Roux-en-Y Gastric Bypass

Hand-assisted Laparoscopy and Investigation of the Excluded Stomach

BY

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ACTA UNIVERSITATIS UPSALIENSIS
UPPSALA 2003
ABSTRACT


Roux-en-Y gastric bypass (RYGBP) sustains weight loss and ameliorates diseases common in the morbid obese (BMI>40 kg/m²), but leaves the stomach and duodenum inaccessible. Morbidly obese patients have increased operative risks and in other fields minimal surgery is known to facilitate the postoperative course.

The aim of this thesis was to evaluate hand-assisted laparoscopy in RYGBP and develop techniques to study the excluded stomach.

The hand-assisted technique was developed in 13 patients and subsequently compared to open surgery in a blinded, prospective, randomised trial of 50 patients. Hand-assistance was feasible with a low need for conversions or re-operations. The duration of surgery was longer (150 versus 85 minutes) and postoperative results were similar to those in open surgery. Thus, the patients did not appear to derive benefits from hand-assisted laparoscopy. Interventional radiology accessed the excluded stomach and allowed endoscopy, barium studies and acid measurements. Chronic gastritis and low acid production were found. After RYGBP, 8 of 22 patients (36%) had duodenogastric bile reflux (DGBR), when studied by HIDA-scintigraphy. No DGBR was seen among controls. The gastric mucosa was evaluated by serology (pepsinogen I (PGI), H. pylori and H,K-ATPase) in 64 patients before and 1-4 years after operation. RYGBP, in contrast to gastric restriction, had reduced PGI levels postoperatively. According to serology, the mucosa is atrophic or in a resting state.

This study focuses on safety in RYGBP. Hand-assisted laparoscopy was feasible, but not favourable compared to an optimised open procedure. The excluded stomach is no longer inaccessible and characterised by chronic gastritis, low acid production and frequent bile reflux.

Key words: Gastric bypass, morbid obesity, laparoscopy.
To my family
This thesis is based on the following papers, which will be referred to in the text by their Roman numerals (I-V)


II Sundbom M and Gustavsson S. Hand-assisted Laparoscopic versus Open Roux-en-Y Gastric Bypass: A Prospective, Randomised Study. Submitted for publication.


V Sundbom M, Mårdh E, Mårdh S, Öhrvall M, Gustavsson S. Reduction in Serum Pepsinogen I After Roux-en-Y Gastric Bypass. Accepted for publication in J Gastrointest Surg

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<td>AGB</td>
<td>Adjustable gastric banding</td>
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<td>BAO</td>
<td>Basal acid output</td>
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<td>BMI</td>
<td>Body mass index</td>
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<td>BPD</td>
<td>Bileo-pancreatic diversion</td>
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<tr>
<td>CCK</td>
<td>Cholecystokinin</td>
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<td>CLO</td>
<td>Campylobacter like organism</td>
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<td>CRP</td>
<td>C-reactive protein</td>
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<td>CT</td>
<td>Computed tomography</td>
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<td>DGBR</td>
<td>Duodeno-gastric bile reflux</td>
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<td>HIDA</td>
<td>Hepatic iminodiacetic acid</td>
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<tr>
<td>H,K-ATPase</td>
<td>Hydrogen potassium adenosine tri-phosphatase</td>
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<td>H. pylori</td>
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<tr>
<td>Lap-RYGBP</td>
<td>Laparoscopic Roux-en-Y gastric bypass</td>
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<tr>
<td>LCD</td>
<td>Low calorie diet</td>
</tr>
<tr>
<td>JIB</td>
<td>Jejuno-ileal bypass</td>
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<tr>
<td>MAO</td>
<td>Maximal acid output</td>
</tr>
<tr>
<td>NIH</td>
<td>National Institute of Health</td>
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<tr>
<td>NSAID</td>
<td>Non-steroid anti-inflammatory drugs</td>
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<tr>
<td>PPI</td>
<td>Proton-pump inhibitor</td>
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<tr>
<td>PGI</td>
<td>Pepsinogen I</td>
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<td>PCA</td>
<td>Patient controlled analgesia</td>
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<td>RYGBP</td>
<td>Roux-en-Y gastric bypass</td>
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<tr>
<td>VBG</td>
<td>Vertical banded gastroplasty</td>
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<tr>
<td>WHR</td>
<td>Waist hip ratio</td>
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<td>WHO</td>
<td>World Health Organisation</td>
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</table>
Introduction

In the last 20 years, the number of obese people has doubled [1] and obesity has become the most common form of malnutrition [2]. It is paradoxical that in a world where millions of humans are dying of hunger and starvation, many others suffer from overeating. By damaging our health, reducing the quality of our lives, and leading us to a premature death, obesity is becoming the greatest health problem in the developed world [3, 4].

Food type and availability are the most likely reasons for the upward drift in the prevalence of obesity during the last decades. However, the recent explosion is considered the result of rapidly decreasing levels of physical activity [5]. The most common obesity-related complications are non-insulin-dependent diabetes, high blood pressure, myocardial infarction, sleep apnoea, joint problems, gallbladder disease and some cancers [4, 6, 7]. Obese people report a lower quality of life than the population at large [8, 9]. People who suffer from obesity bear the double burden of a serious health hazard and a social stigma.

Dietary modification with an increase in physical activity and reduction in sedentary habits forms the basis of obesity therapy. Low calorie diets (LCD) can be used to replace meals and there are also drugs on the market to help promote weight loss. Unfortunately, for most obese patients these medical treatments are unsuccessful in the long run.

At present, surgery is necessary to counter extreme obesity [10-15]. However, most surgical procedures imply major life-long rearrangement of the gastrointestinal tract to obtain the massive weight reduction. The changes in gastrointestinal physiology can often be controlled by medication and supplements, but not all long-term effects are fully understood. In addition, obese patients have an increased risk of complications secondary to surgery, such as wound dehiscence [16], hernias [17, 18], pneumonia [19] and pulmonary
embolism [20]. In spite of all precautions, operative mortality is one percent. The patient must be aware of these risks and be committed to lifelong follow-up.

The introduction of minimal invasive techniques in general surgery has given patients benefits in form of reduced postoperative pain, earlier mobilisation, shorter hospital stay and reduced sick leave. Obesity was initially considered a contraindication and laparoscopic surgery in the morbid obese has mainly been performed in specialised centres due to the technical difficulties. The results have been promising and the interest from patients and surgeons in laparoscopic surgery for morbid obesity is now enormous.

The development of surgical treatment has been investigational. The different procedures can be divided into two categories: gastric restrictive and malabsorptive. Gastric restriction mechanically prevents the patient from overeating and the latter interferes with the absorption of ingested nutrients. Roux-en-Y gastric bypass (RYGBP) has components of both principles and is well tolerated by the patients. RYGBP is known to sustain weight loss and ameliorate diseases common in the morbid obese [10-12, 21]. However, the stomach and duodenum are bypassed and concerns have been raised about the environment in the excluded stomach.

This thesis focuses on the safety of the Roux-en-Y gastric bypass and has evolved along two different lines. First, we have studied the role of minimal invasive surgery for RYGBP, in particular the so-called hand-assisted laparoscopic technique. Second, we have been concerned about the environment in the inaccessible excluded stomach and studied the state of the gastric mucosa and postoperative changes in gastrointestinal physiology.
Background

BMI

A number of methods are used to determine whether an individual is overweight or obese. Body mass index, BMI, has been found by body densitometry studies to indicate most accurately the degree of “fatness” for all heights [22]. BMI is defined as weight in kilograms divided by height in meters squared.

\[ \text{BMI} = \frac{\text{kg}}{\text{m}^2} \]

Normal weight is defined as a BMI between 18 and 25 kg/m². WHO identifies overweight as a BMI above 25 kg/m² and obesity above 30 kg/m² [1]. A BMI > 40 kg/m² implies morbid obesity, a term that will be used extensively in this summary. In the American literature, morbid obesity can sometimes be defined as being 100 pounds (~ 45 kg) overweight.

<table>
<thead>
<tr>
<th>Height (m)</th>
<th>&gt;25 kg</th>
<th>&gt;30 kg</th>
<th>&gt;40 kg</th>
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<tr>
<td>1.70</td>
<td>72 kg</td>
<td>87 kg</td>
<td>116 kg</td>
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<tr>
<td>1.80</td>
<td>81 kg</td>
<td>97 kg</td>
<td>130 kg</td>
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<tr>
<td>1.90</td>
<td>90 kg</td>
<td>108 kg</td>
<td>144 kg</td>
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</table>

BMI does not consider whether the excess weight is due to fat or muscular tissue, neither does it reflect the distribution of fat in the body. Studies indicate that abdominal fat is more hazardous than fat concentrated around the hips [23, 24]. This can be measured by waist circumference and waist-hip circumference ratio, WHR.

Excess body weight, EBW, is used to describe weight above an ideal weight. The ideal weight is often taken from the 1983 Metropolitan Life Statistics Table [25] and used as a reference when describing weight loss after surgery. The excess weight lost is presented in percent of the original excess body weight, EWL%. The concomitant use of BMI and EWL% in European and
American studies, respectively, is confusing and does not facilitate comparisons. However, the use of BMI is gaining in popularity.

**Prevalence**

The prevalence of obesity is epidemic. A majority of adults in Western societies are overweight and approximately 20% are obese (BMI > 30) [1]. In the last 20 years, the number of obese people has nearly doubled [4]. It is estimated that 5 to 6 million Americans are morbidly obese (BMI > 40). In some subgroups, such as Afro-American women aged 40 to 60, individuals with morbid obesity exceed 10% [26].

Throughout the world obesity is increasing and a similar pattern as that in the USA is occurring in most of Europe, several South American and Asian countries [1]. In Sweden, the number of overweight 18-year-olds was 6% in 1971 and had risen to 16% in 1995. Today, the number of obese Swedes is estimated to be 500,000.

The aetiology of morbid obesity is multifactorial. Current research suggests that in genetically predisposed individuals, factors related to lifestyle (diet and exercise) and society, culture and behaviour determine whether or not obesity develops [5, 27-31].

**Risks with morbid obesity**

Young overweight people of both sexes die sooner than their lean contemporaries [32]. A twelve-fold increase in mortality in the 25- to 34-year age group and a six-fold increase in the 35- to 44-year age group have been described among morbidly obese [3].

The most frequent co-morbid conditions to morbid obesity are:

- Cardiovascular; hypertension, atherosclerosis, heart failure and angina pectoris
- Metabolic; hyperlipidemia, impaired glucose tolerance and non-insulin-dependent diabetes mellitus
- Respiratory; dyspnea, sleep apnea and pulmonary embolism
• Gastrointestinal; hepatic steatosis, gallbladder disease, and colon carcinoma
• Genitourinary; infertility, amenorrhea, incontinence, breast and prostate carcinoma
• Degenerative; arthritis of weight-bearing joints, chronic venous insufficiency, hernias, and fungal skin infections
• Psychological; depression, isolation and loss of self-esteem

Several of these improve or even disappear with an appropriate weight reduction [20, 33, 34]. Weight loss may also have an additional benefit in the psychological aspects of morbid obesity improving quality of life [9, 35].

Non-operative treatment
Diet and increase in physical activity are conventional strategies in obesity management. Patients need to change food preparation, adopt to low-fat products, reduce take-away foods as initial dietary changes, as well as reduce portion size. LCD can be used to replace all meals for several weeks or single meals over a longer period, often 3-4 months. At present, the choice of pharmacotherapy is limited and not targeted. In Sweden, two drugs are approved orlistat (Xenical®) [36, 37] and sibutramine (Reductil®) [38]. In morbid obese, the non-operative methods are seldom effective in achieving significant long-term weight loss [39].

Operative treatment
Since 1954 surgery has been performed in an attempt to control severe overweight. These surgical procedures have been called bariatric after Baros, Greek for fat. Bariatric surgery, like all other surgical interventions, has been developmental and has had an incidence of failure. However, the outcome has improved steadily, mainly during the last 10 to 20 years [40].

Several bariatric procedures are currently used, having a variety of advantages and drawbacks. Most bariatric procedures have a mortality rate of about 1% and an early postoperative morbidity of 10% or more (wound infections, various
pulmonary problems, thrombosis or stomal stenosis). However, the most serious complications, anastomotic leaks and pulmonary embolism occur, in only 1%. The operative treatment does not involve removal of any adipose tissue and is in no way cosmetic. After the massive weight loss however, plastic surgery is often required.

The demand for bariatric surgery is rising world-wide. The understanding of the serious obesity-related morbidity, in the general public and among health care professionals, has increased markedly during the past decade. The continuous improvement in both safety and long-term integrity of the surgical procedures, and the introduction of laparoscopic techniques have resulted in a “boom” for bariatric surgery. In 2001, the number of bariatric procedures in the USA was 40,000; in 2002, it was projected to be 86,000 [41]. This can be compared to 6,425 in 1992 [42].

**Indications for bariatric surgery**

According to the National Institute of Health (NIH) consensus [43] and the established criteria for bariatric surgery as expressed by the International Federation of Surgery for Obesity (IFSO) [44], the weight requirement for an operation is a BMI > 40 kg/m², or > 35 in the presence of severe co-morbidity. All patients should have failed in long-term professional weight reduction programs including medication. The option of surgical treatment should be offered to patients who are well informed and able to participate in treatment. Patients with manifest psychopathology that jeopardises co-operation in long-term follow-up may need to be excluded. A multidisciplinary team should evaluate all patients and the operation should be performed at well-equipped medical centres capable of managing all types of surgical complications. This team has also the responsibility to arrange the life-long follow-up program after surgery. At present, only adults (> 18 years) are accepted for bariatric surgery. Morbid obesity has even affected the adolescents and some
centres have operated on adolescents with good results [45, 46].

**Evolution of bariatric procedures**

Various surgical procedures have been tried for the treatment of obesity, many of which later proved to have serious complications precluding their use. The more powerful the procedure is, the greater the risk of gastrointestinal complications and nutritional deficiencies.

**Intestinal bypass**

The fact that individuals who had the short-bowel syndrome lost weight led to the performance of the jejuno-colic bypass in the 1950s. The intestinal limb lengths used resulted in persisting fluid and electrolyte imbalance, and liver failure.

These major disadvantages led to the development of the **jejuno-ileal bypass** (JIB) in the 1960s.
The JIB was performed by anastomosing the proximal jejunum to the distal ileum.

The malabsorption resulted in weight loss. Initial fluid and electrolyte imbalances were controllable, but renal stones, migratory polyarthritis, abdominal bloating and liver dysfunction followed. These required close surveillance and gave JIB a bad reputation. The weight loss was good (60% loss of excess body weight) and many patients alive today would have died without their JIBs.

In spite this powerful modification, the digestive tract was able to adapt by proliferation of the intestinal epithelium, leading to weight regain in the long run. The JIB is nowadays only performed by a few surgeons after additional modifications.

**Gastric bypass**

Ed Mason observed in the 1960s, that most patients lost weight after gastric resection (Billroth II) and he developed the gastric bypass for weight loss surgery [47]. The major part of the stomach was bypassed, instead of resected, to produce early satiety and sustained weight loss with fewer surgical complications. He divided the stomach horizontally across the upper fundus and anastomosed a jejunal loop to the greater curvature. The early results were good, but the procedure resulted in a high incidence of bile reflux to the gastric pouch and ulcers in the anastomosed jejunum. The high frequency of bile gastritis was reduced by changing the jejunal loop to a Roux limb [48]. The gastric fundus would often dilate and could reach large proportions, allowing the patient to resume large food intake. Mason reoriented the gastric pouch to the lesser curvature and developed another bariatric procedure, the vertical banded gastroplasty (VBG) [49]. This vertical lesser-curvature pouch was included in Roux-en-Y gastric bypass in 1983 [50]. In 1993, the operation was adapted to laparoscopy by Wittgrove and Clark [51]. This has increased its popularity, making RYGBP the most performed bariatric procedure worldwide today [42].
We have chosen RYGBP as our standard procedure and have performed almost 400 operations since 1996. We create a small completely transsected gastric pouch on the lesser curvature by linear staplers. The Roux limb is made 50-75 cm long and placed behind the transverse colon and excluded stomach. It is anastomosed to the gastric pouch by staplers or hand suturing.

The RYGBP produces massive weight loss and is well tolerated by the patients. However, bypassing the stomach and duodenum has two disadvantages, nutritional deficiencies and the inaccessibility.

**Nutritional deficiencies**

Iron, B\textsubscript{12}, folic acid and fat-soluble vitamin A, D, and E deficiencies occur. Iron is absorbed in the duodenum and jejunum in the ferrous form and after RYGBP, the absorption in the first 50-cm of the jejunum (the Roux limb) is severely limited due to achlorhydria [52]. Vitamin B\textsubscript{12} absorption is severely affected by difficulties of releasing the protein-bound vitamin [53, 54] and insufficient secretion of intrinsic factor [55]. Therefore vitamin B\textsubscript{12} must be available at doses compatible with passive diffusion rather than dependent on the intrinsic factor mechanism. We encourage all patients to take daily dietary supplements of vitamins and minerals, and we prescribe vitamin B\textsubscript{12} to all patients and iron to menstruating women. During pregnancy supplements must be increased and liaison between the obstetrician and bariatric surgeon is
necessary. The absorption of ethanol is fast and results in higher peak concentrations after RYGBP [56]. This is noticed by several patients as an enhanced feeling of inebriation. This rapid absorption, due to the absence of normal stomach emptying might also have implications for the pharmacological effect of other drugs. This phenomenon could exist also in patients after total gastrectomy.

The mucosa in the excluded stomach

The unknown fate of the bypassed segments is a major drawback. The excluded stomach and entire duodenum are not readily available for radiographic or endoscopic examinations. The fundus pouch has been studied after the earlier loop gastric bypass by endoscopy. Frequent findings were chronic gastritis, bile reflux, and occasional intestinal metaplasia [48, 57-59]. There are only sparse reports on the excluded stomach after RYGBP, probably due to its inaccessibility. Eight patients, in a series of 3000, had bleeding from the bypassed segment that did not respond to conservative treatment and required gastric resection [60]. Eleven patients, out of 4300, had perforated peptic duodenal or gastric ulcer [61] and two cases of gastric cancer has been reported [62, 63].

The state of the gastric mucosa can now be assessed by a combination of serological tests: S-pepsinogen I, antibodies against H. pylori and H,K-ATPase. This analysis has been developed as a screening test for selecting patients for endoscopy [64]. Serum pepsinogen levels have also been correlated to pernicious anaemia [65, 66], ulcers [67] and Helicobacter pylori infection [68]. In Japan, measurements of serum pepsinogens have been used as a screening test to detect subjects with extensive atrophic gastritis, who have a high risk of developing gastric cancer [69-71]. The accuracy is as good as the routine photofluorography [72].
Vertical Banded Gastroplasty, VBG

In the mid-1970s, Mason and Printen performed the first horizontal gastroplasties [73]. They failed to control weight because the pouch was too large and the outlet on the greater curvature not stabilized. In 1980, Gomez refined the procedure by enforcing the outlet by a nonabsorbable, seromuscular suture [74], but the fundus distended easily. The stomach was therefore partitioned vertically, as mentioned above, and the outlet reinforced by a band, creating the vertical banded gastroplasty, VBG [49].

The pouch was made by stapling a hole near the lesser curvature and from there stapling the front and back wall of the stomach together up to the angel of Hiss. The narrow channel was calibrated by a 28- to 32-Fr boogie and a collar of Marlex mesh reinforced the outlet. VBG had a high frequency of vertical staple line rupture leading to passage of food into the main stomach and subsequent weight regain. This was overcome by dividing the stomach, instead of just stapling it together.

VBG has been used for several years; it is reputable and rather straightforward to perform. The attraction of VBG is the maintained passage through the duodenum, which preserves iron, phosphate and calcium absorption, and normal vitamin D metabolism [75]. However, many patients suffer frequent reflux and vomiting, due to the restrictive outlet. VBG is still used today, but has lost its supremacy to RYGBP [42].
**Bilio-Pancreatic Diversion, BPD**

The bilio-pancreatic diversion was designed in the late 1970s by Nicola Scopinaro [76] to overcome the bacterial overgrowth in the blind loop of the jejuno-ileal bypass, JIB.

The distal part of the stomach is resected to avoid marginal ulceration and restricts food intake initially. The small bowel is divided 250 cm proximal to the ileo-cecal valve and anastomosed to the gastric remnant. The bilio-pancreatic limb (from the duodenum) is anastomosed 50 cm proximal to the ileo-cecal valve, to form a 200-cm alimentary limb and a 50-cm common limb. The digestion with juices from the upper gastrointestinal tract can only occur in these most distal 50 cm of ileum. Cholecystectomy is done to prevent gallstone problems.

The weight loss is related to restriction of food intake and maintained by malabsorption of starches and fats in the common limb. BPD provides the greatest weight loss (80% excess weight loss) but requires close long-term follow-up since severe nutritional deficiencies may develop.

**BPD with Duodenal Switch**

The original BPD by Scopinaro has been modified by Hess and Marceau [13, 77] into the BPD with duodenal switch.

The greater curvature of the stomach is resected, instead of the distal part, leaving the pylorus intact. The
alimentary limb is anastomosed to the divided duodenum (and stomach) proximal to the entry of the common bile duct. The biliopancreatic limb is connected 100 cm proximal to the ileocecal valve, creating a common limb for absorption. Dumping and marginal ulceration is reduced by the intact pylorus and sleeve gastrectomy, which also produces initial weight loss.

The metabolic drawbacks are similar to those of the original BPD. Super obese patients (BMI>60 kg/m²) benefit particularly from this procedure, since it produces massive weight loss [78]. The BPD with duodenal switch can also be used when correcting severe complications after adjustable gastric banding, since no pouch or anastomosis has to be created at the scarred proximal stomach [79].

**Gastric Banding**

In the 1970s, a restricting band of fixed length was placed around the upper part of the stomach to achieve gastric partitioning without stapling. However, it was difficult to achieve the optimal stoma diameter at surgery. If the band was too loose, weight reduction was minimal or absent and if the stoma was too tight, the proximal pouch would dilate and the patient would experience gastro-oesophageal reflux and frequent vomiting. Band slippage or migration was other problems. A few surgeons reported good results in large series [80, 81].

BPD with Duodenal Switch
Adjustable Gastric Banding, AGB

Most bariatric surgeons had disappointing experiences with the fixed band. This stimulated the development of adjustable inflatable devices in the late 1980s [82, 83].

A non-elastic band equipped with an inflatable silicon balloon on the gastric side is placed around the stomach creating the small proximal reservoir. The balloon is connected to a subcutaneous injection port, and adding or removing fluid postoperatively changes the inner diameter of the stoma.

The weight loss is inferior to that obtained by the more complex methods, but the main advantage of AGB is simplicity: laparoscopic placement and no alteration of the normal anatomy. There are two large manufacturers and more than 80,000 bands have been placed, mostly in Europe. There are concerns about reflux-oesophagitis, vomiting due to band slippage, pouch dilatation and band erosions into the stomach. Long-term follow-up has shown that the AGB method is far from ideal. The cumulative re-operation rate has been 10 to 58% [84-87]. Revisional operations after band erosions are challenging from a technical point of view and are associated with increased morbidity.
Summary of bariatric procedures used today:

<table>
<thead>
<tr>
<th></th>
<th>AGB</th>
<th>VBG</th>
<th>RYGBP</th>
<th>BPD with DS</th>
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<tbody>
<tr>
<td>Type of procedure</td>
<td>Restrictive</td>
<td>Restrictive</td>
<td><strong>Restrictive/ Malabsorptive</strong></td>
<td>Malabsorptive</td>
</tr>
<tr>
<td>Excess weight loss (%)</td>
<td>40-50</td>
<td>40-50</td>
<td><strong>50-70</strong></td>
<td>60-80</td>
</tr>
<tr>
<td>Relief of co-morbidities</td>
<td>Good</td>
<td>Good</td>
<td><strong>Very good</strong></td>
<td>Excellent</td>
</tr>
<tr>
<td>Advantages</td>
<td>No changed metabolism of ingested foods.</td>
<td><strong>Well tolerated</strong></td>
<td>Very durable results.</td>
<td></td>
</tr>
<tr>
<td>Disadvantages</td>
<td>Band erosion.</td>
<td>Staple line breakdown</td>
<td><strong>B₁₂ and iron deficiency</strong></td>
<td>Protein and calorie malnutrition</td>
</tr>
<tr>
<td></td>
<td>Inadequate weight loss and frequent vomiting.</td>
<td><strong>Dumping</strong></td>
<td>Diarrhoea, gas, and kidney stones</td>
<td></td>
</tr>
</tbody>
</table>
Laparoscopy

Laparoscopy has become a major part of general surgery with the introduction of laparoscopic cholecystectomy in the late 1980s. This new operative technique has started a worldwide revolution of minimal invasive surgery for abdominal surgeons and the development of new instruments and operative procedures. Today, there is a strong demand of laparoscopy from both patients and surgeons, even in bariatric surgery.

Laparoscopy is an old technique of examining the abdominal cavity and its contents. In 1901, Kelling introduced a cystoscope in the abdominal cavity of a dog during high-pressure insufflation of air and Jacobeus reported on laparoscopy in humans ten years later. In 1937, Veres described the use of a needle for the creation of pneumoperitoneum [88] and Hasson later developed a blunt trocar to eliminate the blind puncture of the abdominal wall [89]. Semm, a gynaecologist, performed the first laparoscopic appendectomy in 1983 - a major contribution to the development of laparoscopy in general surgery [90]. In 1985, Muhe performed the first laparoscopic cholecystectomy, but was poorly received [91]. Finally, the technique spread throughout the world and has become a stimulus for expanding the possibilities of minimal invasive procedures in general surgery [92].

The presented benefits of laparoscopy are earlier mobilisation, reduced postoperative pain, shorter hospital stay and shorter sick leave in comparison with the corresponding open procedure. The risk of incisional hernias, as well as intra-abdominal adhesions is also diminished [93]. Laparoscopic appendectomy, inguinal hernia repair, and hiatal hernia fundoplication have become common surgical procedures. All types of gastrointestinal surgery, and even autopsy can be performed laparoscopically [94].
Laparoscopy in bariatric surgery

Laparoscopy requires special skills of the surgeon and morbid obesity poses an added challenge. The establishment of pneumoperitoneum, exposure and intra-abdominal dissection is more demanding due to the large quantity of fat. Laparoscopy in morbidly obese is also associated with other problems, such as impaired respiratory function, high intra-abdominal pressure and liver steatosis contributing to the lack of exposure.

The laparoscopic approach in bariatric surgery began in 1991 with the development of the Lap-band for adjustable gastric banding [82]. In 1994, the band became available and has engendered heated discussions among bariatric surgeons. Nevertheless, placement of an adjustable band is the least invasive operative procedure that can be offered to patients with morbid obesity. In 1993, Wittgrove and Clark started to perform laparoscopic Roux-en-Y gastric bypass (lap-RYGBP) [51]. A complex bariatric procedure like lap-RYGBP, where extensive dissection is necessary and multiple anastomoses are constructed is a major challenge for the laparoscopic surgeon. The procedure is recognised to be one of the most difficult laparoscopic procedures in general surgery [95]. The learning curve has been shown to be very long. Besides, to obtain good results one must perform a large number of these procedures on a regular basis, which is why lap-RYGBP is performed mainly in large specialised centres [12, 96, 97].

A survey of the American Society for Bariatric Surgery in 1999 revealed that only 3% of all bariatric cases in the USA were done by laparoscopy, but this number will probably rise in the near future.

Nguyen has compared lap-RYGBP to open procedures in several randomised studies. Patients have significantly less impairment of pulmonary function after lap-RYGBP than open on the first three days [98]. The systemic stress was similar, but concentrations of ACTH, C-reactive protein and IL-6 were lower after lap-RYGBP. These findings may suggest less operative trauma [99]. The
postoperative length of stay was shorter after laparoscopy, three versus four days. Furthermore, wound-related complications, such as infection (1.3 vs. 10.5%) and incisional hernia (0 vs. 7.9%) were less frequent after laparoscopy [16].

On the other hand, the operative time is prolonged and side-effects peculiar to the laparoscopic approach must be avoided. Urinary output is lower throughout the operation, probably due to the increased intra-abdominal pressure [100]. The prolonged pneumoperitoneum does not impair cardiac function if proper attention is taken to intravascular volume resuscitation and normal acid-base status, at least in patients without compromised cardiac function [101]. The trocars must be placed in the direction of the operative field through the rich subcutaneous fat; otherwise, too much force is needed to obtain the correct angle making the handling of the instruments less sensitive. The defects in the fascia are difficult to close and hernias have been described, at all trocar sites and of all sizes [102, 103]. In addition, hernias never encountered in open surgery have resulted, such as the Petersen’s hernia between the Roux limb and mesocolon.[104, 105]

**Hand-assisted laparoscopy**

Lack of tactile gnosis is a problem inherent in most types of laparoscopic procedures and is especially unfavourable in technically demanding procedures. In 1995, Cuschieri and Shapiro described an extracorporeal pneumoperitoneum access bubble [106] and different hand-assisted devices have subsequently been developed. The hand-assisted device is applied in the abdominal wall and seals airtight against the surgeon’s wrist, allowing him or her a helping hand in the abdomen with maintained pneumoperitoneum.

The development of hand-assisted laparoscopic techniques for advanced procedures in other fields, such as splenectomy [107], colo-rectal surgery [108] and living-donor nefrectomy [109] has been promising. More than 100 hand-assisted procedures have been
now described in the literature, including pancreatico-duodenotomy [110] and abdominal aortic aneurysm repair [111]. The reports on hand-assistance in morbid obese subjects include adjustable gastric banding, VBG, RYGBP and BPD with duodenal switch and are reviewed in Seminars of Laparoscopic Surgery 2001 by Sundbom and Gustavsson [112]. Forstieri et al found that hand-assistance facilitated the placement of the adjustable gastric band and in VBG the technique has been used by Watson [113], Gerhart [114] and Vasallo [115], both for correction or first choice operation. The main advantage was increased control, here in positioning the circular stapler for the gastric hole and subsequent mesh.
Aims of the Thesis

This thesis deals with two different issues. First, we wanted to evaluate the use of hand-assistance, proposed to be valuable in other demanding laparoscopic procedures. Second, we wanted to establish an access route to the bypassed stomach and design a variety of techniques to investigate the changes in gastrointestinal physiology and to evaluate the gastric mucosa over time.

The specific aims of the different studies were:

I to develop a new laparoscopic operative technique by hand-assistance to reduce our high conversion and re-operation rate in laparoscopic Roux-en-Y gastric bypass;

II to compare our hand-assisted laparoscopic technique for RYGBP to the conventional open procedure in a prospective, randomised study;

III to obtain access to the excluded stomach after RYGBP by means of interventional radiology, and to perform endoscopy with biopsy and measure the production of hydrochloric acid;

IV to study the occurrence of duodeno-gastric bile reflux to the excluded stomach by HIDA-scintigraphy (99mTc-labelled mebrofenin);

V to evaluate the state of the gastric mucosa before and after RYGBP by means of serology (pepsinogen I, antibodies towards H. pylori and K,H-ATPase)
Material and Methods

Paper I:
Thirteen consecutive women with median age of 38 (26-53) years and BMI of 45 (38-50) kg/m², not previously operated on for morbid obesity, accepted to have their Roux-en-Y gastric bypass (RYGBP) performed by hand-assisted laparoscopy. All patients had undergone a thorough medical work-up and were motivated to undergo surgical treatment. Five patients had previously undergone open cholecystectomy and six patients had had lower abdominal operations. The hand-assisted device was introduced through a right subcostal incision after merely separating the muscle fibres. In one patient, we placed the hand-assisted device in the upper part of a previous midline-incision. The operative technique developed for the hand-assisted laparoscopic RYGBP is described in detail below. Patient controlled analgesia (PCA) with intravenous morphine was used. Per- and postoperative data ware collected. All patients were seen at a clinical visit 4-6 weeks postoperatively and in complying patients a gastroscopy was performed to evaluate the gastrojejunostomy.

Paper II:
Fifty patients (45 women and 5 men) with a median age of 38 years (19-54) and a median BMI of 44 kg/m² (34-54) scheduled for Roux-en-Y gastric bypass were randomised to either hand-assisted laparoscopic or open operation. The RYGBP technique was identical for both procedures (a small totally transsected pouch, a >50-cm retrocolic and retrogastric Roux limb, and a gastrojejunostomy by a 21-mm circular stapler) and is described in detail below. The randomisation was done after the induction of anaesthesia. Dressings were applied for both techniques and the selected operative technique was blinded for the patient and staff at the ward. The amount of morphine taken by the patients themselves (PCA) was recorded daily. C-reactive protein (CRP) was measured as an indicator of inflammatory response and systemic stress. Per- and postoperative data were collected
continuously. At discharge, a two-week sick leave was given and subsequently prolonged, if needed. The patients were examined at 1, 6 and 12 twelve months.

**Technical description of the hand-assisted laparoscopic Roux-en-Y gastric bypass, used in paper I and II**

The patient was placed supine in a slight anti-Trendelenburg position. The surgeon stood on the patient’s right side and the assistant on the left. We used an 8-cm right subcostal incision for the hand-assisted device, and divided the subcutaneous fat by blunt fraction. The rectus fascia was incised and the muscle separated in the fibre direction, usually without cutting muscle tissue. The hand-assisted device was applied and the surgeon introduced his left hand into the abdomen. He could protect the intra-abdominal contents while the first 10-mm trocar was introduced in the supraumbilical region. The 45-degree laparoscope was inserted, pneumoperitoneum applied and four additional trocars introduced under direct vision in the direction of the operative field.

The enlarged left lobe of the liver was kept aside with a steel retractor. The gastrophrenic ligaments were exposed and incised with cautery and by gentle finger dissection the lesser sac was entered from above. Next the flaccid part of the lesser omentum was opened and the lesser sac entered below the coronary vein. The intra-abdominal hand could easily remove adhesions between the back wall of the stomach and the retroperitoneum creating pathways for the coming EndoGia blue 45-mm linear staplers (Tyco Healthcare).
At a distance of 4 cm from the angle of Hiss, a third opening into the lesser sac was made by finger dissection, very close to the lesser curvature of the stomach. The **gastric pouch** was divided horizontally by linear stapler and next a gastrotomy was made on the anterior corpus by cautery. The helping hand was withdrawn and re-entered with the anvil of the 21-mm circular stapler (Ethicon Endo-surgery). It was passed through the gastrotomy by a 10-mm Anvil grasper (Ethicon Endo-surgery) and taken out near the horizontal gastric staple line at the intended position of the gastro-jejunal anastomosis. A linear stapler closed the gastrotomy. The proximal pouch was completely separated from the remaining stomach by two cutting linear staplers directed towards the angle of Hiss.

The ligament of Treitz was identified after retracting the transverse colon and the major omentum cranially. The small bowel was transsected with a linear stapler 20 to 30 cm further distally without dividing the small bowel mesentery.

The **Roux limb** was made more than 50 cm long and the enteroanastomosis was stapled side-to-side using linear stapler. The intra-abdominal hand was used to manipulate the small bowel, totally avoiding maltreatment by laparoscopic instruments. The mesocolon was

![Diagram of surgical procedure](image-url)
opened near the ligament of Treitz, where the distance to the retrogastric bursa is short. A purse-string suture was placed in-between the lower part of the mesocolon, the ligament of Treitz and the root of the small bowel mesentery, for future closure of this defect to prevent entrapment of the small bowel. The surgeon could digitally check that the retrocolic window was wide enough and placed the Roux limb beside the proximal gastric pouch without tension or rotation.

The circular stapler was introduced through a jejunotomy into the Roux limb as shown in the earlier figure. The circular stapler created the end-to-end gastrojejunostomy and was left obturating the porthole. A linear stapler closed the jejunotomy and the Roux limb was straightened by hand from below the mesocolon. The purse-string suture was tied and three interrupted sutures were placed between the serosa of the Roux limb and the mesocolon to prevent internal hernias. The circular stapler was removed after placing absorbable sutures in the fascia laparoscopically. A running suture and PDS loop closed the incision for the hand-assisted device. All skin incisions were closed by sutures.

The entero-enterostomy is made side-to-side by linear staplers.
Open RYGBP
An identical procedure was performed, using laparoscopic instruments, through a short upper midline incision always sparing the periumbilical region. The incision was closed by a PDS loop and skin sutures.

Paper III:
Three men, 50 to 64 years old, experienced obscure gastrointestinal bleeding six months to seven years after RYGBP. They had tarry stools and required blood transfusions repeatedly. A thorough investigation with repeated upper endoscopies and colonoscopy could not find the bleeding lesion. In this clinical situation, we needed to examine the excluded stomach to rule out serious disease. We therefore developed a technique for percutaneous access to the excluded stomach, which was first identified by a CT scan. Under local anaesthesia and light sedation, a guide wire was introduced into the stomach using ultrasound guidance. A pigtail catheter (Ch 14) was introduced with Seldinger technique. One to two weeks later, the gastrostomy channel was dilated to 18 Ch. The excluded stomach and duodenum were examined by percutaneous endoscopy with multiple histological biopsies. Conventional barium studies were also done. The pigtail catheter could also be used for subsequent determination of gastric acid. We measured the basal acid output (BAO) and maximal acid output (MAO), after pentagastrin stimulation (0.5 mg sc). Serum gastrin and serology for H. pylori were studied. Four women, 38 to 63 years old, with gastrostomy catheters after complicated RYGBP, served as controls in the acid determinations.

Paper IV:
Twenty-two patients with a median age of 44 (30-58) years and a BMI of 29 (17-38) kg/m² were studied 18 (13-33) months after RYGBP by HIDA-scintigraphy to evaluate the rate of duodeno-gastric bile reflux (DGBR) to the excluded stomach. Nine patients had had previous cholecystectomy. ⁹⁹ᵐ⁻Tc-labelled mebrofenin was given intravenously and the fate of the tracer was recorded every 2 minutes for 90 minutes in a dual-head gamma camera. The bile flow was enhanced by
intravenous cholecystokinin (CCK, 20 dog units) given 20 minutes after the mebrofenin injection in the first 15 patients. Two of these patients had a repeated examination without CCK. The excluded stomach was visualised by $^{99m}$Tc-pertechnetate in the last 12 patients. Eight patients with a median age of 48 (35-67) years and of BMI 24 (23-25) kg/m$^2$ who had not undergone upper gastrointestinal surgery served as controls. They were examined due to suspected liver disease during this period at the same laboratory. In all patients both anterior and posterior images were recorded, allowing subsequent computer analysis.

**Paper V:**

We evaluated the gastric mucosa in 64 patients before and one to four years after surgery for morbid obesity by a combination of serological tests: S- pepsinogen I (PGI), antibodies against H. pylori and H,K-ATPase. Thirty-four patients (mean age 39 years and mean BMI 44 kg/m$^2$) had a RYGBP excluding the stomach and duodenum. Thirty patients (42 years and BMI 44 kg/m$^2$) had simple gastric restriction (10 VBG and 20 adjustable gastric banding) not altering the normal passage of food through the stomach and duodenum. Sera were obtained at the study intervals and kept at $-70^\circ$ C. Clinical data, especially abdominal pain and the use of PPI, were collected in all patients. The serological probe had been constructed and evaluated against endoscopic biopsies at the University of Linköping, Sweden. All our tests were analysed in duplicates at that laboratory in the same run: PGI by Gastroset$^\circledR$ and the antibodies by in-house ELISA.

**Statistics**

The results are presented as median and range in paper I, II, III, and IV. In paper V mean, standard deviation and range are used. Comparisons between groups were conducted using t-tests and the chi-squared test. P values of less than 0.05 were defined as significant. In paper V univariate and multivariate associations were evaluated. Details are given in each paper.
Results and Discussion

Paper I:

Results
The hand-assisted device could be successfully placed and allowed good working conditions in all patients. Duration of surgery (including learning-curve time) was 205 minutes (135-280). One patient (8%) was converted to full laparotomy for a safe closure of a small perforation of the proximal gastric pouch caused by the anvil of the circular stapler. In another patient, a small accidental gastric perforation caused by a Babcock clamp was closed by laparoscopically placed sutures. The amount of morphine taken by the patients (PCA) during postoperative day 1-3 was in median 45, 32 and 18 mg, respectively. All patients made an uneventful recovery and the postoperative hospital stay was 5 days (4-7). No sign of leakage, pneumonia or deep venous thrombosis was seen. At the clinical visit after 4-6 weeks, weight loss was 14 (12-23) kg. Two patients needed endoscopic dilatation of a relative stricture at the gastro-jejunostomy.

Discussion
Laparoscopic RYGBP is considered one of the most technically demanding laparoscopic procedures, since it requires creation of two anastomoses and dissection in two operative fields, i.e. above and below the transverse colon and greater omentum. The large amounts of intra-abdominal fat in the morbid obese contribute to a major lack of exposure, which makes the lack of tactile gnosis especially unfavourable.

The hand-assisted technique was feasible. In comparison with our earlier study by Westling et al [116], the conversion rate was reduced (23% to 8%). In retrospect, we could even have completed the converted operation by suturing the small rupture at the horizontal staple-line laparoscopically, as we did for the instrumental perforation. No patient developed any sign of Roux-limb obstruction, which occurred in as many as 20% in our previous total lap-RYGBP. To focus on the new technique, all 13 operations were performed during three months by two surgeons, alternating as surgeon
and assistant. We decided to use the 21-mm circular stapler to facilitate the creation of the gastro-jejunostomy. We chose to enter the anvil through a small gastrotomy, as described by de la Torre [117] and Hedenbro [118], since the transoral route is controversial [119] and possibly dangerous [119-121].

We believe that hand-assistance has four main advantages: the blind abdominal puncture with the Veres’ needle is avoided, the hand can be used for dissection, for handling the small bowel and checking a newly constructed anastomosis, and for exposure of the surgical field.

In a thick abdominal wall, even the ordinary blind puncture with the Veres’ canula can be difficult. The use of an open approach to introduce a Hassan trocar is not so easy through the thick subcutaneous fat. By first establishing the hand-assisted device we could introduce one hand into the abdomen and guide the introduction of the first trocar.Entry access injuries occur in total laparoscopy [122] and the small bowel is the most commonly injured organ, often with a delayed diagnosis [123]. Vascular injuries are a major cause of death from laparoscopy, second only to anaesthesia, with a mortality rate of 15% [124]. Studying injury-based data, Chandler found 506 injuries, resulting in 65 deaths (13%). Most injuries were severe (bowel or retroperitoneal vascular injuries in 76%) and done when establishing primary entry access [125]. Aortic injuries have been reported even with the use of a Hasson trocar [126]. The complication rates for urologic laparoscopic surgery on massively obese patients (BMI>30), were higher than in the general population undergoing laparoscopic surgery, 21% and 0.3%, respectively [127].

The surgeon’s hand can be used for dissection of the tissue as an alternative to conventional laparoscopic instruments. The tactile gnosis was an invaluable complement to pure vision, especially in opening the retrogastric bursa and creating the mesocolic tunnel for the Roux limb. The laparoscopic dissectors are at least 8 times less sensitive than the human
hand [128] and not optimal [129], with a low percentage of successful grasping [130]. For a surgeon, the performance of the hand is superior to any mechanical device.

One can handle delicate structures, such as the small bowel, more safely than with a Babcock clamp. High pressures are generated at the tip of laparoscopic dissectors locally on the tissue [131], resulting in damage or even perforation, as in our patient. In addition, a small accidental perforation can pass unnoticed. The patency of a newly constructed anastomosis can be checked by the thumb and index finger. If the entero-enterostomy is too narrow there is an increased risk both for leakage at the gastro-jejunostomy and gastric distension with subsequent blow-out. After having fired the gastro-jejunostomy, the circular stapler is not easy to remove, since it has to pass through the inverted tissue at the fragile anastomosis. The countertraction by the intra-abdominal hand increases the surgeon’s comfort level during this disengagement.

In bariatric surgery, large amounts of intra-abdominal fat contribute to a severe lack of exposure. The left lobe of the enlarged fatty liver has to be held aside when working at the lesser curvature. The steel retractors constructed for normal weight patients are sometimes not sufficient and can tear the fragile capsule and hepatic parenchyma, resulting in annoying bleeding. The mere handling of the fatty transverse colon and thick omentum can be difficult. The intra-abdominal hand can reliably handle the adjacent organs, while total laparoscopy of course requires mechanical retractors.

In addition, the hand is also in place should sudden major haemorrhage occur. Moreover, a difficult bowel anastomosis or concomitant cholecystectomy can be performed through the incision for the hand, should this be necessary. Undoubtedly, hand assistance provides more control during a difficult operation.

The drawback of the hand-assisted technique is of course the 8-cm incision for the hand, which could omit the
benefits of laparoscopy. In addition, the hand-assisted technique places the intra-abdominal hand in awkward positions not encountered during open surgery, which can result in fatigue and ache. The hand-assisted device itself provides wrist and forearm constriction that can result in numbness [132]. These difficulties are related to the surgeon's experience and length of the procedure. The cost of the hand-assisted device is probably justified by the reduction in theatre time.

Four devices are now available: the Dexterity Pneumo Sleeve® (Dexterity Surgical Inc), the HandPort System® (Smith and Nephew Endoscopy), the Intromitt® (MedTech), and the LapDisc® (Ethicon Endosurgery). They have similar working mechanism, but specific advantages and disadvantages. The Dexterity Pneumo Sleeve is applied by an adhesive base to the skin after pneumoperitoneum has been obtained. Failure to maintain pneumoperitoneum and skin reactions from the adhesive have been described. In addition, the device does not eliminate the blind puncture of the abdominal wall for the creation of pneumoperitoneum. The HandPort System is secured by an intra-abdominal ring with an inflatable outer portion. After the device is placed, the surgeon can guide the introduction of the first trocar (for subsequent pneumoperitoneum) by the intra-abdominal hand. Both these two devices require an additional sleeve. The Intromitt has a taut valve and is secured to the abdominal wall by an adhesive flange. An insufflation port on the device is used to establish pneumoperitoneum and the hand can then be introduced without the use of an extra sleeve. The LapDisc consists of two rings to create an iris effect. The device is placed around the surgeon's hand and inserted into the abdomen. The seal around the gloved intra-abdominal hand is tightened by turning the rings and pneumoperitoneum applied by a separate trocar. In addition, instruments can be placed through this device by tightening the iris valve even more.

Schweitzer et al [133] have reported another approach to the hand-assisted
technique for RYGBP, by using the Dexterity Sleeve. They had to start the operation by applying pneumoperitoneum with a Visiport, since, as already mentioned, the adhesive layer of this device requires the abdomen to be distended for an airtight seal. The incision for the sleeve was placed in the midline, near the umbilicus, to be able to elongate the incision should a full laparotomy become necessary. Furthermore, the proximal small bowel was eviscerated for the construction of the entero-enteroanastomosis. We have by using the HandPort System been able to protect the intra-abdominal contents while introducing the first trocar. Our operative technique has been totally intra-abdominal, withdrawing the hand only for the introduction of the 21-mm anvil.

At one year, the weight loss was 42 kg and the BMI 28 kg/m², i.e. fairly similar to conventional open RYGBP. One patient, who had endoscopic balloon-dilatation due to stenosis, has later been re-operated due to recurring strictures. No patient has developed incisional hernia or small bowel obstruction. Obstruction due to adhesions is rare, but RYGBP can be followed by a specific and potentially dangerous complication, namely internal herniation of the small bowel [104, 134]. Three internal hernias are created: the Petersen hernia (behind the mesentery of the Roux limb), beside the Roux limb in the mesocolon [135], and at the entero-enterostomy [136]. We believed that the hand-assistance facilitated the closure of these defects at the primary operation. Aggressive operative treatment is warranted in RYGBP patients with severe cramping abdominal pain whose symptoms have no other obvious explanation [105].

At that time, we were very satisfied with our hand-assisted technique for laparoscopic RYGBP. In 2000, we started study II; a prospective, randomised trial between hand-assisted laparoscopic and open RYGBP to evaluate the new technique.
Paper II:

Results
Duration of surgery in the hand-assisted laparoscopic and open group was 150 (110-265) and 85 (60-150) minutes, respectively, (p<0.001). The median peroperative bleeding was 250 ml in both groups. One patient in each group required two units of blood, due to postoperative anaemia. The median amount of morphine taken by the patients (PCA) for postoperative day 1-3 was for the hand-assisted group 48, 36, and 28 mg, respectively. The corresponding values for the open group was 32, 30, and 25 mg, respectively. The total amount of morphine required after hand-assisted and open operation during the three first postoperative days was in median 98 and 66 mg, respectively. The systemic inflammatory response, as measured by C-reactive protein, did not differ between the groups. One patient in the hand-assisted group was re-operated due to leakage from the gastro-jejunostomy. She was treated by large bore drains and intravenous antibiotics, and made a full recovery. The median postoperative stay was 6 days in both groups. Six patients (12%) needed endoscopic dilatation of a relative stricture in the gastro-jejunostomy, two after hand-assisted laparoscopy and four after open surgery. There was no difference in wound or pulmonary complications. The sick leave could be evaluated in 40 patients and was in the hand-assisted and open group, 30 and 37 days, respectively. The median weight loss was 13 kg 4-6 weeks postoperatively in both groups. It was at one year, 39 kg after hand-assisted and 41 kg after open operation, resulting in a BMI of 29 and 30 kg/m², respectively. Accordingly, BMI had been reduced by 14 and 15 units. At one year, one symptomatic incisional hernia was seen in the open group.

Discussion
The hand-assisted laparoscopic procedure felt very stable and there was no need for conversions to open surgery. The operative time was acceptable, 150 minutes. It even decreased by 55 minutes, from 205 minutes in the pilot study (paper I). Our earlier problem in total
laparoscopy, obstruction of the Roux-limb in the mesocolon was still absent. However, the hand-assisted technique had no benefits, compared to the open procedure, in terms of reduced morphine consumption, postoperative hospital stay or sick leave.

In comparing the two techniques, one must remember that our open group was favoured by the use of laparoscopic instruments. The advancement in laparoscopic surgery has supplied new surgical instruments with many attributes (jaw design, long shafts and handles) which make them especially valuable in the deep, obese abdomen. The standard GIA or TA stapler can be technically difficult to position across the stomach in patients with a large, immobile left hepatic lobe. The long shaft of the laparoscopic EndoGIA stapler allows the working handpiece of the instrument to remain outside the abdomen when constructing the gastric pouch, which improves visualisation. The division of the proximal stomach can be made under better control reducing the risk of leakage and remaining gastro-gastric fistula. The new stapler with roticulating head can be used in especially demanding situations. The laparoscopic ultrasonic coagulating shears can also simplify tissue dissection and division of small vessels, but has not been used in this study, except to fenestrate a liver cyst in one patient. The routine use of laparoscopic instruments in open RYGBP has recently been advocated by Harold [137].

The upper-abdominal incision could, using laparoscopic instruments be short, 12-15 cm, and always spare the periumbilical region. This could facilitate postoperative mobilisation and reduce the increased risk of incisional hernia. The open procedures performed in this study might therefore not be representative of ordinary open RYGBP performed in clinical routine. However, in planning the present study we thought it was correct, from a scientific point of view, to make all efforts to achieve the best outcome in both groups.
The most crucial part of the procedure, often done at the end of a demanding laparoscopy, is construction of the gastro-jejunostomy. We decided to use the circular stapling technique for this anastomosis, since it is completely automatic and obviates the need for hand suture. Leakage from the gastro-jejunostomy is one of the most feared complications after RYGBP. The clinical symptoms can be vague, tachycardia, general discomfort and impaired oxygenation [138], as in our patient and justify an immediate Gastrograffin swallow [139]. At laparotomy, the defect in the anastomosis can often not be visualised and surgically repaired, but large bore drains are most important. A few leakages are contained within the retrogastric bursa with no free contrast seen in the abdomen. These can perhaps, in selected cases, be treated by percutaneous drains and intravenous antibiotics, not laparotomy. Several methods have been tried to reduce leakage: oversewing the staple lines [140], invaginating the anastomosis, methylene-blue test [141], air insufflation under water [142], peroperative endoscopy [143], reinforcing the anastomosis by tissue glue or bio-membrane [144, 145], and routine use of drains [146]. Most centres report leakage in 0.5 to 3% of primary RYGBP [134, 142, 147-150]. We have a rate of 1% without using any of these techniques routinely. Even if a leakage is diagnosed early and treated adequately, patients may die.

We used the smallest stapler (21 mm), according to Wittgrove et al [12], to achieve a stoma of standardised width with restrictive properties. However, the incidence of strictures in the gastro-jejunostomy requiring endoscopic balloon dilatation was rather high (12%). In a recent report of Gonzalez [151], the stricture rate was 31% for the 21-mm circular stapler, compared to 3% for a hand sewn anastomosis, which they now favour. According to our recent experience a lower incidence of strictures can be obtained by using the 25-mm circular stapler. An added advantage of this stapler is the tilting anvil head, which facilitates its removal after completing the anastomosis.
The length of **postoperative stay** as reported in the present study (6 days in median) might seem long. As stated in the paper, the in-hospital stay depends on many factors and varies between centres using the same operative technique. Our patients are not motivated to an early discharge for economic reasons, due to the socialised medical system. However, this should have been affected both groups equally and not biased our comparison.

We found a low incidence of symptomatic **incisional hernias**, only one (4%) in the open group. This is probably a reward for leaving the periumbilical region intact. The hand-assisted device was placed in a right-subcostal incision and the midline incisions were always short. DeMaira et al place the hand-assisted device supraumbilical and report a 20% rate of hernias [152]. The same group has in an earlier study of 968 patients found greater risk of incisional hernia in morbid obese than in steroid-dependent patients, 20% and 4%, respectively [17]. Brolin et al have, in a randomised study of 229 patients, closed the midline incision extended to the umbilicus by either interrupted figure-eight technique by non-absorbable sutures or continuous double-stranded PDS. They report incisional hernias in 18 and 10%, respectively, during the 30 months follow-up [18]. Jones [153] performs open RYGBP through a left subcostal incision and reports few hernias.

**The main finding** in this prospective, randomised study was that the patients do not appear to derive significant benefit from having their RYGBP performed by the hand-assisted laparoscopic technique in comparison to open surgery. Initially, when the hand-assisted approach was introduced into our surgical practice, we were rather enthusiastic about the results of this new technique [154]. However, now that we have appropriate controls it appears that we have lost the benefits of laparoscopy. Also, DeMaria et al [152] have found that hand-assistance does not improve patient outcome and increases costs when compared to the open procedure. Many arguments in favour of the hand-assisted technique
(tactile gnosis, eased dissection and orientation) are in fact arguments for open surgery.

I am personally disappointed by our results. The hand-assisted laparoscopic technique has been valuable for our climb on the learning curve, but to obtain all the proposed benefits the operation has to be done by total laparoscopy [16, 116]. The learning curve for total laparoscopy is long, at least 75 to 100 cases [96, 155] for an individual surgeon. In Sweden, the annual number of potential laparoscopic cases would be about 30 to 40 at the largest hospitals. It is therefore questionable whether one can acquire enough experience to perform this technically demanding procedure with good results in these conditions.

Paper III:
Results
Access to the excluded stomach was obtained without complications. We could perform endoscopy, barium studies and measurements of the gastric acid output through the gastrostomy. Neither endoscopy nor barium studies showed any ulcers, post-ulcerous deformities or tumours in the excluded stomach or duodenum. Mucosal biopsies revealed chronic antral gastritis in all patients and intestinal metaplasia in one. CLO test, histology and culture for H. pylori were all negative. The basal acid output (BAO) was 0-2.6 mmol/h and the maximal acid output (MAO), after pentagastrin stimulation, was 0.6 to 9.0 mmol/h. These values are lower than the reference value for normal persons. Serum gastrin was normal and serology for H. pylori was negative in all patients.

Discussion
The excluded stomach is a potential hazard. The fact that the excluded stomach and duodenum cannot be studied by conventional endoscopy or barium studies may lead to a delay in diagnosis of a serious disease. It is an accepted clinical rule that patients with alarm symptoms from the upper gastrointestinal tract should undergo endoscopy to exclude malignancy. After RYGBP, an exploratory laparotomy with gastrostomy may be the
only alternative to confidently exclude serious gastric disease.

In our experience access to the excluded stomach has been needed in less than one percent of the cases; hence the routine placement of a gastrostomy tube in the bypassed stomach [156] or a radio-opaque marker [157] seems unnecessary. Retrograde endoscopic intubation of the excluded stomach and duodenum has been used in the earlier gastric bypass procedure with a loop gastro-jejunostomy [48, 57]. The currently favoured retrogastric, retrocolic Roux-en-Y technique makes endoscopic intubation of the afferent loop almost impossible, due to the sharp angle at the entero-enterostomy. CT-guided catheter placement [158] and direct Chiba needle punction [159] have been used in selected cases. We believe that ultrasonographic guidance is technically easier and safer to perform. Virtual CT endoscopy is now being introduced for examination of the colon [160] and also demonstrated for lesions in the excluded stomach [161].

We were able to exclude serious disease in the stomach and duodenum as the cause for the bleeding episodes in our patients. However, the actual cause of the bleeding remains obscure [162]. A temporal relation with cessation of PPI therapy indicates that overlooked stomal ulcers could be the cause in spite of the repeated normal upper endoscopies. We were also able to confirm that the mucosa in the excluded stomach showed histological changes of chronic gastritis and intestinal metaplasia. The future clinical significance of these mucosal changes is not known, but still worrying. The excluded stomach could harbour quiet dysplastic progression.

The amount of acid produced in the excluded stomach was less than expected when compared to the reference values for normal persons [163]. Mason [164, 165] and Printen [165] has earlier described this in the loop gastric bypass. The increase in acid production after stimulation by pentagastrin proves that the parietal cells in the excluded stomach still react to stimuli.
Most gastrostomies have bile-stained fluid, implying duodeno-gastric bile reflux. Bile reflux is known to cause chronic gastritis after subtotal gastrectomy, which can promote an increased risk of malignancy in the long-term [166-169]. We therefore wanted to investigate the occurrence of bile reflux to the excluded stomach after RYGBP.

**Paper IV: Results**

The examination was easily tolerated by all patients. Eight (36 %) of the RYGBP patients had scintigraphic evidence of duodenogastic bile reflux (DGBR). The tracer appeared in the excluded stomach after a median of 28 (21-45) min after the mebrofenin injection. DGBR occurred equally often in patients with or without scintigraphic evidence of a functioning gallbladder. A semi-quantitative analysis showed that most of the tracer was transported in an aboral direction and the amount found in the excluded stomach did not exceed 20 % in any patient. However, the radioactivity remained in the excluded stomach throughout the study period of 90 minutes.

Repeat examinations were performed without cholecystokinin (CCK) in two RYGBP patients and confirmed the presence of DGBR. The tracer appeared in the excluded stomach at about the same time in the first examination (with CCK), as in the second (without CCK). In addition, three patients without a history of cholecystectomy were found to have a non-functioning gallbladder.

No scintigraphic evidence of DGBR was found in any of the eight controls. Three were found to have a non-functioning gallbladder. The suspected liver disease did not disturb the tracer’s conjugation to the bile, giving an examination of good quality in which
the distribution of the tracer was easy to follow.

**Discussion**

We performed this exploratory study to investigate whether, and to what extent, DGBR occurred after RYGBP. To our surprise, DGBR occurred in as much as 36% of the patients. In addition, the bile-refluxate was not emptied from the excluded stomach during the study time. This leads to a prolonged and enhanced interference of bile with the gastric mucosa, since it cannot be diluted by ingested food and normal gastric contents after RYGBP.

DGBR has been postulated to contribute to the development of gastritis and the increased risk of malignancy after partial gastrectomy [167, 168, 170-172]. The risk is estimated to be increased by a factor of two or three when evaluated 15-20 years postoperatively [166]. Bile reflux is also a component in oesophagitis [173] and a potential component in the development of Barrett’s oesophagus [174]. DGBR in individuals with an intact upper gastrointestinal tract is unusual. None of our controls had any scintigraphic evidence of DGBR. Although the gastric bypass procedure does not involve manipulation of the antroduodenal area, the physiology of the upper gastrointestinal tract is profoundly changed after RYGBP. Bile flow is co-ordinated from the gastroduodenal area by nervous and hormonal pathways and the absence of passing food could disturb this tuning system leading to bile reflux.

HIDA-scintigraphy has been a reliable method to determine enterogastric reflux after partial gastrectomy [175-177]. The method is non-invasive and determines the fate of labelled bile without disturbing tubes or endoscopes, simulating physiological conditions. Moreover, all images are recorded and allow later assessment. Special regions of interest can be identified and specific indexes calculated, based on the amount of measured activity [178].
This high incidence of bile reflux warranted additional evaluation of the mucosa in the excluded stomach.

**Paper V:**

**Results**

Serum pepsinogen I

Before surgery, serum Pepsinogen I (PGI) was 69.3 µg/l and 65.1 µg/l in the RYGBP and control group, respectively, not significantly different.

One year postoperatively, all RYGBP patients, except one, had developed a reduced PGI titre. The reduction was on average 18.7 µg/l. In addition, eight patients (24%) showed abnormally low values, i.e. below the reference value of 28 µg/l (not shown in the figure).

![Graph showing RYGBP, change in PGI one year postop](image-url)
In the control group, the mean reduction in pepsinogen I was 3.7 µg/l at one year. No clear pattern was seen among the individual patients, as illustrated in the figure. The difference between RYGBP and controls, -18.7 µg/l and -3.7 µg/l, respectively, was statistical significant (p<0.0001). One to four years postoperatively, the change in mean PGI for the RYGBP patients (-13.7, -12.8, -16.6, and -12.5 µg/l) remained throughout the study and was highly significant compared to the controls.
The reduction for the RYGBP patients did not significantly correlate to age, gender, BMI, PPI treatment, smoking, status in H. pylori or H,K-ATPase.

Three RYGBP and six control patients had increased titres of antibodies against H. pylori. Six patients in both groups had increased titres of antibodies against H,K-ATPase. These abnormalities remained unchanged during the study. No additional patient developed increased titres of antibodies against H. pylori or H,K-ATPase.

**Discussion**

Pepsinogen is produced in the gastric mucosa as an inactive precursor of the protein-digestive enzyme pepsin. A small amount of pepsinogen leaks into the blood and can be measured as an indicator of the histological state of the gastric mucosa [64, 179, 180]. Serum pepsinogen is low in pernicious anemia [64, 65] due to the severe atrophy of the mucosa. Chronic gastritis, intestinal metaplasia, and gastric cancer are also characterised by low levels (REF). High levels of serum pepsinogen are associated with mucosal inflammation; superficial gastritis, duodenal ulcer [181, 182] or H. pylori infection [68]. The excluded stomach after RYGBP is hence not characterised by acute mucosal inflammation or ulcers.

How can the low PGI values be interpreted and are there clinical implications for patients who have had or are thinking of undergoing a gastric bypass?

On the one hand, the environment in the excluded stomach could favour the development of chronic atrophic gastritis. These epithelial changes could have pre-malignant potential, similar to the situation in the gastric remnant after subtotal Billroth II gastrectomy, where an increased risk of adenocarcinoma has been proposed24. If this is true, an increased awareness of the state of the gastric mucosa and readiness for invasive investigation would be warranted for the safety of the RYGBP patients.

Second, the absence of food stimulation in the excluded stomach and duodenum contributes to a substantial change in
upper gastrointestinal physiology. The normal regulatory system is affected, which could set the mucosa in the excluded stomach in a resting state. Pepsinogen secretion is known to be reduced in hibernating animals, after vagotomy and with diminished blood supply. The fact that the PGI values are fully reduced as early as one year afterwards strengthens this interpretation, whereas a dysplastic process would be expected to give a more progressive year-by-year pattern.

In our study, the BMI is similar in both groups, but it is well known from prospective, randomised studies that RYGBP is followed by a better weight loss than gastric restriction. That similarity simplified the comparisons of PGI in the study and was probably due to selection bias. We converted patients with poor weight loss after gastric restriction into RYGBP, leaving only the successful cases to be evaluated in the control group. It would be interesting to measure the PGI values in VBG patients with a subsequent late staple line rupture.

No additional patient showed an increased titre of antibodies against H. pylori during the four-year period as a sign of an acquired H. pylori infection. Unfortunately, our sample is too small to evaluate whether patients with gastric and duodenal bypass, for example after RYGBP, are protected against H. pylori infection. In addition, no patients showed serological signs of being cured from the H. pylori infection. We do not routinely perform endoscopy or H. pylori eradication preoperatively, as done in other centres.

The typical RYGBP patient is young and with the weight loss induced by the operation, life expectancy is long. Therefore, all potential adverse effects in the excluded stomach have to be taken seriously. A permanent solution is of course the resectional gastric bypass, described by Curry et al. Instead of excluding the main stomach, they resect it and leave only a 30- to 50-cc gastric pouch, which is anastomosed to a 50-cm retrocolic Roux limb. The Tacoma group perform the resectional bypass due to the potential problems in
the in situ defunctionalized stomach, lacking easy diagnostic access. They believe that the preservation of the stomach is unnecessary from three standpoints: First, in practice, full reversal of a gastric bypass is infrequently performed. Second, obesity is a chronic disease and a major weight regain is known to follow reversal. Third, there is extensive experience with long-term nutritional outcome, both after total gastrectomy performed for reasons other than obesity and in traditional gastric bypass (with the main stomach excluded). In addition, they report improved exposure for the gastro-jejunal anastomosis by the absence of the main stomach, especially in revisional procedures. Armstrong et al, share the worry about the potential problems in the excluded stomach and also perform a 95% gastrectomy, as well as a simultaneous cholecystectomy and appendectomy.

However, a gastrectomy implies an additional risk to the morbid obese patient, as it can be technically demanding. Leakage from the divided duodenum is infrequent, but more common than leakage from the staple lines of the excluded stomach, and requires subsequent drainage. Moreover, a gastrectomy obviates all production of gastric acid and intrinsic factor. The gastric acid provides protection of the natural bacterial environment in the small bowel. The risk for bacterial overgrowth in the Roux limb is increased after RYGBP, when evaluated by culture and the activity in the Paneth cells, as a marker of the innate immune system (Sundbom, unpubl data). A resectional bypass is of course totally irreversible. Most centres have reversed patients due to postoperative complications, such as small bowel gangrene or severe anorexia, thus preventing severe malnutrition or death.
Conclusions

Paper I
We were able to develop a hand-assisted laparoscopic technique for Roux-en-Y gastric bypass that reduced our earlier high conversion and re-operation rate in total laparoscopy. The hand-assisted laparoscopic technique for RYGBP is feasible.

Paper II
In a prospective, randomised study we did not find hand-assisted laparoscopy to be superior to conventional open RYGBP. The operative time was longer and no postoperative benefits were seen. The hand-assisted technique cannot replace total laparoscopic RYGBP.

Paper III
We could obtain access to the excluded stomach after RYGBP. Endoscopic biopsies showed chronic gastritis and intestinal metaplasia and we could exclude serious disease. The basal, as well as maximal, production of hydrochloric acid was lower than normal, indicating that the excluded stomach is not ulcerogenous.

Paper IV
Thirty-six percent of our patients have duodenogastric bile reflux to the excluded stomach after RYGBP. This frequent exposure to bile can imply long-term risks, similar to those after subtotal gastric resections where the risk of malignancy is increased.

Paper V
The state of the gastric mucosa in the excluded stomach can be assessed by serology. The pepsinogen I values are reduced and persistently low after RYGBP. The mucosa is probably in a resting state, even if genuine atrophy cannot be excluded.
Svensk sammanfattning (Summary in Swedish)

Roux-en-Y gastric bypass (RYGBP) är en operation vid sjuklig övervikt (BMI>40 kg/m²) som ger kraftig viktminskning, men lämnar magsäcken urkopplad och svårundersökt för resten av livet. RYGBP är möjlig att utföra med laparoskopi (tittålskirurgi) men tekniskt krävande. Inom andra fält har handassisterad laparoskopi, en hybrid där man kan ha en hjälpande hand inne i buken varit lovande. Målet med avhandlingen har varit att studera om handassisterad laparoskopi ger fördelar vid RYGBP och att utveckla tekniker för att undersöka den urkopplade magsäcken.

Vi utvecklade en handassisterad operationsteknik i en pilotserie på 13 konsekutiva patienter. Handporten fungerade bra och endast en patient behövde konverteras till öppen operation. Operationstiden var 205 minuter och alla patienter återhämtade sig väl. Vi randomiserade sedan 50 patienter med median BMI på 46 kg/m² till handassisterad eller öppen operation. Ingen handassisterad operation behövde konverteras, men operationstiden var längre, 150 mot 85 minuter jämfört med öppen operation. Det var ingen skillnad i patienternas återhämtning (vårdtid 6 dagar) eller viktnedgång (40 kg) efter 1 år.

Hos patienter med oklara blödningar efter RYGBP kunde vi punktera den urkopplade magsäcken med ledning av ultraljud. Gastroskopi genom denna kanal visade inga sår eller tumörer men kronisk magkatarr. Saltsyraproduktionen i den urkopplade magsäcken var lägre än normalt. 22 patienter undersöktes i gamma-kamera och 36 % hade reflux av galla till magsäcken: Magsäcksslemhinnan undersöktes hos 64 opererade patienter med en nyutvecklad analys (mätning av pepsinogen, antikroppar mot H pylori samt H,K-ATPas i blod). Hos alla som genomgått RYGBP hade pepsinogenvärdena sjunkit, talande för slemhinneatrofi eller inaktivitet.

Arbetet har varit inriktat på säkerhet vid RYGBP. Handassisterad laparoskopi var genomförbar men gav inte patienterna några fördelar. Den urkopplade magsäcken kännetecknas av kronisk magkatarr, låg saltsyraproduktion samt backflöde av galla. Magsäcksslemhinnan förefaller vara i ett vilostadium, men dessa fynd skulle kunna innebära ge ökad cancerrisk på lång sikt.
Acknowledgements

I would like to express my sincere gratitude to everyone involved in these studies, for all their encouragement and assistance. My special thanks are due to:

**Sven Gustavsson**, my supervisor, for introducing me into the fields of bariatric surgery and research, daily encouragement and outstanding support. I am especially grateful for your unselfish sharing of operative skills and for placing a “however” in every paragraph in all my manuscripts.

**Ulf Haglund**, head of the Department of Surgery and **Lars Wiklund**, head of the Department of Surgical Sciences, for providing the facilities for me to perform these studies simultaneously with my surgical work.

My co-authors, **Margareta Öhrvall, Hans Hedenström, Rikard Nyman, Sven Mårdh and Erik Mårdh** for contributing with your expertise and good advice.

Friends and colleagues in the upper gastrointestinal team, **Britt-Marie Karlsson, Rikard Henriksson, Ib Rasmussen, Rune Sandbu, Bengt Wallner** and **Agneta Westling**, for daily support and encouragement.

**Friends and colleagues** at the Department of Surgery, Uppsala

**Anita Ohlin**, for a genuine interest and never ending care of the obese patients

**The staff of 70AII**, for creating a pleasant atmosphere at the ward for upper gastrointestinal surgery

**The staff at the operating theatre**, for invaluable help and patience

**Martin Lidholt**, for transforming my sketches into understandable, high class illustrations and generous assistance

**Steve Scott-Robson**, for friendship and fast, skilful linguistic revision

Former **colleagues** at the Department of Surgery, Eskilstuna, for giving me a sound start in general surgery

My wife **Ann** and our children **Sofia** and **Johan**, for support, immense understanding and just being who you are

My mother **Gunnel**, father **Lennart**, and brothers **Stefan** and **Håkan** with family, for giving me a good start in life and constant concern

My parents-in-law **Cecilia and Gustaf**, for always helping out when needed
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