Surgical and patient reported outcomes after novel techniques for gastrostomy insertion and fundoplication in children

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2. Summary

Gastrostomy tube (GT) insertion and fundoplication are two of the most performed gastrointestinal surgical procedures in children. A GT provides enteral nutritional support and fundoplication treats gastroesophageal reflux disease (GERD). The two procedures may be performed concomitantly or in sequence and are offered to many of the same patient populations. Both GT and fundoplication may improve somatic outcome and health-related quality of life. However, both procedures are associated with a risk for complications, and there is an ongoing discussion on indications and operating techniques. During the last decades surgical techniques for both GT and fundoplication have changed significantly. Laparoscopic fundoplication has almost completely substituted open fundoplication, and several novel techniques for GT insertion, including laparoscopy, now exist. The studies in this thesis were initiated because we wanted to evaluate results after introduction of new techniques for GT insertion and fundoplication.

To study trends and changes in techniques for GT insertion we retrospectively reviewed the medical charts of 649 patients undergoing GT insertion at Oslo University Hospital (OUS) Rikshospitalet from 1994-2012. We found that the number of GT insertions more than doubled, from 24 per year in 1994 to 57 in 2012 (p<0.001). Children with neurologic impairment (NI) constituted the largest patient group (48 %). During the latter part of the study period, GT was increasingly offered to other patient populations, such as children with cardiac disease and other congenital malformations. Percutaneous endoscopic gastrostomy (PEG) was the most common (62 %) technique throughout the study period. 7 % was with laparoscopic technique (LAP-G), and this number increased during the period (p<0.009).

To get more information about complications related to change of techniques for GT insertions, we retrospectively evaluated postoperative complications after the two most novel techniques for GT insertion; PEG with T-fastener gastropexy (PEG-T) and LAP-G. Eighty-seven patients undergoing PEG-T insertion during 2010-14 at OUS Ullevål and 104 patients getting a LAP-G at OUS Rikshospitalet 2005-14 were included. Early (<30 days) complications were common and were reported in nearly half of patients after PEG-T insertions. Most were minor; such as peristomal infection (26 %) and tube dislodgement (10 %). Major complications requiring laparotomy or endoscopy, occurred in 7 %. Early and late complications related to T-fasteners occurred in 11 % and 13 % of patients, respectively. No risk factor for complications was identified, and we did not demonstrate any learning curve for either operating time or
complication rate. As for PEG-T, gastrostomy-related complications were common (38%) also after LAP-G. Peristomal infection and granulation tissue both occurred in 13% of the patients, whilst major complications occurred in 10%. Patients with NI had fewer complications than those without NI (46% vs 22%, p=0.01). We also found that the operation time significantly decrease from the first to the second half of the study period (46 vs. 35 minutes, p=0.04).

The most important change in operative technique for fundoplication was the introduction of laparoscopy. Due to few high-quality studies comparing laparoscopic and open technique, we performed a randomized controlled study between 2003 and 2009. Eighty-eight children were randomized to either laparoscopic Nissen fundoplication (LNF) or open Nissen fundoplication (ONF). Seventy (82%) of the patients were included in a study for long-term assessment median 12 years postoperatively. We confirmed previous findings of significantly more recurrences after LNF than after ONF. After median 12 years follow-up, 56% experienced recurrent GERD after LNF versus 31% after ONF (p=0.004). We also found that recurrence occurred earlier after LNF. 86% of patients reported no reflux symptoms at follow up. Satisfaction with outcome of the fundoplication was high in both groups; 81% after LNF and 88% after ONF (p=0.5).

It is debated whether NI patients have worse outcome after fundoplication than other patients. We therefore compared results in NI and non-NI patients included in the randomized controlled trial. NI-patients had longer hospital stay, but there was no overall difference in postoperative complications. Median four years postoperatively, there was no difference in recurrence rates between patients with and without NI (27% vs. 17%, p=0.31). Satisfaction was high as 97% of parents in both groups would choose fundoplication again.

When reviewing results after primary fundoplication in the randomized controlled trial, it became apparent that a substantial number of patients underwent redo fundoplication (RF). RF is by many considered to have worse outcomes than primary fundoplication, and in the last study in this thesis we investigated outcomes after RF. We included 24 patients who had undergone RF between 2002 and 2020 at OUS Rikshospitalet. In addition to a retrospective chart review, patients/parents answered a questionnaire recording signs of recurrent GERD, troublesome symptoms and satisfaction with the RF. Recurrent GERD was the most common indication for RF (75%). Half of the patients experienced early postoperative complications. Five (21%) patients had recurrent GERD after RF, of which three were satisfactorily treated. Only one child had more than one RF. Lastly, 96% of patients said they would recommend RF to someone in a similar situation.
The main finding in this thesis is that novel surgical techniques are not necessarily better than more traditional techniques. Recurrent GERD was more common after LNF than after ONF, and recurrence occurred earlier after LNF. Furthermore, we found that many patients experienced complications after PEG-T and LAP-G, and some complications were related to the specific technique for GT insertion. Our findings suggest that continuous evaluation of results and a structured introduction of new techniques are important.
3. List of papers

**Paper 1**

**Paper 2**

**Paper 3**

**Paper 4**

**Paper 5**

**Paper 6**
4. Abbreviations

CCI: Complex Complications Index

ESPGHAN: European Society for Paediatric Gastroenterology Hepatology and Nutrition

GER: Gastroesophageal reflux

GERD: Gastroesophageal reflux disease

GT: Gastrostomy tube

LAP-G: Laparoscopic gastrostomy tube

LNF: Laparoscopic Nissen fundoplication

NI: Neurologic impairment

ONF: Open Nissen fundoplication

OUS: Oslo University Hospital

PEG: Percutaneous endoscopic gastrostomy

PEG-P: Percutaneous endoscopic gastrostomy with pull technique

PEG-T: Percutaneous endoscopic gastrostomy with T-fastener gastropexy

PPI: Proton pump inhibitor

RCT: Randomized controlled trial

RF: Redo fundoplication

RI: Reflux index

UGI: Upper gastrointestinal
5. Introduction

Pediatric surgery is a surgical specialty that covers many different diseases and conditions in children. This thesis focuses on two of the most common gastrointestinal procedures performed in children: Gastrostomy tube (GT) insertion and fundoplication. These procedures aim to improve well-being and decrease morbidity in pediatric patients with feeding problems and gastroesophageal reflux disease (GERD). Fundoplication is a major procedure whilst GT insertion is considered a minor procedure. The two operations are intertwined because they are often performed simultaneously or in sequence and performed in many of the same patients. This introduction provides a brief overview of these two procedures; their indications, how they are performed and postoperative outcomes.

5.1 Feeding problems

Feeding problems of various severity are common in children. Studies report feeding problems in 50 % of otherwise healthy children, and in up to 80 % of children with neurologic impairment (NI) (1). The term “feeding problems” is used inconsistently and may include many conditions, ranging from picky eaters without comorbidity to patients with NI and severe oropharyngeal dysfunction and intestinal dysmotility (2,3). Goday and coworkers recently proposed the following definition for pediatric feeding disorder: “Impaired oral intake that is not age-appropriate, and is associated with medical, nutritional, feeding skill, and/or psychosocial dysfunction” (4). Diagnostic evaluation of feeding problems is dependent on presentation and severity and many children with feeding problems can be treated in primary care. If the feeding problems are severe, examination and treatment by a multidisciplinary team consisting of pediatricians, clinical nutritionists, speech therapists, psychologists and nurses are needed (5). Treatment can range from simple dietary advice to interventions aimed at behavioral modifications and long-term parenteral nutrition. This thesis focuses on patients with feeding problems in whom enteral nutritional support via tubes is required.

Enteral nutritional support is defined as special diet formulations provided orally and/or feeds delivered to the gastrointestinal tract via tubes (6). The two most common routes for tube feeding are a nasogastric tube or a GT. Both deliver feeds to the stomach. Tubes ending in the small intestine may also be used, including nasojejunal tubes, transgastric jejunal tubes and jejunostomy tubes. A gastrostomy is established during a surgical procedure that creates an artificial stoma channel between the abdominal wall and the stomach. This allows insertion of a GT directly into the lumen of the stomach and can be used to administer feeds (7).
5.2 Gastrostomy tube

5.2.1 Indications for gastrostomy insertion
GT feeding is used in patients with need for long term enteral nutrition support. Failure to thrive and dysphagia are the most common indications (8). Administration of specific diets (e.g. in metabolic diseases and ketogenic diets for epilepsy), maintaining hydration, preventing malnutrition (e.g. related to chemotherapy and radiotherapy), and delivering medications are other reasons for establishment of a GT (8,9). GT may also be inserted in newborns with congenital malformations such as long gap esophageal atresia (10). Thus, the population of pediatric patients undergoing GT placement is heterogenous with various underlying comorbidities. Patients with NI constitute the majority, of which cerebral palsy is the most common diagnosis (11–13). Other underlying diagnoses include cardiac disease, respiratory disorders, malignancies, various congenital anomalies, renal disease, metabolic syndromes, and Crohn’s disease (12).

Deciding on the optimal timing for GT placement can be challenging. According to the European Society for Paediatric Gastroenterology Hepatology and Nutrition (ESPGHAN), GT insertion should be considered when there is need for enteral nutrition support of minimum 4-6 weeks, and in most cases even longer (6). According to web published guidelines from the Norwegian Pediatric Association, GT insertion is indicated when there is suspected need for enteral nutrition support for more than 3-4 months (14). Deciding on GT placement should be based on a multidisciplinary approach and in each case be an individual assessment (9). Many children have been fed through a nasogastric tube for a long time before GT insertion (15,16). Some parents may delay the decision to start GT feeding because they are worried about the effect on oral feeding and the risk related to the procedure (17). Interestingly, nine out of ten parents would accept earlier GT placement had they known the positive outcome (18).

5.2.2 Techniques for gastrostomy insertion
There are various techniques for GT insertion. In addition to the techniques outlined below, radiologically inserted GT is used in some centers (19). This technique is rarely used in children in Norway and is therefore not discussed further in this introduction.

Open gastrostomy insertion
The Stamm procedure for open GT insertion dates back to 1886 and is, with slight modifications, still in use today (7). The technique involves a mini-laparotomy, and under direct visualization, an ideal site for the gastrostomy can be chosen. Usually, one or two purse-string
sutures are placed at the site for the gastrostomy. After the GT has been placed, the purse-string sutures are tightened, and the stomach is fixed to the abdominal wall (20). Some surgeons prefer Malecot catheters, whereas others insert low-profile buttons or balloon tubes.

Although less invasive techniques for GT insertions have been introduced, open GT is still used when other techniques are not suitable, for instance because of extensive adhesions from previous abdominal surgery or when open abdominal surgery is performed concomitantly (21–23).

Percutaneous endoscopic gastrostomy

In 1980, Gauderer and Ponsky introduced a new technique for GT insertion without laparotomy; the percutaneous endoscopic gastrostomy (PEG) (24). Using an endoscope, the stomach is insufflated, and transillumination and indentation used to secure a safe puncture site. A needle is pushed through the abdominal wall into the stomach lumen. Then, a guide wire is passed through the needle, grasped with forceps before the endoscope is withdrawn. The PEG tube is fastened to the guide wire and then pulled antegrade through the mouth and esophagus, into the stomach and through the abdominal wall. Hence, this is known as the pull technique (PEG-P) (Figure 1). An internal retaining device, "bumper", secures contact between the stomach and the abdominal wall, and the tube is further secured externally (24). PEG-P was first described in children, but quickly gained popularity both in adults and children and is by many considered the preferred method for GT insertion (6). PEG has few absolute contraindications, but care should be taken in patients with previous abdominal surgery, ventriculoperitoneal shunt, severe scoliosis and needing peritoneal dialysis (9,25).

Figure 1. Insertion of a percutaneous endoscopic gastrostomy with the pull technique. Reprinted from. “Percutaneous endoscopic gastrostomy in children: The technique in detail” by Gauderer, MWL and Stellato, TA. Pediatric Surgery International volume 6, page 82–87, 1991, with permission from SpringerLink.
The PEG-P tube is often changed to a skin-level device, such as a low-profile button, because of convenience (12). This should be performed no earlier than 2-3 months postoperatively, as replacement before the stoma channel has healed may lead to separation of the stomach from the abdominal wall, with risk for peritonitis (9,26). In adults, change to a skin-level button is usually done with the “cut and push-technique”; the tube is cut at skin level and allowed to pass via the gastrointestinal tract. However, this technique has in children been associated with severe complications such as esophageal perforation or lodging of the bumper in the esophagus (27,28). Most PEGs with bumpers are in children removed either endoscopically under general anesthesia or by traction under light sedation or general anesthesia if the PEG has a collapsible bumper (26). In older children and adolescents, the cut and push-technique may be safe.

**Percutaneous endoscopic gastrostomy with T-fastener gastropexy**

To allow direct placement of balloon tubes or low-profile buttons, one-step PEG techniques have been developed (29). The GT is introduced directly into the stomach lumen, and this technique is known as “push” technique. There are several variations of the “push” technique, and PEG with T-fastener gastropexy (PEG-T) is one common push technique used in children.

During PEG-T, gastropexy is first performed by placing metal T-fasteners with resorbable sutures in a trigonal fashion. The T-fasteners are fastened with external suture locks. The GT is then introduced via a Seldinger “push“ technique, and a gastrostomy is established in the middle of these sutures. Either a low-profile balloon button or a balloon tube is inserted (Figure 2) (30). A major advantage of PEG-T, is that it can be changed in an outpatient setting without sedation (30). Among 105 patients getting PEG-P or PEG-T, only 3 % of PEG-T changes required general anesthesia, compared to 72 % of PEG-P changes (31). A proposed advantage with push techniques is a lower the risk for peristomal infections as the oral flora is omitted during insertion of the GT (32).
Laparoscopic gastrostomy insertion

The use of laparoscopy has increased significantly during the last decades, and techniques for GT insertion using laparoscopy (LAP-G) have gained popularity (33). LAP-G is inserted under direct visualization, thus avoiding the risk for perforation of intraabdominal organs. The camera is inserted through the umbilicus and a left subcostal port inserted at the site for the GT. The stomach is grasped at a suitable site (Figure 3). Then, gastropexy is provided with internal or external suturing, and various techniques have been described (34,35). LAP-G, as PEG-T, omits the oral flora and allows insertion of a primary balloon tube or low-profile button (36). This technique has few absolute contraindications. Previous abdominal surgery is a relative contraindication, due to the risk of intraabdominal adhesions. LAP-G may be difficult to perform in obese patients because a thick abdominal wall can make it difficult to deliver the stomach without making the abdominal wall opening to big (36). In such cases, some have suggested combining the traditional PEG technique with laparoscopic surveillance, a so-called laparoscopically assisted PEG technique (37). LAP-G requires more technical equipment and occupies operating theater capacity, compared to PEG techniques that can be performed in an endoscopy unit.
5.2.3 Trends in gastrostomy tube insertion

GT insertion is a commonly performed surgical procedure in pediatric patients. A birth cohort study from Australia found a prevalence of around 7 GT insertions per 10 000 births (11). Several studies report an increase in the number of GT insertions, and a decrease in the number of children getting a nasogastric tube for long-term enteral feeding (38–41). A national registry study from the United States reported an increase in GT insertions from 16.6 procedures/100 000 children in 1997 to 18.5 procedures/100 000 children in 2009, and LAP-G insertions became more common during this period (39). The increase is especially apparent in younger patients. Another study from the United States found that usage of PEG vs. LAP-G and open GT varied between centers (42). Furthermore, GT has become more common in populations other than patients with NI. Fox and co-authors found that the number of patients with cardiac disease and prematurity getting a GT increased from 1997 to 2009, but the number of patients with NI was stable (39).

5.2.4 Outcomes after gastrostomy tube insertion

Nutritional outcomes

The efficacy of GT feeding has been thoroughly investigated. The main benefit is improvement in nutritional status and weight gain (15,43–46). In a retrospective study of 300 pediatric patients undergoing LAP-G, weight-for-length z-scores improved significantly (47). In malnourished children, nutritional restitution and improved nutritional status may optimize growth and development (48). Many parents fear that inserting a GT means giving up on oral
feeding. However, a study of 58 children found that 49% experienced increased oral feeding after GT insertion (15). In patients where the condition that necessitate GT feeding is transient or improved, reducing or stopping GT feeding can be challenging. However, the majority of these children can successfully wean of GT feeding with time and adequate follow-up (49).

Although GT feeding is shown to have many positive effects, adverse effects may occur. GT feeding may lead to overfeeding and overweight, especially in patients with low energy requirements such as children with severe NI (50). There are also concerns that GT feeding can cause both deficiency and excess of micronutrients such as minerals and vitamins due to the compositions of feeds (6,51).

Patient and parent reported outcomes

The impact of GT feeding on health-related quality of life in pediatric patients is not well studied. The only study that has used validated questionnaires found that overall health-related quality of life did not improve in children undergoing LAP-G, but psychosocial health-related quality of life improved (52). A prospective study of children with NI compared health related quality of life before and after GT insertion and found no significant difference (53). However, 84% of the parents said that the GT had a positive impact on their child’s health. A previous study from our center found that GT insertion improved parent-child communication and satisfaction during meals (15). Furthermore, studies have shown improvements in health-related quality of life of caregivers after GT insertions (54,55). A previous a study from our center, found decreased levels of distress and parental stress in mothers 18 months after GT insertion (56).

Complications after gastrostomy insertion

Complications after GT insertion are common, although complication rates vary immensely between studies. In their prospective study of 92 patients, Brewster and coworkers report a complication rate of 14% during the first 90 postoperative days (57). However, other studies find that up to 74% are affected by one or more complications after GT insertion (47,58). Complications are defined and classified differently in various studies. ESPGHAN guidelines on management of PEG classify early and late complications as before and after 30 days postoperatively (9), and further as minor or major. A complications is major if it leads to additional hospitalization, surgical or radiological interventions (59).
Minor complications

Minor complications are by far the most common and are for the most part stoma related. Although not life threatening, they cause trouble, discomfort and concern for patients and caregivers and are associated with frequent health-care visits and costs (60).

Hypergranulation is newly formed connective tissue with micro vessels occurring during wound healing and is commonly reported after GT insertion in children (Figure 4). In prospective and retrospective studies using questionnaires or interviews, hypergranulation is reported in as many as 38-70 % of patients (58,61–63). Hypergranulation can cause continuous secretion, bleeding and infection, and is considered troublesome by many patients and care-givers (64). Many cases can be treated with topical administration of silver nitrate or corticosteroids, but some patients have recurring symptoms and require surgical debridement or revision of the GT (60).

![Figure 4. Gastrostomy with low-profile balloon tube and hypergranulation that needed surgical debridement. Parental consent for use of the photo has been obtained.](image)

Peristomal wound infection is another common complication after GT insertion in children. Prospective studies with a follow-up time of 3-4 months find that peristomal wound infection occurs in 6-9 % (57,63), and infections are also noted long term (58,62). Most infections are treated with topical or oral antibiotics. Intravenous antibiotics and hospitalization may be required for recurrent infections or severe infections with cellulitis or abscess formation (59,60). Prophylactic antibiotics before GT insertion is often administered to lower the risk of peristomal wound infection and is recommended by ESPGHAN (9). A Cochrane analysis of randomized controlled trials (RCT) in adults found fewer infections in patients given prophylactic
antibiotics (65). A recent retrospective study in children found no difference in infections between those with and without prophylactic antibiotics (66).

Leakage from the stoma site is commonly reported, and leakage will in many cases be linked to peristomal wound infection (57). Leakage can, however, be persistent and require temporary stop of GT feeding or surgical refashion of the GT (47,67).

Tube dislodgement is a minor complication if it can be handled with bedside reinsertion, but in some cases surgical, endoscopic or radiological intervention is required. The rate of tube dislodgement varies from 1.6-24 % (47,61,68). Early tube dislodgement is feared because there is a risk for peritonitis if the tube dislodges before the stoma channel is fully healed and the stomach is not fixed to the abdominal wall.

**Major complications**

Depending on how major complications are defined, major complications occur in 2-13 % of patients (47,59,69,70). Major complications include among others peritonitis, internal leakage, bleeding, damage to intraabdominal organs, massive pneumoperitoneum, and pneumonia (9,47,57,59,71). Procedure-related mortality is extremely rare and is only sporadically reported as single cases (70). The overall mortality in patient undergoing GT insertion is, however, high. Three years after GT insertion 18-39 % of patients have died of their underlying disease (72,73).

Some GT related complications appear to be technique specific. Gastro-enteric fistulas and perforation of intraabdominal organs are almost exclusively reported after PEG insertions, A meta-analysis of 3304 PEG patients reported perforation of the colon or small bowel in 0.27 % (74). After PEG-P insertion, the internal retaining device may migrate alongside the stoma tract, into the mucosa or further through the abdominal wall, leading to pain, leakage, infection, perforation, or peritonitis, referred to as “buried bumper syndrome” (75). There are reports of problems related to the T-fasteners used in PEG-T. These include pain, skin problems and suture migration (76–78). LAP-G may be associated with port site herniation (67).

**Risk factors for complications**

Several studies attempt to predict which patients are at risk for complications following GT insertion. Two studies identified the presence of a ventriculoperitoneal shunt as a risk factor for major gastrostomy-related complications (69,70). In one of these studies, NI appeared to be protective of complications (69), whilst another study found higher rates of peristomal infection in patients with NI (8). Furthermore, low age has been investigated as a risk factor, and found
to be protective in one study whilst others find no difference (69,70,79). Concomitant procedures such as fundoplication predicted complications in one study (80), whilst another study found that a concomitant fundoplication did not affect the complication rate (81).

5.3 Gastroesophageal reflux disease

5.3.1 Definition of gastroesophageal reflux disease

Gastroesophageal reflux (GER) refers to the passage of gastric contents into the esophagus with or without regurgitation or vomiting (82). Regurgitation is the passive passage of refluxed contents into the pharynx, into the mouth or out from the mouth, whilst vomiting is the forceful expulsion of refluxate out of the mouth after diaphragmatic contraction (83). Episodes of GER occur in healthy infants, children and adults several times per day without any symptoms, and GER is a normal physiologic process (82). Regurgitation is often reported by care-givers of healthy infants and will in most cases resolve during the first 12-18 months of life (84,85). A questionnaire-based study of healthy infants found a peak (67 %) of reported daily regurgitation at 4 months, but at one year, only 5 % had daily regurgitation (86).

The term gastroesophageal reflux disease (GERD) has been used inconsistently in clinical settings and in research, leading to variations in diagnosis and management (87). In 2009, a consensus statement defined pediatric GERD as “GER that causes troublesome symptoms and/or complications” (83).

5.3.2 Epidemiology and pathophysiology

The estimated prevalence of GERD in children varies from 0-38 % (88). A French cross sectional study estimated a prevalence of GERD in children and adolescents of 6 % (89). The prevalence of GERD is believed to be higher in some groups of children, such as those with NI, esophageal atresia and congenital diaphragmatic hernia (90–92). There are no studies investigating the epidemiology of pediatric GERD in Norway.

The pathophysiology of GERD is multifactorial and not fully understood. Both anatomical, genetic, neurogenic, hormonal, and environmental factors have been suggested (93). Protective mechanisms include the antireflux barrier, an anatomical structure that limits the frequency and volume of refluxed contents, consisting of the lower esophageal sphincter, diaphragmatic crura and the angel of His (94). Esophageal clearance and mucosal resistance are other protective mechanisms (93). A major mechanism for GERD is increased frequency or duration of transient lower esophageal sphincter relaxations (95). These are not related to swallowing and can be triggered by gastric distention (96). Another disposing factor is hiatal hernias (97). Delayed
gastric emptying as a contributing factor to GERD is often discussed, though the importance of delayed gastric emptying remains controversial (98).

5.3.3 Clinical manifestations
Symptoms and signs of GERD vary with age (83,99). Infants, toddlers and patients with NI are often not able to account for their symptoms, and evaluation is dependent on care-giver reports. These patients may present with classic reflux symptoms such as excessive regurgitation or vomiting, but also irritability, back arching, crying, food refusal, poor weight gain, feeding problems, cough, and apneas (83,100,101). These latter symptoms are nonspecific and should lead to investigations to rule out other conditions. “Happy spitters”, infants with regurgitation who appear untroubled and without complications, should not be diagnosed with GERD (83). In older children and adolescents evaluation of symptoms rely on patient reports, and include regurgitation, vomiting and retrosternal pain (86,102). There may also be abdominal pain, food refusal and nausea (99). Patients may also present with more atypical symptoms such as dental erosions and brief resolved unexplained events (103,104). The relationship between GER and respiratory problems such as asthma, chronic cough and laryngitis is unclear and the literature conflicting (105–107). Aspiration pneumonia may be related to GER in children with NI (108).

GERD will in some patients manifest with complications. Refluxate can cause inflammation and damage to the esophageal mucosa, leading to ulceration, esophagitis and esophageal stricture (109). In patients with longstanding GERD, there is an increased risk for Barret’s esophagus, a condition with intestinal metaplasia in the esophagus that over time can evolve to esophageal adenocarcinoma (110). It appears that children with NI and esophageal atresia have a particularly high risk for these complications (110,111).

5.3.4 Diagnosing gastroesophageal reflux disease
Diagnosing GERD in pediatric patients can be challenging. There are no single symptom or diagnostic examination that can diagnose GERD, although typical symptoms (heartburn and regurgitation) in older children and adolescents without NI is highly suggestive of GERD (83,107). An expanded history and clinical examination should be obtained to identify any alarm symptoms or signs of differential diagnoses that need further attention (107). Various questionnaires have been developed to identify symptoms, severity and effects on quality of life in patients of various age groups, but are not validated for diagnostic use (112–115).

Objective examinations can aid in diagnosing GERD, assess severity and complications or rule out other diagnoses that mimic GERD. However, physicians should be aware of the tests’
limitations (107). These tests also have an important role in the assessment of recurrence of GERD after antireflux surgery.

Esophageal 24-hour pH-monitoring has long been used to detect and quantify acid exposure in the esophagus. A catheter is inserted transnasally into the esophagus, and correct position verified by either x-ray or fluoroscopy (116). The most used parameter is the reflux index (RI), which is the percentage of the recording time when pH in the esophagus is <4 (82). The method cannot fully correlate GER symptoms with acidic episodes (117,118), and the sensitivity ranges from 41-81 % (119). As the catheter may be uncomfortable, the child may not eat and behave as it normally would. Another limitation of this test is the inability to detect nonacidic reflux, for instance if acid is buffered by tube feeds or milk (120). Therefore, many physicians now prefer combined esophageal pH and multiluminal impedance monitoring. This method also detects weakly acidic and nonacidic exposure. This technique detects GER to a higher degree than pH monitoring alone, and it appears that weakly acidic reflux can cause symptoms in some patients (121,122).

An upper gastrointestinal (UGI) contrast study is performed by giving the patient a meal or liquid containing a contrast agent such as barium, with subsequent x-ray examinations. This technique can show episodes of GER, but the sensitivity and specificity is low, and a UGI contrast study should not be used as a stand-alone examination to diagnose GERD (123,124). It may, however, be useful to identify anatomical abnormalities (e.g. esophageal stricture, hiatal hernia) or partial bowel obstruction (e.g. malrotation, pancreas annulare) that may cause symptoms mimicking GERD (124).

Endoscopic evaluation of the esophagus can demonstrate erosions, ulceration and strictures that suggest GERD (99). Biopsies may show histological signs of reflux esophagitis, but the negative predictive value of this test is low (109,125). It is, however, useful to rule out conditions resembling GERD, such as eosinophilic esophagitis (126). As pediatric patients will require general anesthesia, endoscopy should not be performed in all patients with suspected GERD, but is recommended in patients with persistent symptoms despite adequate pharmacological treatment (107).

Other diagnostic investigations include scintigraphy and manometry. Gastric scintigraphy can be used to evaluate gastric emptying which can be linked to GERD, but as previously mentioned, this is unclear. If there are clinical signs of delayed gastric emptying, scintigraphy can aid in deciding whether to perform a pyloroplasty concomitantly with fundoplication, but
this remains controversial as fundoplication in itself may accelerate gastric emptying (127). Scintigraphy as a way to diagnose GERD has been investigated, but has too low sensitivity and specificity to be recommended (125). Manometry, in which pressure and motility in the esophagus is measured, is commonly used in adults, but is only recommended in children when an esophageal motility disorder is suspected (107).

5.3.5 Non-surgical treatment of gastroesophageal reflux disease

Treatment of GERD includes for most patients a conservative approach, with the addition of pharmacological agents in some, and surgical treatment in the few. In infants and children with GER without troublesome symptoms or complications, unnecessary treatment should be avoided, as this is not GERD. Reassurance, parental education and anticipatory guidance will often suffice. Conservative treatment is recommend even though the scientific evidence is low (107). Food thickeners can reduce episodes of visible regurgitation in infants, but actual episodes of GER evaluated with pH monitoring are not reduced (128). Furthermore, no such products are approved for use in children under three years in Norway. Smaller and more frequent meals may be beneficial. Placing the child in the left lateral position may reduce reflux episodes (129), but any other position than supine should be avoided in infants under the age of one year during sleep due to the risk of sudden infant death syndrome (130). In older children and adolescents, conservative measures derived from studies on adults include weight loss in obese patients and modification of sleeping position with elevation of the head (131).

Multiple pharmacological agents can be used to treat GERD in children and adolescents. Alginates alter feed viscosity, gastric acid is reduced with antacids, histamine H₂ receptor antagonists or proton pump inhibitors (PPI) and prokinetics changes gut motility (132). Of these, PPI are most often used, and have been shown to heal reflux esophagitis in adults (133). In children, the evidence has poorer quality, but case series and RCTs have shown that PPI can reduce reflux esophagitis and improve symptoms in infants, children and adolescents (102,132). Furthermore, current guidelines suggest a 4-8 weeks trial of PPI as a diagnostic test in older children with typical symptoms of GERD (107). There are concerns about the effects of long-term usage of PPI, including increased risk for infections and osteoporosis (134,135).

5.4 Surgical treatment of gastroesophageal reflux disease in pediatric patients

When optimal pharmacological treatment is unsatisfactory or if the child has severe complications from GERD, antireflux surgery may be indicated (107). No RCTs have compared
antireflux surgery to PPI, thus guidelines are based on expert opinion and results from non-randomized studies. One study from the United States found that the incidence of antireflux procedures varies between different hospitals, and the authors believed this to be caused by different views on indications for surgery (136).

5.4.1 Surgical technique

The most common antireflux operation is a fundoplication. This was first introduced by the surgeon Rudolf Nissen in 1955, and it is therefore called a Nissen fundoplication (137). In this procedure, the fundus is folded around the lower esophagus, creating a wrap (plication) (Figure 5). This was originally an open technique (ONF), and the first laparoscopic Nissen fundoplication (LNF) was performed in 1991, and two years later the first LNF was performed in a child by the American pediatric surgeon Tom Lobe (138). Using blunt and sharp dissection, the intraabdominal part of the esophagus and the two diaphragmatic crura are exposed. A hiatal closure with one or more sutures may be performed to lower the risk for herniation of the wrap. The gastric fundus is then mobilized, wrapped posteriorly around the esophagus and secured with sutures, thus creating a 360° wrap (20). Some may choose to fasten the wrap to the diaphragm and/or to the esophagus.

![Figure 5. Nissen fundoplication. The fundus is wrapped 360° around the lower esophagus. Reprinted from. “Laparoscopic Nissen fundoplication in childhood” by Lobe TE Schropp K and Lundford K. Journal of Pediatric Surgery Volume 28, pages 358-361, 1993. Reprint with permission from Elsevier Science Direct.](image)

The mechanism for why this procedure works is not fully understood. The procedure increases the length of the intraabdominal part of the esophagus, tightens the hiatal diaphragmatic
opening, and the fundoplication itself serves as a one-way valve. It has also been suggested that fundoplication decreases the number of transient lower esophageal sphincter relaxations (139,140). Additional complex explanations have been introduced, including inhibiting effects on the vagus nerve which is responsible for transient lower esophageal sphincter relaxations (141,142).

An alternative to Nissen fundoplication is a partial fundoplication, where the fundus is wrapped only partially around the esophagus (e.g 270°); either anteriorly (Thal) or posteriorly (Toupet). The main arguments in favor of partial fundoplication are to lower the risk for dysphagia. There is a continued academical discussion on which technique is best, and studies find conflicting results with regards to postoperative outcomes (143,144). In Norway, partial fundoplications are rarely performed in children, mainly when a fundoplication is combined with Heller myotomy in children with achalasia.

5.4.2 Outcomes after fundoplication

Symptom improvement and objective measures
Most children experience immediate improvement of GER symptoms such as regurgitation and vomiting in the early postoperative period after fundoplication. However, the rate of patients with complete symptom relief varies. In a systematic review, symptom relief in children within six months after surgery was 57-100 % (145). When asked one month after fundoplication, 96 % of 55 children had relief of GER symptoms (146). Some studies report improvement in respiratory symptoms such as aspiration pneumonia, whilst others find no difference (147,148).

Effectiveness of fundoplication may also be shown with objective measures. 24-hour pH monitoring performed before and after LNF in a study of 127 children found that median RI changed from 10 % preoperatively to 0.5 % in patients with NI and to 0.8 % in patients without NI after 3 months (149). A reduced number of acidic and non-acidic episodes have also been found (150). In forty patients undergoing an UGI contrast study 6 months after fundoplication, 87 % were without signs of GER or a herniated wrap (151). Lastly, weight gain have been reported in patients with NI after fundoplication (152).

Patient reported outcomes
A few studies have reported improvement of health-related quality of life in pediatric patients after fundoplication (153–155). One study of patients undergoing LNF or laparoscopic Thal fundoplication found that improvements in health-related quality of life may be transient, as it diminished after two years (156). It seems that the fundoplication may also have a positive
effect on caregivers’ quality of life (157), and parental satisfaction with the surgery is generally high (158,159). A follow up study in mothers of patients included in the RCT of which parts of this dissertation is based on, found that levels of psychological distress and state anxiety were significantly reduced 12 months after fundoplication (160).

**Complications**

Postoperative complications after fundoplication include wound infection, wound dehiscence, pneumonia, sepsis, feeding problems, and bleeding (161–166). A study of 252 patients reported postoperative complications (excluding wrap dehiscence) in 15 % of patients (163). As insertion of a new GT or refashioning of a previous GT may be performed during fundoplication, complications related to GT are also frequently reported. A common complaint in the immediate postoperative period is dysphagia (146,164). This can be caused by temporary swelling or by a too tight wrap. Persistent dysphagia may necessitate endoscopic dilation or redo fundoplication (RF) in some patients (143,164). Temporary dysphagia after fundoplication was found in 38 % in a retrospective study of 288 patients, whilst 24 % needed endoscopic dilation because of persistent dysphagia (164).

Long-term complications after fundoplication include retching, gas bloat and dumping syndrome. Retching is frequently reported after fundoplication in children, especially in patients with NI (146,167). Retching may also be present before fundoplication and can be difficult to distinguish from vomiting and regurgitation. In a study of 55 patients, 27 % had retching before surgery, and 25 % reported new-onset retching after fundoplication (146). New-onset retching is often not a symptom of GERD, but due to activation of the emetic reflex in patients who are unable to vomit because of the fundoplication, and may be better treated with medication or jejunal feeding (168). In such cases, wrap herniation should be excluded with an UGI contrast study. Gas bloat is a term used to describe early satiety, bloating, abdominal pain and the inability to vomit or belch perceived as troublesome, and is reported in 0-10 % (164,169). Dumping syndrome is a condition where patients may experience postprandial nausea, sweating, diarrhea, hypoglycemia, and lethargy (170). This is believed to be caused by rapid passage of undigested food into the small intestine, and although rarely reported, believed to be common by some researchers (170,171). Adhesive small bowel obstruction is rare and appears to be more frequent after ONF (163,172). A retrospective study of 1383 children found adhesive small bowel obstruction in 1.4 % after LNF and 2.7 % after ONF (p<0.001) (173). Surgery related mortality due is rare and occurs in 0-5 %, mostly in children with severe underlying diseases (149,161,166).
Recurrence of GERD

Rates of recurrent GERD after fundoplication vary immensely in different studies. This may partly be explained by use of different definitions of recurrence. Some report recurrence as relapse of typical symptoms, others use results from investigations, and some only report rates of RF. In a systematic review, symptomatic recurrence of GERD varied from 4 to 30 % six months or more postoperatively (145). Another systematic review pooled eleven studies and found a rate of RF from 3.6-18 %, with lower numbers in high volume centers (148,174). Investigations used to diagnose recurrent GERD include UGI contrast study, 24-hour pH monitoring/impedance and/or endoscopy, and may show a herniated or disrupted wrap, GER and/or esophagitis (175–177).

Several studies have sought to identify risk factors for recurrent GERD after fundoplication. Some find that postoperative retching or forceful vomiting increase the risk for recurrent GERD as this increase intraabdominal pressure and put a mechanical strain on the wrap, causing herniation and/or disruption (167,178). Furthermore, younger age at fundoplication is associated with a higher risk for recurrent GERD, especially in patients under 4 months of age (167,179,180). With regards to comorbidity and recurrent GERD, some report higher recurrence rates in patients with esophageal atresia and congenital diaphragmatic hernia, whilst others find no difference (179,181,182). These patients may have increased risk for recurrence because of anatomical and functional changes associated with esophageal atresia and congenital diaphragmatic hernia. Whether operative technique or NI influence recurrence rate is an ongoing debate and is discussed in a separate section of this introduction.

Recurrent GERD in pediatric patients can be treated with various approaches. Most will undergo a trial of PPI, and this can be effective in treating both symptoms and complications in some (183). The most surgical option is a RF which is discussed below. An alternative option in patients with NI is jejunal feeding; either through a transgastric jejunal tube or a jejunostomy (179). Jejunal tube feeding may be associated with major complications and mortality, as well as frequent tube dislodgements and other mechanical problems (184,185). Furthermore, recurrent GERD may be treated with total esophagogastric dissociation. This procedure is performed by separating the esophagus and stomach, creating a Roux-en-Y esophagojejunostomy and a inserting GT (if not already present) (186).

5.4.3 Redo fundoplication

Most RFs are performed during the first two years postoperatively. Time from the primary fundoplication to RF is median 1.0-2.4 years, but ranges up to 14.7 years (166,175,179,187).
Reported indications for RF are either GERD not responding to conservative treatment, discomfort from a herniated wrap or persistent dysphagia (179,180). RF is considered more technically challenging, mainly due to the altered anatomy and adhesions from the previous operation. RF was traditionally performed with open technique, but laparoscopic technique has become more common also for RF and can be performed in patients who have had previous ONF (180,188). If patients have signs of delayed gastric emptying, a pyloroplasty may be performed concomitantly with RF to lower the risk for recurrent GERD, although this is controversial (187).

Outcomes after RF are rarely reported but appear to be worse than after primary fundoplication. Studies reporting wrap failure after RF or re-RF find recurrent GERD in 6-26 % (180,187,189,190), whilst studies including symptoms and objective findings report recurrent GERD in 26-42 % (175,179). One study of 32 patients undergoing RF found that 61 % were back on PPI, and 42 % had been treated with a re-RF or jejunal feeding (191). Only 17 % of caregivers in this study said the RF had improved symptoms of GERD and that they would proceed with fundoplication again. Two studies have reported worse outcomes after RF for patients with NI when compared to patients without NI (175,190).

5.4.4 Laparoscopic vs. open fundoplication

LNF quickly gained popularity among both adult and pediatric surgeons. Early reports from adult studies reported shorter convalescence, fewer postoperative complications and similar rates of recurrent GERD compared to ONF, which was later confirmed with multiple RCTs (192). Non-randomized studies in children also reported similar or better results after LNF (193), and therefore, fundoplication with laparoscopic technique is now considered the gold standard for surgical treatment of GERD in children (107). However, a retrospective study of 762 patients from 2005 found higher recurrence after LNF than after ONF (194).

Three RCTs comparing LNF and ONF have been performed during the last decade. In two RCTs, both with around forty participants, no statistically significant difference in recurrent GERD was found (155,195). Pacilli and coworkers reported recurrent GERD in 20 % after LNF and 12.5 % after ONF (155). In the RCT by Papandria and coauthors, 12 % of LNF patients had a RF compared to 4 % of ONF patients (195). The third RCT has been carried out at the department where I have written my thesis. This study of 87 children found no difference in length of stay or postoperative complications, but recurrent GERD was significantly more frequent after LNF than after ONF after a follow up of median four years (37 % vs. 7 %).
Two meta-analyses have pooled the results of these RCTs, and both report higher rates of recurrent GERD and longer operating time after LNF compared to ONF (196,197).

There have been suggested modifications to improve the LNF technique and to lower the risk for recurrent GERD. One such modification is to use pledgeted mattress sutures for closure of the crura and construction of the wrap. Curtis and co-workers found a significantly lower risk of recurrent GERD after changing their LNF technique from single sutures to included pledgeted sutures (23 % vs. 6 %) (198). There is also evidence suggesting that minimal esophageal dissection during LNF can reduce the risk for wrap herniation. In an RCT comparing traditional maximal to minimal dissection, wrap herniation and RF was significantly less common after minimal esophageal dissection (199).

5.4.5 Fundoplication in patients with neurologic impairment

Children with NI constitute a large proportion of the population undergoing fundoplication. Several retrospective studies have reported worse outcomes after fundoplication in children with NI compared to children without NI; complications, recurrent GERD and mortality were more common (200,201). Newer studies, both retrospective and prospective, are inconclusive (167,178). In a study by Capito and coauthors, recurrent GERD was found in 12 % of patients with NI compared to 2 % in patients without NI (149). Recurrent GERD symptoms was found in 31 % with NI compared to 25 % without NI in a study by Mauritz and coworkers (202). A recent meta-analysis including both retrospective and prospective studies found higher rates of recurrence in patients with NI, but concluded that there is poor quality of studies on postoperative outcomes after fundoplication in patients with NI (203).

5.5 Gastroesophageal reflux and gastrostomy tube feeding

Whether GT causes, worsens, or reduces GERD has been widely debated and investigated. In the 1980s and 90s, some would perform antireflux surgery concomitantly with GT insertion, as it was believed that GT insertion precipitated or worsened GERD. This has, however, been contradicted in several later studies, as shown in a systematic review on the subject (204). A study using 24-hour pH monitoring and symptom reports before and after PEG insertion, found that most patients remained without signs of GERD, and some patients with preexisting GERD continued to have reflux after PEG insertion (205).

Patients undergoing GT insertion often have comorbidities that increase the risk for GERD, and current recommendations state that children undergoing GT insertion should be evaluated for GERD (9). GT insertion with prophylactic antireflux surgery is associated with higher risk of
complications compared to GT insertions alone (206). In most cases, antireflux surgery can be performed at a later stage if GERD proves to be unsatisfactorily relieved with conservative and medical treatment (207).
6. Aims of thesis

Main aim: To study outcomes after introduction of new techniques for GT insertion and antireflux surgery in children

Secondary aims:

1. To study trends in GT insertion in children
2. To study complications after novel techniques for GT insertion and antireflux surgery
3. To compare long-term surgical and patient-reported outcomes between LNF and ONF
4. To study surgical and patient-reported outcomes after RF
5. To compare results of fundoplication in patients with and without NI
7. Materials and methods

This section briefly outlines the methods that have been applied in the various studies of this thesis. A more detailed description can be found in the attached manuscripts.

7.1 Paper 1

“Trends in the use of gastrostomies at a tertiary paediatric referral centre”

7.1.2 Subjects

Patients <15 years who underwent primary GT insertion at Oslo University Hospital (OUS) Rikshospitalet from 1994 to 2012 were included. The only exclusion criterion was lack of necessary information from the medical records. Of 655 patients identified, 649 were included in the study.

7.1.3 Methods

A retrospective chart review was performed to record demographics and perioperative data, including type of GT. Mortality during the follow-up period was obtained from the National Population Registry. Subsequent fundoplications were recorded.

7.1.4 Statistics

Categorical data were presented as frequencies and percentages, numerical data as median and range. Data were aggregated according to year, and a Spearman’s correlation coefficient (rho) calculated. To compare mortality and the number of patients with concomitant and subsequent fundoplication, data were aggregated into 5-year periods and a chi squared test performed.

7.2 Paper 2

“Initial experience with percutaneous endoscopic gastrostomy with T-fastener fixation in pediatric patients”

7.2.1 Subjects

The study included patients under 18 years who had undergone primary PEG-T insertion at OUS Ullevål between 2010 and 2014. There were no exclusion criteria, and 87 patients were included.

7.2.2 Methods

Data were collected retrospectively and included demographics, perioperative data, and postoperative complications. Complications were graded according to the Clavien Dindo Classification (208) (Table 1). Early complications (<30 days) included all complications,
whilst late complications included only GT related complications. The technique for PEG-T was done according to the manufacturer’s procedure as described in the introduction of this thesis.

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Table 1. Clavien Dindo Classification of surgical complications (208).

7.2.3 Statistics
Categorical data were presented as frequencies and percentages, numerical data as median and range. Risk factors for postoperative complications such as NI, age less than one year and weight under 10 kg, were analyzed using the chi squared test. Complications and operating time were compared in the first and second half of patients to investigate a potential learning curve. Complication rates were compared with the chi squared test. Operating time was not normally distributed, and therefore presented as median and compared with the Mann Whitney U-test.

7.3 Paper 3
“Laparoscopic gastrostomy placement in children has few major, but many minor early complications”

7.3.1 Subjects
Patients under 16 years of age who had a LAPG inserted in the period from 2005 to 2018 at OUS Rikshospitalet were included. There were no exclusion criteria, and 104 patients were included.

7.3.2 Methods
A retrospective chart review recorded demographics, perioperative data and early postoperative complications (<30 days). Complications were graded according to the Clavien Dindo Classification (table 1) and recorded as GT related or general.

7.3.3 Statistics
Categorical data were presented as frequencies and percentages, numerical data as median and range. Potential risk factors for gastrostomy related complications were investigated using the
chi squared test and included NI, age <1 year, surgeon’s rank (junior/consultant), and tube size. Calculations for a potential learning curve were performed as described for paper 2.

7.4 Papers 4 and 5

“Nissen fundoplication in children with and without neurological impairment: A prospective cohort study”

“Outcome a decade after laparoscopic versus open Nissen fundoplication in children; results from a randomized controlled trial”

7.4.1 Subjects

Papers 4 and 5 present data from a prospective, randomized controlled trial where the primary outcome was to compare recurrence of GERD after LNF and ONF. The study population was the same in papers 4 and 5 and included patients referred for fundoplication at OUS Rikshospitalet 2003-2009 and at Ullevål 2007-2009. Inclusion criteria were GERD verified with 24-hour pH monitoring and/or UGI contrast study, and insufficient effect of conservative antireflux treatment. 105 patients were eligible for inclusion, and 11 were excluded because of comorbidity not compatible with laparoscopy (n=8), need for urgent operation and no time for randomization (n=2), and parents did not speak Norwegian (n=1). Six were unwilling to participate (figure 6). Consequently, 88 patients were included and randomized to LNF or ONF. Two patients died before the first scheduled clinical follow-up six months postoperatively and could not be evaluated for recurrence. One patient was excluded for analysis of recurrence because the indication for fundoplication was a paraesophageal hernia. Consequently, outcomes could be evaluated in 85 patients, of whom 44 had NI. Later, 13 patients died and two emigrated, leaving 70 patients eligible for the long-term follow-up (paper 5).

7.4.2 Methods

Patients were randomized to either LNF or ONF in blocks of ten. Randomization was unstratified, and the study was non-blinded. Operative technique for the Nissen fundoplication was standardized and identical except from laparoscopy or laparotomy. Postoperative care was also standardized and included prophylactic antiemetics the first 24 hours to avoid retching. All LNFs were performed by trained laparoscopic surgeons, whilst ONFs were performed by consultants or junior doctors under the supervision of a consultant.

Demographics and GER symptoms were recorded preoperatively. All patients were scheduled for clinical examination and diagnostic investigations six months after the fundoplication, and later if indicated. Semi-structured telephone interviews recording symptoms of GER and
Troublesome side effects were scheduled after one, two, and four years for paper 4 and after 12 years for paper 5. The interviews also included questions on parental and patient satisfaction with the outcome of the fundoplications and improvement in well-being.

**Figure 6.** Flow-chart of patients included in a randomized controlled trial comparing laparoscopic and open Nissen fundoplication.

In paper 4, early postoperative complications were graded according to the Clavien Dindo Classification (table 1), and a Complex Complications Index (CCI) was calculated, in which complications are summed and weighted for severity (209). This creates a scale from 0 to 100; 0 implying no burden from complications and 100 meaning death.

Recurrence of GERD was in paper 4 defined as a combination of clinical symptoms of GER and objective verification of GER (RI >4 on 24-hour pH monitoring and/or GER/herniated wrap

34
on an UGI contrast study). Paper 5 adapted a wider definition of recurrence, where recurrence was defined as presence of any of the following criteria: Heartburn, regurgitation and/or vomiting more than once a week, weekly or more frequent use of antisecretory drugs because of GERD, jejunal or parenteral feeds due to GER symptoms, endoscopic macroscopic esophagitis or new-onset Barrett’s esophagus, RI>4, GER on UGI contrast study, wrap herniation on UGI contrast study or endoscopy, or RF.

7.4.3 Statistics
Comparison of categorical data between patients with and without NI in paper 4 was performed with a chi squared test or Fishers exact test as suited. Operating time was compared with Student’s T-test whilst other numerical data was compared with Mann-Whitney U test as data were not normally distributed. To compare recurrence of GERD between patients with and without NI in paper 4, a logistic regression model was used, correcting for surgical technique as LNF had been shown to have higher rates of recurrence (151). Comparison of patient reported outcomes between the patients with and without NI and over time was performed using Generalized Estimation Equation with a poisson-regression type model.

In paper 5, continuous data were presented as mean (standard deviation) if normally distributed or as median [interquartile range] if not normally distributes. Categorical data were compared with chi squared test or Fisher’s exact test as appropriate and expressed by risk ratio and 95 % confidence interval. The McNemars test was used to compare the proportion of patients using antisecretory drugs before and after the fundoplication. To compare recurrence of GERD, Kaplan-Meier plot and log rank test were used. Furthermore, a hazard ratio for recurrence of GERD in LNF vs. ONF was calculated using univariate Cox regression.

7.5 Paper 6
Short and long-term outcomes after pediatric redo fundoplication

7.5.1 Subjects
Patients who underwent RF in childhood (age <18) at OUS Rikshospitalet between 2002 and 2020 were eligible. Patients were included if consent to participate was obtained. Exclusion criteria were emigration and death at follow-up. 24/31 patients were included. Of the six who were not included, four did not reply, two were dead, and one had emigrated.

7.5.2 Methods
This study was a retrospective chart review with a cross sectional follow-up. Demographics, data from the primary fundoplication, investigations prior to RF and perioperative data were
collected from medical records. Early complications were graded according to the Clavien Dindo Classification. GER symptoms, treatment of recurrent GERD or troublesome gastrointestinal symptoms were recorded retrospectively. A questionnaire was sent during the period 2019 to 2020 to either patients or caregivers according to age and NI (attachment 1). The questionnaire was derived from the Pediatric Quality of Life Inventory Gastrointestinal Symptoms Scale (210) and included questions on GER symptoms, stomach pain and troublesome side effects. All items were answered on a 5-point Likert scale (0: never, 1: almost never, 2: sometimes, 3: often, 4: almost always). The questionnaire also included questions on use of antisecretory drugs and satisfaction with the RF.

7.5.3 Statistics
The answers from questionnaires were transformed to dichotomous variables; 3 and 4 were reported as “yes” and 0, 1 and 2 as “no”. Categorical data were presented as frequencies and percentages, and numerical data as median and range as they were not normally distributed.

7.6 Classification of comorbidity
The same definition of NI was used in all papers; “a static or progressive, central or peripheral neurologic condition associated with chronic functional or intellectual impairment “ (211). In paper 4, patients with NI were further classified as having severe NI if three or more of the following criteria were found: Cerebral palsy, mostly or exclusively tube-fed, daily epilepsy medication, and non-ambulatory.

7.7 Statistical software
All studies used IBM SPSS Statistics for Windows (IBM, Amonk, NY). Version 20.0 was used in paper 4, version 21.0 in paper 2, version 25.0 for paper 3 and 6 and version 27.0 for paper 5. In paper 4, we used STATA version 11 (StataCorp LP, College Station, TX) to perform the Generalized Estimation Equation analyses, whilst Kaplan-Meier analyses was performed with STATA version 15 in paper 5. A p-value <0.05 was considered statistically significant in all papers.
8. Ethics

All papers followed the ethical principles outlined in the Declaration of Helsinki. Studies in papers 1, 2, 3 and 6 were approved by the Data Protection Officer at OUS, and for paper 6 written consent was obtained before inclusion. The RCT of which papers 4 and 5 were part of was approved by the Regional Committees for Medical and Health Research Ethics, and renewed approval was obtained for paper 5. Participation was voluntary, and written consent obtained from all patients/parents before inclusion. The RCT is registered at https://clinicaltrials.gov (reference number NCT01551134).
9. Summary of main results

This section outlines the main results of the studies included in this thesis. A complete overview of results can be found in the attached manuscripts.

9.1 Paper 1

“Trends in the use of gastrostomies at a tertiary paediatric referral centre”

The annual number of patients undergoing GT insertions nearly doubled during the 19-year study period from 24 per year in 1994 to 57 per year in 2012 (Spearman’s rho 0.90, p<0.001). The most common comorbidity was NI which accounted for nearly half of the patients (48 %). The number of patients with comorbidities other than NI increased during the study period, especially for those with cardiac disease (Spearman’s rho 0.88, p<0.001) and other congenital malformations (Spearman’s rho 0.62, p=0.005). The median age at GT insertion was 1.2 years, and decreased during the study period (Spearman’s rho -0.83, p<0.001).

The most common surgical technique was PEG (62 %), followed by open technique (31 %) and LAP-G (7 %). The number of PEG and LAP-G insertions increased (Spearman’s rho 0.83 and 0.65, p<0.01). The proportion of patients undergoing a concomitant fundoplication (8 %) decreased (p<0.001), whereas the proportion of patients having a fundoplication after the GT insertion (7 %) remained stable (p=0.8).

9.2 Paper 2

“Initial experience with percutaneous endoscopic gastrostomy with T-fastener fixation in pediatric patients”

Complications were common after PEG-T, and most were Clavien-Dindo grade I or II. Nearly half of 87 patients experienced one or more early postoperative complications (Table 2). The most common complications were stoma infections (26 %), tube dislodgement (10 %) and pneumonia (6 %). The Grade IIIb complications (7 %) were handled with laparotomy (4/6 patients) and endoscopy (2/6 patients). Early and late complications related to T-fastener were reported in 11 % and 13 % of patients, respectively.

There was no difference in complication rates between patients with and without NI (49 % vs. 47 %, p=0.86), patients below or over 1 year (48 % vs. 49 %, p=0.95) or weight below or over 10 kg (50 % vs. 47 %, p=0.77). No learning curve could be demonstrated as operating time (28
vs. 27 minutes, p=0.26) and complication rate (44 % vs. 52 %, p=0.45) were similar when comparing the first and second halves of patients.

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<td>Age</td>
<td>1.9 years (2.9 months-16.4 years)</td>
<td>1.2 years (1 day-15.2 years)</td>
</tr>
<tr>
<td>Patients with neurologic impairment</td>
<td>61 % (53/87)</td>
<td>52 % (54/104)</td>
</tr>
<tr>
<td>Patients undergoing concomitant procedures</td>
<td>7 % (6/87)</td>
<td>33 % (34/104)</td>
</tr>
<tr>
<td>Operating time</td>
<td>28 minutes (10-65)</td>
<td>37 minutes (19-86)</td>
</tr>
<tr>
<td>Patients with early complications</td>
<td>47 % (41/87)</td>
<td>38 % (40/104)</td>
</tr>
<tr>
<td>Patients with grade III or IV complications</td>
<td>7 % (6/87)</td>
<td>10 % (10/104)</td>
</tr>
<tr>
<td>Patients with early tube dislodgement</td>
<td>10 % (9/87)</td>
<td>6 % (6/104)</td>
</tr>
</tbody>
</table>

Table 2. Demographics, perioperative data and complication rates in patients undergoing insertion of percutaneous endoscopic gastrostomy with T-fastener gastropexy (paper 2) and laparoscopic gastrostomy (paper 3). Median (min-max) values are given for age and operating time.

9.3 Paper 3

“Laparoscopic gastrostomy placement in children has few major, but many minor early complications”

Early gastrostomy-related complications were common after LAP-G. Of 104 patients, 38 % experienced complications, and most were grade I or II (table 2). The most common complications were stoma infections (13 %), granulation tissue (13 %), leakage (8 %), and tube dislodgement (6 %). Because of massive leakage in two patients, enteral feeding was stopped, and a central venous catheter inserted for parenteral nutrition. Non-gastrostomy related complications, such as respiratory complications were recorded in 11 % of patients. Patients without NI had more complications than patients with NI (46 % vs 22 %, p=0.01), but age (<1 year: 35 %, >1 year:32 %, p=0.7) and tube size (12 Fr: 44 % vs. 14 Fr: 30 %, p=0.19) did not influence complication rates. Furthermore, patients operated by a junior doctor did not experience more complications that those operated by consultants (35 % vs. 32 %, p=0.7). A significant learning curve for operating time was found (46 vs. 35 minutes, p=0.04). We did not find that more experience with the technique led to fewer gastrostomy related complications (37 % vs. 31 %, p=0.5).
9.4 Paper 4

“Nissen fundoplication in children with and without neurological impairment: A prospective cohort study”

Outcomes after fundoplications did not differ between patients with and without NI. Recurrent GERD occurred in 12 (27%) patients with NI and in 7 (17%) without NI (p=0.31). Parental satisfaction was high and similar in both groups. Median four years after fundoplication, 97% of parents in both groups would choose fundoplication again. Fundoplication ensured significantly reduced vomiting and regurgitation in both groups, and this remained significant four years after the antireflux surgery (p<0.001). Patients with NI spent more days at the hospital postoperatively (9 vs. 4 days, p<0.001), but there was no significant difference in CCI score between those with and without NI (20.9 vs. 8.7, p=0.09).

9.5 Paper 5

“Outcome a decade after laparoscopic versus open Nissen fundoplication in children; results from a randomized controlled trial”

43 and 42 patients were randomized to LNF and ONF, respectively. The follow-up time for the included 70 patients was median 11.9 years [9.9-12.8]. Recurrence of GERD was significantly more common after LNF (56%) than after ONF (31%) (p=0.004). The hazard ratio for recurrence after LNF was 2.6 (95% confidence interval 1.3-5.1, p=0.006). Recurrent GERD occurred earlier after LNF than after ONF (figure 7). The most common treatment for recurrent GERD was antisecretory drugs, and RF was performed in 19% and 7% after LNF and ONF, respectively (p=0.16).

No GER symptoms were reported in 86% of the patients at follow-up, with no difference between the two groups. Patient and parent satisfaction were high in both groups: 81% and 88% were completely satisfied with the LNF and OND, respectively (p=0.5), and over 95% in both groups would recommend fundoplication to others if in the same situation (p=0.47).
Figure 7. Kaplan-Meier plot of recurrence of gastrosophageal reflux disease after laparoscopic and open Nissen fundoplication.

9.6 Paper 6

Short and long-term outcomes after pediatric redo fundoplication

The most common indication for RF was recurrence of GER symptoms (75 %), followed by discomfort from a herniated wrap (21 %) and slipped Nissen (4 %). 67 % of patients had NI. All patients had at least one investigation showing recurrent GER before RF. The RF was performed with laparoscopy in 21 % of the patients, and with open technique in the remaining patients. 50 % of the patients experienced postoperative complications, and 33 % had more than one complication. The majority (70 %) of complications were grade I or II.

One in five patients (21 %) reported recurrent GERD after the RF. Of the five patients with recurrent GERD, three had either improved or complete relief of symptoms with appropriate treatment. Only one patient had more than one RF. 18/22 (82 %) patients or caregivers would choose surgery again, and 21/22 (96 %) said they would recommend RF to someone in a similar situation. The most common symptoms reported at follow-up were excessive flatulence (39 %), and stomach pain (37 %). One patient (4 %) had new onset delayed gastric emptying, and one (4 %) patient had new onset retching, and both were successfully treated with jejunal feeding.
10. Discussion of main findings

10.1 Trends in gastrostomy insertion

In our first study we investigated if there had been any changes in the use of GT during the last two decades and our most important finding was that the number of gastrostomy insertions more than doubled. This is in line with other similar studies (11,39). One of the most likely reasons for the observed changes is probably evidence showing that GT feeding is safe and effective. Nutritional support is important for improving outcomes and general well-being in pediatric patients, and there is an increased focus on nutrition and feedings problems in children (212,213). Moreover, there has a been shift from feeding through a nasogastric tube to GT feeding because nasogastric tube-feeding is associated with discomfort, repeated dislocations and more oral food aversion than GT feeding (16). GT feeding can also be used in shorter time periods in patients with transient underlying comorbidity such as cardiac disease and cancer, and weaning of GT feeding in such patients is often successful (49).

The introduction of the PEG technique was a real game changer, because it is less invasive than the traditional open gastrostomy. Minor interventions are associated with less stress and anxiety in parents compared to major interventions (214). Furthermore, the newer techniques LAP-G and PEG-T allow primary insertion of a low-profile balloon button, and clinical experience suggests that low-profile balloon buttons are something caregivers want because they are less irritating and esthetically more appealing (215). The introduction of PEG and later improvement in GT techniques may have lowered physicians’ and caregivers’ threshold to insert a GT, so that GT insertion is offered to a more extended group of patients.

Just about every patient with the need for GT feeding has one or more complex and chronic conditions. Patients with NI constitute the largest group of patients undergoing GT insertion, but we found that GT insertions was increasingly used in other patients as well. In particular, there was a relative increase of patients with cardiac disease and other congenital malformations, consistent with the results of Fox and co-workers (39). During the last decades, the survival in such patients has improved (216,217), and those who survive with sequelae may need GT feeding. Since these patients often need nutritional support early in life, we found, as expected, that the median age at GT insertion has decreased. It has later been found that most GTs are inserted before the age of 2 years (13). Furthermore, 1 in 5 patients undergoing GT insertion in our cohort were born preterm. Preterm babies have an increased risk for comorbidities leading to feeding problems (218). An increase in survival has been linked to
increased use of GT feeding in ex-premature children (40). Lastly, our clinical experience suggest that it is now more common to give patients with serious comorbidity a GT, because of increased anesthetic competence and because of the known benefits of GT feeding in these patients. Supporting this is our finding that GT was inserted also in patients with a short life expectancy.

10.2 Postoperative complications after gastrostomy tube insertion

GT insertion is considered a minor procedure, but the complication rate is high. We wanted to explore whether complications also were common after two new techniques for GT insertion: PEG-T and LAP-G. We found that many patients experienced complications after both PEG-T and LAP-G, but most of the complications were minor (Claviern-Dindo grade I or II). Major complications (Clavien-Dindo grade III or higher) were rare.

10.2.1 Minor complications

Peristomal infections are of the most common minor complications after GT insertion, both in our studies and in the literature (47,58,72). Peristomal infections may occur immediately or long after the child got the GT, and for some, it is a recurrent problem. It is suggested that PEG-T and LAP-G have lower risk for early peristomal infections because these push techniques, as opposed to PEG-P, omit the oral flora. This has been confirmed in a metanalysis of adult of PEG push techniques (219), whilst studies in children are conflicting (30,32). Gothberg and coworkers found higher rates of peristomal infection after PEG-T compared to PEG-P (6 % vs 3 %), whilst Jacob and coauthors found lower rates after PEG-T (11 % vs 29 %) (30,32). Compared to these two studies, the rate of peristomal infection in our cohort of PEG-T patients was rather high. Furthermore, we found that peristomal infections appeared to be more common after PEG-T (26 %) than after LAP-G (13 %). No studies have compared the peristomal infection rate between LAP-G and PEG-T, but studies comparing LAP-G to PEG-P find similar rates of peristomal infection (34,220,221). Based on the retrospective chart reviews after PEG-T and LAP-G, the threshold to start antibiotic treatment for suspected peristomal infection was low. Some cases classified as infection may in fact have been leakage and/or local inflammation. Both our studies were retrospective, and there was no standardization for classification of peristomal infection. A better designed study may have improved diagnostic accuracy (222).

Leakage was reported after both PEG-T and LAP-G and was in some related to peristomal infection. Both our studies reported lower rates of leakage than several previous studies.
In a study of 346 PEG-P and LAP-G insertions, chronic leakage was found in 16\%, suggesting that this also is a long-term problem (22). In many cases, leakage can be handled with conservative measures such as adjustment of the GT, giving smaller volumes of feeds or temporarily stopping feeds through the GT. In a few, interventions such as surgical revision is needed (67). In our studies, two patients had so severe leakage after LAP-G that feeds had to be stopped, and a central venous catheter was placed to provide parenteral nutrition. Furthermore, four patients had their PEG-Ts changed early due to leakage. Since leakage is common after both PEG-T and LAP-G, this may be a complication not directly related to technique, but to the GT itself. A reason for leakage after LAP-G may be that the opening in the abdominal wall is too wide. Our clinical experience is that the U-stitch method for LAP-G can be performed with a smaller incision compared to the purse string method. 24\% of LAP-G insertions in our study was with the U-stitch method and the remaining 76\% with the purse string technique. We could not, however, demonstrate a difference in complication rate between the two methods, which is in line with Backman and coworkers’ findings of similar leakage rate between these two techniques (223). Although we did not find that age or weight was a risk factor for complications, our clinical experience is that that a wider incision is needed to insert the LAP-G in patients with more subcutaneous fat. Lastly, it has also been suggest that size of the balloon tube may influence the leakage rate (224), but we did not find that tube size influenced the overall complication rate.

We found lower rates of hypergranulation tissue after PEG-T and LAP-G compared to other studies with longer follow-up (58,61,63). In our cohort of PEG-T patients, hypergranulation was found in only 3\% during the first 30 days, but this increased to 20\% long-term. This supports the assumption that hypergranulation is a problem that occurs more long-term (58). Based on the numbers from our two studies, hypergranulation may be more common after LAP-G, as suggested by Sutherland and coworkers (225). In their retrospective study of 450 patients undergoing GT insertion with various techniques, higher rates of hypergranulation was found after fascial techniques (mainly LAP-G) compared to push techniques (including PEG-T). They suggested that the fascial sutures used for LAP-G might be the explanation for this observed difference, as they can cause local inflammation. Many techniques for LAP-G have been described, and not all techniques use fascial sutures. Backman and coauthors found lower rates of hypergranulation after implementing the U-stitch method compared to their previous purse string method (223).
Many physicians consider minor complications an unavoidable problem after GT insertion. Although not life threatening, minor complications are troublesome and time consuming for both patients and caregivers. Furthermore, they are associated with a substantial clinical burden and costs due to telephone calls and clinic visits. In a study of 219 children undergoing GT insertion, 20% of patients returned to the emergency room during the first 30 days (226). Interestingly, 39% of these visits were problems that were considered preventable or that could have been handled at home (e.g., hypergranulation or minor clogs). Similarly, many parents of patients in our studies contacted the hospital for minor stoma problems that were preventable or not classified as complications (unpublished data). Standardization of pre-, per- and postoperative investigations and care have been shown to reduce emergency department visits and improve satisfaction (227,228). Furthermore, educational programs aiming to improve outcomes after GT insertion have been developed (229,230). At our two departments, educational material is distributed, and dedicated nurses provide information and instructions on use to caregivers before and after GT insertions. These nurses are also available for telephone consultations. This may contribute to better care and fewer complications. Considering our findings of many minor complications, such services such be strengthened to further lower complication rates after GT insertion.

**10.2.2 Tube dislodgement**

Tube dislodgement is a commonly reported problem after GT insertion, and our findings after PEG-T and LAP-G are in line with previous reports (47,61,68). Dislodgement is especially problematic if it occurs in the early postoperative period, when the stoma channel has not fully healed. If the stomach detaches from the abdominal wall, this can lead to leakage of gastric contents into the abdominal cavity and peritonitis. A metanalysis found lower rates of early tube dislodgement with operative management after LAP-G compared to PEG-P (231). Both PEG-T and LAP-G include gastropexy with sutures to secure the stomach to the abdominal wall in the event of GT dislodgement. It is therefore assumed that early dislodgement after PEG-T and LAP-G can be handled with bedside reinsertion, without the need for surgery or endoscopy. All patients experiencing early dislodgement after LAP-G could have a new GT inserted bedside, as in line with other studies (47,67). Surprisingly, we found that half of the patients who experienced early dislodgement after PEG-T required intervention with either surgery or endoscopy. This contrasts previous reports. Gothberg and coworkers reported tube dislodgement needing reinsertion under general anesthesia in only two of 206 children undergoing PEG-T insertion, both during the first postoperative day (30). Interestingly, none
of the patients with tube dislodgement in our study had signs of detachment of the stomach from the abdominal wall. Since the technique was new, and we had little experience with the patency of the gastropexy, treatment of tube dislodgement with surgical or endoscopic intervention may have been a precautionary approach. It is possible that we will see an institutional learning curve with more experience, and that operative management of tube dislodgement after PEG-T can be avoided. The role of T-fasteners and timing of cutting of sutures is further discussed below.

10.2.3 T-fastener complications

The high rate of complications related to the T-fasteners was a surprising finding after PEG-T insertion, especially that migration caused pain and need for operative management. Migration of T-fasteners has previously only been reported in a few pediatric patients (78,79). Optimal timing for cutting the T-fastener is controversial, and late removal of the T-fasteners has been proposed as a reason for T-fastener migration and problems related to migration. Livingston and coworkers changed their protocol from cutting sutures at 3-4 weeks to 5 days postoperatively and reported no T-fastener related complications after this (78). In another study in children, sutures were cut after 2-3 weeks, and there were no reports of migrated sutures (30). The procedure at our center was that sutures should be cut 3-4 weeks postoperatively if not spontaneously detached. When performing the chart review, we found that this was not done in all patients. We could not link late removal of sutures to migration of the T-fasteners, because it was not adequately reported in the patients’ charts. We have now changed our protocol and cut sutures after 2 weeks. We recently performed a prospective study of 82 patients undergoing PEG-T between 2017 and 2020, and T-fastener related complications occurred in only 1 % (unpublished data). Although there is a lot of focus on not cutting the sutures too late, we do not know if late cutting of sutures in fact is the cause of T-fastener migration. In a study in adults, CT after PEG-T demonstrated that after 4 weeks, 36 % of T-fasteners had migrated into the abdominal wall, and the authors suggested that migration occurs early after the procedure, possibly already during tract dilation and insertion of the GT (77). This should also be taken into consideration if early tube dislodgement occurs, because it is necessary to have a patent gastropexy if bedside reinsertion is to be considered safe. Furthermore, cutting the sutures too early can be problematic in case of early tube dislodgement, if the stoma channel has not matured sufficiently. Results from an animal study suggest that the stoma channel matures already one week after PEG-T (232), but the evidence on when to cut sutures children is poor and should be further investigated.
10.2.4 Major complications

Major complications after GT insertion are feared because they can lead to substantial morbidity and in the worst case, mortality. In our studies, early major complications after GT insertion occurred in 7% after PEG-T and 10% after LAP-G, comparable to results from other studies (47, 59, 69, 70). There were no procedure related mortalities in any of the three studies.

In our study of LAP-G, two major complications were related to the placement of the GT itself (short gastrostomy button and gastric outlet obstruction). This shows the importance of being aware of potential pitfalls and awareness of correct placement of the GT. Furthermore, there were two laparoscopy-specific complications that occurred after LAP-G (omentum trapped in umbilical port and suspected facial defect). Such complications have been reported earlier and appear to be rare. In a study of 461 patients undergoing LAP-G, port hernia occurred in only 0.7% of patients (67). Major complications after PEG-T were related to either tube dislodgement or suspected injury of intraabdominal organs. Perforation of intraabdominal organs is a feared complication after PEG because insertion of the tube into the stomach is performed blindly. Consequently, PEG techniques are associated with a higher risk for perforation of intraabdominal organs than LAP-G (74, 231). As expected, there were no reports of such complications after LAP-G. In contrast, this was suspected in two patients after PEG-T, but the suspicion was refuted during surgery. As discussed earlier, because we had little institutional experience with PEG-T, the threshold to perform laparotomy when intraabdominal organ injury was suspected may have been lower compared to after other GT techniques with whom we had more experience. Some choose to perform PEG insertion with laparoscopic assistance to avoid injury to intraabdominal organs (37). This was done in five of the patients in paper 1, mainly due to inadequate transillumination (unpublished data).

10.2.5 Risk factors for complications after gastrostomy insertion

As discussed, GT insertion is associated with a high frequency for complications. Many have therefore tried to identify risk factors for complications, but studies are inconclusive. Having a ventriculoperitoneal shunt has been shown to increase the complication rate (69, 70). There were too few patients with a ventriculoperitoneal shunt in our two studies to investigate this as a risk factor. Whether NI is related to reduced or increased complications rate is also debated (8, 22, 69). In our study on LAP-G, patients with NI had lower complication rates. In contrast, the complication rate was not different between patients with and without NI after PEG-T. McSweeney and co-authors found that American Society of Anesthesiologists class III and age under 6 months decreased the risk for complications after PEG-P. As patients with NI or high
American Society of Anesthesiologists class are known to have higher morbidity, it is possible that postoperative monitoring and care are more meticulous, and that this lower the risk for complications. Furthermore, many parents of patients with NI have experience with medical equipment and may therefore have an easier time dealing with the GT.

10.3 Techniques for gastrostomy tube insertion

There is an ongoing debate as to which technique for GT insertion is the best one. The only RCT comparing techniques for GT insertion compared PEG-P to radiologically inserted GT and found no difference in complication rates (19). No RCT has compared various PEG techniques to LAP-G. Multiple retrospective and prospective studies comparing PEG-P to LAP-G have been published, and many favor LAP-G (22,34,36,220,233). Most of these studies find more complications after PEG-P compared to LAP-G, particularly major complications such as perforation of intraabdominal organs. A metaanalysis of GT insertion in 1550 children found major complications in 5.4 % of PEG-P patients compared to 1.0 % in LAP-G patients (234). Based on these numbers, the number needed to treat to avoid one major complication by using LAP-G as a substitute for PEG-P was 23. As none of the studies comparing LAP-G to PEG are RCTs, there is a risk for selection bias. Another argument for LAP-G compared to PEG-P is that one can omit a second anesthesia when changing the tube to a balloon tube. This is an advantage with PEG-T as well. Based on the literature, the U-stitch method may be preferred over the purse string method (67,223). The open GT technique is still in use and has been found to have similar outcomes as LAP-G and may be preferred in patients with previous abdominal surgery (21). It is not possible, based on the two studies in this thesis, to decide which technique is superior – PEG-T or LAP-G. It appears that choice of GT technique is a matter of tradition, surgeons’ preference and experience with one’s own results.

10.4 Recurrence after primary and redo fundoplication

An important reason for performing a fundoplication is to relieve a child of troublesome GER symptoms and complications. Therefore, it is crucial to investigate whether the symptoms disappear and if they come back. When comparing recurrence rates between different techniques and studies, it is important to acknowledge that recurrence rates varies. A systematic review from 2016 pooled data from 18 retrospective studies including 14 580 children found unfavorable outcomes in 5-77 % (148). This is not unexpected, as different outcome measures were used. Some report only RF rate, others results from objective investigations and/or symptoms of GER and some define recurrence as reintroduction of PPI. Variation in recurrence
rates may also be explained by different study designs; inclusion criteria (e.g. indication for surgery) and the number of included patients. Prospective studies are likely to report higher rates of recurrence. Studies with a long follow-up will diagnose patients with late onset recurrence, as was the case for our long-term follow up of patients after LNF and ONF. Also, cohorts with many patients with comorbidity such as NI, previous esophageal atresia and congenital diaphragmatic may have higher failure rates, as such diagnoses have been suggested as risk factors for an unfavorable outcome after surgery (179). Lastly, it is possible that difference in reported recurrence rate is caused by varying quality of care between different centers, especially between high and low-volume centers.

10.4.1 Laparoscopic vs. open fundoplication

We found that recurrent GERD was significantly more common after LNF compared to ONF. This was reported first after median 4 years, and later confirmed twelve years postoperatively (151). There are only two other RCTs comparing LNF to ONF in children. Pacilli and coworkers reported 4-year results from their RCT of 39 children (155). Recurrence of GERD occurred in 20 % after LNF and 12.5 % after ONF. In the RCT by Papandria and coauthors, 39 patients under 2 years were randomized to LNF or ONF, and median 42 months after surgery, 12 % of LNF patients had a RF compared to 4 % of ONF patients (195). The difference was not statistically significant in either of these studies. However, both studies were underpowered, and hence, there is a chance for type 2-error. Furthermore, when the three RCTs are combined in metanalyses, the difference is statistically significant in favor of ONF (196,197).

Most pediatric studies comparing LNF to ONF are retrospective or prospective studies with a median follow-up time around one to two years (193), and there appear to be no studies, retrospective or prospective, that have compared LNF to ONF with a minimum follow-up time beyond five years. A retrospective study of laparoscopic and open Thal in children with a median follow-up time of 6.5 years found similar results with the two techniques (235). However, the minimum follow-up time in this study was only two years. Two RCTs have investigated long-term results 15 and 17 years after LNF and ONF in adults, and both find LNF to be superior to ONF (236,237). Thus, the findings from our study and the combined results in the metanalyses of the three pediatric RCTs are surprising. The reason for why we found higher rates of recurrent GERD after LNF is not clear. One explanation may be that more adhesions are formed after fundoplications with the open technique (238). These adhesions may lower the risk for disruption or herniation of the wrap, especially in patients with retching, seizures and coughing. Such symptoms are more common in children than in adults, which could explain
why there are different results in children compared to adults. Lastly, it has been suggested that minimal esophageal dissection can lower the risk for wrap herniation after LNF (239). We have now changed our technique to minimal dissection, and it remains to be seen if this will lower recurrence rates at our department.

The overall recurrence rate after LNF and ONF was 44%. There are very few studies reporting long-term outcomes after fundoplication in children. Although many have a median follow-up time beyond five years, the minimum follow-up time is considerably shorter (149,161). Thus, late recurrences will not have been reported in most of these studies. There is only one other study that has reported results after Nissen fundoplication with a minimum follow-up time beyond five years. This retrospective study by Esposito and coworkers included 32 patients undergoing LNF, and recurrence of GERD was defined as symptoms of GERD based on answers from questionnaires and 13% of patients had recurrence (169). This study excluded patients with NI. A prospective study of 57 children undergoing laparoscopic Thal fundoplication found that 43% had recurrence after minimum 10 years follow-up (202). Thus, taking results from studies with shorter follow-up into consideration, the recurrence rate from our study is comparable to what has been found previously. The Kaplan-Meier plot in paper 5 clearly shows that most cases of recurrent GERD occur during the first two years, especially after LNF. This is in line with previous reports (194). Still, cases of recurrent GERD continue to occur many years after primary fundoplication, and both patients, parents and physicians should be aware of the risk for late onset recurrence.

10.4.2 Redo fundoplication
Seeing that recurrence after primary fundoplication is common and that a significant part of patients need a RF, we wanted to investigate outcomes after RF in our population. We found recurrent GERD after RF in 21% of patients, and this in line with previous studies (175,179). Furthermore, only one of the five patients with recurrent GERD underwent more than one RF. RF is believed to have inferior results compared to primary fundoplication. In a study of 360 pediatric patients undergoing primary fundoplication, 35 patients underwent RF, and the recurrence rate after RF was higher than after primary fundoplication (12% vs 26%) (179). It is not possible to directly compare results from primary fundoplications in paper 5 to results after RF in paper 6, due to difference in study design and follow-up protocol. However, it appears that the results after RF are not significantly inferior to primary fundoplication; our center has previously reported recurrent GERD in 22% after median 4 years (151). Importantly, most patients in our study are without symptoms of recurrence after RF, and many of the
patients with recurrent GERD were successfully treated without a second RF or other surgical interventions.

Parents and physicians may be reluctant to perform RF when the primary fundoplication has failed and may be even more reluctant to perform a re-RF after failed RF. As in our series, many with recurrent GERD after RF undergo other treatments than re-RF (175). In addition to conservative and pharmacological treatment, alternatives to RF are jejunal feeding or total esophagogastric dissociation. A metaanalysis comparing primary fundoplication to jejunal feeding reported similar outcomes after the two interventions, but the quality of the evidence was deemed low (240). When compared to primary fundoplication, total esophagogastric dissociation has similar efficiency, but appear to be more invasive (intensive care admittance and length of stay) (241).

10.5 Complications and troublesome symptoms after fundoplication

Although recurrence rate is the most reported outcome fundoplication, other outcomes such as complications and troublesome symptoms are also important and say something about the burden of the operation. In our three studies of children undergoing primary fundoplication and RF, we found that a substantial number of patients experienced postoperative complications. How postoperative complications are classified and to what extent they are recorded, vary. Therefore, it is difficult to compare rates of complications to other studies. Compared to results after primary fundoplication and RF, the complications rate in our studies appears to be high (163,177). Because the Clavien Dindo classification of surgical complications includes any deviance from expected postoperative course, the complication rate may be higher compared to studies including only typical complications such as wound infection and pneumonia. When comparing complication rates after primary fundoplication and RF, it appears that RF has a higher degree of major complications. Possible explanations are a technically more challenging operation and that patients needing RF have more serious comorbidities.

With regards to long-term complications, discomfort during meals and excessive flatulence were common both after primary fundoplication and RF and might be a sign of gas bloat. These symptoms may also be a consequence of the patients’ comorbidity and a generalized gastrointestinal dysmotility, especially in patients with NI, and is therefore difficult to interpret. Preoperative retching was more common in patients with NI in study 4, but retching decreased in both groups four years after fundoplication, and there was no difference in retching after LNF and ONF. In contrast, Pacilli and co-authors found lower rates of retching after LNF compared
to ONF (155). Retching is a feared symptom after antireflux surgery, especially in the immediate postoperative period, because it increases the risk for wrap disruption or herniation and is troublesome for patients (178). Retching may be present before fundoplication or it may be new onset (146), and postoperative retching may be explained by other causes than the fundoplication, such as high bolus volume and osmolarity of feeds (242). Frequent venting of the GT and careful feeding regimes may alleviate symptoms (242), but some patients will need jejunal feeding, as was the case for one patient after RF. Patients and caregivers in the RCT were given instructions on how to handle retching postoperatively and during follow-up, which may explain the low number of patients with retching observed long-term.

### 10.6 Surgical and patient-reported outcomes after antireflux surgery in patients with neurologic impairment

There is an ongoing debate if patients with NI benefit from fundoplications (149,202). The most common explanation for inferior results in patients with NI has been their comorbidity. Seizures has been shown as a risk factor for recurrent GERD (243), and autonomic dysregulation, altered gut motility and scoliosis may also play a role. Furthermore, it has been suggested that weak crural muscles due to malnutrition and altered anatomy in patients with NI, increase the risk for recurrent GERD (244). The crural muscles are important for hindering wrap herniation and to maintain the angle of His.

Several studies have found higher rates of recurrence in patients with NI, as summarized in a systematic review from 2018 (203). In contrast, we did not find a difference in recurrent GERD between patients with and without NI. Mauritz and coworkers found, in a prospective study, recurrence in 23 % of patients with NI and 18 % in patients without NI, 1 to 5 years after Thal fundoplication (202). The difference was not statistically significant. The discrepancy in the literature may have many of the same explanations as discussed earlier; inconsistent definitions of recurrence, number of patients included or study design. In addition, diagnosing recurrence in patients with NI is particularly difficult, because these patients have GER symptoms that can be unspecific and difficult to interpret (245). NI is a general term, and definitions of NI vary between studies or may be completely lacking, making it difficult to compare results (246). We attempted to better differentiate the specter of NI by classifying patients as having either mild or severe NI based on four criteria. There was, however, no difference in recurrent GERD between these two groups. Many of the retrospective studies that found higher rates of recurrent GERD in patients with NI are studies from the 1980s and 1990s. Improved overall survival and care for patients with NI may have led to better results in later years. Furthermore, the results
from these older studies may have influenced surgeons with regards to patient selection and risk assessment, meaning that some of the patients with severe NI are offered other treatment modalities than fundoplication.

Half of patients in our study undergoing RF had NI. The number of patients undergoing RF was too low to compare results between patients with and without NI. Pacilli and coauthors identified NI as a risk factor for recurrence after RF (175). An important finding from our study of RF patients, was that recurrent GERD can be missed in patients with NI. Two adult patients with NI had symptoms related to a herniated wrap, but this was not adequately investigated and treated. This highlights the need for adequate transitioning from pediatric to adult care for patients treated with antireflux surgery (247).

It has previously been reported that patients with NI have a higher risk for postoperative complications (248). We did not find such a difference in our study. The overall postoperative complication rate was not statistically different, but pneumonia was more common in patients with NI. Patients with NI may be at risk for respiratory problems due to respiratory muscle weakness, aspiration tendency, scoliosis, and malnutrition (249). Also, patients with NI more commonly have a GT inserted or refashioned during fundoplications. The CCI was considerably lower for patients with NI in paper 4 when GT related complications were excluded. We found that patients with NI had a significantly longer hospital stay after fundoplication, in line with previous reports (250). Because of these patients’ comorbidity, they will require more time at the hospital to recover.

Based on the available literature and the results of the studies in this thesis, most patients with NI benefit from antireflux surgery, but to a cost, as they may be subject to a higher risk for recurrence and postoperative complications. It is necessary to acknowledge that these patients are different from patients without comorbidity. They may require a more thorough diagnostic evaluation, not only to excluded conditions that mimic GERD, but also to decide on the optimal treatment.

10.7 Patient-reported outcomes after antireflux surgery

We found a high degree of parental satisfaction in all studies on results after fundoplication. Importantly, satisfaction remained high even after more than ten years follow-up. Our long-term follow-up in paper 5 is the first study to investigate satisfaction with a follow-up time of this magnitude and is in line with previous reports with a shorter follow-up (158,159). Furthermore, there was no difference between patients with and without NI, and between those
undergoing LNF compared to ONF. Satisfaction was also high after RF, in contrast to the only previous study reporting satisfaction in RF, which reported satisfaction in only 17% of parents (191).

The high level of satisfaction may be explained in several ways. The primary aim of antireflux surgery is to relieve the patient of GER symptoms, and if successful, this may lead to satisfaction with the operation. In paper 4, classical GER symptoms such as heartburn and regurgitation were significantly reduced one, two and four years postoperatively, and there was also a reduction in pulmonary infections. Consequently, antireflux surgery may improve health-related quality of life in patients (251). Moreover, fundoplication may also have beneficial effects on the patients’ parents. We found that the mothers of patients included in the RCT comparing LNF and ONF had significantly reduced psychological distress and state anxiety after fundoplication (160). These factors are likely to contribute to the high levels of satisfaction. Lastly, many patients undergo GT insertion simultaneously with the primary fundoplication, and satisfaction may partly be attributed to the GT as this may improve nutrition and health-related quality of life (56).

The high levels of satisfaction are especially interesting since a significant part of patients both after primary fundoplication and RF had recurrent GERD. Recurrent symptoms and/or newly onset troublesome symptoms have previously been found to be the cause for dissatisfaction after laparoscopic fundoplication in adults (252). The follow-up in paper 5 found that most patients with recurrent GERD were adequately treated. Furthermore, based on parental reports from the telephone interviews, some patients with recurrence had less severe symptoms compared to before the surgery. Some parents of patients with recurrence said they would choose the operation again despite recurrence, because the child had benefitted from the years without symptoms of GERD. Bourne and coworkers found similar results: 10/13 parents of patients with symptomatic recurrence were satisfied because symptoms were considerable improved (158). Several patients in our studies had milder symptoms compared to before the initial operation; the symptoms did not need further treatment or could be handled with PPI. This may explain the fact that even though recurrence is more common after LNF compared to after ONF, the satisfaction is the same, both in our study and in the RCT by Pacilli and co-workers (155).

Satisfaction with an operation will undoubtedly be related to the expectations one had beforehand (253). It is important to provide realistic information on expected results and potential complications when deciding to go through with antireflux surgery, especially because
the literature shows that a substantial portion of patients will experience complications and/or recurrent GERD. Clarification of expectations and thorough preoperative delivery of information have been standard at our department and have likely contributed to the high satisfaction.

10.8 Improving outcomes after novel surgical techniques

The aim of new surgical techniques is usually to improve patient outcomes. This was also the rationale for implementation of the new surgical techniques investigated in this thesis. It is typical for pediatric surgery that, very often, studies in adults are used as a knowledge foundation when implementing new techniques in children. For both LNF and push-PEG techniques such as PEG-T, the evidence in current guidelines for children are derived from studies of adults (9,107). However, as shown in this thesis, the results are not necessarily the same in adults and children. Therefore, it is important to perform studies in children and not just assume they are the same as in adults.

Implementation of new techniques should ideally be done following a predefined framework. Strong and co-authors highlight the need for adequate training and evaluation of outcomes as paramount when implementing a new technique (254). Teaching in surgery has traditionally been based on a master-apprentice relationship, but in the last decades there has been a shift towards a combination of a master-apprentice relationship and a more structured approach to teaching of surgical skills (255). This includes the use of simulation training and structured evaluation of performance (256,257). In our two studies of PEG-T and LAP-G, many different surgeons were involved, and there was no standardized protocol for training or specific guidelines for the operative techniques. Furthermore, complications were common, and the nature of the complications different, than we expected. This became especially apparent when we performed chart reviews after PEG-T, as a surprisingly high number of patients experienced complications with the T-fasteners. These are complications that we hope and believe are possible to avoid.

In order to quantify improvement in outcomes, the term “learning curve” is commonly applied. A learning curve describes the relationship between proficiency and the surgeon’s experience, and the number of procedures needed to reach a plateau is often presented as a marker of proficiency (258). A common method for evaluation of the learning curve is splitting data into two or three time periods and comparing outcomes such as operating time and complications for individual surgeons, but more sophisticated statistical methods may also be used (259).
Pediatric studies on learning curves after fundoplication report proficiency after between 20 and 60 procedures (260). There has also been found a learning curve for GT insertion (78,261). We did not observe a learning curve for complications in our studies of PEG-T and LAP-G. This may be explained by the relatively high number of surgeons involved. Furthermore, one can expect an institutional learning curve over time. It may lower the risk for complications if each surgeon’s experience with the technique and its complications are shared with others in the department. This requires continuous critical review of one’s own results.

Both fundoplication and GT insertion are associated with a relatively high degree of adverse events. To improve these outcomes, one could look at the procedure itself and investigate ways to perfect the various steps involved. One way of doing this is to standardize protocols (262). Holcomb and St. Peter used comparative studies to evaluate different approaches to some of the technical aspects of LNF, and found that avoiding extensive esophageal mobilization can improve outcomes (263). The complications after PEG-T and LAP-G reported in this thesis give insight to steps in these techniques that require particular attention. With LAP-G, this can for instance be avoiding a too large incision to lower the risk for leakage and skin problems. Careful insertion of T-fasteners to avoid traction and migration into the abdominal wall and cutting of T-fastener sutures at the right time may further improve outcomes after PEG-T.

The results of this thesis show that implementation of new techniques should not be taken lightly, and evaluation of outcomes is important to see if new techniques are better than the traditional ones. To give patients the best possible care, it is necessary to examine one’s own results and openly look for ways to avoid complications and improve outcomes. We acknowledge, that in retrospect, the implementation of PEG-T and LAP-G could have been done more thoroughly, with a more standardized protocol for training and ongoing evaluation of results.
11. Methodological considerations

11.1 Participants

Patients undergoing GT insertion and fundoplication are heterogenous in both age and presence of comorbidities. This was also the case for the patients included in the studies in this thesis. The cohorts in our studies are like those in many other studies, and the results should therefore be generalizable to other pediatric surgery centers with a similar volume (12,30,155,195). Including patients of all comorbidities is a strength of the studies in this thesis, as the results can be applied to the everyday life in the clinic. It may, however, be useful to evaluate outcomes in specific groups, such as children with NI, to better aid decision-making.

The patients in the three studies on GT were reviewed retrospectively and were included if they have had the surgery performed. Consequently, there were very few exclusion criteria in these studies, and we were able to include almost all patients that had undergone the procedure. This is a strength when investigating postoperative complications. As the studies on GT insertions mainly looked at demographics and postoperative complications, and not the effects of the surgery, we did not have specific inclusion criteria or look at whether the indications for GT insertion were correct. The indication for GT insertions is mostly decided by pediatricians, and patients are often referred to the pediatric surgery department after the decision is made.

In papers 4 and 5, the inclusion criteria in the RCT were subjective and objective signs of GERD and unsatisfactory effect of conservative treatment. Patients with all comorbidities were involved, strengthening the generalizability of the results. As expected, some patients died during the follow-up time, but in many of these, results were evaluated at least once. For the long follow-up in paper 5, we were able to contact and include all patients, except for those who were dead or who had emigrated. This is a particular strength with regards to the high level of satisfaction reported in this study because the risk for non-response bias is low. Non-response bias occurs when responders differs from non-responders, e.g. if patients with negative outcomes decline to participate (264). Patients who had died may have had more severe underlying comorbidity, and therefore a higher risk for negative outcomes.

Paper 6 only included patients who gave consent and returned the questionnaires, and four out of 28 (16 %) eligible patients did not return questionnaires. Whether these patients can be considered missing at random is difficult to say. Patients who were unsatisfied or who
experienced recurrent GERD may be less likely to respond to questionnaire-based studies. On the other hand, such patients may want to participate, because they were given the opportunity to contact us and possibly get a new evaluation.

11.2 Study design

11.2.1 Number of included patients

Many conditions in pediatric surgery are rare, and consequently many studies have few included patients (265). This was also the case for the studies in this thesis. To include more patients, we would have needed to do multi-center studies and/or have longer study periods. For instance, we were able to include only 24 patients undergoing RF over an 18-year period, because the procedure is so rare. With few patients there is a chance that rare complications do not occur. No episodes of intraabdominal organ perforation occurred after PEG-T in 87 patients, but occurred in one patient in our recent prospective study of PEG-T.

An RCT with too few patients included has risk for type 2 error; reporting no difference between groups when in fact there is a difference. The initial power calculation for the RCT in this thesis found that 91 patients were needed in each group to detect a difference in recurrence of at least 20% (151). The RCT was initially meant to be a multicenter study, but in the end only two centers participated. Furthermore, there were fewer patients referred for fundoplication during the study period compared to the previous years. Consequently, fewer patients than anticipated were included. The number of included patients is higher than in the other two RCTs on fundoplication in children (155,195) and comparable to the two RCTs in adults with a similar follow up (86 and 111 patients) (236,237). Even though the number of patients were lower than anticipated, the long-term follow-up still found a significant difference in recurrent GERD between LNF and ONF. We do not believe this to be a type 1 error, in which a difference is reported when there actually is none. The demographics, comorbidity and mortality of the two groups were comparable, and the overall loss to follow-up was low. Although the power calculation was not performed with regards to NI, our finding of no difference in recurrent GERD between patients with NI and patients without NI may be a type 2-error. Our results may, however, be useful in future metanalyses.

11.2.2 Retrospective chart reviews

The studies on PEG-T, LAP-G and RF were all retrospective chart reviews. Retrospective chart reviews are common in pediatric surgery (266,267). Advantages of a retrospective chart review are that they rely on data that is already available and that they are easy to perform.
without high costs (268). The main limitation is the risk for missing data. The nature of the retrospective studies in this thesis means that some complications were missed. For instance, complications handled at local hospitals or in primary care were not registered. Thus, the true rates of minor complications are probably higher. We find it unlikely, however, that major complications requiring operative management were missed, because these are managed at the hospital where the initial procedure was performed.

In paper 1, we retrospectively reported demographics of patients undergoing GT insertion over a 19-year period. The study did not fully evaluate the indication for GT insertion, but rather used underlying comorbidity as a proxy outcome. We did not include indication because it was not adequately reported in the patients’ charts. OUS Rikshospitalet is a tertiary referral center with national and regional functions for many conditions such as cardiac disease and congenital malformations. This has likely influenced the demographics of patients undergoing GT insertion in paper 1 as these comorbidities are more common at our center compared to local hospitals. GT insertions are performed at other hospitals in Norway, but patients with high risk for anesthesia are often referred to a center like ours. It is unlikely that this affects the trends observed in the study because the referral routines have been the same for such conditions during the whole study period. Lastly, it would have strengthened the findings if the study had included results from several hospitals, ideally from the whole country. There is, however, no national registry available that would have made this possible.

11.2.3 Randomized controlled trial

RCTs are considered the gold standard when comparing treatments. Still, it is an uncommon study design in pediatric surgery. A review from 2010 found that RCTs stood for less than 0.05 % of all publications in pediatric surgery, and the quality of RCTs was generally low (266). Our RCT is one of only three RCTs comparing LNF to ONF. The main advantage of RCTs are lower risk for selection bias. Thus, known and unknown prognostic factors are balanced and confounding less likely when comparing two treatments (269). Performing a RCT in pediatric surgery is especially difficult (265). As previously mentioned, many conditions are rare, and the volume of procedures low. Blinding participants and investigators are challenging in surgical RCTs, and more so when children are involved and was therefore not prioritized in our RCT. However, the two other RCTs in children were able to blind their patients and the health care personnel responsible for postoperative care (155,195), and should perhaps have been prioritized in the postoperative period in our study as well. Knowing which group one was randomized to may have affected the results of patient and
parent reported outcomes, such as satisfaction (270). It is, however, less likely that this influenced the rate of recurrent GERD because this is based on objective findings in addition to subjective reports. Lastly, it would be impossible to blind the participants long-term because of the different scars.

11.2.4 Follow-up time

We reported long-term complications in the study after PEG-T, in addition to early complications, because we suspected that T-fasteners would cause problems more long term. It would have strengthened the study of LAP-G if long-term complications had been reported, which probably would have led to a higher rate of minor complications such as hypergranulation. The range in follow-up after RF was 1.6 months to 17.7 years, and it is likely that more cases of recurrent GERD would have been found if the minimum follow-up time was longer.

A major strength with the RCT comparing LNF to ONF is the meticulous follow-up, including both a clinical examination and investigations 6 months preoperatively, and later telephone interviews one, two, four and twelve years postoperatively. Furthermore, patients and parents were encouraged to contact the department if they had signs of recurrence or troublesome side effects between the scheduled follow-up, and many did. If so, they were invited to undergo adequate investigations. Thus, it is unlikely that symptomatic recurrence was left undiagnosed.

It would have strengthened the study after LNF and ONF if investigations such as 24-hour pH monitoring had been performed at all time points, making it possible to link symptoms to objective findings. It was, however, considered unlikely that all patients would agree to these investigations if they were without symptoms. We instead chose to perform investigations in patients with symptoms suggestive of recurrent GERD or troublesome side effects. Most patients had at least one investigation performed after six months. In those who had a pathological 24 hour pH-monitoring after six months, only one had a history of symptoms that suggested the operation never worked (151).

11.2.5 Questionnaires

In paper 4 and 5, self-made questionnaires were used to perform semi-structured telephone interviews. These were the same at the various time points and recorded typical symptoms of recurrent GERD as well as troublesome symptoms such as retching and dysphagia. The interviews were performed by study personnel not involved in the treatment of the patients,
making it less likely that questions were answered in a way that would please the researchers (response bias) (264).

It would have strengthened our conclusions if validated questionnaires had been used. Various standardized questionnaires have been developed, including questionnaires that are GERD specific or questionnaires that cover gastrointestinal symptoms overall (112–115,210). Using such questionnaires would make it easier to compare our results to that of other studies. However, no such questionnaire has been translated and validated to Norwegian. We used the Pediatric Quality of Life Inventory Gastrointestinal Symptoms Scale as a basis for questionnaires that were sent to patients and parents after RF in paper 6 (Appendix 1) (210), and started a process to translate the questionnaire into Norwegian. Two independent translators translated the questionnaires to Norwegian, which was then reviewed by a physician. The questionnaire was further translated back to English for review, and then tested on a patient with recurrent GERD. The Norwegian version of the questionnaire has not yet been tested for validity. Moreover, we learned that many of the questions were not relevant for GERD patients, that many would be difficult to answer for parents of patients with NI and that retching was not covered in the English questionnaire. We therefore used only parts of the questionnaire in paper 6 and added questions on retching.

11.2.6 Surgical technique

There was no standardization of surgical technique for PEG-T, LAP-G and RF. PEG-T was for the most part performed according to the instructions from the manufacturer. Two techniques for LAP-G were used in the study period, mainly because of surgeon’s preference. It is a weakness of our study that two techniques for LAP-G were used, because others have reported difference in outcomes between various LAP-G techniques (223). Most of the RFs were done with open technique, and the numbers of included patients are too low to compare laparoscopic RF to open RF. Surgical technique was standardized in the RCT comparing LNF to ONF and this is a strength of this study.

11.3 Outcome measures

11.3.1 Postoperative complications

Postoperative complications are an important focus area for research and is often used as a surrogate marker for quality in health services. To improve objectivity and make comparison between studies easier, classifications systems for surgical complications have been introduced. There is no consensus of what constitute a surgical complication. First proposed in 1992 and
then improved in 2004, the Clavien-Dindo classification grades complications according to how they are treated (208). A definition that was proposed by Clavien and Dindo is “any deviation from the ideal postoperative course”, but this has been opposed as too wide by others (271,272). Other classifications include Accordion Severity Grading System of Surgical Complications (273). Such classification systems are now widely used in surgical research, and although they are not validated for children, they are increasingly applied in pediatric surgery research (184,274). We used the Clavien-Dindo classification in our studies after GT insertion and fundoplication and believe this to be a major strength. Terms such as “minor” and “major” complications have been used inconsistently for many years and complications are mainly events that could be directly linked to the operation (275,276). Most define major complications as complications that require surgical intervention, and therefore we defined major complications as grade IIIb or higher in this thesis. This is not entirely consistent with what has been proposed by ESPGHAN, where in addition to surgical or radiological interventions, complications leading to hospitalization after GT are classified as major.

The Clavien Dindo classification include any deviation from the ideal postoperative course, not only those directly attributed to the procedure. Reporting such complications is important because it says something about the burden of the procedure. For instance, longer operating time with RF means a longer general anesthesia, and thus a higher risk for complications such as pneumonia (277). A limitation of the Clavien-Dindo classification is that it grades complications based on how they are treated, and this does not necessarily correlate with the burden or cost of the complication. Lastly, the use of the Clavien-Dindo classification in children has been criticized as it was created for adults and has not been validated in children (278). Future studies should aim at validating this classification system in pediatric surgery cohorts.

11.3.2 Recurrence of gastroesophageal reflux disease

Recurrence of GERD was defined differently in the three studies reporting results after antireflux surgery. In papers 4 and 6, recurrence of GERD was defined as symptoms of GERD and at least one objective finding. Thus, some patients with a herniated wrap or who used PPIs but were without symptoms were classified to not have recurrence. We used a wider definition for recurrent GERD for the long-term follow-up in paper 5. Consequently, we found patients who had objective signs of GERD (herniated wrap or pathological pH monitoring), but who did not have symptoms or who had symptoms that were so mild they did not want treatment. A herniated wrap or pathological pH monitoring is a sign of a
fundoplication that has failed, and therefore gives insight to the patency of the fundoplication. Moreover, symptoms can be difficult to interpret in patients with NI, and there may be patients with recurrence that was undiagnosed even though objective investigations and telephone interviews were performed. There were six patients whom, with the new definition in paper 5, were classified with recurrence. Three of these underwent LNF and three ONF. Therefore, it is unlikely that the new definition affected the conclusion of the study.

11.3.3 Satisfaction after fundoplication

We used closed questions to record the parents’ and patients’ satisfaction in the studies after LNF, ONF and RF, and aimed at investigating the overall satisfaction with the surgery. Studies reporting satisfaction with antireflux surgery have for the most part used a similar approach (158,159). This method has several limits. Using closed questions means we are unable to say why parents/patients were satisfied. As mentioned previously, satisfaction is closely related to expectations. Overall satisfaction further covers the satisfaction with the procedure and care itself, e.g. before, during and after the surgery, and also the improvement of the child’s symptoms and quality of life (279). Using a qualitative approach would have given more insight to this matter. During the telephone interviews, the interviewers would talk to the parents about their overall impression of the surgery, and some parents would spontaneously say something about why they were satisfied or not. Although this was not recorded systematically, it gave a valuable insight to what patients and parents experienced after the fundoplication. An alternative approach could be to use validated questionnaires to assess satisfaction, but no questionnaire for children has been translated to Norwegian (280,281).

11.3.4 Parent proxy reports

For the most part, subjective outcomes in this thesis were reported by parents, as is common in the pediatric literature. There are reports of disagreement in subjective outcome assessment between parents and children; parents of children with health conditions tend to underestimate the health related quality of life compared to the child’s own reports (282,283). This may have affected the reports on symptoms and satisfaction in our studies. For the long-term follow-up after LNF and ONF in paper 5, we contacted the patient if they were adult and without NI, and we would always talk to patients without NI in addition to parents if this was age appropriate. Furthermore, we sent questionnaires to all adults without NI in our follow-up of RF in paper 6, and to both patients and parents if without NI and age between 12 and 16.
years. However, in younger children and in patients with NI, using a proxy report from parents is the only possible option.

11.4 Ethical considerations

It was challenging to justify performing an RCT comparing LNF and ONF because the general opinion was that LNF was better with regards to short- and long-term outcomes. Critics, both at our department and at other centers, said it was unethical not to offer LNF to all patients, and there was a considerable debate in advance. However, a retrospective review from our department gave a hunch that LNF had poorer results, and this was also suspected based on clinical experience at the time (161). Thus, in addition to the poor quality of evidence, it was considered ethically sound to perform the RCT, and the study was approved by the Regional Committees for Medical and Health Research Ethics. Participation in the RCT was voluntary, and informed consent obtained before randomization. No parents withdrew their child after randomization. In addition to the scheduled follow-ups, patients and parents were instructed and encouraged to contact the department if they had signs of recurrent GERD or for some other reason had worries and would then be offered adequate investigations and follow-up at our department.

The studies in paper 1, 2 and 3 were retrospective chart reviews, and with permission from the Data Protection Officer at OUS, no consent was obtained. This was because the studies meant no new investigations or interventions for the patients, and because privacy was handled by deidentifying data. As paper 5 meant sending questionnaires and obtaining new information from the patients, consent was deemed necessary and therefore obtained. There were no negative aspects related to inclusion in this study, and as with the RCT, patients were offered diagnostic evaluation if they had signs of recurrent GERD or troublesome symptoms.

Ethical dilemmas may arise with medical research in children (284). To ethically defend research in children, it is important that the studies generate new and useful knowledge and that the risks are minimized. This was considered the case for all studies in this thesis. A main issue is the ability to give information and to obtain consent. Patients older than 16 years provided their own consent, and consent was obtained from both patients and parents in paper 6 if the age of the patient was between 12 and 16 years.
12. Conclusions

The number of GT insertions at our tertiary pediatric surgery center more than doubled over a 19-year period. Furthermore, the age at GT insertion decreased, and comorbidities other than NI became more common.

Postoperative complications after two novel techniques for GT insertion, PEG-T and LAP-G, were common. Most of the complications were minor, and major complications were rare.

Recurrence of GERD was significantly more common median 12 years after LNF compared to after ONF. Moreover, recurrent GERD occurred earlier after LNF than ONF. Still, patient and parental satisfaction was high in both groups.

RF is a valid treatment option in pediatric patients with recurrent GERD after primary fundoplication, and most patients are without symptoms of GER after RF.

There was no significant difference in outcomes after fundoplication in patients with and without NI. The rate of recurrent GERD and postoperative complications in patients with NI was comparable to patients without NI. Also, improvement of symptoms and parental satisfaction were similar in the two groups.

Our experience after introducing new techniques for GT insertion and fundoplication show that new techniques are not necessarily better than the traditional techniques. Implementation of new techniques should be done with a structured framework and an ongoing evaluation of results.
13. Implications and future perspectives

Our findings that complications are common after GT insertion and that the number getting a GT steadily increases, suggest that health services must have the necessary capacity and qualifications to handle problems that can arise in patients with a GT. Adequate information on what to expect and ways to prevent negative outcomes, should be provided to those who care for patients with a GT.

Because of the results after PEG-T reported in this thesis, a prospective study was performed at OUS Rikshospitalet and Ullevål in the period 2017 to 2020. Follow-up was done after 14 days and three months postoperatively. Fewer surgeons perform the PEG-T technique and all sutures locks were removed 14 days postoperatively if not spontaneously detached. Unpublished results from this study find a significant reduction of early tube dislodgments and T-fastener related complications after PEG-T, and the operating time was nearly halved.

The findings from the studies on primary fundoplication and RF provide information on expected outcomes after antireflux surgery and is therefore valuable in shared decision-making with patients with GERD and their parents. Parents and patients are now informed about the findings from the RCT and are involved when deciding on technique. ONF may be a better alternative because of the lower risk for recurrent GERD in patients with severe comorbidity, in whom later RF or other surgical interventions are especially unwanted. Unpublished data from our department show that ONF has become more common after the results from the RCT were published, especially in patients with NI. The results after RF are new, but support RF as a good treatment option in patients with recurrent GERD after primary fundoplication.

The experience with introducing new techniques reported in this thesis has inspired the department of pediatric surgery at OUS to better evaluate outcomes when new procedures or techniques are introduced. Examples of this are research projects investigating results after a new technique for surgical treatment of Hirschsprung’s disease and a new initiative to evaluate outcomes after minimal invasive surgery in neonates. This is especially important as we now see an improvement in results in the recent prospective study of PEG-T.

In the Nordic pediatric surgery consortium, it has in later years become more common to do multicenter studies to be able to include more patient. It is important to make use of such networks to be able to perform multicenter studies, preferably RCTs, and thereby provide evidence of higher academic quality.
With regards to future perspectives, there is a need for further studies to evaluate results after GT insertion and fundoplications. Ideally, an RCT should be performed to compare the various techniques for GT insertions. Future studies should continue investigate difference in outcomes after LNF and ONF with attention to improvement in technical aspects. Larger studies are needed to evaluate outcomes in patients with NI of varying severity. It might also be beneficial to compare fundoplication to other treatments for GERD such as jejunal feeding.
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15. Appendix 1

Spørreskjema for oppfølging etter ny operasjon etter Nissen fundoplokusjon


Vi setter veldig pris på om du fyller ut svar på alle spørsmålene og refunderer skjemaet i vedlagt ferdig frankert konvolutt.

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<td>4 hvis det nesten alltid er et problem</td>
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Det finnes ikke noen riktige eller gale svar.
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<td>3</td>
<td>4</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>UBEHAG I MAGEN UNDER SPISING</strong> (problemer med ...)</th>
<th>Aldri</th>
<th>Nesten alderi</th>
<th>Noen ganger</th>
<th>Ofte</th>
<th>Nesten altid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jeg blir uvel i magen når jeg spiser</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Jeg føler meg dårlig i magen når jeg spiser</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Magen min gjør vondt når jeg spiser</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Magen føles tung når jeg spiser</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Jeg føler meg mett med det samme jeg begynner å spise</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
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</table>

<table>
<thead>
<tr>
<th><strong>BEGRENSNINGER NÅR DET GJELDER MAT OG DRIKKE</strong> (problemer med ...)</th>
<th>Aldri</th>
<th>Nesten alderi</th>
<th>Noen ganger</th>
<th>Ofte</th>
<th>Nesten altid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Det er noen typer mat jeg ikke kan spise</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Det er noen typer drikke jeg ikke kan drikke</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Jeg kan ikke spise det jeg har lyst på</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Jeg kan ikke drikke det jeg har lyst på</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Jeg kan ikke spise enkelte matvarer fordi jeg blir dårlig av dem</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Jeg kan ikke spise samme type mat som vennene mine spiser</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>PROBLEMER MED Å SVELGE</strong> (problemer med ...)</th>
<th>Aldri</th>
<th>Nesten alderi</th>
<th>Noen ganger</th>
<th>Ofte</th>
<th>Nesten altid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Det er vanskelig for meg å svelge maten</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Det gjør vondt når jeg svelger</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Maten blir sittende fast på veien ned</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>HALSBRANN OG SURE OPPSTØT</strong> (problemer med ...)</th>
<th>Aldri</th>
<th>Nesten alderi</th>
<th>Noen ganger</th>
<th>Ofte</th>
<th>Nesten altid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jeg får en brennende følelse i halsen</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Jeg har vondt i brystet</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Jeg raper mye</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Maten kommer opp igjen i munnen etter at jeg har spist</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
</tbody>
</table>
I løpet av den **SISTE** måneden, hvor stort problem har dette vært for deg ...

### BREKNINGER (problemer med ...)

<table>
<thead>
<tr>
<th></th>
<th>Aldri</th>
<th>Nesten alrdi</th>
<th>Noen ganger</th>
<th>Ofte</th>
<th>Nesten alltid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jeg brekker meg når jeg spiser</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Jeg brekker meg etter at jeg har spist</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Jeg brekker meg utenom måltider</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Jeg brekker meg til jeg kaster opp</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
</tbody>
</table>

### KVALME OG OPPKAST (problemer med ...)

<table>
<thead>
<tr>
<th></th>
<th>Aldri</th>
<th>Nesten alrdi</th>
<th>Noen ganger</th>
<th>Ofte</th>
<th>Nesten alltid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jeg føler jeg må kaste opp</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Jeg føler jeg må kaste opp når jeg spiser</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Jeg føler jeg må kaste opp etter at jeg har spist</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Jeg kaster opp</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
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</table>

### LUFT OG OPPBLÅSTHET (problemer med ...)

<table>
<thead>
<tr>
<th></th>
<th>Aldri</th>
<th>Nesten alrdi</th>
<th>Noen ganger</th>
<th>Ofte</th>
<th>Nesten alltid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Det kjennes ut som om magen min er full av luft</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Magen min føles veldig full</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Magen min blir stor og hard</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Jeg har mye luft i magen</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Jeg promper mye</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Magen min føles oppblåst</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Magen min lager lyder</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
</tbody>
</table>

### FORSTOPPELSE (problemer med ...)

<table>
<thead>
<tr>
<th></th>
<th>Aldri</th>
<th>Nesten alrdi</th>
<th>Noen ganger</th>
<th>Ofte</th>
<th>Nesten alltid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jeg føler meg full i magen selv etter at jeg har hatt avføring</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Jeg føler at jeg ikke er ferdig etter at jeg har hatt avføring</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Jeg føler jeg ikke får tømt meg skikkelig når jeg har avføring</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Det gjør vondt når jeg har avføring</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Avføringen min er hard</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Avføringen min er klumpete</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Jeg må presse hardt for å få ut avføringen</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Bæsjen blir sittende fast når jeg har avføring</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Jeg har vondt i rumpa etter at jeg har hatt avføring</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Det tar lang tid for bæsjen å komme ut</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Jeg må streve for å få ut bæsjen</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Jeg har ikke lyst til å bæsje fordi det gjør vondt</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Jeg tilbringer mye tid på do når jeg skal ha avføring</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Det gjør vondt i magen når jeg bæsjer</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
</tbody>
</table>
I løpet av den **SISTE** måneden, hvor stort problem har dette vært for deg ...

<table>
<thead>
<tr>
<th>BLOD I AVFØRINGEN (problemer med ...)</th>
<th>Aldri</th>
<th>Nesten aldri</th>
<th>Noen ganger</th>
<th>Ofte</th>
<th>Nesten alltid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Det er blod på toalettpapiret etter at jeg har hatt avføring</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Det er blod i avføringen min</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>DIARÉ (problemer med ...)</th>
<th>Aldri</th>
<th>Nesten aldri</th>
<th>Noen ganger</th>
<th>Ofte</th>
<th>Nesten alltid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jeg må ofte holde meg i nærheten av do</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Jeg må skynde meg på do for å ha avføring</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Jeg føler at jeg alltid er på do og har avføring</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Jeg våkner om natten for å ha avføring</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Avføringen er vandig</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Jeg har uhell med bæsj i undertøyet</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Jeg må ofte ha avføring</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>BEKYMNRINGER OM AVFØRING (problemer med ...)</th>
<th>Aldri</th>
<th>Nesten aldri</th>
<th>Noen ganger</th>
<th>Ofte</th>
<th>Nesten alltid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jeg bekymrer meg for å få avføring i undertøyet</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Jeg bekymrer meg for at jeg ikke skal rekke frem til do i tide</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Jeg bekymrer meg for at det skal gjøre vondt når jeg har avføring</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Jeg bekymrer meg at jeg blir nødt til å gå på toalettet på skolen/jobb</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Jeg bekymrer meg at jeg skal få avføring i undertøyet på skolen/jobb</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>BEKYMRING OM MAGESMERTER (problemer med ...)</th>
<th>Aldri</th>
<th>Nesten aldri</th>
<th>Noen ganger</th>
<th>Ofte</th>
<th>Nesten alltid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jeg bekymrer meg for magesmertene mine</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Jeg bekymrer meg for at jeg skal få vondt i magen på skolen/jobb</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>MEDISINER (problemer med ...)</th>
<th>Aldri</th>
<th>Nesten aldri</th>
<th>Noen ganger</th>
<th>Ofte</th>
<th>Nesten alltid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Det er vanskelig for meg å ta medisinene mine</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Jeg glemmer å ta medisinene mine</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Det er vanskelig for meg å svelge medisinene mine</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Jeg liker ikke å måtte ta medisiner hele tiden</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
</tbody>
</table>
I løpet av den **SISTE** måneden, hvor stort problem har dette vært for deg ...

<table>
<thead>
<tr>
<th>KOMMUNIKASJON (problemer med ...)</th>
<th>Aldri</th>
<th>Nesten aldri</th>
<th>Noen ganger</th>
<th>Ofte</th>
<th>Nesten alltid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Det er vanskelig for meg å fortelle legene og sykepleierne hvordan jeg har det</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Det er vanskelig for meg å stille spørsmål til legene og sykepleierne</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Det er vanskelig for meg å forklare sykdommen min til andre mennesker</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Det er vanskelig for meg å forklare sykdommen min til vennene mine</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Det er vanskelig for meg å snakke med foreldrene mine om sykdommen min</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
</tbody>
</table>

De neste spørsmålene skal du svare på sammen med foreldre eller foresatte. Svar ved å sette kryss ved det svaret som er riktig for deg.

**Har barnet fortsatt gastrostomi:**

- JA
- NEI

**Hvis ja, hva brukes denne til (kan krysse av flere):**

- Lufte magen
- Medisiner
- Mat
- Kun vann

**Bruker du fortsatt syrehemmende medisiner:**

- JA
- NEI

**Hvis ja, hvilke:**

**Disse to spørsmålene gjelder den andre Nissen fundplikasjonen, altså reoperasjonen**

**Med fordelen av å kunne se tilbake, ville du valgt samme reoperasjon igjen?**

- JA
- TROLIG JA
- TROR IKKE DET
- NEI
- USIKKER

**Vil du anbefale reoperasjon til noen andre?**

- JA
- TROLIG JA
- TROR IKKE DET
- NEI
- USIKKER
Introduction

The standard management of pediatric patients requiring long-term enteral nutritional support is a gastrostomy feeding tube [1]. Most centers prefer to insert a percutaneous endoscopic gastrostomy (PEG) owing to its simplicity and low costs [2]. The pull technique (PEG-P) is the most commonly used method, and an internal bumper secures fixation of the stomach to the abdominal wall. In adults, removal of the PEG-P tube is usually done with the “cut and push” technique. This is not recommended in children due to reports of severe complications such as esophageal laceration and intestinal obstruction caused by the internal bumper [3]. Therefore, in pediatric patients, the tube is removed either endoscopically or by traction, under general anesthesia or sedation [4].

An alternative to PEG-P is the push technique, which offers primary insertion of a balloon gastrostomy. Due to limited data on the results of this technique in children, we have investigated peri- and postoperative outcomes after implementation of PEG-T in our department.

Patients and methods

This retrospective chart review included all patients below 18 years who underwent PEG-T placement from 2010 to 2014. Main outcomes were 30-day postoperative complications and late gastrostomy-related complications.

Results

In total, 87 patients were included, and median follow-up time was 2.4 years (1 month – 4.9 years). Median age and weight at PEG-T insertion were 1.9 years (9.4 months – 16.4 years) and 10.4 kg (5.4 – 33.0 kg), respectively. Median operation time was 28 minutes (10 – 65 minutes), and 6 surgeons and 3 endoscopists performed the procedures. During the first 30 days, 54 complications occurred in 41 patients (47%). Most common were peristomal infections treated with either local antibiotics in 11 patients (13%) or systemic antibiotics in 11 other patients (13%). 9 patients (10%) experienced tube dislodgment.

Late gastrostomy-related complications occurred in 33 patients (38%). The T-fasteners caused early and late complications in 9 (10%) and 11 patients (13%), respectively. Of these, 4 patients (5%) had subcutaneously migrated T-fasteners which were removed under general anesthesia.

Conclusion

We found a high rate of complications after PEG-T. In particular, problems with the T-fasteners and tube dislodgment occurred frequently after PEG-T insertion.
secure fixation of the stomach to the abdominal wall as an internal bumper, the stomach must be fixed to the abdominal wall by sutures or T-fasteners. Another postulated benefit of the push technique is decreased risk for peristomal infections because the tube is not exposed to the oral bacterial flora during insertion. Although the push technique is associated with a lower peristomal infection rate than PEG-P in adults [5], a similar advantage has not been shown in pediatric patients [6, 7].

Recently, PEG placement with the push technique and T-fastener gastropexy (PEG-T) has been introduced in pediatric patients [6], and this particular method has gained popularity. So far, there are only a few studies that have evaluated the PEG-T technique in pediatric patients [6–8], therefore, we wanted to report our initial experience with the PEG-T with particular emphasis on peri- and postoperative complications.

Materials and methods

Patients
This retrospective, descriptive study includes all patients <18 years of age who received a PEG-T at Oslo University Hospital Ullevål between January 2010 and November 2014. PEG-T was introduced at our center in January 2010 and was the preferred technique for PEG if no contraindication was found. Patients receiving PEG-T were identified by an electronic search for the PEG procedure and cross-checked with data from a written surgical logbook.

Technique for PEG-T placement
The MIC-KEY Introducer Kit (Kimberly-Clark Corp, Roswell, GA, United States) was used in all patients, and the gastrostomy was placed according to the manufacturer’s procedure as previously described by Göthberg and Björnsson [6]. The standard tube was a 14 Fr bolus gastrostomy balloon tube. A low-profile button was placed initially in some patients according to parents’ wish or if assessed appropriate by the gastroenterologist. All procedures were performed under general anesthesia as well as local anesthesia around the stoma channel. Prophylactic antibiotic (Cefalotin) was given before the procedure. Briefly, the stomach was distended by insufflation, and a suitable location for the gastrostomy tube and surrounding gastropexy points was identified by transillumination. Gastropexy was performed using 3 T-fasteners with resorbable sutures (Saf-T-Pexy T-fasteners, Kimberly-Clark Corp). These were placed in a trigonal fashion and fastened with accompanying external suture locks. A stoma channel for the gastrostomy tube was established in the center of the trigone of T-fasteners using a modified Seldinger technique and a serial 18 Fr dilator. Lastly, the 14 Fr gastrostomy tube was inserted, and the balloon filled with sterile water (Fig. 1).

Before the introduction of the PEG-T procedure, the technique was presented to the team by a representative from the company, and an introduction CD showing the technique was available for the team.

Postoperative treatment
Enteral liquids were started 6 hours after the procedure, and tube feeding started on the first postoperative day. Patients were discharged to their home or to their local hospital as appropriate. The parents or a gastrostomy nurse were instructed to remove the suture locks 3–4 weeks postoperatively if these had not already detached spontaneously. The balloon tube was scheduled to be replaced with a low profile button at our hospital or at the patient’s local hospital 8 weeks after surgery if a button was not inserted primarily.

Collection of data
Patient data were collected from electronic medical records. Demographic data included age, sex, weight, presence of a nasogastric tube at admittance, and underlying diagnosis most likely contributing to the patients’ feeding problems. Neuromotor impairment was defined as a static or progressive, central or peripheral neurologic condition associated with chronic functional or intellectual impairment [9], including conditions such as cerebral palsy, quadriplegia, and genetic syndromes. Duration of the procedure, perioperative complications, and any concomitant procedure were recorded. Operating time was not registered in patients undergoing concomitant procedures.
Postoperative complications were graded according to the Clavien-Dindo classification for surgical complications [10]. Briefly, grade I complications indicate any deviation from the normal postoperative course, but without the need for any pharmacologic treatment. Grade II complications require pharmacologic treatment with drugs. Grade III complications require surgical, endoscopic, or radiologic intervention. Interventions not requiring or requiring general anesthesia were denoted as grade IIIa and IIIb, respectively. Grade IV is life-threatening complications, whereas grade V describes death of a patient.

Postoperative complications were categorized as early (≤30 days) or late (>30 days). Early complications included all types of complications, but non-gastrostomy related complications (e.g., pneumonia) were excluded if concomitant procedures were performed. Late complications were limited to gastrostomy related complications only. Stoma infections were categorized as grade I if treated with topical agents or as grade II if systemic antibiotics were given. Complications specifically related to the T-fasteners were registered as a separate item with attention to when and how they were discovered and when and how they were treated.

Ethical approval
The study has been approved by the hospital’s Commission for Personal Security.

Statistics
Descriptive statistics were used when presenting the data; frequencies and percentages, median and range [min–max]. Median operating time in the first and last half of patients was compared using a Mann-Whitney U test, as data were not normally distributed. The frequency of early postoperative complications in various subgroups was compared using the chi-squared test. All analyses were performed by IBM SPSS software for Windows version 21.0 (IBM Corp, Armonk, NY, United States). P values <0.05 were considered statistically significant.

Results

Patients
A total of 87 patients were identified, of whom 45 (52%) were female. Median age and weight were 1.9 years (2.9 months – 16.4 years) and 10.4 kg (5.4 – 33.0 kg), respectively. The most common underlying diagnosis was neurologic impairment (n = 53, 61%), followed by weight faltering of unknown etiology (n = 13, 15%), malignancy (n = 3, 3%), and other diseases (n = 18, 21%). A nasogastric tube was present in 33 patients (38%) at admittance. The median follow-up time was 2.3 years (1 month – 4.8 years).

Perioperative data
Three consultant pediatric gastroenterologists and 6 pediatric surgeons (5 consultants or 1 trainee) performed the PEG-T procedures during the study period. 6 (7%) patients underwent a concomitant procedure; central venous catheter insertion (n = 2), tooth extraction (n = 1), eye examination (n = 1), bronchoscopy (n = 1), and muscle biopsy (n = 1). The median duration of the PEG-T procedure in the remaining 81 patients was 28 minutes (10 – 65 minutes). In the first 40 patients, the median operating time was 28 minutes compared to 27 minutes in the last 41 patients (P = 0.26).

In 7 patients, 1 or more of the T-fasteners detached or was placed at an unsuitable location and these were therefore replaced by a new T-fastener during the PEG procedure. There were no other perioperative complications.

Early postoperative complications
A total of 54 early postoperative complications were recorded in 41 (47%) patients (Table 1) of which the majority were grade I and II complications. Of these, 45 were gastrostomy related. Of the patients with an early stoma infection treated with topical agents (grade I) or systemic antibiotics (grade II), 5 and 3 patients, respectively, also had an infection around the external suture locks. Of the 6 patients (7%) with early grade

Table 1 Early postoperative complications in pediatric patients undergoing insertion of a percutaneous endoscopic gastrostomy with T-fastener gastropexy.

<table>
<thead>
<tr>
<th>Grade</th>
<th>Early complications (n=54)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>27</td>
</tr>
<tr>
<td>II</td>
<td>21</td>
</tr>
<tr>
<td>IIIa</td>
<td>6</td>
</tr>
<tr>
<td>IIIb</td>
<td>4</td>
</tr>
<tr>
<td>IV</td>
<td>3</td>
</tr>
<tr>
<td>V</td>
<td>2</td>
</tr>
<tr>
<td>Others</td>
<td>2</td>
</tr>
</tbody>
</table>

1 Bedside reintroduction of the tube.
2 Others include for grade I: pneumoperitoneum (n = 1), gastroenteritis (n = 1), urinary retention (n = 1), and for grade II: fungal infection around a central venous catheter (n = 1), laryngitis (n = 1).
3 Tube reinserted under Midazolam anesthesia.
Ilb complications, 4 underwent a laparotomy and 2 an endoscopic procedure (Table 2). The 9 tube dislodgments occurred at a median of 5 days (0–28 days) postoperatively. 5 patients had a new gastrostomy tube inserted bedside. In 3 patients, bedside reinsertion was not possible; of these, 2 had a new 1 inserted endoscopically while one had a laparotomy due to inadequate transillumination during the initial procedure. Lastly, 1 patient had a laparotomy due to clinical signs of peritonitis. In all, the T-fasteners appeared to be in place, without obvious signs of migration. The balloon was noted to have deflated in 2 of the 9 patients. 1 or more early complications occurred in 48% of the infants and in 49% of those older than 1 year ($P=0.95$). In patients weighing less than 10 kg, 50% had early complications, compared to 47% of those weighing more than 10 kg ($P=0.77$). When comparing patients with and without neurologic impairment, 49% and 47% experienced early complications, respectively ($P=0.86$).

When comparing the first half of the patients with the last half, no difference was found concerning the frequency of early postoperative complications (44% vs. 52%, $P=0.45$). With regard to grade Ilb complications, 3 occurred in the first half of patients, and the remaining 3 in the last half.

### Long-term results

After the first 30 postoperative days, 55 gastrostomy-related complications were recorded in 33 (38%) patients. 35 grade I complications were noted and included granulation tissue ($n=17$), stoma infection ($n=12$), and migrated T-fasteners ($n=6$). Grade II complications were stoma infection ($n=12$) and migrated T-fasteners ($n=2$). Lastly, 8 grade Ilb complications were recorded: migrated T-fasteners ($n=5$), tube dislodgement ($n=2$), and stricture of the stoma channel necessitating revision ($n=1$).

Records of change of the initial gastrostomy tube to a low-profile button were found in 43 patients (49%). In 39 patients, the initial tube was changed to a low-profile button as planned after about 2 months. Due to leakage, 4 patients had the tube changed earlier than planned. In 42 of the 43 patients (98%), the change was done without the need for sedation or general anesthesia. In 1 patient, a short general anesthesia was necessary.

### T-fastener related complications

Early and late T-fastener related complications occurred in 9 (11%) and 11 patients (13%), respectively (Table 3). All late T-fastener complications seemed related to suspected migration of the T-fasteners into the stomach or abdominal wall. The late T-fastener complications were diagnosed at a median time of 2 months (4 weeks–17 months) postoperatively. In the 10 patients requiring intervention, this was performed at a median time of 4.5 months (1.3 months–3.5 years) after PEG-T insertion. Pain related to migrated T-fasteners necessitated removal in 7 patients: 4 under general anesthesia and 3 without. Furthermore, 1 patient underwent endoscopy under general anesthesia because the remaining T-fasteners in the stomach wall were suspected of causing pain. However, no T-fasteners were found during the procedure. In 1 patient, pain related to migrated T-fasteners disappeared spontaneously. Lastly, migrated T-fasteners were discovered accidentally in 2 patients, but no procedures were performed because these children were asymptomatic.

### Discussion

The main and surprising findings from this study are that many patients experienced dislodgment of the balloon tube within the first month and that the T-fasteners of the PEG-T system caused considerable problems. Although the use of T-fasteners is becoming increasingly popular in pediatric patients needing a gastrostomy, very few studies have addressed problems with T-fasteners in this population. In 1 retrospective study of 92 pediatric patients undergoing laparoscopic assisted PEG-T, only 3 patients (3%) experienced problems with the T-fasteners; 1 needed an endoscopic evaluation, and 2 had migrated T-fasteners removed under local anesthesia [8]. In contrast, 2 other studies including 201 [6] and 186 [7] children reported no T-fastener related complications. In adults, T-fasteners are often used, especially during insertion of a gastrostomy under radiologic surveillance. None of the 71 adult patients included in a
retrospective study experienced problems with the T-fasteners [11]. In contrast, a prospective study of 48 adults reported complications attributed to T-fasteners, either pain or skin related problems, in 11 patients (23%) [12].

It is largely unknown why and when some T-fasteners migrate through the stomach and abdominal wall and cause problems. Too tight locking of the sutures is considered to be a risk factor. Furthermore, it is possible that children are more prone to experience T-fastener migration than adults because they have thinner tissue layers. Apparently, the migration occurs early after PEG insertion. CT imaging in adult patients performed less than 4 weeks postoperatively, showed that 36% of T-fasteners had migrated into the anterior abdominal wall [11]. It is assumed that the T-fasteners may migrate into the abdominal wall during the initial procedure, especially during tract dilatation. Lastly, how soon the T-fastener sutures are cut after PEG insertion, may also influence the tendency for T-fastener migration.

In studies investigating gastropexy with T-fasteners, the sutures are cut between 5 days and 3 – 4 weeks postoperatively. Livingston et al. changed from cutting the T-fastener sutures 3 – 4 weeks postoperatively to 5 days after PEG insertion. After this change of practice, they did not report any T-fastener related complications [8]. Göthberg and Björnsson cut all sutures after 2 – 3 weeks, and they have not experienced any T-fastener related complications [6]. In our patients, the sutures were supposed to be cut 3 – 4 weeks postoperatively if not already detached. Unfortunately, data on when the sutures were actually cut were incompletely reported in the medical records. We also learned that some caregivers did not understand that the sutures were meant to be cut after 3 – 4 weeks. For instance, in 1 patient later needing surgical removal of a subcutaneous T-fastener, the external sutures were noted to be in place 5 weeks postoperatively. It is possible that the high complication rate related to T-fasteners in the present study may be partly explained by late removal of T-fastener sutures, but we cannot be sure about this since there are insufficient data on suture removal.

Early tube dislodgment is a feared complication after PEG insertion because the gastrocutaneous tract takes time to mature. Among our patients, 10% experienced early dislodgment. Compared to other reported series of PEG-P, this is a high number [13, 14]. In 2 series of PEG-T [6, 7], there was no report of any early dislodgment, while Livingston et al. reported this in 2 of 92 patients [8]. We have no apparent explanation for the high frequency of early dislodgment. To be able to insert a balloon gastrostomy tube, a wider opening in the abdominal wall is needed compared to PEG-P. This may increase the risk for tube dislodgment in the early postoperative period. Other possible explanations for early dislodgment are balloon malfunction, traction by the patient, balloon damage by the T-fasteners, and caregiver error (insertion of fluids in the balloon). One could also speculate that early T-fastener migration or removal may influence the tendency for dislodgment. In the patients who experienced early tube dislodgment in the present series, the T-fasteners appeared to be in place in all.

A major advantage of PEG-T is easy removal without the need for sedation or general anesthesia. This compares well with our experiences where 98% of the patients had their PEG-T removed in the outpatient clinic with no need for sedation or anesthesia. Another proposed benefit of T-fastener gastropexy is the fixation between the stomach and anterior abdominal wall making bedside reinsertion safe in case of early tube dislodgment. In our study, bedside reinsertion was possible in 5 of 9 patients, showing that T-fastener gastropexy cannot guarantee that a new gastrostomy tube may be inserted bedside.

Peristomal infections were common in our series and occurred in 25% of patients during the first 30 days after surgery. A lower infection rate after PEG-T insertion has been reported in 2 other pediatric series [6, 7]. Different classifications and definitions of peristomal infections may explain these differing results. In line with previous studies on peristomal infections after

### Table 3 Early and late complications specifically related to T-fasteners in pediatric patients undergoing insertion of a percutaneous endoscopic gastrostomy with T-fasteners.

<table>
<thead>
<tr>
<th>Grade</th>
<th>Early T-fastener complications (n = 10)</th>
<th>Late T-fastener complications (n = 13)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade I</td>
<td>Infection at site of external suture lock 5</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>Detached external suture lock 1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Migrated T-fastener causing pain</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>Migrated T-fastener without pain</td>
<td>2</td>
</tr>
<tr>
<td>Grade II</td>
<td>Infection at site of external suture lock 3</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Pain from external suture lock 1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Infection at site of migrated T-fastener</td>
<td>2</td>
</tr>
<tr>
<td>Grade IIb</td>
<td>Migrated T-fastener causing pain</td>
<td>5</td>
</tr>
</tbody>
</table>

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PEG-T, the design of this study makes it impossible to support a hypothesis of a lower peristomal infection rate after PEG-T compared to PEG-P. A randomized controlled study would best investigate this.

In addition to peristomal infections, hypergranulation is a common complication after PEG. Fortunately, this tends to become less of a problem with time. In a series from Sweden including 201 pediatric patients, hypergranulation was reported in 23% of patients 6 months after PEG-T insertion [6]. Interestingly, in the same series, hypergranulation was experienced by only 5% in the PEG-P group. In a small series of 10 Korean pediatric patients getting PEG-T, 50% developed granulation tissue [15]. In our series, hypergranulation was only reported in 4% of the patients. Since our data are based on a retrospective chart review, it is likely that the frequency of hypergranulation is underestimated. It has been hypothesized that the wide and deeper abdominal wall incision required to insert the balloon gastrostomy, may explain a higher frequency of hypergranulation after PEG-T.

Complications necessitating intervention under general anesthesia (grade IIIb complications) occurred in 7% of the patients in the present series. Among 92 pediatric patients getting a laparoscopy assisted PEG-T, grade IIB complications were reported in 4% [7]. Fewer grade IIB complications were found in a series of 201 PEG-T insertions, where only 2 children (1%) experienced grade IIB complications [6]. In the present study, 2 patients were suspected of having intraabdominal organ injury because of pneumoperitoneum and/or feces-looking secretion from the gastrostomy site together with impaired general condition. No damage was found during laparotomy; however, a large gastrostomy channel was noted in both patients. Pneumoperitoneum can be a normal finding after PEG insertion, but when found in a patient with signs of possible organ injury, such as fever or signs of peritonitis, further investigations are indicated [16]. Interestingly, in the series from Jacob et al., 7% of the patients were reported to have pneumoperitoneum [7]. In these patients, pneumoperitoneum did not warrant further surgery, but it is reasonable to assume that the patients in Jacob’s series had some clinical symptoms since abdominal X-rays were taken.

When introducing a new technique, a learning curve with regard to operating time and complications is likely to occur. At our center, the mean duration of insertion of a PEG-T was 28 minutes, which is in line with previous literature. In the large Swedish series of 201 patients getting PEG-T, median time for PEG-T placement was 20 minutes [6]. We did not see a decrease in operating time or in the frequency of patients experiencing early complications in our study as reported in other series [7, 8], but this may partly be explained by the relatively high number of physicians involved. Jacob et al. found the PEG-T procedure to be technically challenging, and they experienced a significant learning curve with regard to both complications and operating time [7]. In line with this, Livingston et al. found that all postoperative complications with laparoscopy assisted PEG-T insertion occurred within the first 50 cases and within the first 40 cases for each surgeon [8]. These findings support keeping the number of physicians involved with the procedure to a minimum.

Limitations of this study include the retrospective nature of data collection. Thus, it is likely that some complications are missed since patients may seek help at their general practitioner or local hospital. It would also have strengthened the study and interpretation of results if we had compared PEG-P and PEG-T in the same institution. However, this was not possible since PEG-T was the preferred technique. Strengths include the use of a validated scoring system for complications, including all complications, not only those obviously related to the gastrostomy. The use of the Clavien-Dindo system makes it easier to compare results and avoids subjective terms such as minor and major complications. The Clavien-Dindo classification has been used in trials in adults for a long time and is also increasingly used in pediatric studies [17]. Since none of the previous studies on PEG-T have used a predefined and validated complication classification system, it is difficult to compare results between studies.

To conclude, our study on initial experience with the PEG-T technique shows that the T-fasteners caused considerable short- and long-term complications, and the rate of early tube dislodgment was high. We did not see a lower rate of peristomal infections, but our hypothesis that PEG-T facilitates easy removal of the gastrostomy tube was confirmed. After reviewing these results, we have changed routines so that only 1 team of 1 pediatric surgeon and 2 pediatric endoscopists, inserts the PEG-Ts. Furthermore, there is particular focus on not making the sutures too tight and to avoid traction while dilating the gastrostomy channel. Lastly, all patients are scheduled for removal of the sutures and evaluation of postoperative results 2 weeks postoperatively. Hopefully, this change of practice will reduce the complication rate. Based on our experience with introduction of PEG-T, we recommend that this procedure is performed by a small team until sufficient experience with the method is gained at each center.

Competing interests

None

References


Nissen fundoplication in children with and without neurological impairment: A prospective cohort study

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A B S T R A C T

Background: It is assumed that children with neurological impairment (NI) have inferior results after fundoplication compared to those without NI (non-NI). The aim of this study was to assess outcome after fundoplication in children with and without NI.

Methods: 87/105 patients (46 NI, 41 non-NI) undergoing fundoplication between 2003 and 2009 were included in this prospective two-center cohort study. Complications occurring within the first 30 days were scored from 0 to 100 by the comprehensive complication index (CCI). Follow-up included clinical examination, upper gastrointestinal contrast study and 24-h pH monitoring 6 months postoperatively, then phone-interviews 1, 2 and 4 years later.

Results: There were no statistical differences in age (NI 3.1 years [0.2–15.2] vs non-NI 5.0 years [0.4–15.3], p = .14) or in total CCI score (NI 20.9 [0–44.9] vs non-NI 8.7 [0–40.6], p = .57). Hospital stay was longer for NI children (9 days [4–57] vs non-NI: 4 days [2–16], p < 0.001). More than 90% of parents in both groups reported that the fundoplication had improved the child’s overall condition. Recurrence of gastroesophageal reflux disease (GERD) was diagnosed in 12 NI and 7 non-NI patients (p = .31).

Conclusions: Early complications, GERD recurrence, and long-term parental satisfaction after fundoplication did not differ between NI and non-NI patients.
1. Material and methods

1.1. Inclusion criteria

Patients referred for fundoplication at Rikshospitalet and Ullevål University Hospitals between January 2003 and December 2009 were considered for inclusion. The present study is part of a prospective trial where patients were randomized to either laparoscopic or open Nissen fundoplication. Preoperative work-up included a 24-h pH monitoring and an upper gastrointestinal (UGI) contrast study. The pH monitoring was the main assessment for GERD. However, an UGI contrast study was performed in order to look for any anatomical pathology (e.g., hiatal hernia) or for gastroesophageal reflux (GER) if a pH study was not performed. Indications for surgery were objectively proven GERD with insufficient response to conservative antireflux therapy including proton pump inhibitors [13]. Data on outcome following the two surgical techniques have been published previously [12,13]. The Regional Committee for Medical Research Ethics approved the trial, and participation was voluntary. The study is registered in clinicaltrials.gov (NCT01551134).

1.2. Data collection

At admission patient demographics, feeding patterns and symptoms of GERD were recorded. Retching was defined as an unproductive effort to vomit with contraction of the diaphragm and abdominal muscles, vomiting as contraction of the diaphragm and abdominal muscles with forceful expulsion of gastric contents, and regurgitation as effortless regurgitation of gastric contents to or out of the mouth [14]. The frequency of retching, vomiting and regurgitation was graded on a 4-point scale: never (0), <1 day/week (1), 1–3 days/week (2) and ≥4 days/week (3). Ability to vomit and burp, meal related discomfort, daily GERD medications, seizures, and airway symptoms were recorded as none (0), <4/year (1) and ≥4/year (2).

NI was defined as a static or progressive, central or peripheral neurological condition associated with intellectual disability and/or functional impairment [15]. Severe NI was defined as having three or more of the following criteria: Cerebral palsy, mostly or exclusively tube-fed, daily epilepsy medications, and non-ambulance. Non-ambulance was defined as dependency of a wheelchair or a gross motor function classification system score of 4 or 5 in those less than four years old [16].

Surgical procedure, anesthesia and postoperative analgesia followed standardized guidelines. All patients got a Nissen fundoplication and the fundoplication was performed identically in laparoscopic and open procedures [12]. Briefly, the procedure included opening of the phrenoesophageal membrane and the gastroheptic ligament, complete exposure of the lower 3 cm of the distal esophagus, division of the short gastric vessels, and creation of a loose 1.5–2 cm wrap. At least one suture approximated the crura, and the wrap was also attached to the diaphragm. Complications and readmissions occurring following criteria: Cerebral palsy, mostly or exclusively tube-fed, daily GERD medications, seizures, and airway symptoms were recorded as none (0), <4/year (1) and ≥4/year (2).

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Clinical examination, 24-h pH-monitoring and an upper gastrointestinal (UGI) contrast study were scheduled six months postoperatively. Then, telephone-interviews were performed one, two and four years postoperatively by two independent investigators (CKK, TJF). Parents were asked the same questions as preoperatively. In addition, parental assessment of the child’s overall well-being, airway symptoms, and sleep was registered and classified as worse (0), unchanged (1) or improved (2). Parental satisfaction of outcome after fundoplication was graded as not satisfied (0), partially satisfied (1) and completely satisfied (2), while whether they would choose fundoplication again was recorded as yes or no. Any complications or symptoms suggestive of recurrent GERD or related to the fundoplication were investigated. To be diagnosed as having recurrence a child had to present both clinical GERD symptoms and objective verification of GER (either a reflux index >4%, and/or GER and/or herniation of the wrap by UGI contrast study). Patients with recurrent GERD were also followed by further phone-interviews, and if a redo fundoplication was performed, outcome was registered using a similar follow-up procedure as after the first fundoplication.

1.3. Patient demographics

Out of 105 eligible patients, 17 patients were excluded as described previously [12]. Reasons for exclusion were parents that did not speak Norwegian (n = 1), multiple previous laparotomies (n = 4), comorbidity assessed to be incompatible with laparoscopy (n = 4), need of urgent operation and no time for randomization (n = 2), and unwillingness to participate (n = 6). Eighty-eight patients were included in the study (Fig. 1). One non-NI child was excluded after inclusion because a paraparosophageal hernia was indication for fundoplication. Of the included 41 patients without NI, 34 had no other condition than GERD, four had esophageal atresia, and three children had other comorbidities. In the NI group, diagnoses included cerebral palsy (n = 18), various syndromes (n = 17), central nervous system disorders (n = 6), and brain damage caused by perinatal asphyxia (n = 5). Of these 46 NI patients, 25 (54%) had severe NI. Further clinical data of the NI and non-NI patients are presented in Tables 1 and 2. Preoperatively, frequent vomiting, retching, meal discomfort, and feeding problems were significantly more common among NI than among non-NI children (Tables 1 and 4). Continuous feeds were given to eight NI children and no non-NI child. One or more pulmonary infections requiring antibiotics during the last 12 months were reported in more NI than non-NI children (NI = 28, non-NI = 16, p = .04).

Preoperatively, 84 (97%) patients underwent pH monitoring. A pathological reflux index was found in 79 patients (40 NI, 39 non-NI). Of the remaining five patients (all NI) four had a normal reflux index and in one patient the pH monitoring failed. All these five children had massive reflux on the UGI contrast study and vomited or regurgitated 4–7 days/week. A pH monitoring was not attempted in three children (1 NI and 2 non-NI with esophageal atresia). Two of these three had GER induced stricture shown on endoscopy, GER on UGI contrast study, and vomiting and regurgitation 4–7 days/week. The third child was uncooperative and was considered to be unable to tolerate the test both by parents and doctors and was accepted for the study because of daily vomiting and regurgitation. An UGI contrast study was performed preoperatively in 76 (87%) children, of which 50 had GER and 9 had a hiatal hernia. Laparoscopic fundoplication was performed in 23 NI and in 21 non-NI patients. Eleven children (NI = 5, non-NI = 6) without a preoperative gastrostomy had one established concomitantly with the fundoplication.
1.4. Statistical analysis

Categorical variables were analyzed with Pearson’s χ²-test or Fisher’s exact-test as appropriate. Duration of surgery was compared with Student’s t-test. Age, LOS, days on parenteral fluid, and CCI score were not normally distributed and expressed as median [minimum–maximum] and assessed by Mann–Whitney U test. Because recurrence of GERD was more common after laparoscopic than open fundoplication [13], statistical adjustment for surgical technique using logistic regression was performed when comparing GERD recurrence between NI and non-NI patients. Fulfilment of expectations rated as “completely fulfilled” or “partly fulfilled” was counted together. “Would choose Nissen fundoplication again” only included those answering “yes”. The longitudinal observations on comparison of symptoms between children with and without NI and their change in symptoms over time were assessed using Generalized Estimation Equations (GEE). Thus, a Poisson regression-type model (Poisson distribution family and log link function) with diagnosis and follow-up as independent factors was used to estimate relative risks for selected symptoms over time with 95% confidence intervals. For the symptom “Able to burp” an exchangeable working correlation matrix was used, because of lack of convergence if an unstructured working correlation matrix was applied. The GEE analyses were performed with STATA 11 (StataCorp LP, College Station, TX). All other statistical analyses were performed with IBM SPSS Statistics for Windows, version 20.0 (IBM, Armonk, NY). A P value < .05 was considered statistically significant.

2. Results

2.1. Early postoperative outcome

The distributions of CCI scores among NI and non-NI children are displayed in Fig. 2. Total CCI score was not significantly different between those with and without NI (p = 0.09) (Table 3). There was also no significant difference when gastrostomy related complications were excluded (p = .17) (Table 3). When comparing children with severe and mild NI, there was no significant difference in total CCI score (severe NI 20.9 [0–33.7] vs. mild NI 20.9 [0–44.9], p = .57).

Parenteral fluids were given longer in the NI group (Table 1). After discharge, 5 NI and 18 non-NI children were readmitted to hospital (p = 0.001). Eleven of these children (NI = 3, non-NI = 8) were hospitalized. The other twelve children (NI = 2, non-NI = 10) were treated as outpatients; three received antibiotics for gastrostomy infection, eight had mild feeding problems, and one had mild airway symptoms not needing medical therapy. LOS was longer in the NI group (Table 1). When combining both the index stay and the second hospital stay, LOS was 9.5 days [4–57] in NI patients and 5.0 days [3–16] in non-NI patients (p < .001).

2.2. Long-term outcome

Two NI children died before the scheduled six months follow-up. Consequently, long-term postoperative outcome could be assessed in 85 out of the 87 included children (Table 2, Fig. 1). After the first follow-up six children died (all NI), and none died of causes related to the fundoplication.

---

**Table 1**

<table>
<thead>
<tr>
<th></th>
<th>NI (n = 46)</th>
<th>Non-NI (n = 41)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preoperative ng tube/gastrostomy tube, n</td>
<td>6/33</td>
<td>1/5</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Mostly or exclusively tubefed, n</td>
<td>36</td>
<td>6</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Feeding time &gt;3 h per day, n</td>
<td>27</td>
<td>7</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Scoliosis, n</td>
<td>12</td>
<td>0</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Daily epilepsy medications, n</td>
<td>27</td>
<td>1</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Age, years</td>
<td>3.1 [0.2–15.2]</td>
<td>5.0 [0.4–15.4]</td>
<td>&lt;.14</td>
</tr>
<tr>
<td>Days at Rikshospitalet/Ullevål hospital</td>
<td>7.0 [3–21]</td>
<td>4.0 [2–16]</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Total hospital days, index stay*</td>
<td>9.0 [4–57]</td>
<td>4.0 [2–16]</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Days on parenteral fluids, Rikshospitalet/Ullevål</td>
<td>6.0 [2–9]</td>
<td>2.0 [0–16]</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Transferred to local hospital on parenteral fluids, n</td>
<td>24</td>
<td>4</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

*Includes stay at Rikshospitalet/Ullevål and local hospital.
After fundoplication, vomiting, regurgitation, meal discomfort, and pulmonary infections were significantly reduced, while rectal flatulence increased in both groups. The fundoplication did not change the number in either group receiving feeds mostly or exclusively through a feeding tube (NI = 26, non-NI = 3) or the percentage that were fed N3h/day (NI = 12, non-NI = 6).

2.3. Parental satisfaction and overall evaluation of outcome

Overall, the parents were positive to the surgical outcome, with no reduction over time (Tables 4 and 5). The majority stated that the child’s overall condition was improved, that their expectations of surgery were fulfilled, and that they would have chosen fundoplication again (Table 4). Only four (2 NI, 2 non-NI) of the 85 children had parents that were unsure or would not have chosen fundoplication again during one or more of the follow-up interviews for the following reasons: Complicated postoperative convalescence; recurrence of GERD; troublesome retching, skin problems around the gastrostomy; and unchanged need for dilatations of esophageal stricture after repair of esophageal atresia. In this last child, esophageal stricture not responding to repeated dilatations was the main indication for fundoplication.

2.4. Recurrence of GERD

All 85 patients eligible for long-term follow-up underwent a postoperative pH monitoring and/or an UGI contrast study. Specifically, one or more pH monitorings were performed in 76 (89%) patients and one or more UGI contrast studies in 72 (85%) patients postoperatively [13]. A reflux index above 4% was detected in 12 patients (NI = 6, non-NI = 6). Nine children (3 NI, 6 non-NI) did not undergo any postoperative pH monitoring, either because parents refused and the child was considered unable to cooperate (n = 6) or because the child was absolutely

<table>
<thead>
<tr>
<th>Able to burp</th>
<th>Vomiting 4–7 days/week</th>
<th>Regurgitation 4–7 days/week</th>
<th>Retching 4–7 days/week</th>
<th>Discomfort after meal</th>
<th>Rectal fluctance</th>
<th>Daily airway medications</th>
<th>Pulmonary infections &gt;4/year</th>
</tr>
</thead>
<tbody>
<tr>
<td>NI (n = 46)</td>
<td>Non-NI (n = 41)</td>
<td>NI (n = 40)</td>
<td>Non-NI (n = 39)</td>
<td>NI (n = 36)</td>
<td>Non-NI (n = 37)</td>
<td>NI (n = 32)</td>
<td>Non-NI (n = 38)</td>
</tr>
<tr>
<td>93%</td>
<td>100%</td>
<td>51%</td>
<td>69%</td>
<td>55%</td>
<td>84%</td>
<td>66%</td>
<td>92%</td>
</tr>
<tr>
<td>65%</td>
<td>24%</td>
<td>5%</td>
<td>3%</td>
<td>6%</td>
<td>3%</td>
<td>3%</td>
<td>3%</td>
</tr>
<tr>
<td>46%</td>
<td>76%</td>
<td>5%</td>
<td>3%</td>
<td>0%</td>
<td>8%</td>
<td>0%</td>
<td>3%</td>
</tr>
<tr>
<td>46%</td>
<td>10%</td>
<td>28%</td>
<td>5%</td>
<td>17%</td>
<td>5%</td>
<td>10%</td>
<td>11%</td>
</tr>
<tr>
<td>48%</td>
<td>53%</td>
<td>34%</td>
<td>24%</td>
<td>39%</td>
<td>24%</td>
<td>31%</td>
<td>24%</td>
</tr>
<tr>
<td>26%</td>
<td>25%</td>
<td>58%</td>
<td>67%</td>
<td>46%</td>
<td>64%</td>
<td>57%</td>
<td>63%</td>
</tr>
<tr>
<td>51%</td>
<td>33%</td>
<td>44%</td>
<td>26%</td>
<td>47%</td>
<td>14%</td>
<td>31%</td>
<td>8%</td>
</tr>
<tr>
<td>33%</td>
<td>17%</td>
<td>8%</td>
<td>3%</td>
<td>18%</td>
<td>6%</td>
<td>10%</td>
<td>6%</td>
</tr>
</tbody>
</table>

Only results in children who had a primary fundoplication at the various follow-up times are shown. Results one year p.o. include data from two children who died shortly before the one year follow-up and whose parents were interviewed post-mortem.

Fig. 2. The distribution of comprehensive complication index scores (CCI) among children with neurological impairment (NI) and without NI (non-NI). Complications occurring during the first 30 postoperative days were registered.
In contrast to earlier retrospective studies, this prospective study did not find any major differences in postoperative outcome between children with and without NI. Importantly, more than nine out of ten parents of both NI and non-NI children reported that the Nissen fundoplication improved their child’s overall well-being. The high parental satisfaction did not decrease over a median four-year follow-up period in either group. Furthermore, NI children did not have a higher total CCI score than non-NI patients, and early postoperative mortality and life-threatening complications did not occur in any patient. However, NI children needed intravenous fluids longer and stayed longer in hospital than children without NI. There are several possible reasons why a fundoplication may benefit a child suffering from GERD. These include relief of regurgitation and vomiting, easier feeding, and improved growth [10,19,20]. In the present study both children with and without NI experienced less regurgitation and vomiting postoperatively. Importantly, none of the parents reported exaggerated postoperative retching. There are studies focusing on post fundoplication retching as a serious complication of antireflux surgery in NI children, suggesting that fundoplication may not be a good treatment option for GERD in NI children with frequent preoperative retching [11,21]. Simple measures such as frequent air venting from the gastrostomy, small and frequent meals, and adjustment of meal temperature and formula composition may alleviate postoperative retching and feeding intolerance in many patients [22]. We informed parents about these complications and advised them to follow the above measures if retching occurred, and this has probably been important for the absence of troublesome retching in our cohort of patients. Lastly, improved sleep, fewer respiratory

### Table 3

Postoperative complications occurring the first 30 days after Nissen fundoplication in children with (NI) and without neurological impairment (non-NI), graded according to the Clavien-Dindo classification and comprehensive complication index (CCI) (see Materials and Methods for description).

<table>
<thead>
<tr>
<th></th>
<th>NI</th>
<th>Non-NI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n = 46)</td>
<td>(n = 41)</td>
</tr>
<tr>
<td>Patients with complications</td>
<td>27/46</td>
<td>21/41</td>
</tr>
<tr>
<td>Patients with ≥ 2 complications</td>
<td>9/27</td>
<td>4/21</td>
</tr>
<tr>
<td>Grade I (total number)</td>
<td>6</td>
<td>16</td>
</tr>
<tr>
<td>Dislocated gastrostomy</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Hematoma at the epigastric port site</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Gastroenteritis</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Wound infection</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Feeding problem</td>
<td>3</td>
<td>14</td>
</tr>
<tr>
<td>Grade II (total number)</td>
<td>28</td>
<td>7</td>
</tr>
<tr>
<td>Pulmonary complication</td>
<td>18</td>
<td>4</td>
</tr>
<tr>
<td>Gastrostomy infection</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>Blood transfusion</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>Urinary tract infection</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Gastroenteritis</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Grade IIIb (total number)</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Food impaction</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Port site hernia/wound rupture</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Redo gastrostomy</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Total number of complications</td>
<td>38</td>
<td>27</td>
</tr>
<tr>
<td>CCI all complications</td>
<td>20.9</td>
<td>8.7</td>
</tr>
<tr>
<td>[0.449]</td>
<td>[0.406]</td>
<td></td>
</tr>
<tr>
<td>CCI when excluding gastrostomy-related complications</td>
<td>8.7</td>
<td>8.7</td>
</tr>
<tr>
<td>[0.449]</td>
<td>[0.348]</td>
<td></td>
</tr>
</tbody>
</table>

The total number of complications is higher than the number of patients with complications, as some patients had more than one complication.

* a Gastrostomy balloon in the duodenum. Problems resolved when the gastrostomy tube was correctly replaced into the stomach.

* b Leakage around gastrostomy requiring surgery.

* p < .05.

Well and did show any signs of recurrent GERD and the parents therefore refused (n = 3).

UGI contrast studies displayed reflux in six (NI = 3, non-NI = 3), and herniation of the wrap was found in 11 patients (NI = 9, non-NI = 2) (p = .05). All 11 patients underwent a postoperative pH monitoring, but was unsuccessful in one owing to a technical failure. Four (NI = 3, non-NI = 1) of the children with a herniated wrap were classified as having no recurrence of GERD or any problems related to the herniation, because they had a normal pH monitoring, no reflux on UGI contrast study, and reported no GER symptoms or any other signs of discomfort that could be related to the herniated wrap. 7 of the 11 children with herniated wrap were classified as having recurrent GERD. Two patients had GER symptoms, a pathological reflux index (20% and 7.7%), and no GER on UGI contrast study. These two children with herniated wrap were classified as having recurrent GERD. Two patients developed symptoms that were not managed satisfactorily with medications and underwent a retrofundoplication. In the child with an unsuccessful pH monitoring the UGI contrast study showed GER, and he had symptoms of regurgitation, sour smell from his mouth, and increased frequency of pulmonary infections and a second pH monitoring was therefore not attempted. The remaining four patients with a technically successful pH monitoring had no pathological pH-index and no reflux on UGI contrast study. Two patients developed similar symptoms as preoperatively with frequent vomiting and regurgitation, and the other two patients developed symptoms of feeding problems, pain related to feeds, and volume intolerance necessitating continuous feeding.

Recurrence of GERD was diagnosed in twelve (27%) NI and seven (17%) non-NI patients, with a risk ratio for recurrence of GERD in NI patients of 1.60 (95% confidence interval: 0.70–3.66) (p = .31) (Fig. 3). In a logistic regression model, odds ratio for failure in a NI patient was 1.8 [95% confidence interval 0.63–5.2] (p = .26). When adjusting for surgical technique, the odds ratio for recurrence of GERD in NI patients was 2.04 (95% confidence interval: 0.66–5.32) (p = .21). There was no significant difference in recurrence rates between the groups with severe and mild NI (6/25 vs. 6/21, p = .87). Ten children with recurrent GERD were treated conservatively, and nine (NI = 7, non-NI = 2) underwent a redo fundoplication owing to failure of conservative treatment. All nine children experienced improved overall wellbeing after the redo fundoplication (median follow-up 4.3 years [0.5–6.8]). One non-NI child developed dumping after the redo procedure, but this responded well to dietary treatment.

### 3. Discussion

In contrast to earlier retrospective studies, this prospective study did not find any major differences in postoperative outcome between children with and without NI. Importantly, more than nine out of ten parents of both NI and non-NI children reported that the Nissen fundoplication improved their child’s overall well-being. The high parental satisfaction did not decrease over a median four-year follow-up period in either group. Furthermore, NI children did not have a higher total CCI score than non-NI patients, and early postoperative mortality and life-threatening complications did not occur in any patient. However, NI children needed intravenous fluids longer and stayed longer in hospital than children without NI.

There are several possible reasons why a fundoplication may benefit a child suffering from GERD. These include relief of regurgitation and vomiting, easier feeding, and improved growth [10,19,20]. In the present study both children with and without NI experienced less regurgitation and vomiting postoperatively. Importantly, none of the parents reported exaggerated postoperative retching. There are studies focusing on post fundoplication retching as a serious complication of antireflux surgery in NI children, suggesting that fundoplication may not be a good treatment option for GERD in NI children with frequent preoperative retching [11,21]. Simple measures such as frequent air venting from the gastrostomy, small and frequent meals, and adjustment of meal temperature and formula composition may alleviate postoperative retching and feeding intolerance in many patients [22]. We informed parents about these complications and advised them to follow the above measures if retching occurred, and this has probably been important for the absence of troublesome retching in our cohort of patients. Lastly, improved sleep, fewer respiratory

### Table 4

Parental assessment of outcome reported one, two and four years postoperatively (p.o) in children with neurological impairment (NI) and without NI (non-NI).

<table>
<thead>
<tr>
<th></th>
<th>1 year p.o</th>
<th>2 years p.o</th>
<th>4 years p.o</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>NI (n = 40)</td>
<td>Non-NI (n = 38)</td>
<td>NI (n = 36)</td>
</tr>
<tr>
<td>Expectations fulfilled</td>
<td>100%</td>
<td>97%</td>
<td>97%</td>
</tr>
<tr>
<td>Would chose again</td>
<td>95%</td>
<td>100%</td>
<td>97%</td>
</tr>
<tr>
<td>Improved well-being</td>
<td>98%</td>
<td>100%</td>
<td>94%</td>
</tr>
<tr>
<td>Improved airway symptoms</td>
<td>50%</td>
<td>46%</td>
<td>42%</td>
</tr>
<tr>
<td>Improved sleep</td>
<td>43%</td>
<td>54%</td>
<td>44%</td>
</tr>
</tbody>
</table>

Numbers include all children, with or without recurrence of gastroesophageal reflux disease. Only results in children who had a primary fundoplication at the various follow-up times are shown. Results one year p.o. include data from two children who died shortly before the one year follow-up and whose parents were interviewed post-mortem.
infections, and less need for daily airway medications were other reported benefits of the fundoplication.

NI children did not experience recurrence of GERD more often than non-NI children, and there was also no difference among those with severe and mild NI. A minor difference in recurrence rate among the groups may have been missed in our study owing to the limited number of patients. Opposing this are the findings of the only two other prospective studies comparing NI and non-NI children [10,23] and a large cohort study, which in line with us, did not show inferior results for the NI group [24]. Including the four children with symptomless wrap herniation into the recurrence group would have increased the failure rate in NI patients (NI = 15 (34%) vs non-NI = 8 (20%)), but the difference would have remained non-significant (p = .15). We chose not to include children with symptomless herniated wraps in the recurrence group, since it did not have any consequence for the management of the child. Patients with a herniated wrap and postoperative symptoms were included in the recurrence group, but not all had objective sign of GERD. As continuous feeding may buffer the stomach acid, the pH monitoring may have been false negative in the four patients with troublesome symptoms and herniated wrap. A combined pH impedance examination might have shown pathological reflux in these patients, but such equipment was not available at that time in our department. It is also possible that the symptoms in some of these patients may have been caused by the herniated wrap and not recurrent GERD. In this patient population it is difficult to differentiate whether the symptoms were caused by one condition or the other. Thus, some of the patients we have classified as having recurrent GERD may not have had GERD recurrence, but problems related to the mechanical effects of a herniated wrap. Still, this does not alter the conclusion or main results of the study, but may affect the results presented in Fig. 3.

Interestingly, the majority of parents of children with recurrent GERD reported that the fundoplication had benefited their child. In some children with recurrent GERD, the symptoms were milder than preoperatively and could be successfully managed conservatively. Herniation of the wrap was detected in 13% of our patients, of which 4%, but later developed symptoms of feeding problems, pain related to feeds, and volume intolerance necessitating continuous feeding, and a redo fundoplication was performed. All of the nine patients undergoing a redo fundoplication experienced improved well-being.

The total CCI score was not significantly higher in children with than without NI, nor was there any difference in the total number of early complications between the groups. However, there were some differences among the groups. Postoperative lower airway infections were more common in NI patients. Since NI patients had a higher preoperative incidence of lower airway infections, they are probably also more susceptible to postoperative infections. Readmission to hospital owing to feeding problems was less frequent in NI than non-NI children, possibly because most NI patients had a gastrostomy. We have previously reported that LOS, number, and severity of postoperative complications did not differ between patients randomized to laparoscopic or open fundoplication [12], thus the surgical approach has not influenced these parameters. Duration of intravenous fluids and LOS were longer in the NI group. These findings may partly be explained by the department’s strategy of slowly introducing enteral feeding in NI children to avoid retching, as retching is thought to be particularly harmful to a newly established fundoplication [25,26].
Preoperative examination of NI children’s nervous system, respiratory function, dysphagia, and intolerance to gastric feedings has been suggested to guide decision making for fundoplication [15,27]. Previous studies on outcome of fundoplication have not graded the severity of NI and often the definition of NI is unclear. This makes it difficult to assess outcome after antireflux surgery in NI children and to compare results from different studies. In this study, we graded the severity of NI according to recognized parameters [2]. Interestingly, we found no difference in early and long-term outcome in those with mild and severe NI.

The major strengths of our study are the meticulous follow-up, the classification of NI patients and scoring of complications according to a standardized classification system. A limitation is the limited number of patients and thus a risk for type II error, especially when comparing subgroups such as those with mild and severe NI. Using a validated tool to assess GERD symptoms and outcome after fundoplication would have strengthened our study, but no such form has been developed for the pediatric patient population.

4. Conclusion

We did not find major differences in outcome after Nissen fundoplication between NI and non-NI children. Importantly, more than 90% of parents of both NI and non-NI children reported that the fundoplication had improved their child’s overall well-being. Consequently, given a well-selected NI child, a fundoplication is likely to offer measurable benefits to well-being, albeit at the cost of longer postoperative stay and more frequent early postoperative airway infections compared to children without NI.

Acknowledgments

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References


TITLE: Short and long-term outcomes after pediatric redo fundoplication

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Declaration of interest: none
Abstract

Background: Redo fundoplication (RF) is the most common surgical treatment for recurrent gastroesophageal reflux disease (GERD) in children, but outcomes after RF are rarely reported. The aim of this study was to assess short- and long-term outcomes after RF in childhood.

Methods: The study is a follow-up study of patients undergoing RF from 2002-2020 at a tertiary care center. Patients/parents were sent questionnaires recording symptoms of recurrent GERD, troublesome side-effects and satisfaction. Retrospective chart review was also performed.

Results: 24/28 (86%) patients were included median 9 (1.6 months-17.7 years) years after RF. 16 (67%) had neurologic impairment. Indications for RF was recurrence of GERD (n=18), discomfort or dysphagia from a herniated wrap (n=5) and dysphagia from a slipped fundoplication (n=1). Median operating time was 128 (95-250) minutes. Six (25 %) patients experienced early major complications, of which two were gastrostomy related.

Five (21%) patients experienced recurrence after RF. Three of these were symptom free at follow-up with medical treatment or re-RF. The most common symptom at follow-up was stomach pain (37%) and excessive flatulence (38%). 18/22 (95%) patients/parents would choose RF again, and 21/22 would recommend RF to someone in a similar situation.

Conclusions: RF is successful in treating recurrent GERD after primary fundoplication, and patient/parental satisfaction is high.

Key words
- Redo fundoplication
- Antireflux surgery
- Pediatric surgery
- Gastroesophageal reflux disease
- Postoperative complications
- Satisfaction
1. Introduction

Fundoplication is one of the most commonly performed major gastrointestinal surgical procedures in pediatric patients. Indications for fundoplication are symptoms or complications of gastroesophageal reflux (GER) disease (GERD) not sufficiently relieved with conservative treatment [1]. Most patients report initial disappearance of GER symptoms after fundoplication, but a substantial number of patients experiences recurrent GERD after some time. A systematic review from 2011 including studies with at least six months follow-up after primary fundoplication, reported recurrence of symptoms in 4-30% [2]. When recurrence occurs, there is no agreed-on algorithm for treatment. Treatment options include conservative management, redo fundoplication (RF), jejunal feeding either through a transgastric jejunal (TGJ) tube or a jejunostomy, parenteral nutrition, or esophagogastroduodenal disconnection and Roux-en-Y esophagojejunostomy [1,3–5].

In most centers, RF is the most common surgical option to treat recurrent GERD. Despite being the primary choice of surgical treatment, the literature is sparse on outcome after RF in children. Most studies are small retrospective case series and often only re-RF rates are reported [3,6–11]. The re-RF rate varies from 6-26% [7–12]. However, the re-RF rate does not reflect the true recurrence rate since some patients are treated conservatively, and some undergo other interventions than re-RF. In line with this, when recurrence after RF was defined as vomiting and objectively proven GER, two studies including 81 and 35 children, reported higher recurrences rate after RF; 42% and 25%, respectively [3,6]. Only one previous study has assessed outcome after RF beyond retrospective chart reviews. In this study including 31 children, family members reported that 61% of the children were back on anti-secretory drugs, and 45% vomited regularly median 3.6 years after the RF [13]. Even more concerning was that only 17% of the parents were satisfied with the outcome of the RF [13].

Due to the paucity of studies on outcome after RF in children, and especially the lack of studies where patients’ and parents’ evaluation of outcome has been addressed, we undertook this study where the main aim was to report frequency of recurrent GERD and troublesome symptoms after RF. Furthermore, we wanted to explore the short-term complication rate and patient and parental satisfaction with the RF.
2. Methods

2.1 Study design and patients

The current study is a cross sectional follow-up study of outcome in pediatric patients under 18 years undergoing RF between January 2002 and July 2020 at Oslo University Hospital Rikshospitalet. This is a tertiary pediatric surgery referral center, with an average of twelve primary fundoplications per year, and neurologically impaired (NI) children constitute around half of the patients [14]. The patients were identified from a surgical logbook. Patients who had undergone primary fundoplication at other hospitals were also included. Exclusion criteria were patients who were no longer alive or had emigrated. Data were collected by questionnaires and chart reviews. All fundoplications, both primary and redo, were performed with the Nissen technique by at least one attending surgeon.

Patients and/or parents got the questionnaires by mail in the period from November 2019 to August 2020. The questionnaires were filled out by parents of NI children and non-NI children below 12 years, by non-NI patients over 16 years, and by both non-NI patients between 12 and 16 years and their parents. Patients or parents were contacted by one of the authors if they had questions or symptoms that might be related to the fundoplication, and they were offered appropriate investigations if indicated.

Patients that already were included in a randomized controlled trial comparing laparoscopic and open fundoplication at our center, were not separately approached for this study since questions about postoperative outcome covered the same topics in the randomized trial as in this study [14,15]. In the randomized trial, patients were interviewed one, two, four and twelve years postoperatively, recording signs of recurrent GERD, troublesome side effects and parental/patient satisfaction.

2.2 Questionnaire

The questionnaire sent to patients and parents included questions about heartburn, vomiting, regurgitation, abdominal pain, dysphagia, discomfort during meals, retching, belching, and excessive flatulence. The questions were derived from the Pediatric Quality of Life Inventory Gastrointestinal Symptoms Scale [17]. Answers were given on a 5-point Likert scale (0: never, 1: Almost never, 2: Sometimes, 3: Often, 4: Almost always). When analyzing the results, the answers were transformed into dichotomous variables; 3 and 4 were reported as “yes” and 0, 1 and 2 as “no”. The questionnaire also addressed use of anti-secretory drugs (yes/no), if the patients had undergone any investigations for recurrent GERD or experienced...
any side effect of the fundoplication (yes/no and if yes, what had been done). The patient or parents were also asked if they had any questions related to the surgery or if they wanted investigations for symptoms that may be related to the fundoplication. Lastly, the questionnaire recorded satisfaction with the redo NF: “With the benefit of being able to look back, would you choose a RF again?” and “Would you recommend a RF to others in a similar situation?” (yes/probably yes/do not think so/no/unsure).

2.3 Retrospective chart review

Patient demographics, perioperative data regarding both the primary fundoplication and the RF, time from primary fundoplication to RF, and results from all investigations for GERD after the primary fundoplication and RF were recorded retrospectively. Recurrence of GERD was defined as symptoms of GERD and investigations confirming GER and/or herniated wrap. Indication for RF was registered as free text and categorized based on main complaint. NI was defined as a static or progressive, central or peripheral neurologic condition associated with chronic functional or intellectual impairment [18]. Complications during the first 30 postoperative days after the RF were graded according to the Clavien Dindo classification [19]. Grade 3 complications or higher were considered major complications.

2.4 Ethics

The study was approved by the hospital’s commission for personal security (19/22925). Consent was obtained from parents of patients under 12 years and NI patients, from both parents and patients between 12 and 16 years, and from patients only if older than 16 years.

2.5 Statistics

Data were presented with descriptive statistics; categorical data as frequencies and percentages and numerical data as median and range using IBM SPSS Statistics for Windows Version 25.0 (IBM, Amonk, NY).

3. Results

3.1 Patients

31 patients underwent a RF during the study period. Three were excluded; one had emigrated, and two were no longer alive. Six patients were already included in the above-mentioned randomized trial. Consequently, questionnaires were sent to 22 patients, and replies received from 18 (2 by patient only, 4 by both patient and parents and 12 by parents only). Thus, 24
out of 28 eligible patients (86%) were included in the current study, and the median follow up time was 9 (1.6 months-17.7 years) years.

The majority (67%) of patients had NI, and only 21% had no comorbidity (Table 1). The primary fundoplications were performed according to the Nissen technique, and hiatal closure was performed in all. A gastrostomy was established before or concomitantly with the RF in 17 (74%) patients. The median time from primary fundoplication to RF was 2.8 years (2 days-13 years). The RFs were performed by seven consultants. There were almost always two consultants performing the procedure, and senior author K.B was involved in 18/24 procedures.

3.2 Investigations before RF

All 24 patients had at least one investigation showing recurrent GER before the RF. Eight had a reflux index >4 on 24-hour pH monitoring, eight patients had GER on upper gastrointestinal (UGI) contrast study, and radiographic or endoscopic wrap herniation was demonstrated in 18 patients.

3.3 Indications for RF and perioperative data

The most common reason for RF was recurrence of GER symptoms such as heartburn, regurgitation and/or vomiting not satisfactorily relieved by conservative treatment (n=18, 75%). In five patients, the indication for RF was discomfort or dysphagia assumed to be caused by a herniated wrap. One of these patients presented with severe pain the first postoperative day and was reoperated the second day. Lastly, in one patient, the RF was performed because of dysphagia, and the UGI contrast study suggested that the fundoplication was wrapped around the upper part of the stomach (slipped Nissen).

RF was performed laparoscopically in five patients, of whom all had the primary fundoplication done laparoscopically. One of these procedures was converted because of extensive adhesions. The operating time, available in 18 (85%) patients, was median 128 (95-250) minutes. Wrap herniation was confirmed in all 18 patients where it was demonstrated at preoperative investigations, and the wrap was intact in half of these (table 2). In one patient the wrap had slipped and was situated around the upper part of the stomach as shown on the preoperative barium swallow. A hiatal closure was performed in 22 (92%) patients. A Gore-Tex mesh was used to reinforce the hiatal closure in two patients because of weak crural muscles.
Concomitant procedures were performed in seven (29%) patients; pyloroplasty (n=2), pyloroplasty and gastrostomy (n=1), umbilical hernia repair (n=1), removal of a pyloric hamartoma (n=1), endoscopic dilation of esophageal stricture (n=1), and Roux-en-Y-jejunostomy (n=1). The Roux-en-Y jejunostomy was performed to provide jejunal feeding in a patient with severe intestinal dysmotility. The RF in this patient was performed because a herniated wrap was believed to cause discomfort.

3.4 Early postoperative complications after RF

Twenty early postoperative complications occurred in 12 (50%) patients; four grade I complications (pneumothorax (n=1), wound infection (n=1), dislocated gastrostomy tube (n=1), gastrostomy site infection (n=1)), ten grade II complications (pneumonia (n=5), infection of unknown origin (n=2), bleeding needing transfusion (n=1), wound infection (n=1), central venous catheter related infection (n=1)) and six grade IIIB complications (revision of a central venous catheter (n=2), gastrointestinal bleeding necessitating endoscopy and blood transfusion (n=1), gastrostomy revision with drainage of peristomal abscess (n=1), dislocated gastrostomy tube reinserted under general anesthesia (n=1), respiratory problems requiring reintubation (n=1)).

3.5 Long term outcomes after RF

Five (21%) patients had recurrent GERD after redo NF (Table 3). Three had NI, one had previous esophageal atresia, and one had no comorbidity. Only one patient had more than one RF. This patient had no comorbidity, underwent a third RF due to recurrent symptoms and later a fourth RF due to a herniated wrap, and is now without symptoms. Based on the follow-up questionnaire, three of the five patients had, with appropriate treatment, either no symptoms or improved symptoms compared to before the RF (Table 4). The two patients with persisting symptoms had investigations confirming recurrent GERD and reported vomiting at follow-up. They did not receive satisfactory treatment for their symptoms. Furthermore, three patients used PPI for other indications than GERD; gastritis (n=2), to reduce gastric secretion because of severe gastrointestinal dysmotility (n=1).

The most reported gastrointestinal symptoms at follow-up were troublesome flatulence and abdominal pain (Table 4). One patient with new onset retching and one patient who got delayed gastric emptying after the RF had been successfully treated with insertion of a TGJ feeding tube. Four parents and one patient were contacted by telephone because they wanted
further follow-up. In addition, one patient had been operated two months and two years after the RF because of adhesion ileus.

Questions regarding satisfaction with outcome after the RF were answered by 22/24 (92%). 18 (82%) would choose RF again. Three would not, two were parents of patients with stomach pain and a herniated wrap and one patient with uncharacteristic upper abdominal pain, where endoscopy was normal. One parent of a child without any symptoms was unsure if she would choose RF again. Lastly, 21 (96%) said they would recommend RF to someone in a similar situation.

4. Discussion

This study on short and long-term outcome after RF in childhood demonstrates that most patients were successfully treated for their recurrent GERD. A large majority of parents and patients was satisfied with the outcome and would recommend RF to others in a similar situation. Those who experienced recurrent GERD or troublesome side effects after the RF, could often be satisfactorily treated without a new RF.

The most commonly reported results after both primary fundoplication and RF are recurrence and re-RF rates. Previous studies have reported symptomatic recurrence after RF in 25-45% of patients [3,6,13]. Thus, our finding of recurrent GERD in 21% is comparable to what has been reported earlier. Only one patient in our study underwent a re-RF (4%), reflecting previous findings of re-RF in 6-26% of patients [7–12]. Many pediatricians and pediatric surgeons assume that the success rate is considerably lower after RF than after primary fundoplication [9,10,19]. Interestingly, the recurrence rate after RF was similar to the recurrence rate after primary fundoplication at our center, questioning the opinion of significantly poorer results after RF [15].

Most patients reported no GERD symptoms at follow-up. Some mentioned early satiety and excessive flatulence, which are common complaints also after primary fundoplication [21]. Another frequently reported symptom was stomach pain. This is a symptom that is difficult to interpret, especially in NI patients. Retching in NI patients may be present before fundoplication or may occur after surgery [22], and has been linked to increased risk of wrap herniation or disruption [23]. One patient experience new onset retching after the RF, which was completely resolved after initiating jejunal feeding, supporting jejunal feeding as a treatment option for severe post-fundoplication retching [24].
Almost all patients and parents were satisfied with the outcome of the RF. In contrast, the only other study that has addressed satisfaction after RF in children, found that only 17% of parents were satisfied [13]. One explanation for the discrepancy may be the definition of satisfaction. Baerg and coworkers defined satisfaction as improvement of GERD symptoms and that parents would proceed with fundoplication again. We separated these two measures and found that most parents were satisfied even if their child had recurrence or troublesome side effects. Another explanation for this surprising finding could be that symptoms were less severe compared to before the RF and often could be managed successfully without surgery. Furthermore, all patients had tried conservative treatment without satisfactory effect, and this may have contributed to tolerance for mild GERD symptoms and troublesome side effects.

Deciding how to treat recurrent GERD after RF that is unresponsive to antireflux medication, is challenging. In this series, none but one patient had a third fundoplication. Reluctance to undertake a third fundoplication is in line with results from other series [6]. Jejunal feeding is an alternative to primary fundoplication in NI patients, and may be even more relevant if recurrence occur after RF [1,4,25]. Total esophagogastric dissociation is another treatment option [5,26].

RF is technically more challenging than primary fundoplication, particularly after open surgery. Consequently, operation time is longer and the complication rate higher. In this series the mean operation time of 128 minutes is comparable with other studies reporting mean operating time for RF from 82-177 minutes [10,27]. We previously reported operating times of 89 and 150 minutes for open and laparoscopic fundoplication, respectively, reflecting that RF is a more complicated procedure than a primary fundoplication [28].

Half of the patients experienced early postoperative complications, and a third of complications were major. There are few previous reports on complication rates after RF. In a study of 130 children undergoing RF, Dalla Vecchia and coauthors reported postoperative complications in 35% [9]. We have previously reported early complications in half (54%) of patients after primary fundoplication of whom one in ten were major, supporting the opinion of RF as a technically demanding procedure [28].

Five patients or parents wanted follow-up because of troublesome symptoms. Two adult NI patients were according to parents not properly handled by the local healthcare providers. Both patients had symptoms from a herniated wrap. These cases show that transition from pediatric to adult health care is important also for children having undergone fundoplication,
since recurrence may occur many years after the RF, and symptoms, particularly in NI patients, may be difficult to interpret [29,30].

Major strengths of this study are that we obtained patient/parent reported outcome measures and the long follow-up. The main limitation is the low number of patients. It would have strengthened the study if all patients had undergone postoperative investigations and if validated questionnaires for GERD had been applied.

In conclusion, this study finds that most patients undergoing RF were successfully treated. Regardless of recurrence or not, the patient and parental satisfaction was high. Based on these results and what is known in the literature, we believe that RF is a suitable treatment alternative when primary fundoplications fails. Careful patient selection and involvement of patients and parents in shared decision-making is important.

References


[8] Celik A, Loux TJ, Harmon CM et al. Revision Nissen fundoplication can be completed laparoscopically with a low rate of complications: a single-institution experience with 72


**Table 1.** Demographics of 24 patients undergoing redo fundoplication at Oslo University Hospital in the period 2002-2020.

<table>
<thead>
<tr>
<th></th>
<th>N=24</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at primary fundoplication, median (range)</td>
<td>3 yrs (2.6 mts-14.3 yrs)</td>
</tr>
<tr>
<td>Age at redo fundoplication, median (range)</td>
<td>9 yrs (1.0-16.0 yrs)</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>14 (58%)</td>
</tr>
<tr>
<td>Comorbidity</td>
<td></td>
</tr>
<tr>
<td>Neurologic impairment, n (%)</td>
<td>16 (67%)</td>
</tr>
<tr>
<td>Repaired esophageal atresia, n (%)</td>
<td>3 (13%)</td>
</tr>
<tr>
<td>No comorbidity, n (%)</td>
<td>5 (21%)</td>
</tr>
<tr>
<td>Primary fundoplication, open/laparoscopic</td>
<td>10/14</td>
</tr>
<tr>
<td>Follow up time after redo fundoplication, median (range)</td>
<td>9 yrs (1.6 mts-17.7 yrs)</td>
</tr>
</tbody>
</table>

**Table 2:** Perioperative findings from redo fundoplication in children

<table>
<thead>
<tr>
<th></th>
<th>N=24</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intact and herniated wrap</td>
<td>9 (38%)</td>
</tr>
<tr>
<td>Disrupted and herniated wrap</td>
<td>9 (38%)</td>
</tr>
<tr>
<td>Disrupted wrap</td>
<td>5 (21%)</td>
</tr>
<tr>
<td>Fundoplication wrapped around upper part of stomach</td>
<td>1 (4%)</td>
</tr>
</tbody>
</table>
Table 3. Patients with recurrent gastroesophageal reflux disease after redo fundoplication.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Presenting symptoms</th>
<th>Objective findings</th>
<th>Treatment</th>
<th>Status at follow up</th>
</tr>
</thead>
<tbody>
<tr>
<td>#1</td>
<td>Vomiting</td>
<td>Reflux index &gt;4. Macrosopic esophagitis on endoscopy.</td>
<td>PPI</td>
<td>No symptoms</td>
</tr>
<tr>
<td>#2</td>
<td>Vomiting and abdominal pain</td>
<td>GER and wrap herniation on UGI</td>
<td>PPI</td>
<td>Persistent symptoms, parents reluctant to further surgical treatment</td>
</tr>
<tr>
<td>#3</td>
<td>Vomiting and regurgitation</td>
<td>Reflux index &gt;4.</td>
<td>Redo fundoplication x2</td>
<td>No symptoms</td>
</tr>
<tr>
<td>#4</td>
<td>Abdominal pain</td>
<td>Wrap herniation on UGI</td>
<td>PPI</td>
<td>Improved symptoms</td>
</tr>
<tr>
<td>#5</td>
<td>Abdominal pain, vomiting and respiratory symptoms</td>
<td>Wrap herniation on UGI</td>
<td>PPI</td>
<td>Persistent symptoms, referred for jejunal feeding</td>
</tr>
</tbody>
</table>

PPI: Proton pump inhibitor  
GER: Gastroesophageal reflux  
UGI: Upper gastrointestinal contrast study

Table 4. Symptoms occurring “often” or “almost always” in patients median 9 years after redo Nissen fundoplication. Not all questions were applicable to all patients.

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>N=24</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vomiting</td>
<td>8% (2/24)</td>
</tr>
<tr>
<td>Regurgitation</td>
<td>0% (0/22)</td>
</tr>
<tr>
<td>Heartburn</td>
<td>0% (0/8)</td>
</tr>
<tr>
<td>Stomach pain</td>
<td>37% (7/19)</td>
</tr>
<tr>
<td>Retching</td>
<td>17% (4/24)</td>
</tr>
<tr>
<td>Discomfort during meals</td>
<td>17% (3/18)</td>
</tr>
<tr>
<td>Excessive flatulence</td>
<td>39% (9/23)</td>
</tr>
<tr>
<td>Dysphagia</td>
<td>25% (2/8)</td>
</tr>
<tr>
<td>Belching</td>
<td>18% (3/17)</td>
</tr>
</tbody>
</table>