



Does pyloric drainage have a role in the era of minimally invasive esophagectomy?

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Received: 19 July 2018 / Accepted: 28 November 2018 / Published online: 10 December 2018
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Abstract

Introduction Pyloric drainage during minimally invasive esophagectomy (MIE) may be more technically challenging than with an open approach. Alternatives to classic surgical drainage have increased in popularity; however, data are lacking to demonstrate whether one technique is superior in MIE. The purpose of this study was to compare post-operative outcomes after MIE between different pyloric drainage methods.

Methods We performed a retrospective review of a prospectively maintained database of patients undergoing MIE at a single academic institution. Patients were divided into three groups for analysis: no drainage, intrapyloric Botulinum Toxin injection, and surgical drainage (pyloroplasty or pyloromyotomy). The primary outcome was any complication within 90 days of surgery; secondary outcomes included reported symptoms and need for pyloric dilation at 6 and 12 months post-operatively. Comparisons among groups were conducted using the Kruskal Wallis and Chi Square tests.

Results There were 283 MIE performed between 2011 and 2017; of these, 126 (45%) had drainage (53 Botulinum injection and 73 surgical). No significant difference in the rate of post-operative complications, pneumonia, or anastomotic leak was observed between groups. At 6 and 12 months, patients that received Botulinum injection and surgical drainage had significantly more symptoms than no drainage ($p < 0.0001$) and higher need for pyloric dilation at 6 months ($p = 0.007$).

Conclusions Pyloric drainage was not significantly associated with lower post-operative complications or long-term symptoms. While Botulinum injection appears safe post-operatively, it was associated with increased morbidity long-term. Pyloric drainage in MIE may be unnecessary.

Keywords Esophagectomy · Pyloric drainage · Post-operative complications · Pyloric stricture

Increasing emphasis on improvement of post-operative outcomes and quality of life in conjunction with evolution of surgical technologies has led to growing utilization of minimally invasive esophagectomy (MIE). MIE has been associated with reduced post-operative blood loss and fewer major complications as compared to open surgery [1, 2].

Despite the benefits of MIE, certain morbidities are inherent to esophagectomy regardless of the operative approach.

Vagal nerve resection commonly necessary for oncologic quality may result in conduit dysmotility and pyloric dysfunction with subsequent post-operative delayed gastric emptying (DGE) reported in 4 to 50% of patients [3]. Resultant stasis within the conduit may result in symptoms (i.e., nausea, vomiting, and early satiety) which complicate eating, and increase risk of aspiration pneumonia, anastomotic stricture and anastomotic leak [4].

Pyloric drainage procedures are often used to minimize the negative sequelae attributed to DGE; however, available data are inconsistent about associated benefits [3, 5, 6]. Some surgeons argue against intervention as DGE may impact only a minority of patients and nerve regeneration gradually allows for recovery of gastric function [7]. Additionally, drainage has been associated with complications including increased gastric dumping, esophagitis and biliary reflux [8, 9].

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Surgical drainage with pyloromyotomy or pyloroplasty has historically been the most common pyloric intervention; however, these approaches are more technically challenging and take more time in the minimally invasive setting. Intrapyloric injection with Botulinum Toxin has become a popular alternative since it was first introduced in 2007 as a less invasive, simpler approach to drainage in MIE. Additional proposed benefits included the short-term nature of this therapy—improved gastric emptying may be useful in the immediate post-operative period but the effects mitigate as gastric function recovers and therefore, negative long-term effects of drainage are minimized [10]. Current data comparing Botulinum injection as an alternative to surgical drainage procedures (pyloroplasty or pyloromyotomy) are inconclusive as to whether one approach is superior in reducing associated morbidity [9, 11].

Although previous studies have questioned the role of pyloric drainage following open esophagectomy, there is a paucity of data in MIE. As surgeon experience with MIE rises, it is important to determine whether pyloric drainage has a benefit in this setting and whether one approach is safer with fewer side effects. Therefore, the purpose of this study was to compare outcomes between pyloric intervention group (none, surgical, and Botulinum injection) in patients undergoing MIE.

Materials and methods

Consecutive patients that underwent minimally invasive esophagectomy (MIE) for esophageal malignancy between January 2011 and December 2017 were identified from a prospectively maintained institutional database of esophagectomies performed at Memorial Sloan Kettering Cancer Center. Data on patient demographics, esophageal pathology, treatment selection, and post-operative outcomes were abstracted from patient charts. Post-operative clinical notes and endoscopic reports were reviewed for patient reported symptoms and subsequent interventions. This study was exempt by the Institutional Review Board.

Patients were divided into three groups by pyloric intervention, including: no drainage, Botulinum injection, and surgical drainage. Patients that received pyloroplasty or pyloromyotomy were analyzed together within the surgical group. Only patients that underwent esophagectomy for malignancy and dysplasia were included. We excluded patients that underwent pharyngo-laryngo-esophagectomy to eliminate confounders linked to case complexity. Additionally, we excluded patients that had conversion of the abdominal portion from minimally invasive to open. Patients that had conversion of the thoracic portion to thoracotomy were still analyzed as our primary interest was in a minimally invasive approach to the abdominal portion.

Surgical technique

Each patient underwent clinical staging using a combination of endoscopy, endoscopic ultrasound, positron emission tomography, and computed tomography scan, as is the standard at our institution. Neoadjuvant therapy with chemoradiation was given to all patients with node-positive disease and/or $\geq T2$ disease. Resection was performed 5–8 weeks after completion of therapy. Patients with in situ/T1N0 tumors or other pathology (GIST) were offered MIE alone without neoadjuvant therapy. All operations were performed by surgeons within the Department of Thoracic Surgery.

Surgical approach to MIE was selected by surgeon preference and tumor location. We prefer a transthoracic approach for cancer to better enable mediastinal lymphadenectomy, with anastomosis in the chest (Ivor Lewis) or neck (3-hole). Most patients in the United States present with distal esophageal adenocarcinoma, and consequently, Ivor Lewis is most commonly performed. All patients received a bronchoscopy and endoscopy prior to initiation of surgical resection. For Ivor Lewis, the procedure generally begins with a laparoscopic or robotic approach to the abdomen. A complete lymphadenectomy of the celiac branches is performed. The stomach and distal esophagus are mobilized at the hiatus, and the dissection is continued as far as proximally into the mediastinum as possible. Adjunct procedures, including feeding jejunostomy and pyloric drainage, are then performed. The stomach is tubularized to create a conduit approximately 5 cm in width. Thoracoscopic mobilization and lymphadenectomy is then performed via a right posterolateral approach with subsequent intrathoracic anastomosis using either a circular or a linear stapler. In the 3-hole (McKeown) approach, the procedure begins with en block dissection of the esophagus and lymphadenectomy. Laparoscopic gastric mobilization and nodal dissection is then performed. Finally, a cervical anastomosis is performed via a left neck incision using a stapled or hand-sewn approach.

Intra-operative pyloric interventions

The decision of whether and which type of pyloric intervention to use was dependent upon surgeon preference. Pyloric drainage included intra-operative pyloroplasty, pyloromyotomy or Botulinum Toxin A (Botox) injection. Botulinum injection was first used at our institution in 2016; as such, use was more frequent in the last 2 years of the study.

The pyloric intervention is performed after creation of the gastric conduit. Pyloromyotomy is performed using

hook electrocautery in a longitudinal fashion across the pylorus without entering the gastric mucosa. Patients that were noted to have full thickness perforation into the gastric lumen are converted to pyloroplasty. During pyloroplasty the entire muscle and the gastric mucosa are divided. The pylorus is then closed in a Heineke-Mikulicz transverse fashion using an endosuture device in an interrupted fashion. Our preference for Botulinum Toxin injection is well described, but involves a transabdominal approach utilizing a 7 inch 22-gauge spinal needle into the pyloric musculature [12]. By decreasing the insufflation pressure, the pylorus is easily reached in each case.

Post-operative evaluation and follow-up

All patients received a nasogastric tube post-operatively. Radiologic studies for DGE were not routinely performed. Operative data collected included operative procedure type, operative time, estimated blood loss (EBL) in milliliter (ml), and drainage procedure used.

Post-operative data included length of stay (LOS) in days, any complications, serious complications, anastomotic leak, pneumonia, tracheoesophageal fistula (TEF), empyema, readmission, reoperation, and death within 90 days of surgery. Serious complications were defined as complications classified as Clavien-Dindo grade ≥ 3 [13]. Leak and TEF were diagnosed by swallow study, computed tomography, or endoscopic assessment. Pneumonia was diagnosed by combination of clinical symptoms suggestive of the diagnosis, leukocytosis, and infiltrates on imaging. Diet was advanced according to surgeon preference. High nasogastric tube output on post-operative day 3, defined as > 300 ml, was assessed as a measure of DGE. However, as an additional measure of DGE, we determined time in days to liquid diet and removal of jejunostomy tube as the ability to tolerate oral diet as these measures may be more objective than NGT removal, which may be a function of surgeon preference. Lastly, we identified whether any patients required pyloric dilation within 90 days of surgery. The decision for post-operative endoscopy with pyloric or anastomotic dilation was based on symptoms of conduit dysfunction or gastric outlet obstruction (dysphagia, early satiety, nausea, vomiting, bloating). Patients that had not received any intra-operative intervention but required subsequent post-operative dilation were maintained in the no drainage group for intent to treat.

Late outcomes included symptoms and need for endoscopic dilation (pyloric or anastomotic) at 6 months and 12 months. Patients completed a standard review of symptoms. Gastrointestinal symptoms of interest included reflux, coughing, dysphagia, early satiety, poor PO tolerance, regurgitation, nausea, vomiting, diarrhea, aspiration, and post-prandial pain. Dumping was defined as the presence of one

or more symptoms commonly associated with dumping including flushing, sweating, light-headedness, or tachycardia. Aspiration events were deemed to have occurred in patients that had either been hospitalized or treated for aspiration related pulmonary complications.

Statistical analysis

Demographic data were summarized and compared between the three pyloric intervention groups using the Kruskal–Wallis test for continuous variables and Fisher's exact test or Chi Square test as appropriate for categorical variables. Odds ratios (OR) from logistic regression models were used to estimate the association between pyloric intervention groups and selected binary endpoints. Outcomes included symptoms at 6 and 12 months, need for pyloric dilation at 6 and 12 months and selected symptoms with sufficient event numbers (at least 10 events) to provide reliable estimates. All multivariable logistic models were adjusted for clinically relevant variables decided upon a priori: age and BMI at time of surgery [14]. Full multivariable selection procedure was not possible due to limited numbers of events. Two-sided $p < 0.05$ was considered significant. Data were analyzed using Stata 15.0 (StataCorp, College Station, TX).

Results

Demographics

Of 1738 esophagectomies performed during the study period, 299 were MIE (17.2%). Changes in use of MIE at our institution during the study period are presented in Fig. 1. Use of the MIE approach increased during the study period from 22.9% in 2011 to 64.4% in 2017. After excluding patients with esophagopharyngeal anastomosis ($n = 1$) and conversion of the abdominal portion to laparotomy ($n = 15$), 283 patients met inclusion criteria. The majority (55%) of patients did not have any pyloric drainage procedure

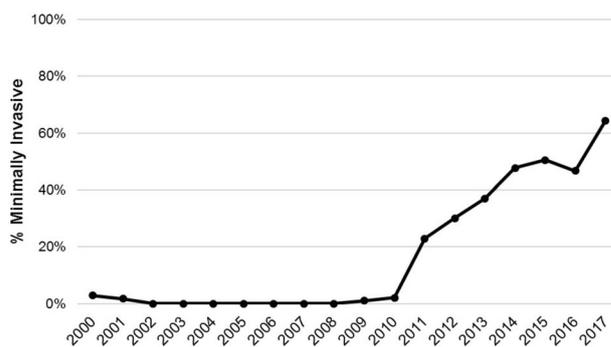


Fig. 1 Institutional use of MIE over time

performed at the index surgery. Amongst remaining patients, 73 (26%) underwent surgical drainage and 53 (19%) received Botulinum Toxin. Changes in trends of pyloric intervention strategies over the study period are demonstrated in Fig. 2. Botulinum injection first came into use at our institution in 2016.

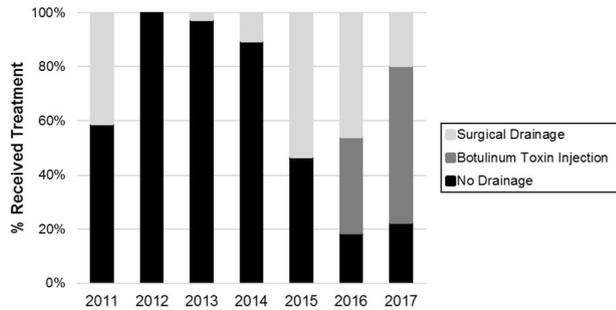


Fig. 2 Institutional variability in selection of pyloric intervention group over time

Median patient age was 62 years (25th–75th percentile, 56–69). Adenocarcinoma was the most common pathology (250/283; 82.8%) and most patients received neoadjuvant treatment (209/283; 69.2%). Overall 90-day complication rate was 61.3% ($n = 185$), with serious complication rate of 28.6% ($n = 81$) and mortality 3% (9/283). Comparison of key factors between pyloric intervention groups are presented in Tables 1 and 2. There was no difference in age, BMI, ASA score, or neoadjuvant therapy use between groups. Patients who received Botulinum injection had significantly longer median operative time (528 min versus 478 surgical drainage and 439 no drainage; $p < 0.0001$) but lower median estimated blood loss (EBL) (150 ml versus 200 for surgical and no drainage; $p = 0.01$). (Table 2) There was no significant difference in length of stay between groups.

Post-operative outcomes

Post-operative 90-day outcomes are compared between intervention groups in Table 2. There were no differences

Table 1 Characteristics of 283 patients that underwent MIE compared by pyloric intervention group

	No drainage ($N = 157$; 55%)	Botulinum injection ($N = 53$; 19%)	Pyloroplasty ($N = 73$; 26%)	<i>p</i>
Age, years	62.0 (55.0, 68.0)	59.0 (54.0, 70.0)	62.0 (58.0, 70.0)	0.10
Male	123 (78%)	44 (83%)	62 (85%)	0.5
Comorbid conditions				
Pulmonary	15 (10%)	9 (17%)	6 (8.2%)	0.3
Cardiac	70 (45%)	33 (62%)	40 (55%)	0.058
Diabetes	26 (17%)	12 (23%)	9 (12%)	0.3
ASA				0.5
2	24 (15%)	7 (13%)	9 (12%)	
3	126 (80%)	40 (75%)	59 (81%)	
4	7 (4.5%)	6 (11%)	5 (6.8%)	
BMI	28.7 (24.6, 32.2)	29.4 (24.9, 34.2)	27.9 (25.3, 31.0)	0.5
Pre-operative chemotherapy	119 (76%)	42 (79%)	52 (71%)	0.6
Pre-operative radiation	114 (73%)	40 (75%)	48 (66%)	0.4
Procedure type				0.4
Ivor Lewis	144 (92%)	48 (91%)	63 (86%)	
3-hole	13 (8.3%)	5 (9.4%)	10 (14%)	
EBL, ml	200.0 (125.0, 350.0)	150.0 (100.0, 230.0)	200.0 (100.0, 300.0)	0.010
Operative time, minutes	439.0 (384.0, 518.0)	528.0 (477.0, 577.0)	478.0 (435.0, 555.0)	<0.0001
Histology				0.8
Adeno	139 (89%)	45 (85%)	66 (90%)	
SCC	13 (8.3%)	7 (13%)	6 (8.2%)	
Other	5 (3.2%)	1 (1.9%)	1 (1.4%)	
Tumor location				0.001
Proximal	0 (0%)	1 (1.9%)	0 (0%)	
Mid	1 (0.6%)	5 (9.4%)	4 (5.5%)	
Distal	156 (99%)	47 (89%)	69 (95%)	

Values presented as N (%) or median (25th, 75th percentile)

Table 2 90-day post-operative outcomes of 283 patients that underwent MIE compared by pyloric intervention group

	No drainage (<i>N</i> =157; 55%)	Botulinum injection (<i>N</i> =53; 19%)	Pyloroplasty (<i>N</i> =73; 26%)	<i>p</i>
Length of stay, days	9.0 (8.0, 11.0)	8.0 (7.0, 12.0)	8.0 (7.0, 11.0)	0.2
Complications				
Any	104 (66%)	34 (64%)	47 (64%)	1
Serious ^a	47 (30%)	14 (26%)	18 (25%)	0.7
Readmission	35 (22%)	10 (19%)	12 (16%)	0.6
Reoperation	6 (3.8%)	4 (7.5%)	7 (10%)	0.2
Leak	35 (22%)	8 (15%)	11 (15%)	0.3
Tracheoesophageal fistula (TEF)	6 (3.8%)	1 (1.9%)	4 (5.5%)	0.6
Empyema	15 (10%)	5 (9.4%)	7 (10%)	1
Pneumonia	31 (20%)	7 (13%)	15 (21%)	0.5
Days to liquid diet (<i>N</i> =269)	7.0 (6.0, 8.0)	6.0 (6.0, 8.0)	10.0 (7.0, 14.0)	<0.0001
Days to jejunostomy removal	26.0 (22.0, 47.0)	25.0 (20.0, 34.0)	36.5 (23.0, 57.0)	0.009
Days to nasogastric tube removal	6.0 (4.0, 7.0)	4.0 (4.0, 5.0)	3.0 (2.0, 4.0)	<0.0001
High nasogastric tube output (≥300 ml), post-operative day 3	103 (66%)	36 (68%)	62 (85%)	0.007
Post-operative pyloric dilation	10 (6.4%)	2 (3.8%)	1 (1.4%)	0.30
Mortality	5 (3.2%)	0 (0%)	4 (5.5%)	0.20
In-hospital mortality	2 (1.3%)	0 (0%)	4 (5.5%)	0.069

Values presented as *N* (%) or median (25th, 75th percentile)

^aClavien-Dindo classification ≥ 3

in complication, serious complication, reoperation, or readmission rates between groups. Similarly, observed rates of leak, pneumonia or TEF did not differ. Patients with surgical drainage had slower median time to starting liquid diet (10 days versus 6 for Botulinum injection and 7 for no drainage, $p < 0.0001$) and removal of jejunostomy tube (36.5 days versus 25 Botulinum injection and 26 no drainage, $p = 0.009$). Patients without drainage had the longest median time to removal of nasogastric tube (6 days versus 4 Botulinum injection and 3 surgical drainage) ($p < 0.0001$); however, patients with surgical drainage had a significantly higher rate of high nasogastric tube output on post-operative day 3 compared to no drainage and Botulinum injection ($p = 0.007$).

There were 10 (6.4%) patients without drainage that required pyloric dilation within 90 days of surgery compared to 2 (3.8%) and 1 (1.4%) in the Botulinum injection and surgical drainage groups, respectively ($p = 0.30$). Patients that received surgical drainage displayed slightly higher rate of in-hospital mortality following the index procedure but was not statistically significant (5.5% vs. 0% Botulinum injection and 1.3% no drainage, $p = 0.069$). Of the 4 patients with surgical drainage, 3 died from pneumonia/aspiration and 1 from cardiac complications. There were 2 in-hospital deaths in the no drainage group, 1 due to pneumonia/aspiration and the other due to cardiac issues. Three additional patients without drainage died within 90 days after surgery following hospital discharge because of aspiration/pneumonia ($n = 1$),

complications from anastomotic leak ($n = 1$) and failure to thrive ($n = 1$).

6 and 12 month post-operative outcomes

There were 257 (91%) patients that had a 6-month post-operative visit and 203 (80%) with a 12-month visit. Patients with pyloric drainage procedures reported a significantly larger proportion of patients with any symptoms at 6 months (81% Botulinum injection and 75% surgical drainage) and 12 months (81% and 77%, respectively) compared to patients without drainage (53% at 6 and 52% at 12 months) ($p < 0.0001$) (Fig. 3). Reported symptoms by group at 6

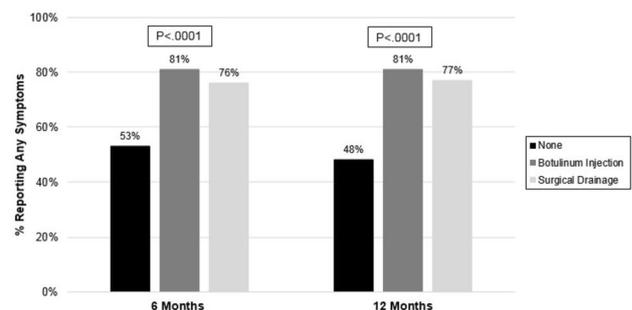


Fig. 3 Frequency of reported symptoms by pyloric intervention group at 6 and 12 months

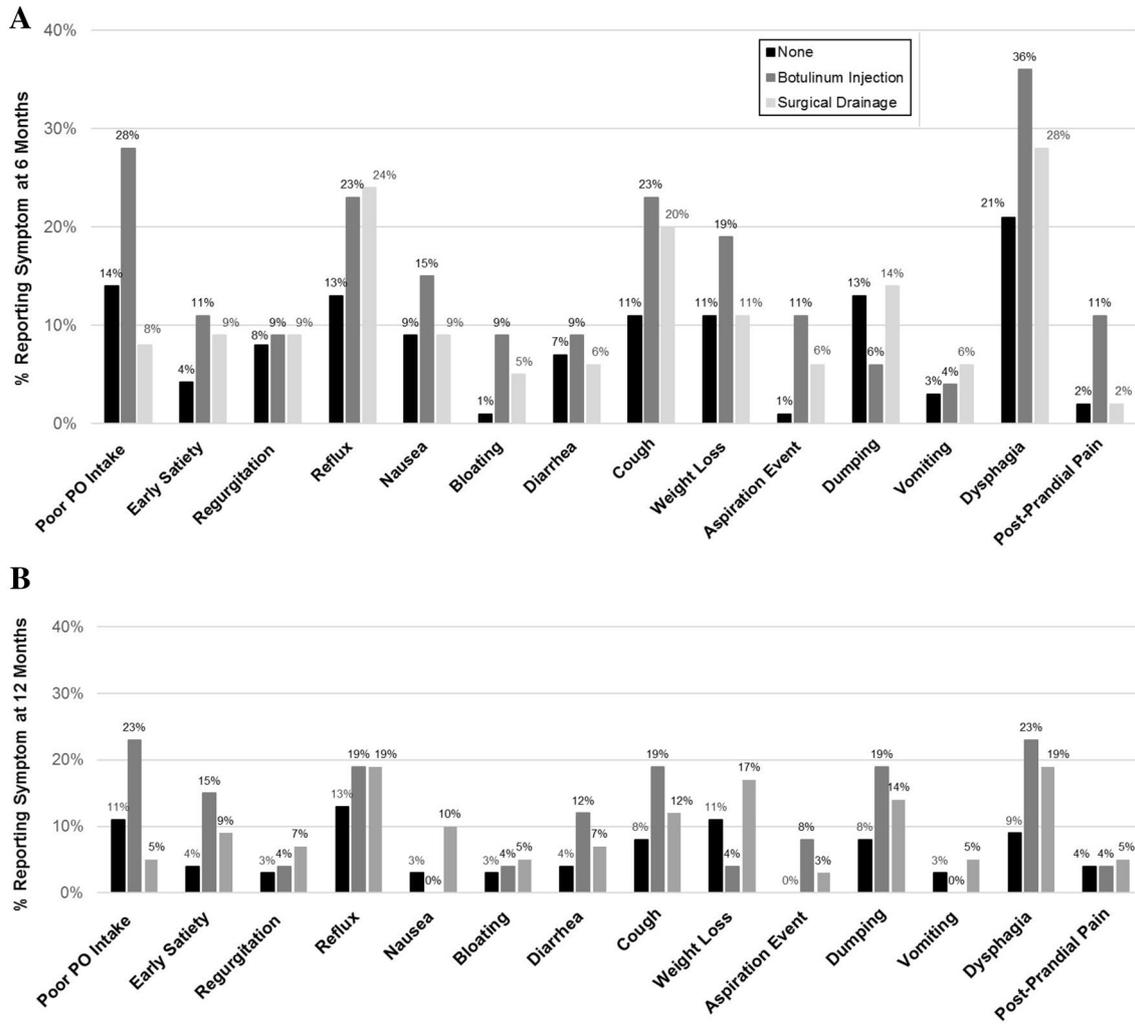


Fig. 4 Comparison of reported symptoms by pyloric intervention group at: **A** 6 months, **B** 12 months

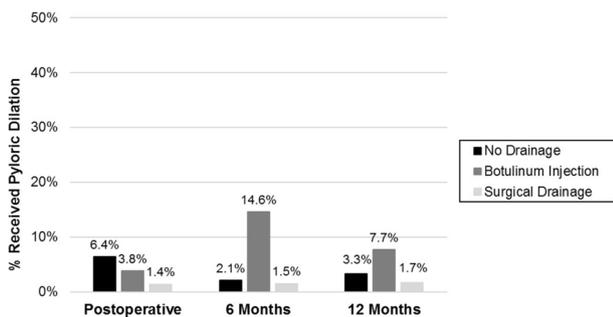


Fig. 5 Pyloric dilation by pyloric intervention group

and 12 months are presented in Figs. 4 and 5. At 6 months, patients with Botulinum injection had higher rates of poor PO tolerance (28%), post prandial pain (11%), and aspiration events (11%) compared to the other groups ($p < 0.02$). Although not significant, a larger proportion of patients that

received Botulinum injection or surgical drainage reportedly experienced reflux, cough and dysphagia compared to no drainage. Patients that received Botulinum injection received pyloric dilation more often than other groups at 6 months (14.6% vs. 1.5% surgical drainage and 2.1% no drainage) ($p < 0.002$). Although not significant, patients that received Botulinum injection underwent pyloric dilation more than the other groups at 12 months (7.7% Botulinum injection versus 3.3% no drainage and 1.7% surgical drainage, $p = 0.40$).

Logistic regression was performed to estimate the association between pyloric intervention group and selected outcomes. As demonstrated in Table 3, univariable analysis demonstrated that patients that received Botulinum injection and surgical drainage had greater odds of reporting any symptoms at 6 months compared to no drainage OR 3.93 (95% CI 1.77–8.71; $p = 0.001$ and 2.83 (1.48–5.44); $p = 0.002$, respectively). At 12 months, patients that

Table 3 Univariable and multivariable logistic regression for any and specific symptoms reported at 6 and 12 months

	Univariable		Multivariable ^a	
	OR (95% CI)	<i>p</i>	OR (95% CI)	<i>p</i>
Any symptoms				
6 Months				
Botox versus no drainage	3.93 (1.77–8.71)	0.001	4.14 (1.83–9.35)	0.001
Surgical versus no drainage	2.82 (1.48–5.44)	0.002	3.16 (1.62–6.16)	0.001
Surgical versus Botox	0.72 (0.29–1.81)	0.5	0.76 (0.30–1.95)	0.6
12 months				
Botox versus no drainage	2.23 (0.92, 5.38)	0.08	2.26 (0.93, 5.52)	0.07
Surgical versus no drainage	2.08 (1.09, 3.95)	0.026	2.15 (1.12, 4.14)	0.021
Surgical versus Botox	0.93(0.35, 2.46)	0.9	0.95 (0.36, 2.54)	0.9
Pyloric dilation				
6 months				
Botox versus no drainage	7.97 (1.97, 32.2)	0.004	8.68 (2.1, 35.8)	0.003
Surgical versus no drainage	0.72 (0.07, 7.0)	0.8	0.63 (0.06, 6.2)	0.7
Surgical versus Botox	0.09 (0.01, 0.76)	0.027	0.07 (0.01, 0.6)	0.017
12 months				
Botox versus no drainage	2.46 (0.43, 14.2)	0.3	2.45 (0.42, 14.2)	0.3
Surgical versus no drainage	0.52 (0.06, 4.74)	0.6	0.57 (0.06, 5.30)	0.6
Surgical versus Botox ¹	0.21 (0.02, 2.43)	0.3	0.23 (0.02, 2.74)	0.2
Dumping				
6 months				
Botox versus no drainage	0.44 (0.12, 1.55)	0.2	0.39 (0.11, 1.42)	0.2
Surgical versus no drainage	1.01 (0.43, 2.38)	1	1.12 (0.47, 2.67)	0.8
Surgical versus Botox	2.32 (0.59, 9.06)	0.2	2.89 (0.7, 11.9)	0.14
12 months				
Botox versus no drainage	1.37 (0.27, 7.0)	0.7	1.02 (0.17, 6.14)	1
Surgical versus no drainage	1.90 (0.61, 5.92)	0.3	2.45 (0.75, 8.05)	0.14
Surgical versus Botox	1.38 (0.26, 7.37)	0.7	2.39 (0.36, 15.81)	0.4
Poor PO tolerance				
6 months				
Botox versus no drainage	2.33 (1.05, 5.16)	0.037	2.33 (1.05, 5.20)	0.038
Surgical versus no drainage	0.50 (0.18, 1.40)	0.2	0.51 (0.18, 1.43)	0.2
Surgical versus Botox	0.21 (0.07, 0.65)	0.007	0.22 (0.07, 0.67)	0.008
12 Months				
Botox versus no drainage	3.03 (1.00, 9.12)	0.049	3.04 (1.00, 9.25)	0.050
Surgical versus no drainage	0.55 (0.15, 2.05)	0.4	0.60 (0.16, 2.29)	0.5
Surgical versus Botox	0.18 (0.04, 0.80)	0.024	0.20 (0.04, 0.88)	0.034
Early satiety				
6 Months				
Botox versus no drainage	2.70 (0.78, 9.29)	0.12	2.6 (0.75,9.04)	0.13
Surgical versus no drainage	2.27 (0.70, 7.32)	0.2	2.41 (0.74, 7.86)	0.14
Surgical versus Botox	0.84 (0.24, 2.93)	0.8	0.93 (0.26, 3.34)	0.9
12 months				
Botox versus no drainage	4.25 (1.06, 17.11)	0.041	3.94 (0.94, 16.54)	0.061
Surgical versus no drainage	2.21 (0.61, 7.95)	0.2	2.34 (0.62, 8.64)	0.2
Surgical versus Botox	0.52 (0.13, 2.12)	0.4	0.59 (0.14, 2.55)	0.5

OR odds ratio

^aMultivariable models were adjusted for age and BMI at the time of surgery

underwent surgical drainage were more likely to report symptoms compared to patients without drainage procedures ($p=0.023$). Patients that received Botulinum injection were also more likely to require pyloric dilation at 6 months compared to no drainage ($p=0.009$); however, no difference was observed between surgical drainage and no drainage. Patients with Botulinum injection were more likely to report poor PO tolerance compared to both no drainage and surgical drainage at 6 and 12 months. Multivariable analysis is presented in Table 3. Adjusted odds ratio demonstrated that the observed increased odds of reporting any symptoms persisted at 6 months in both the Botulinum injection (OR 4.14; 95% CI 1.83–9.35; $p=0.001$) and surgical drainage groups (OR 3.16; 95% CI 1.62–6.16; $p=0.001$) compared to no drainage, and persisted at 12 months in patients with surgical drainage (2.15; 95% CI 1.12–4.14; $p=0.021$). Patients with surgical drainage had lower odds of undergoing pyloric dilation at 6 months compared to Botulinum injection (0.07; 95% CI 0.01–0.70; $p=0.023$) and had lower odds of poor PO tolerance at 6 and 12 months ($p<0.05$).

Discussion

Despite advances in surgical technique and morbidity benefits attributed to use of a minimally invasive approach to esophagectomy, DGE and pyloric hypertonia resulting from vagal disruption are an inherent part of esophagectomy for malignancy regardless of operative approach. Pyloric drainage was adopted into practice based on studies from the 1990s that demonstrated reduced DGE, post-operative complications and symptoms in patients that underwent surgical drainage procedures for open esophagectomy [5, 6, 15]; however, more recent literature has failed to demonstrate similar benefits and has even shown increased complications with drainage leaving the role of these techniques unclear [4, 8]. As MIE increased in use, Botulinum injection was introduced as an alternative approach to the pylorus with the potential for improved morbidity and technical ease compared to surgical drainage techniques. As use of MIE continues to rise, identification of the optimal management of the pylorus with this surgical approach will better facilitate minimization of DGE associated sequelae following esophagectomy.

This study presents the largest comparison series of pyloric interventions in MIE alone to date, and the only study to evaluate post-operative outcomes and long-term symptoms. Our results demonstrated no difference in post-operative complications between patients that received no drainage, Botulinum injection or surgical drainage; and furthermore, patients that received drainage (Botulinum injection and surgical drainage) had increased reported symptoms compared to no drainage. Our findings support

previous studies in open esophagectomy that demonstrated no improvement in post-operative complications in patients that underwent pyloric drainage [4, 8, 11, 16].

Early studies with use of Botulinum injection found no clinical evidence for DGE in the post-operative period [10, 17]. A 2009 comparative study demonstrated improved post-operative DGE with use of Botulinum injection compared to surgical drainage approaches; however, the authors found no difference in morbidity and these results have not been replicated [11]. In fact, a subsequent study found that patients that received Botulinum injection may even have increased risk of pneumonia and post-operative mortality when compared to pyloroplasty [9]. Although we failed to demonstrate a difference in morbidity, it is interesting to note that patients that underwent surgical drainage and no drainage had a trend towards increased pneumonia. It is possible that in the immediate post-operative period, patients that receive surgical drainage techniques have edema at the pylorus which may impede function and result in stasis. This hypothesis is further supported by the observation that patients in this group had a significantly longer period to post-operative jejunostomy removal compared to the other groups, perhaps as a reflection of poor oral feeding tolerance as a result of DGE. Additionally, it is interesting to note that the 90-day reoperation rate in the no drainage group was almost $2\times$ lower than the Botox group and $2.6\times$ lower than the surgical drainage group. None of the reoperations in the no drainage group were indicated for DGE. Post-operative endoscopic dilation for early DGE is a safe, short procedure and the demonstrated 90-day reintervention dilation rate in the no drainage group was low compared to previously published studies [3, 9].

Results of long-term outcomes are less conclusive. Our study demonstrated that patients in both drainage groups had higher reported long-term symptoms at 6 and 12 months and increased need for pyloric dilation at 6 months as compared to no drainage. Patients with Botulinum injection had a trend towards higher reported symptoms and need for pyloric drainage at all time points compared to surgical drainage, although there were too few patients at 12 months to demonstrate a significant result. Drainage has previously been associated with increased bile reflux and esophagitis [8]. Studies comparing long-term outcomes between approaches have demonstrated conflicting findings regarding reflux, dumping, and need for pyloric dilation [9, 11]. In a study comparing drainage techniques in an exclusively MIE group of 146 patients, Giugliano et al. failed to demonstrate superiority of any approach in reducing need for subsequent post-operative pyloric dilation [18]. Although patients with no drainage required the highest rate of pyloric dilation in the immediate post-operative period, we demonstrated increased long-term symptoms and need for pyloric dilation in patients that receive Botulinum injection, even at

12 months after the effects would have certainly worn off. A possible explanation for this finding may be consequent fibrosis of the pylorus, as has been postulated in achalasia, resulting in continued dysfunctional emptying. Similarly, it is possible that surgical drainage techniques result in stricture of the pylorus in some patients leading to continued problems with gastric emptying despite recovery of nerve function. In a propensity matched comparison of patients with open esophagectomy that received surgical drainage against MIE without any drainage, Mehran and colleagues demonstrated no difference in reported dumping, reflux, or overall satisfaction at a median of 12-month follow-up [16]. Similarly, a series of 145 patients comparing pyloroplasty versus no drainage in MIE demonstrated that drainage could be safely omitted with minimal difference in gastric emptying and reduced operative time [19]. In the peri-operative and long-term period neither Botulinum injection nor surgical drainage has been shown to provide a definitive benefit over no drainage; as such, foregoing pyloric drainage may be a safe, reasonable option in MIE.

Our study was composed of 283 patients with more than 50 patients in each pyloric intervention group which supports the strength of our findings. However, the retrospective design of this study yields several limitations. We attempted to minimize confounding through multivariable analysis. There were 11 surgeons that performed MIE during the study period and there were too few events to adjust for surgeon as a variable in our analysis. Although differences in operative technique and peri-operative patient management may impact immediate short-term post-operative outcomes, the primary focus for this study was presence of symptoms and need for dilation long-term at 6 and 12 months by which point these peri-operative differences should no longer have an impact. Additionally, given that the decision to perform pyloric drainage is based upon specific surgeon practice rather than patient characteristics, it is less likely that there was selection bias in treatment allocation. Also, most of Botulinum injections were performed in the last 2 years of the study. Although we did not account for relative experience with MIE in this study, variation in surgeon experience should have had minimal to no impact on observed outcomes given that it is standard for junior attendings or attendings with minimal MIE experience to have two attendings present to perform the procedure. Lastly, the subjective assessment of symptoms does complicate the ability to quantify symptoms into broader categories, such as reflux or dumping; however, this method is consistent with other studies on this subject [9, 11]. These findings highlight the need for development of a unified system for classification of post-operative symptoms following esophagectomy. A currently ongoing prospective randomized study comparing Botulinum injection and no intervention in MIE may yield

further insight into the current controversies surrounding the role of pyloric drainage [20].

In conclusion, this study demonstrated that use of surgical drainage and Botulinum injection in MIE does not reduce post-operative morbidity and has increased long-term symptoms and need for pyloric dilation.

Funding This study was supported, in part, by the National Institutes of Health /National Cancer Institute Cancer Support Grant P30 CA008748. Tamar Nobel is supported, in part, by a grant from the American Cancer Society.

Compliance with ethical standards

Disclosures Tamar Nobel, Kay See Tan, Arianna Barbetta, Prasad Adu-sumilli, Manjit Bains, Matthew Bott, David Jones and Daniela Molena have no conflict of interest or financial ties to disclose.

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