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Diaphragmatic Hernia after Minimally Invasive Esophagectomy

Keywords: Esophageal cancer; Diaphragmatic hernia; Esophagectomy; Outcomes

Abstract

Background: Diaphragmatic Hernias (DH) are a known, yet poorly studied, post-surgical complication of esophagectomy. The aim of this study was to analyze the Minimally Invasive Esophagectomy (MIE) experience at a single high-volume academic institution, in order to identify risk factors associated with DH.

Methods: we reviewed data from MIEs performed at our institution (July 2013 - January 2018). Patients who developed a DH at any time post operatively were compared to those who did not. We compared pre-, intra- and postoperative clinical variables of interest in the two groups using Fisher's exact test for all categorical variables and Mann-Whitney test for continuous variables.

Results: 103 patients underwent MIE during the study period; eight developed DH in a time frame ranging from one week to two years post operatively. All identified DH involved >1 intraabdominal organs other than the stomach; seven patients required reoperation. DH patients appeared to have lower Body Mass Index (BMI) and lower incidence of reported gastroesophageal reflux disease. Furthermore, the DH population tended to have an overall more advanced cancer stage (p=0.028) and a higher incidence of occult microscopically positive margins in the resected specimen (p=0.027). There were no statistically significant differences in intraoperative variables between the two groups, nor where there differences in incidence of postoperative complications other than DH.

Conclusion: DH occurred in approximately 8% of patients undergoing MIE. Lower BMI and more advance cancer stage appear to be significantly associated with DH, perhaps pointing towards more extensive dissection as a potential risk factor.

Introduction

Esophagectomy represents the mainstay of treatment for many esophageal malignant and benign conditions. Over the last two decades, an increasing number of surgical centers have adopted minimally invasive techniques in an effort to reduce the significant mortality and morbidity classically associated with this operation. The incidence of esophageal cancer in the western world is on the rise, with more than 17000 new cases in the US in 2018 [1]. The most common subtype in the US is adenocarcinoma, and Ivor Lewis Minimally Invasive Esophagectomy (MIE) has gained popularity as a particularly well suited technique to treat this disease, which prevalently involves the lower third of the esophagus. Some advantages of this approach include excellent magnified visualization for abdominal and thoracic lymphadenectomy and need for decreased conduit length, due to the intrathoracic location of the gastroesophageal anastomosis [2]. Randomized data have shown that MIE yields several advantages over open esophagectomy, such as fewer pulmonary infections, shorter LOS, and better short-term quality of life, without compromising the oncological quality of the resection [3].

As often happens, with new techniques come new benefits but also

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new complications. In fact, there is increasing evidence suggesting that MIE patients could be particularly prone to develop Diaphragmatic Hernias (DH), a known yet relatively rarely reported complication of open esophagectomy [4-7]. Messenger et al. performed a review of the literature available at the time which included 11 studies totaling 4669 esophagectomy patients, 16% being MIE and 84% open procedures. Their results suggested that MIE appears to have a higher incidence of DH when compared to open esophagectomy[8]. Results from several other series point towards the same conclusion [6,7]. A stronger level of evidence towards the same finding was achieved by a recent meta-analysis from the Netherlands, which showed that symptomatic DH occur more frequently after MIE compared to traditional esophagectomy, with a pooled incidence of 4.5% versus 1.0% [9].

Esophagectomy is inherently predisposed to formation of postoperative DH – the resective portion of any esophagectomy, in fact, entails disruption of the phrenoesophageal ligament, an important means of stabilization of the gastroesophageal junction. This results in loss of a physiological mechanism of retention of abdominal contents within the abdominal domain. Despite the increase in the incidence of DH after esophagectomy, there are limited data on the factors associated with this complication, nor is it well understood why using minimally invasive techniques increases its incidence. Various techniques have been used in an effort to mitigate its occurrence, such as tacking of intra-abdominal contents to the abdominal wall, crural tightening and pexy of conduit to the diaphragm[10]. However, there is no convincing evidence that any of the above listed procedures significantly decreases the incidence of DH.

The aim of this study was to determine the association of DH following MIE with pre-operative, intra-operative and post-operative factors.

Materials and Methods

Data source

Patients who underwent MIE between 2013 and 2018 at the University of Colorado Hospital were included. The dataset is collected and populated prospectively. Additional data that was specific for this study was collected retrospectively via chart review.

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Table 1: Inclusion and exclusion criteria.

Inclusion criteria	Exclusion criteria
Age < 18	Age < 18
Operation between 2013 and 2018	Planned laparotomy
Esophageal, esophagogastric and proximal gastric malignancies	Planned thoracotomy
Minimally invasive approach for both abdomen and chest	

Table 2: Baseline demographic and clinical characteristics.

	DH						
	No			Yes		P-value	
	No.	%	No.	%	No.	%	
Sex							
Male	83	87.37	6	75	89	86.41	0.297
Female	12	12.63	2	25	14	13.59	
BMI							
Median (IQR)	26.5	(24.30-29.30)	23.57	(22.80-26.51)	26.3	(24.19-29.09)	0.04
Comorbidity	84	88.42	6	75	90	87.38	0.265
Previous Surgery							
No	45	47.37	6	75	51	49.51	0.326
Yes	49	51.58	2	25	51	49.51	
Unknown	1	1.05	0	0	1	0.97	
Atrial Fibrillation	6	6.32	0	0	6	5.83	>0.999
Coronary Artery Disease	18	18.95	0	0	18	17.48	0.345
Anemia	19	20	0	0	19	18.45	0.346
Hiatal Hernia	33	34.74	2	25	35	33.98	0.713
Diabetes	14	14.74	0	0	14	13.59	0.594
Deep Vein Thrombosis	9	9.47	0	0	9	8.74	>0.999
Reflux	59	62.11	4	50	63	61.17	0.708
Hypertension	46	48.42	2	25	48	46.6	0.279
Steroids	12	12.63	0	0	12	11.65	0.591
GERD	73	76.84	3	37.5	76	73.79	0.028
Barret's Esophagus	41	43.16	1	12.5	42	40.78	0.137
Current Smoker	5	5.26	0	0	5	4.85	>0.999
Former Smoker	57	60	7	87.5	64	62.14	0.253
Pre-Operative Stage							
Stage 1	18	18.95	0	0	18	17.48	0.029
Stage 2	29	30.53	0	0	29	28.16	
Stage 3	32	33.68	6	75	38	36.89	
Stage 4	8	8.42	0	0	8	7.77	
N/A or Unknown	8	8.42	2	25	10	9.71	
Chemotherapy	75	78.95	8	100	83	80.58	0.349
Radiation							
No	23	24.21	0	0	23	22.33	0.256
Yes	71	74.74	8	100	79	76.7	
Unknown	1	1.05	0	0	1	0.97	
Neoadjuvant Treatment Complete							
No	4	4.21	1	12.5	5	4.85	0.241
Yes	71	74.74	7	87.5	78	75.73	
No chemo/radiation	19	20	0	0	19	18.45	
Unknown	1	1.05	0	0	1	0.97	
Chemoradiation							
No chemoradiation or chemotherapy only/radiation only	25	26.32	0	0	25	24.27	0.194
Yes	70	73.68	8	100	78	75.73	

BMI: Body Mass Index; IQR: Interquartile Range; GERD: Gastroesophageal Reflux Disease

We employed a systematic data collection on relevant preoperative and intraoperative variables, as well as postoperative morbidity up to the most recent outpatient follow up or inpatient admission. This study was approved by our institutional review board.

Inclusion criteria

This study was restricted to patients who underwent MIE for esophageal, esophagogastric and proximal gastric malignancies during the study period. Patients who underwent either a planned

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Figure 1: Appearance of the diaphragmatic hiatus during dissection. Notice the hiatal width necessary to safely pull the tubulized gastric conduit in the thorax.

laparotomy or a thoracotomy were excluded from the study, even if the remaining portion of the operation was performed with thoracoscopic surgery or laparoscopy. The DH group consisted of patients who developed a symptomatic diaphragmatic hernia or a sizable asymptomatic hernia after MIE. The non-DH group consisted of all patients who did not develop a hernia, and of those who developed small asymptomatic sliding hernias not involving intraabdominal organs other than the gastric conduit.

Baseline characteristics of patients

Baseline characteristics were compared between the groups of patients, including gender, Body Mass Index (BMI), preoperative comorbidities such as presence of hiatal hernias, Barrett's esophagus, Gastroesophageal Reflux Disease (GERD) and history of previous abdominal surgeries. Information on preoperative oncologic staging and neo-adjuvant treatment was collected as well. Finally, intraoperative variables were compared between the two groups, including operative time, anastomosis type, use of an omental flap to cover the anastomosis, conversion to open and use of DH mitigating techniques. The latter included the techniques of pexy of the transverse colon omental attachment to the abdominal wall and partial crural closure. All the procedures were performed as a team approach with a surgical oncologist performing the laparoscopic portion of the operation and a thoracic surgeon performing the thoracoscopic portion.

Outcomes

Short term surgical outcomes, such as bleeding, atrial fibrillation, Deep Vein Thrombosis (DVT), penumonia and leak were analyzed. Additional long term outcomes compared between the DH and the non-DH group included feeding tube complications and delayed gastric emptying. We also gathered information on oncological outcomes such as cancer histology on final pathology, margin status, number of lymph nodes retrieved and lymph node involvement.

Statistical analysis

Patients' baseline characteristics and outcomes were compared between the two groups using Fisher's exact test for all categorical variables and Mann-Whitney test for continuous variables. All data analyses and management were performed using Stata version 15.1 (StataCorp, College Station, TX, USA). Statistical significance was indicated by p < 0.05.

Results

Patient characteristics

During the study period, 103 patients were identified who underwent MIE for esophageal cancer. Baseline differences and comparison of pre-operative variables between the two groups are detailed in (Table 1 and 2). Median follow up was 390 days (IQR 97-895). Eight patients (7.7%) developed DH after MIE, seven requiring surgical repair. Patients in the DH group were found to have significantly lower BMI, lower incidence of reported GERD and more advanced pre-operative cancer stage compared to patients in the non-DH group. History of prior abdominal surgical procedures was found to be associated with lower incidence of diaphragmatic hernias only when small, asymptomatic, sliding hernias were included in the analysis. This did not remain true when DH (large symptomatic hernias) and non-DH groups where instead compared (Figure 1).

Outcomes

We found no significant differences in intraoperative variables between the two groups (Table 3). DH mitigating procedures where performed in four (50%) of the DH patients (three underwent pexy of the transverse colon omental attachment to the abdominal wall, one underwent pexy of the conduit to the crura) and in sixty-three (63.1%) of the non-DH patients. Operative attempts to prevent DH occurrence did not appear to be effective in decreasing its incidence (P=0.473). The overall incidence of postoperative complications (all-comers) was not significantly different between DH and non-DH patients (Table 4). Post-operative staging confirmed an overall more advanced cancer stage in the DH population. Furthermore, DH patients showed a higher incidence of positive margins. Of the three (37.5%) occultly positive margins in the DH group, two had positive distal gastric lesser curve margins and one had a positive radial esophageal margin. By comparison, five (5.26%) non-DH patients had positive margins. Patients who developed a symptomatic DH were significantly more likely to undergo a reoperation when compared to the non-DH group (Figure 2).

Discussion

Post-esophagectomy development of diaphragmatic hernia



Figure 2: Axial and coronal sections of CT imaging of DH in our case series.

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Table 3: Intra-operative variables.

	DH						
	No		Yes		Total		P-value
	No.	%	No.	%	No.	%	
Operative Time (minutes)							
Median (IQR)	473.5	(425-557)	420	(385-488)	471	(423-556)	0.103
Anastomosis							
Other	11	11.58	1	12.5	12	11.65	>0.999
Circular stapled	84	88.42	7	87.5	91	88.35	
Omental Flap							
No	14	14.74	0	0	14	13.59	0.656
Yes	79	83.16	8	100	87	84.47	
Unknown	2	2.11	0	0	2	1.94	
Conversion to Open	8	8.42	2	25	10	9.71	0.173
Operative Attempt to Prevent DH	60	63.16	4	50	64	62.14	0.473
Feeding Tube*	47	49.47	6	75	53	51.46	0.271

IQR: Interquartile Range; DH: Diaphragmatic Hernia

*at any point during the course of treatment

is a poorly understood and infrequently reported postoperative complication. In our study of 103 patients undergoing MIE at a single institution, approximately 8% developed a DH postoperatively. These occurred and became symptomatic between a few weeks to two years after the initial procedure. The majority of these required operative repair for acute symptoms.

Since recent increase in development and adoption of MIE techniques, there is a paucity of literature focusing on its longterm complications, such as DH. In addition, long term survival for esophageal cancer remains low, further complicating long term collection of postoperative data. The first report of DH after MIE in the English language literature dates back to 2004, when Aly et al. described a sizable hernia in the left chest of a patient 20 months after MIE [11]. The DH rate observed at our institution correlates well with those reported in some other series. Benjamin et al., for example, described 5.8% incidence of hernia after 120 MIEs, with more than 70% of the DH patients requiring operative repair [12]. Matthews et al. reported a 6.8% incidence of DH after their MIE which, of note, was remarkably higher than the 1.8% DH rate among their open esophagectomies [4]. Almost 90% of their patients with DH ended up requiring an operation, and 26% of the patients who had a repair developed a recurrence. Similar to what we observed in our series, the timing of their DH from the index operation varied widely, ranging from a few weeks to years, with a peak at 90-365 days after surgery.

Our results also show that more advanced cancer stage and positive margins appear to be significantly associated with DH, perhaps pointing towards more extensive dissection as a risk factor. This has been observed by other authors as well, with high T-stage in particular being a predictor of DH [4].

It has been previously described that extended iatrogenic enlargement of the hiatus during esophagectomy in order to facilitate passage of the gastric conduit and prevent conduit compression is a risk factor for DH [13]. While it is hard to quantify the extent of the dissection on retrospective review, it is not unreasonable to postulate that bulkier, more advanced disease of the gastroesophageal junction could prompt a surgeon to be more aggressive. The exact amount of dissection needed to achieve the best oncological outcome is an intraoperative judgment decision. Some authors have recently brought attention to this, raising the question of whether it is worth pursuing aggressive hiatal dissection at the expense of increased risk of DH when the evidence of decreased survival in the presence of positive circumferential margins is conflicting [14].

It is somewhat counterintuitive in the context of hernias that lower rather than higher BMI appeared to be significantly associated with DH. Yet, this matches the findings of other authors and could represent a consequence of more advanced disease or malnutrition, ultimately leading to poor healing and predisposing to herniation [15,16]. On the other hand, larger patients may have an intrinsically bulkier intestinal mesentery that could theoretically limit the ability of the large and small bowel to migrate into the chest.

The technical operative approach to MIE may influence the risk of DH as some data seem to suggest that Ivor Lewis MIE is particularly prone to forming DH. Gooszen et al. describe a 9.4% incidence of DH with this technique versus 2.3% with transhiatal MIE, 1.6% with McKeown and around 1% with their open counterparts [5].

As it commonly occurs when faced with this complication, we also repaired the majority (87.5%) of DH, since all but one of them were acutely symptomatic. We were able to perform laparoscopic repair in three patients (42.8%). Of the open repairs, one was converted due to inability to achieve reduction, and the rest were approached in an open fashion from the start for a variety of factors. Although DH repair after esophagectomy has been reported to be associated with a mortality as high as 20% in some series, we did not experience any mortality in our cohort, nor recurrences we are aware of [4].

Interestingly, intraoperative attempts at tacking the transverse colon omental remnant to the abdominal wall to promote adhesions and fix the most common organ to herniate did not appear to prevent the occurrence of DH. To our knowledge there is no method to date that has been reliably proven to decrease the incidence of DH after MIE. The approach we initially adopted to reduce herniation of intestinal contents was fixing the transverse colon omental remnant to the abdominal wall. This strategy is employed by other authors and has the benefit of not adding significant time or morbidity to the procedure [4,17]. However the data on its efficacy is lacking and this maneuver did not appear to reduce the incidence of DH as some patients still developed a DH despite the attempt. In more recent

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Table 4: Post-operative variables.

		DH					
		No Yes				P-value	
	No.	%	No.	%	No.	%	
Length of Stay (days)							
Median (IQR)	11	(9-15)	10.5	(9-12)	11	(9-15)	0.295
Post-operative Complications (any)							
No	34	35.79	0	0	34	33.01	0.123
Yes	60	63.16	8	100	68	66.02	
Unknown	1	1.05	0	0	1	0.97	
Bleeding	7	7.37	0	0	7	6.8	>0.999
Atrial Fibrillation	17	17.89	0	0	17	16.5	0.347
Deep Vein Thrombosis	7	7.37	0	0	7	6.8	>0.999
Feeding Tube Complication							
No	30	31.58	5	62.5	35	33.98	0.222
Yes	17	17.89	1	12.5	18	17.48	
N/A	48	50.53	2	25	50	48.54	
Delayed Gastric Emptying	16	16.84	2	25	18	17.48	0.626
Pneumonia	15	15.79	2	25	17	16.5	0.616
Leak	17	17.89	0	0	17	16.5	0.347
Stricture	10	10.53	1	12.5	11	10.68	>0.999
NSAID Use	15	15.79	0	0	15	14.56	0.599
Weight Gain	7	7.37	0	0	7	6.8	>0.999
Post-op Stage							
Stage 0	18	18.95	0	0	18	17.48	0.028
Stage 1	25	26.32	0	0	25	24.27	
Stage 2	23	24.21	5	62.5	28	27.18	
Stage 3	22	23.16	2	25	24	23.3	
Stage 4	1	1.05	1	12.5	2	1.94	
N/A or Unknown	6	6.32	0	0	6	5.83	
Histology							
Adenocarcinoma	89	93.68	8	100	97	94.17	>0.999
Squamous	2	2.11	0	0	2	1.94	
Other or Unknown	4	4.21	0	0	4	3.88	
Margins							
Negative	86	90.53	5	62.5	91	88.35	0.027
Positive	5	5.26	3	37.5	8	7.77	
N/A or Unknown	4	4.21	0	0	4	3.88	
Lymph nodes retrieved							
Median (IQR)	20	(14-28)	24	(14.5-33.5)	21	(14-28)	0.55
Lymph nodes positive							
Median (IQR)	0	(0-1)	0	(0-4)	0	(0-1)	0.413
Reoperation							
No	83	87.37	1	12.5	84	81.55	<0.001
Yes	7	7.37	7	87.5	14	13.59	
Unknown	5	5.26	0	0	5	4.85	

IQR: Interquartile Range; Nonsteroidal anti-inflammatory drug

times we began using anterior crural closure in an attempt to narrow the hiatus, since some authors advocate that prophylactic cruroplasty should be the standard of care for this patient population [5]. This technique is used frequently by other centers, however it has some disadvantages; for example crural closure is more easily achieved from the abdomen and therefore may necessitate re-positioning the patient and re-entering the abdomen after the thoracic portion of the procedure is completed. In order to avoid this inconvenience we now perform a modification of the technique originally described by Wells, et al. [18]. We start with placing crural sutures laparoscopically from the abdomen after completion of the abdominal dissection. The ends of the untied sutures are clipped to the conduit itself so that they can be secured and pulled into the chest with the pull through. Finally, after the anastomosis is complete, the crural sutures are tied from the chest. Alternatively, one of the surgeons in our group prefers instead repositioning the patient after the thoracic portion of the MIE is completed and perform from the abdomen crural closure from the abdomen, also fixating the conduit to the hiatus with interrupted sutures. While it has been hypothesized that the latter might disturb vascularization of the conduit, we have not experienced this in our series [19]. It is too early in our experience to determine if these additional maneuvers will make a difference in post-op MIE DH. Some authors advocate for primary closure and reinforcement with

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biological mesh sutured to the gastric wall as a preventive measure, but we have not yet tried this approach [20].

The major strength of our study is the granularity of our database, which allowed for in-depth review of every studied complication. Furthermore all the surgeons who perform MIEs at our institution favor Ivor Lewis with minimal interpersonal variations in technique; this allowed for minimal intraprocedural confounders when comparing surgical outcomes.

On the other hand, the most significant limitations of our study reside in its retrospective nature and in the small size of the DH group, which limits the statistical power. It is also worth mentioning that while we had a chance to see and treat all patients with a symptomatic hernia, many of our patients continue their oncological follow up outside of our institution. This likely translates in us failing to capture at least some of the small asymptomatic diaphragmatic hernias incidentally found during follow up.

The literature on DH after MIE is scarce and, due to the low incidence of this complication, lack of power is a recurrent issue. In this setting, we believe that data from a large volume tertiary center constitutes a meaningful addition to the knowledge on this topic. Our results also suggest that intraoperative attempts at tacking the transverse colon omental remnant to the abdominal wall are not effective in preventing DH. This is relevant, as it highlights the need to focus on different strategies to mitigate this complication.

Conclusion

Our results confirm that DH occurs in a non-negligible percentage of patients undergoing MIE. Lower BMI, more advance cancer stage and positive margins appear to be significantly associated with DH, perhaps pointing towards more extensive dissection as a risk factor. Efforts to reduce post-minimally invasive esophagectomy DH deserve further investigation.

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