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Does illness severity matter? A comparison of laparoscopic esophagomyotomy with fundoplication and esophageal dilation for achalasia

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Abstract
Introduction There is scarce evidence regarding optimal treatment options for achalasia in patients with varying illness severity risk. The objective of this study was to evaluate and compare outcomes with laparoscopic esophagomyotomy with fundoplication (LM) and esophageal dilation (ED) for hospitalized patients with different illness severity.
Methods The University HealthSystem Consortium (UHC) is an alliance of more than 100 academic medical centers and nearly 200 affiliate hospitals. UHC's Clinical Data Base/Resource Manager (CDB/RM) allows member hospitals to compare patient-level risk-adjusted outcomes for performance improvement purposes. The CDB/RM was queried for patients with achalasia who underwent LM ($n = 1{,}390$) or ED ($n = 492$) during a 3-year period between 2006 and 2008.
Results Overall esophageal perforation rates were significantly higher for ED (0.4% LM vs. 2.4% ED; $p < 0.001$). Patients undergoing LM with minor/moderate illness severity showed higher morbidity (9.42% LM vs. 5.15% ED; $p < 0.05$). However, LM patients in this illness severity group showed significantly lower 30-day readmission rate (0.38% LM vs. 7.32% ED; $p < 0.001$) and length of stay (2.23 ± 1.78 LM vs. 4.88 ± 4.42 days ED; $p < 0.001$), but comparable cost ($9,539 LM vs. $8990 ED; $p > 0.05$). In the major/extreme illness severity group mortality was comparable (1.37% LM vs. 2.44% ED; $p > 0.05$). Overall morbidity was significantly greater in LM (50.48% LM vs. 19.57% ED; $p < 0.001$). However, the length of stay was significantly increased in the ED group (8.96 ± 7.86 LM vs. 11.72 ± 11.05 days ED; $p = 0.04$).
Conclusion In hospitalized patients with minor/moderate illness severity, laparoscopic myotomy for achalasia showed comparable or better outcomes than ED. For major/extreme illness severity, dilation showed comparable or better profile for hospitalized achalasia patients. These results highlight the importance and impact of illness severity on outcomes of achalasia patients.

Keywords Achalasia · Digestive · General · Therapeutic/palliation · Heller myotomy · Esophageal dilation · Outcomes · Illness severity · Esophageal perforation

Achalasia is a rare, incurable esophageal motility disorder. Management of symptoms by decreasing resting lower esophageal sphincter pressure is the goal of treatment, because food trapped in the esophagus can ferment and produce discomfort similar to gastroesophageal reflux [1, 2]. Current therapeutic options for achalasia include pharmacologic therapy with calcium channel blockers or nitroglycerin, endoscopic options with pneumatic dilation or botulinum toxin injection, and surgical management with Heller myotomy [3]. Of these, pharmacologic therapy clearly appears to be limited for early disease or intermediate therapy in patients expecting future definitive treatment [4]. Among the endoscopic options, botulinum toxin injection therapy [5] seems to be associated with extremely high symptomatic relapse rate beyond 2 years and perhaps may be inferior to pneumatic dilation in the long-term [6, 7]. As a result, endoscopic pneumatic dilation and surgery

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with Heller myotomy presently remain the standard management options for achalasia.

Several studies have demonstrated the safety and efficacy of esophageal dilation (ED) with low risk of complications and excellent short- and long-term symptom management [8–10]. Esophageal dilation is considered to be the most effective nonsurgical treatment option for achalasia [7, 8]. Heller myotomy with or without fundoplication has produced excellent long-term results in achalasia patients [11]. In contrast to open or thoracoscopic approach to Heller myotomy, laparoscopic esophagomyotomy has been shown to be associated with lower morbidity, shorter hospital stay and better perioperative outcomes, subsequently resulting in greater adoption of laparoscopic myotomy [12–15]. This has shifted the focus of surgical management of achalasia from an ancillary procedure for failed dilation patients to the primary approach for achalasia.

Although both esophageal dilation and laparoscopic myotomy have shown excellent results in achalasia, dilation has been associated with a higher risk of esophageal perforation and a higher rate of symptomatic recurrence requiring repeat interventions [8]. In a randomized, controlled trial comparing endoscopic dilation to laparoscopic myotomy with fundoplication, the surgical arm showed significantly fewer treatment failures at both the 5- and 15-year follow-up [16, 17]. In addition to decreased need for repeat interventions, studies have shown improved quality of life after surgical management [18–20]. Thus, it appears that laparoscopic myotomy with fundoplication may offer a clear clinical benefit and may be a superior alternative to endoscopic dilation for the management of achalasia.

Despite these results, the question of optimal treatment option for achalasia in patients with varying illness severity risk has never been examined. Indeed, patient illness severity risk can impact not only the optimal treatment decision but also therapy outcomes. It is quite possible that the risk profile of postintervention morbidity, such as perforation risk with dilation or postoperative morbidity risk with myotomy, may alter the treatment algorithm particularly in high-risk hospitalized patients compared with low-risk patients with achalasia. Despite the well-recognized impact of illness severity on treatment outcomes in general, there is scarce evidence on optimal treatment options for achalasia patients with varying illness severity risk. The objective of this study was to evaluate and compare outcomes with esophageal dilation and laparoscopic myotomy for hospitalized patients with different illness severity. These results will help to define optimal treatment option and ultimately help to develop a treatment algorithm for achalasia management, based on illness severity risk.

Methods

Database description

The University HealthSystem Consortium (UHC) is an alliance of more than 100 academic medical centers and nearly 200 affiliate hospitals. UHC's Clinical Data Base/Resource Manager (CDB/RM) allows member hospitals to compare patient level, risk-adjusted outcomes for performance improvement purposes. This database has previously been utilized for many studies [21–23]. Discharge data and specific demographics, including age, gender, and race, are accessible for specific diagnosis and procedure queries. International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) diagnosis and procedure codes were used to track patient data. Information concerning length of stay (LOS), morbidity, mortality, intensive care unit (ICU) admission, comorbidities, specific complications, and 30-day readmission rates also is available. Patient level data are collected by hospital staff via consolidated patient data feed electronic encounter forms and submitted to UHC monthly. Risk adjustment is assessed by utilizing logistic regression models.

The estimated cost of patient care is calculated using a ratio of cost-to-charge (RCC) methodology. RCC is created for each service using specific costs and revenues from the Centers for Medicare & Medicaid Services (CMS). Detailed patient charges are collected at the revenue code level and estimated service center costs are then calculated by multiplying these charges by the RCC. Summation of individual cost center estimates reveals the total costs.

The UHC database stratifies patients into four illness severity groups: minor, moderate, major, and extreme. A total of 29 comorbidities and patient characteristics, such as age, sex, race, admission status, admission source, socioeconomic status, and specific patient population variables, are assessed utilizing the 3M APR-DRG [24].

Study design

Institutional Review Board (IRB) and University HealthSystem Consortium (UHC) approval was obtained before performing this study. A retrospective, observational study design was used to analyze multicenter outcomes using the UHC database. Discharge data of all patients with a diagnosis of achalasia who underwent laparoscopic esophagomyotomy with fundoplication or endoscopic dilation during a 3-year period from 2006–2008 in adult patients older than aged 18 years was accessed. For data collection, UHC database was accessed electronically with diagnosis and procedural ICD-9-CM codes. The ICD-9-CM codes for achalasia (530.0), perforation of esophagus (530.4), esophagomyotomy (42.7), laparoscopic procedures for

creation of esophogastric sphincteric competence (44.67), and dilation of esophagus (42.92) were used.

Main outcome measures

Observed mortality, overall patient morbidity, ICU admission rate, 30-day readmission rate, length of hospital stay, and hospital costs were compiled for each patient group. Data on demographic characteristics, such as age, gender, and race, also was collected. Age was further divided into subgroups as 18–30 years, 31–50 years, 51–64 years, and ≥65 years. Racial groups were further classified as Caucasians, African-Americans, Hispanics, Asians, and other group, including Native Americans and undetermined categories. Rates of esophageal perforation secondary to procedure performed were accessed. Patient groups were compared overall and based on severity of illness subgroups.

Data analysis

Prism 5.0 software (GraphPad Software; San Diego, CA) was used for statistical analysis. Continuous variables were expressed as mean ± standard deviation (SD) and compared with a *t*-test. Categorical variables were expressed as percentage and Fisher's exact test was performed for comparison. Significance for the study was set at $p < 0.05$.

Results

As shown in Table 1, a total of 1,390 hospitalized patients with achalasia underwent laparoscopic myotomy with fundoplication (LM) and 492 patients underwent endoscopic dilation (ED). In the surgery group, the majority of patients ($n = 1{,}317$) had minor or moderate severity of illness scores with only 73 patients with major or extreme severity of illness. Hospitalized patients who had endoscopic dilation for achalasia were evenly distributed across severity of illness groups, with 246 patients in both the minor/moderate group and the major/extreme group. Esophageal dilation population had significantly higher proportion of patients aged ≥65 years compared with the laparoscopic myotomy group (53.3% ED vs. 21.3% LM; $p < 0.001$). Caucasian patients constituted approximately 68% of both the surgery and dilation groups.

Esophageal perforation risk was significantly lower in the surgery group (0.4% LM vs. 2.4% ED; $p < 0.001$). Stratification by severity of illness revealed that in minor/moderate risk group (Table 2), the overall morbidity was significantly higher in the surgery group (9.42% LM vs. 5.15% ED; $p = 0.03$). There were no reported deaths in the minor/moderate severity groups in LM or ED. In addition, minor/moderate-risk patients who underwent LM had a significantly lower 30-day readmission rate (0.38% LM vs. 7.32% ED; $p < 0.001$) and significantly reduced length of stay than ED (2.23 ± 1.78 LM vs. 4.88 ± 4.42 days ED; $p < 0.001$). The trend toward ICU admission was increased in the ED group (5.26% LM vs. 7.02% ED; $p > 0.05$). In this group of patients, there was no statistically significant difference in cost between LM and ED (9,539 ± 6,750 LM vs. 8,990 ± 7,544; $p > 0.05$).

In the major/extreme severity illness group (Table 3), mortality was higher, but not statistically different, in the dilation group compared with the surgery group (1.37% LM vs. 2.44% ED; $p > 0.05$). Overall morbidity was greater in the surgery group (50.48% LM vs. 19.57% ED; $p < 0.001$). Readmission rate within 30 days was greater but not statistically different in the ED group (1.97% LM vs. 6.72% ED; $p > 0.05$). Length of stay was significantly increased in the esophageal dilation group (8.96 ± 7.86 LM vs.

Table 1 Demographic characteristics of study population

	Dilation ($n = 492$)	Myotomy ($n = 1{,}390$)
Age, *n* (%)		
18–30 years	28 (5.7%)	193 (13.9%)
31–50 years	106 (21.5%)	516 (37.2%)
51–64 years	96 (19.5%)	385 (27.7%)
≥65 years	262 (53.3%)	296 (21.3%)
Gender, *n* (%)		
Female	266 (54.1%)	682 (49.1%)
Male	226 (45.9%)	708 (50.9%)
Race, *n* (%)		
Caucasian	331 (67.3%)	949 (68.3%)
African-American	113 (23.0%)	194 (14.0%)
Hispanic	16 (3.3%)	72 (5.2%)
Asian	7 (1.4%)	28 (2.0%)
Other	25 (5.0%)	147 (10.5%)
Illness severity, *n* (%)		
Minor/moderate	246 (50.0%)	1,317 (94.7%)
Major/extreme	246 (50.0%)	73 (5.3%)

Table 2 Outcomes of all hospitalized patients with minor/moderate illness severity

	Myotomy ($n = 1{,}317$)	Dilation ($n = 246$)
Mortality (%)	0.00	0.00
Overall morbidity (%)	9.42	5.15*
LOS (days, mean ± S.D.)	2.23 ± 1.78	4.88 ± 4.42*
30-Day readmission (%)	0.38	7.32*
Cost ($, mean ± S.D.)	9,539 ± 6,750	8,990 ± 7,544

* Denotes $p < 0.05$ compared to LM

Table 3 Outcomes of all hospitalized patients with major/extreme illness severity

	Myotomy ($n = 73$)	Dilation ($n = 246$)
Mortality (%)	1.37	2.44
Overall morbidity (%)	50.48	19.57*
LOS (days, mean ± S.D.)	8.96 ± 7.86	11.72 ± 11.05*
30-Day readmission (%)	1.97	6.72
Cost ($, mean ± S.D.)	35,589 ± 44,943	25,806 ± 33,167*

* Denotes $p < 0.05$ compared to LM

Table 4 Outcomes of all hospitalized patients including all illness severity

	Myotomy ($n = 1,390$)	Dilation ($n = 492$)
Mortality (%)	0.07	1.22*
Overall morbidity (%)	11.01	12.31
LOS (days, mean ± S.D.)	2.59 ± 2.91	8.3 ± 9.08*
30-Day readmission (%)	0.65	7.20*
Cost ($, mean ± S.D.)	10,302 ± 16,201	17,436 ± 25,502*

* Denotes $p < 0.05$ compared to LM

11.72 ± 11.05 days ED; $p = 0.04$). The trend toward ICU admission was increased in the LM group (26.39% LM vs. 20.99% ED; $p > 0.05$). However, costs were significantly increased in the surgical group (35,589 ± 44,943 LM vs. 25,806 ± 33,167 ED; $p = 0.04$).

When patient groups were evaluated with combined illness severity groups (Table 4), clinical outcomes surprisingly appeared to favor LM. Mortality (0.07% LM vs. 1.22% ED; $p < 0.05$), length of stay (2.59 ± 2.91 LM vs. 8.3 ± 9.08 days ED; $p < 0.05$), 30-day readmission rate (0.65% LM vs. 7.20% ED, $p < 0.05$), and cost ($10,302 ± 16,201 LM vs. $17,436 ± 25,502 ED, $p < 0.05$) were significantly improved in LM patients. There was no significant difference in overall morbidity between the groups (11.01% LM vs. 12.31% ED; $p > 0.05$).

Discussion

Despite the well-recognized impact of illness severity on treatment outcomes, there is hardly any data on optimal treatment options for achalasia patients with varying illness severity risk. The objective of this study was to evaluate and compare outcomes with ED and LM for hospitalized patients with differing illness severity. Study results demonstrated that severity of illness may impact choice of treatment for achalasia.

For hospitalized patients with a minor/moderate illness severity, mortality between the two study treatment options was comparable, indicating safety of both options consistent with previous studies [8, 18]. Although overall morbidity was higher with the myotomy group, the length of stay and 30-day readmission rate with myotomy were lower compared with the dilation group. The morbidity in the minor/moderate risk patients was approximately 9%. Previous studies have shown the overall morbidity with laparoscopic myotomy to be as high as 35% [25] with a recent meta-analysis showing 6.3% overall morbidity [8]. However, previous study estimates were not risk-specific as opposed to the estimates in the present study. The duration of hospitalization with laparoscopic myotomy has been shown previously to be in the range of 1 to 5 days, which is consistent with results from our study [1]. The mean duration of hospitalization was 5.7 days with myotomy and 3.6 days with esophageal dilation in a recent large database study [18]. However, this study compared open myotomy with esophageal dilation, and hence the length of stay with myotomy may be higher compared with our study. Furthermore, the present study captured only inpatient admissions, whereas the previous study utilized both inpatient and outpatient data for esophageal dilation. This may explain the vast difference in duration of hospitalization between these studies. Hospital costs appear to be a function of length of stay, overall morbidity, and serious morbidity with a need for ICU admissions and operative costs. Costs between the two procedures were comparable for minor/moderate severity patients. This may be due to the fact that costs from increased length of stay in hospitalized patients undergoing dilation may be offset by a decreased overall morbidity in this group compared with the laparoscopic myotomy group.

For major/extreme illness severity, LM showed higher morbidity and costs but lower length of stay compared with ED. Although the exact reason for shorter length of stay in laparoscopic myotomy group despite higher morbidity was not known, it might be due to the higher proportion of serious complications in the esophageal dilation group requiring extended hospitalization. The dramatically increased morbidity together with increased operative costs with laparoscopic myotomy may have contributed to the increased costs in this group. The esophageal dilation group showed a slightly higher, but not significantly different, readmission rate, suggesting the increased incidence of complications during the immediate postintervention period. Although these complications may not be necessarily intervention-related, they definitely suggest the possibility that the morbidity rate with esophageal dilation may be underestimated.

Overall, both procedures were found to be safe. Esophageal dilation was associated with a higher risk of perforation compared with the laparoscopic myotomy group as seen in previous study [8]. The duration of

hospitalization was significantly longer for the dilation than laparoscopic myotomy, reflecting, in part, a similar effect seen in the various illness severity groups. Surprisingly, when all patients are considered without regard to illness severity, laparoscopic myotomy showed lower morbidity and costs with compared with esophageal dilation. This conflicting result may be due to the Yule-Simpson effect, in which overall outcomes may change when subgroups are analyzed [26]. These results highlighted the significance of stratifying risk severity in studies that may impact outcomes and lead to false conclusions based on overall combined risk estimates between comparative treatment options. Previous studies have not examined the importance of risk severity and hence the generalization of results regarding optimal treatment option across illness severity in achalasia patients may be difficult.

This was the first retrospective comparative analysis of efficacy of therapeutic options for achalasia in risk-stratified patients utilizing a large administrative database. Population-based estimates of surgical outcomes for these procedures in achalasia patients were never examined previously, although a similar large patient database study between esophagomyotomy and esophageal dilatation showed safety and efficacy of these procedures [18]. The previous study, however, did not differentiate between open and laparoscopic myotomy, and data on antireflux procedures were not available for all surgical patients. Furthermore, the study included both inpatient and outpatient esophageal dilation procedures in contrast to our study, which only included inpatient admissions. Although this is one of the drawbacks of this study, previous studies have outlined outcomes that are not necessarily differentiated by admission status [10, 27–29]. In one retrospective study, admission after ED was 17% [30], but these patients were not analyzed separately as a group. Outcomes of esophageal dilation may differ by admission status and currently no study has captured data on hospitalized patients with achalasia.

The quality of life in achalasia patients has been shown previously to improve with laparoscopic myotomy [19, 20]. In addition, the need for further or repeat interventions appears to be significantly higher for esophageal dilation [18]. This study did not examine the need for repeat interventions or quality of life outcomes for either procedure. Whether previous attempts at esophageal dilation adversely affect outcomes with subsequent surgery for achalasia is still controversial. Several studies have shown worse or better outcomes with myotomy in patients that have needed prior multiple dilation attempts [31, 32]. Data on previous failed esophageal dilation in either treatment group was not available in the database; how this may have affected outcomes in our study is not known.

The study has several limitations. Effect of confounding variables, such as age, gender, and race, on these outcome measures was not known because of our inability to perform multivariate analysis with the CDB/RM. Although several studies have evaluated the role of the Nissen, Dor, and Toupet fundoplication and also the outcomes of standard versus extended esophagomyotomy in the treatment of achalasia [33–35], currently this information is unavailable through our database search. Outcomes concerning symptom improvement, quality of life improvement, need for further treatment, and postoperative gastroesophageal reflux could not be ascertained in this study. Furthermore, there is no differentiation between esophageal dilation performed though fluoroscopic or endoscopic guidance. The retrospective nature of this study does not allow for patient randomization, and the criteria for patient selection are unknown. The fact that higher risk patients represent an increased portion of the ED group suggests that patients with major/extreme severity of illness were selected for endoscopic treatment compared with surgical treatment, which would constitute a selection bias. Conversely, it is possible that lower-risk patients were selected for surgical treatment because most patients in the surgery group are categorized as minor/moderate severity of illness. All patients in this study were hospitalized, and hospitalized patients with achalasia may represent a group that is distinctly different than those treated on an outpatient basis. Although this study matches patient groups for severity of illness, their comparison is not precisely equivalent secondary to the aforementioned reasons. However, a prospective, randomized study of this size would require several years and a large multicenter cooperative to complete as a consequence of the rarity of this disease. For this reason, we find this data to be of significant value, especially in terms of counseling patients concerning the safety and efficacy of these procedures.

Conclusions

Our study has demonstrated the safety and efficacy of both laparoscopic esophagomyotomy with fundoplication and esophageal dilation for the treatment of achalasia. Hospitalized patients with a minor/moderate illness severity laparoscopic myotomy for achalasia showed comparable or better outcomes than esophageal dilation. For major/extreme illness severity, dilation showed comparable or better profile for hospitalized achalasia patients for most outcome measures. These study results highlight the importance and impact of illness severity on outcomes of achalasia patients and, in the future, may be used to develop a treatment algorithm for achalasia patients with different illness severity.

Disclosures Drs. Jason F. Reynoso, Manish M. Tiwari, Albert W. Tsang, and Dmitry Oleynikov have no conflicts of interest or financial ties to disclose.

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