Title: Hiatal hernia following esophagectomy for cancer

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Abstract

Background: Hiatal hernia (HH) after esophagectomy is becoming more relevant due to improvements in survival. This study aimed to evaluate and compare the occurrence and clinical course of HH following open and minimally invasive esophagectomy (MIE).

Methods: The prospectively recorded characteristics of patients treated with esophagectomy for cancer at two tertiary referral centers in the UK and the Netherlands between 2000-2014 were reviewed. All CT reports were reviewed to identify HH.

Results: Of 657 patients, MIE was performed in 432 (66%) and open esophagectomy in 225 (34%) patients. A CT-scan was performed in 488 (74%) patients. HH was diagnosed in 45 patients after a median of 20 (0-101) months. The development of HH after MIE was comparable to the open approach (8% vs. 5%, p=0.267). A total of 14 patients presented as a surgical emergency at the time of diagnosis. Of the remaining 31 patients, 17 were symptomatic and 14 were asymptomatic. Elective surgery was performed in 10 symptomatic patients, all others were treated conservatively. During conservative treatment, 2 patients presented as a surgical emergency. Emergency surgery resulted in a prolonged intensive care unit stay compared to elective surgery (3 vs. 0 days, p<0.001). In-hospital mortality was solely seen after emergency surgery (19%).

Conclusion: HH is a significant long-term complication after esophagectomy, occurring in a substantial proportion of the patients. The occurrence of HH after MIE and open esophagectomy is comparable. Emergency surgery is associated with dismal outcomes and should be avoided.

Introduction

Esophagectomy is the cornerstone of multimodality treatment for esophageal cancer. This includes dissection and removal of the esophagus, followed by restoration of the alimentary tract with a gastric tube in the majority of cases[1, 2]. During this procedure, the normal anatomy around the esophageal hiatus of the diaphragm is disrupted, which could lead to an increased risk of developing a post-operative hiatal hernia (HH). A recent systematic review reported a mean HH incidence of 2.6%, occurring up to 32 months after surgery[3]. This is likely to be an underestimate of the true incidence due to the limited long-term survival in the included studies and because some studies only reported rates of HH requiring surgical repair[3]. With improvements in overall survival due to the routine use of neoadjuvant treatment and modern-day esophageal cancer surgery[4], the development of HH after esophagectomy is becoming more relevant.

Minimally invasive esophagectomy (MIE) has been performed more frequently in recent years due to promising short-term outcomes such as decreased postoperative morbidity, shorter hospital stays and faster recovery[2, 5, 6]. These potential benefits could be offset by short and long-term complications specific to the minimally invasive approach. There is surgical concern that HH presenting as a surgical emergency, with potentially catastrophic consequences, is increasingly being seen in patients who are long-term survivors after MIE [7-9]. The aims of the current study were to document the occurrence and clinical course of HH following open and minimally invasive esophagectomy.

Patients and Methods

Study population

Consecutive patients treated with transhiatal or transthoracic esophagectomy followed by gastric tube reconstruction at two designated cancer centers, one in the United Kingdom and one in the Netherlands, between October 2000 and December 2014 were reviewed. All patients were diagnosed with a clinically resectable tumor (cT1a-T4a) without evidence of metastatic disease (cM0) according to the AJCC TNM staging system[10]. A small group of patients who underwent a hybrid procedure procedure (n=37) were excluded. Furthermore, patients who died in the hospital during the postoperative course were also excluded. Neoadjuvant therapy was given to eligible patients with locally advanced tumors (≥T2 or N+) and consisted of perioperative chemotherapy or neoadjuvant chemoradiation as previously described[4, 11]. In the UK, most patients received perioperative chemotherapy as this was the standard approach. In the Netherlands, most patients received perioperative chemotherapy before 2012. Hereafter, protocols were changed due to the results of the CROSS-trial and most patients received neoadjuvant chemoradiotherapy. Institutional Review Board approval for both centers was obtained and informed consent requirement was waived for this study.

Surgical procedure

In all patients, an esophagectomy with gastric tube reconstruction was performed, which included the following subtypes: Ivor Lewis, McKeown, and transhiatal esophagectomy. All types of procedures were performed minimally invasive and open based on institutional, surgeon and patient preference. The McKeown and transhiatal approach were predominantly performed at University Medical Center Utrecht (UMC Utrecht), Netherlands, whereas the Ivor Lewis procedure was predominantly performed at University Hospital Southampton (UHS), UK. The surgical procedures were performed as previously described[6, 12]. In short, a 4-5 cm gastric tube was constructed and positioned prevertebrally, in the esophageal bed, and cruroplasty and fixation of the gastric tube were not performed in any patient. The intraoperative techniques were comparable for open esophagectomy and MIE. In the UMC Utrecht a robot-assisted minimally invasive transthoracic approach is used in case of a MIE. This includes a robot-

assisted thoracoscopic phase in the left lateral decubitus position, with three ports placed for the robotic system and two ports placed for the assisting surgeon. For the abdominal phase, the patient is placed in a supine position and 5 ports are used for dissection of the stomach and adequate lymphadenectomy. After that, the left para-umbilical trocars pot is widened to a 5 to 7cm transverse transabdominal incision for removal of the resection specimen[12]. In case of a transhiatal esophagectomy, the abdominal phase is performed similarly as described above. In the UHS the Ivor Lewis procedure starts with abdominal laparoscopy in supine position via 5 ports for gastric mobilization and abdominal lymphadenectomy. After that, a thoracoscopic esophageal mobilization and mediastinal lymphadectomy using 5 ports in prone position is performed. For removal of the resected specimen, the lower most thoracic port is enlarged to 3 – 6 cm[6].

Evaluation of hiatal hernia

Postoperative follow-up of all surviving patients consisted of outpatient clinic assessment every 3 months in the first year, every 6 months in the second and third year and every 12 months thereafter until discharge of follow-up after 5 years. According to national guidelines, patients did not undergo routine imaging during follow-up, but only underwent radiological imaging or endoscopy if they were symptomatic suggestive of tumor recurrence, or long-term complications [13-15]. To identify hiatal hernia after esophagectomy, all computed tomography (CT) reports of patients who underwent a scan during the follow-up period (≥2 months after surgery) were reviewed. Some patients had their follow-up in another hospital, in which case these hospitals were contacted and asked to send the radiological reports. The diagnosis of HH was made if there was herniation of abdominal organs other than the gastric tube through the hiatus into the thorax. The electronic patient records were reviewed to evaluate the clinical course associated with HH including clinical presentation, treatment (surgical or conservative), and postoperative course after surgical repair. Patients were considered symptomatic if imaging was performed for symptoms that may have been attributable to HH such as pain, dysphagia, vomiting or dyspnea. Patients who underwent imaging for other indications were defined as “asymptomatic”. The

percentages of HH was calculated in the group of patients who had a follow up CT scan and in all patients.

Hiatal hernia treatment

During the study period, there was no standardized treatment protocol for HH following esophagectomy. In general, asymptomatic patients were treated with a watchful waiting policy (conservative management). The treatment of symptomatic patients was based on individual assessment of symptoms, patient fitness, risk factors and prognosis. Surgical repair of HH was performed through an open or minimally invasive abdominal approach. During the procedure, the content of the HH was dissected completely from the mediastinal structures and returned to the abdomen, the hiatal defect was repaired by approximation of the left and right crus, and a mesh was performed according to the surgeon's preference. Lastly, the gastric conduit was attached to the crus.

Statistical analysis

First a comparison was made between the UHS and UMC Utrecht to determine the equality of both databases regarding patient demographics. These data were evaluated by means of the Mann-Whitney U (MWU) test for continuous variables and the Pearson's Chi-squared (χ^2 test) – or Fisher's exact test in case of small cell count – for categorical variables. To determine risk factors for HH, all patients were taken into account. Factors with a p-value < 0.250 on univariable analysis were entered in a multivariable logistic regression model using the Enter-method. Further analysis was performed in patients who underwent a transthoracic esophagectomy. To compare the incidence of HH after OG and MIG, propensity score matching was used to build comparable groups and to deal with possible confounding factors. The optimal matching technique was used to generated matched sets of cases in which each set contain one open esophagectomy case and one MIE case [16]. Covariate balance of the matched cohort was assessed using the mean standardized differences, with differences less than 10% taken to indicate good balance [17]. Data were considered significant if $p<0.05$.Data were analyzed using the IBM SPSS

Statistics (version 21; IBM Corporation, Armonk, NY) and R 3.1.2 open-source software (http://www.R-project.org; ‘MatchIt’ and ‘optmatch’ packages) for PSM..

Results

Patients

A total of 657 consecutive patients underwent transhiatal or transthoracic esophagectomy for esophageal cancer in one of the participating hospitals (Table 1). MIE was performed in 432 (66%) patients; open esophagectomy in 225 (34%) patients. A comparison was made between the UHS and UMC Utrecht to compare cohorts between both centers. Patients treated at UHS had a higher ASA score (ASA 3: 24% vs. 17%, $p<0.001$). Chemotherapy was given more often given at UHS (67% vs. 29%, $p<0.001$), whereas chemoradiation was given more often in the UMCU (31% vs 5%, $p<0.001$). In the UHS more patients underwent open surgery (46% vs 25%, $p<0.001$). A transhiatal approach was only performed in the UMC Utrecht. All other parameters were comparable. A univariable analysis was conducted to determine equality of baseline characteristics between patients treated with MIE and open esophagectomy. With regard to age, BMI, ASA score and neoadjuvant treatment no differences were found.

Hiatal hernia

The median follow-up of the entire cohort was 31 months (range 6-107). Out of the 657 patients, 488 (74%) underwent a CT-scan during follow-up. The last CT-scan of each patient was performed at a median of 18 months (range 2-149) after esophagectomy. A total of 45 patients were diagnosed with a HH; 7% (45/657) of the total study population and 9% (45/488) in the group of patients who underwent a CT-scan. At the time of diagnosis, 31/45 (69%) patients experienced symptoms; 5% (31/657) of the total study population. Of the remaining 14/45 (31%) asymptomatic patients, HH was considered as an incidental finding. The HH was located in the left chest in 41 (91%) patients and involved the colon in 37 (82%) patients, the small intestines in 19 (42%) patients (Figure 1), the pancreas in 6 (13%) patients, the liver in 3 (7%) patients and the spleen in 1 (2%) patient. The median time of HH diagnosis was 20 months (range 0-101) after esophagectomy; 5 patients were diagnosed <1 month after surgery; all presented as a surgical emergency. Figure 2 demonstrates the time to HH diagnosis for those patients

presenting electively (31; 69%) compared with patients presenting as a surgical emergency (14; 31%) during follow-up. The majority of the patients who presented as a surgical emergency did so between 12 and 24 months after esophagectomy. Of note, 203 (31%) patients died before the median time of HH diagnosis (20 months), and in 33 (5%) patients follow-up did not yet reach the median time of HH diagnosis of 20 months.

Of the 31 patients who presented electively, 17 (55%) were symptomatic, with abdominal or thoracic pain as the most common presenting symptom (12/17, 71%), and 14 (45%) were asymptomatic (Figure 3). All 14 patients who presented as a surgical emergency experienced acute symptoms that were not present during routine follow-up. Only 4 of these patients had symptoms in the weeks before presentation that could be attributable to HH, whereas the other 10 patients experienced a sudden onset of symptoms.

Treatment

All 14 patients who presented as an emergency underwent immediate surgery (Figure 3). In the remaining 31 patients a choice between conservative treatment and elective surgery could be made on the basis of symptoms and patient preference. Elective surgery was performed in 10 symptomatic patients, at a median of 4 (0-25) months after diagnosis of HH. All other patients (7 symptomatic; 14 asymptomatic) were treated conservatively. After a median follow-up of 14 (0-66) months, conservative management was successful in 19 patients, and 2 patients (1 symptomatic; 1 asymptomatic) needed emergency surgery. As a results, in total 16 patients required emergency surgery (2.4% of total cohort).

In patients undergoing emergency surgical repair, a laparotomy was performed in 12 cases and laparoscopy in 4 cases. One procedure was converted from laparoscopy to laparotomy. For elective repair, laparotomy was performed in 4 patients and laparoscopy was performed in 6 patients. A mesh was used in 5 patients for crural reinforcement.

Clinical course

Postoperative complications occurred in 9/26 (35%) patients after HH repair: 8/16 (50%) after emergency and 1/10 (10%) after elective surgery (p=0.087). Postoperative complications included pneumonia (*n*=5), atrial fibrillation (*n*=3), bowel ischaemia (*n*=1), pleural effusion (*n*=1) and anaphylactic reaction to anesthetics (*n*=1). In-hospital mortality was only seen after emergency surgery (*n*=3, 19%); two patients died due to respiratory failure after a pneumonia and one patient died due to an anaphylactic reaction of anesthetics. A total of 15 patients who underwent emergency surgery were admitted to the Intensive Care Unit (ICU) for a median of 3 (0-18) days, compared to none after elective surgery (p<0.001). Median hospital stay was 10 (4-121) days after emergency surgery compared to 4 (1-17) days after elective surgery (p=0.051). After a median follow-up of 9 (range 0 – 65) months, recurrent HH was found in 4 (15%) patients after surgical repair. Three of these patients had primary repair and in 1 patient a mesh was used (p=1.000). Furthermore, 3 patients had laparotomy and 1 patient laparoscopy (p=0.604). HH recurrence was treated by redo surgery in 2 (50%) patients, whereas the other 2 were treated conservatively. Of all patients with HH, 3 (7%) died during hospital admission of HH repair, 20 (44%) died due to non-hernia related causes, and 22 were alive after a median follow-up of 14 (0-66) months.

Risk factors

A comparison was made between patients who developed HH and patients who did not develop HH after esophagectomy (Table 1). There was no difference in HH incidence after a transthoracic or transhiatal approach (7% vs. 9%; p=0.837). The development of HH after MIE was comparable to the open approach when transhiatal and transthoracic surgery was considered together (8% vs. 5%, p=0.267), with similar follow-up in both groups (28 vs. 26 months, p=0.405). Also in subgroup analyses in patients treated either with a transhiatal or transthoracic approach, there was no difference between MIE or open esophagectomy (transhiatal: 4% vs. 11%, p=0.258; transthoracic: 8% vs. 4%, p=0.055).

The multivariable analysis included all patient and tumor characteristics with p<0.250 (Table 2). In the analysis of all patients who underwent esophagectomy, low BMI (<25 kg/m2) (OR 2.0, 95% CI [1.1 –

3.7] p=0.026) was identified as a risk factor for hiatal hernia. The analysis of patients treated with transthoracic esophagectomy demonstrated no specific risk factors for developing HH.

Open vs. Minimally Invasive Esophagectomy

In the entire cohort, differences were found between the open esophagectomy and MIE groups regarding smoking status, surgical approach, tumor histology and tumor stage (Table 3). After propensity score matching, the 2 groups were well-balanced with 225 patients in each group. In this cohort the development of HH after MIE was comparable to the open approach (7% vs. 5%, p=0.559) with similar follow-up in both groups (28 vs. 26 months, p=0.405).

Discussion

Major findings

In this large cohort of consecutive patients treated with esophagectomy for cancer, the incidence of postoperative hiatal hernia (HH) was 7-10%. The incidence of HH after MIE in all patients was comparable to open surgery (8% vs. 5%). Hiatal herniation presented acutely in 32% of patients, who were at high risk of perioperative death. A conservative management strategy was safe in asymptomatic patients with HH.

Occurrence

HH following esophagectomy is a significant long-term complication, which occurs in a substantial group of patients. In this study, the incidence of 7% from the total study population is probably underestimated, as 26% of the patients did not undergo a CT-scan. On the other hand, the incidence of 10% calculated from patients who underwent a CT-scan probably overestimates the true incidence, as the incidence of HH in patients who did not undergo a CT-scan is probably lower. Thus, the true incidence of HH is most likely between 7% and 10%. These numbers are comparable to a recent meta-analysis and a recent UK study[18, 19], which reported an incidence of 5% and 6% respectively. HH

following esophagectomy will become an increasing clinical problem as cancer survival improves. In this study 2.4% of patients required emergency surgery for HH following esophagectomy, a figure that is comparable with current postoperative mortality after esophagectomy. All surgeons discuss mortality at the time of primary resection with their patients, but HH was not specifically considered in a recently defined core disclosure information set for patients undergoing esophagectomy[20]. Patients clearly prioritized long-term outcomes such as eating and drinking and overall quality of life, which can be significantly impacted by the development of HH and subsequent surgery (14). This makes the disclosure of the potential for HH after esophagectomy and the identification of risk factors for HH important.

In this study, lower BMI was associated with a higher risk of developing a HH following esophagectomy. A lower BMI has been reported as a risk factor for HH post-esophagectomy before by Ganeshan et al.[9] An explanation could be that a higher BMI results in a reduced mobility of intra-abdominal structures.

The influence of MIE on the occurrence of HH is currently an important topic of debate. In a recent meta-analysis of 6058 patients a higher incidence of a symptomatic HH was found after MIE (4.5%, 95% CI [2.8-6.2]) compared to open esophagectomy (1.0%, 95% CI [0.6-1.3])[18]. A frequently reported explanation is the reduced formation of peritoneal adhesions after MIE, although there is no evidence to prove this theory. However, the included studies in this meta-analysis were heterogeneous, as they had different follow-up periods and used different surgical techniques in the open and MIE groups. In the present study propensity score matching was used to build comparable groups and after that, the overall incidence of HH between the open and minimally invasive group was similar. Due to improvements in overall survival, it is possible that HH will become a more common problem facing esophageal surgeons and strategies to mitigate HH will need to be considered. A possible prevention method could be closure of the crurae during initial esophagectomy, which is advocated by some surgeons[7]. Crural closure can be performed from the abdomen during a 3-phase McKeown or transhiatal esophagectomy, and from the thorax during a 2-phase Ivor Lewis esophagectomy. However,

there is no solid evidence supporting this technique and very large studies will be required to validate this technique.

Diagnosis

In this study the acute presentation of HH was associated with high mortality (19%), which is in keeping with recent data[19]. Surviving patients were at risk of significant complications and long ICU stay. Unfortunately, 14 out of the 16 patients that underwent emergency surgery were not diagnosed with HH before and presented with acute symptoms at the time of diagnosis. Whether HH was already present in these patients remains unclear: only a minority of the patients had mild nonspecific symptoms, which suddenly became worse, but the majority had an acute onset of symptoms after an event such as vomiting or coughing. As many patients have mild non-specific symptoms after esophagectomy, it is difficult to differentiate between HH and non-HH symptoms. Another option for HH detection could be routine screening during follow-up. Based on the results in this study, one might perform routine screening at 12-18 months (Figure 2). CT scanning would be the preferred investigation, but chest x-ray could be considered depending on local circumstance.

Treatment

The current study evaluated treatment decisions made in patients who were diagnosed electively with HH. Although there was no standardized treatment protocol for HH after esophagectomy, all asymptomatic patients were initially treated conservatively at the time of HH diagnosis. This is in line with the Society of American Gastrointestinal and Endoscopic Surgeons (SAGES) guidelines of the treatment of asymptomatic HH in the general population [21]. In contrast, some surgeons advocate surgical repair in all patients, including asymptomatic patients, to prevent the need for emergency surgery after an acute presentation[7, 22]. However, the risk for acute presentation should be balanced against the risks that accompanies surgical repair and patient prognosis. In this study only 1 (7%) asymptomatic patient who was treated conservatively eventually needed emergency surgery after a follow-up of 13 months. In addition, most of the patients died from non-hernia related causes. Therefore,

in asymptomatic patients conservative management appears to be safe and could prevent postoperative complications accompanied with surgery. For patients with symptomatic HH in the general population, the SAGES guidelines recommend surgical repair due the high risk of emergency presentation compared to asymptomatic patients[21, 23]. Since evidence concerning the management of symptomatic HHs after esophagectomy is lacking, it remains unclear if the SAGES guidelines should also be followed for this population. In the present study, after a follow-up of 13 months, conservative treatment was successful in 90% of symptomatic patients with HH after esophagectomy. Whether to perform surgery in these patients should therefore depend on the severity of symptoms, patient fitness and prognosis taking into account the outcomes of surgery for HH in the emergency setting.

Limitations

There are some limitations of this study that should be addressed. First, there were some baseline differences between the 2 participating centers with regard to ASA score, neoadjuvant treatment and surgical approach. Second, this study did not evaluate the preoperative occurrence of HH, which could influence the risk of developing postoperative HH. Third, due to the retrospective character of this study, lack of routine imaging during follow-up, and as some patients only had a short follow-up, the exact incidence of HH might be underreported. Nevertheless, 73% of all patients could be evaluated and within this group, 9% developed a HH, which demonstrates the importance and significance of this long-term complication. Fourth, in this study reconstruction was performed with a 4-5cm wide gastric tube and the esophageal bed was used in all cases as the reconstruction route. Although this is a commonly performed approach, the results may not be generalizable to other procedures. Last, there is selection bias in the chosen treatment for HH. Currently, there is no standard treatment for HH after esophagectomy and therefore the chosen treatment is based on the surgeon’s individual preferences.

Conclusion

As hiatal hernia after esophagectomy is expected to occur more frequently in the future due to prolonged survival. More attention is warranted for this significant long-term complication. In general, HH following MIE and open esophagectomy is comparable. Since a substantial number of patients with HH require emergency surgery, which is associated with poor outcomes, focus should lie on prevention. After elective presentation, conservative management appears to be safe for asymptomatic patients, whereas individual risk assessment should determine the need for surgical therapy in symptomatic patients.

Disclosures

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Table 1. Comparison of patients with and without hiatal hernia after esophagectomy.

	Hiatal hernia (n=45)		No hiatal hernia (n=612)		
	n	(%)	n	(%)	p-value
Gender					0.196
Male	38	(8)	465	(92)	
Female	7	(5)	147	(95)	
Age (years) [a]	62.8	[8.1]	65.0	[9.3]	0.118
BMI during esophagectomy (kg/m^2) [a]	24.7	[3.5]	26.1	[4.0]	**0.029**
Smoking history	29	(64)	322	(53)	0.158
ASA					0.888
I	9	(7)	112	(93)	
II	29	(7)	376	(93)	
III	7	(5)	123	(95)	
IV	0	(0)	1	(100)	
Neoadjuvant therapy					0.657
None	12	(5)	214	(95)	
Chemotherapy	24	(8)	276	(92)	
Radiotherapy	0	(0)	2	(100)	
Chemoradiotherapy	9	(7)	120	(93)	
pT-stage					0.943
T0 / IS	4	(5)	75	(95)	
T1	9	(7)	112	(93)	
T2	8	(8)	92	(92)	
T3	23	(7)	313	(93)	
T4	1	(5)	20	(95)	
Tumor location					0.243
Upper 1/3	0	(0)	4	(100)	
Middle 1/3	2	(3)	67	(97)	
Lower 1/3	21	(7)	302	(93)	
GEJ	22	(9)	225	(91)	
Procedure type					0.265
Open					
Ivor Lewis	5	(4)	122	(96)	
McKeown	2	(4)	52	(96)	
Transhiatal	5	(11)	39	(89)	
MIE					
Ivor Lewis	13	(10)	118	(90)	
McKeown	17	(7)	215	(93)	
Transhiatal	3	(4)	66	(96)	

Table 2. Univariable and multivariable logistic regression of risk factors associated with the occurrence of hiatal hernia after esophagectomy.

All patients (*n*=657)						
	Univariable			**Multivariable**		
	OR	95% CI	p	OR	95%CI	p
Male gender	1.7	[0.8 – 3.9]	0.201	1.8	[0.8 – 4.1]	0.191
BMI <25 kg/m2	1.9	[1.0 – 3.5]	**0.037**	2.0	[1.1 – 3.7]	**0.026**
MIE	1.5	[0.7 – 2.9]	0.269	1.4	[0.7 – 2.9]	0.317
Transhiatal	1.0	[0.5 – 2.3]	0.915	-	-	
Age >65	0.6	[0.4 – 1.2]	0.170	0.7	[0.4 – 1.3]	0.234
Smoking history	1.6	[0.8 – 3.0]	0.161	1.4	[0.7 – 2.8]	0.286
ASA 3-4	0.7	[0.3 – 1.7]	0.447	-	-	
CRTx vs. CTx	0.9	[0.4 – 1.9]	0.729	-		
pT-stage 3-4	1.0	[0.5 – 1.8]	0.889	-	-	
GEJ tumor	1.6	[0.9 – 3.0]	0.108	1.7	[0.9 – 3.1]	0.106

Transthoracic esophagectomy (*n*=544)						
	Univariable			**Multivariable**		
	OR	95% CI	p	OR	95%CI	p
Male gender	1.4	[0.6 – 3.2]	0.449	-	-	
BMI <25 kg/m2	1.6	[0.8 – 3.1]	0.173	1.6	[0.8 – 3.2]	0.174
MIE	2.2	[1.0 – 5.2]	0.061	2.2	[1.0 – 5.3]	0.060
McKeown	0.9	[0.5 – 1.9]	0.877	-	-	
Age >65	0.6	[0.3 – 1.1]	0.100	0.6	[0.3 – 1.1]	0.110
Smoking history	1.2	[0.6 – 2.4]	0.577	-	-	
ASA 3-4	0.7	[0.3 – 1.8]	0.447	-	-	
CRTx vs. CTx	0.8	[0.3 – 1.8]	0.524	-	-	
pT-stage 3-4	1.0	[0.5 – 2.0]	0.907	-	-	
GEJ tumor	1.6	[0.8 – 3.2]	0.163	1.7	[0.8 – 3.2]	0.109

Figures

Figure 1. HH of the small intestines after esophagectomy. GT; Gastric Tube. AO; Aorta. HH; Hiatal hernia.

Figure 2. Time to diagnosis of HH after esophagectomy according to presentation at diagnosis

Figure 1. Flowchart of treatment decisions at the time of HH diagnosis.

Table 3. Baseline characteristics and the occurrence of HH of the original and propensity matched cohort

	Original Cohort (*n*=657)					**PSM Cohort (*n*=450)**				
	Open (*n*=225)		MIE (*n*=432)			Open (*n*=225)		MIE (*n*=225)		
	n	(%)	*n*	(%)	p-value	*n*	(%)	*n*	(%)	p-value
Male gender	181	(80)	322	(75)	0.090	181	(80)	174	(77)	0.488
Age (years) (mean, SD)	65.2	±9.4	64.7	±9.2	0.546	65.2	±9.4	65.8	±9.4	0.498
BMI (kg/m^2) (mean, SD)	26.0	±3.8	26.0	±4.1	0.938	26.0	±3.8	26.1	±3.6	0.754
Smoking history					**0.013**					0.123
No	98	(44)	181	(42)		98	(44)	95	(42)	
Yes	111	(49)	240	(56)		111	(49)	123	(55)	
Unknown	16	(7)	11	(3)		16	(7)	7	(3)	
ASA					0.221					0.445
I	46	(20)	75	(17)		46	(20)	36	(16)	
II	129	(57)	276	(64)		129	(57)	140	(62)	
III	49	(22)	81	(19)		49	(22)	49	(22)	
IV	1	(0)	0	(0)		1	(0)	0	(0)	
Neoadjuvant therapy					0.316					0.798
None	77	(34)	149	(34)		77	(34)	77	(34)	
Chemotherapy	111	(49)	189	(44)		111	(49)	111	(49)	
Radiotherapy	1	(0)	1	(0)		1	(0)	0	(0)	
Chemoradiotherapy	36	(16)	93	(22)		36	(16)	37	(16)	
Surgical approach					**<0.001**					0.694
Ivor Lewis	127	(56)	131	(30)		127	(56)	123	(54)	
McKeown	54	(24)	232	(54)		54	(24)	57	(25)	
Transhiatal	44	(20)	69	(16)		44	(20)	45	(20)	
Histology					**0.018**					1.000
CIS	0	(0)	7	(2)		0	(0)	0	(0)	
Adenocarcinoma	192	(85)	334	(77)		192	(85)	192	(85)	
Squamous cell carcinoma	33	(15)	91	(21)		33	(15)	33	(15)	
Tumor location					0.313					0.640
Upper 1/3	0	(0)	4	(1)		0	(0)	1	(0.4)	
Middle 1/3	22	(10)	54	(13)		22	(10)	17	(8)	
Lower 1/3	113	(50)	217	(50)		113	(50)	116	(52)	
Cardia	90	(40)	157	(36)		90	(40)	91	(40)	
pTNM-stage					**0.030**					0.323
0	13	(6)	55	(13)		13	(6)	19	(8)	
I	58	(26)	96	(22)		58	(26)	54	(24)	
II	56	(25)	119	(28)		56	(25)	68	(30)	
III	98	(44)	160	(37)		98	(44)	83	(37)	
IV	0	(0)	2	(0)		0	(0)	1	(0.4)	
Hiatal Hernia	12	(5)	33	(8)	0.267	12	(5)	16	(7)	0.559