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Incidence and Risk Factors of Symptomatic Hiatal Hernia Following Resection for Gastric and Esophageal Cancer

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Abstract. *Background/Aim: Symptomatic hiatal hernia (HH) following resection for gastric or esophageal cancer is a potentially life-threatening event that may lead to emergent surgery. However, the incidence and risk factors of this complication remain unclear. Patients and Methods: Data of patients who underwent resection for gastric or esophageal cancer between 2005 and 2012 were assessed and the incidence of symptomatic HH was evaluated. Factors associated with an increased risk for HH were investigated. Results: Resection of gastric or esophageal cancer was performed in 471 patients. The primary tumor was located in the stomach, cardia and esophagus in 36%, 24%, and 40% of patients, respectively. The incidence of symptomatic HH was 2.8% (n=13). All patients underwent surgical hernia repair, 8 patients (61.5%) required emergent procedure, and 3 patients (23%) underwent bowel resection. Morbidity and mortality after HH repair was 38% and 8%, respectively. Factors associated with increased risk for symptomatic HH included Body-Mass-Index (median BMI with HH 27 (23-35) vs. BMI without HH 25 (15-51), p=0.043), diabetes (HH rate: with diabetes, 6.3% vs. without diabetes, 2%, p=0.034), tumor location (HH rate: stomach, 1.2% vs. esophagus, 1.1% vs. cardia, 7.9%, p=0.001), and resection type (HH rate: total/subtotal gastrectomy, 0.7% vs. transthoracic esophagectomy, 2.7% vs. extended gastrectomy, 6.1%, p=0.038). Conclusion: HH is a major adverse event after resection for gastric or esophageal cancer especially among patients undergoing extended gastrectomy for cardia cancer requiring a high rate of repeat surgery. Therefore, intensive follow-up examinations for high-risk patients and early diagnosis of asymptomatic patients are essential for selecting patients for elective surgery to avoid unpredictable emergent events with high morbidity and mortality.*

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Esophageal and gastric cancer are reported as leading causes of cancer-related deaths with rapidly increasing incidence. Worldwide, more than 450,000 people are affected by tumors located in the esophagus (1). Gastric cancer is described as the fifth most common type of cancer in the world (2). Despite advances in endoscopic and systemic therapy, oncological resection in the form of esophagectomy and gastrectomy remain the mainstay of treatment for these serious malignancies of the digestive system (3, 4). In recent studies, morbid postoperative complications, such as *de novo* hiatal hernia (HH) have attracted attention among surgeons and oncologists. Diaphragmatic herniation following esophagectomy has been the subject of current reports in medical literature with an estimated incidence of 0.4-19.4% (5-15). Gastrectomy accompanied by extensive hiatal dissection is also correlated with hernia formation postoperatively (16). The incidence of HH after gastrectomy ranges from 0.19-47% (17-26).

Even though postoperative HH following esophagectomy and gastrectomy is still considered a rare complication, HH may be a potentially life-threatening event that remarkably deteriorates the postoperative and long-term outcome of patients. Operative hernia repair is recommended (27), especially in case of symptomatic herniation or a progressive increase in size of HH (9). More importantly, HH may also present with grievous complications, such as severe respiratory compromise, intestinal ischemia with perforation (16), bowel obstruction, and strangulation (27) leading to emergent surgery.

However, studies in which risk factors for HH have been accurately investigated are lacking. Thus, the aim of this study was to evaluate the incidence of symptomatic HH in

patients who underwent resection for gastric or esophageal cancer with curative intent and identify factors associated with an increased risk for the development of this potentially life-threatening complication.

Materials and Methods

Patient inclusion criteria. Following approval from the institutional review board (EA4/052/14), a retrospective review of clinicopathological data of all consecutive patients treated with curative resection for gastric and esophageal cancer between 2005 and 2012 at the Charité, Campus Virchow-Klinikum in Berlin, Germany was conducted. Patients with stage IV disease and those who underwent palliative resection were excluded from the database. Patients undergoing surgery for benign disease were also excluded from the analysis.

Esophageal resections during this period were predominantly performed using a transthoracic approach and a gastric pull up as previously reported (28). Anastomotic reconstruction after gastric resection included a Roux-en-Y-esophagojejunostomy (28).

Surgical management of the esophageal hiatus. During the initial operation, the hiatus was first dissected and in cases of esophageal resection or transhiatally extended gastric resection, the diaphragm was opened strictly anteriorly up to the left inferior diaphragmatic vein, which was transsected during esophageal resection. Both diaphragmatic crurae were preserved. After mediastinal lymphadenectomy and reconstruction, the hiatus was not closed on a routine basis.

Diagnosis and perioperative management of HH. For the purpose of this study, HH was defined as an anatomic defect of the hiatus diaphragmaticus following esophagectomy or gastrectomy that allowed elements of the abdominal cavity to herniate into the thorax, usually associated with a striking left-sided predominance (5-7).

Patients were included in the study if they presented with HH related symptoms making surgical intervention necessary. For the diagnosis of HH and preoperative assessment of the patients, medical history, physical examination, serum laboratory tests, computed tomography (CT) with contrast agent of the chest and the abdomen, and an anesthesia evaluation were performed.

The extent of the surgery depended on whether the procedure was elective or emergent as well as from the intraoperative findings including ischemia of the herniated intestine and the need for bowel resection. In general, after reduction of the herniated bowel, the crurae were approximated posteriorly by non-resorbable sutures, if possible. Mesh augmentation was used if the hiatus could be closed upon surgeon's discretion. If the hiatus could not be reapproximated, in cases of a retrocolic Roux-Y esophagojejunostomy, the transverse mesocolon was used as a "curtain" in front of the hiatus and the alimentary jejunal loop was straightened between the anastomosis and the mesocolon and sewed to the mesocolon. In cases of esophageal resection and a large diaphragmatic defect, which could not be closed, a non-resorbable mesh was used as an inlay patch to the diaphragm anterior to the gastric conduit.

In case of emergency surgery, patients were postoperatively admitted to a specialized surgical intensive care unit and were closely observed for postoperative complications including intra-abdominal infection, bowel ischemia, wound infection, pneumonia, pleural effusions, and organ failure. Postoperative morbidity was defined as any complication within 90 days and postoperative mortality was defined as any in-hospital death after surgery.

Statistical analysis. The primary endpoint of this study was to evaluate the incidence of symptomatic HH requiring surgical treatment, and identify risk factors associated with an increased risk for HH. Quantitative and qualitative variables were expressed as medians (range) and frequencies. Chi-squared or Fisher's exact test and the Mann-Whitney *U*-test were used to compare categorical and continuous variables, as appropriate. To identify factors associated with an increased risk for HH following resection for gastric and esophageal cancer, we evaluated the following clinicopathologic variables: sex (male *vs.* female), median age at resection in years, median body-mass-index (BMI), tumor location (esophagus *vs.* cardia *vs.* stomach), resection type (transthoracic esophagectomy *vs.* extended gastrectomy *vs.* total/subtotal gastrectomy), the presence of diabetes (yes *vs.* no), the presence of cardiovascular disease (yes *vs.* no), the presence of pulmonary disease (yes *vs.* no), the presence of liver cirrhosis (yes *vs.* no), the presence of renal insufficiency (yes *vs.* no), American Society of Anesthesiologists (ASA) physical status (I *vs.* II *vs.* III *vs.* IV), the use of preoperative chemotherapy (yes *vs.* no), the use of preoperative radiotherapy (yes *vs.* no), median duration of resection time in minutes, the need for intraoperative transfusions (yes *vs.* no), T stage (T1 *vs.* T2 *vs.* T3 *vs.* T4), N stage (N0 *vs.* N1 *vs.* N2 *vs.* N3), Union for International Cancer Control (UICC) stage (I *vs.* II *vs.* III), presence of lymphangiosis carcinomatosa (yes *vs.* no), presence of venous invasion (yes *vs.* no), tumor differentiation (G3 *vs.* G1/2), resection margins (R1 *vs.* R0), histologic type of tumor (adenocarcinoma *vs.* squamous cell carcinoma), presence of anastomotic leak (yes *vs.* no), the use of postoperative chemotherapy (yes *vs.* no), and the use of postoperative radiotherapy (yes *vs.* no).

p-Values <0.05 were considered statistically significant. Statistical analyses were performed using the SPSS software package, version 22 (IBM, Armonk, NY).

Results

Patient characteristics. During the study period, a total of 471 esophageal and gastric resections for malignant disease were performed. The clinicopathological data of these patients are summarized in Table I. Thirteen patients suffered symptomatic HH. All of them were men and the median age was 63 (range=39-78 years) years. Among patients with symptomatic HH, the primary tumor was located in stomach, cardia, and esophagus in 17%, 69%, and 16% of patients, respectively. Total or subtotal gastrectomy, extended gastrectomy, and transthoracic esophagectomy was performed in 32%, 20%, and 48% of patients who developed HH, respectively.

Incidence of symptomatic HH and clinical presentation. After a median follow-up time of 35 months, the incidence of symptomatic hiatal hernia following esophageal and gastric resection for carcinoma was 2.8% (n=13) (Table II) and the median time between oncologic resection and diagnosis of the HH was 15 (range=0.1-57 months) months. With regards to the tumor location, 1.1% of patients with esophageal cancer (n=2), 7.9% of patients with cardia cancer (n=9), and 1.2% of patients with gastric cancer (n=2) developed symptomatic *de novo* HH requiring surgical

Table I. *Clinicopathological characteristics of 471 patients who underwent resection for gastric or esophageal carcinoma.*

Characteristics	All Patients (N=471)	No Hiatal Hernia (N=458)	Hiatal Hernia (N=13)	*p*-Value*
Male gender, %	75	74	100	0.035
Median age at resection (range), years	65 (28-89)	65 (28-89)	63 (39-78)	0.937
Median BMI (range)	25 (15-51)	25 (15-51)	27 (23-35)	0.043
Tumor location, %				0.001
Esophagus	40	40	16	
Cardia	24	23	69	
Stomach	36	37	15	
Resection Type, %				0.038
Transthoracic esophagectomy	48	48	46	
Extended gastrectomy	20	20	46	
Total/subtotal gastrectomy	32	32	8	
Diabetes, %	16	16	39	0.034
Cardiovascular disease, %	57	57	62	0.720
Pulmonary disease, %	15	16	8	0.440
Liver cirrhosis, %	2	2	0	0.572
Renal insufficiency, %	8	8	0	0.279
ASA physical status, %				0.562
I	4	4	8	
II	40	41	25	
III	54	53	67	
IV	2	2	0	
Preoperative chemotherapy, %	53	52	77	0.081
Preoperative radiotherapy, %	14	14	8	0.517
Median duration of resection (range), min	288 (96-687)	288 (96-687)	292 (195-389)	0.856
Need for intraoperative transfusions, %	21	21	8	0.290
T Stage, %				0.597
T1	20	21	8	
T2	17	17	23	
T3	60	59	69	
T4	3	3	0	
N Stage, %				0.364
N0	54	54	69	
N1	17	17	23	
N2	15	15	0	
N3	14	14	8	
UICC Stage, %				0.203
I	24	25	23	
II	48	47	69	
III	28	28	8	
Lymphangiosis carcinomatosa, %	31	31	31	0.986
Venous invasion, %	12	11	15	0.653
Poorly differentiated carcinoma (G3), %	49	48	73	0.104
Positive resection margins (R1), %	8	8	8	0.982
Histologic type, %				0.088
Adenocarcinoma	82	82	100	
Squamous cell carcinoma	18	18	0	
Anastomotic leak, %	9	9	0	
Postoperative chemotherapy, %	37	37	62	0.067
Postoperative radiotherapy, %	7	7	8	0.882

*Comparison of patients with and without hiatal hernia. BMI: Body-mass-index; UICC: Union for International Cancer Control; ASA: American Society of Anesthesiologists.

treatment (Table II). Abdominal pain (n=8, 62%) was the most common presenting symptom, followed by emesis (n=6, 46%), and bowel obstruction (n=6, 46%) (Table III).

Surgical management of patients with symptomatic HH and postoperative results. All patients underwent open operative hernia repair including 8 patients (62%) who required an

Table II. *Incidence of hiatal hernia (HH) according to the location of the resected tumor.*

Tumor location	Number of HH (n)	Incidence of HH (%)
Esophagus (n=171)	2	1.1
Cardia (n=114)	9	7.9
Stomach (n=186)	2	1.2
Total (n=471)	13	2.8

Table III. *Perioperative characteristics of 13 patients who underwent repair of hiatal hernia (n=13).*

Characteristics	Number of patients (%)
Emesis	6 (46%)
Abdominal pain	8 (62%)
Bowel obstruction	6 (46%)
Emergent procedure	8 (62%)
Bowel resection	3 (23%)
Postoperative morbidity	5 (38%)
Postoperative mortality	1 (8%)

emergent procedure, and 3 patients (23%) who underwent resection of ischemic herniated bowel (Table III). Primary repair of the HH was performed by re-approximating the diaphragmatic crura with (n=3) or without (n=10) the use of a mesh implant.

The in-hospital mortality rate was 8% (n=1). Postoperative death was related to myocardial infraction following emergency surgery for acute mechanical ileus due to incarcerated and torqued small bowel in the thoracic cavity. The 64-year-old patient underwent resection of the ischemic intestinal segments and developed postoperative sepsis requiring admission in the surgical intensive care unit. Postoperative 90-day morbidity was 38% (n=5) and included pulmonary complications (pneumonia, pneumothorax, pleura effusions), bleeding complications, and infectious complications in 3, 1, and 1 patient, respectively.

Prognostic factors for symptomatic HH. Factors associated with an increased risk for the development of symptomatic HH are summarized in Table I and included Body-Mass-Index (median BMI with HH 27 (23-35) *vs*. BMI without HH 25 (15-51), p=0.043), diabetes (HH rate: with diabetes, 6.3% *vs*. without diabetes, 2%, p=0.034), tumor location (HH rate: stomach, 1.2% *vs*. esophagus, 1.1% *vs*. cardia, 7.9%, p=0.001), and resection type (HH rate: total/subtotal gastrectomy, 0.7% *vs*. transthoracic esophagectomy, 2.7% *vs*. extended gastrectomy, 6.1%, p=0.038).

Discussion

In the past decade, several studies have reported the development of HH following resection for gastric or esophageal cancer (9, 29). However, factors associated with an increased risk for symptomatic *de novo* HH remain unclear and recommendations for the management of patients undergoing resection for gastric or esophageal cancer are still not established. Our current study examined factors associated with symptomatic *de novo* HH and indicated that patients with tumors located in the cardia requiring extended gastrectomy have a significant risk for this complication. Diabetes and obesity were additional considerable risk factors.

Iatrogenic alterations of the upper GI anatomy, such as enlargement of the hiatus during esophagectomy was the only investigated risk factor in previous analyses that has been considered to be significantly associated with postoperative herniation (9, 29). Van Sandwick *et al*. have postulated already in 1999, that the main cause of HH may be the extensive blunt dissection of the hiatus (29). A series published in 2011 hypothesized that HH is a result of increased intraabdominal pressure and suction effect of the negative intrathoracic pressure leading to progressive hiatal dilation (5, 6).

Price *et al*. presented their results on the incidence of diaphragmatic hernia following minimally invasive esophagectomy (6). Laparoscopic surgery is generally known to decrease the extent of postoperative peritoneal adhesions (9, 16, 27). The reduction of adhesions and the perioperative enlargement of the hiatus may increase the risk of HH after esophagectomy compared to open approaches (7, 9, 16, 27). The outcome of previous reports was in accordance with our results showing that esophagectomies are essentially more frequently associated with HH compared to total/subtotal gastrectomy (17) and that transhiatal procedures correlated with an even higher incidence due to the enlargement of the hiatus (9, 14). In our study, HH rates after esophagectomy using a transthoracic approach and extended gastrectomy were also significantly higher than after total/subtotal gastrectomy (2.7% *vs*. 6.1% *vs*. 0.7%, respectively, p=0.038). Thus, the surgical techniques should be taken into consideration when evaluating the risk for HH among surgically treated patients with gastric and esophageal cancer especially in the current era of increased utilization of minimal invasive techniques.

The histological type and stage of the tumor was not significantly associated with the occurrence of HH in univariate analyses as shown in Table I. This finding is in discordance with a report by Matthews *et al*. (16) who introduced T-stage as a significant predictor of HH. The majority of oncologic resections in our study were performed in patients with locally advanced esophageal or gastric cancer and correspondingly impaired long-term survival.

Therefore, late complications such as HH may be more frequent in studies in which benign disease or more early stage carcinomas are included.

Our data suggested that the presence of preoperative comorbidities, such as diabetes mellitus also significantly affected the development of postoperative HH. In a recent study, the combination of transient neonatal diabetes mellitus (TNDM) and congenital diaphragmatic hernia (CDH) was presented initially, postulating that a common genetic or embryologic etiology may underlie TNDM and CDH (30, 31). Diabetes as a potential predictor for HH following gastrectomy and esophagectomy has not been previously investigated. However, the correlation between the impairment of wound healing and diabetes (32, 33) may have contributed to the increased frequency of HH. Yahchouchy-Chouillard *et al*. referred to type II diabetes as an important patient-related risk factor for developing incisional hernia following abdominal surgery (34). Further studies reported on the association between diabetes and incisional hernia (35, 36), confirming the plausibility of our finding. Finally, Hornby *et al*. found that diabetes may be a risk factor for recurrent incisional hernia after laparoscopic hernia repair presumably due to impaired wound healing and increased postoperative wound infection complications (37).

Obesity was also found to have an influence on the frequency of HH in our study and we showed that higher BMI was associated with an increased risk for the development of symptomatic HH (median BMI with HH 27 (range=23-35 kg/m^2) *vs*. BMI without HH 25 (range=15-51 kg/m^2), p=0.043). Surprisingly, another clinical study by Ganeshan *et al*. performed in 2013 indicated opposing results showing that patients with high BMI were less prone to develop HH after esophagectomy (9). This could be explained by the fact that ''the abdominal contents in patients with BMI >25 kg/m^2 are increased and therefore may obscure the hiatus'' (9). Additionally, Ganeshan *et al*. considered that less mobility of abdominal contents in patients with high BMI may prevent HH (9). However, a recent study which assessed the prevalence of HH in morbidly obese patients based on preoperative upper GI contrast studies, nearly 40% of patients were identified with HH (38). Che *et al*. referred to previous studies showing that obesity is associated with an increased intraabdominal pressure, which may lead to a higher risk of developing abdominal and hiatal herniation (38-41).

Our current retrospective study has some limitations. In this database, different tumor entities were pooled together. However, patients who underwent resection for gastric or esophageal cancer were both included to achieve a representative study size for the investigation of risk factors for the development of HH. Despite the relative small number of patients included, this study is one of the largest from a western comprehensive cancer center providing data regarding potential factors associated with *de novo* HH and thus facilitating optimal management of patients at risk.

Conclusion

De novo HH is a major adverse event following resection for gastric or esophageal cancer. Among patients undergoing oncological upper GI surgery, extended gastrectomy for carcinoma of the cardia is significantly associated with an increased HH rate requiring for revisional surgery. The fact that emergent procedures for HH correlated with high morbidity and mortality underlines the importance of intensive follow-up examinations for high-risk patients and diagnosis of asymptomatic HH in order to select patients for elective surgery.

Conflicts of Interest

The Authors report no conflicts of interest relevant to this article.

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