is often found in OSA patients, and OSA associated hypertension may be particularly drug-resistant [Attal et Chanson 2010].

2.9. Treatment of OSA

Patient compliance with OSA treatment is challenging while many patients even with severe OSA are asymptomatic. The relation between OSA and obesity is well known, and the beneficial effect of weight reduction on mild OSA was shown in a randomised trial of VLCD and lifestyle intervention. In mild OSA obesity treatment should be the first-line treatment [Tuomilehto et al 2008].

The current golden standard of OSA treatment is continuous positive airway pressure (CPAP) during sleep via nasal or oronasal mask. CPAP prevents collapsing of upper airways. It relieves symptoms but does not cure OSA. Compliance with CPAP therapy varies between 50% and 70% [Barbè et al 2012, Sawyer et al 2011]. In a meta-analysis of randomised trials comparing CPAP and mandibular advancement devices CPAP was the most effective treatment in reducing AHI in moderate to severe OSA [Sharples et al 2015]. However, CPAP treatment does not improve metabolic variables, such as insulin sensitivity, glucose metabolism, lipids, fat

distribution, and adipokines, according to the currently available data [Schlatzer et al 2014].

Mandibular advancement devices are intraorally worn devices that prevent upper airway collapse by holding the mandibula and tongue forward. For patients intolerant of CPAP treatment, mandibular advancement device was effective in reducing AHI and was better than no treatment. In reducing subjective daytime sleepiness, mandibular advancement device was nearly as effective as CPAP [Sharples et al 2015]. The range of surgical treatment options of OSA is wide, from nasal to oro- and hypopharyngeal surgery, and from maxillofacial to bariatric surgery. Upper airway surgery is rarely effective, a careful patient selection is critical to ensure the best result, and surgery should be individually tailored according to each patient's needs [Kotecha et Hall 2014].

Since obesity is the most important risk factor for OSA; at least 70% of OSA patients are obese, the patients may also have other obesity related co-morbidities besides OSA. In fact, metabolic syndrome, hyperglycaemia, and OSA are often present in the same individual, and it has been proposed that the co-existence of these conditions could have an even more widespread impact on the cardiovascular and metabolic sequelae than any of the conditions on their own [McArdle et al 2007]. For all these conditions weight reduction – which may result in reduction of visceral fat in particular – should be the first-line treatment when they are linked to excess body weight.

By knowing the key role of obesity as an independent risk factor for OSA, and by knowing the challenges of long-term results of conservative treatment of obesity, bariatric surgery could be an option for a selected OSA patient population. The mechanisms of OSA resolution after bariatric surgery are the decrease of adiposity, which may relieve the physical pressure on the neck and upper airways, and beneficial anatomical changes in airway size and collapsibility. There are also systemic effects due to a reduction in systemic inflammation and insulin resistance. Also the alteration of bile and nutrients flow after certain surgery types and modulation of gut hormones may affect the resolution of OSA [Ashrafian et al 2012].

3 Aims of the study

1) To identify the most common findings in upper gastrointestinal endoscopy (UGI) performed routinely prior to a bariatric operation to see if the findings influenced the decision to operate or even cancelled the operation. (**I**)
2) To test the safety of the enhanced recovery after surgery (ERAS) programme for consecutive primary LRYGB patients operated in a general hospital, and to compare the results to those reported from high-volume, dedicated bariatric centres. (**II**)
3) To investigate the prevalence of OSA in all bariatric surgery candidates prior to the operation. (**III**)
4) To investigate the impact of LRYGB on the prevalence and symptoms of OSA 12 months after surgery. (**IV**)

4 Methods and patient material

4.1. Methods

4.1.1. Upper gastrointestinal endoscopy (UGI) (I)

Standard UGI with flexible endoscope was performed in all the bariatric surgery candidates. In rare cases general anaesthesia was needed, and UGI was performed in an operating room prior to the LRYGB. Local anaesthesia such as lidocaine spray was provided if the patient wanted it. UGI was performed by experienced surgeons in 86.8% of the cases. Routine biopsies were taken from duodenum, antrum, and corpus and additional biopsies were taken if abnormalities were seen. Clinical findings were compared to histological findings. Helicobacter pylori (HP) was determined from biopsies, and if detected eradication therapy was given. Eradication of HP was confirmed with a blood antibody test, a stool antigen test, or a carbon urea breath test. UGI was not repeated to confirm the eradication.

4.1.2. Enhanced recovery after surgery (ERAS) programme (II)

Patients were treated by an ERAS pathway as introduced by Kehlet and Wilmore [Kehlet et al 2002]. Basically a similar protocol was utilised as for colorectal surgery patients. The protocol includes modifications of pre-, intra-, and postoperative routines.

Preoperatively, patients visited the outpatient clinic 1–2 weeks before the scheduled operation and received extensive information and counselling by a nurse, an anaesthesiologist, and the operating surgeon. Other specialties were consulted if found necessary for optimising the patient's condition for the forthcoming operation. Oral carbohydrate intake was allowed until two hours before surgery (ProvideXtra® or lower carbohydrate preparation PreOp® in case of T2DM). Patients arrived at the hospital 1–2 hours before the scheduled start of the operation and were guided walking to the operating room. No sedative pre-anaesthetic medications were given. In the operating room patients were equipped with pneumatic anti-thrombotic stockings and received 1.5 g of cefuroxime as antibiotic prophylaxis during induction of the anaesthesia. The use of urine catheters was avoided in all cases. Anti-thrombotic agents were not used routinely. Patients were encouraged to follow a VLCD for 2–6 weeks preoperatively (depending on baseline BMI), aiming at approximately 8 % weight loss before surgery. However, insufficient preoperative weight loss was not regarded as an absolute exclusion

criterion. Subsequent weight loss calculations were based on the initial weight measured at the start of the VLCD.

Intraoperatively short-acting and standardised intravenous anaesthesia was used (propofol–remifentanil–desflurane and rocuronium for muscle relaxation) instead of traditional inhalation anesthesia (oxygen-sevoflurane and cis-atracurium for muscle relaxation), and special care to avoid hypothermia was taken. Non-steroidal anti-inflammatory drugs (NSAIDs) and paracetamol were given at the end of surgery. To prevent postoperative nausea and vomiting, dexamethasone was administered intravenously at the beginning of the surgery and ondansetron at the end. The operations were completed by laparoscopy in all cases, and a restrictive perioperative fluid regimen (≤30 ml/kg/24 h) was followed. Nasogastric tubes and drains were avoided postoperatively, and perioperative inspired oxygen fractions were kept at 50–60%. All port site wounds were infiltrated with bupivacaine preperitoneally at the beginning and subcutaneously at the end of the operation.

Postoperatively early mobilisation was emphasized. All patients were extubated immediately after surgery and were asked to move by themselves from the operating room table to their bed. They were admitted to the surgical ward after a follow-up in the awakening room for 2–4 hours. A liquid diet was initiated immediately when the patient was fully awake, usually 1–2 hours after surgery if no signs of complications could be detected. Patients were also encouraged to stand up and walk 10–20 minutes at this time. At the ward patients were allowed and encouraged to move around freely. Postoperative pain was treated mainly by administration of paracetamol and/or NSAIDs. Epidural analgesia was not used, and the use of opioids was avoided and used only for breakthrough pain. Antiemetic medication was used on demand. Liquid food and protein drinks were allowed without limitations from the first postoperative day, and the patients were instructed in detail, by the dietician before discharge, on how to keep to a liquid diet for the first two postoperative weeks. Clinical non-invasive parameters, such as pulse, blood pressure, oxygen saturation, respiratory frequency, and body temperature, were regularly recorded during the immediate postoperative period (24 hours). Patients were discharged if these parameters were in the normal range and patients were fully mobilised, able to eat liquid food, had adequate pain control on oral analgesics, and adequate home support. Postoperative laboratory blood tests were taken only on clinical demand, not routinely. The patients were followed up at regular intervals postoperatively, with the first outpatient visit at three months after surgery.

4.1.3. Laparoscopic Roux-en-Y gastric bypass (LRYGB) (II, III, and IV)

LRYGB was performed via five trocars; three 10-mm and two 5-mm trocars introduced on the upper part of abdomen. A liver retractor was put in place to obtain a good visibility in the operation area. A small gastric pouch was then divided from upper part of stomach with linear staplers. If the omentum was heavy and fatty, it was split with ultrasound scissors. A biliary limb of 50 cm to 75 cm, measured from the ligamentum of Treitz, was lifted up beside the pouch and a gastro-jejunostomy was created with linear stapler and suturing. An alimentary limb of 150 cm was measured onward from the gastro-jejunostomy and a jejuno-jejunostomy was stapled and sutured. Both anastomoses were tested with methylene blue for leakage. The pathway between anastomoses was transected. Both mesenteric defects were closed by a running, non-absorbable suture.

4.1.4. Cardiorespiratory recording Embletta (III and IV)

Standard overnight ambulatory cardiorespiratory recording by Embletta® (Embla, Broomfield, CO, U.S.A.) was conducted for all the participants in accordance with accepted guidelines for diagnosing OSA prior to the LRYGB operation [Qaseem et al 2014].

Embletta® is a type-3 multi-channel American Academy of Sleep Medicine compliant portable recorder. For the study purposes the following channels were used: airflow (thermistor and pressure), respiratory effort (abdomen and thorax), body position, pulse, and oxygen saturation.

4.1.5. Symptom questionnaire for OSA patients (III and IV)

The patients filled a symptom questionnaire for OSA patients prior to the operation and 3, 6, and 12 months after the operation. Study nurses helped the patients with the questionnaire if needed. Questionnaires used in studies III and IV are seen in the Appendices.

The questionnaire consists of a modification of three different validated questionnaires: SOS (Snore Outcome Survey), BNSQ (Basic Nordic Sleep Questionnaire), and ESS (Epworth Sleepiness Scale). SOS is designed to evaluate sleep-related QoL, and the questions consider the intensity, duration, frequency, and impact of snoring. BNSQ is a quantitative scale to assess sleep quality designed by the Scandinavian Sleep Research Society. It consists of 21 standardised questions, but only 11 of them were included in our symptom

questionnaire. ESS consists of 8 questions and it measures the level of daytime sleepiness.

4.1.6. Statistics

In studies I and II the databases were built in Microsoft Excel, and statistical analyses were performed with Excel.

In studies III and IV statistical analyses were carried out using IBM SPSS Statistics 22. Statistical significance of differences between means in different sleep apnoea groups was tested with t-test and Pearson's Chi-Square test. Kruskal Wallis test, including pairwise comparison test, was used to evaluate differences between individual groups. The paired samples t-test was used to analyse the statistical significance of changes within the groups, except in those variables where deviation in distribution of values was detected and Wilcoxon test was used instead. P-value less than 0.05 was considered statistically significant.

4.2 Patient material

4.2.1. Study I

The data of 412 patients undergoing preoperative UGI in Vaasa Central Hospital between the years 2006 and 2010 was evaluated retrospectively. Complete data was found in 342 patients, and they were included in this study. Seventy patients were excluded because of missing UGI documents, even though we knew that the patients went through the investigation in some other hospital or in the private sector. If the patient had a previous UGI for other reasons in the last 2 years, the investigation was not repeated if the data were available.

4.2.2. Study II

Between March 2011 and March 2015, altogether 514 patients were treated for their morbid obesity by bariatric surgery at our hospital. Patients were accepted for surgery by a multi-disciplinary team consisting of an endocrinologist, a dietician, a nurse specially trained for handling bariatric patients, an anaesthesiologist, and a surgeon. Psychiatric counselling was used if considered necessary. The NIH consensus guidelines (BMI more than 40 kg/m^2, or more than 35 kg/m^2 with obesity related co-morbidity, and failed conservative weight loss attempts) were followed, with the exception of four patients with severe metabolic syndrome

accepted for surgery with BMI less than 35 kg/m^2 (31–34 kg/m^2). Of the total 514 patients, 388 were operated by primary LRYGB and included in this analysis, as they were all eligible for at least three months of follow-up. One hundred and twenty-six patients were excluded because of revisional surgery in 84 patients (mainly failed gastric banding procedures), sleeve gastrectomies in 24 patients, and short follow-up in 18 patients (not yet eligible for their three-month follow-up). Data were entered prospectively in the hospital's database for bariatric patients, including demographic details, baseline co-morbidities, operative time, length of stay (LOS), morbidity before and after 30 days, mortality, readmissions, reoperations, weight loss parameters, and improvements/resolutions of co-morbidities. The diagnosis of T2DM was based on the presence of anti-diabetic medication or HbA1c more than 6.5%. The diagnosis of hypertension was based solely on the presence of medication for high blood pressure.

4.2.3. Study III and IV

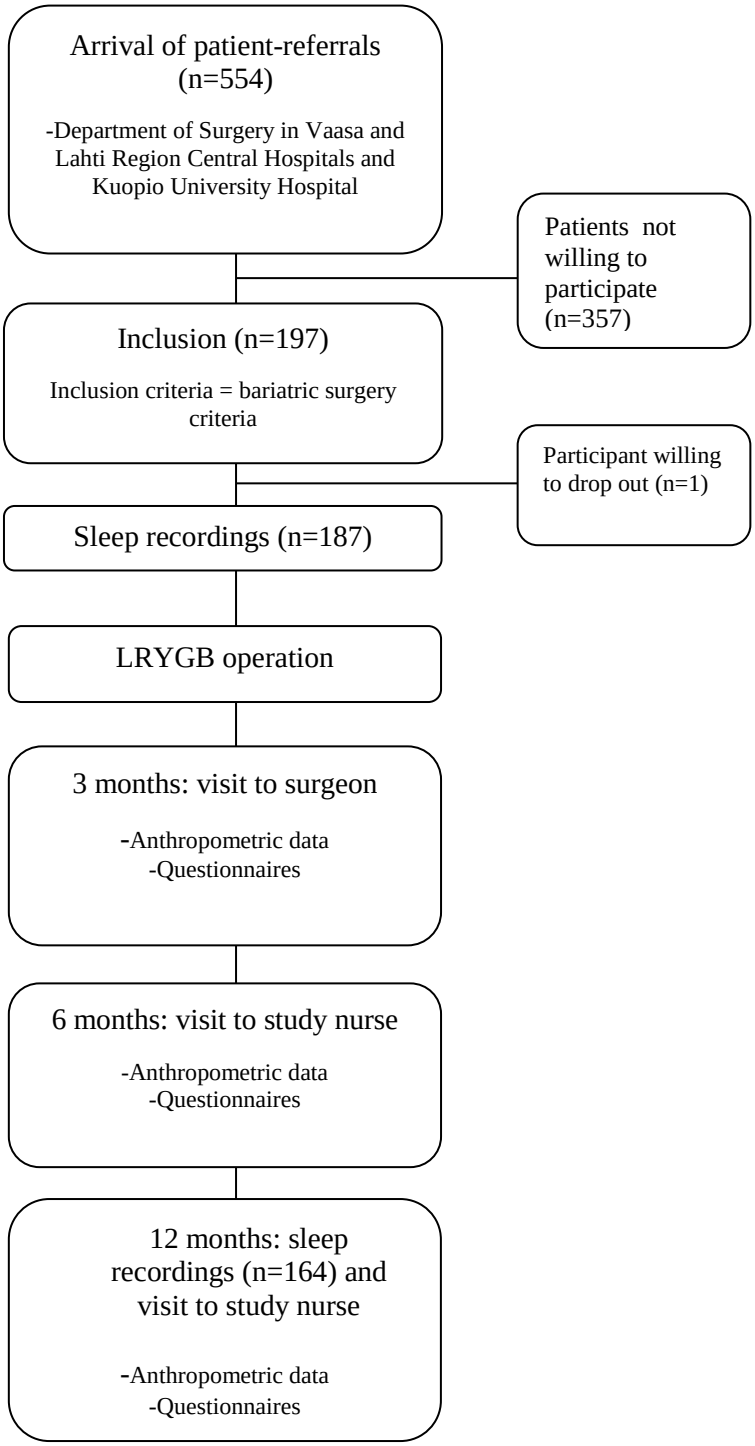
A total of 554 consecutive patients planned to undergo bariatric surgery in three different hospitals were recruited to this prospective multicentre study between November 2010 and September 2013. Of these, 197 patients (36%) signed informed consent and agreed to participate. A total of 103 patients were recruited in Vaasa Central Hospital, 48 patients in Lahti Region Central Hospital, and 46 patients in Kuopio University Hospital. Inclusion criteria for the study were the same as for bariatric surgery: age 18–65 years, BMI more than 35 kg/m^2 with co-morbidity or BMI more than 40 kg/m^2, and co-operative patient. Written consent from the patients was required for the study. The exclusion criteria were alcohol or drug abuse, severe eating disorder, depression, or other severe disease contra-indicating bariatric surgery.

All patients referred for bariatric surgery in participating hospitals were recruited to participate in this trial regardless of whether they had prior symptoms or a diagnosis of OSA. They had all undergone the hospital's normal preoperative routines for bariatric surgery and had failed conservative treatment for weight management. Before the operation patients followed a VLCD a minimum of four weeks.

Study nurses met the patients before the operation, recorded the anthropometric data, and helped patients to fill out a symptom questionnaire for OSA patients, consisting of three validated questionnaires: SOS, BNSQ, and ESS. The later visits to surgeon and study nurse are shown in the study flow chart (Figure 7).

In study III the baseline data of all 197 patients was analysed. A total of 132 patients with OSA in baseline analysis were included in study IV.

Figure 7. Study flow chart for studies III and IV



5 Results

5.1. Study I. Clinical and histological findings in a routine preoperative UGI

Out of the total of 342 patients 208 (60.8%) were women. Routine biopsies, which included a HP test, were taken in all but 16 patients. HP test via UGI was taken in 12 of these 16 patients. The final results of the biopsies were missing in 19 patients. UGI was considered normal in 191 (55.8%) patients. All the endoscopic findings and their prevalence are shown in Table 1.

Table 1. Endoscopic findings in UGI and their prevalence

Endoscopic findings	Prevalence (n,%)
Normal	191 (55.8%)
Hiatal hernia	87 (25.4%)
Gastritis	47 (13.7%)
mild	25 (53.2 % of all gastritis)
chronic	5 (10.6 % of all gastritis)
severity not mentioned	17 (36.2 % of all gastritis)
Oesophagitis	46 (13.4%)
mild or LA A	28 (60.9 % of all oesophagitis)
LA B or C	13 (28.3 % of all oesophagitis)
severity not mentioned	5 (10.9 % of all oesophagitis)
Gastric ulcer	7 (2.0%)
Gastric polyps	23 (6.7%)
Duodenitis	3 (0.9%)
Barrett	3 (0.9%)
Benign oesophageal tumour	1 (0.3%)

Histology was found normal in 185 (54.1%) patients. Clinical and histological findings of the patients did not always match. The reasons for this might be that some clinical findings, i.e. hiatal hernias, are not histological conditions at all, and i.e. esophagitis when mild is not necessarily biopsied. It is always possible that the biopsy has missed the lesion. The histological findings are shown in Table 2.

Table 2. Histological findings of routine UGI biopsies and their prevalence

Histological findings	Prevalence (n,%)
Normal	185 (54.1%)
H. Pylori positive	41 (12%)
Gastritis	98 (28.7%)
Esophagitis	10 (2.9%)
Gastric polyps	10 (2.9%)
Duodenitis	7 (2.0%)
coeliac disease	1 (0.3%)
Barrett	4 (1.2%)
Gastric atrofia	3 (0.9%)
Leiomyoma	1 (0.3%)

5.2. Study II Outcome of ERAS in LRYGB patients.

Of the total 388 patients scheduled for LRYGB in Vaasa Central Hospital, 253 (65%) were women and 135 were men. The mean age was 45.1 years, mean preoperative weight was 134.1 kg, and BMI 46.4 kg/m^2. VLCD was successfully performed prior to bariatric surgery, and mean preoperative weight loss was 13.7 kg (10%).

Mean length of hospital stay was 1.3 days, and 323 (83%) patients were discharged on the first postoperative day. Another 49 (13%) patients were discharged on the second day; 42 (86%) of them were considered surgically fit already on the first postoperative day, but stayed one extra day for social reasons (lack of home support). Postoperative morbidity was classified according to Dindo-Clavien [Dindo et al 2004] and divided into short-term (less than 3 days) and long-term (more than 30 days, less than 2 years) morbidity. Altogether 43 complications and their treatment in 38 patients are explained in Table 3.

Table 3. Classification of short-term and long-term complications and the choice of treatment

Dindo-Clavien classification	**<30 days**	**Treated by**	**>30 days <24 months**	**Total**
Minor morbidity:	n (%)		n (%)	n (%)
Grade I-II	21 (5.4)		1 (0.3)	22 (5.7)
Bleeding[a]	8	Transfusion		
Urinary retention	1	Catheterisation		
Marginal ulcer[b]	1	Endoscopy (PPI)	1	
Infection[a]	11	Iv antibiotics		
Dumping	1	Modified diet		
Nausea[b]	3	PPI, modified diet		
Major morbidity:				
Grade III a-b	10 (2.6)		3 (0.8)	13 (3.4)
Abscess	4	Drainage (radiol 2, surgical 2)		
Internal hernia		Laparoscopy	2	
Bleeding[c]	3	Laparoscopy		
Colon obstruction	1	Laparoscopy		
Anastomotic stricture	1	Dilatation	2[d,e]	
Retention	1	Gastrostomy		
Life threatening:				
Grade IV a-b	2 (0.5)		1 (0.3)	3 (0.8)
Bowel perforation[c]	1	Suturing		
Anastomotic rupture[d]		Laparoscopy	1	
GJ-leakage[e]	1	Laparoscopy		
Death: Grade V	0		0	0
Overall Morbidity	33 (8.5)		5 (1.3)	38 (9.8)

[a] Both bleeding and infection in three patients. All infections were intra-abdominal and treated with intravenous (iv) antibiotics only

[b] Nausea and a small marginal ulcer, both occurring in a smoker. Resolved with proton pump inhibitor (PPI) treatment

[c] Bowel perforation during re-laparoscopy for bleeding

[d] Anastomotic rupture (perforation) during dilatation of a stricture in the gastro-jejunal anastomosis

[e] Late complication of gastro-jejunal (GJ) leakage. Leakage treated by re-laparoscopy, drainage, and endoscopic tissue gluing

5.3. Study III Prevalence of OSA in bariatric surgery candidates.

Of the recruited 197 patients, 125 (64 %) were women and 72 (36 %) were men. One patient dropped out before the first cardiorespiratory recording, and the recording failed for nine patients. Baseline cardiorespiratory recording data was available in 187 patients. The mean age in non-OSA group was 44 years and 51 years in OSA group ($p<0.001$). Weight and BMI were 119.9 kg and 42.7 kg/m^2 in non-OSA, and 128.0 kg and 43.9 kg/m^2 in OSA groups. The waist and neck circumferences were 122.5 cm and 41.2 cm in non-OSA group, and 133.2 cm and 45.5 cm in OSA group. There seemed to be a significant difference between groups, but when the groups were divided by sex, a significant difference was found only in female neck circumference.

The prevalence of OSA in baseline data was 71% (n=132). In male patients the prevalence was 90% compared to 60% in females ($p<0.001$). According to the preoperative co-morbidity questionnaire, the prevalence of OSA was only 24 % (n=45), which means that 66% (n=87) of the baseline OSA patients were unaware of their OSA diagnosis. The data of cardiorespiratory recordings and symptoms related to OSA are shown in Table 4.

Table 4. Cardiorespiratory recording and OSA symptom data showing frequencies (%) or mean values with standard deviation (SD)

	Male	Female	Total
Patients with AHI <5, n (%)	7 (10.3)	48 (40.3)	55 (29.4)
Patients with AHI 5-15, n (%)	18 (26.5)	39 (32.8)	57 (30.5)
Patients with AHI 15-30, n (%)	17 (25.0)	17 (14.3)	34 (18.2)
Patients with AHI > 30, n (%)	26 (38.2)	15 (12.6)	41 (21.9)
AHI, total, mean (SD)	30.6 (25.8)	14.2 (20.2)	20.1 (23.7)
AHI, supine, mean (SD)	33.8 (29.0)	18.1 (24.3)	23.7 (27.1)
AHI, other than supine, mean (SD)	28.7 (30.6)	10.9 (18.7)	17.3 (25.1)
SpO_2 %, mean (SD)	91.3 (3.1)	93.4 (2.1)	92.6 (2.7)
SpO_2 time below 90%, minutes, mean (SD)	89.2 (97.2)	36.9 (65.6)	56.4 (82.6)
SpO_2 time below 80%, minutes, mean (SD)	15.2 (35.6)	4.7 (13.1)	9.8 (27.0)
Heart rate, beats/min, mean (SD)	65.6 (10.4)	67.8 (9.1)	67.0 (9.6)
ESS, points, mean (SD)	7.22 (3.9)*	7.68 (4.5)*	7.51 (4.3)*
SOS, points, mean (SD)	66.0 (15.2)	63 (15.7)	64.5 (15.6)

AHI= apnoea-hypopnea index (the number of apnoea-hypopnea events per hour)

OSA= obstructive sleep apnoea

SpO_2= arterial oxygen saturation (pulse oximetry)

SOS= Snore Outcomes Survey

ESS= Epworth Sleepiness Scale

* In Epworth Sleepiness Scale N=177, data missing from 20 patients

A higher age was associated with the severity of OSA. In non-OSA group mean age was 43.8 years, in mild OSA 49.8 years, in moderate OSA 51.9 years, and in severe OSA 52.1 years ($p<0.001$).

ESS and SOS values calculated from the OSA symptom questionnaires did not have a significant correlation to OSA, except SOS values in female patients.

5.4. Study IV Effect of LRYGB on OSA 12 months after surgery.

In study III, in the baseline cardiorespiratory recordings, 132 (71%) patients were found who fulfilled the diagnostic criteria for OSA. Those OSA patients were selected to the study IV and followed for 12 months after surgery. The mean initial BMI of the patients with OSA was 43.9 kg/m^2. The decrease in BMI after bariatric surgery was 10.1 kg/m^2. Mean per cent of total weight loss (%TWL) was 24.6% and mean excess BMI loss per cent (%EBMIL) was 59.6%.

The prevalence of OSA decreased from 71% at baseline to 44% at one year after surgery ($p<0.001$). A second cardiorespiratory recording, conducted one year after the operation, was available for 164 patients: 102 women and 62 men. Of these patients 40 women (39%) and 32 men (52%) had OSA. Again the difference of prevalence between genders was significant ($p<0.05$). However, six patients were diagnosed with de novo OSA (8%) in the second recording; five of them with mild OSA, one of them with severe OSA. There was also one patient with mild OSA at baseline who had moderate OSA at the one-year recording. When evaluating the change in AHI and BMI in these patients, the mean AHI had increased from 3 events/h to 15 events/h ($p=0.023$) and BMI had decreased from 45 kg/m^2 to 32 kg/m^2 ($p<0.001$).

Of those 132 patients, who were diagnosed with OSA at baseline, the second cardiorespiratory recording was available for 119 (90%) patients. Sixty-five (55%) of them still had OSA, but the number of patients with AHI more than 15 events/h had decreased from 40% at baseline to 20% at one-year follow-up. Total AHI decreased from 27.8 events/h to 9.9 events/h ($p<0.001$). Of those 54 patients (45%), who had their OSA in remission after one year, 29 (24%) had formerly a mild OSA, 18 (15%) moderate OSA, and 7 (6%) severe OSA. The data of the baseline, one-year cardiorespiratory recording data, and symptom questionnaire scores are shown in Table 5.

The resolution of co-morbidities was also evaluated at one year after LRYGB. (Table 6)

Table 5. Sleep registration data of patients with diagnosed OSA at baseline and at one year after LRYGB, and p-values of differences between groups.

	Baseline (n=132)	1 year (n=119)	p-value
Patients with AHI 5-15, n (%)	57 (30.5)	41 (34.5)	0.26
Patients with AHI 15-30, n (%)	34 (18.2)	16 (13.4)	0.012
Patients with AHI > 30, n (%)	41 (21.9)	8 (6.7)	<0.001
AHI, total, mean (SD)	27.6 (24.6)	9.9 (11.2)	<0.001
AHI, supine, mean (SD)	32.1(27.8)	15.8 (17.7)	<0.001
AHI, other than supine, mean (SD)	24.4 (27.4)	6.3 (12.0)	<0.001
SpO_2 %, mean (SD)	92.0 (2.8)	93.3 (8.4)	0.11
SpO_2 below 90%, min, mean (SD)	71.4 (88.2)	19.4 (37.1)	<0.001
Heart rate, beats/min, mean (SD)	66.4 (9.6)	59.4 (8.1)	<0.001
ESS, points, mean (SD)	7.7 (4.5)*	4.6 (3.2)	<0.001
SOS, points, mean (SD)	63.5 (15.2)**	65.2 (6.2)	0.26

AHI= apnoea-hypopnea index (the number of apnoea-hypopnea events per hour)

SpO_2= arterial oxygen saturation, pulse oximetry

SOS= Snore Outcomes Survey

ESS= Epworth Sleepiness Scale

* In Epworth Sleepiness Scale n=119, both at baseline and at one year

** In Snore Outcomes Survey n=132 at baseline and n=126 at one year

Table 6. The co-morbidities of patients at baseline and at one year.

	At baseline	At one year
Healthy obese subjects, n (%)	13 (7)	23 (14)
One co-morbidity, n (%)	33 (18)	50 (30)
2 - 3 co-morbidities, n (%)	80 (43)	71 (42)
More than 3 co-morbidities, n (%)	59 (32)	23 (14)
OSA, n (%)	133 (71)	72 (44)
Hypertension, n (%)	114 (62)	84 (50)
T2DM, n (%) / with insulin n (%)	70 (38) / 21 (11)	33(20) / 8 (5)
Asthma, n (%)	42 (23)	25 (15)
Hyperlipidemia, n (%)	35 (19)	13 (8)
Depression, n (%)	31 (17)	21 (12)
Hypothyreosis, n (%)	38 (21)	36 (21)
Other, n (%)	122 (66)	86 (51)

6 Discussion

Bariatric surgery has proven to be the most effective long-term treatment for severe and morbid obesity. Even though bariatric surgery has been performed from the early 1960s, it became more popular after laparoscopic techniques were introduced in the 1990s. In Finland the first laparoscopic bariatric procedures were mostly AGBs, which have now mostly been abandoned. From 2006 LRYGB has been the dominant operation. From the 99 operations performed in 2006, the number of operations increased evenly till 1000 operations at 2011 [www.limery.fi]. Even though the estimated need of bariatric operations was at least 3000 per year [THL Report 16/2009], the number of bariatric operations stayed at 1000 operations per year and has even decreased during past two years. In 2015 a total of 882 bariatric operations were performed, 76 % of them being LRYGBs.

6.1. Clinical value of a routine UGI prior to a bariatric operation

The role of routine preoperative UGI is controversial. Randomised prospective studies have been requested for years, but none was found. In five prospective and seven retrospective studies the number of abnormal findings varied from 4.9% to 91%, but the percentage did not seem to correlate with the recommendations whether UGI should be performed routinely prior to bariatric surgery or not [Schirmer et al 2002, Sharaf et al 2004, Azagury et al 2006, Zeni et al 2006, Mong et al 2008, Loewen et al 2008, Munoz et al 2009]. In 2015 The Standards of Practice Committee of the American Society of Gastrointestinal and Endoscopic Surgeons (ASGE) prepared guidelines, where they recommended UGI prior to bariatric surgery at least in patients with symptoms of GERD and in patients with chronic use of anti-secretory medications. They pointed out that an alteration of surgical approach or delay in surgery occurred in less than 1% to 9% of patients owing to the endoscopic findings in mostly asymptomatic patients [ASGE Guideline 2015]. Another study reported clinically important findings altering surgical treatment or timing in 61.5% of cases [Sharaf et al 2004], while in most of the studies the operative plan was altered in less than 10% of cases [Schirmer et al 2002, Azagury et al 2006, Zeni et al 2006, Mong et al 2008, Loewen et al 2008, Munoz et al 2009]. To recommend preoperative UGI for symptomatic patients is problematic, since Küper et al showed that 80% of the patients with pathological findings are asymptomatic [Küper et al 2010]. In eight studies UGI was recommended for all bariatric surgery candidates [Madan et al 2004, Munoz et al

2006, Csendes et al 2007, de Moura Almeida et al 2008, Mong et al 2008, Küper 2010, D'Hondt et al 2013, Wong et al 2015].

The most recent study of the role of routine UGI prior to bariatric surgery in 613 patients reported that HP was the strongest predictor of an abnormal endoscopy, and endoscopically diagnosed ulceration was the only predictor of postoperative complications. In the series all patients with gastro-duodenal ulcers were infected with HP. A routine HP testing is needed and eradication of HP recommended [Fernandes et al 2016]. Schirmer et al (2002) also detected significantly lower incidence of marginal ulcers at the gastro-jejunal anastomosis in patients who had UGI prior to the surgery and HP eradicated. This also supports the routine testing of HP, which can be tested with a blood antibody test, a stool antigen test, or a carbon urea breath test, and thereby HP testing alone is not an indication for UGI. HP testing was recommended to all patients in six studies [Schirmer et al 2002, Azagury et al 2006, Vanek et al 2006, Csendes et al 2007, de Moura Almeida et al 2008, Fernandes et al 2016]. However, there are also studies that did not associate HP with increased risk of marginal ulcers [Papasavas et al 2008, Almazeedi et al 2014].

The most common findings in UGI in our study were hiatal hernias and GER, which are both relative contraindications for SG but not for LRYGB. Rather both conditions are improved after LRYGB. Therefore UGI may be indicated prior to SG to exclude these possible contraindications. UGI also could be considered in patients with previous abdominal operations, when the risk of conversion from LRYGB to SG is increased due to intra-abdominal adhesions.

6.2. ERAS programme after LRYGB

Outcomes following LRYGB with ERAS programmes have been reported in ten articles including this study. The results of these studies are shown in Table 7.

Table 7. Reported outcomes of LRYGB with ERAS in nine studies found in literature and outcome of this study.

Authors	Year of publication	Number of patients	Surgical time (minutes)	Mean LOS[a] (days)	% 1 day discharge	Readmis-sions (%)	Overall morbidity (%)	Mortality n (%)
McCarthy al	2005	2000	54	NR	84	1.7	6.2	2 (0.1)
Bergland et al	2008	500	57	2	NR	NR	0.6	0 (0.0)
Jacobsen et al	2012	2000	41	2.3	NR	1.9	2.8	2 (0.1)
Bamgadeet al	2012	406	100	1	65	0.0	3.4	0 (0.0)
Awad et al	2014	150	NR	1.8	37	NR	4.4	1 (0.7)
Geubbels et al	2014	360	71	1	NR	8.3	18.3	0 (0.0)
Dogan et al	2015	75	56	2	NR	1.3	8	0 (0.0)
Pike et al	2015	112	NR	1	87.5	0.9	4.5	0 (0.0)
Matlock et al	2015	170	128	2.9	NR	1.7	10.5	1 (0.6)
This study	2015	388	74	1.1	83	4.9	9.8	0 (0.0)

[a] Length of stay

The literature remains scarce and all these aforementioned publications come from high-volume and specialised bariatric centres. Whether the reported outcomes are a result of specific ERAS programmes or merely reflect the vast experience of the surgical teams remains unclear. According to a recent systematic review, the ERAS management of patients undergoing LRYGB is feasible, but the authors concluded that further studies from independent researchers are required to determine the safety of a generalised adoption of this approach outside of dedicated bariatric units [Elliott et al 2013]. Therefore, it was important to see if ERAS programmes may be applied equally successfully in a lower volume, less specialised hospital.

Vaasa Central Hospital has previously reported the outcome of the first 325 LRYGBs during the learning curve. Length of stay (LOS) dropped from the initial four days during the first 108 operations to two days during the last 109 patients. The mean operative time dropped from 110 minutes to 74 minutes. Operative time kept falling during the first 325 operations [Victorzon et al 2012]. After introducing the ERAS programme as explained in this study, LOS dropped from two days to one day. Overall morbidity dropped from 19% to 10% and major complications from 4.6% to 3.4%. The results of this study compared to those shown in Table 7 confirm that outcomes mostly reported in high-volume centres are reproducible in lower volume, less specialised centres.

6.3. Prevalence of OSA in bariatric surgery candidates

Prevalence of OSA in bariatric surgery candidates has been reported to range between 64% and 97%. In this study the prevalence was 71%, and it reached even 90% in males, supporting the earlier findings. In all studies there was a strong male dominance among OSA patients [Valencia-Flores et al 2004, Lee et al 2009, Sharkey et al 2010, Sareli et al 2011, Kolotkin et al 2011, Carneiro et al 2012, Aguiar et al 2014, Koeck et al 2014].

The number of undiagnosed OSA patients is extremely high. Young et al estimated that 93% of women and 82% of men with moderate to severe OSA are undiagnosed [Young et al 1997]. In most of the studies questionnaires are used for screening OSA patients even though the diagnosis of OSA is always based on cardiorespiratory recording, which was scheduled to all patients at baseline in our study. In a prospective study of adult surgical patients the ARES OSA screening questionnaire was used, and patients with high risk for OSA were investigated further on with home sleep studies resulting in 82.1% prevalence of undiagnosed OSA [Finkel et al 2009]. In many trials different kinds of screening tools have been tested for prediction of OSA among bariatric patients. Dixon et al. (2003) introduced a simple scoring system of six factors predicting AHI more than 15: observed sleep apnoea, male sex, higher BMI, older age, and higher fasting insulin and glycosylated haemoglobin (HbA1c). ESS questionnaire was also used, but as in our study, it did not correlate with OSA. One validated tool for screening OSA is STOP-Bang questionnaire predicting OSA from loud snoring, tiredness, observed apnoea, high blood pressure, BMI, age, neck circumference, and gender. A STOP-Bang score of three had a sensitivity of 90% and a positive predictive value of 85% for identifying obese patients with OSA. A high STOP-Bang score (three or more) has also been associated with more postoperative complications and increased length of hospital stay in undiagnosed OSA patients not using CPAP compared to patients with CPAP treated OSA [Chung et al 2013, Proczko et al 2014]. Even a severe OSA can be asymptomatic, which means that predicting OSA solely on the basis of symptoms is difficult. In the present study with diagnostic cardiorespiratory recordings, SOS scores correlated with OSA in women, but not in men. So far there is no feasible tool to predict OSA, and cardiorespiratory recording is always needed to verify the diagnosis when suspected.

Whether screening for undiagnosed OSA has any impact on perioperative outcome in bariatric surgery patients is controversial. Finkel et al (2009), whose study group routinely screened patients for undiagnosed OSA prior the operation, reported a

lower number of postoperative respiratory complications in patients with OSA than many previous studies. The study population was not bariatric, but adult surgical patients, and the complication data were gathered retrospectively. The Longitudinal Assessment of Bariatric Surgery Consortium also reported an association between OSA and a possible adverse surgical outcome [Flum et al 2009]. According to the report of the American Academy of Sleep Medicine Clinical Practice Review Committee in 2003, sleep-disordered breathing increased the risk for anaesthetic and sedative complications, including life threatening cardiorespiratory complications [Meoli et al 2003]. No increased risk associated with OSA was found in a retrospective study comparing bariatric and orthopaedic surgery groups, which were screened for OSA prior to the operations [Nepomnayshy et al 2013]. Another retrospective study was investigating the relationship between perioperative complications and the severity of OSA in bariatric surgery patients, and did not detect any independent associations [Weingarten et al 2011].

A routine screening for OSA was recommended in at least three studies. One prospective and one retrospective study with prevalence of OSA of 64% and 86% recommended cardiorespiratory recording for all bariatric patients [Carneiro et al 2012, Sharkey et al 2010]. One prospective study, showing an OSA prevalence of 77%, recommended a routine sleep study for patients over 49 years of age [Sareli et al 2011].

The surgical risk for severe complications following LRYGB is low, around 1% to 4% [Kim et Wolfe 2012], but generally considered increased for older patients, males, and especially for more obese and older male patients [Buchwald et al 2007]. It is well demonstrated that OSA is associated with an increased risk for cardiovascular morbidity and mortality in the longer term, and most patients with OSA remain undiagnosed. Therefore bariatric patients represent a unique possibility to identify a novel risk group and a possibility to prevent cardiovascular complications. In the perioperative care, OSA patients are given CPAP ventilation in the recovery room. Otherwise the perioperative care does not differ from that of non-OSA patients. The remission of OSA after bariatric surgery is not predictable, and several patients are likely to still have severe or moderate OSA after surgery. This may be important knowledge considering the possible severe complications associated with OSA in the long run. In our study the overall OSA prevalence was 71%, and 90% in males. It is also noteworthy that 66% of OSA patients were discovered because of this study. This is important to keep in mind when investigating obese male surgery candidates. In our opinion sleep recordings should be recommended at least for all bariatric male patients.

6.4. Effect of LRYGB on OSA 12 months after surgery

Effect of bariatric surgery on OSA has been reported in many trials, and the results are variable. The study populations have been heterogeneous, and the criteria for OSA resolution have varied. In our study the diagnosis of OSA as well as the resolution of OSA was based on cardiorespiratory recording and was defined as AHI less than 5 events/hour. In two systematic reviews OSA was improved or resolved in 75% to 84% of the patients after the operation [Sarkosh et al 2013, Buchwald et al 2004]. In a meta-analysis of twelve studies, a significant reduction in AHI was observed, but it was pointed out that the mean AHI after surgical weight loss was still 15.8 events/hour, which equals to moderate OSA, and additional treatment of OSA may still be needed after surgery [Greenburg et al 2009]. The study of 58 moderate to severe OSA patients undergoing gastric bypass did not report any total resolution of OSA after bariatric surgery. However, only 11 (19%) patients had polysomnography recorded 3–21 months after bariatric surgery. In these 11 patients respiratory disturbance index decreased from 56 (severe) to 23 (moderate). Nevertheless, the authors concluded that gastric bypass is an effective treatment for OSA [Rasheid et al 2003]. In another study of 24 patients with OSA at baseline, who all had significant weight loss after gastric banding, only one (4%) patient experienced a resolution of OSA and 71% still had moderate to severe OSA one year after the operation. The mean AHI changed from 47.9 to 24.5 events/hour [Lettieri et al 2008].

In a study comparing LRYGB with intensive lifestyle intervention (ILI), the operation was demonstrated to be more effective in inducing remission of OSA (66% vs. 40% remission). However, the study analysis suggested that it was the weight loss that explained the beneficial effects rather than the surgical procedure. In this study the weight loss was 8% in ILI group and 30% in the bariatric surgery group [Fredheim et al 2013]. Surgical and conventional therapies were also compared in a randomised controlled trial of 60 obese patients with recently diagnosed (less than six months) OSA and AHI 20 events/hour or more. CPAP had been prescribed to all patients. Even though gastric banding operation resulted in greater weight loss (27.8 kg vs. 5.1 kg), it did not result in a statistically greater reduction in AHI compared to the conventional therapy group. Also CPAP adherence did not differ between the groups. The study confirmed that weight loss is associated with improvement in AHI, but suggested that much of the benefit is already associated with mild to moderate weight loss [Dixon et al 2012].

Our study is one of the largest prospective studies on the topic, and it demonstrates that bariatric surgery is an effective treatment for OSA. Following surgery the total AHI decreased from 27.8 events/h to 9.9 events/h ($p<0.001$), and the prevalence of OSA reduced from 71% to 44% ($p<0.001$). Of all 119 OSA patients who underwent bariatric surgery 90% had either the disease improved or totally dissolved at 12 months; 54 patients had OSA in remission (45%), 33 patients (28%) moved into a milder OSA-group, and 20 patients (17%) had their total AHI improved even though the OSA group did not change. Particularly those patients who had severe OSA prior to the operation experienced beneficial changes in the severity of OSA; 22% had severe OSA before the operation, but only 7% at 12 months ($p<0.001$). In addition, at baseline especially men had a very high prevalence of OSA (90%), which decreased to 52% at 12 months after the operation.

7 Conclusions

On the basis of the present investigations the following conclusions can be drawn

Study I. All the findings in routine preoperative upper GI endoscopies (UGI) were benign and mild and did not influence the operative plan. Our results do not support the performance of routine UGI prior to gastric bypass.

Study II. Our ERAS programme was found to be safe and effective, and it did not increase postoperative morbidity or readmissions. Our results confirmed that ERAS may be equally successful outside high-volume, highly dedicated bariatric centres.

Study III. Obstructive sleep apnoea (OSA) was found to be very common in bariatric surgery candidates (71%), especially in men (90%). Considering our results and the increased morbidity and mortality related to OSA, we recommend routine screening for OSA in bariatric surgery patients, particularly men.

Study IV. The prevalence of OSA decreased from 71 % to 44 %, and OSA was either improved or totally resolved in 90% of patients 12 months after surgery. We conclude that LRYGB is an effective treatment for OSA, but postoperative cardiorespiratory recordings are recommended to all OSA patients in order to find the approximately 20% of patients with persisting moderate to severe OSA.

8 Acknowledgements

This thesis was carried out at the Departments of Surgery in Vaasa Central Hospital and in Hatanpää Hospital and in association with Departments of Surgery in Kuopio University Hospital and Lahti Region Central Hospital.

My endless gratitude is due to my supervisors Professor Mikael Victorzon and Docent Henri Tuomilehto. Thank you, Mikael, for warmly welcoming me into the world of bariatric surgery. You have believed in me and supported me in clinical work and in writing. I always could count on your fast and honest feedback. This doctoral thesis would not exist without you. Thank you, Henri, for your support and patience trying to explain the wonders of sleep apnea to a surgeon. Your advice in scientific work has been invaluable.

I gratefully acknowledge the reviewers Docent Timo Heikkinen and Docent Tom Scheinin for their valuable comments to improve my manuscript.

I also wish to express my gratitude to my co-authors: Professor Jussi Pihlajamäki for his contribution to the OSA study design, his constructive advice and revisions of the last two articles; Tilda Hahl, MD, for her work in the ERAS study and her contribution to the second article; Pekka Tarkiainen, MD, and Otto Knutar, MD for their revisions in ERAS study and Markku Luostarinen, MD, PhD, Jyrki Kössi, MD, PhD, Juha Virtanen, MD, and Pirjo Käkelä, MD, for revisions in OSA articles.

I want to thank Jaana Elberkennou, MD, MA, for your expertise in revising the English language and your very flexible working hours. I cordially thank my dear friend Miia Artama, PhD, as well as Jani Raitanen, MSc, for your critical assistance and guidance in statistical analysis. I am thankful to the research nurses Synnöve Liukku, Helinä Mäkipää, Taina Poutiainen, Matti Laitinen and Marjo Soini and research assistant Ville Ruohoranta for your assistance. I want to thank colleagues and nurses and other staff members in Vaasa Central Hospital, who contributed by recruiting patients and collecting the data for the trials. I also want to thank all the patients who participated in these studies.

I warmly thank the hospital director Arto Ranta in Hatanpää Hospital for supporting me in this project and accepting my endless trips to Vaasa. I also wish to thank the Head of Surgical Department Susanna Niemeläinen, MD, for support

and my bariatric colleagues Anu Välikoski, MD, in Hatanpää Hospital and Tuula Tyrväinen, MD, in Tampere University Hospital; it has been a pleasure to start bariatric operations in Tampere with you.

I want to owe my warm gratitude to my friends. Special thanks belong to Virve Korhonen MD, for mind-clearing conversations and walks (even in snowstorm) over the years. I thank Loimaan Naistenkerho for refreshing annual meetings: Thank you Miia, Anu, Riikka, Ansku, Laura and Maria for the good memories and good laughs. I also want to thank the Kangasala Gang (which does not mean you have to live in Kangasala): Kristiina, Tuomas, Lisa, Janne, Miia, Antti, Pauliina and Mika for your friendship.

My deepest thanks go to my family. My parents Tuija and Pekka, I thank you for your unconditional love. My need to challenge myself has sometimes surprised you, but no matter what I decide to do, you support me all the way. Your help with Hermanni has been invaluable. I thank my dear sister Tiina and her family Hannu and Ilona and Helinä for love and support. I warmly thank my parents-in-law Tarja and Antti for your time and support. Academic writing with a 2-year-old son is not easy and you have given me the peaceful moments to write knowing my son is enjoying himself with grandparents. I also thank my sister-in-law Miia and Tomi and Rasmus for your support and help.

The family business Hämeen Kirjapaino is warmly thanked for this fine, quality edition you are holding in your hand at the moment.

Finally, I want to thank my beloved husband Miika for being my personal 24/7 IT-service, for saving all the research data from the destroyed computer and for editing and printing this book. During this project we have been blessed with a wonderful son Hermanni. You are the best thing that ever happened! Thank you Hermanni for pushing me to use my time efficiently and finishing this project. I love you!

9 References

Abdeen, G. & le Roux, C. W. (2016) Mechanism Underlying the Weight Loss and Complications of Roux-en-Y Gastric Bypass. Review. *Obes Surg*, 26(2), 410-21.

Abelson, J. S., Afaneh, C., Dolan, P., Chartrand, G., Dakin, G. & Pomp, A. (2015) Laparoscopic Sleeve Gastrectomy: Co-morbidity Profiles and Intermediate-Term Outcomes. *Obes Surg*.

Aguiar, I. C., Freitas, W. R., Jr., Santos, I. R., Apostolico, N., Nacif, S. R., Urbano, J. J., Fonseca, N. T., Thuler, F. R., Ilias, E. J., Kassab, P., LeitaoFilho, F. S., Laurino Neto, R. M., Malheiros, C. A., Insalaco, G., Donner, C. F. & Oliveira, L. V. (2014) Obstructive sleep apnea and pulmonary function in patients with severe obesity before and after bariatric surgery: a randomized clinical trial. *Multidiscip Respir Med*, 9(1), 43.

Almazeedi, S., Al-Sabah, S., Alshammari, D., Alqinai, S., Al-Mulla, A., Al-Murad, A., Al-Enezi, K. & Jumaa, T. (2014) The impact of Helicobacter pylori on the complications of laparoscopic sleeve gastrectomy. *Obes Surg*, 24(3), 412-5.

American Society of Gastrointestinal and Endoscopic Surgeons (ASGE) Standards of Practice Committee. Evans, J. A., Muthusamy, V. R., Acosta, R. D., Bruining, D. H., Chandrasekhara, V., Chathadi, K. V., Eloubeidi, M. A., Fanelli, R. D., Faulx, A. L., Fonkalsrud, L., Khashab, M. A., Lightdale, J. R., Pasha, S. F., Saltzman, J. R., Shaukat, A., Wang, A., Stefanidis, D., Richardson, W. S., Kothari, S. N. & Cash, B. D. (2015) The role of endoscopy in the bariatric surgery patient. *Gastrointest Endosc*, 81(5), 1063-72.

Angrisani, L., Santonicola, A., Iovino, P., Formisano, G., Buchwald, H. & Scopinaro, N. (2015) Bariatric Surgery Worldwide 2013. *Obes Surg*, 25(10), 1822-32.

Arnold, M., Leitzmann, M., Freisling, H., Bray, F., Romieu, I., Renehan, A. & Soerjomataram, I. (2016) Obesity and cancer: An update of the global impact. *Cancer Epidemiol*, 41, 8-15.

Ashrafian, H., le Roux, C. W., Rowland, S. P., Ali, M., Cummin, A. R., Darzi, A. & Athanasiou, T. (2012) Metabolic surgery and obstructive sleep apnoea: the protective effects of bariatric procedures. *Thorax*, 67(5), 442-9.

Attal, P. & Chanson, P. (2010) Endocrine aspects of obstructive sleep apnea. *J Clin Endocrinol Metab*, 95(2), 483-95.

Awad, S., Carter, S., Purkayastha, S., Hakky, S., Moorthy, K., Cousins, J. & Ahmed, A. R. (2014) Enhanced recovery after bariatric surgery (ERABS): clinical outcomes from a tertiary referral bariatric centre. *Obes Surg*, 24(5), 753-8.

Azagury, D., Dumonceau, J. M., Morel, P., Chassot, G. & Huber, O. (2006) Preoperative work-up in asymptomatic patients undergoing Roux-en-Y gastric bypass: is endoscopy mandatory? *Obes Surg*, 16(10), 1304-11.

Barbe, F., Duran-Cantolla, J., Sanchez-de-la-Torre, M., Martinez-Alonso, M., Carmona, C., Barcelo, A., Chiner, E., Masa, J. F., Gonzalez, M., Marin, J. M., Garcia-Rio, F., Diaz de Atauri, J., Teran, J., Mayos, M., de la Pena, M., Monasterio, C., del Campo, F. &

Montserrat, J. M. (2012) Effect of continuous positive airway pressure on the incidence of hypertension and cardiovascular events in nonsleepy patients with obstructive sleep apnea: a randomized controlled trial. *Jama*, 307(20), 2161-8.

Berghöfer, A., Pischon, T., Reinhold, T., Apovian, C. M., Sharma, A. M. & Willich, S. N. (2008) Obesity prevalence from a European perspective: a systematic review. *BMC Public Health*, 8, 200.

Biertho, L., Simon-Hould, F., Marceau, S., Lebel, S., Lescelleur, O. & Biron, S. (2016) Current Outcomes of Laparoscopic Duodenal Switch. *Ann Surg Innov Res*, 10, 1.

Borg, P., Kukkonen-Harjula, K., Fogelholm, M. & Pasanen, M. (2002) Effects of walking or resistance training on weight loss maintenance in obese, middle-aged men: a randomized trial. *Int J Obes Relat Metab Disord*, 26(5), 676-83.

Buchwald, H. (2014) The evolution of metabolic/bariatric surgery. *Obes Surg*, 24(8), 1126-35.

Buchwald, H., Avidor, Y., Braunwald, E., Jensen, M. D., Pories, W., Fahrbach, K. & Schoelles, K. (2004) Bariatric surgery: a systematic review and meta-analysis. *Jama*, 292(14), 1724-37.

Buchwald, H., Estok, R., Fahrbach, K., Banel, D. & Sledge, I. (2007) Trends in mortality in bariatric surgery: a systematic review and meta-analysis. *Surgery*, 142(4), 621-32; discussion 632-5.

Bächler, T., Schiesser, M., Lutz, T. A., le Roux, C. W. & Bueter, M. (2014) Where to begin and where to end? Preoperative assessment for patients undergoing metabolic surgery. *Dig Surg*, 31(1), 25-32.

Caballero, B. (2007) The global epidemic of obesity: an overview. *Epidemiol Rev*, 29, 1-5.

Carneiro, G., Florio, R. T., Zanella, M. T., Pradella-Hallinan, M., Ribeiro-Filho, F. F., Tufik, S. & Togeiro, S. M. (2012) Is mandatory screening for obstructive sleep apnea with polysomnography in all severely obese patients indicated? *Sleep Breath*, 16(1), 163-8.

Chen, Y., Corsino, L., Shantavasinkul, P. C., Grant, J., Portenier, D., Ding, L. & Torquati, A. (2015) Gastric Bypass Surgery Leads to Long-term Remission or Improvement of Type 2 Diabetes and Significant Decrease of Microvascular and Macrovascular Complications. *Ann Surg*, 263(6), 1138-42

Chung, F., Yang, Y. & Liao, P. (2013) Predictive performance of the STOP-Bang score for identifying obstructive sleep apnea in obese patients. *Obes Surg*, 23(12), 2050-7.

Csendes, A., Burgos, A. M., Smok, G. & Beltran, M. (2007) Endoscopic and histologic findings of the foregut in 426 patients with morbid obesity. *Obes Surg*, 17(1), 28-34.

Current Care Guidelines: Obesity, adults (2013) Käypähoito –suositus: Lihavuus, aikuiset. *Duodecim*.http://www.kaypahoito.fi/web/kh/suositukset/suositus?id=hoi24010

D'Hondt, M., Steverlynck, M., Pottel, H., Elewaut, A., George, C., Vansteenkiste, F., Van Rooy, F. & Devriendt, D. (2013) Value of preoperative esophagogastroduodenoscopy in morbidly obese patients undergoing

laparoscopic Roux-en-Y gastric bypass. *Acta Chir Belg*, 113(4), 249-53.

Dargent, J. (2016) Novel Endoscopic Management of Obesity. *Clin Endosc*, 49(1), 30-6.

de Moura Almeida, A., Cotrim, H. P., Santos, A. S., Bitencourt, A. G., Barbosa, D. B., Lobo, A. P., Rios, A. & Alves, E. (2008) Preoperative upper gastrointestinal endoscopy in obese patients undergoing bariatric surgery: is it necessary? *Surg Obes Relat Dis*, 4(2), 144-9; discussion 150-1.

Diamantis, T., Apostolou, K. G., Alexandrou, A., Griniatsos, J., Felekouras, E. & Tsigris, C. (2014) Review of long-term weight loss results after laparoscopic sleeve gastrectomy. *Surg Obes Relat Dis*, 10(1), 177-83.

Dindo, D., Demartines, N. & Clavien, P. A. (2004) Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Ann Surg*, 240(2), 205-13.

Dixon, J. B., Schachter, L. M. & O'Brien, P. E. (2003) Predicting sleep apnea and excessive day sleepiness in the severely obese: indicators for polysomnography. *Chest*, 123(4), 1134-41.

Dixon, J. B., O'Brien, P. E., Playfair, J., Chapman, L., Schachter, L. M., Skinner, S., Proietto, J., Bailey, M. & Anderson, M. (2008) Adjustable gastric banding and conventional therapy for type 2 diabetes: a randomized controlled trial. *Jama*, 299(3), 316-23.

Dixon, J. B., Schachter, L. M., O'Brien, P. E., Jones, K., Grima, M., Lambert, G., Brown, W., Bailey, M. & Naughton, M. T. (2012) Surgical vs conventional therapy for weight loss treatment of obstructive sleep apnea: a randomized controlled trial. *Jama*, 308(11), 1142-9.

Dogan, K., Gadiot, R. P., Aarts, E. O., Betzel, B., van Laarhoven, C. J., Biter, L. U., Mannaerts, G. H., Aufenacker, T. J., Janssen, I. M. & Berends, F. J. (2015) Effectiveness and Safety of Sleeve Gastrectomy, Gastric Bypass, and Adjustable Gastric Banding in Morbidly Obese Patients: a Multicenter, Retrospective, Matched Cohort Study. *Obes Surg*, 25(7), 1110-8.

Driscoll, S., Gregory, D. M., Fardy, J. M. & Twells, L. K. (2016) Long-term health-related quality of life in bariatric surgery patients: A systematic review and meta-analysis. *Obesity (Silver Spring)*, 24(1), 60-70.

Elliott, J. A., Patel, V. M., Kirresh, A., Ashrafian, H., Le Roux, C. W., Olbers, T., Athanasiou, T. & Zacharakis, E. (2013) Fast-track laparoscopic bariatric surgery: a systematic review. *Updates Surg*, 65(2), 85-94.

Fernandes, S. R., Meireles, L. C., Carrilho-Ribeiro, L. & Velosa, J. (2016) The Role of Routine Upper Gastrointestinal Endoscopy Before Bariatric Surgery. *Obes Surg*, Jan 10. Epub ahead of print.

Finkel, K. J., Searleman, A. C., Tymkew, H., Tanaka, C. Y., Saager, L., Safer-Zadeh, E., Bottros, M., Selvidge, J. A., Jacobsohn, E., Pulley, D., Duntley, S., Becker, C. & Avidan, M. S. (2009) Prevalence of undiagnosed obstructive sleep apnea among adult surgical patients in an academic medical center. *Sleep Med*, 10(7), 753-8.

Finkelstein, E. A., Trogdon, J. G., Cohen, J. W. & Dietz, W. (2009) Annual medical spending attributable to obesity: payer-and service-specific estimates. *Health Aff (Millwood)*, 28(5), w822-31.

Flum, D. R., Belle, S. H., King, W. C., Wahed, A. S., Berk, P., Chapman, W., Pories, W., Courcoulas, A., McCloskey, C., Mitchell, J., Patterson, E., Pomp, A., Staten, M. A., Yanovski, S. Z., Thirlby, R. & Wolfe, B. (2009) Perioperative safety in the longitudinal assessment of bariatric surgery. *N Engl J Med*, 361(5), 445-54.

Fobi, M. (1991) Why the Operation I Prefer is Silastic Ring Vertical Gastric Bypass. *Obes Surg*, 1(4), 423-426.

Fogelholm, M. & Kukkonen-Harjula, K. (2000) Does physical activity prevent weight gain--a systematic review. *Obes Rev*, 1(2), 95-111.

Fogelholm, M., Kukkonen-Harjula, K., Nenonen, A. & Pasanen, M. (2000) Effects of walking training on weight maintenance after a very-low-energy diet in premenopausal obese women: a randomized controlled trial. *Arch Intern Med*, 160(14), 2177-84.

Fredheim, J. M., Rollheim, J., Omland, T., Hofso, D., Roislien, J., Vegsgaard, K. & Hjelmesaeth, J. (2011) Type 2 diabetes and pre-diabetes are associated with obstructive sleep apnea in extremely obese subjects: a cross-sectional study. *Cardiovasc Diabetol*, 10, 84.

Fredheim, J. M., Rollheim, J., Sandbu, R., Hofso, D., Omland, T., Roislien, J. & Hjelmesaeth, J. (2013) Obstructive sleep apnea after weight loss: a clinical trial comparing gastric bypass and intensive lifestyle intervention. *J Clin Sleep Med*, 9(5), 427-32.

Geubbels, N., Lijftogt, N., Fiocco, M., van Leersum, N. J., Wouters, M. W. & de Brauw, L. M. (2015) Meta-analysis of internal herniation after gastric bypass surgery. *Br J Surg*, 102(5), 451-60.

Greenburg, D. L., Lettieri, C. J. & Eliasson, A. H. (2009) Effects of surgical weight loss on measures of obstructive sleep apnea: a meta-analysis. *Am J Med*, 122(6), 535-42.

Hachem, A. & Brennan, L. (2015) Quality of Life Outcomes of Bariatric Surgery: A Systematic Review. *Obes Surg*, 26(2), 395-409.

Harlan, W. R., Landis, J. R., Flegal, K. M., Davis, C. S. & Miller, M. E. (1988) Secular trends in body mass in the United States, 1960-1980. *Am J Epidemiol*, 128(5), 1065-74.

Helmiö, M., Victorzon, M., Ovaska, J., Leivonen, M., Juuti, A., Peromaa-Haavisto, P., Nuutila, P., Vahlberg, T. & Salminen, P. (2014) Comparison of short-term outcome of laparoscopic sleeve gastrectomy and gastric bypass in the treatment of morbid obesity: A prospective randomized controlled multicenter SLEEVEPASS study with 6-month follow-up. *Scand J Surg*, 103(3), 175-181.

Henriksson, V. (1952) Kan tunntarmsresektion försvaras som terapi mot fettsot. *Nordisk Medicin*, 47, 744.

Himpens, J., Dobbeleir, J. & Peeters, G. (2010) Long-term results of laparoscopic sleeve gastrectomy for obesity. *Ann Surg*, 252(2), 319-24.

Hyysalo, J., Männistö, V. T., Zhou, Y., Arola, J., Karja, V., Leivonen, M., Juuti, A., Jaser, N., Lallukka, S., Käkelä, P., Venesmaa, S., Simonen, M., Saltevo, J., Moilanen, L., Korpi-Hyövalti, E., Keinanen-Kiukaanniemi, S., Oksa, H., Orho-Melander, M., Valenti, L., Fargion, S., Pihlajamäki, J., Peltonen, M. & Yki-Järvinen, H. (2014) A population-based study on the prevalence of NASH using scores validated against liver histology. *J Hepatol*, 60(4), 839-46.

Ikramuddin, S., Korner, J., Lee, W. J., Connett, J. E., Inabnet, W. B., Billington, C. B., Thomas, A. J., Leslie, D. B., Chong, K., Jeffery, R. W., Ahmed, L., Vella, A., Chuang, L. M., Bessler, M., Sarr, M. G., Swain, J. M., Laqua, P., Jensen, M. D. & Bantle, J. P. (2013) Roux-en-Y Gastric Bypass versus Intensive Medical Management for the Control of Type 2 Diabetes, Hypertension and Hyperlipidemia: An International, Multicenter, Randomized Trial. *Jama*, 309(21), 2240-9.

Kehlet, H. & Wilmore, D. W. (2002) Multimodal strategies to improve surgical outcome. *Am J Surg*, 183(6), 630-41.

Kim, J. H. & Wolfe, B. (2012) Bariatric/metabolic surgery: short- and long-term safety. *Curr Atheroscler Rep*, 14(6), 597-605.

Koeck, E. S., Barefoot, L. C., Hamrick, M., Owens, J. A., Qureshi, F. G. & Nadler, E. P. (2014) Predicting sleep apnea in morbidly obese adolescents undergoing bariatric surgery. *Surg Endosc*, 28(4), 1146-52.

Koehestanie, P., de Jonge, C., Berends, F. J., Janssen, I. M., Bouvy, N. D. & Greve, J. W. (2014) The effect of the endoscopic duodenal-jejunal bypass liner on obesity and type 2 diabetes mellitus, a multicenter randomized controlled trial. *Ann Surg*, 260(6), 984-92.

Kolotkin, R. L., LaMonte, M. J., Walker, J. M., Cloward, T. V., Davidson, L. E. & Crosby, R. D. (2011) Predicting sleep apnea in bariatric surgery patients. *Surg Obes Relat Dis*, 7(5), 605-10.

Koski, S.(2011) Diabetesbarometri 2010, Suomen Diabetesliitto ry.

Kotecha, B. T. & Hall, A. C. (2014) Role of surgery in adult obstructive sleep apnoea. *Sleep Med Rev*, 18(5), 405-13.

Kremen, A. J., Linner, J. H. & Nelson, C. H. (1954) An experimental evaluation of the nutritional importance of proximal and distal small intestine. *Ann Surg*, 140(3), 439-48.

Kumar, N. (2015) Endoscopic therapy for weight loss: Gastroplasty, duodenal sleeves, intragastric balloons, and aspiration. *World J Gastrointest Endosc*, 7(9), 847-59.

Küper, M. A., Kratt, T., Kramer, K. M., Zdichavsky, M., Schneider, J. H., Glatzle, J., Stuker, D., Konigsrainer, A. & Brucher, B. L. (2010) Effort, safety, and findings of routine preoperative endoscopic evaluation of morbidly obese patients undergoing bariatric surgery. *Surg Endosc*, 24(8), 1996-2001.

Lahti-Koski, M., Seppänen-Nuijten, E., Männistö, S., Härkänen, T., Rissanen, H., Knekt, P., Rissanen, A. & Heliövaara, M. (2010) Twenty-year changes in the prevalence of obesity among Finnish adults. *Obes Rev*, 11(3), 171-6.

Lassailly, G., Caiazzo, R., Buob, D., Pigeyre, M., Verkindt, H., Labreuche, J., Raverdy, V., Leteurtre, E., Dharancy, S., Louvet, A.,

Romon, M., Duhamel, A., Pattou, F. & Mathurin, P. (2015) Bariatric Surgery Reduces Features of Nonalcoholic Steatohepatitis in Morbidly Obese Patients. *Gastroenterology*, 149(2), 379-88.

le Roux, C. W., Welbourn, R., Werling, M., Osborne, A., Kokkinos, A., Laurenius, A., Lönroth, H., Fandriks, L., Ghatei, M. A., Bloom, S. R. & Olbers, T. (2007) Gut hormones as mediators of appetite and weight loss after Roux-en-Y gastric bypass. *Ann Surg*, 246(5), 780-5.

Lee, J., Meyerhardt, J. A., Giovannucci, E. & Jeon, J. Y. (2015) Association between body mass index and prognosis of colorectal cancer: a meta-analysis of prospective cohort studies. *PLoS One*, 10(3), e0120706.

Lee, W. J. & Lin, Y. H. (2014) Single-anastomosis gastric bypass (SAGB): appraisal of clinical evidence. *Obes Surg*, 24(10), 1749-56.

Lee, Y. H., Johan, A., Wong, K. K., Edwards, N. & Sullivan, C. (2009) Prevalence and risk factors for obstructive sleep apnea in a multiethnic population of patients presenting for bariatric surgery in Singapore. *Sleep Med*, 10(2), 226-32.

Lettieri, C. J., Eliasson, A. H. & Greenburg, D. L. (2008) Persistence of obstructive sleep apnea after surgical weight loss. *J Clin Sleep Med*, 4(4), 333-8.

Loewen, M., Giovanni, J. & Barba, C. (2008) Screening endoscopy before bariatric surgery: a series of 448 patients. *Surg Obes Relat Dis*, 4(6), 709-12.

Lozano, R., Naghavi, M., Foreman, K., Lim, S., Shibuya, K., Aboyans, V., Abraham, J., Adair, T., Aggarwal, R., Ahn, S. Y., Alvarado, M., Anderson, H. R., Anderson, L. M., Andrews, K. G., Atkinson, C., Baddour, L. M., Barker-Collo, S., Bartels, D. H., Bell, M. L., Benjamin, E. J., Bennett, D., Bhalla, K., Bikbov, B., Bin Abdulhak, A., Birbeck, G., Blyth, F., Bolliger, I., Boufous, S., Bucello, C., Burch, M., Burney, P., Carapetis, J., Chen, H., Chou, D., Chugh, S. S., Coffeng, L. E., Colan, S. D., Colquhoun, S., Colson, K. E., Condon, J., Connor, M. D., Cooper, L. T., Corriere, M., Cortinovis, M., de Vaccaro, K. C., Couser, W., Cowie, B. C., Criqui, M. H., Cross, M., Dabhadkar, K. C., Dahodwala, N., De Leo, D., Degenhardt, L., Delossantos, A., Denenberg, J., Des Jarlais, D. C., Dharmaratne, S. D., Dorsey, E. R., Driscoll, T., Duber, H., Ebel, B., Erwin, P. J., Espindola, P., Ezzati, M., Feigin, V., Flaxman, A. D., Forouzanfar, M. H., Fowkes, F. G., Franklin, R., Fransen, M., Freeman, M. K., Gabriel, S. E., Gakidou, E., Gaspari, F., Gillum, R. F., Gonzalez-Medina, D., Halasa, Y. A., Haring, D., Harrison, J. E., Havmoeller, R., Hay, R. J., Hoen, B., Hotez, P. J., Hoy, D., Jacobsen, K. H., James, S. L., Jasrasaria, R., Jayaraman, S., Johns, N., Karthikeyan, G., Kassebaum, N., Keren, A., Khoo, J. P., Knowlton, L. M., Kobusingye, O., Koranteng, A., Krishnamurthi, R., Lipnick, M., Lipshultz, S. E., Ohno, S. L., et al (2012) Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet*, 380(9859), 2095-128.

Madan, A. K., Speck, K. E. & Hiler, M. L. (2004a) Routine preoperative upper endoscopy for laparoscopic gastric bypass: is it necessary? *Am Surg*, 70(8), 684-6.

Maggard, M. A., Yermilov, I., Li, Z., Maglione, M., Newberry, S., Suttorp, M.,

Hilton, L., Santry, H. P., Morton, J. M., Livingston, E. H. & Shekelle, P. G. (2008) Pregnancy and fertility following bariatric surgery: a systematic review. *Jama*, 300(19), 2286-96.

Mannaerts, G. H., van Mil, S. R., Stepaniak, P. S., Dunkelgrun, M., de Quelerij, M., Verbrugge, S. J., Zengerink, H. F. & Biter, L. U. (2016) Results of Implementing an Enhanced Recovery After Bariatric Surgery (ERABS) Protocol. *Obes Surg*, 26(2), 303-12.

Martin-Rodriguez, E., Guillen-Grima, F., Marti, A. & Brugos-Larumbe, A. (2015) Comorbidity associated with obesity in a large population: The APNA study. *Obes Res Clin Pract*, 9(5), 435-47.

Mason, E. E. & Ito, C. (1967) Gastric bypass in obesity. *Surg Clin North Am*, 47, 1345-51.

Mason, E. E. (1982) Vertical banded gastroplasty for obesity. *Arch Surg*, 117, 701-6.

McArdle, N., Hillman, D., Beilin, L. & Watts, G. (2007) Metabolic risk factors for vascular disease in obstructive sleep apnea: a matched controlled study. *Am J Respir Crit Care Med*, 175(2), 190-5.

Mehaffey, J. H., LaPar, D. J., Clement, K. C., Turrentine, F. E., Miller, M. S., Hallowell, P. T. & Schirmer, B. D. (2016) 10-Year Outcomes After Roux-en-Y Gastric Bypass. *Ann Surg*, 264(1), 121-6.

Meoli, A. L., Rosen, C. L., Kristo, D., Kohrman, M., Gooneratne, N., Aguillard, R. N., Fayle, R., Troell, R., Kramer, R., Casey, K. R. & Coleman, J., Jr. (2003) Upper airway management of the adult patient with obstructive sleep apnea in the perioperative period--avoiding complications. *Sleep*, 26(8), 1060-5.

Milone, M., De Placido, G., Musella, M., Sosa Fernandez, L. M., Sosa Fernandez, L. V., Campana, G., Di Minno, M. N. & Milone, F. (2016) Incidence of Successful Pregnancy After Weight Loss Interventions in Infertile Women: a Systematic Review and Meta-Analysis of the Literature. *Obes Surg*, 26(2), 443-51.

Mingrone, G., Panunzi, S., De Gaetano, A., Guidone, C., Iaconelli, A., Leccesi, L., Nanni, G., Pomp, A., Castagneto, M., Ghirlanda, G. & Rubino, F. (2012) Bariatric Surgery versus Conventional
Medical Therapy for Type 2 Diabetes. The New England Journal of Medicine.

Miras, A. D. & le Roux, C. W. (2013) Mechanisms underlying weight loss after bariatric surgery. *Nat Rev Gastroenterol Hepatol*, 10(10), 575-84.

Mong, C., Van Dam, J., Morton, J., Gerson, L., Curet, M. & Banerjee, S. (2008) Preoperative endoscopic screening for laparoscopic Roux-en-Y gastric bypass has a low yield for anatomic findings. *Obes Surg*, 18(9), 1067-73.

Munoz, R., Ibanez, L., Salinas, J., Escalona, A., Perez, G., Pimentel, F., Guzman, S. & Boza, C. (2009) Importance of routine preoperative upper GI endoscopy: why all patients should be evaluated? *Obes Surg*, 19(4), 427-31.

Muraja-Murro, A., Eskola, K., Kolari, T., Tiihonen, P., Hukkanen, T., Tuomilehto, H., Peltonen, M., Mervaala, E. & Toyras, J. (2013) Mortality in middle-aged men with

obstructive sleep apnea in Finland. *Sleep Breath*, 17(3), 1047-53.

Mühlig, Y., Wabitsch, M., Moss, A. & Hebebrand, J. (2014) Weight loss in children and adolescents. *Dtsch Arztebl Int*, 111(48), 818-24.

Mäklin, S., Malmivaara, A., Linna, M., Victorzon, M., Koivukangas, V. & Sintonen, H. (2011) Cost-utility of bariatric surgery for morbid obesity in Finland. *Br J Surg*, 98(10), 1422-9.

National institute of health and welfare, Terveyden ja hyvinvoinnin laitos, Inkonen T, Anttila H, Gylling H, Isojärvi J, Koivukangas V, Kumpulainen T, Mustajoki P, Mäklin S, Saarni S, Saarni S, Sintonen H, Victorzon M, Malmivaara A (2009) Sairaalloisen lihavuuden leikkaushoito. THL Report 16/2009.

National Institute for Health and Welfare, Terveyden ja hyvinvoinnin laitos, Borodulin K,Levälahti E, Saarikoski L, Lund L, Juolevi A, Grönholm M, Jula A, Laatikainen T, Männistö S, Peltonen M, Salomaa V, Sundvall J, Taimi M, Virtanen S and Vartiainen E. (2013) FINRISKI 2012 National Survey. THL Report 22/2013.

National Institutes of Health conference. (1991) Gastrointestinal surgery for severe obesity. Consensus Development Conference Panel. *Ann Intern Med*, 115, 956-61.

Nepomnayshy, D., Hesham, W., Erickson, B., MacDonald, J., Iorio, R. & Brams, D. (2013) Sleep apnea: is routine preoperative screening necessary? *Obes Surg*, 23(3), 287-91.

Nguyen, D. M. & El-Serag, H. B. (2010) The epidemiology of obesity. *Gastroenterol Clin North Am*, 39(1), 1-7.

Obeid, N. R., Malick, W., Concors, S. J., Fielding, G. A., Kurian, M. S. & Ren-Fielding, C. J. (2016) Long-term outcomes after Roux-en-Y gastric bypass: 10- to 13-year data. *Surg Obes Relat Dis*, 12(1), 11-20.

O'Brien, P. E., MacDonald, L., Anderson, M., Brennan, L. & Brown, W. A. (2013) Long-term outcomes after bariatric surgery: fifteen-year follow-up of adjustable gastric banding and a systematic review of the bariatric surgical literature. *Ann Surg*, 257(1), 87-94.

O'Brien, P. (2000-2016) Surgical Treatment of obesity, in De Groot, L. J., Beck-Peccoz, P., Chrousos, G., Dungan, K., Grossman, A., Hershman, J. M., Koch, C., McLachlan, R., New, M., Rebar, R., Singer, F., Vinik, A. & Weickert, M. O. (eds), *Endotext*. South Dartmouth (MA): MDText.com, Inc. www.endotext.org

Ogden, C. L., Carroll, M. D., Fryar, C. D. & Flegal, K. M. (2015) Prevalence of Obesity Among Adults and Youth: United States, 2011-2014. *NCHS Data Brief*, 219, 1-8.

Omotosho, P., Mor, A., Shantavasinkul, P. C., Corsino, L. & Torquati, A. (2016) Gastric bypass significantly improves quality of life in morbidly obese patients with type 2 diabetes. *Surg Endosc*, 30(7), 2857-64.

Osland, E., Yunus, R. M., Khan, S., Alodat, T., Memon, B. & Memon, M. A. (2016) Postoperative Early Major and Minor Complications in Laparoscopic Vertical Sleeve Gastrectomy (LVSG) Versus Laparoscopic Roux-en-Y Gastric Bypass (LRYGB) Procedures: A Meta-Analysis and

Systematic Review. *Obes Surg*, Feb 19. Epub ahead of print.

Papasavas, P. K., Gagne, D. J., Donnelly, P. E., Salgado, J., Urbandt, J. E., Burton, K. K. & Caushaj, P. F. (2008) Prevalence of Helicobacter pylori infection and value of preoperative testing and treatment in patients undergoing laparoscopic Roux-en-Y gastric bypass. *Surg Obes Relat Dis*, 4(3), 383-8.

Parikh, M., Ayoung-Chee, P., Romanos, E., Lewis, N., Pachter, H. L., Fielding, G. & Ren, C. (2007) Comparison of rates of resolution of diabetes mellitus after gastric banding, gastric bypass, and biliopancreatic diversion. *J Am Coll Surg*, 205(5), 631-5.

Peeters, A., Barendregt, J. J., Willekens, F., Mackenbach, J. P., Al Mamun, A. & Bonneux, L. (2003) Obesity in adulthood and its consequences for life expectancy: a life-table analysis. *Ann Intern Med*, 138(1), 24-32.

Pekkarinen, T. & Mustajoki, P. (1997) Comparison of behavior therapy with and without very-low-energy diet in the treatment of morbid obesity. A 5-year outcome. *Arch Intern Med*, 157(14), 1581-5.

Pekkarinen, T., Mustonen, H., Sane, T., Jaser, N., Juuti, A. & Leivonen, M. (2016) Long-Term Effect of Gastric Bypass and Sleeve Gastrectomy on Severe Obesity: Do Preoperative Weight Loss and Binge Eating Behavior Predict the Outcome of Bariatric Surgery? *Obes Surg*, Feb 3. Epub ahead of print.

Pekurinen, M.(2006) Mitä lihavuus maksaa? Tuhti taakka terveydenhuollolle. *Duodecim*, p. 1213-4.

Pontiroli, A. E. & Morabito, A. (2011) Long-term prevention of mortality in morbid obesity through bariatric surgery. A systematic review and meta-analysis of trials performed with gastric banding and gastric bypass. *Ann Surg*, 253(3), 484-7.

Proczko, M. A., Stepaniak, P. S., de Quelerij, M., van der Lely, F. H., Smulders, J. F., Kaska, L. & Soliman Hamad, M. A. (2014) STOP-Bang and the effect on patient outcome and length of hospital stay when patients are not using continuous positive airway pressure. *J Anesth*, 28(6), 891-7.

Puzziferri, N., Roshek, T. B., 3rd, Mayo, H. G., Gallagher, R., Belle, S. H. & Livingston, E. H. (2014) Long-term follow-up after bariatric surgery: a systematic review. *Jama*, 312(9), 934-42.

Qaseem, A., Dallas, P., Owens, D. K., Starkey, M., Holty, J. E. & Shekelle, P. (2014) Diagnosis of obstructive sleep apnea in adults: a clinical practice guideline from theAmerican College of Physicians. *Ann Intern Med*, 161(3), 210-20.

Rasheid, S., Banasiak, M., Gallagher, S. F., Lipska, A., Kaba, S., Ventimiglia, D., Anderson, W. M. & Murr, M. M. (2003) Gastric bypass is an effective treatment for obstructive sleep apnea in patients with clinically significant obesity. *Obes Surg*, 13(1), 58-61.

Ribaric, G., Buchwald, J. N. & McGlennon, T. W. (2014) Diabetes and weight in comparative studies of bariatric surgery vs conventional medical therapy: a systematic review and meta-analysis. *Obes Surg*, 24(3), 437-55.

Rissanen, A., Heliövaara, M., Knekt, P., Reunanen, A., Aromaa, A. & Maatela, J. (1990) Risk of disability and mortality due to overweight in a Finnish population. *Bmj*, 301(6756), 835-7.

Rodriguez, J. E. & Campbell, K. M. (2016) Past, Present, and Future of Pharmacologic Therapy in Obesity. *Prim Care*, 43(1), 61-7.

Romeo, S., Maglio, C., Burza, M. A., Pirazzi, C., Sjöholm, K., Jacobson, P., Svensson, P. A., Peltonen, M., Sjöström, L. & Carlsson, L. M. S. (2012) Cardiovascular Events After Bariatric Surgery in Obese Subjects With Type 2 Diabetes, *Diabetes Care*, 2613-7.

Roslin, M. S., Cripps, C. & Peristeri, A. (2015) Bariatric and metabolic surgery: current trends and what's to follow. *Curr Opin Gastroenterol*, 31(6), 513-8.

Rubino, F., R'Bibo S, L., del Genio, F., Mazumdar, M. & McGraw, T. E. (2010) Metabolic surgery: the role of the gastrointestinal tract in diabetes mellitus. *Nat Rev Endocrinol*, 6(2), 102-9.

Rucker, D., Padwal, R., Li, S. K., Curioni, C. & Lau, D. C. (2007) Long term pharmacotherapy for obesity and overweight: updated meta-analysis. *Bmj*, 335(7631), 1194-9.

Sakran, N., Raziel, A., Goitein, O., Szold, A. & Goitein, D. (2016) Laparoscopic Sleeve Gastrectomy for Morbid Obesity in 3003 Patients: Results at a High-Volume Bariatric Center. *Obes Surg*, Jan 12. Epub ahead of print.

Salameh, J. R. (2006) Bariatric surgery: past and present. *Am J Med Sci*, 331(4), 194-200.

Sanchez-Pernaute, A., Herrera, M. A., Perez-Aguirre, M. E., Talavera, P., Cabrerizo, L., Matia, P., Diez-Valladares, L., Barabash, A., Martin-Antona, E., Garcia-Botella, A., Garcia-Almenta, E. M. & Torres, A. (2010) Single anastomosis duodeno-ileal bypass with sleeve gastrectomy (SADI-S). One to three-year follow-up. *Obes Surg*, 20(12), 1720-6.

Sareli, A. E., Cantor, C. R., Williams, N. N., Korus, G., Raper, S. E., Pien, G., Hurley, S., Maislin, G. & Schwab, R. J. (2011) Obstructive sleep apnea in patients undergoing bariatric surgery--a tertiary center experience. *Obes Surg*, 21(3), 316-27.

Sarkhosh, K., Switzer, N. J., El-Hadi, M., Birch, D. W., Shi, X. & Karmali, S. (2013) The impact of bariatric surgery on obstructive sleep apnea: a systematic review. *Obes Surg*, 23(3), 414-23.

Sawyer, A. M., Gooneratne, N. S., Marcus, C. L., Ofer, D., Richards, K. C. & Weaver, T. E. (2011) A systematic review of CPAP adherence across age groups: clinical and empiric insights for developing CPAP adherence interventions. *Sleep Med Rev*, 15(6), 343-56.

Schauer, D. P., Arterburn, D. E., Livingston, E. H., Coleman, K. J., Sidney, S., Fisher, D., O'Connor, P., Fischer, D. & Eckman, M. H. (2015) Impact of bariatric surgery on life expectancy in severely obese patients with diabetes: a decision analysis. *Ann Surg*, 261(5), 914-9.

Schirmer, B., Erenoglu, C. & Miller, A. (2002) Flexible endoscopy in the management of patients undergoing Roux-en-Y gastric bypass. *Obes Surg*, 12(5), 634-8.

Schlatzer, C., Schwarz, E. I. & Kohler, M. (2014) The effect of continuous positive airway pressure on metabolic variables in patients with obstructive sleep apnoea. *Chron Respir Dis*, 11(1), 41-52.

Seidell, J. C. & Halberstadt, J. (2015) The global burden of obesity and the challenges of prevention. *Ann Nutr Metab*, 66 Suppl 2, 7-12.

Sharaf, R. N., Weinshel, E. H., Bini, E. J., Rosenberg, J., Sherman, A. & Ren, C. J. (2004) Endoscopy plays an important preoperative role in bariatric surgery. *Obes Surg*, 14(10), 1367-72.

Sharkey, K. M., Machan, J. T., Tosi, C., Roye, G. D., Harrington, D. & Millman, R. P. (2010) Predicting obstructive sleep apnea among women candidates for bariatric surgery. *J Womens Health (Larchmt)*, 19(10), 1833-41.

Sharples, L. D., Clutterbuck-James, A. L., Glover, M. J., Bennett, M. S., Chadwick, R., Pittman, M. A. & Quinnell, T. G. (2015) Meta-analysis of randomised controlled trials of oral mandibular advancement devices and continuous positive airway pressure for obstructive sleep apnoea-hypopnoea. *Sleep Med Rev*, 27, 108-124.

Sjöström, L., Rissanen, A., Andersen, T., Boldrin, M., Golay, A., Koppeschaar, H. P. & Krempf, M. (1998) Randomised placebo-controlled trial of orlistat for weight loss and prevention of weight regain in obese patients. European Multicentre Orlistat Study Group. *Lancet*, 352(9123), 167-72.

Sjöström, L., Lindroos, A. K., Peltonen, M., Torgerson, J., Bouchard, C., Carlsson, B., Dahlgren, S., Larsson, B., Narbro, K., Sjöström, C. D., Sullivan, M. & Wedel, H. (2004) Lifestyle, diabetes, and cardiovascular risk factors 10 years after bariatric surgery. *N Engl J Med*, 351(26), 2683-93.

Sjöström, L., Narbro, K., Sjöström, C. D., Karason, K., Larsson, B., Wedel, H., Lystig, T., Sullivan, M., Bouchard, C., Carlsson, B., Bengtsson, C., Dahlgren, S., Gummesson, A., Jacobson, P., Karlsson, J., Lindroos, A. K., Lönroth, H., Näslund, I., Olbers, T., Stenlof, K., Torgerson, J., Agren, G. & Carlsson, L. M. (2007) Effects of bariatric surgery on mortality in Swedish obese subjects. *N Engl J Med*, 357(8), 741-52.

Sjöström, L., Peltonen, M., Jacobson, P., Sjöström, C. D., Karason, K., Wedel, H., Ahlin, S., Anveden, A., Bengtsson, C., Bergmark, G., Bouchard, C., Carlsson, B., Dahlgren, S., Karlsson, J., Lindroos, A. K., Lonroth, H., Narbro, K., Näslund, I., Olbers, T., Svensson, P. A. & Carlsson, L. M. (2012) Bariatric surgery and long-term cardiovascular events. *Jama*, 307(1), 56-65.

Sjöström, L. (2013) Review of the key results from the Swedish Obese Subjects (SOS) trial - a prospective controlled intervention study of bariatric surgery. *J Intern Med*, 273(3), 219-34.

Skubleny, D., Switzer, N. J., Gill, R. S., Dykstra, M., Shi, X., Sagle, M. A., de Gara, C., Birch, D. W. & Karmali, S. (2016) The Impact of Bariatric Surgery on Polycystic Ovary Syndrome: a Systematic Review and Meta-analysis. *Obes Surg*, 26(1), 169-76.

Smith, K. B. & Smith, M. S. (2016) Obesity Statistics. *Prim Care*, 43(1), 121-35.

Spieker, E. A. & Pyzocha, N. (2016) Economic Impact of Obesity. *Prim Care*, 43(1), 83-95.

Stenberg, E., Szabo, E., Agren, G., Näslund, E., Boman, L., Bylund, A., Hedenbro, J., Laurenius, A., Lundegardh, G., Lönroth, H., Moller, P., Sundbom, M., Ottosson, J. & Näslund, I. (2014) Early complications after laparoscopic gastric bypass surgery: results from the Scandinavian Obesity Surgery Registry. *Ann Surg*, 260(6), 1040-7.

Stenberg, E., Szabo, E., Agren, G., Ottosson, J., Marsk, R., Lönroth, H., Boman, L., Magnuson, A., Thorell, A. & Näslund, I. (2016) Closure of mesenteric defects in laparoscopic gastric bypass: a multicentre, randomised, parallel, open-label trial. *Lancet*, 387(10026), 1397-404.

Stroh, C., Kockerling, F., Volker, L., Frank, B., Stefanie, W., Christian, K., Christiane, B. & Thomas, M. (2016) Results of More Than 11,800 Sleeve Gastrectomies: Data Analysis of the German Bariatric Surgery Registry. *Ann Surg*, 263(5), 949-55.

Subak, L. L., King, W. C., Belle, S. H., Chen, J. Y., Courcoulas, A. P., Ebel, F. E., Flum, D. R., Khandelwal, S., Pender, J. R., Pierson, S. K., Pories, W. J., Steffen, K. J., Strain, G. W., Wolfe, B. M. & Huang, A. J. (2015) Urinary Incontinence Before and After Bariatric Surgery. *Jama Intern Med*, 175(8), 1378-87.

Tasali, E., Mokhlesi, B. & Van Cauter, E. (2008) Obstructive sleep apnea and type 2 diabetes: interacting epidemics. *Chest*, 133(2), 496-506.

Telem, D. A., Talamini, M., Shroyer, A. L., Yang, J., Altieri, M., Zhang, Q., Gracia, G. & Pryor, A. D. (2015) Long-term mortality rates (>8-year) improve as compared to the general and obese population following bariatric surgery. *Surg Endosc*, 29(3), 529-36.

Tolonen, P. (2008) Laparoscopic adjustable gastric banding for morbid obesity. Primary, intermediate, and long-term results including quality of life studies. *Acta Universitatis Ouluensis* D982.

Tuomilehto, H., Peltonen, M., Partinen, M., Seppä, J., Saaristo, T., Korpi-Hyövalti, E., Oksa, H., Saltevo, J., Puolijoki, H., Vanhala, M. & Tuomilehto, J. (2008) Sleep-disordered breathing is related to an increased risk for type 2 diabetes in middle-aged men, but not in women--the FIN-D2D survey. *Diabetes Obes Metab*, 10(6), 468-75.

Ulrik, C. S. (2016) Asthma and obesity: is weight reduction the key to achieve asthma control? *Curr Opin Pulm Med*, 22(1), 69-73.

Valencia-Flores, M., Orea, A., Herrera, M., Santiago, V., Rebollar, V., Castano, V. A., Oseguera, J., Pedroza, J., Sumano, J., Resendiz, M. & Garcia-Ramos, G. (2004) Effect of bariatric surgery on obstructive sleep apnea and hypopnea syndrome, electrocardiogram, and pulmonary arterial pressure. *Obes Surg*, 14(6), 755-62.

van Huisstede, A., Rudolphus, A., Castro Cabezas, M., Biter, L. U., van de Geijn, G. J., Taube, C., Hiemstra, P. S. & Braunstahl, G. J. (2015) Effect of bariatric surgery on asthma control, lung function and bronchial and systemic inflammation in morbidly obese subjects with asthma. *Thorax*, 70(7), 659-67.

Vanek, V. W., Catania, M., Triveri, K. & Woodruff, R. W., Jr. (2006) Retrospective review of the preoperative biliary and gastrointestinal evaluation for gastric bypass surgery. *Surg Obes Relat Dis*, 2(1), 17-22.

Vgontzas, A. N., Tan, T. L., Bixler, E. O., Martin, L. F., Shubert, D. & Kales, A. (1994)

Sleep apnea and sleep disruption in obese patients. *Arch Intern Med*, 154(15), 1705-11.

Victorzon, M., Peromaa-Haavisto, P. & Tolonen, P. (2012) Perioperative morbidity, mortality and early outcome of the first 360 gastric bypass operations performed in a district hospital. *Scand J Surg*, 101(3), 184-9.

Visscher, T. L. & Seidell, J. C. (2001) The public health impact of obesity. *Annu Rev Public Health*, 22, 355-75.

Wadden, T. A. & Stunkard, A. J. (1986) Controlled trial of very low calorie diet, behavior therapy, and their combination in the treatment of obesity. *J Consult Clin Psychol*, 54(4), 482-8.

Weingarten, T. N., Flores, A. S., McKenzie, J. A., Nguyen, L. T., Robinson, W. B., Kinney, T. M., Siems, B. T., Wenzel, P. J., Sarr, M. G., Marienau, M. S., Schroeder, D. R., Olson, E. J., Morgenthaler, T. I., Warner, D. O. & Sprung, J. (2011) Obstructive sleep apnoea and perioperative complications in bariatric patients. *Br J Anaesth*, 106(1), 131-9.

Weller, W. E. & Rosati, C. (2008) Comparing outcomes of laparoscopic versus open bariatric surgery. *Ann Surg*, 248(1), 10-5.

Wharton, S. (2016) Current Perspectives on Long-term Pharmacotherapy for Obesity. *Can J Diabetes*, 40(2), 184-91.

Wittgrove, A. C., Clark, G. W. & Tremblay, L. J. (1994) Laparoscopic gastric bypass, roux-en-Y: preliminary report of five cases. *Obes Surg*, 4, 353-7.

Wirth, A., Wabitsch, M. & Hauner, H. (2014) The prevention and treatment of obesity. *Dtsch Arztebl Int*, 111(42), 705-13.

World Health Organization. (2006) Obesity and Overweight. http://www.who.int/mediacentre/factsheets/fs311/en/

World Health Organization. (2014) Global status report on noncommunicable diseases 2014. Global target 7, 79-93. http://www.who.int/nmh/publications/ncd-status-report-2014/en/

Wong, H. M., Yang, W., Yang, J. & Wang, C. (2015) The value of routine gastroscopy before laparoscopic Roux-en-Y gastric bypass surgery in Chinese patients. *Surg Obes Relat Dis*, 11(2), 303-7.

Young, M. T., Gebhart, A., Phelan, M. J. & Nguyen, N. T. (2015) Use and Outcomes of Laparoscopic Sleeve Gastrectomy vs Laparoscopic Gastric Bypass: Analysis of the American College of Surgeons NSQIP. *J Am Coll Surg*, 220(5), 880-5.

Young, T., Evans, L., Finn, L. & Palta, M. (1997) Estimation of the clinically diagnosed proportion of sleep apnea syndrome in middle-aged men and women. *Sleep*, 20(9), 705-6.

Zeni, T. M., Frantzides, C. T., Mahr, C., Denham, E. W., Meiselman, M., Goldberg, M. J., Spiess, S. & Brand, R. E. (2006) Value of preoperative upper endoscopy in patients undergoing laparoscopic gastric bypass. *Obes Surg*, 16(2), 142-6.

Zhao, Y. & Encinosa, W. (2006) Bariatric Surgery Utilization and Outcomes in 1998 and 2004: Statistical Brief #23, *Healthcare Cost and Utilization Project (HCUP) Statistical Briefs*. Rockville (MD): Agency for Health Care Policy and Research (US)

10 Appendices

Appendix 1. Uniapnean oirekyselylomake

Appendix 2. Blankett för sömnapné symtomförfrågan

Appendix 1. Uniapnean oirekyselylomake

LIHAVUUS JA OBSTRUKTIIVINEN UNIAPNEA: ESIINTYVYYS JA MAHALAUKUN OHITUSLEIKKAUKSEN VAIKUTUS

NIMI: **Puh:**

Sukupuoli: _____ **Pituus/paino:** _____

Tupakoitteko? 1. En 2. Kyllä, määrä_____

Kuinka paljon käytätte alkoholia? (Kuinka monena päivänä viikossa tai kuukaudessa, kuinka suuria määriä?)

_____

Perussairaudet: _____

_____

Säännöllisesti käyttämänne lääkkeet: _____

_____

Viimeisen neljän viikon aikana kun olette nukkunut, olette tietääksenne kuorsannut

1. Koko ajan
2. Suurimman osan ajasta
3. Osan ajasta
4. Harvakseltaan
5. En ollenkaan
6. En osaa sanoa

Viimeisen neljän viikon aikana kuinka kuvailisitte/Teille on kuvattu kuorsaamistanne

1. En kuorsaa
2. Lievää
3. Kohtalaista
4. Kovaa
5. Erittäin kovaa
6. En osaa sanoa

Kuorsaamiseni herättää minut öisin/tekee minut väsyneeksi seuraavana päivänä

1. Pitää täysin paikkansa
2. Pitää osittain paikkansa
3. En osaa sanoa
4. Ei pidä paikkaansa
5. Ei pidä ollenkaan paikkaansa

Kuinka paljon kuorsaamisenne on häirinnyt nukkumistanne ja päivittäistä jaksamistanne viimeisen neljän viikon aikana?

1. Ei ollenkaan
2. Jonkin verran
3. Kohtalaisen paljon
4. Paljon
5. Erittäin paljon

Häiritseekö kuorsaamisenne puolisoanne?

1. Erittäin paljon
2. Paljon
3. Kohtalaisen paljon
4. Jonkin verran
5. Ei ollenkaan
6. En osaa sanoa

Verrattuna vuoden takaiseen, kuinka määrittelisitte kuorsaamistanne nyt?

1. Paljon vähäisempää kuin vuosi sitten
2. Jonkin verran vähäisempää kuin vuosi sitten
3. Melko samanlaista kuin vuosi sitten
4. Jonkin verran pahempaa kuin vuosi sitten
5. Paljon pahempaa kuin vuosi sitten

Kuinka puolisonne kuvailee kuorsaamistanne?

1. Erittäin kovaäänistä
2. Kovaäänistä
3. Melko kovaäänistä
4. Vaimeaa
5. En kuorsaa
6. En tiedä

Mikä seuraavista kuvaa parhaiten kuorsaamistanne?

1. En kuorsaa
2. Kuorsaan harvoin
3. Kuorsaan vain tietyssä nukkuma-asennossa
4. Kuorsaan suurimman osan nukkuma-ajasta
5. Kuorsaan jatkuvasti

Onko Teillä kuvattu olevan hengityskatkoja nukkuessanne?

1. Ei
2. Joskus
3. En osaa sanoa
4. Usein
5. Aina tai lähes aina

Nukutteko päiväunet?

1. En
2. Kyllä

Kuinka nopeasti nukahdatte yleensä illalla käydessänne nukkumaan?

1. 10 min. tai nopeammin
2. 10-30 min.
3. Yli 30 min.

Miten nukutte öisin, sen jälkeen kun olette nukahtanut?

1. Hyvin levottomasti
2. Melko levottomasti
3. En osaa sanoa
4. Melko rauhallisesti
5. Hyvin rauhallisesti

Montako kertaa heräätte tavallisesti öisin?

1. En kertaakaan
2. Kerran
3. 2 kertaa
4. 3-4 kertaa
5. Ainakin 5 kertaa

Oletteko kärsinyt unettomuudesta viimeisen kolmen kuukauden aikana?

1. Lähes joka yö
2. Usein
3. Toisinaan
4. Harvoin
5. En koskaan

Tunnetteko itsenne pirteäksi aamulla herättyänne?

1. Kyllä, hyvin pirteäksi
2. Melko pirteäksi
3. En osaa sanoa
4. Olen melko väsynyt
5. Olen hyvin väsynyt aamuisin

Onko Teillä päänsärkyä aamuisin?

1. Ei koskaan
2. Joskus harvoin
3. Toisinaan
4. Usein
5. Säännöllisesti

Oletteko käyttäneet viimeksi kuluneen kolmen kuukauden aikana unilääkkeitä?

1. En koskaan
2. Joskus harvoin
3. Toisinaan
4. Usein
5. Säännöllisesti

Oletteko joskus nukahtanut ajaessanne esim. autoa?

1. En koskaan
2. Kyllä, kerran
3. 2 kertaa
4. 3-4 kertaa
5. Ainakin 5 kertaa

Oletteko koskaan joutunut liikenneonnettomuuteen väsymyksen takia?

1. En koskaan
2. Kyllä, kerran
3. 2 kertaa
4. 3-4 kertaa
5. Ainakin 5 kertaa

Onko työkykynne ollut mielestänne alentunut?

Viimeisen 3 kuukauden aikana
1. Kyllä,_____vrk
2. Ei

Viimeisen vuoden aikana
1. Kyllä,_____vrk
2. Ei

Arvio torkahtamisen todennäköisyydestä (rengasta oikea vaihtoehto):

	Todennäköisyys, että torkahdatte?			
Tilanne:	**En torkahda koskaan**	**Pieni**	**Kohtalainen**	**Suuri**
Istun lukemassa	0	1	2	3
Katson TV:tä	0	1	2	3
Istun passiivisena julkisessa paikassa (esim. teatteri tai esitelmätilaisuus)	0	1	2	3
Olen matkustajana autossa keskeytyksettä tunnin ajan	0	1	2	3
Lepään makuuasennossa iltapäivällä olosuhteiden sen salliessa	0	1	2	3
Istun puhumassa jonkun kanssa	0	1	2	3
Istun kaikessa rauhassa alkoholittoman lounaan jälkeen	0	1	2	3
Istun autossa sen pysähdyttyä liikenteessä muutamaksi minuutiksi	0	1	2	3

Appendix 2. Blankett för sömnapné symtomförfrågan

ÖVERVIKT OCH OBSTRUKTIV SÖMNAPNÉ: FÖREKOMST OCH INVERKAN AV BYPASSOPERATION AV MAGSÄCKEN

Blankett för symtomförfrågan

Undersökningens nummer

Namn: **Tel:**

Kön: _____ **Längd/vikt:** _____

Röker ni? 1. Nej 2. Ja, mängd_____

Hur stort är ert alkoholbruk? (Hur många dagar i veckan eller månaden, hur stora mängder?) _____

Grundsjukdomar: _____

_____

De mediciner som ni använder regelbundet: _____

_____

Vet ni om ni har snarkat när ni har sovit under de senaste fyra veckorna

1. Hela tiden
2. Största delen av tiden
3. En del av tiden
4. Sällan
5. Inte alls
6. Kan inte säga

Hur skulle ni beskriva ert snarkande/hur har ert snarkande beskrivits åt er under de senaste fyra veckorna

1. Jag snarkar inte
2. Lindrigt
3. Måttligt
4. Svårt snarkande
5. Mycket svårt snarkande
6. Kan inte säga

Mitt snarkande väcker mig på nätterna/gör mig trött följande dag

1. Stämmer helt
2. Stämmer delvis
3. Kan inte säga
4. Stämmer inte
5. Stämmer inte alls

Hur mycket har ert snarkande stört sovandet och ert dagliga orkande under de senaste fyra veckorna?

1. Inte alls
2. En aning
3. Tämligen mycket
4. Mycket
5. Riktigt mycket

Stör ert snarkande er maka/make?

1. Riktigt mycket
2. Mycket
3. Tämligen mycket
4. En aning
5. Inte alls
6. Kan inte säga

Hur skulle ni definiera ert snarkande nu jämfört med ett år tillbaka?

1. Mycket mindre än för ett år sedan
2. En aning mindre än för ett år sedan
3. Ganska likadant som för ett år sedan
4. En aning värre än för ett år sedan
5. Mycket värre än för ett år sedan

Hur beskriver er maka/make ert snarkande?

1. Mycket högljutt
2. Högljutt
3. Ganska högljutt
4. Dämpat
5. Jag snarkar inte
6. Jag vet inte

Vilket av följande beskriver ert snarkande?

1. Jag snarkar inte
2. Jag snarkar sällan
3. Jag snarkar bara i viss sömnställning
4. Jag snarkar största delen av sovtiden
5. Jag snarkar ständigt

Har man berättat att ni har andningsuppehåll när ni sover?

1. Nej
2. Ibland
3. Kan inte säga
4. Ofta
5. Alltid eller nästan alltid

Tar ni tupplurer på dagen?

1. Nej
2. Ja

Hur snabbt somnar ni i allmänhet när ni går och sover?

1. 10 min. eller snabbare
2. 10-30 min.
3. Över 30 min.

Hur sover ni på nätterna efter att ni har somnat?

1. Mycket oroligt
2. Ganska oroligt
3. Kan inte säga
4. Ganska lugnt
5. Mycket lugnt

Hur många gånger vaknar ni i allmänhet på nätterna?

1. Inte en enda gång
2. En gång
3. 2 gånger
4. 3-4 gånger
5. Åtminstone 5 gånger

Har ni lidit av sömnlöshet under de senaste tre månaderna?

1. Nästan varje natt
2. Ofta
3. Ibland
4. Sällan
5. Aldrig

Känner ni er pigg då ni vaknar?

1. Ja, mycket pigg
2. Ganska pigg
3. Kan inte säga
4. Jag är ganska trött
5. Jag är mycket trött på morgnarna

Har ni huvudvärk på morgnarna?

1. Aldrig
2. Någon gång sällan
3. Ibland
4. Ofta
5. Regelbundet

Har ni använt sömnmediciner under de senaste tre månaderna?

1. Aldrig
2. Någon gång sällan
3. Ibland
4. Ofta
5. Regelbundet

Har ni någon gång somnat t.ex. när ni kört bil?

1. Aldrig
2. Ja, en gång
3. 2 gånger
4. 3-4 gånger
5. Åtminstone 5 gånger

Har ni någon gång hamnat i en trafikolycka p.g.a. trötthet?

1. Aldrig
2. Ja, en gång
3. 2 gånger
4. 3-4 gånger
5. Åtminstone 5 gånger

Har er arbetsförmåga varit nedsatt enligt er egen åsikt?

Under de senaste tre månaderna
1. Ja,_____dygn
2. Nej

Under det senaste året
1. Ja,_____dygn
2. Nej

Uppskattning över att ni slumrar till (ringa in rätt alternativ):

	Sannolikheten att ni slumrar till?			
	Jag slumrar aldrig till	**Liten**	**Måttlig**	**Stor**
Situation:				
Jag sitter och läser	0	1	2	3
Jag ser på TV	0	1	2	3
Jag sitter passiv på offentlig plats (t.ex. teater eller föreläsningstillfälle)	0	1	2	3
Jag är passagerare i bil utan avbrott i en timmes tid	0	1	2	3
Jag vilar i liggande ställning när omständigheterna tillåter	0	1	2	3
Jag sitter och pratar med någon	0	1	2	3
Jag sitter i lugn och ro efter en alkoholfri lunch	0	1	2	3
Jag sitter i bilen då den har stannat i trafiken ett par minuter	0	1	2	3

TACK FÖR ERA SVAR!