Case Volume-to-Outcome Relationship in Minimally-Invasive Esophagogastrectomy

Running Head: A National Cancer Database Analysis

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Abstract

Background: Outcomes after open esophagectomy (OE) have been shown to depend on institution case volume. We aim to determine whether a similar relationship exists for minimally-invasive esophagogastrectomy (MIE).

Methods: Patients who had OE or MIE (excluding robotic procdures) between 2010 and 2013 in the National Cancer Database were included. Outcomes included 30- and 90-day mortality, length-of-stay, hospital readmission, margin positivity, and number of lymph nodes harvested. Logistic and linear regression were used to adjust for possible confounders including age, gender, tumor size, Charlson score, induction therapy, and type of institution (academic vs. community-based).

Results: We identified 2371 patients in the MIE group and 6285 patients in the OE group. In multivariate analysis, high case volume was an independent predictor for lower 30-day, 90-day mortality, shorter length-of-stay, and higher rate of negative-margin resection in OE ($P<0.001$) but not MIE. After quartile ranking of institutions based on volume, MIE outcomes were found to be better in institutions in the highest volume quartile compared to those in the lowest ($p< 0.0001$).

Conclusions: In this dataset, MIE postoperative outcomes, unlike OE, did not correlate with hospital case volume. Volume-outcome relationships may be affected by surgical approach. The effect of case volume on long-term outcomes after MIE warrants further study.

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Esophageal carcinoma typically presents with locally-advanced or metastatic disease precluding surgical resection[1-4]. For early-stage tumors, esophagogastrectomy (EG) is the best option for cure despite carrying significant risks and post-operative complications compared to other operations with similar complexity[1,2,4]. Within the past decade, minimally-invasive (MIE) esophagogastrectomy has gained increasing popularity due to decreased post-operative pain and lengt-of-stay while maintaining similar outcomes when compared to the traditional open approach[5-22]. However, MIE has an extensive learning curve, and typically are performed routinely only at tertiary referral centers with high-volume[15-19]. While previous reports indicated a direct correlation between open EG case volume and operative outcome[20-28], no studies have evaluated this relationship in MIE. The primary goal of this study is to determine whether short-term and oncologic outcomes for minimally-invasive esophagogastrectomy for esophageal cancer is dependent on institutional case volume.

Patients and Methods

Patients

The National Cancer Database (NCDB) is a de-identified clinical oncology hospital registry data from community, comprehensive community, and academic facilities. Following an exemption granted by the local Institutional Review Board, the NCDB was queried for all esophagectomies performed between January 1 2010 through December 31, 2013. We elected to begin with 2010 and not earlier due to the minimal implementation of MIE prior to this time period. We chose to end data collection at 2013 to allow for a complete 5-year follow-up in our analyses. Patients with concurrent laryngectomy, esophagogastrectomy with staged or non-gastric conduits were excluded. All included patients were categorized into laparoscopic (MIE), open (OE), or robotic. Given the small number of robotic esophagectomies, this group was excluded from final analysis.

Statistical Analysis

Demographics including age and gender, Charlson comorbidity index, neoadjuvant chemoradiation, clinical, and pathological T-stage were described using descriptive statistics. Pearson's Chi-square and student's t-tests were used to analyzed categorical and continuous variables, respectively. Pooled multivariable logistic and linear models were used to examine outcomes including 30 and 90-day mortality, R0 resection, 30-day readmissions, long-term survival, length-of-stay, number of regional nodes collected, and number of positive nodes. All models were controlled for the effect of annual case volume and annual laparoscopic-to-open conversion rates in addition to preoperatibe characteristics. Multicollinearity were tested and highly correlative variables were omitted from our final model[28]. Casewise deletion was used for missing data. Multivariable regression analysis were performed for MIE and OE subgroup.

Volume analysis

The institution annual esophagogastrectomy (MIE and OE) case volume and MIE case volume during the study period were analyzed. Quartiles were created with cut-offs at 25th, 50th, and 75th percentile. For each outcome, we performed interquartile comparisons of the multivariable regression estimates.

Propensity Score Matching

To examine any differences in outcomes between MIE and OE that might explain differences in volume-outcome realtionships due to selection bias[29], we used PSMATCH2[30] command in Stata SE 14.2 to match each MIE to OE case without replacement. The optimal caliper width[31] of 0.10 to match age, gender, tumor size, Charlson's comorbidity score, induction radiation and chemotherapy, and type of institution (academic versus community-based). Multivariable logistic and linear regressions were performed on the matched pairs.

Kaplan-Meier survival analysis

Using time from diagnosis to the last contact and/or death, we performed Kaplan-Meier (KM) analysis to estimate the survival function for unmatched and matched cohorts. Difference in survival between MIE and OE were examined using log-rank tests.

Results

We identifiied 8656 cases of esophagogastrectomy performed between January 1, 2010 through December 31, 2013. 6285 cases were performed open and 2371 cases were performed using the minimally-invasive approach. The median volume of esophagogastrectomy performed per year per facility was 8 (range 1-113). Similarly, the median volume of MIE performed per facility was 5 (range 1-42) with a mean conversion rate of 3.3 cases per year.

Cohorts

Demographics and preoperative factors including tumor size, Charlson score, clinical and pathologic staging, and neoadjuvant chemotherapy and radiation are presented in Table 1. There was no differences in any of the aforementioned factors except for larger tumor size (35 mm versus 31 mm, $p<0.05$) and higher clinical T-stage ($p<0.006$) in OE. No differences in pathologic staging were noted. In bivariate analysis, the MIE group was noted to have a shorter length-of-stay (LOS) ($p<0.001$), lower 30-day and 90-day mortality ($p<0.05$), higher number of lymph nodes collected ($p< 0.001$), and longer 5-year overall survival ($p<0.05$) as compared to the OE cohort (Table 2). Multivariate regression analyses identified the MIE approach as an independent predictor of lower 30 and 90-day mortality, shorter LOS, higher number of examined lymph nodes and higher 5-year survival ($p<0.05$) (Table 3). These findings persisted after propensity matching was performed accounting for age, gender, Charlson Comorbidity Index, tumor size, and stage ($p<0.05$) (Table 4).

When looking at all cases (open and MIE), multivariate analysis revealed that volume was found to be a predictor of all outcome variables except for 30-day readmission (Table 3). Further subgroup analyses indicated that case volume as a continuous variable was a significant predictor of all outcome measures for OE but not MIE (Supplemental Table 1). Conversion from MIE to open approach was associated with a slight increased in 30-day mortality in MIE subgroup but carried no effects on any other outcomes.

Volume quartile analysis.

Institutions were ranked based on the number of total esophagogastrectomy performed annually. The lowest quartile performed an average of 2.4 cases annually and the highest quartile performed an average of 42.5 cases per year (range 20-113 cases). Regression estimates were compared between all quartiles (Table 5). The highest performing centers were found to have reduced 30-day [OR 0.44] and 90-day [OR 0.56] mortality when compared to the two lowest-performing quartiles ($p<0.05$). Centers that performed 20 to 113 cases per year (4^{th} quartile) also had shorter length-of-stay [OR -1.80, $p<0.05$], higher number of lymph nodes collected [OR 6.09, $p<0.001$], and lower rate of incomplete resection [OR 0.63, $p<0.05$] when compared to the first quartile ($p< 0.05$). High-volume centers have decreased long-term mortality compared to all other quartiles ($p<0.05$) (Table 5). These differences dissipated when institutions were ranked based on annual MIE cases (Supplemental Table 2). Similar analyses were performed for matched cohorts and no significant differences were noted for any outcome variables except for the number of lymph nodes collected and long-term mortality (data not shown).

Oncologic outcomes

Case volume and MIE were positive independent predictors of the number of lymph nodes collected in both matched and unmatched cohorts (Table 3, 4). Although no differences were found in final N-stage in pooled results, subgroup analyses revealed that case volume correlates with higher rate of R0 resection and number of collected and lymph nodes in OE but not MIE (Supplemental Table 1). Interquartile comparisons revealed similar findings.

Comment

Analyses of the Medicare database in 2011 indicated that EG operative complications are inversely associated with institutional case volume and thus shifted the paradigm towards centralizing care for esophagogastrectomy[20,21,32]. A similar relationship was recently noted between complex laparoscopic operations and the volume of their open counterparts and suggested institutionally-derived benefits at tertiary care centers[32,33]. In the setting of rapid adoption of minimally-invasive esophagectomies across all institutions, we seek to define the effects of esophagogastrectomy case volume on MIE outcomes.

The NCDB database provided a robust multi-institutional patient population capturing approximately 75 percent of cancer cases in the United states with data regarding type of operations, type of institutions, and case volume over several years. Our study of this patient population corroborated findings from previous reports indicating that volume is an independent predictor of postoperative outcomes and mortality in all esophagectomy cases[22-27]. However, subgroup analysis suggest that this relationship only holds true for open cases and volume as a continuous variable did not contribute an effect on minimally-invasive esophagectomy. We further explored this relationship in a volume-outcome relationships were analyzed as a rank-test. Our quartile analysis suggested that differences in outcomes are only seen between the highest (4th quartile) and lowest (1st quartile) volume centers. This suggests that marginal increases in volume is not a positive predictor of outcome and corroborates with the finding of a large challenging learning curve of MIE in that a threshold case volume is required to achieve a benefit in outcome[34,35,36]. Previous studies determined that mortality benefits arise from high-volume centers that perform at least 20 esophagogastrectomies annually as compared low-volume institutions perform between 1 to 10 cases[34,35]. These divisions correlated with our quartile rankings. Even though our analysis did not determine a cut-off value for the number of cases required to improve outcome, it is reasonable to surmise rankings similar to previous study. It is interesting to note that differences in outcomes are only noted when institutions were ranked based on total volume of esophagectomy cases (open and MI) performed per year. When institutions were ranked based only on the number of MI esophagectomies performed annually, no significant differences were detected in any outcome parameters. These results suggest that outcomes for MIE rely on institutionally-derived benefits including multidisciplinary care rather than on MIE case volume alone. It is unclear at this point how and to what degree the institutional advantages have conferred to these cases and this needs to be explored in future studies[36,37].

Our Kaplain-Meier analysis revealed a long-term survival benefit for MIE patients in matched cohorts with case volume as a significant predictor. This is independent of preoperative clinical staging, surgical margins, complete resection, lymph node status, and final pathology staging. To our knowledge, this survival advantage has not been previously established. Of interest, the number of resected lymph nodes correlated with higher case volumes and was also higher in MIE cases. These effects of institutional case volume on long-term survival warrant further study.

Our study is limited in its retrospective nature and data errors inherent to national databases exist. In addition, the NCDB database also had missing data in several fields including clinical staging, pathology, and accurate description of surgical procedure type. The missingness of our clinical staging was approximately 2.30%. There were 2.59% (n=224) patients with missing pathological stages. To address this, as suggested in the NCDB Public Use File Data Dictionary, we used clinical stage to impute the tumor staging. After this imputation, we had only 2.26% (n=196) patients with missing stages. Because of the small percent of missingness, casewise deletion was done when analyzing the pathological stages. In addition, we do believe that propensity matching eliminates these errors. Another inherent limitation lies in the ability to determining volume association with specific complications of esophagogastrectomy including anastomotic leak. Even though these surgery-specific outcomes were not captured in our dataset, it is assumed that their presence would indirectly prolonged LOS or increased 30-day readmission rate[38]. We found that the MIE approach was a negative predictor of hospital LOS but that was negated in matched cohorts (p=0.051). However, no inferences can be made whether this is due to an equal rate of surgery-specific complications or secondary to the institutions' abilities to mitigate the complications so that surrogate outcomes such as LOS and readmission are not affected. The latter would suggest that case volume have an indirect positive effect on shortening hospital stay but our findings on this were inconclusive. Our study was also unable to account for specific surgical techniques (Ivor Lewis versus McKeown versus transhiatal), transfusions, and operative time which are factors that may mitigate surgical outcomes[38]. However, we do believe that despite these limitations, these statistical reviews of NCDB still has value in defining certain, though not all, factors that contribute to overall outcomes of complex surgical procedures such as esophagectomy[33,39].

In conclusion, our analyses of the NCDB esophagogastrectomy database demonstrates that perioperative outcomes of open cases had a direct linear correlation with case volume. The effect of case volume on the MIE outcomes, however, was only apparent when comparing the highest and lowest volume centers. This may be due to the fact that small incremental changes in MIE volume do not confer any short-term advantages, particulary since the overall MIE outcomes were shown to be better in a parallel, propensity-matched analysis. It is unclear whether the volume outcome relationships also confer a true long-term oncologic benefit. Further studies to investigate these relationships are warranted.

References

1. D'Amico TA. Outcomes After Surgery for Esophageal Cancer. Gastrointest Cancer Res 2007;1(5):188-96.
2. Pennathur A, Gibson MK, Jobe BA, Luketich JD. Oesophageal carcinoma. Lancet 2013;381(9864):400-412.
3. Hagen JA, DeMeester SR, Peters JH, Chandrasoma P, DeMeester TR. Curative Resection for Esophageal Adenocarcinoma: Analysis Of 100 En Bloc Esophagectomies. Ann Surg 2001;234(4):520-31.
4. Zahoor H, Luketich JD, Levy RM et al. A propensity-matched analysis comparing survival after primary minimally invasive esophagectomy followed by adjuvant therapy to neoadjuvant therapy for esophagogastric adenocarcinoma. J Thorac Cardiovasc Surg 2015;149(2):538-47.
5. Biere SS, Maas KW, Bonavina L et al. Traditional invasive vs. minimally invasive esophagectomy: a multi-center, randomized trial (TIME-trial). BMC Surgery 2011;11:2.
6. Biere SS, van Berge Henegouwen MI, Maas KW et al. Minimally invasive versus open oesophagectomy for patients with oesophageal cancer: a multicenter, open-label, randomized controlled trial. Lancet 2012;379(9829):1887-92.
7. Luketich JD, Pennathur A, Franchetti Y et al. Minimally Invasive Esophagectomy: Results of a Prospective Phase II Multicenter Trial- the Eastern Cooperative Oncology Group (E2202) study. Ann Surg 2015;261(4):702-7.
8. Zhou C, Zhang L, Wang H et al. Superiority of Minimally Invasive Oesophagectomy in Reducing In-Hospital Mortality of Patients with Resectable Oesophageal Cancer: A Meta-Analysis. PLoS One 2015;10(7).
9. Mamidanna R, Bottle A, Aylin P, Faiz O, Hanna GB. Short-term outcomes following open versus minimally invasive esophagectomy for cancer in England: a population-based national study. Ann Surg 2012;255(2):197-203.

10. Sihag S, Wright CD, Wain JC et al. Comparison of perioperative outcomes following open versus minimally invasive Ivor Lewis oesophagectomy at a single, high-volume centre†. Euro J Cardiothorac Surg 2012;42(3):430-7.
11. Sihag S, Kosinski AS, Gaissert HA, Wright CD, Schipper PH. Minimally Invasive Versus Open Esophagectomy for Esophageal Cancer: A Comparison of Early Surgical Outcomes From The Society of Thoracic Surgeons National Database. Ann Thorac Surg 2016;101(4):1281-9.
12. Lazzarino AI, Nagpal K, Bottle A, Faiz O, Moorthy K, Aylin P. Open versus minimally invasive esophagectomy: trends of utilization and associated outcomes in England. Ann Surg 2010;252(2):292-8.
13. Luketich JD, Pennathur A, Awais O et al. Outcomes After Minimally Invasive Esophagectomy: Review of Over 1000 Patients. Ann Surg 2012;256(1):95-103.
14. Palazzo F, Rosato EL, Chaudhary A et al. Minimally Invasive Esophagectomy Provides Significant Survival Advantage Compared with Open or Hybrid Esophagectomy for Patients with Cancers of the Esophagus and Gastroesophageal Junction. J Am Coll Surg 2015;220(4):672-9.
15. Dantoc MM, Cox MR, Eslick GD. Does minimally invasive esophagectomy (MIE) provide for comparable oncologic outcomes to open techniques? A systematic review. J Gastrointest Surg 2012;16(3):486-94.
16. van Workum F, Berkelmans GH, Klarenbeek BR et al. McKeown or Ivor Lewis totally minimally invasive esophagectomy for cancer of the esophagus and gastroesophageal junction: systematic review and meta-analysis. J Thorac Dis 2017;9(Suppl 8):S826-S33.
17. Pham TH, Perry KA, Dolan JP et al. Comparison of perioperative outcomes after combined thoracoscopic-laparoscopic esophagectomy and open Ivor–Lewis esophagectomy. Am J Surgery 2010;199(5):594-8.

18. Zingg U, McQuinn A, DiValentino D et al. Minimally invasive versus open esophagectomy for patients with esophageal cancer. Ann Thorac Surg 2009;87(3):911-9.
19. Smithers BM, Gotley DC, Martin I, Thomas JM. Comparison of the outcomes between open and minimally invasive esophagectomy. Ann Surg 2007;245(2):232-40.
20. Birkmeyer JD, Siewers AE, Finlayson EVA et al. Hospital Volume and Surgical Mortality in the United States. New Engl J Med 2002;346(15):1128-37.
21. Finks JF, Osborne NH, Birkmeyer JD. Trends in Hospital Volume and Operative Mortality for High-Risk Surgery. New Engl j Med 2011;364(22):2128-37.
22. Markar SF, Karthikesalingam A, Thrumurthy S, Low DE. Volume-Outcome Relationship in Surgery for Esophageal malignancy: Systematic Review and Meta-analysis 2000-2011. J Gastrointest Surg 2012;16:1055-1063
23. Casson AG, van Lanschott JJB. Improving Outcomes After Esophagectomy: the Impact of Operative Volume. J Surg Onc 2005;92:262-266.
24. Patti MG, Corvera CU, Glasgow RE, Way LW. A hospital's annual rate of esophagectomy influences the operative mortality rate. J Gastrointest Surg 1998;2(2):186-92.
25. Swisher SG, DeFord L, Merriman KW et al. Effect of operative volume on morbidity, mortality, and hospital use after esophagectomy for cancer. J Thorac Cardiovasc Surg 2000;119(6):1126-1134.
26. Fuchs HF, Harnsberger CR, Broderick RC et al. Mortality after esophagectomy is heavily impacted by center volume: retrospective analysis of the Nationwide Inpatient Sample. Surg Endo 2017;31(6):2491-7.
27. Brusselaers N, Mattsson F, Lagergren J. Hospital and surgeon volume in relation to long-term survival after oesophagectomy: systematic review and meta-analysis. Gut 2014;63(9):1393.

28. Berry WD, Feldman S (1985). Multiple Regression in Practice (Quantitative Applications in the Social Sciences (Series 50). 1st ed. Newbury Park: Sage Publications, p. 42.
29. Rosenbaum PR, Rubin DB. The Central Role of the Propensity Score in Observational Studies for Causal Effects. Biometrika 1983;70(1): 41-55.
30. Leuven E, Sianesi B (2003). PSMATCH2: Stata module to perform full Mahalanobis and propensity score matching, common support graphing, and covariate imbalance testing. Available online: http://ideas.repec.org/c/boc/bocode/s432001.html.
31. Austin PC. Optimal caliper widths for propensity-score matching when estimating differences in means and differences in proportions in observational studies. Pharm Stat 2011;10(2):150-161
32. Nilsson M, Kamiya S, Lindblad M, Rouvelas I. Implementation of minimally invasive esophagectomy in a tertiary referral center for esophageal cancer. J Thoracic Dis 2017;9(Suppl 8):S817-S25.
33. Kutlu OC, Lee JE, Kats MH et al. Open Pancreaticoduodenectomy Case Volume Outcome of Laparoscopic Approach: A Population-based Analysis. Ann Surg 2018; 267(3):552-560.
34. Metzer R, Bollschweiler E, Vallbohmer D, Maish M, DeMeester RF, Holscher AH. High Volume centers for esophagectomy: what is the number needed to achieve low post-operative mortality. Dis Esophagus 2004;17(4):310-4.
35. van Lanschott JJ, Hulscher JB, Buskens CJ, Tilanus HW, ten Kate FJ, Obertop H. Hospital volume and hospital mortality for esophagectomy. Cancer 2001;91(8):1574-8
36. van Workum F, Stenstra M, Berkelmans GHK et al. Learning Curve and Associated Morbidity of Minimally Invasive Esophagectomy: A Retrospective Multicenter Study. Ann Surg 2017;Epub ahead of print
37. Tapias LF, Morse CR. Minimally Invasive Ivor Lewis Esophagectomy: Description of a Learning Curve. J Am Coll Surg 2014;218(6):1130-1140.

38. Bailey SH, Bull DA, Harpole DH et al. Outcomes after esophagectomy: a ten-year prospective cohort. Ann Thorac Surg 2003;75(1):217-222.
39. Varghese TK Jr, Wood DE, Farjah F et al. Variation in esophagectomy outcomes in hospitals meeting Leapfrog volume outcome standards. Ann Thorac Surg 2011; 91(4): 1003-1009.

Table 1: Demographics

	Unmatched Cohorts		Matched Cohorts	
	MIE [N=2371]	OE [N=6285]	MIE [N=1819]	OE [N=1819]
Case volume/institution/year,				
Mean(SD)	8.04 (8.69)	11.71 (14.29)	8.15 (8.77)	5.02 (5.86)
Median (range)[b]	5 (1-42)	6 (1-71)	5 (1-42)	9 (1-28)
Age, mean (SD)	63.43 (9.49)	63.11 (9.74)	63.67 (9.66)	63.35 (9.51)
Gender, n(%)				
Male	1982 (27.75)	5161 (72.25)	1507 (82.85)	1537 (84.50)
Female	389 (25.71)	1124 (74.29)	312 (17.15)	282 (15.50)
Tumor size, mean (SD)[a]	36.78 (25.05)	38.15 (25.41)	36.88 (25.14)	37.57 (25.4)
Median (range)[a,c]	31 (0-160)	35 (0-190)	32 (0-160)	33 (0-160)
Charlson score, n(%)				
None	1667 (70.31)	4457 (70.91)	1277 (70.20)	1287 (70.75)
1	557 (23.49)	1463 (23.28)	435 (23.91)	425 (23.36)
>/=2	147 (6.2)	365 (5.81)	107 (5.88)	107 (5.88)
Clinical Stage, n(%)[a]				
TIS	53 (2.27)	113 (1.85)	32 (1.78)	20 (1.12)
T1	477 (20.39)	1099 (17.96)	378 (21.05)	334 (18.79)
T2	440 (18.81)	1127 (18.42)	362 (20.16)	334 (18.79)
T3	1094 (46.77)	2896 (47.34)	809 (45.04)	846 (47.58)
T4	38 (1.62)	138 (2.26)	26 (1.45)	34 (1.91)
Pathological Stage, n(%)				
0	137 (5.90)	319 (5.20)	80 (4.48)	73 (4.05)
1	754 (32.46)	1827 (29.77)	591 (33.07)	549 (30.48)
2	705 (30.35)	1957 (31.89)	547 (30.61)	595 (33.04)
3	689 (29.66)	1913 (31.17)	542 (30.33)	545 (30.26)
4	38 (1.64)	121 (1.97)	27 (1.51)	39 (2.17)
Radiation, n(%)				
None	856 (36.1)	2210 (35.16)	709 (38.98)	650 (35.73)
Neoadjuvant	1395 (58.84)	3681 (58.57)	1013 (55.69)	1054 (57.94)
Adjuvant	97 (4.09)	328 (5.22)	87 (4.78)	102 (5.61)
Chemotherapy, n(%)				
None	720 (30.37)	1805 (28.72)	581 (31.94)	535 (29.41)
Neoadjuvant	1382 (58.29)	3750 (59.67)	1015 (55.80)	1066 (58.60)
Adjuvant	129 (5.44)	398 (6.33)	115 (6.32)	127 (6.98)
MIE conversion, rates/year(SD)	3.3 (8.88)		2.29 (5.78)	

MIE – minimally-invasive esophagectomy, OE- open esophagectomy

[a] Statistically significant for unmatched group

[b]- non-parametric sign test, [c]- Kruskal-Wallis rank test

All comparisons for matched cohorts are not statistically significan

Table 2: Bivariate outcomes

	Full Cohort [N = 8656]	MIE [N=2371]	OE [N=6285]	p-value
30-day mortality, n(%)[a]	335 (3.89)	73 (3.09)	262 (4.19)	0.018
90-day mortality, n(%)	720 (8.46)	175 (7.49)	545 (8.84)	0.046
Length-of-stay, mean (SD)[a]	14.37 (12.06)	13.61 (11.33)	14.67 (12.32)	0.0005
30-day unplanned readmission, n(%)	705 (8.2)	184 (7.79)	521 (8.35)	0.399
R0 resection, n(%)	7873 (92.91)	2202 (93.38)	5671 (92.75)	0.289
Collected LN, mean (SD)[a]	13.96 (9.67)	15.38 (9.92)	13.42 (9.52)	<0.001
Positive LN, mean (SD)	1.18 (2.83)	1.13 (2.68)	1.2 (2.88)	0.3397
5-year overall survival, n(%)[a]	4792 (55.36)	1374 (57.95)	3418 (54.38)	0.003

[a] Significant difference
MIE – minimally-invasive esophagogastrectomy
LN – lymph node
OE – open esophagogastrectomy

Table 3: Regression analysis of unmatched cohorts

	30-day mortality*	90-day mortality*	Length of stay‡	Positive Margin*	LN collected‡	LN positive‡	30-day readmission*	5-year mortality*
Minimally-invasive esophagectomy	0.68[a]	0.83	-1.01[a]	0.98	1.58[a]	-0.04	0.92	0.89
Case volume	0.99[a]	0.99[a]	-0.03[a]	0.99[a]	0.11[a]	0.01[a]	1.00	0.99[a]
Age	1.05[a]	1.05[a]	0.04[a]	1.01[a]	-0.02	-0.01[a]	1.01	1.02[a]
Female	1.14	0.99	0.09	1.18	-0.28	-0.16	1.16	0.87[a]
Tumor size	1.00	1.01[a]	0.01[a]	1.01[a]	0.01[a]	0.01[a]	1.00	1.01[a]
Charlson score								
1	1.01	1.11	0.84[a]	0.99	0.02	0.05	1.39[a]	1.12
>/=2	1.97[a]	1.45[a]	1.47[a]	0.96	-0.09	0.01	1.35	1.33[a]
Pathological Stage								
1	0.75	0.82	0.16	1.16	0.67	-0.53[a]	1.62	1.21
2	0.99	1.06	0.68	3.87[a]	1.50[a]	0.02	1.37	2.53[a]
3	0.90	1.21	0.74	8.09[a]	2.97[a]	2.60[a]	1.41	4.31[a]
4	1.85	3.59[a]	0.70	11.39[a]	1.42	3.04[a]	3.05[a]	6.57[a]
Radiation								
Neoadjuvant	0.80	0.94	-2.20[a]	0.48[a]	-1.59[a]	-0.57[a]	0.92	1.14[a]
Adjuvant	0.25[a]	0.29[a]	-3.49[a]	2.18[a]	-0.97	0.25	0.89	1.27[a]
MIE-to-open conversion[b]	1.01	1.00	0.03	1.01	0.01	0.01	1.01	1.00

[a] Significant difference ($p<0.05$)
[b] Conversion rate/year
LN- Lymph node

Table 4: Multivariable regression analysis of propensity-matched cohorts

	30-day mortality	90-day mortality	Length of stay	Positive Margin	LN collected	LN positive	30-day readmission	5-year mortality
Minimally-invasive esophagectomy	0.40[a]	0.63[a]	-0.98	0.98	2.95[a]	0.07	0.96	0.78[a]
Case volume	1.01	1.00	0.00	0.99	0.11[a]	0.00	1.00	0.99[a]
Age	1.06[a]	1.05[a]	0.02	1.01	-0.03	-0.01	1.02[a]	1.02[a]
Female	1.00	0.90	0.59	0.70	-0.46	-0.25[a]	0.98	0.82
Tumor size	1.00	1.01[a]	0.03[a]	1.01[a]	0.02[a]	0.00	1.00	1.01[a]
Charlson score								
1	1.07	1.30	0.64	1.39	0.01	0.03	1.52[a]	1.20
>/=2	2.22[a]	1.56	0.71	0.98	1.00	-0.05	1.44	1.52[a]
Pathological Stage								
1	0.51	0.63	1.11	+	0.87	-0.29[a]	1.20	0.93
2	0.66	0.84	1.47	+	1.54[a]	0.28[a]	0.86	1.97[a]
3	0.67	0.85	1.84	+	2.97[a]	2.95[a]	0.89	3.80[a]
4	1.04	1.12[a]	2.84	+	1.09	4.20[a]	1.81[a]	4.38[a]
Radiation								
Neoadjuvant	0.96	1.08	-1.93[a]	0.47[a]	-1.82[a]	-0.44[a]	0.96	1.12
Adjuvant	0.32	0.48	-2.99[a]	3.25[a]	-1.77[a]	0.01	0.91	1.49[a]
MIE-to-open conversion[b]	1.02[a]	1.01	0.02	1.00	-0.03	0.00	1.00	1.00

[a] Significant difference (p<0.05)
[b] Conversion rate/year
+ Could not determine statistically
LN- Lymph node

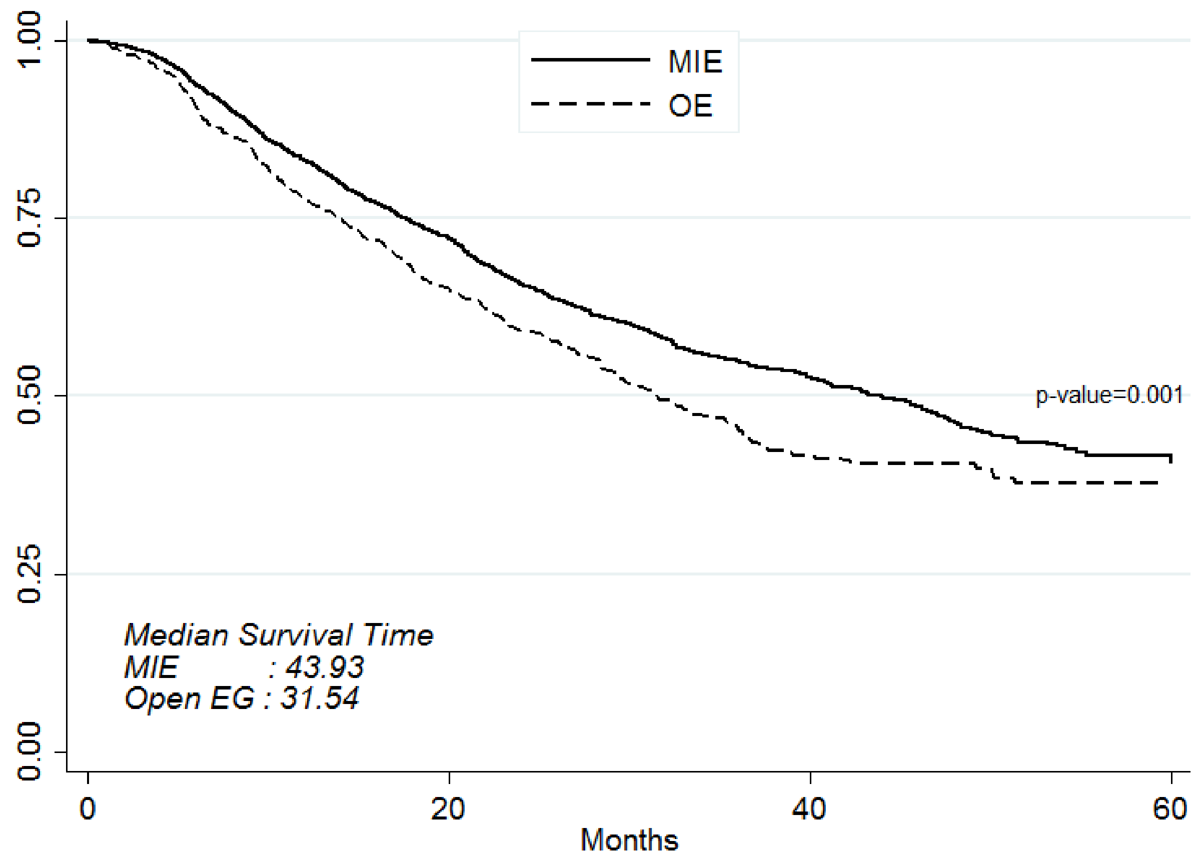
Table 5: Outcomes of MIE after interquartile comparisons based on total annual esophagogastrectomy volume

Dependent variable	Quartiles	AOR*/β-Coefficients‡	p-value
30-day mortality*	4 vs 1	0.44	<0.001
	4 vs 2	0.66	0.048
	4 vs 3	0.79	0.272
90-day mortality*	4 vs 1	0.56	<0.001
	4 vs 2	0.78	0.077
	4 vs 3	0.88	0.383
Length of stay‡[days]	4 vs 1	-1.82 [13.55 vs. 15.56]	<0.001
	4 vs 2	-0.78 [13.55 vs. 14.44]	0.086
	4 vs 3	-0.31 [13.55 vs 13.83]	0.474
Positive Margin*	4 vs 1	0.63	0.001
	4 vs 2	0.86	0.316
	4 vs 3	1.10	0.551
LN collected‡	4 vs 1	6.09	<0.001
	4 vs 2	3.71	<0.001
	4 vs 3	1.20	<0.001
LN positive‡	4 vs 1	0.28	0.003
	4 vs 2	0.22	0.027
	4 vs 3	0.32	0.001
30-day readmission*	4 vs 1	0.89	0.333
	4 vs 2	1.03	0.828
	4 vs 3	1.16	0.282
5-year mortality*	4 vs 1	0.62	<0.001
	4 vs 2	0.68	<0.001
	4 vs 3	0.80	0.003

AOR – Adjusted odds ratio, LN- Lymph node

Figure Legend

Figure 1: Kaplan-Meier curve for propensity matched cohorts; MIE – minimally-invasive esophagogastrectomy; OE – open esophagogastrectomy


1.00
0.75
0.50
0.25
0.00
MIE
OE
p-value=0.001
Median Survival Time
MIE : 43.93
Open EG : 31.54
0
20
40
60
Months