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REVIEW ARTICLE

Diaphragmatic hernia following esophagectomy for esophageal cancer: A systematic review

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Summary

Purpose: *Diaphragmatic hernia following an esophagectomy for esophageal cancer (EC) can be both an early and late complication. The esophageal hiatus within the diaphragm is disrupted during the operation. However, the incidence of Post-Esophagectomy Diaphragmatic Hernia (PEDH) is unknown. PEDH can be life-threatening and surgical treatment is challenging. However, all PEDH do not require surgery. The rate of EC diagnosis is rising. Therefore, esophageal surgery, particularly esophagectomy, is gradually increasing. Undoubtedly, the numbers of PEDH increase as well.*

Methods: *This review describes the presentation and diagnosis of PEDH after surgery for esophageal malignancy, as well as the management options for PEDH.*

Results: *Fifteen papers regarding PEDH have been published. There are many different surgical approaches to complete an esophagectomy, while there are different approaches to repair PEDH.*

Conclusion: *Upper GI surgeons need to have an index of suspicion for PEDH. They must investigate and operate these patients if this complication develops, since an immediate surgery has a high mortality and poor outcome.*

Key words: *diaphragmatic hernia, esophagus, esophageal cancer, esophagectomy*

Introduction

Esophageal cancer (EC) is rising worldwide , with approximately 1700 new cases in the United States during 2015 and an estimated 32% of these patients presenting with locally advanced disease [1,2]. According to the National Comprehensive Cancer Network (NCCN) guidelines, complete surgical resection in eligible patients with EC is the cornerstone for long-term survival [3,4]. Moreover, advances in multimodality treatment and early detection have led to a significant improvement in survival [5]. Nevertheless, during esophagectomy, the normal anatomy of the diaphragmatic hiatus is disrupted, resulting in a risk of both early and late complications including post-esophagectomy diaphragmatic hernia (PEDH).

The true incidence of PEDH is still unknown. According to the literature, the reported incidence of PEDH varies widely from 0.7% to 26% [6,7]. This is likely because many patients are asymptomatic and also because many studies have reported only the rate of PEDH requiring surgical intervention. The magnitude of this complication is very important because some PEDHs lead to life-threatening events. However, it is unclear whether all PEDHs require a repair. Surgical treatment is always challenging, requiring an open or laparoscopic operation.

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We completed the present review of the articles published in MEDLINE database to examine the incidence, clinical presentation, and diagnosis of diaphragmatic hernia after esophagectomy for EC. Additionally, we assessed possible differences in the risk of PEDH related to different surgical approaches for esophagectomy. Finally, we describe the different surgical management options for this complication.

Methods

Search strategy

A comprehensive review of the literature was conducted from Medline, Scopus Embase, Web of Science, and the Cochrane library. The search terms were restricted to the following keywords in different combinations: "Diaphragmatic hernia", "Esophagectomy", "Oesophagectomy", and "Complications postoperative". Cross references and grey literature were also studied. We reviewed the electronic literature and synthesized the findings to present the following review of diaphragmatic hernia following esophagectomy for EC. The last search was completed on June 10, 2017.

Study selection

Titles and abstracts were initially screened. In our review, the literature search was conducted to identify articles that met the following criteria: (1) the reported procedure was open or laparoscopic esophagectomy for cancer in adults, (2) other intraoperative or postoperative complications were clearly mentioned, (3) patient demographics and (4) description of the diagnosis and treatment which was followed for the PEDH were indicated. Studies were excluded for the following criteria: (1) duplicate publication, (2) case reports and small case series, (3) editorials, review articles, and letters to the editors.

Identified studies

The literature search resulted in 5485 studies from PubMed. After initial screening for both the titles and abstracts, 5050 non-eligible studies were excluded. The full text of potentially eligible ones (n=435 were fully analyzed. After a complete evaluation of these papers and exclusion of overlapping series, 17 publications were suitable for this review and 15 studies were finally included in the review (Figure 1).

Results

Fifteen papers regarding diaphragmatic hernias following esophagectomy have been published. The number of patients in each paper varied from 5 to 2182, while the incidence of diaphragmatic hernia varied from 0.69% to 19.4%. All papers included more male patients who underwent esophagectomy and presented with PEDH. Patients undergoing esophagectomy and experiencing diaphragmatic hernia were mostly in the 6th and 7th decades of life. Unfortunately, the body mass index (BMI) of the patients at esophagectomy was reported in only 4 studies.

The stage of tumor, its histology, and the radiological findings determine whether a patient will be treated with neoadjuvant chemotherapy, neoadjuvant chemoradiotherapy, or surgery. This information included in the studies is displayed in Table 1. The majority underwent esophagectomy for adenocarcinoma. The location of the tumor was reported in few studies.

There are many methods to complete an esophagectomy, including open, minimally invasive, and robotic. In addition, patients may have an Ivor Lewis esophagectomy, a McKeown esophagectomy, or a transhiatal esophagectomy. The clinical features of the original esophagectomy were reviewed to explore any possible perioperative factors that contributed to the development of a post-esophagectomy hernia.

Diaphragmatic hernia can occur in acute or late period, with cases reported from 2 days of initial surgery to 12 years following surgery. Some are symptomatic and require immediate surgical

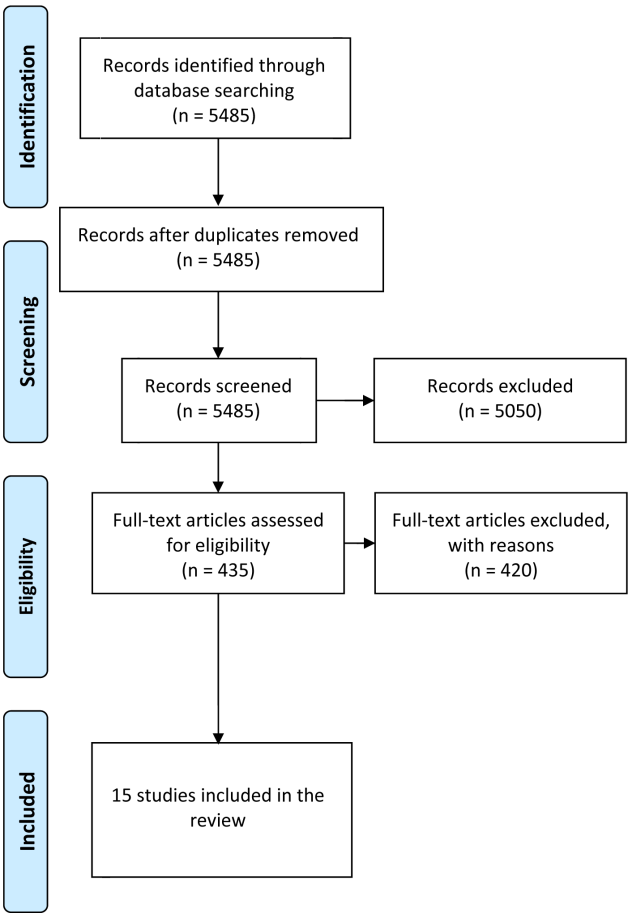

Figure 1. Flow chart of the study.

Table 1. Treatment, staging, tumor location, procedure type and histology prior to diaphragmatic hernia

Author	*Neoadjuvant tx*	*Stage*	*Tumour location (upper v middle v lowe1/3)*	*Procedure type (Open: Ivor Lewis, McKeown, Transhiatal vs MIE: Ivor Lewis vs McKeown vs Transhiatal)*	*Histology (adeno v SCC v other)*
Benjamin et al	71.4% chemorad	NR	NR	MIE	87% adeno, 7% SCC, 4% other
Crespin et al	66% chemo rad	82% stage 2/3	NR	Lap assisted THE	NR
Erkman et al	60% chemorad, 20% chemo, 20% none	80% stage 3A	NR	40% "three hole esophagectomy", 60% lap assisted esophagectomy	NR
Matthews et al	NR	11% T4	NR	2 %(4) open 2 or 3 stage esophagectomy, 10 %(22) lap hybrid esophagectomy, 7 %(5) MIE, 3 %(4) total gastrectomy.	29 (5.9 %) adeno, 6 (5.8 %) SCC
Messenger et al	8 neoadj tx	MIO: 2 HGD, 1 cPR, 22 I, 48 IIA, 15 IIB, 108 III, 8 IV Open: 2 HGD, 2 cPR, 14 I, 11 IIA, 12 IIB, 26 III, 1 IV	NR	205 open: (Ivor-Lewis 144 (70.3 %), transhiatal 42(20.5 %), McKeown 19(9.3 %)); 68 MIE	63(92.6%) Adeno MIO, 165(80.5%) Adeno open
Narayanan	88.9% chemorad	8 % stage 0 (mostly HGD), 13 % stage I, 22 % stage II, 54 % stage III (mostly T3N1), 3 % stage IV disease	NR	9 THE, 1 McKeown	8 adeno, 1 SCC
Willer et al	27 (69.2%) neoadj tx	3 T2N0M0R0, 1 T3N1M0R0, 1 T1N1M0R0	NR	19 MIE, 20 open TTE	30 adeno, 6 SCC, 3 other
Price et al	9 chemorad	2 TNM stage 0, 5 py0, 1 IB, 1 pyIIB , 1 IIIA, 4 pyIIIA, 1 stage IV	NR	Ivor Lewis 9, Transhiatal 5, Substernal colon interposition 1	13 adeno, 1 SCC, 1 HGD
Ganeshan et al	NR	NR	NR	12% (32) Ivor-Lewis, 24% (25) transhiatal esophagectomy, 17% (7)three-field (McKeown) esophagectomy, 10% (3)MIE	58 adeno, 5 SCC, 4 other
Brenkman et al	12 None, 24 Chemo, 9 Chemorad	4 T0, 9 T1, 8 T2, 27 T3, 1 T4	0 Upper, 2 Middle, 21 Lower, 22 GEJ	5 (4) 2 (4) 5 (11) Open: IL 5, MCK 2, TH 5, MIE: IL 13 MCK 17, TH 3	NR Only incl histology for all 657, not the 45
Ulloa Severino et al	8 (25%)None,19 (59.3%) chemo, 5 chemorad	4 (9.3 %) pT0, 5 (15.6 %) pTIA, 7 (21.8 %) pTIB, 5 (15.6 %) pTIIA, 5 (15.6 %) pTIIB, 6 (18.7 %) pTIIIA	7 (21.8 %) Middle, 9 (28.1 %) Lower, 16 (50%)GEJ	390 MIE Ivor Lewis	Adeno 24 (75%), SCC 8 (25%)

NR: Not reported, MIE: minimally invasive esophagectomy, M: month, SCC: squamous cell carcinomas, THE: transhiatal esophagectomy, GEJ: gastro-esophageal junction, HGD: high grade dysplasia

Table 2. Preoperative, perioperative and postoperative results

Author	*Time after oesophagectomy*	*Emergency vs elective*	*Repair method (Suture vs mesh)*	*Operation method (lap vs open)*	*Recurrence (yes/no)*
Benjamin et al	3.4M (1-45M)	20% emergent; 80% elective	40% mesh	Lap	20% Yes
Crespin et al	7.5 M (2D-97M)	All emergency	Open: 3 mesh, 1 suture Lap: all 3 mesh	57%(4) open; 43% (3) lap	1 Open suture repair
Erkman et al	21.4 M	All emergency	3 suture; 1 mesh	Lap	No
Matthews et al	6(17 %) < 7 days of their index surgery; 6 (17 %) 7-90 days, 10 patients (29 %) 90 days-1 year, 6 patients (17 %) 1-2 years; 2 (6 %) 2-3 years; 5 (14%) > 5 years from surgery	20 (57%) emergency, 12 (43%) non-urgent 5 (14%) > 5 years from surgery	24 suture, 7 mesh 12 (43%) non-urgent	Open 12 (39%), Lap 11 (35%), Converted to open 8 (26%)	7 (26%)
Messenger et al	16.5M (6-114M)	5 emergency, 6 elective	Suture (6), mesh (4), omentopexy to anterior abdominal wall without hiatal closure(1)	7 Lap, 4 open	2 (18%)
Narayanan	2.4 years	3 emergency, 6 non urgent	All 9 mesh	All 9 open	No
Willer et al	13.8M (3-20M)	3 elective, 2 conservative	2 suture, 1 mesh 2 conservative	2 lap, 1 open	No
Price et al	21M (3D -12 Y)	2 emergency, 13 elective	2 mesh, 13 suture	open	2
Ganeshan et al	2Y	3 emergency, 9 elective	9 mesh	8 open, 1 lap	4
Brenkman et al	20 M (0-101M)	16 emerg, 10 elective, 19 conservative	Mesh 5. Others suture 19 conservative 20 (62.5%)mesh,	Emerg: Open 12, lap 4. One conversion occurred. Elective: 4 open, 6 lap.	4 (15%) after surgical repair, regardless of mesh (1 mesh vs 3 no mesh) & surgical procedure (3 laparotomy vs 1 laparoscopy). HH recurrence redo operation in 2 patients, 2 conservatively.
Ulloa Severino et al	10M (3D-96M)	6 (19%) emerg	12 (37.5%) primary suture	19 (59 %) lap, 5 (15.6%) midline, 6 (18 %) required conversion to open laparotomy	6 (19%)
Bronson et al	13.7M (1.8–55.6M)	4 emerg, 5 elective	9 mesh	7 lap, 2 open	1 recurrence
Sutherland et al	1 <30D, 1 30-60D, 3 60–120 d, 2 >120 days	2 emerg, 5 elective	7 Primary suture	? Robotic	2
Vallböhmer et al	8M (0.3-30M)	5 emergency, 2 elective	6 Primary suture, 1 mesh	7 Open	NR
van Sandick	4 <7D,5 at 12,19,23,24,44M	NR	NR	5 open, 1 thoracotomy	No

repair, while others are repaired electively or conservatively, as shown in some studies. This is in line with the Society of American Gastrointestinal and Endoscopic Surgeons guidelines of the treatment of asymptomatic hiatus hernia in the general population [8]. The repair method includes the open abdominal approach, laparoscopic approach, and thoracotomy approach (Table 2). The majority of patients underwent a primary suture closure of the diaphragmatic defect, but 13 studies included patients who had a mesh repair. The reason for primary closure or mesh repair was not identified clearly. Four studies did not show any diaphragmatic hernia recurrence. Of those who reported recurrence, this varied between 11-26%.

Discussion

Esophagectomy is the cornerstone of multimodality treatment for EC. This includes dissection and removal of the esophagus, followed by restoration of the alimentary tract with a gastric tube in most patients [9,10]. The two most used routes for esophageal reconstruction after esophagectomy are the posterior mediastinal and the retrosternal route. The mediastinal space is preferred for immediate reconstructions after esophagectomy and the retrosternal approach is used for delayed construction. The retrosternal route might be an alternative option for reconstruction; however, this approach has a major disadvantage, which is the potential risk for graft compression at the level of the thoracic inlet. Moreover, there is lack of data about the correlation of the incidence of PEDH and the above-mentioned reconstruction routes.

Our study evaluated all published papers so far, relating to PEDH following esophagectomy for EC. Diaphragmatic hernia after esophagectomy was first reported in 1987 by Terz and colleagues [11].

A diaphragmatic hernia is the abnormal movement of the abdominal contents into the thoracic cavity. It is an infrequent complication of both thoracic and abdominal surgery. Its incidence is increasing, but the reported incidence is widely variable, ranging from 0.69% to 19.4% from our review of the literature. Variation in surgical approaches and techniques may explain to some extent the variation in the incidence of diaphragmatic hernia. The method of estimating the incidence of diaphragmatic hernia is important to consider. Because, diaphragmatic hernia occurs over variable periods of time, a time-to-event analysis is required to estimate their frequency. Furthermore, because of the very real and competing risk of death after treatment for EC, time-to-event analyses should account for the competing risks [12].

There is no definition regarding the questions of "what is an acute diaphragmatic hernia'' and "what is a late diaphragmatic hernia''. There are varying periods of follow-up and methods of estimating and reporting incidence. Similarly, the method of detection could be a chest x-ray or a CT of the thorax. This complication is potentially life-threatening due to bowel compromise, while others are asymptomatic. Symptomatic patients are usually treated immediately upon diagnosis, but there is no consensus on the treatment of asymptomatic patients who are often diagnosed incidentally. The risk of possible obstruction and ischemia must be weighed against the risk of surgery in these patients, particularly in patients whose life expectancy is reduced due to metastatic disease. Erkmen et al advise surgical treatment of a post-esophagectomy hiatal hernia for any patient who presents with symptoms such as dyspnea, abdominal pain, early satiety, or nausea. In asymptomatic patients with minimal herniation of bowel contents into the chest, they feel there is a role for active observation obtaining a thoracic CT scan every 6 months [13]. Because evidence concerning the management of symptomatic hiatus hernias after esophagectomy is lacking, it remains unclear whether the Society of American Gastrointestinal and Endoscopic Surgeons guidelines should also be followed for this population. Brenkman et al reported that conservative treatment was successful in 90% of their symptomatic patients. Whether to perform an operation in these patients should therefore depend on the severity of symptoms, patient fitness, and prognosis, taking into account the outcomes of the operation for hiatus hernia in the emergency setting [14].

Diaphragmatic hernias were first described in case reports and small case series, but in recent years, larger studies have been reported. The largest study so far by Price et al reviewed 2,182 esophagostomies from 1988 to 2009 and found no difference in the incidence of diaphragmatic hernia between Ivor Lewis transthoracic esophagectomy and transhiatal esophagectomy, with rates of 0.92 and 0.83%, respectively [6]. Ganeshan et al also found that 24% of patients who developed diaphragmatic hernia were subjected to post-transhiatal esophagectomy compared with 12% of patients who had undergone Ivor-Lewis esophagectomy [15]. Kent et al who analyzed 1,075 oesophagectomies, found a higher incidence of diaphragmatic hernia occurrence in minimally invasive esophagectomy (2.8%), compared with open approach (0.8%) [16]. This likely occurs because of an increasingly dilated diaphragmatic hiatus secondary to insufflation as well as high mediastinal dissection with

mechanical arms in the case of robot-assisted esophagostomies [17].

Most hernias occurred in patients who underwent transhiatal esophagectomy because of the technical necessity of widening the esophageal diaphragmatic hiatus to mobilize the gastric conduit into the chest and to safely perform the mediastinal dissection [15]. If this is necessary, an anterior incision in the diaphragm is advocated rather than a lateral extension [18]. At the end of the procedure, the integrity of the diaphragm must always be checked. No preventive measures performed at the time of esophagectomy have been proven effective at reducing the incidence of hernia [19].

Both early and long term outcomes following esophagectomy are improving. With improvements in overall survival resulting from the routine use of neo-adjuvant treatment and modern-day esophageal cancer operations, the development of hiatus hernia after esophagectomy is becoming more relevant.

Hiatal herniation occurs as a result of a combination of factors, including negative intra-thoracic and positive intra-abdominal pressure. Peritoneal adhesions that form due to abdominal surgery serve to anchor abdominal viscera and secure the hiatus around the conduit, but in their absence, the viscera are drawn superiorly and progressively dilate the defect, facilitating their herniation into the thorax. This is relevant in laparoscopic surgery where adhesion formation is reduced in comparison to open surgery and may predispose to an increased risk of herniation following minimally invasive approaches [7]. Increasing intra-abdominal pressure with early mobilization as part of an enhanced recovery program could be another factor. Other studies have suggested the BMI of patients, pre-existing hiatal hernia, and radical surgical resection of the diaphragmatic crura are risk factors. Patients with an elevated BMI (>25 kg/m^2) may be less prone to PEDH. Although the exact reasons are not clear, it is possible that increased intra-abdominal contents in these patients may either obscure the hiatus, helping to prevent herniation or lead to abdominal contents to be less mobile, which could prevent PEDH [15]. Another recent study suggested the incidence is increasing due to improved survival associated with neo-adjuvant oncological therapies [16]. PEDH rates were highest in hybrid operations (10.4%) and minimally invasive esophagectomy (MIE) procedures (6.8%), perhaps going against this hypothesis [20].

The incidence of PEDH is low overall. Diaphragmatic hernia can occur following minimally invasive esophagectomy and may be underreported. MIE appears to have a higher incidence of postoperative herniation when compared to the traditional open esophagectomy [21,22]. Urgent repair of postoperative hernias containing abdominal viscera is important to prevent devastating complications. The technique of repairing the diaphragmatic hiatus primarily with a suture is effective in most cases, preventing recurrence without compromising the neo-esophagus. However, Narayanan et al advocated the use of a biologic mesh which is equally effective and results in fewer complications [23]. The repair can be completed by laparoscope, open surgery, or thoracoscope. The benefits conferred by laparoscopy include better visualization of the right gastroepiploic artery supplying the gastric conduit, minimally invasive evaluation of the field for metastasis and a shorter recovery time [13].

Messenger et al, who described the UK's experience, report a PEDH rate of 13.2% following MIE. This appears high, but several other recent studies report a similar magnitude following their initial experience with MIE. The rate following open esophagectomy (1.0%) is comparable to the rates reported elsewhere in the literature. All of their PEDH were symptomatic and required repair. Furthermore, more than half of the cases following MIE occurred in the early post-operative period (<30 days) [22]. At the time of repair, all were found to have occurred to the left of the conduit, consistent with the findings of previous studies where right-sided herniation has rarely been noted [16,24]. One theory suggests that the staple line along the lesser curve of the gastric conduit promotes adhesion formation to the right crus more readily than that of the smooth, serosal surface of the greater curve to the left crus, thus preventing herniation of the intra-abdominal viscera. In addition, the left lobe of the liver may also act as a mechanical barrier.

Given the increased incidence of PEDH with MIE, several centers have recommended suture fixation of the conduit to the crura. There has been no direct comparison of the rates of PEDH between conduit fixation and non-fixation, although centers who perform routine fixation report the rates of 2.8-7.9% [16,19].

Messenger et al report it is safe to perform a laparoscopic repair of a PEDH following MIE, even in the acute setting as long as the patient does not experience significant cardiopulmonary compromise. It is important to remember that not all hernias can be repaired via an abdominal approach, either laparoscopic or open, and that the surgeon should be prepared to undertake a thoracotomy in cases where intra-thoracic adhesions prevent abdominal reduction of the contents. The key to any successful hernia repair is a tension-free

closure, which is best achieved by complete mobilization of the crura prior to the suture apposition. PEDH repair is a particularly high risk procedure, as achieving a snug closure around the conduit has to be weighed against the potential for vascular compromise. Evidence for the superiority of mesh reinforcement over suture apposition alone for primary hiatus hernia is limited to 2 small-scale randomized controlled trials that demonstrate a reduction in short-term recurrence rates [25,26]. Many surgeons still have concerns over the potential for visceral erosion. For this reason, Mesh placement was avoided in the majority of early postoperative diaphragmatic hernias where the need for an adequately vascularized conduit was at its most crucial. If tension-free closure cannot be achieved due to the size of the hiatal defect, then omentopexy alone may suffice. The recurrence rate of 18% in this study compares favorably to other series where rates of 13-44% have been reported with a similar length of follow-up [6,15,16].

Given the potential for morbidity associated with corrective surgery, careful thought needs to be given when deciding which patients require surgical intervention [27]. However, this finding has to be balanced against the significant mortality rate (20 to 80%) associated with patients who present with a complicated diaphragmatic hernia [28]. There is currently very little data on mesh repair for hiatal hernias after esophagectomy. Prospective randomized data on the use of mesh in conventional para-esophageal hernias demonstrates fewer short-term recurrences and fewer symptomatic recurrences even at 5 years [29].

In conclusion, meticulous careful thought is needed to identify surgical techniques to prevent diaphragmatic hernia forming when both open and minimal access esophagectomy are performed. Upper GI surgeons need to have an index of suspicion to investigate and operate these patients for this complication, as immediate surgery has a high mortality and poor outcome.

Authors' contributions

MH and AA: conceived the idea and prepared the manuscript.

II, ES and DC: critical revision of the article for important intellectual content and final approval of the article.

Conflict of interests

The authors declare no conflict of interests.

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