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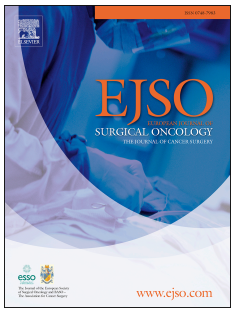

University hospital status and surgeon volume and risk of reoperation following surgery for esophageal cancer

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Abstract

Purpose: Centralization of surgery improves the survival following esophagectomy for cancer, but whether university hospital setting or surgeon volume influences the reoperation rates is unknown. We aimed to clarify whether hospital status or surgeon volume are associated with a risk of reoperation after esophagectomy.

Methods: Patients who underwent esophagectomy for esophageal cancer in 1987-2010 were identified from a population-based, nationwide Swedish cohort study. University hospital status and cumulative surgeon volume were analyzed in relation to risk of reoperation or death (the latter included to avoid competing risk errors) within 30 days of surgery. Multivariable logistic regression provided odds ratios (OR) with 95% confidence intervals (CI), adjusted for calendar period, age, sex, comorbidity, tumor histology, stage, neoadjuvant therapy, resection margin, surgeon volume, and hospital status.

Results: Among 1820 participants, 989 (54%) underwent esophagectomy in university hospitals and 271 (15%) died or were reoperated within 30 days of surgery. Non-university hospital status was associated with an increased risk of reoperation or death compared to university hospitals (adjusted OR 1.56, 95% CI 1.13-2.13). Regarding surgeon volume, the ORs were increased in the lower volume categories, but not statistically significant (OR 1.30, 95% CI 0.89-1.89 for surgeon volume <7 and OR 1.10, 95% CI 0.75-1.63 for surgeon volume 7-16, compared to surgeon volume >16).

Conclusion: The risk of reoperation or death within 30 days of esophagectomy seems to be lower in university hospitals even after adjustment for surgeon volume and other potential confounders. These results support centralizing esophageal cancer patients to university hospitals.

Keywords: neoplasm; esophagus, esophagectomy; surgery

1. Introduction

The curative treatment of esophageal cancer includes surgical resection (esophagectomy) in most patients.[1] One of several potential reasons for the improved 5-year survival of esophageal cancer patients in the last decade is centralization of surgery.[1, 2] Surgeon volume is a known long-term prognostic factor in esophageal cancer surgery,[3] and higher annual esophagectomy volume may lower early postoperative mortality after esophagectomy regardless of comorbidity.[4, 5] However, hospital volume is not prognostic after adjustment for individual surgeon volume.[3, 6]

University hospital status has not been shown to be associated with long-term survival of esophageal cancer patients.[7] However, university hospitals should be more experienced in the perioperative treatment of patients undergoing major thoraco-abdominal surgery due to a higher case load of other procedures, for example cardiac and lung cancer surgery, and have greater staffing and more research activities. Instead of prolonged survival, university hospital status might be associated with lower complication or reoperation rates, which in turn may cause poor quality of life also in the long-term perspective.[8] The collection of data concerning complications, as well as reporting of complications, has varied greatly in individual studies.[9] Therefore, reoperation and short-term mortality could be considered a more robust and specific assessment of poor early postoperative outcomes than complications in historical cohorts. Reoperations are also known to decrease the long-term survival after esophagectomy.[10] Yet, the relation between university hospital status, or surgeon volume and risk of reoperations is not known.

The aim of this study was to test the hypotheses that esophagectomy for esophageal cancer in university hospitals and conducted by high-volume surgeons is associated with lower rates of reoperation than in non-university hospitals and lower volume surgeons.

2. Methods

2.1. Study design

This was a population-based and nationwide cohort study of patients diagnosed with adenocarcinoma or squamous cell carcinoma of the esophagus who had undergone esophagectomy in Sweden between 1987 and 2010, with follow-up until 2016.

2.2. Exposures

The study main exposure was university versus non-university hospital status where the esophagectomy was conducted. University hospital was defined as any of the six hospitals affiliated to a university providing education and training for medical students in Sweden, and the remaining 49 hospitals that had conducted esophagectomies during the study period were considered non-university hospitals. The secondary exposure was the cumulative surgeon volume of the individual surgeon during the study period, where <7 was the lowest quartile, 7-16 was the second quartile, and >16 esophagectomies defined the two highest quartiles. Surgeon volume was chosen instead of hospital volume because surgeon volume is more robust predictor of surgeon skill compared to hospital volume, and because hospital volume is not prognostic after adjustment for individual surgeon volume.[3] The algorithm to determine the surgeon volume has been described earlier.[3] Highest two volume quartile surgeons were grouped into one category because there were much more high-volume surgeons operating in university hospitals, and because esophagectomy-associated short-term mortality has been shown to plateau after cumulative surgeon volume of 15.[11]

2.3. Outcomes

The primary outcome was the occurrence of reoperation or death within 30 days of primary surgery. The secondary outcome was reoperation alone within 30 days of primary surgery.

The primary outcome was chosen to include 30-day all-cause mortality to reduce competing risk errors from mortality before any reoperation was possible. The study was approved by the Regional Ethical Review Board in Stockholm, Sweden.

2.4. Cohort

Earlier versions of the cohort of this study have been used for other studies examining esophageal cancer surgery.[3, 11-13] In brief, the study cohort included at least 98% of all esophageal cancer patients who underwent curatively intended surgery in Sweden during the study period. The patients with esophageal cancer were identified from the Swedish Cancer Registry, which we have shown to have at least 98% completeness for this cancer.[14] Additionally, the Swedish Patient Registry was used for selecting only patients who had undergone esophagectomy, and this registry has 99.6% positive predictive value for this operation.[15] The Patient Registry also provided information about patient characteristics (age, sex, and comorbidity) and hospital status (university or non-university). Comorbidity data were defined and categorized using the most updated and well-validated Charlson Comorbidity Index.[16]

To enable collection of additional and more detailed clinical data, surgery charts and pathology records were retrieved from all hospitals conducting esophageal cancer surgery in Sweden during the study period. The data retrieved from the medical records were assessed and categorized according to a detailed predefined protocol to ensure uniformity. This assessment has been validated for high concordance.[12] The medical records provided information about reoperations, surgeon volume, tumor characteristics (location, stage and histology), as well as details regarding the treatment (type of surgery, radicalness of the resection and neoadjuvant therapy). Tumor stage was classified based on the Union

Internationale Contre le Cancer, using the 7th edition of tumor-node-metastasis (TNM) system.[17] Open transthoracic resection with intrathoracic anastomosis was the dominant (>95%) surgical procedure and a gastric tube which was pulled up and anastomosed to the proximal esophagus was the preferred reconstruction.

Mortality data were obtained from the nationwide Swedish Causes of death Registry, which has 100% complete data for date of death.

The information from the registries and medical records was linked for all individual patients using the Swedish personal identity number, a unique 10-digit identifier assigned to each Swedish resident upon birth or immigration, which is a well-validated tool for research purposes.[18]

2. 5. Statistical analysis

All statistical analyses were carried out by an experienced biostatistician (KW), who followed an *a priori* specified study protocol, defining and categorizing the exposures, outcomes and covariates as well as the statistical methods. To estimate the relative risk for the exposures in relation to the outcomes, multivariable logistic regression was used to calculate odds ratios (OR) with 95% confidence intervals (CI). The following covariates were selected and adjusted for as potential confounders: 1) calendar period of surgery (year 1987-1994, 1995-2002, or 2003-2010), 2) age (categorized into <65, 65-75, or >75 years), 3) sex (male or female), 4) comorbidity (Charlson Comorbidity Index score 0, 1, or ≥2), 5) tumor histology (adenocarcinoma or squamous cell carcinoma), 6) tumor stage (0-I, II or III-IV), 7) neoadjuvant therapy (yes or no), 8) resection margin status (radical [R0] or not [R1/2]), 9) surgeon volume (<7, 7-16, or >16, the cumulative number of esophagectomies per surgeon during the study period), and 10) hospital status (university or non-university). Three

regression models were created, i.e. a crude model without any adjustments, a Model 1 with adjustment for covariates 1-8 above, and Model 2 which additionally adjusted for surgeon volume for the exposure hospital status and hospital status for the exposure surgeon volume. Subgroup analyses were also conducted stratifying by the covariates 1-8 above, with adjustment for the other covariates. Missing data were handled by carrying out a complete case analysis. The statistical software IBM SPSS v24.0 (IBM Corp., Armonk, NY) was used for all statistical analyses.

3. Results

3.1. Patients

Among 1820 participating patients, 989 (54%) underwent esophagectomy in a university hospital and 876 (50%) by surgeons with cumulative volume >16 esophagectomies. The distribution of patient characteristics was similar between those who underwent surgery in university hospitals and in non-university hospitals, except that the proportion of more advanced stage tumors and the proportion of patients operated by surgeons in the highest volume group were higher in university hospitals (Table 1). High-volume surgeons operated proportionally more patients in the most recent time period, and high volume surgeons had higher lymph node yield, compared to low-volume surgeons (Table 2). Reoperation or death within 30 days of surgery occurred in 271 (15%) patients, and reoperations only were found in 200 (11%) patients.

3.2. University hospital status and risk of reoperation

The composite outcome reoperation or death within 30 days of surgery was 64% more likely to occur in non-university hospitals, compared to university hospitals (OR 1.64, 95% CI 1.22 – 2.19 in adjusted Model 1) (Table 3). After additional adjustment for surgeon volume (Model 2), the risk was 56% increased (OR 1.56, 95% CI 1.13 – 2.13).

The risk of reoperation alone was also more likely in non-university hospitals than in university hospitals (OR 1.43, 95% CI 1.03 – 1.98 in adjusted Model 1), and this association was stable (41% increased) after additional adjustment for surgeon volume (adjusted OR 1.41, 95% 0.99 – 2.01 in adjusted Model 2) (Table 3).

Compared to university hospitals, esophagectomy conducted at non-university hospitals was associated with increased point estimates for reoperation or death in all stratified analyses, and were statistically significantly increased in patients operated in 1995-2002, aged <65 years, of female sex, with esophageal squamous cell carcinoma, not receiving neoadjuvant therapy, and in patients with radical (R0) resection (Table 4).

Esophagectomy conducted at non-university hospitals was associated with increased point estimates for reoperation only in almost all stratified analyses, and in patients aged <65 years and those with esophageal squamous cell carcinoma the ORs were also statistically significantly increased (Table 4).

3.3. Surgeon volume and risk of reoperation

The risk of the composite outcome of reoperation or death within 30 days of surgery was higher in the lowest cumulative surgeon volume group compared to highest in the adjusted Model 1 (OR 1.53, 95% CI 1.07 – 2.18 for <7 vs >16 esophagectomies and OR 1.24, 95% CI 0.85 – 1.81 for 7-16 vs >16 esophagectomies) (Table 5). After additional adjustment for university hospital status, the associations were attenuated and no longer statistically significant (OR 1.30, 95% CI 0.89 – 1.89 for <7 vs >16 esophagectomies and OR 1.10, 95% CI 0.75 – 1.63 for 7-16 vs >16 esophagectomies).

Although almost all ORs were above 1, no statistically significant associations were found between surgeon volume and risk of reoperation alone in any of the models (Table 5).

In the stratified analyses, surgeon volume <7 versus >16 was statistically significantly associated with increased HRs of reoperation or death within 30 days of surgery in patients aged 65-75 years and in patients receiving neoadjuvant therapy (Table 6). Cumulative surgeon

volume of 7-16 versus >16 was also associated with higher risk of reoperation or death in 30 days in patients with Charlson's comorbidity score 1 (Table 6).

No statistically significant associations between surgeon volume and reoperations alone were found in the stratified analysis (Table 6).

4. Discussion

The present study suggests that surgery for esophageal cancer conducted at university hospitals is associated with decreased risk of reoperation within 30 days of surgery independent of other variables, including surgeon volume, compared to non-university hospitals. Higher surgeon volume also seemed to decrease the risk of reoperation, but this influence did not remain after adjustment for university hospital status.

One of the main strengths of the study is the population-based design with virtually complete inclusion of all patients undergoing surgery for esophageal cancer in the entire Sweden. Accurate information about the exposures, outcomes and relevant covariates was made possible by virtue of a combination of data retrieval from validated and nationwide registries and ambitious collection of medical records. The use of a predefined data retrieval form and specific study protocol reduced the risk of chance findings and systematic errors. The reliable identification of all eligible patients and the complete follow-up was made possible by the uniquely assigned personal identity numbers and high-quality cancer and patient registries. A limitation of observational studies is confounding. However, this was counteracted by adjusting for several potential confounders, though residual confounding cannot be ruled out. The lower number of high volume surgeons operating in the non-university hospitals compared to university hospitals might be considered a limitation. However, a previous study using the same cohort as in the present study showed that short-term mortality does plateau after 15 cumulative esophagectomies which should alleviate these concerns.[11] Competing risk by mortality is a source of error when studying reoperations, because some patients who might have undergone reoperation may have died before the reoperation could be conducted. Therefore, reoperation and death within 30 days were assessed as a combined outcome and compared with the reoperation alone outcome. The lack of the indications for the reoperations was a limitation of the study, but the assessment of reoperation or death was highly complete

and accurate. Finally, chance might influence the results, particularly in the stratified analyses. However, the large sample size provided robust estimates of the main analyses.

Complications are common following resectional surgery for esophageal cancer. When complications occur and the patient deteriorates, the surgeon might need to choose between reoperation, non-surgical intervention, or "watchful waiting", depending on several factors. Increasing surgeon volume might decrease the risk of reoperations,[11] which might be related to more experienced surgeons encountering fewer complications and being more inclined to watch and wait when complications occur with support from experienced colleagues. Surgeons with more experience in esophagectomy often work in university hospitals, at least in Sweden. Yet, the results of the present study show that the hospital status *per se* influences the incidence of reoperation, i.e. also after adjustment for potential confounders, including surgeon volume. A contributing factor might be that university hospitals have more experience in the intensive care of thoracic and major cancer surgery patients. Psychological factors relating to the surgeons might also affect the decision whether to reoperate or not. Non-university hospitals in Sweden are smaller and have fewer surgeons with experience in a very specialized field, such as esophageal cancer surgery, compared to university hospitals. The lack of feedback from experienced colleagues in non-university hospitals might make the operating surgeon more likely to reoperate, compared to in university hospitals where decisions are more likely made in teams and discussed with other surgeons with experience of these operations. These results may be difficult to generalize to countries with different types of healthcare policies, and therefore it would be important to study the risk of reoperation in relation to hospital status in other countries and settings as well.

Reoperations are associated with worse long-term prognosis,[10] and also clearly worse long-term deterioration in health-related quality of life,[8] and the results of the present study indicate the need for continued centralization of esophageal cancer surgery into high-volume centers within university hospitals. After the end of the inclusion of the current study, esophagectomies have been centralized to university hospitals in Sweden. However, the complex procedure of esophagectomy is still being conducted in many smaller hospitals in Europe. The patients with such malignant disease should be offered the best available care, and the centralization of esophagectomies from smaller units to university hospitals should be carefully considered in the context of each country and area.

In conclusion, this nationwide Swedish study found that risk of reoperation within 30 days of resectional surgery for esophageal cancer is likely favorably influenced by university hospital status, because the association remains after adjustment for surgeon volume and several other potential confounders. Continued and intensified measures to centralize these operations to university hospitals are encouraged.

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6. Role of the funding source

The study sponsors had no role in the design of the study, data collection, analysis or interpretation of the results, the writing of the manuscript or the decision to submit the manuscript for publication.

7. Conflict of Interest Statement

The authors declare no potential conflicts of interest.

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Table 1. Characteristics of the 1820 patients who underwent resectional surgery for esophageal cancer in 1987-2010 in Sweden stratified by hospital status.

	University hospital	**Non-university hospital**	**Total**
	Patients Number (%)	Patients Number (%)	Patients Number (%)
Total	989 (100)	831 (100)	1820 (100)
Time period			
1987-1994	365 (37)	248 (30)	613 (34)
1995-2002	275 (28)	358 (43)	633 (35)
2003-2010	349 (35)	225 (27)	574 (32)
Age (in years)			
<65	468 (47)	384 (46)	850 (47)
65-75	368 (37)	326 (39)	694 (38)
>75	155 (16)	121 (15)	276 (15)
Sex			
Male	733 (75)	627 (74)	1360 (75)
Female	256 (25)	204 (26)	460 (25)
Charlson's comorbidity score			
0	596 (60)	505 (61)	1101 (61)
1	240 (24)	205 (25)	445 (25)
≥2	153 (16)	121 (15)	274 (15)
Tumor histology			
Adenocarcinoma	403 (41)	389 (47)	792 (44)
Squamous cell carcinoma	583 (59)	441 (53)	1024 (56)
Missing	3 (0)	1 (0)	4 (0)
Tumor stage			
0-I	210 (21)	212 (26)	422 (23)
II	353 (36)	309 (37)	662 (36)
III-IV	420 (42)	302 (36)	722 (40)
Missing	6 (1)	8 (1)	14 (1)
Neoadjuvant therapy			
No	678 (69)	553 (67)	1231 (68)
Yes	309 (31)	278 (34)	587 (32)
Missing	2 (0)	0 (0)	2 (0)
Lymph node yield (median [interquartile range])	8 [5 – 18]	7 [4 – 12]	7 [4 – 15]
Missing	231 (23)	242 (29)	473 (26)
Resection margin status			

Radical (R0)	705 (71)	567 (68)	1272 (70)
Non-radical (R1/R2)	155 (16)	126 (15)	281 (15)
Missing	129 (13)	138 (17)	267 (15)
Cumulative surgeon volume			
Low (<7)	176 (18)	313 (38)	489 (27)
Medium (7-16)	179 (18)	216 (26)	395 (22)
High (>16)	608 (61)	268 (32)	876 (48)
Missing	26 (3)	34 (4)	60 (2)
Length of hospital stay (median [interquartile range])	15 [13 – 22]	16 [12 – 23]	15 [12 – 22]
Reoperation			
No	897 (91)	723 (87)	1620 (89)
Yes	92 (9)	108 (13)	200 (11)
Reoperation or death			
No	869 (88)	680 (82)	1549 (85)
Yes	120 (12)	151 (18)	271 (15)

Table 2. Characteristics of patients who underwent resectional surgery for esophageal cancer in 1987-2010 in Sweden stratified by surgeon volume (n=1760).

	Low surgeon volume (<7)	**Medium surgeon volume (7 – 16)**	**High surgeon volume (>16)**	**Total**
	Patients Number (%)	Patients Number (%)	Patients Number (%)	Patients Number (%)
Total	489 (100)	395 (100)	876 (100)	1760 (100)
Time period				
1987-1994	253 (52)	132 (33)	190 (22)	575 (33)
1995-2002	140 (29)	141 (36)	333 (38)	614 (35)
2003-2010	96 (20)	122 (31)	353 (40)	571 (32)
Age (in years)				
<65	221 (45)	183 (46)	426 (49)	830 (47)
65-75	192 (39)	158 (40)	319 (36)	669 (38)
>75	76 (16)	54 (14)	131 (15)	261 (15)
Sex				
Male	368 (75)	305 (77)	642 (73)	1315 (75)
Female	121 (25)	90 (23)	234 (27)	445 (25)
Charlson's comorbidity score				
0	330 (68)	245 (62)	493 (56)	1068 (61)
1	99 (20)	102 (26)	224 (26)	425 (24)
≥2	60 (12)	48 (12)	160 (18)	267 (15)
Tumor histology				
Adenocarcinoma	204 (42)	173 (44)	395 (45)	772 (44)
Squamous cell carcinoma	285 (58)	221 (56)	479 (55)	985 (56)
Missing	0 (0)	1 (0)	2 (0)	3 (0)
Tumor stage				
0-I	102 (21)	97 (25)	212 (24)	311 (23)
II	166 (34)	155 (39)	318 (36)	639 (36)
III-IV	219 (45)	141 (36)	342 (39)	702 (40)
Missing	2 (0)	2 (1)	4 (0)	8 (0)
Neoadjuvant therapy				
No	336 (69)	245 (62)	613 (70)	1194 (68)
Yes	153 (31)	150 (38)	263 (30)	566 (32)
Lymph node yield (median [interquartile range])	5 [3 – 11]	7 [4 - 13]	10 [5 – 18]	7 [4 – 15]
Missing	152 (31)	106 (27)	195 (22)	453 (26)

Resection margin status				
Radical (R0)	309 (63)	270 (68)	652 (74)	1231 (70)
Non-radical (R1/R2)	91 (19)	62 (16)	118 (13)	271 (15)
Missing	89 (18)	63 (16)	106 (12)	258 (15)
Length of hospital stay (median [interquartile range])	16 [13 – 23]	15 [12 – 22]	15 [12 – 22]	15 [12 – 22]
Reoperation				
No	433 (89)	344 (87)	789 (90)	1566 (89)
Yes	56 (11)	51 (13)	87 (10)	194 (11)
Reoperation or death				
No	398 (81)	329 (83)	772 (88)	1499 (85)
Yes	91 (19)	66 (17)	104 (12)	261 (15)

Table 3. Hospital status and risk of reoperation or death within 30 days of resectional surgery in patients with esophageal cancer, expressed as odds ratios (OR) with 95% confidence intervals (CI). Missing values were handled by conducting a complete case analysis.

Model	Number of patients	Reoperation or death		Reoperation	
		University hospital	Non-university hospital	University hospital	Non-university hospital
		OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Crude	1820	1 (reference)	1.61 (1.24 – 2.09)	1 (reference)	1.46 (1.09 – 1.96)
Model 1*	1552	1 (reference)	1.64 (1.22 – 2.19)	1 (reference)	1.43 (1.03 – 1.98)
Model 2**	1501	1 (reference)	1.56 (1.13 – 2.13)	1 (reference)	1.41 (0.99 – 2.01)

*Adjusted for time period, age, sex, Charlson's Comorbidity Index, histology, tumor stage, neoadjuvant therapy and resection margin status.

** Adjusted for the confounders in Model 1, and additionally for surgeon volume.

Table 4. Stratified analysis on hospital status and risk of reoperation or death within 30 days of resectional surgery in patients with esophageal cancer, expressed as odds ratios (OR) with 95% confidence intervals (CI) in each subgroup.

	Reoperation or death		Reoperation	
	University hospital	Non-university hospital	University hospital	Non-university hospital
	OR (95% CI)	OR (95% CI)*	OR (95% CI)	OR (95% CI)*
Time period				
1987-1994	1 (reference)	1.60 (0.93 – 2.75)	1 (reference)	1.22 (0.65 – 2.31)
1995-2002	1 (reference)	1.77 (1.00 – 3.11)	1 (reference)	1.53 (0.81 – 2.86)
2003-2010	1 (reference)	1.33 (0.74 – 2.40)	1 (reference)	1.50 (0.80 – 2.79)
Age (in years)				
<65	1 (reference)	1.91 (1.16 – 3.13)	1 (reference)	1.71 (1.02 – 2.88)
65-75	1 (reference)	1.23 (0.75 – 2.03)	1 (reference)	1.24 (0.70 – 2.19)
>75	1 (reference)	1.78 (0.75 – 4.25)	1 (reference)	0.82 (0.26 – 2.62)
Sex				
Male	1 (reference)	1.38 (0.96 – 2.00)	1 (reference)	1.28 (0.84 – 1.93)
Female	1 (reference)	2.03 (1.08 – 3.80)	1 (reference)	1.64 (0.82 – 3.27)
Charlson's comorbidity score				
0	1 (reference)	1.75 (1.15 – 2.68)	1 (reference)	1.54 (0.97 – 2.45)
1	1 (reference)	1.60 (0.83 – 3.09)	1 (reference)	1.18 (0.58 – 2.39)
≥2	1 (reference)	1.20 (0.56 – 2.58)	1 (reference)	1.59 (0.61 – 4.07)
Tumor histology				
Adenocarcinoma	1 (reference)	1.22 (0.70 – 2.12)	1 (reference)	1.06 (0.58 – 1.93)
Squamous cell carcinoma	1 (reference)	1.77 (1.20 – 2.62)	1 (reference)	1.58 (1.01 – 2.46)
Tumor stage				
0-I	1 (reference)	1.58 (0.81 – 3.06)	1 (reference)	1.42 (0.70 – 2.89)
II	1 (reference)	1.56 (0.96 – 2.56)	1 (reference)	1.40 (0.81 – 2.42)
III-IV	1 (reference)	1.51 (0.87 – 2.61)	1 (reference)	1.39 (0.74 – 2.60)
Neoadjuvant therapy				
No	1 (reference)	1.77 (1.18 – 2.67)	1 (reference)	1.55 (0.97 – 2.47)
Yes	1 (reference)	1.38 (0.83 – 2.30)	1 (reference)	1.32 (0.76 – 2.29)
Resection margin status				
Radical (R0)	1 (reference)	1.46 (1.03 – 2.08)	1 (reference)	1.38 (0.94 – 2.04)
Non-radical (R1/R2)	1 (reference)	1.95 (0.91 – 4.17)	1 (reference)	1.37 (0.54 – 3.44)

***** Adjusted for calendar period, age, sex, comorbidity, histology, tumor stage, neoadjuvant therapy, resection margin status and surgeon volume, except for the covariate that the analysis was stratified by.

Table 5. Cumulative surgeon volume and risk of reoperation or death within 30 days of resectional surgery in patients with esophageal cancer, expressed as odds ratios (OR) with 95% confidence intervals (CI). Missing values were handled by conducting a complete case analysis.

Model	Number of patients	Reoperation or death			Reoperation		
		Surgeon volume >16	Surgeon volume 7-16	Surgeon volume <7	Surgeon volume >16	Surgeon volume 7-16	Surgeon volume <7
		OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Crude	1760	1 (reference)	1.49 (1.07 – 2.08)	1.70 (1.25 – 2.31)	1 (reference)	1.35 (0.93 – 1.94)	1.17 (0.82 – 1.67)
Model 1*	1501	1 (reference)	1.24 (0.85 – 1.81)	1.53 (1.07 – 2.18)	1 (reference)	1.19 (0.79 – 1.80)	1.09 (0.72 – 1.64)
Model 2**	1501	1 (reference)	1.10 (0.75 – 1.63)	1.30 (0.89 – 1.89)	1 (reference)	1.09 (0.72 – 1.67)	0.96 (0.62 – 1.48)

*Adjusted for time period, age, sex, Charlson's Comorbidity Index, histology, tumor stage, neoadjuvant therapy and resection margin status.

** Adjusted for the confounders in Model 1, and additionally for university hospital status.

Table 6. Stratified analysis on cumulative surgeon volume and risk of reoperation or death within 30 days of resectional surgery in patients with esophageal cancer, expressed as odds ratios (OR) with 95% confidence intervals (CI) in each subgroup.

Model	Reoperation or death			Reoperation		
	Surgeon volume >16	Surgeon volume 7-16	Surgeon volume <7	Surgeon volume >16	Surgeon volume 7-16	Surgeon volume <7
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Time period						
1987-1994	1 (reference)	0.92 (0.43 – 1.97)	1.69 (0.88 – 3.16)	1 (reference)	0.76 (0.32 – 1.81)	1.20 (0.58 – 2.45)
1995-2002	1 (reference)	1.61 (0.85 – 3.03)	1.43 (0.73 – 2.80)	1 (reference)	1.75 (0.88 – 3.49)	1.06 (0.47 – 2.37)
2003-2010	1 (reference)	0.85 (0.42 – 1.74)	0.72 (0.32 – 1.62)	1 (reference)	0.85 (0.40 – 1.79)	0.62 (0.25 – 1.51)
Age (in years)						
<65	1 (reference)	1.01 (0.55 – 1.85)	1.06 (0.59 – 1.90)	1 (reference)	1.22 (0.66 – 2.27)	1.01 (0.54 – 1.91)
65-75	1 (reference)	1.38 (0.74 – 2.57)	1.93 (1.08 – 3.47)	1 (reference)	1.16 (0.58 – 2.32)	1.16 (0.59 – 2.28)
>75	1 (reference)	1.03 (0.36 – 2.91)	0.95 (0.34 – 2.66)	1 (reference)	1.06 (0.29 – 3.95)	0.55 (0.13 – 2.38)
Sex						
Male	1 (reference)	1.06 (0.67 – 1.67)	1.26 (0.81 – 1.94)	1 (reference)	1.00 (0.61 – 1.65)	0.95 (0.57 – 1.56)
Female	1 (reference)	1.33 (0.61 – 2.86)	1.57 (0.73 – 3.39)	1 (reference)	1.45 (0.64 – 3.29)	1.07 (0.44 – 2.57)
Charlson's comorbidity score						
0	1 (reference)	0.76 (0.43 – 1.33)	1.14 (0.70 – 1.85)	1 (reference)	0.84 (0.47 – 1.51)	0.88 (0.51 – 1.52)
1	1 (reference)	2.13 (1.03 – 4.43)	1.17 (0.49 – 2.76)	1 (reference)	2.10 (0.95 – 4.63)	1.13 (0.44 – 2.92)
≥2	1 (reference)	1.01 (0.38 – 2.68)	1.74 (0.71 – 4.25)	1 (reference)	0.89 (0.27 – 2.90)	0.85 (0.26 – 2.75)
Tumor histology						
Adenocarcinoma	1 (reference)	1.06 (0.53 – 2.12)	1.58 (0.53 – 2.12)	1 (reference)	1.20 (0.57 – 2.50)	1.40 (0.69 – 2.86)
Squamous cell carcinoma	1 (reference)	1.10 (0.69 – 1.78)	1.19 (0.74 – 1.91)	1 (reference)	1.01 (0.60 – 1.72)	0.79 (0.45 – 1.39)

Tumor stage						
0-I	1 (reference)	0.76 (0.33 – 1.79)	1.40 (0.65 – 3.02)	1 (reference)	0.94 (0.40 – 2.23)	0.94 (0.38 – 2.28)
II	1 (reference)	1.44 (0.81 – 2.57)	1.59 (0.88 – 2.87)	1 (reference)	1.16 (0.61 – 2.21)	1.17 (0.60 – 2.27)
III-IV	1 (reference)	0.92 (0.44 – 1.90)	1.08 (0.57 – 2.07)	1 (reference)	1.20 (0.55 – 2.59)	0.91 (0.43 – 1.93)
Neoadjuvant therapy						
No	1 (reference)	0.96 (0.58 – 1.59)	0.93 (0.67 – 1.52)	1 (reference)	1.11 (0.64 – 1.90)	0.63 (0.35 – 1.15)
Yes	1 (reference)	1.26 (0.66 – 2.37)	2.07 (1.13 – 3.81)	1 (reference)	1.00 (0.50 – 2.01)	1.64 (0.85 – 3.15)
Resection margin status						
Radical (R0)	1 (reference)	0.94 (0.60 – 1.46)	1.20 (0.79 – 1.82)	1 (reference)	0.94 (0.59 – 1.51)	0.90 (0.56 – 1.45)
Non-radical (R1/R2)	1 (reference)	2.09 (0.82 – 5.32)	2.05 (0.82 – 5.15)	1 (reference)	2.15 (0.72 – 6.38)	1.41 (0.47 – 4.25)

***** Adjusted for calendar period, age, sex, comorbidity, histology, tumor stage, neoadjuvant therapy, resection margin status and surgeon volume, except for the covariate that the analysis was stratified by.

Title: University hospital status and surgeon volume and risk of reoperation following surgery for esophageal cancer

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