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Looking Beyond Age and Co-morbidities as Predictors of Outcomes in Paraesophageal Hernia Repair

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Abstract
Introduction Paraesophageal hernia (PEH) repair is a technically challenging operation. These patients are typically older and have more co-morbidities than patients undergoing anti-reflux operations for gastroesophageal reflux disease (GERD), and these factors are usually cited as the reason for worse outcomes for PEH patients. Clinically, it would be useful to identify potentially modifiable variables leading to improved outcomes.
Methods We performed a retrospective analysis of a representative sample from 37 states, using the Nationwide Inpatient Sample database over a 5-year period (2001–2005). Patients undergoing any anti-reflux operation with or without hiatal hernia repair were included, and comparison was made based on primary diagnoses of PEH or GERD. Exclusion criteria were diagnosis codes not associated with reflux disease or diaphragmatic hernia, emergency admissions, and age <18. Primary outcome was in-hospital mortality. Two sets of multivariate analyses were performed; one set adjusting for pre-treatment variables (age, gender, race, Charlson Comorbidity Index, hospital teaching status, hospital volume of anti-reflux surgery, calendar year) and a second set adjusting further for post-operative complications (splenectomy, esophageal laceration, pneumothorax, hemorrhage, cardiac, pulmonary, and thromboembolic events, (VTE)).
Results Of the 23,458 patients, 6,706 patients had PEH. PEH patients are older (60.4 vs. 49.1, $p<0.001$) and have significantly more co-morbidities than GERD patients. On multivariate analysis, adjusting for pre-treatment variables, PEH patients are more likely to die and have significantly worse outcomes than GERD patients. However, further adjustment for pulmonary complications, VTE, and hemorrhage eliminates the mortality difference between PEH and GERD patients, while adjustment for cardiac complications or pneumothorax did not eliminate the difference.
Conclusions While PEH patients have worse post-operative outcomes than GERD patients, we note that differences in mortality are explained by pulmonary complications, VTE, and hemorrhage. The impact of hemorrhagic complications on this group underscores the importance of careful dissection. Additionally, age and co-morbidities alone should not preclude a patient from PEH repair; rather, attention should be focused on peri-operative optimization of pulmonary status and prophylaxis of thromboembolic events.

Keywords Paraesophageal hernia · Hiatal hernia · GERD · Gastroesophageal reflux disease · Nissen fundoplication · Anti-reflux · Surgical outcomes

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Introduction

Paraesophageal hernia (PEH) is defined as a protrusion of the gastric fundus through the diaphragmatic hiatus while the lower esophageal sphincter remains in its normal anatomic position (type II hiatal hernia).[1] In a type III hiatal hernia, both the fundus and the lower esophageal sphincter herniate into the thorax. The majority of PEHs are actually type III (90%).[2] PEHs account for only 5–10% of all hiatal hernias; yet, they are important because they represent a potentially serious disease. The majority of

PEHs are asymptomatic but they do pose a significant risk for the patient in terms of life threatening complications including hemorrhage, strangulation, volvulus, and perforation. In the past, surgeons agreed that once diagnosed, regardless of presence or absence of symptoms, a PEH should be repaired.[3] Recent data has shown that a more selective approach may be implemented when considering surgical repair of PEH.[4]

PEH repair is a technically challenging operation. This may be due to the large amount of herniated contents, need for reduction and resection of a large hernia sac, consideration of a potentially fore-shortened esophagus, and the need to close a large hiatal defect.[2,3] Considerable debate exists regarding the technical specifics of this operation. The relative heterogeneity in technique has resulted in numerous studies, institutional series, and reports in the literature. There is an ongoing effort to identify and establish uniform technique(s) that would ideally result in improved outcomes in terms of recurrence and other quality-of-life outcome variables. Despite the differences in techniques, it seems that the laparoscopic approach to PEH repair and management of GERD has replaced open repair.[4–9]

PEH patients are typically older with more co-morbidities than patients undergoing anti-reflux operations for gastroesophageal reflux disease (GERD).[2,3,5] Based on these observations, it makes intuitive sense that PEH patients may have worse outcomes compared to GERD patients undergoing similar foregut surgery. It is a generally accepted surgical dogma that older patients and those with co-morbidities are subjected to a potentially higher surgical risk. However, there is a paucity of statistically rigorous studies that examine the relationship between traditional surgical risk factors (such as age and co-morbidities) and clinical outcomes in patients undergoing foregut surgery for PEH or GERD on the population level. It would be useful to identify specific variables in an effort to improve selection, risk stratification, and optimization of patient outcomes. The purpose of this study is two-fold: to better characterize PEH patients compared to GERD patients undergoing foregut surgery and to identify any potentially modifiable risk factors to improve outcomes.

Methods

Data Source

We performed a retrospective analysis of a representative sample from 37 states using the Nationwide Inpatient Sample (NIS) database over a 5-year period (2001–2005). The NIS compiles discharge data from inpatient hospitalizations from 20% of all hospitals from 37 participating states, maintained by the Agency for Healthcare Research and Quality as part of the Healthcare Cost and Utilization Project-3. It consists of roughly 7 million patient discharge records per year, originating from approximately 1,000 different hospitals per year, although not necessarily the same hospitals each year. Data available within the NIS include patient and hospital demographics, payer information, treatment and concomitant diagnoses, inpatient procedures, inpatient mortality, and length of stay. The Johns Hopkins Institutional Review Board deemed this public-domain anonymous data set as exempt from review.

Patient Selection

Patients undergoing any anti-reflux operation with or without PEH repair were included in the analysis. Comparison was made based on primary diagnoses of PEH or GERD. This was accomplished by searching for the relevant ICD-9 diagnosis and procedure codes (Table 1). ICD-9 codes 44.65, 44.66, and 44.67 were used to identify patients who underwent an anti-reflux procedure. Since code 44.65 is a very general description, we included any records with this code (44.65) only if they also included diagnosis codes for esophagitis, gastroesophageal reflux, esophageal ulcer, diaphragmatic hernia and diaphragmatic hernia with obstruction (530.10, 530.11, 530.19, 530.81, 530.20, 553.3, 552.3). Procedure codes associated with a code for thoracic repair of diaphragmatic hernia (530.8) were excluded from our analysis as well. For all procedure codes, esophageal cancer (150.0–150.5, 150.8–150.9) and gangrene (551.3) were excluded. Other exclusion criteria included emergency admissions and age <18. Our primary outcome was in-hospital mortality.

Statistical Analysis

Two sets of multivariate analyses were performed. The first set adjusted for pre-treatment variables—age, gender, race,

Table 1 ICD-9 Codes Used for Patient Selection

Code	Description
44.65	Esophagogastroplasty
44.66	Esophagogastric sphincteric competence
44.67	Same as above, laparoscopic
530.10	Esophagitis
530.11	Reflux esophagitis
530.19	Other esophagitis
530.20	Ulcer of esophagus without bleeding
530.81	Esophageal reflux
553.3	Diaphragmatic hernia
530.0	Achalasia and cardiospasm
552.3	Diaphragmatic hernia with obstruction
551.3	Diaphragmatic hernia with gangrene

Charlson score, hospital teaching status, hospital volume of anti-reflux surgery, and calendar year. The second set adjusted for peri-operative complications—splenectomy, esophageal laceration, pneumothorax, hemorrhage, cardiac, pulmonary, and thromboembolic events (VTE).[10]

Analysis was performed using the software package STATA/MP 10 (College Station, Texas). Bivariate analysis of categorical data was performed using the Chi-Squared test. Analysis of continuous data was performed using the Student's *t* test. Multivariate analysis was performed using multiple logistic regression models, adjusting for age, gender, race, Charlson score, hospital teaching status, elective status, year of procedure, and type of procedure. A p value of <0.05 was considered to be statistically significant.

Results

Patient Characteristics

Patients (23,458) underwent foregut surgery for GERD and/or PEH. In the univariate analysis, of the 23,458 patients, 6,706 (28.6%) patients had PEH. The mean age of patients was 52.3 (median age was 52); 14,670 (62.8%) patients were women; 14,111 (87.9%) patients were white, 676 (4.21%) black, and 838 Hispanic (5.22%); 10,921 patients (46.6%) were treated at teaching hospitals (Table 2). In-hospital mortality for all patients was 0.38% (88 patients). Two hundred twenty-nine (0.98%) patients required splenectomy; 132 (0.56%) patients underwent laceration repair; 210 (0.90%) patients were diagnosed with pneumothorax; 1,549 (6.6%) patients underwent unexpected re-operation; 594 (2.53%) patients experienced hemorrhagic complications; 157 patients (0.67%) had wound-related complications; 703 (3%) patients had obstructive complications; 1,007 (4.29%) patients had pulmonary complications; 254 (1.08%) had cardiac complications; 111 (0.47%) patients had thromboembolic complications. Mean length of stay was 3.4 days with a median of 2 days (Table 2).

Table 2 Univariate Analysis: Patient Demographics and Adverse Outcomes—All Patients

Variable	*N*	%
All patients (total *N*)	23,458	
PEH	6,706	28.6
Age in years	52.3 (mean)	52 (median)
Female gender	14,670	62.8
Race—White	14,111	87.9
Race—Black	676	4.21
Race—Hispanic	838	5.22
Teaching hospital	10,921	46.6
In-hospital mortality all patients	88	0.38
Splenectomy	229	0.98
Laceration repair	132	0.56
Pneumothorax	210	0.90
Unexpected re-op	1,549	6.6
Hemorrhagic	594	2.53
Wound related	157	0.67
Obstructive	703	3
Pulmonary	1,007	4.29
Cardiac	254	1.08
Thromboembolic	111	0.47
LOS in days	3.4 (mean)	2 (median)

LOS Length of stay

PEH vs. GERD Patients

On bivariate analysis, PEH patients were significantly older (60.5 vs. 49.1, $p<0.001$). A significantly higher percentage of PEH patients were women (68.3% vs. 60.52%, $p<0.001$). Mean length of stay was significantly higher for PEH patients (Table 3).

PEH patients were more likely to die than those without PEH (0.75% vs. 0.23%, $p<0.001$). Patients with PEH had a significantly higher risk of undergoing splenectomy (1.52% vs. 0.76%, $p<0.001$). Similarly, these patients had a significantly higher proportion of laceration repair, pneumothorax, pulmonary complications, cardiac complications, thromboembolic, and hemorrhagic complications (Table 3).

The first set of multivariate analyses, adjusting for pre-treatment variables (age, gender, race, Charlson score, hospital teaching status, hospital volume of anti-reflux surgery, and calendar year), demonstrates that PEH patients are more likely to die and have a significantly higher likelihood of complications compared to GERD patients (Table 4).

In the second multivariate analysis, the previously noted difference in mortality between PEH and GERD is maintained when adjusting for splenectomy ($p<0.043$), laceration

Table 3 Bivariate Analysis: Patient Demographics and Adverse Outcomes—PEH & GERD

Variable	GERD *N* (%)	PEH *N* (%)	*p* value
Age in years (mean)	49.1 (mean)	60.5 (mean)	<0.001
Female gender	10099 (60.52)	4571 (68.3)	<0.001
LOS in days (mean)	3.01 (mean)	4.32 (mean)	<0.001
Mortality	38 (0.23)	50 (0.75)	<0.001
Splenectomy	127 (0.76)	102 (1.52)	<0.001
Laceration repair	59 (0.35)	73 (1.09)	<0.001
Pneumothorax	107 (0.64)	103 (1.54)	<0.001
Pulmonary	575 (3.43)	432 (6.44)	<0.001
Cardiac	118 (0.70)	136 (2.03)	<0.001
Thromboembolic	51 (0.30)	60 (0.89)	<0.001
Hemorrhagic	343 (2.05)	251 (3.74)	<0.001

Table 4 Multivariate Analysis: Odds Ratio of Adverse Events in PEH vs. GERD Undergoing Foregut Surgery

	Adverse event	Odds ratio (95% CI)	*p* value
	Mortality	1.81 (1.06–3.09)	0.030
Technical	Laceration repair	2.00 (1.29–3.10)	0.002
	Splenectomy	1.44 (1.03–2.01)	0.033
	Pneumothorax	2.45 (1.64–3.65)	0.000
	Hemorrhagic	1.53 (1.22–1.92)	0.000
Peri-op	Pulmonary	1.48 (1.26–1.75)	0.000
	Cardiac	2.11 (1.43–3.11)	0.000
	Thromboembolic	2.34 (1.29–4.23)	0.005

repair ($p<0.028$), pneumothorax ($p<0.034$), and cardiac complications ($p<0.04$). This effect is lost when adjusting for pulmonary ($p=0.079$), hemorrhagic ($p=0.106$), and VTE ($p=0.05$) complications.

Discussion

PEH is a disease that poses unique clinical challenges. Despite its apparent benignity, it has the potential for severe complications. The actual mechanistic sequence of events leading to the development of PEH is not completely understood. It is likely that the process involves stretching of the phrenoesophageal membrane and attendant weakening and enlargement of the diaphragmatic hiatus.[3,11] This process likely evolves with increasing age.[3] Patients may present with heartburn, regurgitation, post-prandial fullness, chest pain, dysphagia, as well as signs and symptoms suggestive of anemia.

PEH repair continues to raise controversy and questions—ranging from the indications for surgery to the actual technical specifics of the operation. These questions have engendered many good studies examining the experience and outcomes of various institutes. Almost all of these single-center series have consistently observed that PEH patients tend to be older, with more co-morbidities. Gangopadhyay et al. examined the relationship between age, co-morbidities, and PEH in their 2006 paper.[2] However, they determined that complication rates are higher in elderly patients. Brunt et al. examined outcomes in elderly patients undergoing laparoscopic anti-reflux surgery for patients with type 1 hiatal hernias and compared them to younger patients.[12] Even though type 1 hiatal hernias are not as complex as PEHs, they noted that elderly patients had more minor complications compared to younger patients, and that there was no increase in major complications.[12] Flum et al. studied outcomes in patients undergoing anti-reflux surgery on a population level, perhaps one of the few such studies in the literature to date.[13] They observed that nationally, even though morbidity and mortality associated with anti-reflux surgery performed in the 1990s was quite low, it was still higher than suggested by case series. Further, they noted that surgeon experience with the procedure was linked to better outcomes. This relationship has been demonstrated by other authors reviewing their results for anti-reflux surgery,[14–16] as well as in other advanced laparoscopic surgical procedures.[17–19]

In our study, 28.6% of the NIS cohort underwent foregut surgery for PEH. The overall in-hospital mortality was quite low—0.38%. As noted, complication rates were also quite low. When we compared PEH to GERD patients in our bivariate analysis, several interesting observations were noted. First, PEH patients were significantly older than GERD patients—60.5 vs. 49.1. This is similar to what has been reported in the literature.[3,20] PEH is an insidious condition. Clinically, patients with PEH may be asymptomatic and may in fact be unaware of the fact that they even have a PEH for many years. More often, they may be tolerating a variety of vague, nondescript symptoms for many years prior to diagnosis.[3] The delayed presentation and progress of symptoms may explain the difference in age. Even though the overall mortality for PEH patients was low (0.75%), it was significantly higher than GERD patients (0.23%). It is interesting to note that a significantly higher percentage of the PEH patients were women when compared to the GERD group (68.3% vs. 60.52%, $p<0.0001$). Overall, on univariate analysis, women make up the majority of the cohort (62.8%). This has been observed in other series as well.[2,3,21] Several studies in the cardiac, obstetric and geriatric literature have demonstrated that women tend to live longer than men, attributable to vascular, hormonal and genetic differences.[22] This, coupled with the fact that PEH may not be diagnosed or symptomatic until the later years in life, may explain, in part, why PEH patients are older and tend to be women. PEH patients had a significantly longer mean length of stay in hospital than their GERD counterparts—mean of 4.32 vs. 3.01 days, $p<0.001$. Similar trends have been noted in other studies.

In our first multivariate analysis, the odds of mortality, technical, and peri-operative complications (Table 4) was significantly higher in PEH patients, even adjusting for the effect of hospital case volume. In our second set of multivariate analyses, we wanted to see if our primary outcome, mortality, remained significantly higher in PEH patients after adjusting for our peri-operative complications. The difference in mortality is no longer significant after adjusting for pulmonary complications. Bivariate analysis demonstrates that PEH patients have a significantly higher rate of pulmonary complications (6.44% vs. 3.43%, Table 3; OR 1.48, Table 4). It is also worth noting that on bivariate analysis, pulmonary complications rank first among the list of chosen adverse-outcome variables. An intra-thoracic stomach may affect ventilation and perfusion, and may even make these patients more sensitive to the pneumo-peritoneum.

Further, dissection in the chest/mediastinum through an abdominal/laparoscopic approach is known to be a difficult and complex undertaking that requires a high level of skill and comfort with laparoscopic and foregut surgery, as has been noted elsewhere.

PEH patients have a higher rate of hemorrhagic complications (3.74% vs. 2.05%, OR 1.53). However, when adjusting for this adverse event, the mortality difference is once again eliminated. This underscores, in part, the importance of minimizing intraoperative hemorrhage through careful dissection during this type of advanced laparoscopic procedures. The dissection of the viscera and hernia sac across two domains—the abdomen and the thorax—is indeed a difficult undertaking. There are several important named vessels in this area (i.e., left gastric), as well as the highly vascular spleen, and the short gastrics, which may be difficult to appreciate in a patient with a significant PEH and associated intra-thoracic abdominal viscera. The intra-thoracic stomach itself may be friable and prone to bleeding. The hernia sac itself may also bleed, secondary to long-term inflammatory changes and edema that result.

After adjusting for VTE complications, the mortality difference is also eliminated. While the overall rate of VTE was only 0.47%, on bivariate analysis, patients with PEH had a significantly higher rate (0.89% vs. 0.30%, $p<0.0001$). This compares similarly with multiple single-center series from 1994–1997.[23] DVT and PE following major surgical procedures remain significant causes of major morbidity and mortality. Factors specific to laparoscopic surgery such as carbon dioxide pneumoperitoneum, reverse Trendelenberg position, and increased operative time may increase the risk of DVT development. It is known that the pneumo-peritoneum actually impedes venous return leading to venous stasis. Conversely, the salutary effects of laparoscopic surgery, such as early ambulation and the potential decrease in postoperative hypercoagulation may actually decrease the risk of DVT development.[23] Furthermore, non-operative factors, or patient factors such as age, for example, are known to increase the risk of DVT and PE. PEH patients are significantly older than the GERD patients, but it is likely that age alone is not the sole contributing factor to mortality in these patients.

Conclusion

In an era when health policy and surgical practice is increasingly driven by evidence-based guidelines and outcomes, there is a clear dearth of population-based analyses of outcomes in patients undergoing PEH repair. Single-center series are subject to selection and publication bias and may not accurately reflect the population-level risk of adverse outcomes.[13] Our study is unique in that we attempt to quantify, on a population level, a number of observations: (1) the incidence of adverse events in all patients undergoing foregut surgery for PEH and GERD from 2001–2005; (2) the difference, if any, in demographics and adverse events/outcomes between these patients and (3) if there are any specific features unique to the two cohorts that may explain the difference in outcomes.

There are some inherent limitations in this study. First, since our data is drawn from a large population-based database, it is very difficult to discern the clinical specifics or details associated with each adverse-outcome variable. Second, despite being high-powered in terms of the number of records, it is difficult to make definitive conclusions given the inherent heterogeneity that may exist given the lack of knowledge about the actual technical specifics about the surgical approach, as well as other unique clinical identifiers. Another limitation is our inability to precisely differentiate between laparoscopic and open repairs. This is because there were no specific ICD-9 codes to identify whether anti-reflux procedures were performed laparoscopically before 2004.

In conclusion, albeit low, the incidence of adverse events is significantly higher in PEH patients compared to GERD patients. PEH patients are significantly older, and a significantly higher percentage are women. The most common adverse events were pulmonary and hemorrhagic, both on univariate and bivariate analyses. On multivariate analysis, PEH patients had a significantly higher percentage of pulmonary and hemorrhagic complications. Finally, adjustment for pulmonary, hemorrhagic and VTE complications eliminated the difference in mortality between PEH and GERD patients. Perhaps a combination of improved peri-operative care focusing on pulmonary physiology and respiratory mechanics, improved surgeon experience with principles of laparoscopic PEH repair, concurrent attention to meticulous hemostasis and attention to DVT prophylaxis will continue to improve outcomes, such that age and co-morbidities alone will not preclude PEH repair.

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