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Pattern of Postoperative Mortality After Esophageal Cancer Resection According to Center Volume: Results from a Large European Multicenter Study

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ABSTRACT

Background. High center procedural volume has been shown to reduce postoperative mortality (POM); however, the cause of POM has been poorly studied previously. The aim of this study was to define the pattern of POM and major morbidity in relation to center procedural volume.

Methods. Data from 2,944 consecutive adult patients undergoing esophagectomy for esophageal cancer in 30 centers between 2000 and 2010 were retrospectively collected. Data between patients who suffered 30-day POM were compared with those who did not. Factors associated with POM were identified using binary logistic regression, with propensity matching to compare low- (LV) and high-volume (HV) centers.

Results. The 30-day and in-hospital POM rates were 5.0 and 7.3 %, respectively. Pulmonary complications were the most common, affecting 38.1 % of patients, followed by surgical site infection (15.5 %), cardiovascular complications (11.2 %), and anastomotic leak (10.2 %). Factors that were independently associated with 30-day POM included American Society of Anesthesiologists grade IV, LV center, anastomotic leak, pulmonary, cardiovascular and neurological complications, and R2 resection margin status. Surgical complications preceded POM in approximately 30 % of patients compared to medically-related causes in 68 %. Propensity-matched analysis demonstrated LV centers were significantly associated with increased 30-day POM, and POM secondary to anastomotic leak, and pulmonary- and cardiac-related causes.

Conclusions. The results of this large, multicenter study provide further evidence to support the centralization of esophagectomy to HV centers, with a lower rate of morbidity and better infrastructure to deal with complications following major surgery preventing further mortality.

On behalf of the FREGAT (French Eso-Gastric Tumors) Working Group – FRENCH (Fédération de Recherche EN CHirurgie) – AFC (Association Française de Chirurgie). The FREGAT working group – FRENCH – AFC Collaborators' list is given in Appendix.

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INTRODUCTION

In recent years there has been steady improvement in short-term outcome parameters, including postoperative mortality (POM), following esophagectomy.[1–3] The reasons for this improvement are multifactorial but include better patient selection, preoperative optimization, advances in surgical technique, and vast improvements in perioperative care.[4–6] The centralization of esophageal cancer services to high-volume (HV) centers with the appropriate infrastructure to manage these complex patients and deliver a consistently high level of care has been shown to reduce esophagectomy-associated morbidity and mortality.[7,8]

DThe impact of procedural volume on POM in esophagectomy is therefore well established;[9] however, the mechanisms underlying this are less well understood. Furthermore, little data are currently published regarding the causes of POM in relation to center procedural volume. The relative importance and identification of individual complications related to mortality is important as reducing the occurrence and severity of these complications can further reduce mortality following esophagectomy. The concept of the same complication increasing the likelihood of mortality in a low-volume (LV) center compared to an HV center due to a combination of severity and available treatment is clearly an important issue influencing service configuration.[10]

DPreoperative identification of high-risk patients for esophagectomy has received much attention by researchers for many years, with several risk-scoring systems being developed.[11,12] Other important factors that continue to be evaluated in relation to esophagectomy-associated POM include the utilization of neoadjuvant therapy, especially neoadjuvant chemoradiotherapy, and variation in operative technique.[13,14]

The aim of this study was to define the pattern and causes of POM and major morbidity in relation to center procedural volume.

METHODS

Patient Eligibility Criteria

Data from 2,944 consecutive adult patients undergoing surgical resection for esophageal cancer (including Siewert type I and II junctional tumors) with curative intent in 30 French-speaking European centers between 2000 and 2010 were retrospectively collected through a dedicated website (http://www.chirurgie-viscerale.org), with an independent monitoring team auditing data capture to minimize missing data and to control concordance, as well as inclusion of consecutive patients. Data collected included demographic parameters, details regarding perioperative and surgical treatments, postoperative outcomes, and histopathological analysis. Missing or inconsistent data were obtained from e-mail exchanges or phone calls with the referral center. The study was accepted by the regional Institutional Review Board on 15 July 2013, and the database was registered on the Clinicaltrials.gov website under the identifier NCT01927016.

Data Collection

Patient demographic data that were collected included patient age, sex, American Society of Anesthesiology (ASA) grade, and nutritional status. Patient malnutrition was defined by weight loss of more than 10 % over a 6-month period prior to surgery. Data regarding tumor location (upper, middle, or lower esophagus), clinical stage, and use of neoadjuvant therapy were also collected. Approach to surgery varied between three techniques—Ivor–Lewis, three-stage, or transhiatal esophagectomy. Postoperative morbidity was assessed, including esophageal anastomotic leak, surgical site infection, chylothorax, gastroparesis, pulmonary, cardiovascular, thromboembolic, neurological complications, and reoperation. The Clavien–Dindo scale was used to grade the severity of all postoperative morbidity.[15] Histologic staging of tumors was based on the 7th edition of the Union for International Cancer Control (UICC)/TNM classification.[16] Postoperative complications were defined using the previously reported definitions[17] (Appendix 1). The cause of mortality was considered as the first major complication that occurred, and mortality was defined as secondary to anastomotic leak, pulmonary, cardiac, or neurological complications.

Procedural-Center Volume

Each center was classified by the number of patients undergoing esophagectomy during the 10-year study period. Centers were initially divided into quartiles based on contribution to the study cohort (<30, 31–80, 81–135, >135) and according to the median (≤80 defining LV centers, and >80 defining HV centers).

Statistical Analysis

Continuous variables were expressed as the mean ± standard deviation or the median (range), and categorical variables as a percentage. A Mann–Whitney test was used for intergroup comparisons of continuous variables, whereas a Chi-square test or Fisher test was used to compare categorical data. A binary logistic regression was used to identify predictors of POM.

In a second step, we conducted a propensity score-matching analysis to compensate for the differences in some baseline characteristics between the LV and HV groups.[18] First, we compared all available patient and tumor variables using a Chi-square test, and a propensity score was then calculated using a logistic regression with the imbalanced variables. Finally, all analyses regarding POM and morbidity were adjusted based on the generated propensity score. Adjustment was also carried out for malnutrition as some missing variables did not allow us to integrate this into the propensity score. All tests were two-sided and the threshold for statistical significance was set to $p < 0.05$. Analyses were performed with SPSS® version 19.0 software (IBM Corporation, Armonk, NY, USA).

RESULTS

In total, 2,944 patients were included in the study; the 30-day and in-hospital POM rates were 5.0 % (147 patients) and 7.3 % (215 patients), respectively. The median age of the study group was 61 (20–93) years, with 82.4 % being male, 58.1 % were ASA grade II, and 24.4 % showed evidence of preoperative malnutrition. An Ivor–Lewis surgical technique was employed in 74.2 % of cases, neoadjuvant chemotherapy was utilized in 46.1 %, and in combination with radiotherapy in 28.8 % of cases. Clinical stage III disease was seen in 47.9 % of patients, with 50.7 % presenting with adenocarcinoma; the most common site affected was the lower oesophagus (53 %).

Pulmonary complications were the most common type of complication following esophagectomy, affecting 38.1 % of patients, followed by surgical site infection (15.5 %), cardiovascular complications (11.2 %), and anastomotic leak (10.2 %). When complications were graded according to the Clavien–Dindo classification, 13.3 % were grade I, 32.3 % grade II, 9.3 % grade IIIa, 11.9 % grade IIIb, 17.1 % grade Iva, and 3.5 % grade IVb. The median intensive care unit (ICU) stay was 7 (1–28.7) days, and the median length of hospital stay was 18 (1–21.6) days for the patients studied. Assessment of pathology showed the most common stage was stage III in 36.7 % of patients, and macroscopically positive resection margins (R2) were seen in 3.3 % of cases.

30-Day Mortality: 5.0 % (147 patients)

Preoperative factors associated with 30-day POM included ASA grade IV and low center procedural volume (Table 1). Analysis for in-hospital mortality (7.3 %) suggested similar factors were associated with mortality, with the only additional factors being patient age ≥60 years and the requirement for reoperation. The causes of mortality of 30-day POM were, most commonly, medically related in 68.7 % of cases. With respect to individual complications, pulmonary complications were responsible for approximately 51.6 % of POM, with anastomotic leak responsible for 19.1 %.

Comparison of Low- and High-Volume Centers

Centers were initially divided into quartiles based on contribution to the study cohort (<30, 31–80, 81–135, >135). However, there was little difference seen in 30-day POM between the two LV groups (8.5 % [<30 resections] vs. 11.2 % [31–80 resections]) and the two HV groups (3.4 % [81–135 resections] vs. 2.8 % [>135 resections]); therefore, the centers were re-classified into two groups as LV and HV based on the median number of resections ($n = 80$).

There was a significant decrease in surgery performed in LV centers after 2006 (45.5 % [LV] vs. 51.7 % [HV]). Analysis of patient demographics showed that in LV centers there was a greater proportion of male patients and those with ASA grade III; however, malnutrition and clinical stage III disease were reduced compared with HV centers. These differences in clinical stage may also have been reflected by the reduction in the utilization of neoadjuvant chemoradiotherapy and three-stage esophagectomy seen in LV centers. Pathological stage may also have been affected by this difference in practice pattern, with a reduction in stage 0 and increase in stage IV disease observed in LV centers (Table 2).

Thirty-day POM (10.5 vs. 3 %) was significantly increased in LV centers. Specifically, mortality related to anastomotic leak, and pulmonary and cardiac complications were increased in LV centers (Table 3). Furthermore, in LV centers there was a greater incidence of major morbidities, including anastomotic leak, postoperative hemorrhage, pulmonary, cardiovascular, thromboembolic and neurological complications, surgical site infections, and reoperation. When the severity of complications was assessed using the Clavien–Dindo classification, the incidence of Clavien–Dindo III (15.2 vs. 11.2 %) and IV (13.9 vs. 11.2 %) were increased in LV centers.

Propensity-Matched Analysis

Thirty-day POM was significantly greater in LV centers when compared with HV centers (odds ratio [OR] 0.30; 95 % confidence interval [CI] 0.20–0.44; $p < 0.001$). POM secondary to anastomotic leak (OR 0.30; 95 % CI 0.15–0.61; $p = 0.001$), pulmonary-related (OR 0.41; 95 % CI 0.26–0.64; $p < 0.001$) and cardiac-related (OR 0.32; 95 % CI 0.13–0.81; $p = 0.017$) causes were all increased in LV centers.

Analysis of morbidity demonstrated that LV centers were associated with a significantly increased incidence of anastomotic leak (OR 0.54; 95 % CI 0.41–0.72; $p < 0.001$), surgical site infection (OR 0.63; 95 % CI 0.49–0.80; $p < 0.001$), pulmonary (OR 0.47; 95 % CI 0.39–0.56; $p < 0.001$), cardiovascular (OR 0.68; 95 % CI 0.51–0.90; $p = 0.006$) and thromboembolic (OR 0.51; 95 % CI 0.30–0.88; $p = 0.014$) complications, along with reoperation (OR 0.54; 95 % CI 0.42–0.69; $p < 0.001$).

DISCUSSION

This large, multicenter study of 2,944 patients undergoing esophagectomy for cancer demonstrated that the

TABLE 1 30-day mortality analysis

Variable	Overall incidence [$n = 2{,}944$ (%)]	Univariable analysis			Multivariable analysis		
		Mortality group [$n = 147$ (%)]	Control group [$n = 2{,}797$ (%)]	p Value	OR	95 % CI	p Value
Surgery after 2006	1,473 (50.0)	63 (42.9)	1,410 (50.4)	0.074	–	–	–
Age ≥60 years	1,518 (51.6)	85 (57.8)	1,433 (51.2)	0.119	1.36	0.92–2.00	0.125
Male incidence	2,427 (82.4)	122 (83.0)	2,305 (82.4)	0.856	–	–	–
Malnutrition at presentation	601 (24.4)	33 (22.4)	568 (20.3)	0.161	–	–	–
ASA score							
1	479 (16.3)	16 (10.9)	463 (16.6)	<0.001	1.0		0.006
2	1,711 (58.1)	79 (53.7)	1,632 (58.3)		1.04	0.57–1.91	0.897
3	719 (24.4)	44 (29.9)	675 (24.1)		1.04	0.54–2.01	0.907
4	35 (1.2)	8 (5.4)	27 (1.0)		6.07	2.00–18.44	0.001
Tumor location							
Upper	403 (13.7)	36 (24.5)	367 (13.1)	<0.001	1.18	0.65–2.14	0.599
Middle	980 (33.3)	49 (33.3)	931 (33.3)		0.84	0.52–1.35	0.461
Lower	1,561 (53.0)	62 (42.2)	1,499 (53.6)		1.0		0.457
Clinical TNM stages							
I	726 (24.7)	26 (17.7)	700 (25.0)	0.209	–	–	–
II	770 (26.1)	43 (29.3)	727 (26.0)				
III	1,409 (47.9)	75 (51.0)	1,334 (47.7)				
IV	39 (1.3)	3 (2.0)	36 (1.3)				
Surgical technique							
Ivor–Lewis	2,185 (74.2)	99 (67.3)	2,086 (74.6)	0.006	1.0		0.719
Three-stage	344 (11.7)	21 (14.3)	323 (11.5)		1.01	0.55–1.84	0.989
Transhiatal	415 (14.1)	27 (18.4)	388 (13.9)		1.24	0.73–2.09	0.428
Center volume[a]							
≤80	781 (26.5)	82 (55.8)	699 (25.0)	<0.001	2.62	1.77–3.87	<0.001
>80	2,163 (73.5)	65 (44.2)	2,098 (75.0)		1.0		
Neoadjuvant chemoradiotherapy	847 (28.8)	50 (34.0)	797 (28.5)	0.161	1.22	0.78–1.90	0.382
Anastomotic leak	299 (10.2)	53 (36.1)	246 (8.8)	<0.001	5.05	1.86–13.69	0.001
Surgical site infection	457 (15.5)	58 (39.5)	399 (14.3)	<0.001	1.54	0.58–4.08	0.385
Chylothorax	70 (2.38)	2 (1.4)	68 (2.4)	0.581	–	–	–
Postoperative hemorrhage	10 (0.3)	9 (6.1)	1 (0.04)	<0.001	179.12	21.09–1,521.05	<0.001
Gastroparesis	39 (1.3)	1 (0.7)	38 (1.4)	0.720	–	–	–
Pulmonary complication	1,122 (38.1)	110 (74.8)	1,012 (36.2)	<0.001	3.35	2.17–5.18	<0.001
Cardiovascular complication	331 (11.2)	46 (31.3)	285 (10.2)	<0.001	2.80	1.74–4.51	<0.001
Thromboembolic event	84 (2.9)	13 (8.8)	71 (2.5)	<0.001	1.19	0.54–2.59	0.666
Neurological complication	21 (0.7)	6 (4.1)	15 (0.5)	<0.001	1.01	0.80–1.28	0.929
Reoperation	429 (14.6)	55 (37.4)	374 (13.4)	<0.001	1.48	0.94–2.34	0.094
Histology							
SCC	1,363 (46.3)	91 (61.9)	1,272 (45.5)	0.001	1.19	0.33–4.30	0.787
Adenocarcinoma	1,494 (50.7)	53 (36.1)	1,441 (51.5)		0.80	0.22–2.87	0.729
Other	87 (3.0)	3 (2.0)	84 (3.0)		1.0		0.238

TABLE 1 continued

Variable	Overall incidence [$n = 2{,}944$ (%)]	Univariable analysis			Multivariable analysis		
		Mortality group [$n = 147$ (%)]	Control group [$n = 2{,}797$ (%)]	p Value	OR	95 % CI	p Value
Tumor differentiation							
Good	880 (29.9)	39 (26.5)	841 (30.1)	0.327	–	–	–
Average	1,026 (34.9)	61 (41.5)	965 (34.5)				
Poor	479 (16.3)	24 (16.3)	455 (16.3)				
Not reported	559 (18.9)	23 (15.7)	536 (19.2)				
Pathological stage							
0	292 (9.9)	14 (9.5)	278 (95.2)	0.045	1.0		0.275
I	854 (29.0)	34 (23.1)	820 (96.0)		4.20	1.0–17.68	0.051
II	666 (22.6)	34 (23.1)	632 (94.9)		2.96	0.77–11.32	0.113
III	1,079 (36.7)	58 (39.5)	1,021 (94.6)		2.91	0.77–11.00	0.115
IV	53 (1.8)	7 (4.8)	46 (1.6)		3.47	1.00–12.06	0.050
Resection margin							
R0	2,600 (88.3)	111 (75.5)	2,489 (89.0)	<0.001	1.0	0.81–2.69	<0.001
R1	248 (8.4)	19 (12.9)	229 (8.2)		1.47		0.205
R2	96 (3.3)	17 (11.6)	79 (2.8)		8.16	3.41–19.54	<0.001

() Values percentages

[a] Hospitals were divided into two groups based on the number of patients included during the study from each hospital, with division at 80 patients (the median value for the cohort)

30-day POM was 5 % in the current era. Factors that were independently associated with 30-day POM included ASA grade IV, LV center, anastomotic leak, postoperative hemorrhage, pulmonary and cardiovascular complications, and R2 resection margin status. Esophagectomy performed by LV was associated with an increase in 30-day POM, specifically mortality secondary to anastomotic leak, and pulmonary and cardiac causes. Morbidity including anastomotic leak, surgical site infection, and pulmonary, cardiovascular and thromboembolic complications, as well as reoperation were all seen to increase in LV centers.

Major complications, including anastomotic leak, pulmonary and cardiovascular complications, and requirement for reoperation were significant predictors of POM. In the short-term, major complications such as anastomotic leak can lead to devastating mediastinitis and overwhelming sepsis, causing fatality.[19,20] The combination of the severity of these complications and the management ensued is clearly important in determining the overall risk of mortality from the complication.

A threshold of 80 esophagectomy procedures over the 10-year period, on average eight per year, was utilized to define LV and HV centers based on the median of the dataset. A reduced proportion of resections have been performed in LV centers since 2006, which may represent a shift towards centralization of esophagectomy to HV centers over time, as seen in other countries.[21] LV centers had a greater proportion of patients with ASA grade III or IV, which may represent an issue associated with patient selection for esophagectomy. The utilization of neoadjuvant chemoradiotherapy was reduced in LV centers and may be responsible for the decrease in pathological stage 0 and increase in stage IV disease observed. This may, in part, be due to differences in practice patterns associated with more specialized multidisciplinary tumor boards in HV centers to appropriately allocate multimodality treatment for advanced esophageal cancer. Similarly, positive resection margin status was increased in LV centers, which may be a reflection of the reduced usage of neoadjuvant chemoradiotherapy or, alternatively, the quality of surgery offered in LV centers.

Propensity scoring to adjust for these confounding variables showed center procedural volume remained an important factor significantly associated with 30-day POM. Furthermore, LV centers were significantly associated with an increase in mortality secondary to anastomotic leak. As has been previously argued, greater procedural volume may impart a higher level of technical ability seen by surgeons in HV centers, translating into a reduction in surgically-related morbidity and mortality. Therefore, this may be a reflection of the greater incidence of these surgical complications in LV centers, or a difference in the management of these complications due to resource availability, i.e. interventional radiology and endoscopy.

TABLE 2 Comparison of demographic and therapeutic characteristics of the study population according to low- versus high-volume centers before matching

Characteristic	Overall incidence [$n = 2{,}944$]	Low volume [$n = 781$]	High volume [$n = 2{,}163$]	p Value
Surgery after 2006	1,473 (50.0)	355 (45.5)	1,118 (51.7)	0.003
Age ≥60 years	1,518 (51.6)	413 (52.9)	1,105 (51.1)	0.390
Male incidence	2,427 (82.4)	673 (86.2)	1,754 (81.1)	0.001
Malnutrition	601 (24.4)	142 (18.2)	459 (21.2)	0.008
ASA score				
1	479 (16.3)	129 (16.5)	350 (16.2)	0.047
2	1,711 (58.1)	426 (54.5)	1,285 (59.4)	
3	719 (24.4)	213 (27.3)	506 (23.4)	
4	35 (1.2)	13 (1.7)	22 (1.0)	
Tumor location				
Upper	403 (13.7)	107 (13.7)	296 (13.7)	0.151
Middle	980 (33.3)	281 (36.0)	699 (32.3)	
Lower	1,561 (53.0)	393 (50.3)	1,168 (54.0)	
Clinical TNM stage				
I	726 (24.7)	209 (26.8)	517 (23.9)	0.002
II	770 (26.1)	221 (28.3)	549 (25.4)	
III	1,409 (47.9)	334 (42.7)	1,075 (49.7)	
IV	39 (1.3)	17 (2.2)	22 (1.0)	
Surgical technique				
Ivor–Lewis	2,185 (74.2)	616 (78.9)	1,569 (72.5)	<0.001
Three-stage	344 (11.7)	58 (7.4)	286 (13.2)	
Transhiatal	415 (14.1)	107 (13.7)	308 (14.2)	
Neoadjuvant chemoradiotherapy	847 (28.8)	162 (20.7)	685 (31.7)	<0.001
Histology				
SCC	1,363 (46.3)	416 (53.3)	947 (43.8)	<0.001
Adenocarcinoma	1,494 (50.7)	349 (44.7)	1,145 (52.9)	
Other	87 (3.0)	16 (2.0)	71 (3.3)	
Tumor differentiation				
Good	880 (29.9)	228 (29.2)	652 (30.1)	0.312
Average	1,026 (34.9)	292 (37.4)	734 (33.9)	
Poor	479 (16.3)	125 (16.0)	354 (16.4)	
Not reported	559 (18.9)	136 (17.4)	423 (19.6)	
Pathological stage				
0	292 (9.9)	49 (6.3)	243 (11.2)	<0.001
I	854 (29.0)	224 (28.7)	630 (29.1)	
II	666 (22.6)	185 (23.7)	481 (22.2)	
III	1,079 (36.7)	300 (38.4)	779 (36.0)	
IV	53 (1.8)	23 (2.9)	30 (1.4)	
Resection margin				
R0	2,600 (88.3)	665 (85.1)	1,935 (89.5)	0.006
R1	248 (8.4)	84 (10.8)	164 (7.6)	
R2	96 (3.3)	32 (4.1)	64 (3.0)	

Furthermore, low procedural volume was significantly associated with medically-related mortality, specifically mortality secondary to pulmonary and cardiac complications. This may, in part, be due to the global package of care imparted by surgery in HV centers, including advanced anesthetic, ICU, and medical care, improving outcomes in patients following major surgery such as esophagectomy.

TABLE 3 Comparison of mortality and morbidity in the study population according to low- versus high-volume centers

Characteristic	Overall incidence [$n = 2{,}944$]	Low volume [$n = 781$]	High volume [$n = 2{,}163$]	p-Value
30-day mortality	147 (5.0)	82 (10.5)	65 (3.0)	<0.001
In-hospital mortality	215 (7.3)	107 (13.7)	108 (5.0)	<0.001
Mortality cause				
Anastomotic leak	41 (1.4)	24 (3.1)	17 (0.8)	<0.001
Pulmonary	111 (3.8)	51 (6.5)	60 (2.8)	<0.001
Cardiac	25 (0.8)	12 (1.5)	13 (0.6)	0.015
Neurological	7 (0.2)	2 (0.3)	5 (0.2)	0.902
Morbidity				
Anastomotic leak	299 (10.2)	118 (15.1)	181 (8.4)	<0.001
Surgical site infection	457 (15.5)	163 (20.9)	294 (13.6)	<0.001
Chylothorax	70 (2.4)	18 (2.3)	52 (2.4)	0.876
Postoperative hemorrhage	10 (0.3)	8 (1.0)	2 (0.1)	0.001
Gastroparesis	39 (1.3)	9 (1.2)	30 (1.4)	0.623
Pulmonary	1,122 (38.1)	396 (50.7)	726 (33.6)	<0.001
Cardiovascular	331 (11.2)	107 (13.7)	224 (10.4)	0.011
Thromboembolic	84 (2.9)	32 (4.1)	52 (2.4)	0.015
Neurological	21 (0.7)	4 (0.5)	17 (0.8)	<0.001
Reoperation	429 (14.6)	163 (20.9)	266 (12.3)	<0.001
Clavien–Dindo classification				
I	226 (13.3)	57 (7.3)	169 (7.8)	<0.001
II	549 (32.3)	140 (17.9)	409 (18.9)	
IIIa	158 (9.3)	48 (6.1)	110 (5.1)	
IIIb	202 (11.9)	71 (9.1)	131 (6.1)	
IVa	291 (17.1)	88 (11.3)	203 (9.4)	
IVb	59 (3.5)	20 (2.6)	39 (1.8)	

There are limitations of this study that must be considered when evaluating the significance of the outcomes presented, including its design as a retrospective, observational study. As a large, multicenter database study, the results generated are dependent on the reliability of the methodology of data collection. To minimize any bias associated with data collection methodology during this study an independent monitoring team audited data capture to minimize missing data and to control concordance, as well as ensure inclusion of consecutive patients. One would argue that LV and HV groups are not comparable. This prompted us to use propensity score matching to compensate for some differences in baseline characteristics. The definition of complications following major surgery is an important issue that is a limitation of large database studies. However, the definition of complications employed at the outset of this study, along with the methodology of data collection employed, suggests that this present study provides good evidence regarding the influence of complications on mortality. ASA grade was used to provide assessment of patients' physiological status prior to undergoing surgery. However, previous authors have suggested that ASA grade provides a crude assessment of the operative risk imparted by the patients' physiological status.[5] The results of this multicenter study suggest that ASA grade can identify patients at risk of POM following esophagectomy, when this ranges from 5–7 %. However, ASA grade is less likely to be able to identify these patients in HV centers with a very low incidence of POM. The threshold to define LV and HV centers was set at eight resections, which some clinicians may argue is low. However, no differences were observed between the two HV groups and the two LV groups in 30-day mortality when the centers were divided into quartiles based on procedural volume. Furthermore, a recent systematic review of the volume–outcome relationship in esophagectomy identified that seven of nine articles used a threshold of nine resections per year or less to define LV centers.[7] This suggests the threshold used in this study is true to the data presented and consistent with the published literature on this subject.

CONCLUSIONS

This large, multicenter study of 2,944 patients undergoing esophagectomy for cancer suggests that 30-day POM is 5 % in the modern era. Center procedural volume is an important factor associated with mortality and morbidity. In LV centers, mortality secondary to anastomotic leak, and pulmonary and cardiac complications were all increased. The results of this study provide further evidence to support the centralization of esophagectomy to HV centers, with a lower rate of morbidity and better infrastructure to deal with complications following major surgery preventing further mortality.

CONFLICTS OF INTEREST None.

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APPENDIX 1

Surgical Complications

Anastomotic leak was defined as any esophagogastric anastomosis dehiscence that was clinically symptomatic (abscess, mediastinitis, digestive liquid externalizing drainage) or asymptomatic detected by contrast study. In case of doubt, the diagnosis was confirmed by gastroscopy without insufflation performed by an experienced physician.

Surgical site infection was defined as superficial pus expressed from the abdominal, thoracic, or drains incision sites, requiring surgical debridement and antibiotic treatment.

Chylothorax was suspected when a major pleural effusion was seen in the first postoperative week upon resumption of feeding, and was defined by the presence of pleural or abdominal fluid, rich in chylomicrons and lymphocytes.

Postoperative hemorrhage was defined as blood loss requiring endoscopic or surgical intervention.

Gastroparesis was defined as the occurrence of vomiting after removal of the nasogastric tube or distension of the gastric conduit on plain radiograph after day 5 postoperatively, requiring repositioning of the nasogastric tube despite prokinetic treatment.

Medical Complications

Pulmonary complications included bronchial congestion, disorders of ventilation, atelectasis, pneumonia, respiratory failure, and acute respiratory distress syndrome.

Cardiovascular complications included angina, myocardial infarction, arrhythmia, and cardiac insufficiency.

Thromboembolic complications included deep venous thrombosis and pulmonary embolism.

Neurological complications included temporospatial disorientation, transient ischemic attack, and cerebrovascular accident.

APPENDIX 2

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