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COMPLICATIONS OF UPPER GASTROINTESTINAL ENDOSCOPY AND SURGERY FOR COMMON BENIGN ESOPHAGEAL DISEASES

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ACADEMIC DISSERTATION

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ABSTRACT

Background and aims: Complications and medical errors strain healthcare systems and societies, and surgery is attributable to a significant number of adverse events. Benign diseases of the esophagus are common disorders, and diagnostic procedures and surgical treatment are commonplace to alleviate symptoms caused by them and improve the quality of life. This thesis consists of three studies that investigate the morbidity caused by complications of upper gastrointestinal endoscopy (esophagogastroduodenoscopy, EGD), antireflux surgery (AS), paraesophageal hernia repair (PEHR), and surgery for Zenker's diverticulum (ZD).

EGD is the core diagnostic tool used to investigate esophageal disorders and is also increasingly used for therapeutic interventions. As more complex procedures are carried out endoscopically, real-life evidence is warranted to justify their use, especially in frail and elderly patient populations.

Gastroesophageal reflux disease (GERD) is one of the most common gastrointestinal disorders, affecting 10-20% of adults in Western countries. ARS, particularly laparoscopic Nissen's fundoplication, is the golden standard for interventional treatment of GERD, and although its popularity has decreased after the introduction of efficient medical treatment alternatives, it is still commonly performed. GERD is often, but not always, related to a hiatal hernia, the prevalence of which increases with age. Small hiatal hernias are operated on only if ARS is indicated. Larger paraesophageal hernias are surgically repaired if they are symptomatic.

ZD is the most common diverticulum of the esophagus. If symptomatic, surgical treatment by either an open or endoscopic approach is recommended.

Surgical treatment of benign esophageal diseases is generally safe but associated with rare serious adverse events such as esophageal perforation. The burden of morbidity on public health resulting from complications of surgery for benign esophageal disorders in the era of minimally invasive surgery is largely unknown. The aim of this thesis is to investigate the complications of surgery for benign esophageal disease and hiatal hernia through malpractice claims on a national level.

Patients and Methods: A population-based retrospective register study of patient injury claims related to EGD, ARS, PEHR, and surgery for ZD was obtained from the registry of the national Patient Injury Centre (PIC) between Jan 2010 and Dec 2020. Furthermore, a baseline cohort concerning all procedures for EGD, ARS, PEHR, and surgery for ZD was collected from national registries from Jan 2010 to Dec 2018 for ARS, PEHR, and EGD and from Jan 1996 to Dec 2015 for ZD.

Results: In study I, 1,044 surgical procedures for ZD were identified from the baseline data, 6.7% of which included postoperative complications. The mortality rate was 0.9%. Nine patient injury claims related to surgery for ZD were identified, 6 of which regarded the transoral approach. Seven of all claims included leakage, and two included a recurrent laryngeal nerve injury.

In study II, 5734 ARS and PEHR operations were done during the study period, and 60 related patient injury claims were identified from the PIC database. Of all operations, 79.9% were ARS, 20.1% were PEHR, 92.5% were laparoscopic, and 5.9% were related to redo surgery. Of the PIC claims, 50.0% were related to PEHR. The mean Comprehensive Complication Index scores were 47.6 (± 20.8) and 35.9 (± 20.7) ($p = 0.033$) for PEHR and ARS, respectively. Of the claims, 18.3% were related to redo surgery.

In study III, 409,153 EGD were performed in Finland. During the study, the annual rate of EGDs increased by 2.5% and was 9.30 EGDs per 1,000 inhabitants. The 30-day and 90-day overall mortality was 1.70% and 3.84%, respectively. Eighty-four malpractice claims related to EGD were identified, with a rate of 0.23 claims per 1,000 patients treated.

Conclusions: Malpractice claims related to surgery for ZD, EGD, ARS, and PEHR remain rare. The surgery outcomes for ZD were more related to approach than patient characteristics. There were nine claims related to surgery for ZD, resulting in a moderate incidence of 15 claims per 1,000 operations. The popularity of paraesophageal hernia repair has increased in Finland during the study period, with a concurrent decline in the rate of ARS. Malpractice claims related to ARS and PEHR, albeit rare, included serious complications overrepresenting redo surgery and PEHR. The annual rate of EGD activity increased during the study time, but overall mortality declined simultaneously, and procedure-specific mortality and the number of malpractice claims are very low. The increase in EGDs was primarily due to diagnostic EGDs.

TIIVISTELMÄ

Huomattava osa hoitovirheistä, komplikaatiosta ja muista lääketieteellisistä haittatapahtumista liittyy toimenpiteisiin tai muuhun kirurgiseen hoitoon. Ruokatorven hyvänlaatuiset sairaudet ovat yleisiä ja toimenpiteet ovat keskeinen osa niiden tutkimista ja hoitoa. Ruokatorven hyvänlaatuisten sairauksien kirurgisen hoidon tiedetään aiempien tutkimusten perusteella olevan suhteellisen turvallista ja siihen liittyvien vakavien komplikaatioiden, kuten ruokatorven puhkeamisen, olevan harvinaisia mutta mahdollisia. Näiden komplikaatioiden aiheuttamaa sairastavuutta ei tunneta väestötasolla.

Tämän väitöskirjan osatyöt ovat retrospektiivisiä rekisteritutkimuksia ruokatorven, mahalaukun ja duodenumin tähystystyksiin, antirefluksikirurgiaan, palleatyrien kirurgiaan ja Zenkerin divertikkelien kirurgiaan liittyvistä potilasvahinkotapauksista aikaväliltä 2010 - 2020. Aineisto on kerätty kansallisen Potilasvahinkokeskuksen rekisteristä. Lisäksi tausta-aineistona käytetään kansallisesta hoitoilmoitusrekisteristä (Hilmo) sekä Tilastokeskuksen kuolinsyyrekisteristä kerättyä dataa kyseisten toimenpiteiden esiintyvyydestä ja niihin liittyvästä kuolleisuudesta.

Ensimmäisessä osatyö käsitteli Zenkerin divertikkelin leikkaushoitoa. Tarkastelujakson aikana Suomessa tehtiin 1044 Zenkerin divertikkelin leikkausta. Kuolleisuus leikkauksen jälkeen oli 0.9%. Yhdeksän potilasvahinkotapausta todettiin ja näistä kuusi liittyi transoraaliseen lähestymistapaan. Toisessa osatyössä tutkittiin antirefluksikirurgiaa ja palleatyräleikkauksia, joita tehtiin tarkastelujakson aikana 5734 kappaletta ja niihin liittyen todettiin 60 potilasvahinkotapausta. Potilasvahinkotapauksista 50.0% liittyi palleatyrien kirurgiaan. Komplikaatioindeksin (the Comprehensive Complication Index) mediaani antirefluksileikkauksiin liittyvissä potilasvahinkotapauksissa oli 47.6 (± 20.8) ja palleatyrien kirurgiaan liittyvissä potilasvahinkotapauksissa 35.9 (± 20.7) (p=0.033). Kolmannessa osatyössä todettiin ruokatorven, mahalaukun ja pohjukaissuolen tähystysten lisääntyneen tarkastelujakson aikana 2.5%. Kokonaiskuolleisuus 30 vuorokautta tähystyksestä oli 1.7%. Potilasvahinkotapausten esiintyvyys tähystysten jälkeen oli 0.23 per 1000 potilasta.

Potilasvahinkotapaukset ovat harvinaisia ruokatorven hyvänlaatuisten sairauksien kirurgisen hoidon jälkeen, mutta liittyvät yleensä vakaviin komplikaatioihin. Palleatyräleikkausten määrä on lisääntynyt Suomessa ja niihin liittyvät potilasvahinkotapaukset olivat aineistossa yliedustettuina. Palleatyräleikkauksiin liittyvät potilasvahinkotapaukset sisälsivät vakavampia komplikaatioita kuin antirefluksikirurgiaan liittyvät potilasvahinkotapaukset.

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I. Uoti S, Nurminen N, Andersson S, Egan, C, Tapiovaara L, Kytö V, Ilonen I. Postoperative Complications and Reoperative Surgery in the Treatment of Patients With Zenker Diverticulum. JAMA Otolaryngol Head Neck Surg. 2023;149(8):690–696. doi:10.1001/jamaoto.2023.1284 *

II. Nurminen NMJ, Järvinen TKM, Kytö VJ, Salo SAS, Egan CE, Andersson SE, Räsänen JV, Ilonen IKP. Malpractice claims after antireflux surgery and paraesophageal hernia repair: a population-based analysis. Surg Endosc. Published online November 27, 2023. doi:10.1007/s00464-023-10572-2

III. Nurminen, N., Järvinen, T., Robinson, E., Zhou, N., Salo, S., Räsänen, J., Kytö, V., & Ilonen, I. Upper gastrointestinal endoscopy procedure volume trends, perioperative mortality, and malpractice claims: Population-based analysis. Endosc Int Open. 2024;12(3):E385-E393. Published 2024 Mar 18. doi:10.1055/a-2265-8757

* This publication has previously been used as a part of Sandra Uoti's thesis "Zenker's Diverticulum: Epidemiology, Management, and Treatment Outcomes; 2024, University of Helsinki; ISBN 978-951-51-9621-7"

ABBREVIATIONS

EGD = Esophagogastroduodenoscopy, upper gastrointestinal endoscopy
ARS = Antireflux surgery
PEHR = Paraesophageal hernia repair
ZD = Zenker's diverticulum
GERD = Gastroesophageal reflux disease
PIC = Patient Injury Centre
NOMESCO = The Nordic Medico-Statistical Committee
CDC = Clavien-Dindo Classification
UES = Upper esophageal sphincter
LES = Lower esophageal sphincter
GEJ = Gastroesophageal junction
ASGE = The American Society of Gastrointestinal Endoscopy
ACG = American College of Gastroenterology
ESGE = European Society of Gastrointestinal Endoscopy
EMR = endoscopic mucosal resection
ESD = endoscopic submucosal dissection
II = Charlson Comorbidity Index
PEG = Percutaneous endoscopic gastrostomy
TLESR = Transient lower esophageal sphincter relaxation
PPI = Proton Pump Inhibitor
AET = acid exposure time
SI = Symptom Index
SAP = Symptom Association Probability
HRM = High-resolution manometry
DMS = DeMeester Score
NERD = Non-erosive reflux disease
H-KATPase = Hydrogen potassium Adenosine 5'-TriPhosphatase
BE = Barret's esophagus
MSA = magnetic sphincter augmentation
TIF = transoral incisionless fundoplication
CT = Computed Tomography
SAGES = Society of American Gastrointestinal and Endoscopic Surgeons
EAES= European Association for Endoscopic Surgery

CT = computed tomography
SD = standard deviation

1 INTRODUCTION

Medical errors and complications cause remarkable morbidity to individual patients and society.[1] Reportedly, 50% of in-hospital adverse events are related to interventional operations.[2] This thesis investigates the morbidity associated with procedures for benign esophageal diseases and paraesophageal hernias through processed malpractice claims and register data on a national level.

Malpractice claims represent the defined, measurable endpoints of adverse events and are a feasible source for studying serious complications and analyzing patterns of errors.[3,4] Surgery and endoscopic procedures for benign esophageal diseases and hiatal hernias are deemed safe but associated with rare serious complications such as iatrogenic esophageal perforations and severe long-term dysphagia.[5,6] The rate of malpractice claims related to surgery for benign esophageal diseases has not been studied at the population level. A previous historical study estimated the relative risk of malpractice after upper gastrointestinal endoscopy (esophagogastroduodenoscopy, EGD) to be 1.2 compared to sigmoidoscopy.[7]

In 1987, Finland became the first country to establish a national non-fault system to handle medical malpractice claims covering all healthcare provided.[8] All medical malpractice claims in Finland are handled by the Patient Injury Centre (PIC), a national insurance organization that deems the claims compensable and pays the compensation. PIC is a centralized insurance pool for all Finnish medical care.

This thesis consists of three studies focusing on mortality, morbidity, and malpractice claims for EGD, antireflux surgery (AS), paraesophageal hernia repair (PEHR), and surgery for Zenker's diverticulum (ZD). Most of these procedures aim to increase the quality of life and alleviate the symptoms related to the conditions. Only emergency repair of paraesophageal hernias is considered lifesaving.[9] Therefore, the morbidity caused by the treatment of these conditions should be strictly monitored to justify the procedures.

All these procedures carry a small risk of iatrogenic esophageal perforation, which is a severe complication that can lead to esophagectomy or mortality.[10,11] A Danish study published in 2011 examining all esophageal perforations found a mortality rate of 21%.[12] Awareness and contemporary minimally invasive treatment modalities may have decreased the morbidity of the condition.[10,13,14]

In a recent national study of all surgical procedures in Finland, the rate of claims was six per 1,000 procedures, and the rate of compensated claims was two per 1,000 procedures.[8] The purpose of this thesis is to establish a claim rate per surgery regarding the aforementioned procedures to serve as a benchmark for healthcare providers. This thesis also aims to produce real-life evidence to confirm the safety of surgery for these benign causes during the era of minimally invasive surgery. Furthermore, this paper explores the trends and epidemiology of the aforementioned surgeries.

2 REVIEW OF THE LITERATURE

2.1 ANATOMY OF THE ESOPHAGUS

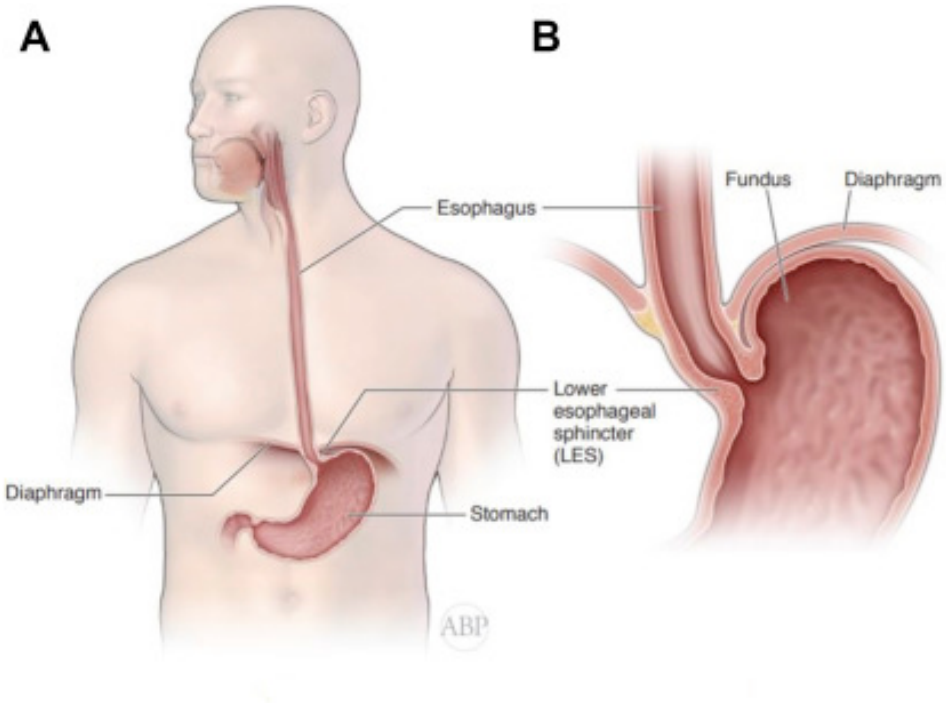

Figure 1 A) Anatomy of the esophagus; B) Anatomy of the gastroesophageal junction and proximal stomach. From Thoracic Surgery Clinics, 2019-11-01, Volume 29, Issue 4, Pages 359–368, Copyright © 2019 Elsevier, Inc. Reprinted with permission from Elsevier.

The esophagus is a hollow tube-like organ that connects the pharynx to the stomach (Figure 1).[15] The esophagus wall consists of four layers: mucosa, submucosa, muscularis propria, and adventitia. The mucosa is further divided into three layers: epithelium and the basement membrane, lamina propria, and muscularis mucosa. Unlike other parts of the gastrointestinal tract, the esophagus does not have a serosal layer.[15] The mucosa of the esophagus is a squamous cell type until the z-line, where it transforms into a columnar epithelium that continues in the stomach. The upper third of the muscle layer of the esophagus is striated muscle, and the lower two-thirds are smooth muscle.

The esophagus is topographically divided into three sections: the cervical, thoracic, and abdominal esophagus. Commonly, the point considered the end of the pharynx and the beginning of the esophagus is at the level of the sixth cervical vertebra, anterior to which the esophagus runs. The muscularis propria layer of the esophagus consists of linear fibers, on the inner side of which is a layer of circular fibers, with a myenteric plexus consisting of neurons between them.[16]

Two muscular sphincters prevent the reflux of gastric contents to the esophagus and the pharynx: the upper esophageal sphincter (UES) and the lower esophageal sphincter (LES).[15] The UES is located in the cervical esophagus. The UES divides the pharynx from the esophagus and consists of the cricopharyngeus muscle, the inferior pharyngeal constrictor, and the longitudinal fibers of the esophagus.[17] The LES is located in the esophagus near the gastroesophageal junction (GEJ) spanning over the hiatus.[15] The LES and the crura of the diaphragm form a complex that functions as a barrier, preventing the reflux of acidic gastric contents from the stomach to the esophagus.[18] The phrenoesophageal ligament holds the LES in place. The angle between the esophagus and the cardia is called the angle of His, and it works as a valve that permits the passage of a food bolus to the stomach but prevents reflux backwards.[19]

2.2 DEFINITION OF A COMPLICATION

There are several definitions for surgical complications.[20,21] Currently, the most widely accepted is the definition introduced by Clavien et al. in 1992, according to which negative outcomes are differentiated into complications, sequelae, and failures.[22] According to the authors, "complications and sequelae result from procedures, adding new problems to the underlying disease. However, complications are unexpected events not intrinsic to the procedure, whereas sequelae are inherent to the procedure. Failures are events in which the purpose of the procedure is not fulfilled."[22] Thus, the inability to walk after an above-the-knee amputation is a sequela, not a complication. Also, if a procedure is performed for GERD and the patient still suffers from heartburn, it is considered a failure to cure, not a complication.

The terms "adverse event" and "complication" are to some extent used interchangeably, although not all authors consider them synonymous.[20] A landmark report on patient safety published in 1999 by the US Institute of Medicine defined an adverse event as "injury caused by medical management rather than the underlying condition of the patient".[1]

Medical errors differ from adverse events and complications. Not all adverse events or complications are the result of a medical error. The previously mentioned report defines error as "a failure of a planned action to be completed as intended or the use of a wrong plan to achieve an aim".[1] A medical error can be, but is not always, a result of negligence, determined by legal criteria for meeting the standard of care.[23]

2.3 UPPER GASTROINTESTINAL ENDOSCOPY

Upper gastrointestinal endoscopy (esophagogastroduodenoscopy, EGD) is the first-line standard diagnostic tool for all esophageal disorders. Kussmaul performed the first EGD in 1868.[24] Additional development and innovations have provided the scope with a light source, flexibility, and video images, enabling the modern endoscope to perform visualization, tissue sampling, and therapeutic maneuvers of the upper gastrointestinal tract.[25] In an article by Peery et al., an estimated 7.4 million EGDs were performed in the USA in 2019.[26]

Performing the flexible EGD begins with intubation of the scope through the mouth and pharynx to the esophagus. Air or carbon dioxide is then used to fill the lumen of the GI tract to enable visualization. The scope is then advanced through the esophagus, to the gastrointestinal junction, and to the stomach. The corpus and antrum of the stomach are then visualized, the pylorus is intubated with the scope, and the duodenum is entered. To visualize the cardia and fundus, the tip of the scope is turned to offer a cephalad (retroflexion) view inside the stomach. At the end of the procedure, the scope is pulled from the GI tract with the suction of excessive air.[27]

The use of procedural sedation during EGD varies globally. In Finland, it is not a common practice, whereas in the USA, sedation is usually administered.[28,29] Pharyngeal anesthesia with topical agents is widely used in non-sedated EGD.[30,31]

In addition to being an essential diagnostic tool, EGD is also used to perform several different therapeutic procedures of the esophagus, such as balloon and bougie dilatations, esophageal stent placements, radiofrequency ablation of Barrett's esophagus, endoscopic mucosal resection, endoscopic submucosal dissection, and ligation of varices.[32-35] Also, peroral endoscopic myotomy (POEM) is increasingly used to treat achalasia and diverticula of the esophagus.[36,37]

There are two statements concerning the quality of EGD: the American Society of Gastrointestinal Endoscopy (ASGE) and American College of Gastroenterology (ACG) quality indicators published in 2015 and the European Society of Gastrointestinal Endoscopy (ESGE) quality improvement initiative published in 2016 that act as benchmarks for centers performing EGDs.[38,39]

Adverse events related to EDG are rare.[40-42] The risk of complications is higher in interventional EGDs than in diagnostic endoscopies.[41] ASGE has published a lexicon for documenting adverse events related to endoscopies and defines an adverse event as "an event that prevents completion of the planned procedure or results in admission to hospital, prolongation of existing hospital stay, another procedure or subsequent medical consultation."[43]

The most frequent adverse events after EGD are cardiopulmonary, such as hypoxemia or respiratory depression, which are related to procedural sedation.[42] In a national study by Sharma et al. from the USA, the incidence of cardiopulmonary events after EGD was 0.6% (n=852 of 139,840 EGDs).[44] In a large German prospective multicenter study consisting of 368,206 endoscopies, of which 52.6% were EGD, 314,190 endoscopies were performed under sedation, and the complication rate related to anesthesia was 0.3% (n=1054).[45] Several guidelines concerning procedural anesthesia during endoscopies have been published regarding staffing of the procedures, regimens used, and patient monitoring.[46,47]

Aspiration of gastric contents and the related potential pneumonia is a potential but uncommon complication of EGD, and it may be related to sedation.[48] In a study by Thomson et al., where 50 patients were given technetium-labeled water perorally before the endoscopy and a gamma scan was run before and after the procedure, no aspiration was detected.[49]

Methemoglobinemia is a rare but serious condition related to the use of topical anesthetics. The risk of methemoglobinemia was 3.5 in every 10,000 cases in a large case-control study by Chowdhary et al. and one case per 1499 in a retrospective single-center study by Kane et al. from Mayo Clinic. [50,51]

Overall, the risk of iatrogenic perforation related to EGD is low. In previous studies, the risk of esophageal perforation after diagnostic EGD was estimated to be 0.0009%–0.03%.[52-54] However, endoscopy is estimated to be responsible for 46.5%–60% of esophageal perforations, which are primarily due to endoscopic procedures and are associated with remarkable morbidity and mortality (Figure 2).[55-57] According to the ESGE position statement of diagnosis and management of iatrogenic endoscopic perforations updated in 2020, esophageal dilatations, endoscopic mucosal resection (EMR), endoscopic submucosal dissection (ESD), septotomy for ZD, and foreign body removal are to be considered high-risk procedures for esophageal perforation.[6] In a population-based study from the United States by Goual et al. published in 2017, the perforation risk after endoscopic dilatation was 0.5% for benign and 0.9% for malign strictures.[58] In addition to esophageal perforations, gastric and duodenal perforations are also possible.[53]

The EGD is also increasingly used to treat iatrogenic esophageal perforations and is recommended by the previously mentioned ESGE position statement.[6] Both through-the-scope and over-the-scope clips can be used, as well as temporary self-expandable metal stents and endoscopic vacuum therapy (Figure 2).[59-61] A recent multicenter trial by Luttikhold et al. concluded a success rate of 89% with esophageal perforations treated with vacuum therapy.[61]

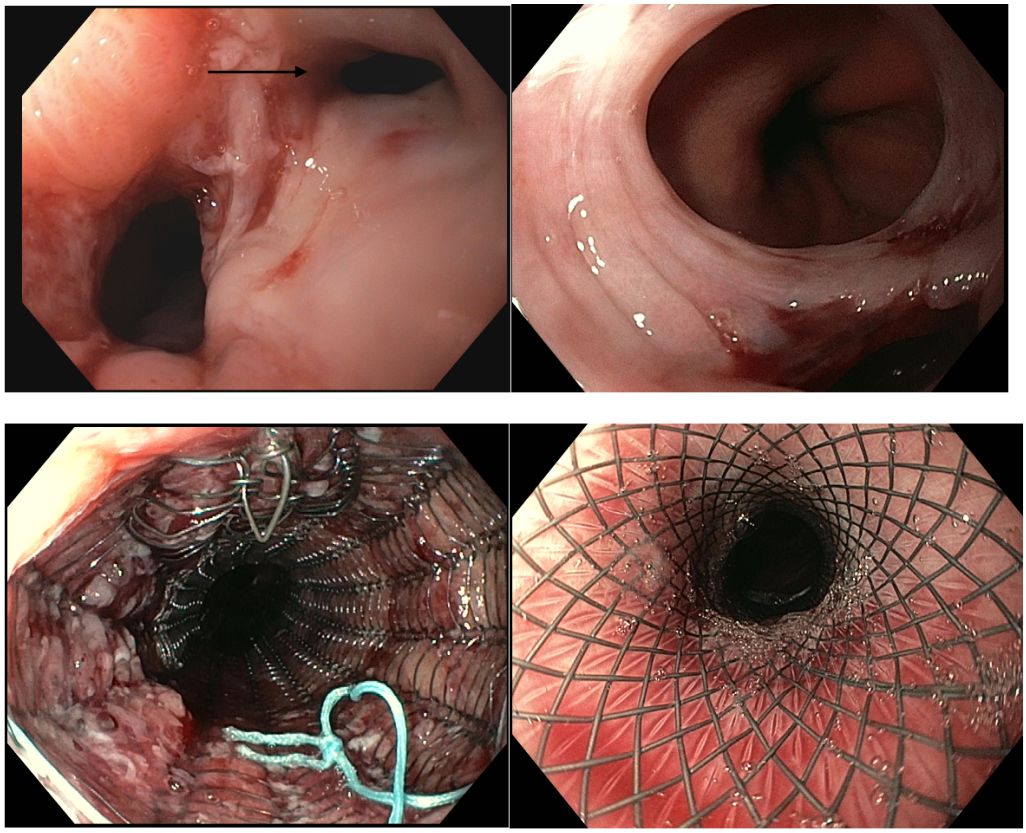

Figure 2 Iatrogenic perforations after esophageal dilatation and stents placed for treatment.

Clinically significant bleeding is a rare adverse event in EGD, especially after diagnostic EGD, even if the patient is taking anticoagulants.[54,62,63] The risk of bleeding is greater if EGD involves procedures and varies depending on the procedure. In a systematic review and meta-analysis by Libanio et al., the risk of bleeding after gastric ESD and EMR was 5.1%.[64]

Endogenic and exogenic infections following EGD have been reported.[65] GI endoscopy has been associated with transient bacteremia, supposedly because of mucosal trauma and the translocation of oral or intestinal microorganisms.[66] Transient bacteremia has especially been related to esophageal dilatation.[66,67] However, clinically significant endogenic infections, such as infectious endocarditis, are extremely rare, and guidelines recommend against routine use of antibiotic prophylaxis.[68] The exogenous infections after EGD have decreased over time because of the evolution of endoscope reprocessing, but outbreaks have still been reported.[65,69] In a systematic review by Deb et al., the most common culprit

organism was Pseudomonas aeruginosa, and the overall infection rate was 0.123% following EGD.[65] Transmission of multidrug-resistant organisms has been reported from duodenoscopes, where the elevator mechanism may generate a biofilm and stay contaminated even after reprocessing.[70]

Missed pathology is a possible complication of EGD. A population-based study by Chadwick et al. from the UK assessed the rate of previous EGDs within three to 36 months of the diagnosis of esophageal cancer and concluded that 7.8% of patients with the condition may have had their diagnosis missed at the first endoscopy.[71] In a recent population-based study from Poland, the risk of missed pathology was 6.0%, and the risk factors were endoscopy performed in primary care, female sex, and a higher Charlson Comorbidity Index (CCI).[72]

Percutaneous endoscopic gastrostomy (PEG) tube insertion has a characteristic complication profile. PEG tube placement was first introduced by Ponsky-Gauderer in 1980 as an alternative to surgical gastrostomy placement and has since gained popularity.[73] Several techniques are available for PEG tube placement, such as the pull-string and push methods.[74] Acute complications of PEG tube placement include colon perforation, small bowel perforation, liver injury, peritonitis, aspiration, infection of the stomal area, and bleeding.[70,75-77] The 30-day mortality rate after PEG placement is reportedly 2.4%–5.3%.[75,78,79] The rate of infectious complications can be reduced with the use of prophylactic antibiotics.[77]

2.4 ANTIREFLUX SURGERY AND PARAESOPHAGEAL HERNIA REPAIR

2.4.1 Gastroesophageal reflux disease

GERD affects 10%–20% of the population in Western countries, and its prevalence is increasing.[80] [81-83] To some extent, reflux of gastric contents is physiological. According to the Montreal consensus statement from 2006, the definition of GERD is the reflux of gastric contents to the esophagus, resulting in symptoms or complications.[84]

The pathophysiology of GERD is multifactorial and related to the incompetence of the GEJ, which can be caused by transient LES relaxation (TLESR), hypotensive LES, or anatomic disruption of the GEJ.[85] TLESR was first described by Dent et al. in 1980, and it defines the vagovagal reflex that results in spontaneous relaxation of the LES without swallowing and enables physiologic venting of gas from the stomach.[86] It is hypothesized to be the basic pathologic mechanism of GERD.[87] TLESR occurs more often in patients with GERD than in healthy controls but is associated with acid reflux at a higher frequency.[88] [89] Hypotensive LES is a cofactor of GERD in a minority of patients with the disease but can manifest even as a free reflux from the stomach to the esophagus. [90] Also, the diaphragm contributes to EGJ integrity, so hiatal hernias or other laxity in the attachment of the esophagus to the crura can result in increased reflux.[90] In addition, the pH of the refluxate, peristalsis of the esophagus, saliva production, and esophageal hypersensitivity contribute to the disease. [85,91-93]

Known risk factors for GERD are obesity, age, and smoking.[94,95] Furthermore, caffeine, alcohol, and several foods and drugs, such as anticholinergics, can induce LES hypotension and, therefore, reflux.[96]

According to the Montreal statement, the classic symptoms of GERD are heartburn and regurgitation, the first of which is characterized by postprandial burning pain rising from the epigastrium towards the throat, and the latter as perception of the flow of the gastric contents in the mouth or hypopharynx.[84] The other symptoms of GERD are chest pain and extraesophageal symptoms such as coughing and hoarseness. GERD is also common in patients with asthma and can cause exacerbations of the disease.[97]

According to guidelines, the diagnosis of GERD can be established empirically if the patient has classic symptoms of GERD, although the diagnosis only has 70% sensitivity and 67% specificity, even when given by an experienced gastroenterologist.[98,99] An eight-week proton pump inhibitor (PPI) trial is suggested by guidelines and widely used, but according to a meta-analysis by Numans et al., its sensitivity and specificity are only 78% and 54%, respectively.[100]

EGD with biopsies is recommended if the patient has alarming symptoms, such as weight loss, dysphagia, or anemia, or if the PPI trial fails to detect cancer, explicit evidence of GERD, rule out other diseases, and screen for Barret's metaplasia.[98]

The Lyon consensus statement from 2018 formed the definition of GERD in esophageal testing.[101] Ambulatory pH monitoring is used to differentiate GERD from reflux hypersensitivity or functional heartburn, and it is recommended in refractory disease if there are no explicit signs of GERD in EGD.[102] The monitoring produces measurements on acid exposure time (AET), reflux events, and the correlation of the events to the symptoms of the patient. This procedure can be performed with a transnasal catheter or wireless system. pH impedance monitoring also detects non-acid reflux and is therefore considered the standard test when feasible.[103] According to the Lyon consensus statement, AET is considered abnormal if it is over 6% of the study time, normal if under 4%, and inconclusive if it takes 4%–6% of the time. The association between reflux and the symptoms can be described using the Symptom Index (SI) and Symptom Association Probability (SAP), which are the percentage of symptom events preceded by reflux and a calculation of the probability that the symptom events and reflux are associated, respectively.[104,105] High-resolution manometry (HRM) can provide information to support the diagnosis of GERD, but it is generally considered to rule out other diseases, such as motility disorders or rumination.[106]

The DeMeester Score (DMS) was introduced in 1974 to define GERD in 24-hour pH testing.[107] The score defines acid reflux as a pH under 4 measured 5 cm above the upper border of LES.[107] The DMS gives a composite score that considers total, upright, and recumbent AET, number of reflux episodes, duration of the longest reflux episode, and acid reflux episodes over five minutes. The Porto consensus group suggested that overall, AET should be used instead of DMS because of AET's reproducibility; however, DMS is still widely used, especially by surgeons.[108,109] DMS is considered diagnostic if over 14.7, mild if under 50, moderate if between 50 and 100, and severe if over 100.[110]

GERD can be divided into erosive and non-erosive GERDs. The hallmark of erosive GERD is mucosal injury of the distal esophagus (erosive esophagitis), which can also be considered a complication of GERD. Non-erosive reflux disease (NERD) indicates reflux-related symptoms and pathologic pH recording without objective findings on upper endoscopy. Normal esophageal mucosa is the most common finding in patients with suspected GERD.[111] According to Holmberg et al., NERD is not associated with an increased incidence of esophageal adenocarcinoma compared to the general population, whereas patients with erosive esophagitis have a remarkably increased risk of esophageal adenocarcinoma.[112] Nevertheless, there are also histopathological changes associated with NERD that resolve after adequate reflux treatment, such as dilation of intracellular spaces, although these findings have limited value in

clinical workup.[113,114] Esophageal acid hypersensitivity (hypersensitive esophagus, reflux hypersensitivity) is defined as heartburn with normal endoscopy and AET in pH-monitoring but positive SAP or SI.[115] Functional heartburn is defined as heartburn with a normal endoscopy, a normal AET, and a negative symptom association in pH monitoring.[116] Esophageal acid hypersensitivity and functional heartburn are classified as functional esophageal disorders according to Rome IV criteria.[117]

It is intended that GERD is a collection of different diseases rather than just a single disease with a spectrum of severity.[118] Also, other conditions like eosinophilic esophagitis or esophageal hypersensitivity may be misdiagnosed as GERD based on the PPI test.[119]

Treatment of GERD comprises lifestyle changes, medication, and, in selected cases, ARS.[98] Lifestyle changes, such as losing weight, diet restrictions, smoking cessation, and modifications to sleeping habits, are often proposed, but the studies supporting them are sparse and contradictory.[96,120-123] The first PPI, omeprazole, was introduced in 1989, and since then, PPIs have revolutionized the treatment of GERD.[124,125] The PPIs inhibit the H-KATPase of gastric parietal cells, thus decreasing the acid secretion of the stomach. A recent systematic review shows that nearly 25% of the adult population uses PPIs.[126] H2-receptor antagonists are also used but are less efficient than PPIs in healing esophagitis or relieving symptoms.[125,127] Antacids, sucralfate, and sodium alginate are used for on-demand symptom relief.[98]

2.4.2 Complications of GERD

According to the Montreal statement, complications are definitive signs of GERD.[84] Patients with complications can also be symptom-free. Complications of GERD include erosive esophagitis, Barret's esophagus (BE), and peptic stricture.

Erosive esophagitis is seen in 30% of patients with GERD. The most widely used classification of its severity is the Los Angeles classification, presented at the Los Angeles World Congress of Gastroenterology in 1994.[128,129] This classification grades the disease by the extent of mucosal breaks in the esophagus. According to animal studies and a prospective trial by Dunbar et al., erosive esophagitis is a cytokine-mediated inflammation rather than a caustic injury of the acid refluxate.[130,131] According to the Lyon consensus statement, grades C and D are considered definitive signs of GERD, whereas grades A and B are not because they are prone to interobserver variability.[101]

Peptic strictures can result when erosive esophagitis heals; they are usually simple and located near the GEJ.[132] Potential esophagitis should be treated before procedures, as dysphagia may resolve with it.[133] Otherwise, a dilatation with a bougie or a balloon dilatator can be done if the patient has dysphagia.[133]

BE occurs when interstitial-type epithelium replaces the normal stratified squamous epithelium of the distal esophagus in a process called metaplasia.[134,135] The condition predisposes to the development of esophageal adenocarcinoma, an association first made by Naef et al. in 1975.[136] BE results from GERD as a reflux of acid or otherwise noxious gastric content, such as bile, causing injury to the mucosa of the esophagus.[137] The diagnosis of BE is completed via endoscopy and biopsies, with the definition differing from country to country. In the USA, intestinal metaplasia that extends over 1 cm of the distal esophagus is considered BE, the histologic hallmark of which is the presence of goblet cells.[134] The British Society of Gastroenterology and some other countries also consider cardiac metaplasia to be BE.[138] If the metaplastic segment is over 3cm, it is considered long, and segments less than 3cm are considered short.[134] BE does not usually lengthen gradually; instead, it appears to reach its full extent quickly.[135] Cancers that develop in BE may do so through stepwise worsening dysplasia or directly because of the genetic instability of the metaplastic mucosa.[135]

To detect the potential transformation of metaplasia into dysplasia or cancer, guidelines recommend surveillance for BE, although the benefits are unclear, and there are known harms associated with the surveillance.[134,139] Since the length of the BE is linked to the risk of dysplasia, according to several guidelines, the surveillance should be tailored based on the length of the BE.[134,140,141] Overall, the risk of BE without dysplasia progressing to cancer is low, and it is more likely that patients with these conditions will die of other causes than esophageal adenocarcinoma.[139]

Dysplastic BE is related to a significant risk of esophageal adenocarcinoma and can be treated endoscopically with radiofrequency ablation or endoscopic mucosal resection.[134,140,141] If this intervention fails, high-grade dysplasia can require an esophagectomy.[142]

2.4.3 Indications for antireflux surgery

ARS is recommended by several guidelines as an option for medical treatment for patients with typical symptoms and objective evidence of GERD, especially if there is severe reflux esophagitis or a large hiatal hernia.[98,143,144] ARS is also a potential option for refractory GERD. In a randomized trial by Spechler et al., surgery was

significantly superior (67% vs. 28%, relative risk 2.38 [95% CI, 1.20 to 4.71]) to medical treatment in patients with refractory GERD.[145] ARS has also been used in the treatment of GERD with extraesophageal symptoms, although the symptom response has been poorer than in patients with typical symptoms.[146,147]

The preoperative workup before ARS should include pH-impedance testing to establish the presence of abnormal reflux and the relationship between reflux and symptoms.[98] If the patient has other objective signs of GERD, such as Los Angeles C or D esophagitis or Barrett's esophagus, the pH monitoring can be performed on PPIs.[98]

In refractory disease, EGD with biopsies should be performed before ARS to rule out other possible reasons for the symptoms. Of patients with suspected refractory GERD, eosinophilic esophagitis (EoE) has been seen in 2%–4%.[145,148] The EGD should be performed off PPIs to rule out EoE because the use of PPIs compromises the histologic diagnosis of EoE.[146]

2.4.4 Antireflux procedures

The original and most popular antireflux procedure is Nissen's fundoplication, introduced by Rudolf Nissen in 1956.[149] The first laparoscopic Nissen's fundoplication was performed in 1991.[150] The procedure has been modified by Nissen and other surgeons, and the contemporary version includes mobilization of the esophagus, closing the crura with sutures (hiatoplasty) and fundoplication, which involves passing the gastric fundus behind the esophagus and wrapping it around the distal esophagus with sutures.[151] The benefits of dividing the short gastric vessels are a matter of debate, and according to a meta-analysis by Markar et al., it does not affect the outcome whether the vessels are divided or not.[152] The tightness of the fundoplication wrap can be "calibrated" with a bougie, but its usefulness is not supported by the literature.[153]

Nissen fundoplication is a so-called "complete" or 360° fundoplication, and several partial fundoplications were introduced after it, such as the posterior 270° Toupet fundoplication and anterior 180° Dor fundoplication.[154,155] A recent guideline from a multi-society consensus conference suggests, based on 70 studies, that a partial fundoplication may be beneficial and provide equally effective symptom control when compared to a complete fundoplication.[156] A 2023 meta-analysis by Li et al. compared laparoscopic posterior Toupet fundoplication to Nissen fundoplication and found Toupet as effective as Nissen but with fewer complications.[157]

It is generally accepted that the esophagus should be mobilized before the fundoplication to achieve at least 2cm of abdominal esophagus without any tension. [158,159] It has been proposed that the inability to achieve this may be due to a short esophagus, which is thought to be a complication of GERD or paraesophageal hernia.[159] The literature related to the true short esophagus is controversial, and not all authors believe the entity exists.[160-162] An esophageal lengthening procedure (Collis gastroplasty) was introduced in 1957 to address the issue and is performed by many esophageal surgeons.[163,164] A recent prospective trial by Lugaresi et al. compared Collis gastroplasty to a stomach around stomach fundoplication in patients with esophagus deemed to be shortened intraoperatively and found no difference between the groups.[165] In the study, GEJ was assessed by intraoperative EGD and marked with clips.[165] Collis gastroplasty is associated with increased morbidity compared to fundoplication without it.[166]

Hill gastropexy, introduced in 1967, is another procedure for treating GERD.[167] Compared to Nissen's fundoplication, the method's outcomes have been equivalent.[168] The two repairs have been combined with good results.[169]

Other antireflux procedures include magnetic sphincter augmentation (MSA) with the LINX Reflux Management System, usually implanted either laparoscopically or robotically. A meta-analysis involving 1,211 patients found MSA safe and effective at one-year follow-up and comparable to Nissen's fundoplication.[170] The device was approved by the US Food and Drug Administration in 2012 but is not currently used in Finland. MSA has not been compared with Nissen's fundoplication in prospective trials.

Endoscopic antireflux procedures include transoral incisionless fundoplication (TIF), which a meta-analysis from 2018 found TIF to be inferior to fundoplication, and the ACG recommends it as a possible choice for patients who do not wish to undergo surgery.[98,171]

Roux-en-Y gastric bypass has also been utilized as an antireflux procedure, especially in the obese, and as a possible salvage operation after failed ARS.[172] Its efficacy, however, has been questioned in a recent population-based study by Lagergren et al. from Sweden, where 48.8% of the operated patients were back on antireflux medication two years following the operation. [173]

2.4.5 Paraesophageal hernia

Paraesophageal hernia is a herniation of abdominal organs to the chest through the esophageal hiatus of the diaphragm.[174] Hiatal hernias are classified into four types (Figure 3).[175] In type I, only the GEJ migrates through the hiatus to the chest (sliding hernia). In type II, the GEJ remains below the diaphragm, but the fundus

herniates (paraesophageal hernia). Type III (mixed hiatal hernia) combines types I and II, as both GEJ and the gastric fundus herniate in it. In type IV, organs other than the stomach, such as the transverse colon, are in the chest cavity. Types II, III, and IV are also commonly referred to as paraesophageal hernias, although only in type II does the herniated fundus lie "para esophageal," hence, next to the esophagus. Type II hernias are rare, and recent literature suggests that parahiatal hernia would be a more accurate term as the hernia enters the chest lateral to hiatus.[176] The term giant paraesophageal hernia is also used, but the definition varies, as some authors classify all type III and type IV hernias as giant paraesophageal hernias, whereas others refer to them as hernias where at least a third of the stomach is above the diaphragm.[177,178] Most hiatal hernias are type I, and of the paraesophageal hernias, type III is most common.[179] Hiatal hernias are usually acquired as the phrenoesophageal ligament weakens and the GEJ moves the cephalad (sliding hernias) or as the stomach herniates through the hiatus but stays fixed to the EGJ as the gastrocolic and gastrosplenic ligaments stretch.[180]

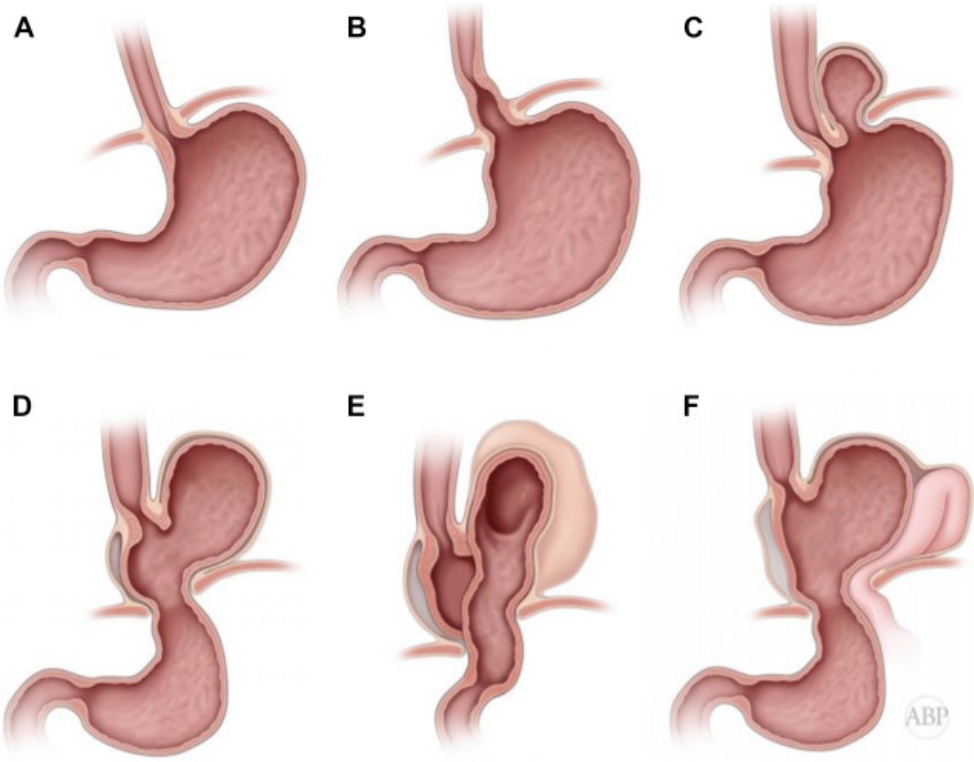

Figure 3 Types of hiatal hernias. A) Normal anatomy. B) Type I (sliding) hiatal hernia C) Type II "true"paraesophageal hernia. D-E) Type III (mixed) hiatal hernia F) Type IV paraesophageal hernia. From Thoracic Surgery Clinics, 2019-11-01, Volume 29, Issue 4, Pages 359-368, Copyright © 2019 Elsevier Inc. Reprinted with permission from Elsevier.

Paraesophageal hernias can be asymptomatic and found incidentally in studies done for other reasons. On the other hand, a paraesophageal hernia can present itself as a life-threatening gastric volvulus, resulting in ischemia and necrosis.[180] Type I hiatal hernias are related to GERD and can present as heartburn, regurgitation, or chest pain.[98] Paraesophageal hernias may manifest as substernal pain, difficulties eating, or shortness of breath.[181] Paraesophageal hernias can be associated with so-called Cameron lesions, which are erosions of the gastric mucosa at the level of the hiatus, which can cause bleeding and, hence, anemia.[182] The diagnosis of a paraesophageal hernia can be made by multiple methods, such as computed tomography (CT), endoscopy, or oral barium swallow fluroscopy.[183]

There are only a few studies on the natural course of paraesophageal hernias. In a single-center study from the Netherlands by Nijhuis et al., the mean follow-up was 64.0 ± 58.8 months, and the hernia-related mortality of conservatively treated patients was 1.6%, and 8.1% had hernia-related complications.[184]

Two guidelines on the topic include the Society of American Gastrointestinal and Endoscopic Surgeons (SAGES) published in 2013 and the European Association for Endoscopic Surgery (EAES) guidelines from 2023.[183,185] The SAGES guideline recommends repair of a type I hernia should be addressed as ARS and thus should not be repaired if they do not cause symptoms, and both guidelines attest to repair symptomatic paraesophageal hernias (type II, type III and type IV), but the SAGES guideline does not suggest repairing of asymptomatic paraesophageal hernias routinely, as EAES also recommends repair of asymptomatic hernias if the patient is not frail. A recently published Markov analysis by DeMeester et al. showed that elective repair of the paraesophageal hernia leads to increased life expectancy.[186] This contradicts the previous analysis of Stylopoulos et al. from 2002. [187] In a population-based study from Finland by Sihvo et al. from 2009 of deaths related to paraesophageal hernias, 13% (n=4) might have been prevented with elective intervention during the study period of 14 years.[9]

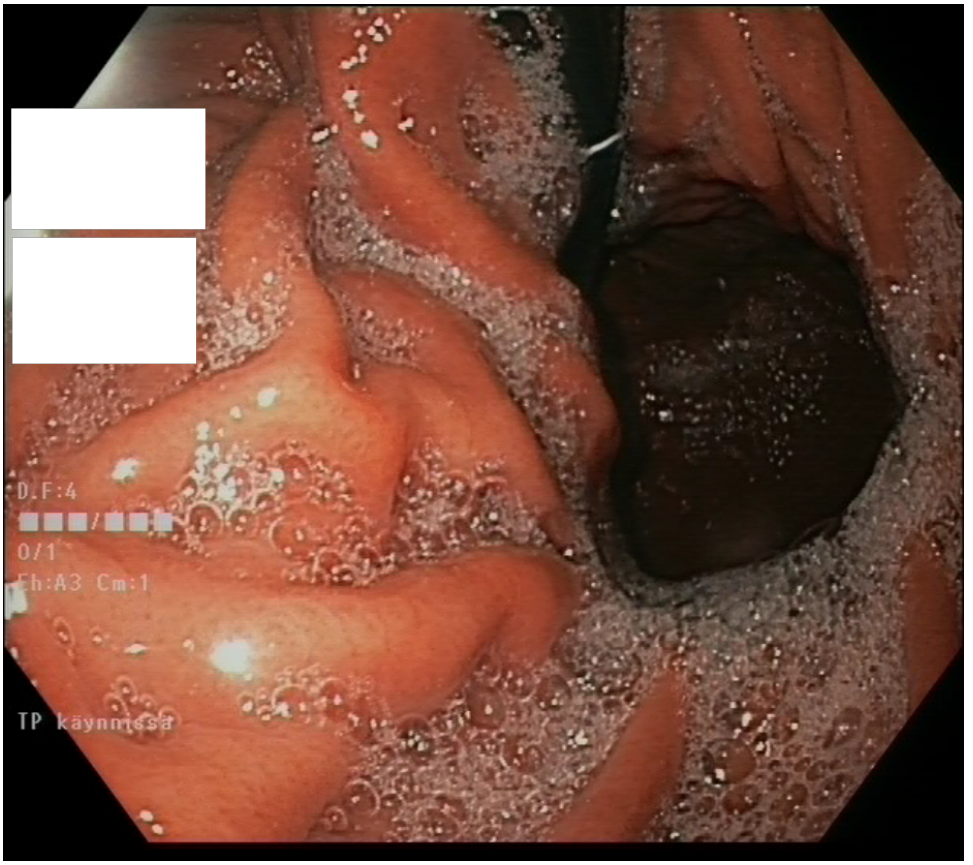

Figure 4 A large mixed (type III) paraesophageal hernia. Endoscopic view.1

As recommended by SAGES, the preoperative workup before paraesophageal repair consists of an EGD (Figure 4) and either a barium swallow or a CT scan.[183] Manometry of the pH impedance test may be difficult to perform in the setting of a large paraesophageal hernia; hence, those are not routinely recommended.[183]

2.4.6 Repair of paraesophageal hernia

The first hiatal hernia was operated on by Soresi in 1919.[150] Studies suggest that PEHR operations improve quality of life.[188-190]

PEHR overlaps with ARS, but it begins with the reduction of the hernia back to the abdomen, eversion of the hernia sac, and complete mobilization of the esophagus to the level of the inferior pulmonary veins.[191] Though the literature on the topic is limited and inconsistent, the operation is usually continued with a fundoplication to prevent recurrence and to anchor the stomach to the abdomen. A gastropexy is an option, especially in acute settings, such as incarceration of the stomach.[185,192,193] Like antireflux operations, paraesophageal hernias can be operated on openly and minimally invasively.[166] The paraesophageal hernia can also be approached via the chest, as in the Belsey Mark IV operation done from the left posterolateral thoracotomy.[150] Simultaneous sleeve gastrectomy and PEHR are further options for obese patients with paraesophageal hernias.[194]

Achieving tension-free repair of the hiatus is an essential goal in PEHR and has led to the development of several techniques.[195] The use of mesh to reinforce the hiatal closure is a matter of significant debate.[196] A recent meta-analysis by Angeramo et al. found no difference in recurrence rates after hiatoplasty with mesh or sutures.[197] A feared long-term complication after reinforcing the hiatoplasty with a mesh is the migration or erosion of the mesh to the esophagus or the stomach.[198] However, the EAES guideline gives a conditional recommendation to use mesh for hiatal repair.[185] Another technical option to minimize tension is to perform a diaphragmatic relaxing incision, which can be done right, left, or bilaterally and closed with a mesh.[199]

2.4.7 Complications of antireflux surgery and paraesophageal hernia repair

Mortality related to ARS and PEHR is low. The 90-day mortality after elective ARS was 0.13% in a population-based study from the Nordic countries published in 2021 which is comparable to an older national analysis from the USA, where inpatient mortality was 0.08%-0.21%.[200,201] In a retrospective single-center study of 662 patients, 30-day mortality after elective or urgent laparoscopic primary PEHR was 1.7%.[166] A national report from Finland published in 2008 found the 30-mortality rate after ARS or PEHR to be 1.0 per 1000 operations, 37% of which were open surgery.[202] Advanced age, obesity, and comorbidity have been related to an increased risk of mortality after PEHR.[166] A large retrospective single-center study on transthoracic PEHR reported 1.7% in-hospital mortality.[203] Gastric volvulus or incarceration of paraesophageal hernia are associated with high mortality, and thus mortality and morbidity after emergency PEHR are high compared to elective repair.[9,204,205]

The incidence of recurrent GERD-related symptoms after ARS is high.[206] In a population-based study from Sweden, 17.7% of patients needed antireflux medication or redo surgery after primary ARS.[207] However, in a study of 86 patients with GERD symptoms after Nissen fundoplication who underwent 24-hour esophageal pH monitoring, the result was abnormal in only 23% of the group.[208] Excellent long-term results of ARS have also been reported in a study by Neuvonen et al., where only 15.8% of patients had used antireflux medication 31 to 33 years after open Nissen fundoplication.[209]

The risk of reherniation after laparoscopic PEHR is reportedly 15.7%-42%.[166,189,190,210,211] The herniation is usually small and rarely affects the quality of life.[189,211] In a study of 165 patients after laparoscopic PEHR, the recurrence rate was 29.3.% (median follow-up time 39 months), but only 4.3% had > 5cm of the stomach above the diaphragm, and the recurrence did not affect quality of life.[190]

Serious complications related to ARS are rare. In a historical population-based study from Finland, the prevalence of life-threatening complications was 0.8% (n=43 of 5502 operations).[5] The potentially serious acute complications related to ARS and PEHR are reportedly esophageal or gastric perforations, bleeding, splenic injury, pneumothorax, perioperative reherniation, and cardiovascular adverse events.[5,166,202,207] In a large institutional retrospective study of 1,223 foregut operations, 1% (n=4 of 381) of the ARS and 1.8% of the primary PEHR (n=7 of 379) cases involved a perforation.[212] In a large national cohort study from the US, the incidence of perforations for ARS and PEHR was 0.04% and 0.7% respectively.[213]

Dysphagia is common, especially after laparoscopic ARS during the first weeks after the surgery.[202] In a historical prospective study, 16-54% of the patients had moderate to severe dysphagia one month after the operation, and 2-11% still had it three months after the operation.[214] The risk of dysphagia is reportedly higher after Nissen's fundoplication compared to partial fundoplications.[215] A meta-analysis by Du et al. based on eight randomized controlled trials found that laparoscopic Nissen fundoplication is related to more dysphagia than laparoscopic Toupet fundoplication, but the difference disappeared over time.[216] A recent meta-analysis comparing laparoscopic Nissen and Toupet fundoplications found that the risk of postoperative dysphagia was greater after Nissen fundoplication, both short-term and long-term.[157] Persistent dysphagia is a common cause of revisional surgery.[217]

Gas-bloat syndrome is common after ARS or PEHR and manifests as bloating, flatulence, and an inability to belch.[218-220] Studies are inconsistent, but a complete fundoplication may result in worse gas-bloat than partial fundoplications.[216,219] Postsurgical gastroparesis is a possible complication after ARS or PEHR as a consequence of a vagal nerve injury.[221,222]

Redoing ARS and PEHR is indicated in selective cases as it improves the quality of life.[223,224] According to a meta-analysis by Schlotmann et al. covering 2,095 operations, laparoscopic redo fundoplication reported major morbidity in 6% of operations.[225] However, redoing PEHR is a challenging operation and is associated with an elevated risk of perforations and other complications compared to primary surgery.[212]

2.5 DIVERTICULA OF THE ESOPHAGUS

Diverticulum is an outpouching of a hollow organ. Esophageal diverticula are classified based on their location in the esophagus: ZD is located near UES, traction diverticulum in the mid esophagus and an epiphrenic diverticulum above LES.[226,227]

2.5.1 Zenker's diverticulum

ZD is a so-called false diverticulum, which means it does not involve all layers of the esophageal wall, only the mucosa and submucosa.[228] ZD is located in the posterior part of the esophagus, where it outpouches through a triangular weak part in the wall of the hypopharynx between the lower inferior constrictor muscle and cricopharyngeus muscle (Killian's triangle).[229] The primary pathophysiological mechanism of ZD is hypothesized to be decreased compliance of the UES, which leads to its incomplete opening, leading to increased pressure in the hypopharynx.[17,226] ZD has also been associated with esophageal dysmotility and GERD, though the causality is unclear.[230,231] ZD is a rare disease typically diagnosed at an older age. In a recent population-based study from Finland by Uoti et al., the incidence of ZD was 2.9 per 100,000 person-years, and the median age of the patient population was 72.[232] ZD can be asymptomatic, especially if small, but it can cause dysphagia, regurgitation, hoarseness, cough, and malnutrition.[226] A squamous cell carcinoma can develop into the ZD, although the risk is small.[233] The diagnosis of ZD includes an esophagogram (Figure 5) and an EGD to verify or rule out malignancy, as patients are often elderly.

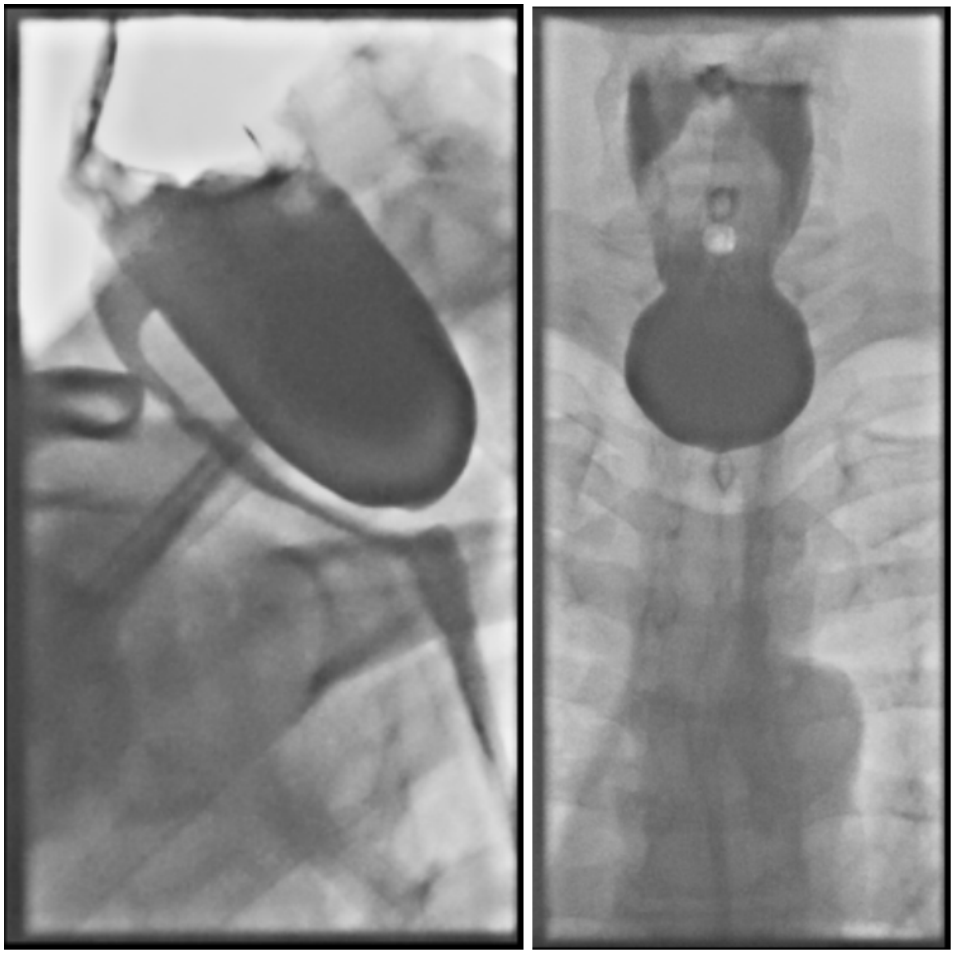

Figure 5 Zenker's diverticulum on an esophagogram.

2.5.2 Surgical treatment of Zenker's diverticulum

The treatment of ZD is surgical, adopting either an open, transoral, or endoscopic approach. These methods have not been compared directly in randomized trials. The open transcervical approach typically consists of cervicotomy, cricopharyngeal myotomy, and usually either diverticulectomy, diverticulopexy, or inversion of the pouch.[234,235] The cervicotomy incision is usually made on the left side of the neck along the anterior border of the sternocleidomastoid muscle, and

the choice between diverticulotomy and diverticulopexy is made based on the size of the diverticulum.[226]

The endoscopic procedure can be performed with a rigid endoscope or a flexible endoscope.[226] The rigid endoscopic procedure was introduced in 1917 by Mosher and popularized by Dohlman et al. in 1960. It includes the division of the common wall of the esophagus and the diverticulum and, hence, the division of the cricopharyngeus muscle.[236,237] The division can be performed with electrocautery, stapling devices, or a laser.[238,239] The flexible endoscopic procedure was introduced in 1995 and involves the division of the common wall, originally with electrocautery.[240,241] POEM has also been successfully used to treat ZD.[37,242]

The size of the diverticulum and patient characteristics direct the choice between open and endoscopic procedures. The rigid endoscopic approach presupposes a pouch being aligned against the posterior wall of the esophagus, sufficient jaw opening, and neck extension; hence, it is not an option for all patients.[243] Also, diverticula less than 2cm long and thus considered small are usually treated endoscopically.[244] In a meta-analysis of 11 studies by Albers et al., the endoscopic procedure for ZD was associated with a shorter length of stay and a lower complication rate, but there were more symptom recurrences compared to the open approach.[245]

2.5.3 Complications of surgery for Zenker's diverticulum

The recurrence of symptoms after the treatment of ZD is not infrequent. In a systematic review by Verdonck et al., the risk of recurrence was 4.2%–18.4%.[246] According to the literature, the recurrence rate of ZD is higher after endoscopic treatment than after open treatment.[245-247] Performing the cricopharyngeal myotomy may prevent recurrences.[248]

In a meta-analysis by Crawley et al. on adverse events of endoscopic treatment for ZD, the overall perioperative mortality after rigid and flexible endoscopic procedures was 0.3% and 0.2%, respectively.[247] Reported complications in the studies were infection, mediastinitis, abscess formation, bleeding, and subcutaneous or mediastinal emphysema.[247] In the aforementioned meta-analysis by Albers et al., the main complications were cervical leak, aspiration pneumonia, perforation, chest pain, and hoarseness.[245] The systematic review by Verdonck et al. reported that mediastinitis and emphysema were more often related to endoscopic approach, fistula formation, and hematoma to open approach.[246] The risk of recurrent nerve injury is higher after the open approach.[246]

2.5.4 Epiphrenic diverticulum

The other diverticula of the esophagus are very rare and linked to motility disorders of the esophagus (Figure 6).[227] They can be treated surgically, either with a transthoracic or transabdominal approach or with POEM.[227,249,250] In a systematic review by Zaninotto et al., mortality after operative treatment was 4.0%–9.0%, and the most common complication was leakage.[251]

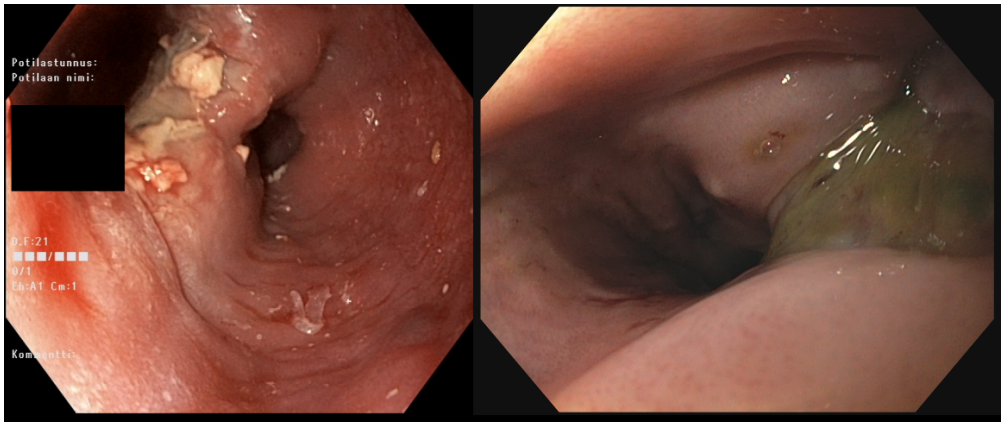

Figure 6 A large epiphrenic diverticulum of the esophagus and a fistula after the treatment.

2.6 MOTILITY DISORDERS OF THE ESOPHAGUS

The most common and best-defined motility disorder of the esophagus is achalasia, with a prevalence of 10.82–32.58/100,000 in the North American population.[252,253] Idiopathic achalasia results from a loss of inhibitory cells in the myenteric plexus for an unknown reason, leading to the inability of the LES to relax and concomitant aperistalsis of the body of the esophagus.[254] An autoimmune etiology of the disease has been hypothesized.[255] The most common symptoms include dysphagia, regurgitation, heartburn, and chest pain.[256] HMR is the golden standard diagnostic test for achalasia, but an EGD should be performed to rule out malignancy (pseudoachalasia).[257,258] Based on findings on HMR, achalasia is divided into three types, which also guide the choice of therapy.[259,260]

The achalasia can be treated with graded pneumatic dilatation, Heller myotomy, or POEM.[257,258] Botulinum toxin injections can be used as a treatment for patients who cannot tolerate more invasive procedures.[258] Heller myotomy, usually combined with a fundoplication as an antireflux procedure, was described by Heller in 1914 and is usually performed laparoscopically or with robot assistance.[261,262] The procedure currently includes the cutting of LES muscle fibers from the anterior side.[263] The success rates of Heller myotomy and POEM are high.[264,265]

The rate of complications and mortality related to laparoscopic Heller myotomy is low.[266] In a systematic review by Lynch et al., the most common major complication after laparoscopic Heller myotomy and pneumatic dilatation was the esophageal perforation, rate of which was 2.0% and 0.37%, respectively.[267] A systematic review by Van Hoeji et al. reported the rate of perforations to be 1.0%–9.3% after pneumatic dilatation, most of which occurred in the initial dilatation, where a 35mm balloon was associated with high risk.[268]

Other motility disorders of the esophagus are rare.[269] They include esophagogastric junction outflow obstruction and spastic and hypomotile disorders of the esophageal peristalsis.[270] The diagnosis is made with HMR, and the diseases are classified based on the Chicago classification.[271] Studies related to the natural course of these diseases are limited, but the progression of spastic diseases to achalasia has been reported, although it is uncommon.[272]

2.7 ESOPHAGECTOMY FOR BENIGN DISEASE

Esophagectomy is indicated for benign conditions on rare occasions, such as spontaneous esophageal rupture (Boerhaave syndrome, Figure 7) when other treatment options fail or are not feasible, or as the last option in chronic conditions, such as achalasia, or as a salvage antireflux operation.[273] Many esophagectomies for benign disease are performed as emergency operations, and the procedure is related to high morbidity.[274] Nevertheless, according to a recent registry study by Worrell et al. consisting of 1,521 esophagectomies for benign indications compared to a propensity-matched group of esophagectomies with malign indications, the benign group had more open surgery and complications, even in the elective setting. [275] In a retrospective register study by Chang et al., early mortality after esophagectomy for recurrent GERD or hiatal hernia was 2%.[273]

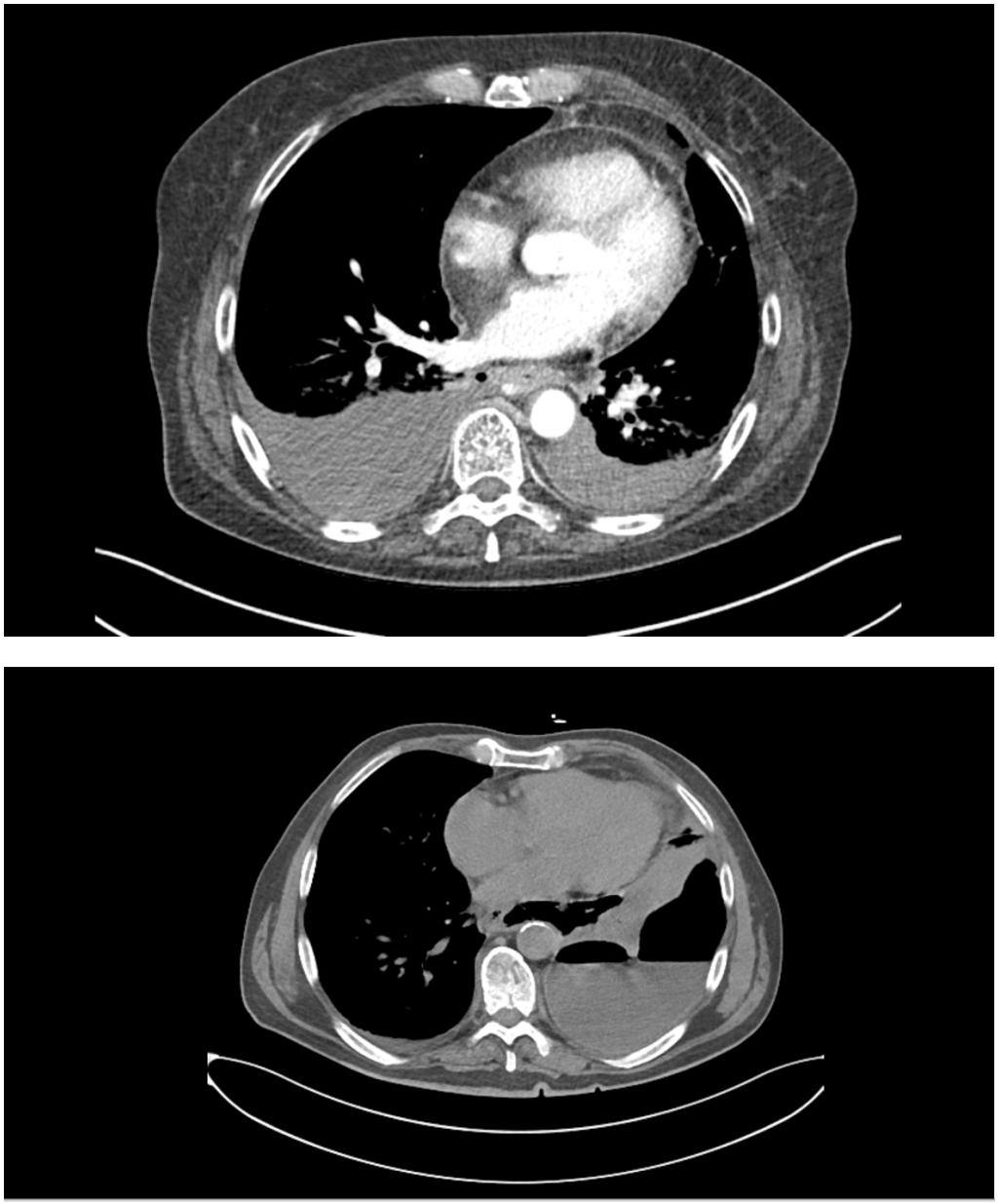

Figure 7 Spontaneous esophageal perforations on CT.

3 AIMS OF THE STUDY

The aim of this thesis was to analyze complications and medical errors associated with upper gastrointestinal endoscopy and surgery for common benign esophageal diseases and hiatal hernias at the national level. The specific aims of the studies involved were as follows:

I. To investigate the rate of complications and malpractice claims after both open and endoscopic repair of Zenker's diverticulum in the national comprehensive care registry and to determine the associations between patient characteristics, comorbidities, and treatment outcomes.
II. To analyze the mortality, morbidity, and malpractice claims after antireflux surgery and paraesophageal hernia repair and the associations of patient and procedure characteristics with the outcomes.
III. To analyze the trends in endoscopic activity, mortality, morbidity, and malpractice claims after EGD and EGD interventional procedures, excluding ERCP.

4 PATIENTS AND METHODS

4.1 PATIENTS

4.1.1.1 Study I

From 1996 to 2015, 2,736 patients with ZD were identified from the Care Register of Finland. Of these, 1,044 (38.2%) were operatively treated. The median age of the patients was 70.0, and 39.8% (n=416) were women. Using ICD-10 and NOMESCO (The Nordic Medico-Statistical Committee) coding systems, complications were identified and classified according to the Clavien-Dindo classification (CDC) of postoperative complications.[276] Adverse events occurring during the perioperative inpatient stay and up to 30 days after the operation were included, except for damage of recurring laryngeal nerve, which was listed as a complication even if more time had passed since the initial surgery.

Nine resolved patient injury claims concerning the treatment of ZD were identified for the period 2010 to 2020. The mean age of these patients was 72.9 (SD ±11.8), and 55.6% (n=5) of the group were female. Of the patients, 44.4% (n=4) had CCI 0, 33.8% had CCI 1, and 22.2% (n=2) had CCI that was 2 or greater.

4.1.1.2 Study II

As a baseline cohort, we obtained data regarding all ARS and PEHR operations in Finland from the Finnish Care Register from 2010 to 2018. A total of 5734 operations were done during the study period. Of primary operations, 79.9% (n=4384) were ARS and 20.1% (n=1101) PEHR. 1.7% (n=92) of the primary operations were coded to be both ARS and PEHR. Multiple ARS or PEHR operations were done on 341 (5.9%) of the patients. The mean age of the patients was 54.9 ± 14.7 SD years, and 59.3% (n=3402) were women. Of the patients,

58.6% (n=3160) had a CCI score of 0, 34.6% had a CCI score of 1-2, and 6.8% (n=367) had a CCI score of ≥ 3.

Then we collected data on patient injury claims from the PIC database related to ARS and PEHR. A total of 61 claims were identified. One claim was excluded because a Heller myotomy was also done during the operation. The mean age of the patient population was 57.2 years (SD = 12.4, rage32–82 years), and 65.0% (n=39) were women.

4.1.1.3 Study III

We collected a population-based cohort of all upper GI endoscopies performed in Finland from 2010 to 2018 to estimate the annual volume of the procedures. Data was collected from the national Care Register according to NOMESCO codes related to upper endoscopies, covering 409,153 procedures performed on 298,082 individual patients. Of these, 53.2% (n=22,361) were female, and the mean age of this patient population was 61.2 (SD=16.6) years.

Additionally, 85 claims regarding upper endoscopies performed on adults were identified from the PIC database, two of which were excluded in further analysis, one because the index endoscopy had occurred before the timeframe of the study and the other because it was related to fundoplication rather than an upper endoscopy. The median age of these patients was 64.1 (IQR 19, range 30-92 years).

4.2 CARE REGISTER AND CAUSES OF DEATH REGISTER

The Finnish Institute for Health and Welfare holds a national Care Register detailing the care given in Finland. The register was established in 1969 and was previously referred to as the Finnish Hospital Discharge Register. All hospitals must report given care to the institute annually; thus, the register contains all inpatient hospital discharges linked to the personal identification codes.[277] According to a systematic review by Sund, the positive predictive value for common diagnoses ranged from 75% to 95%.[277]

Statistics Finland has held a national registry of causes of death in Finland since 1936.[278] The data is published annually and has been coded with the ICD-10 since 1996.

4.3 PATIENT INJURY CLAIMS

Data concerning malpractice in studies I, II, and III was obtained from the Finnish Patient Injury Centre (PIC). The PIC is a national institution established in 1987 that processes all claims filed concerning healthcare, deems whether an injury is compensable, and pays the compensation.[279] Duties of PIC and criteria for compensation are described in the Patient Injury Act (948/2019), according to which all care providers are also obliged to have patient insurance.[8] The PIC holds a database of claims, their outcomes, and the associated patient records.[280] The commonest criterion for compensability is the preventability rule, which states that an experienced physician would have avoided the injury by acting differently.[279] The criteria are applied by PIC expert physicians case-by-case.[8]

The PIC In Finland Is a so-called no-fault system similar to systems in other Nordic countries.[8] The purpose of a non-fault system is to ascertain why an injury occurred instead of deciding who is to blame for it, foster safety, and encourage healthcare providers to report adverse events. The system is patient-driven: The process starts when a patient files a claim. The timeframe for filing is three years after the patient first noticed the injury. Filing a claim is free for the patient.

In a study published in 2023 involving the PIC register about claims made after any kind of surgery, the claims rate was six per 1,000 procedures, and it decreased during the study period.[8]

4.4 CLAVIEN-DINDO CLASSIFICATION OF POSTOPERATIVE COMPLICATIONS AND THE COMPREHENSIVE COMPLICATION INDEX

We used the Clavien-Dindo classification of postoperative complications to classify the complications observed in studies I, II, and III, and a Comprehensive Complication Index was calculated for each patient. The CDC, introduced in 1992 and updated in 2004 with subcategories, is a widespread system used to evaluate surgical complications in a structured manner.[22,276] The classification has been validated in research on complications after a broad range of surgical specialties and procedures.[281-287]

The CDC is based on the corrective efforts needed to address the complications. The classification has seven grades and uses the suffix “d” to represent disability or long-lasting (over six months) symptoms caused by a complication. The list of grades, including definitions, is presented in Table 1.

The 2013 presented Comprehensive Complication Index is a tool based on the CDC that considers all complications the patient has experienced after the procedure to better estimate the morbidity caused by complications.[287] The index's formula is a sum that considers the severity of the complications by weighing them using coefficients. The result is a scale from 0 – 100, where 0 stands for no complications and 100 indicates the death of a patient. The Comprehensive Complication Index correlates more strongly with treatment costs and more strongly than the highest CDC-graded complication.[288] The Comprehensive Complication Index has been validated in several patient populations and specialties.[289-292]

Neither the CDC nor the Comprehensive Complication Index have been directly validated after surgery for benign esophageal diseases, but both have been used in studies on the topic.[293-295]

Table 1 Modified Clavien-Dindo Classification of postoperative complications.

Grade I	Any deviation from the normal postoperative course that did not need interventions or pharmacological treatment. Antipyretic, antiemetic, diuretics, electrolytes, diuretics, and physiotherapy are allowed. Wound infections treated bedside
Grade II	Blood transfusions Total parenteral nutrition Pharmacological treatment other than allowed in grade I
Grade IIIa	Intervention, no general anesthesia
Grade IIIb	Intervention under general anesthesia
Grade IVa	Single-organ dysfunction (treated in ICU)
Grade IVb	Multiorgan dysfunction
Grade V	Death of a patient

4.5 STATISTICAL ANALYSIS

Studies I, II, and III used SPSS statistics version 27.0.2.0 (IBM Corp, Armonk, NY, USA) and SAS version 9.2 (SAS Institute, Cary, NJ, USA). A chi-square test or a Fischer exact test was used when applicable to compare results with categorical variables. A Student's t-test was used when comparing continuous variables, and the Mann-Whitney U-test was used to compare non-parametric continuous variables. To measure the effect side, Cohen's *d* was used to measure the effect

size. The Welch and Games-Howell post hoc tests were applied in cases where equal variances were assumed. Cramer V was used to measure associations. A logistic regression was used to investigate the association of conditions that could be associated with the outcomes. Two-tailed p-values <0.05 were considered statistically significant.

4.6 ETHICAL CONSIDERATIONS

Studies I, II, and III were approved by PIC on April 20, 2021. All studies were approved by THL and Statistics Finland (THL/1469/5.03.00/2016, THL/164/14.02.00/2021 and TK/923/07.03.00/2022). Because of the retrospective nature of the studies, no approval from the ethics committee was warranted.

5 RESULTS

5.1 STUDY I

Of all patients who underwent primary surgery for ZD during the study period, 67 (6.4%) had complications, 54 of which were postoperative and nine intraoperative. The 30-day mortality was 0.9% (n=9). The median length of stay was 3.0 days (range, 0-85.0) after the primary operation but 8.0 days (range, 0-85.0) among the patients with complications. Patients with complications were older (3.39 years, 95% CI 0.072 - 0.212) than those without. The existence of preoperative comorbidity was not associated with complications. Patient characteristics, operative details, and associations with outcomes are presented in Table 2.

Table 2 Association Between Demographic Characteristics, Comorbidity, Operative Approach, and Operative Specialty and Various Outcomes. Reproduced with permission from JAMA Network Journals of the American Medical Association. Uoti S., et al. Postoperative Complications and Reoperative Surgery in the Treatment of Patients with Zenker Diverticulum. JAMA Otolaryngol Head Neck Surg. 2023;149(8):690–696. Copyright © 2023, American Medical Association. All rights reserved.

Variable	Total No.	Compli-cation, No. (%)	Comprehensive complication index score, mean (SD)	Length of stay, *B*[a] (95% CI)
Age, y				
18-49	55	3 (5.5)	21.2 (17.7)	1 [Reference]
50-59	151	7 (4.6)	30.8 (12.8)	0.98 (−0.83 to 2.79)
60-69	285	17 (6.0)	29.2 (8.3)	0.74 (−0.96 to 2.43)
70-79	334	17 (5.1)	43.3 (27.1)	0.90 (−0.78 to 2.57)
80-89	198	18 (9.1)	47.0 (36.2)	1.46 (−0.30 to 3.21)
≥90	21	5 (23.8)	57.7 (39.0)	4.85 (1.90 to 7.80)
Sex				
Female	416	29 (7.0)	39.2 (27.9)	1 [Reference]
Male	628	38 (6.1)	41.5 (28.8)	−0.57 (−1.3 to 0.16)
Charlson Comorbidity Index score				
0	606	38 (6.3)	36.3 (23.0)	1 [Reference]
1	193	7 (3.6)	25.5 (13.5)	−0.22 (−1.17 to 0.74)
2	140	14 (10)	53.2 (37.5)	−0.57 (−1.65 to 0.52)
≥3	105	8 (7.6)	51.0 (34.7)	−0.35 (−1.57 to 0.88)
Operative approach				
Mixed endoscopic	550	23 (4.2)	46.3 (33.0)	1 [Reference]
Transcervical	241	30 (12.4)	41.8 (28.7)	3.70 (2.85 to 4.56)
Transoral stapling	253	14 (5.5)	26.7 (6.7)	−0.72 (−1.56 to 0.12)
Operative specialty				
Otorhinolaryngology	759	32 (4.2)	34.5 (24.9)	1 [Reference]
Thoracic surgery	109	16 (14.7)	43.1 (26.7)	3.94 (2.80 to 5.08)
Gastroenterological surgery	68	7 (10.3)	21.1 (12.5)	1.09 (−0.32 to 2.50)
General surgery	104	11 (10.6)	52.8 (33.0)	3.92 (2.75 to 5.08)
Gastroenterology	4	1 (25)	100	−0.84 (−6.42 to 4.75)

As indicated in a previously published study of the same data, of all patients, 227 (21.7%) had two or more operations to treat ZD during the study period.[232] The patients with a complication after the primary operation were less likely to need a reoperation because of a recurrence of ZD (9.0%, n=6). From the data, the incidence of complications after a redo ZD operation could not be estimated.

Of the patient injury claims, all dealt with at least one complication, and 55.6% (n=5) included more than one complication. None of the claims included a complication that resulted in the death of the claimant. Classified via CDC by the index complication, 5 (55.6%) of patients had grade 2, one (11.1%) had grade 3a, two (22.2%) had grade 3b, and one (11.1%) had grade 4a. The median comprehensive complication index was 20.9 (IQR 31.4, range 20.9–76.8). Of the claims, six (66.7%) had been deemed compensable by PIC. Of the claims, seven (77.7%) included a complication that required at least one reoperation. Of the index complications observed, seven (77.8%) were leakages. Two (22.2%) of all claims included a recurring laryngeal nerve injury.

5.2 STUDY II

Of all ARS and PEHR operations, 7.5% (n=432) were open surgery and 92.5% (n=5302) were laparoscopic surgery. Of the patients involved, 5.9% had several ARS or PEHR operations during the study period. Of all operations, 0.56% (n = 30) were converted from laparoscopic to open.

The total number of primary ARS or PEHR operations during the study period was 5,393 (94.1%), and for statistical accuracy, only index operations were used in comparative analyses. The annual trends are presented in Figure 8.

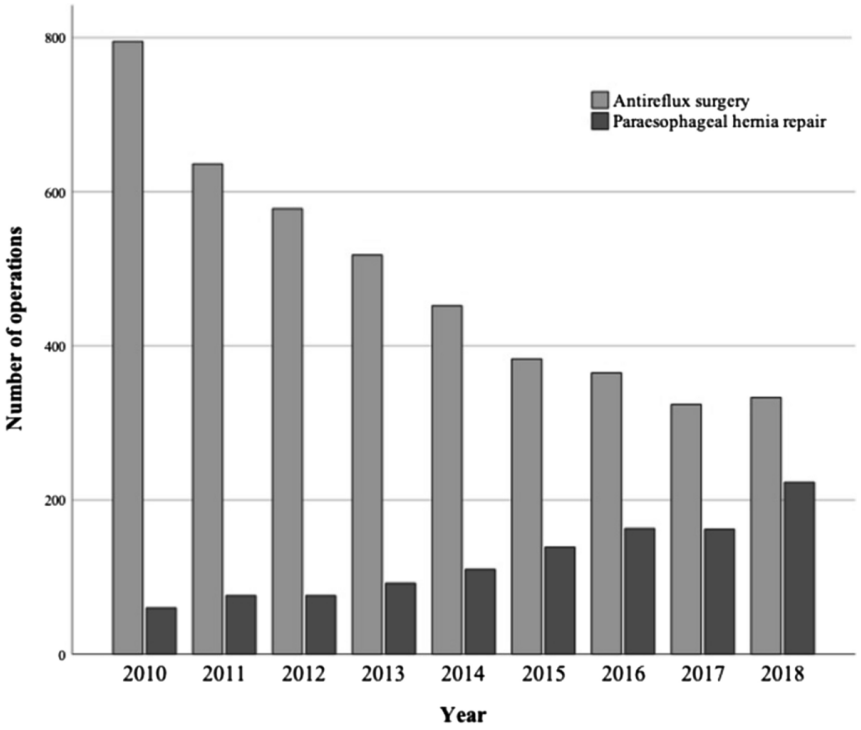

Figure 8 Trends in antireflux surgery and paraesophageal hernia repair in Finland from 2010 to 2018. Adapted from Nurminen et al. Malpractice claims after antireflux surgery and paraesophageal hernia repair: a population-based analysis. Surg Endosc (2023). https://doi.org/10.1007/s00464-023-10572-2

The 30-day and 90-day overall mortality rates of ARS were 0.23% (n=10) and 0.27% (n=12), respectively, and 1.36% (n=15) and 2.1 % (n=23) of PEHR, respectively. Of those whose operation was coded as PEHR, 12.8% (n=200) had a diagnosis related to incarceration or necrosis of a hiatal hernia (ICD-10 codes K44.0 and K44.1). We ran a logistic regression analysis of preoperative factors and found that older age, CCI over 3, and open surgery were related to higher mortality.

Of the patient injury claims, 50.0% (n=30) did not have hiatal hernia or had type 1 hiatal hernia and were coded ARS. Of the others, 50.0% (n=30) of the claims concerned patients with type 3 or type 4 hiatal hernias and were coded PEHR. None had type 2 hiatal hernias. The characteristics of the operations are described in Table 3. Collis gastroplasty was not performed during any of the operations.

Table 3 Perioperative characteristics of patients concerning patient injury claims resolved in the period 2010–2020 in the Finnish Patient Insurance Centre database. Adapted from Nurminen et al. Malpractice claims after antireflux surgery and paraesophageal hernia repair: a population-based analysis. Surg Endosc (2023). https://doi.org/10.1007/s00464-023-10572-2

	AS n = 30 Mean ± SD or % (n)		PEHR n = 30 Mean ± SD or % (n)		*p*
Hospital					0.110
Academic	27	(8)	50	(15)	
Other	73	(22)	50	(15)	
Hospital volume*					0.002
< 8	17	(5)	3	(1)	
8–20	10	(3)	27	(8)	
> 20	50	(15)	70	(21)	
Unknown	23	(7)	0	(0)	
Surgical approach					0.319
Laparoscopic	90	(27)	87	(26)	
Laparotomy	10	(3)	3	(1)	
Thoracotomy	0	(0)	10	(3)	
Intraoperative conversion	10	(3)	13	(4)	
Fundoplication type					0.409
Nissen	93	(28)	80	(24)	
Partial fundoplication	3	(1)	13	(4)	
None or gastropexy	3	(1)	7	(2)	
Hiatal mesh repair	0	(0)	20	(6)	0.024
Reoperation	23	(7)	13	(4)	0.506
Urgent surgery	0	(0)	7	(2)	0.492

ARS = Antireflux surgery
PEHR = Paraesophageal hernia repair
* = Annual volume of ARS and PEHR operations in a hospital

One of the claims dealt with an injury that involved the death of the patient (1.7%). A complication was identified in 93.3% (n=56) of the claims, and 61.7% (n=37) had several complications. Four claims did not include any complications, but the patients had residual symptoms or were unhappy with how they were treated. Of the claims, 36.7% (n=22) were compensated. A detailed summary of the complications is presented in Table 4.

Table 4 Summary of adverse events of ptients concerning patient injuy claims resolved in the period 2010–2020 in the Finnish Patient Insurance Centre database. Adapted from Nurminen et al. Malpractice claims after antireflux surgery and paraesophageal hernia repair: a population-based analysis. Surg Endosc (2023). https://doi.org/10.1007/s00464-023-10572-2

	AS n = 30 Mean ± SD or % (n)		PEHR n = 30 Mean ± SD or % (n)		*p*
Perforation	23	(7)	33	(10)	0.567
Esophageal	3	(1)	23	(7)	0.052
Gastric	13	(4)	7	(2)	0.067
Intestinal	10	(3)	3	(1)	0.061
Re-herniation	17	(5)	27	(8)	0.532
Early*	13	(4)	13	(4)	
Late	3	(1)	13	(4)	
Dysphagia	23	(7)	10	(3)	0.299
Bleeding	10	(3)	3	(1)	0.612
Splenectomy	7	(2)	0	(0)	0.492
Vagal nerve injury	7	(2)	3	(1)	1.000
Loss of esophageal continuity	0	(0)	7	(2)	0.492
Long-term disability**	17	(5)	17	(5)	1.000
No identified complications	10	(3)	3	(1)	0.612

ARS = Antireflux surgery
PEHR = Paraesophageal hernia repair
* = Re-herniation that occurred in the hospital or within 30 days of the index operation
** = Severe symptoms lasting over six months

All the complications in the claims were classified using the CDC system, and the Comprehensive Complication Index was calculated for patients. The mean Comprehensive Complication Index for the patients was 41.8 SD ± 21.2. Of patients within the ARS group, the mean Comprehensive Complication Index was 35.9 ±20.7 and 47.6 ±20.8 (p =.033) for patients in the PEHR group. The highest CDC grade was I for 3.3% (n=2) patients, II for 13.3% (n=8) patients, IIa for 3.3%

(n=2), IIIb for 46.7% (n=28), IVa for 20.0% (n=12), IVb for 4.9% (n=3), and V for 1.7% (n=1). Because of complications, reoperation was required for 65% (n=39) of the patients, and 16.7.% (n=10) had long-term disability (more than six months) resulting from the complications.

5.3 STUDY III

For further analysis, we divided the upper endoscopy procedures into five subgroups: diagnostic, interventional esophageal, PEG insertion, interventional gastric, and ligation of esophageal varices. The rate of procedures and the number of patients are presented in Table 5, and the distribution of NOMESCO codes is shown in Table 6. During our study time, the annual upper gastrointestinal activity increased from 42,108 procedures in 2010 to 51,341 in 2018. This shift was due to an increase in diagnostic endoscopies. Annual rates of procedures per year are presented in Figure 9.

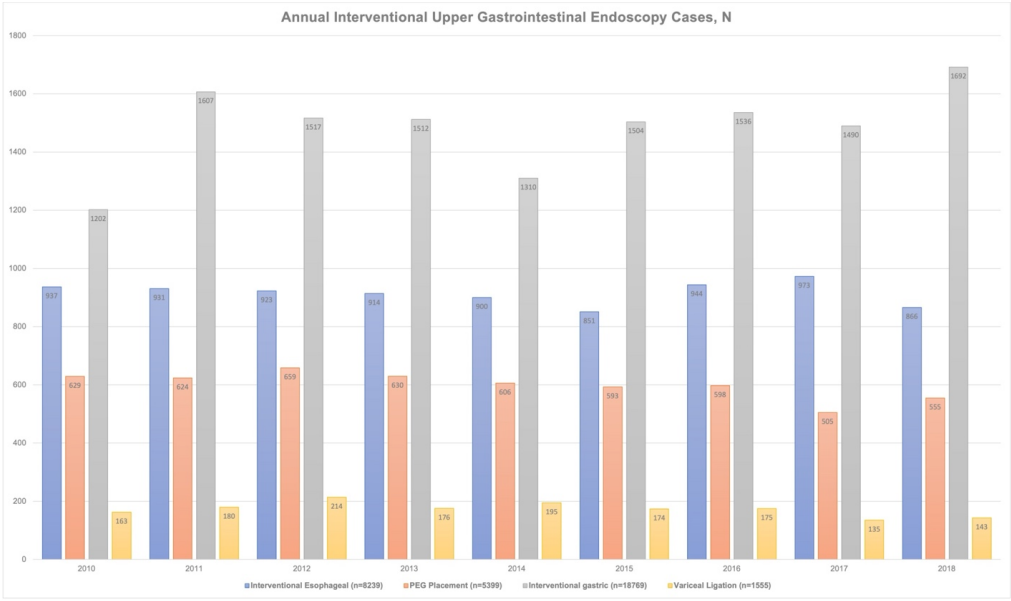

Figure 9 Annual case trends of interventional upper gastrointestinal endoscopies between 2010 and 2018, divided by the type of intervention.

Table 5 The rate of upper endoscopies in Finland by type and number of patients

Group	Rate of Procedures n (%)	Number of patients n (%)
Diagnostic	380,590 (93.0)	287,036 (96.3)
Interventional esophageal	8,239 (2.0)	4,878 (1.6)
PEG Insertions	5,399 (1.3)	4,706 (1.6)
Interventional gastric	13,370 (3.3)	8,076 (2.7)
Variceal ligation	1,555 (0.4)	1,088 (0.4)
Total	409,153 (100)	298,082 (100)

Table 6 The Nordic Medico-Statistical Committees (NOMESCO) Classification of Surgical Procedure Codes used in identifying procedures and claims related to upper gastrointestinal endoscopies in 2010-2020 in Finland.

Diagnostic procedure	
UJD10	Esophagoscopy, gastroscopy and duodenoscopy
UJC02	Rigid esophagoscopy
UJC12	Flexible esophagoscopy
UJD02	Gastroscopy
Interventional Esophageal	
JCA08	Endoscopic removal of foreign body from esophagus
JCA42	Other endoscopic procedure for hemostasis; esophagus
JCA45	Endoscopic mucosal or submucosal resection in esophagus
JCA52	Other endoscopic procedure using diathermy or heat in esophagus
JCA55	Endoscopic dilatation of esophagus
JCA98	Other local endoscopic operation on esophagus
JCF12	Endoscopic insertion of prosthetic tube into esophagus
Percutaneous Gastrostomy	
JDB10	Percutaneous gastrostomy
Interventional Gastric	
JDA05	Endoscopic polypectomy in stomach or pylorus
JDA08	Endoscopic removal of foreign body from stomach or pylorus
JDA12	Endoscopic insertion of gastric stent
JDA22	Endoscopic ligature of varices of stomach
JDA32	Endoscopic injection in stomach or pylorus
JDA35	Endoscopic contact coagulation in stomach or pylorus
JDA38	Endoscopic laser therapy in stomach or pylorus
JDA42	Other endoscopic hemostatic procedure in stomach or pylorus
JDA45	Endoscopic mucosal or submucosal resection in stomach or pylorus
JDA52	Other endoscopic procedure using diathermy or heat in stomach or pylorus
JDA55	Endoscopic dilatation of stomach, pylorus, or anastomosis of stomach
JDW98	Other transluminal endoscopic operation on stomach or duodenum

Variceal Ligation	
JCA20	Ligature of esophageal varices
JCA22	Endoscopic ligature of esophageal varices
JCA32	Endoscopic injection in esophagus for varices
JCA35	Endoscopic contact coagulation in esophagus
JCA38	Endoscopic laser therapy in esophagus for varices

In our study, 30-day and 90-day all-cause mortality were 1.70% (n=7133) and 3.84% (16.106), respectively. During the study period, 30-day mortality decreased from 2.14% (n=900) to 1.41% (n=721), and 90-day mortality decreased from 4.76% (n=2003) to 3.34% (n=1714). Of all patients, 611 (n=0.002) were excluded from the analysis of mortality rates because they were lost in follow-up. We calculated the mortality rates according to the first EGD for patients who underwent multiple endoscopies during our study period. The 30-day mortality rates of the various procedure groups are presented in Figure 10.

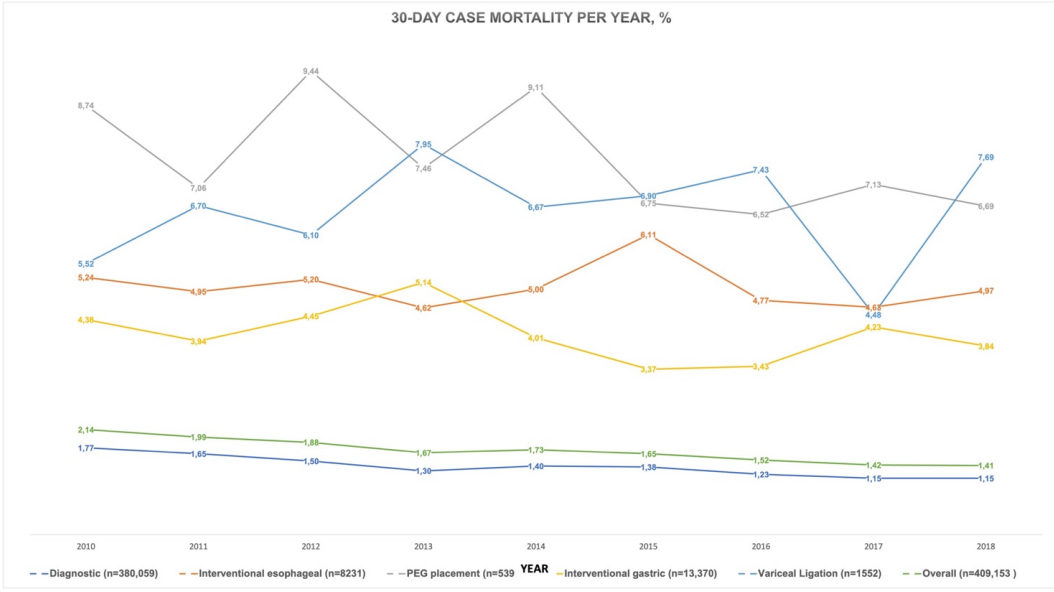

Figure 10 Annual trends for 30-day mortality in upper gastrointestinal endoscopies between 2010 and 2018, categorized by procedure type.

Of the patients who died within 30 days after the endoscopy, the cause of death was a perforation during an endoscopy for two (0.03%) patients. For the rest, the most common causes of death were malignancy (n=3198, 44.95%), benign gastrointestinal (n=1533, 21.55%), and cardiovascular (n=1448, 20.36%).

During 2010–2020, the patient injury claims were divided as follows: 53.7% (n=44) concerned diagnostic EGD, 19.5% (n=16) esophageal dilatation, 11.0% (n=9) PEG placement, 3.7% (n=3) esophageal stent placement, and 2.4% (n=2) foreign body removals. Of the procedures, 42.7% (n=35) were performed under sedation or general anesthesia. The characteristics of the patients and procedures within the claims are described in Table 7. The incidence of claims was 0.23/1000 patients who underwent upper endoscopy during 2010–2018.

Of the claims, 26.5% (n=21) were deemed to be compensated. The claims that dealt with a diagnostic EGD were compensated more often than interventional (29.5%, n=13 and 21.1% n=8, respectively), but the difference was not statistically significant (p= .452).

The root complication was perforation in 36.9% (n=31), dental injury in 14.3% (n=12), and bleeding in 10.7% (n=9). The perforations were mostly of the esophagus (n=25), with five duodenal and two gastric perforations. The claims are categorized according to the root complications in Table 8.

Table 7 Patient and procedure characteristics of claims related to upper gastrointestinal endoscopies 2010-2020 in Finland.

		Diagnostic n=44 Median [IQR] or % (n)		Interventional n=38 Median [IQR] or % (n)		*p*
Age		67.0	[18]	62.5	[20]	.494
Sex						.280
	Male	43.2	(19)	31.6	(12)	
	Female	56.8	(25)	68.4	(26)	
Charlson Comorbidity Index						.383
	0	54.5	(24)	47.4	(18)	
	1	25.0	(11)	15.8	(6)	
	2	11.4	(5)	18.4	(7)	
	3 ≤	9.1	(4)	18.4	(7)	
Hospital						.001
	Non-academic	50.0	(22)	63.2	(24)	
	Academic	18.2	(8)	36.8	(14)	
	Other	31.8	(14)	0	(0.0)	
Procedural sedation		9.1	(4)	81.6	(31)	.001

Table 8 Adverse events of claims related to upper gastrointestinal endoscopies 2010–2020 in Finland.

	Diagnostic n=44 Median [IQR] or % (n)		Interventional n=42 Median [IQR] or % (n)		*p*
Adverse events					
Perforation	16.7	(7)	57.1	(24)	.001
Dental	23.8	(10)	4.8	(2)	.026
Bleeding	11.9	(5)	9.5	(4)	1.00
Neurologic	9.5	(4)	0	(0)	.116
Infection	0	(0)	4.8	(2)	.494
Delay in diagnosis	7.1	(3)	0	(0)	.241
Pancreatitis	2.4	(1)	2.4	(1)	1.00
Missed diagnosis	2.4	(1)	0	(0)	1.00
Cardiopulmonary	0	(0)	2.4	(1)	1.00
Other	14.3	(6)	9.5	(4)	.738
No	11.9	(5)	9.5	(4)	1.00
Comprehensive Complication Index	20.9	[20.1]	33.7	[23.1]	.001

In 6.1% (n=3) of the claims, the patient had died. Of these, two concerned a delay in the diagnostics. One death was the result of severe pancreatitis after duodenal biopsies. No complications were detected in 14.3% (n=12) of the claims, but the diagnosis was delayed (3.5%, n=3), or the patients were unhappy with how they were treated. Complications that resulted in long-lasting (over six months) symptoms were observed in 7.3% (n=6) of the claims.

Of those claims related to PEG tubes, four were related to the insertion of the tube (intraperitoneal placement, bleeding, transhepatic placement, peritonitis, esophageal perforation), one was related to procedural sedation, and four were late complications (cutaneous infection, migration of the internal bumper).

The median Comprehensive Complication Index of the claims was 26.2 (IQR 33.7, range 0-100). Of the claims, 24.4% (n=20) included complications that required intensive care. According to the highest CDC grade within the claim, the claims are divided as follows: grade I for 18.3% (n=15), II for 18.3% (n=15), IIIa for 7.3% (n=6), IIIb for 19.5% (n=16), IVa for 22.0% (n=18), IVb for 1.2% (n=1), and V for 1.2% (n=1). Several complications occurred in 25.6.% (n=21) of claims.

6 DISCUSSION

6.1 STUDY I

This study revealed that operative treatment of ZD by open and endoscopic approaches is safe and seldom leads to complications or patient injury claims. The mortality rate in the cohort was low and comparable to previous literature.[246]

Previous studies have associated comorbidities with complications. Our study did not concur with this, although the literature on the topic is sparse since only a few papers report comorbidity.[296] Instead, we found that older age was associated with complications and longer LOS, against a study by Boruk et al. (2005), where age alone was not a prognostic factor in head and neck surgery.[297]

An endoscopic approach has been recommended for patients with ZD who are not good surgical candidates.[298,299] However, we found that the choice of surgical approach was impacted by the comorbidity level of the patient only to a minor extent. This finding may be explained by the lack of information on the size of the ZD, the rigidity of the neck, and other possible confounding factors that might have influenced the choice of approach.

Although operative treatment of ZD is safe, it still carries a risk of potentially serious complications. Patient injury claims, albeit rare, dealt with major complications such as esophageal leakages. There were only nine claims from 2010 to 2020, and compared to the baseline data, where approximately 54.9 ZDs were operated per year, the incidence of claims was 15 per 1,000 operations, which is relatively high compared to the overall rate of 6 per 1,000 operations as found in a national study by Welling et al. concerning claims related to surgery.[8]

Our findings should be interpreted within the context of the study's limitations. As this is a register study, it is prone to information bias. Thus, we were not able to point out the causality of individual cases. Because national registries do not collect information on a granular level, we could not assess confounding factors, such as obesity, frailty, performance status, or smoking history. We could not estimate the effectiveness of the operation on the symptoms of the patients and their quality of life. Also, our insight is that not all complications were consistently reported in the care register, and not all major complications were reported to the PIC. The PIC system is driven by patient-

submitted claims, so it does not represent all complications but rather those that crossed the individual threshold for filing.

6.2 STUDY II

In this study, we found that mortality after ARS and PEHR was low and at the same level as in reports from other populations—in a 2021 Danish report by Ljungdahl et al., the 30-day and 90-day mortality after ARS ranged from 0%–1.2%, while in our study it was 0.23%–0.27%.[300] The incidence of PIC claims was nine per 1,000 operations between 2010 and 2018, slightly higher than the rate generally after surgery in the same population.[8] Compared to baseline data from the Care Register, PIC claims, PEHR, and redo surgery were overrepresented. Moreover, PIC claims related to PEHR had higher Comprehensive Complication Indexes than claims related to ARS. Comparing the mortality of ARS to PEHR, the latter was higher, which may be explained by the need for urgent surgery for incarcerated paraesophageal hernias, which bear higher mortality.[301,302]

PEHR has increased in popularity since the previous national report on the topic, where the rate of PEHR per year was 37.8, while in our report, it was 137.6 per year.[9] The rate of ARS has diminished simultaneously (Fig 1). These trends are also evident when compared to the previous historical report from Finland on ARS and PEHR combined, where the rate was 1,400 in 2001 and 611 in 2018, according to our study.[202] The same trends can be seen in studies of other populations.[300,303,304] The trend of diminishing ARS can be attributed to the use of PPI. The increase in PEHR can be explained by the aging of the population, an increase in computer tomography imaging, and the utilization of minimally invasive techniques.[305,306]

Our study showed that older age was related to higher overall mortality after ARS or PEHR. This finding contradicts some previous studies, such as an institutional 2017 register study by Parker et al., where there was no difference in mortality after PEHR between older and younger patients, and a 2019 propensity-matched register study by Staerkle et al., where PEHR in octogenarians was not associated with an increase in mortality, complications, or reoperations.[307,308] Furthermore, patients in the PIC cohort were older and more likely to have PEHR than ARS. Although age should not be an ultimate contradiction to the ARS of PEHR, it should not be neglected as a risk factor when weighing the risks and benefits of operating older individuals.

The patient population in the PIC data had suffered major objective complications, and only a few claims did not include any complications. The ARS

group had more dysphagia, though the difference was not statistically significant. It may be related to the ARS group having more (ARS 93%, n=28 whereas PEHR 80%, n=24) complete 360 fundoplications done, which is known to be related to an increased risk of dysphagia.[215] Also statistically insignificant, the PEHR group suffered more perforations, which aligns with the previous literature.[212] This may be related to the mediastinal dissection needed when performing PEHR.

Our study has several limitations. Some claims related to ARS or PEHR during the study period might not be filed yet, since it is possible to claim up to three years after the injury. Also, because of changes in laws concerning secondary use of health data, we were unable to get baseline data from the Care Registry for 2019 and 2020. As a retrospective study, our study is affected by reporting bias and cannot indicate causality. We were unable to obtain data on several confounding factors, including prior surgeries, smoking, the use of PPIs, and obesity, because the registries do not provide this information. We were unable to gain information on quality of life or the severity of symptoms. In the Care Registry, some cases may be coded incorrectly, and in our study, the differentiation of procedures could only be made according to their NOMESCO codes instead of the size of paraesophageal hernias. We could not report disease-specific mortality. The PIC system is based on patients filing claims, so it does not represent all complications. Furthermore, there was no data on the volume of single surgeons.

6.3 STUDY III

This study is a large population-based study of EGDs, and we were able to point out that even though the EGD activity has increased, the mortality has diminished, and malpractice claims remain rare.

The observed 30-day overall mortality of 1.7% in our study is comparable to previous literature, such as the recently published institutional study of Chatelanat et al. from Switzerland conducted in a large tertiary hospital, where the 30-day mortality was 1.89%.[309] Although we were only able to report the overall mortality, the analysis of the causes of death indicates that most of the deaths were related to the primary disease or other underlying health condition rather than to the procedure.

Within our claim data, the most common complication that was related to EGDs with an intervention was perforation. In diagnostic EGDs, dental injuries were the most common. However, a small number of perforations also happened during diagnostic EGDs; thus, perforation, albeit rare, should not be neglected as

a possible adverse event in that setting, too. Our data also pointed out that complications after interventional EGD happened more often in non-academic hospitals (63.2% at non-academic vs. 38.2% academic), which may be related to the volume of these procedures.

Though the percutaneous endoscopic technique to establish a gastrostomy is known to be safe compared to other techniques, it is still known to be related to morbidity and high short-term mortality, which our findings reflect.[310] In our study, 11% (n=9) of the claims were related to PEG tubes, though only four (4.7%) were directly related to the tube insertion, while in the baseline data, only 1.3% of all endoscopies were PEG tube placements. In the baseline data, the 30-day mortality after PEG placement varied annually from 6.52% to 9.44%, which is low compared to a recent multicenter study from Sweden that included 389 patients, where the 30-day overall mortality was 15% and to a nationwide study from the US published in which the in-hospital mortality rate after PEG placement was 11%.[310,311] The complication types related to PEG in the claim data, such as passing the tube through the liver or colon, were in line with the previous literature.[76,312] The late complications could not be assessed from the baseline data. It remains unclear whether PEG is overused in the terminal phase of advanced illnesses, and there are no guidelines available on the topic. More real-life data is warranted to evaluate the actual usage and safety of PEG to improve patient selection.

As a retrospective study, our paper cannot indicate causality, and it is prone to reporting bias. Moreover, some procedures may have been miscoded as diagnostic endoscopies and, therefore, underreported in the baseline data. From the baseline data retained from the Care Register, we were unable to evaluate significant confounding factors, such as the indication for the EGD and the use of procedural sedation. Due to changes in the law regarding the secondary use of healthcare data, we could not retain data from 2018 to 2020 from the Care Register. During our study time, the peroral endoscopic myotomy (POEM) and endoscopic ultrasound (EUS) did not have NOMESCO codes, so their impact could not be investigated. Furthermore, we could not differentiate between urgent and elective procedures.

7 CONCLUSIONS

Malpractice claims after benign esophageal surgery are rare but deal primarily with serious adverse events.

The mortality after operative treatment for ZD was 0.9%, and complications were observed after 6.4% of operations. Increased age was associated with complications, whereas comorbidities were not. The endoscopic approach was less likely to result in complications but was associated with more reoperations. There were only nine patient injury claims related to ZD during the study period. The rate of claims related to ZD was 15 per 1,000 operations.

The 90-day mortality rates after ASR and PEHR were 0.27% and 2.1% respectively. PEHR is associated with higher mortality and more serious complications compared to ARS. PEHR and redo cases were overrepresented in the claims compared to the baseline data, due primarily to elective operations.

The claims related to EGD remained low despite the growing volume of endoscopic activity. The 30-day overall mortality after EGD was 1.7%, which is comparable to previous studies. Our data shows that the deaths were mainly due to baseline illnesses, and only a few were due to complications.

8 FUTURE PROSPECTS

A prospective nationwide register of benign esophageal and foregut surgery is warranted to better understand the association between technical and patient-related factors and complications. Further population-based studies related to benign esophageal diseases such as achalasia and Boerhaave syndrome are needed to achieve a more complete analysis of the effect of the morbidity on the population. As there may be growing interest in the repair of symptom-free paraesophageal hernias, more studies are needed to investigate the possibilities of decreasing PEHR-related morbidity.

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