Overall Volume Trends in Esophageal Cancer Surgery Results From the Dutch Upper Gastrointestinal Cancer Audit

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Objective: In the pursuit of quality improvement, this study aimed to investigate volume-outcome trends in oncologic esophagectomy in the Netherlands.
Summary of Background Data: Concentration of Dutch esophageal cancer care was dictated by introducing an institutional minimum of 20 resections/yr.
Methods: This nationwide cohort study included all esophagectomy patients registered in the Dutch Upper Gastrointestinal Cancer Audit in 2016–2019 from hospitals currently still performing esophagectomies. Annual esophagectomy hospital volume was assigned to each patient and categorized into quartiles. Multivariable logistic regression investigated short-term surgical outcomes. Restricted cubic splines investigated if volume-outcome relationships eventually plateaued.
Results: In 16 hospitals, 3135 esophagectomies were performed. First volume quartile hospitals performed 24–39 resections/yr; second, third, and fourth quartile hospitals performed 40–53, 54–69, and 70–101, respectively. Compared to quartile 1, in quartiles 2 to 4, overall/severe/technical complication, anastomotic leakage, and prolonged hospital/intensive care unit stay rates were significantly lower and textbook outcome and lymph node yield were higher. When raising the cut-off from the first to second quartile, higher-volume centers had less technical complications [Adjusted odds ratio (aOR): 0.82, 95% confidence interval (CI): 0.70–0.96], less anastomotic leakage (aOR: 0.80, 95% CI: 0.66–0.97), more textbook outcome (aOR: 1.25, 95% CI: 1.07–1.46), shorter intensive care unit stay (aOR: 0.80, 95% CI: 0.69–0.93), and higher lymph node yield (aOR: 3.56, 95% CI: 2.68–4.77). For most outcomes the volume-outcome trend plateaued at 50–60 annual resections, but lymph node yield and anastomotic leakage continued to improve.
Conclusion: Although this study does not reflect on individual hospital quality, there appears to be a volume trend towards better outcomes in high-volume centers. Projects have been initiated to improve national quality of care by reducing hospital variation (irrespective of volume) in outcomes in The Netherlands.

Keywords: centralization, esophageal cancer, esophagectomy, hospital volume

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Worldwide, esophageal cancer is the sixth most common cause of cancer-related death.[1,2] Curative treatment generally consists of neoadjuvant chemotherapy or chemoradiotherapy followed by surgical resection, after which 5-year survival rates approximate 50%.[3] Esophageal cancer surgery is associated with significant surgical risk, as postoperative morbidity and mortality rates vary around 65% and 2%, respectively.[4] Some studies found that esophageal cancer surgery in high-volume centers was associated with lower morbidity and mortality rates compared to low-volume hospitals.[5–8] These studies hypothesized that more experienced surgeons, surgical teams, and intensive care and hospital ward personnel lead to lower complication rates and more appropriate and timely treatment of complications. This resulted in a consensus on improving outcomes by centralization of esophageal cancer surgery and caused the introduction of a Dutch volume standard. In 2006, a threshold of at least 10 esophageal cancer operations per year was adopted which was raised to 20 in 2011.[9] This triggered a wave of centralization, which appeared to be completed in 2019 when the number of Dutch esophagectomy centers was reduced to 16 and all centers reached the volume threshold (Fig. 1). Outcomes, like short-term mortality and surgical radicality, improved over this time period.[10] However, it remains unknown whether these improvements are caused by centralization and whether currently (ie, with a volume threshold of 20) there still is a volume trend in clinical outcomes and if this trend eventually reaches a plateau.[11]

The Dutch Upper Gastrointestinal Cancer Audit (DUCA) aims to improve Dutch esophagogastric cancer surgery by providing clinicians with benchmarked outcome feedback.[12] In the Netherlands, these results are transparently discussed in annual meetings with all Dutch upper gastrointestinal surgeons. By discussing hospital variation and identifying best practices, various projects have been initiated to pursue nationwide quality improvement. In addition, certain structure and outcome measures are made transparent to patients and other stakeholders. Annual esophagectomy hospital volume is one of the transparent structure parameters the DUCA employs. To improve quality of care and reduce outcome measure hospital variation, information on the presence of a volume trend in current Dutch practice is highly relevant.

This study aimed to investigate the presence of a volume trend in outcomes of esophageal cancer surgery in a country where all centers perform at least 20 annual esophagectomies, and whether this trend eventually reaches a plateau.

METHODS

Study Design

This nationwide cohort study retrieved data from the DUCA database. This is a mandatory surgical audit registering all esophagogastric cancer patients undergoing surgery with the intention of

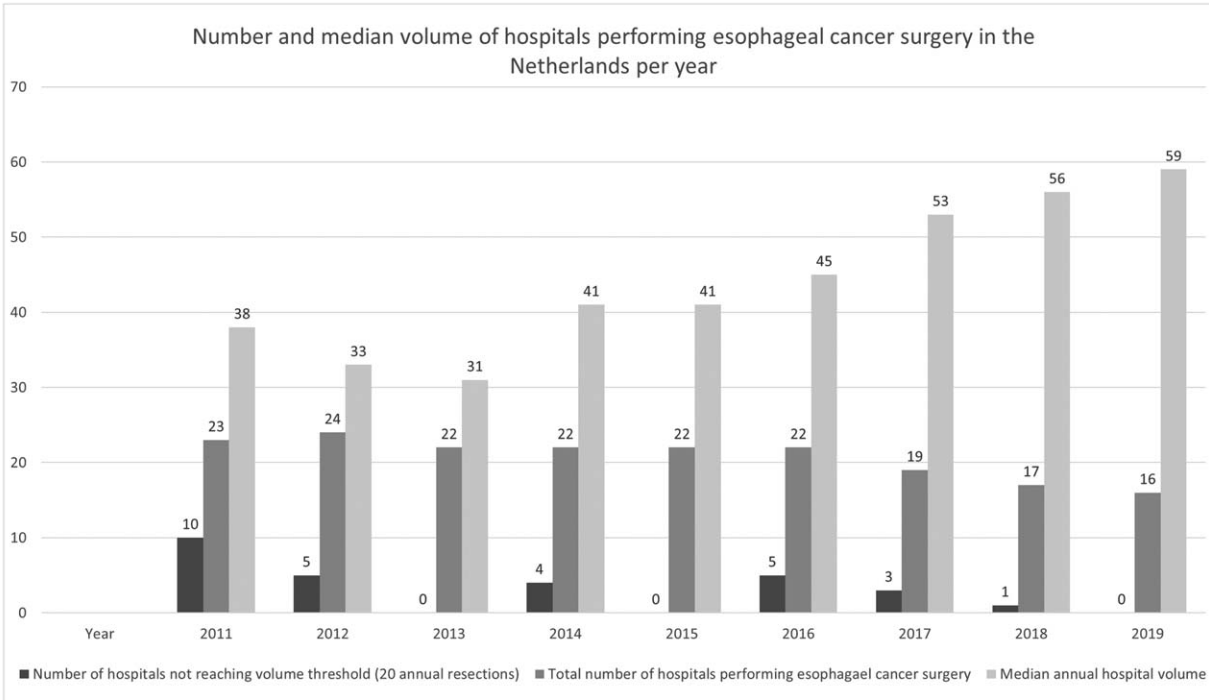

FIGURE 1. Number and median volume of hospitals performing esophageal cancer surgery in the Netherlands from 2011 to 2019.

resection in the Netherlands since 2011. The data completeness and outcome measure accuracy are estimated at 99.2% and 95.3%–100%, respectively.[13] Study approval was received from the DUCA scientific committee (DUCA202008); ethical approval or informed consent was not required according to Dutch legislation.

Patient Selection

All patients undergoing potentially curative esophageal cancer surgery in the Netherlands between January 1, 2016 and December 31, 2019 were included. Centers that stopped performing esophagectomies during this period were excluded in order to review the situation when all centers reached the volume-threshold of 20 annual resections. The 2016–2019 timeframe was selected to prevent redundant exclusion of patients undergoing surgery in centers where esophageal surgery was stopped.

Variables for Analyses

Annual potentially curative esophageal cancer surgery hospital volume was assigned to each patient in the dataset and thereafter divided into volume quartiles [cut-offs at percentiles 25, 50, (median) and 75]. The following baseline characteristics were used in multivariable analyses: sex, age in years (<65, 65–75, >75), body mass index (<20, 20–25, 26–30, >30), reported preoperative weight loss in kilograms (none, 1–5, 6–10, >10), American Society of Anesthesiologists (ASA) grade (1–2, 3+), Charlson Comorbidity Index[14] (0, 1, 2+), clinical T-stage (T0–2, T3–4, Tx), clinical N-stage (N0, N+, Nx), tumor location (intrathoracic, gastro-esophageal junction), previous esophagogastric or hiatal surgery (no, yes), histology (adenocarcinoma, squamous cell carcinoma), and salvage surgery (no, yes; defined as esophagectomy after previous chemoradiotherapy in a definitive scheme without initial intent of resection).

Outcome Measures

The impact of hospital volume on the following outcomes was investigated: postoperative complications (any Clavien-Dindo), severe postoperative complications (Clavien-Dindo ≥IIIa), anastomotic leakage, pulmonary complications, surgical/technical complications, 30-day/in-hospital mortality, surgical radicality, lymph node yield, prolonged hospital stay, prolonged intensive care unit (ICU) stay, and textbook outcome. Textbook outcome is a composite outcome measure that combines several single outcome measures into one.[15] This has important statistical advantages, is easier to interpret for patients and is associated with long-term survival even though it is measured over a short time-period enabling short-loop feedback which is essential in surgical auditing.[16–19] Outcome definitions are depicted in Supplemental Digital Content Table 1, http://links.lww.com/SLA/D190.

Statistics

Comparison of baseline and treatment characteristics between patients undergoing surgery in the first and second volume quartiles versus the third and fourth quartiles (creating groups of comparable sizes) was made using descriptive statistics. The impact of hospital volume on the outcomes was investigated using multivariable logistic regression analyses corrected for patient and tumor characteristics. Ten (non-)events of the investigated outcome measure were considered required per (category of a) variable. In case of insufficient events for the entire correction model, only confounders leading to a 10% change in the odds ratio of the hospital volume variable were included in the model.[20,21] First, the first volume quartile was compared to the pooled second, third, and fourth volume quartiles. Subsequently the first and second quartiles were compared to the third and fourth quartiles. For all outcomes statistically associated with hospital volume in the latter analyses, restricted cubic splines analyses, corrected for baseline characteristics, investigated whether this volume-outcome relationship eventually reached a plateau. Restricted cubic splines are flexible tools able to model nonlinear effects of continuous variables.[22] The number of knots was determined by assessing the Akaike's Information Criterion of the univariable models with 3, 4, and 5 knots.[23]

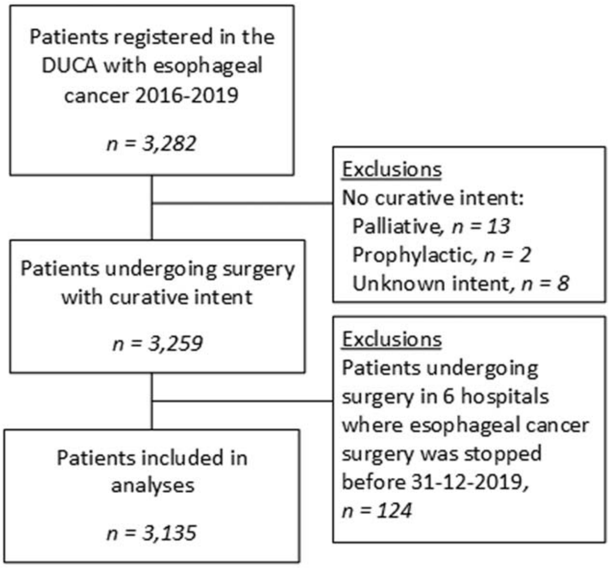

FIGURE 2. Flowchart of the study.

Two-sided P values of <0.05 were considered statistically significant. Missing variables were analyzed as a separate category when comprising >5% of that variable. Patients with missing outcome measures were excluded. A variance inflation factor >2.5 was considered indicative of multicollinearity. R-studio version 3.5.1, The R Foundation for Statistical Computing was used for all analyses.[24]

Additional Analyses

Additional analyses were performed to investigate whether a volume-outcome trend exists in patients with a complicated postoperative course. High-volume hospitals were defined as the third and fourth volume quartiles to create groups of equal sizes. For these analyses, only patients having at least 1 postoperative complication (any Clavien-Dindo) were included. The impact of hospital volume was investigated on: failure to rescue (ie, 30-day/in-hospital mortality in this complicated cohort of patients), prolonged hospital stay, prolonged ICU stay, 30-day hospital readmission, and reinterventions.

Sensitivity Analyses

To check if categorizing hospital volume into quartiles would introduce bias, the impact of volume on the outcome measures was also investigated with hospital volume as continuous variable.

RESULTS

In total, 3135 esophageal cancer patients were included from the 16 hospitals still performing esophageal cancer surgery in 2019 (Figs. 1 and 2). In the 2016–2019 period, the first volume quartile ranged from 24 to 39 annual esophageal resections. The second, third, and fourth volume quartiles ranged from 40 to 53, from 54 to 69 and from 70 to 101, respectively. In total, 886 patients underwent surgery in 10 first quartile hospitals. A total of 697, 800, and 752 underwent surgery in 9 second, 8 third, and 4 fourth quartile hospitals, respectively.

Patient, Tumor, and Treatment Characteristics

Baseline and treatment characteristics of patients undergoing surgery in first and second quartile hospitals versus third and fourth quartile hospitals are presented in Table 1. Preoperative weight loss differed significantly between both groups. In addition, higher-volume hospitals treated more advanced T and N stage tumors, Tx and Nx stages occurred less frequently. Higher-volume centers performed salvage surgery significantly more often (3.9% vs 2.3%, $P = 0.019$). In first and second quartile hospitals, patients were significantly more often treated with neoadjuvant chemoradiotherapy (88.1% vs 80.6%) whereas higher-volume hospitals tended to administer neoadjuvant chemotherapy more often (11.5% vs 5.3%; $P < 0.001$). In addition, in third and fourth volume quartile hospitals the proportion of patients undergoing transthoracic surgery was higher. In these hospitals, the preferred anastomotic location was intrathoracic (63.9%), whereas this was cervical in first and second volume quartile centers (51.8%; $P < 0.001$).

Outcomes

Table 2 shows the incidence and multivariable logistic regression analyses of the outcome measures in first quartile hospitals (≤39 annual esophagectomies) compared to the second, third, and fourth volume quartiles (≥40 annual resections). In the higher-volume group, the overall postoperative complication, severe complication, technical complication, prolonged hospital stay, prolonged ICU stay, and anastomotic leakage rates were significantly lower than in the first volume quartile. In addition, textbook outcome rates and lymph node yield were significantly higher in the second, third and fourth volume quartiles. Separate analyses of cervical and intrathoracic anastomotic leakage rates show that both were lower in the higher-volume centers (23.0% vs 26.5% for cervical and 14.9% vs 19.3% for intrathoracic anastomosis). Postoperative mortality, surgical radicality, and pulmonary complication rates did not differ between both groups.

Table 3 shows the comparison of outcomes in first and second volume quartile hospitals (≤53 annual esophagectomies) versus third and fourth quartile hospitals (>53). In the latter group, technical complication, prolonged hospital stay, prolonged ICU stay, and anastomotic leakage rates were significantly lower and lymph node yield and textbook outcome rates were higher. Figure 3 depicts the restricted cubic spline associations between these outcome measures and hospital volume. Textbook outcome, technical complications, and length of ICU stay improved when hospital volume increased but eventually plateaued at around 60 annual resections. Lymph node yield and anastomotic leakage continued to improve with rising volumes.

Additional Analyses

A total of 2024 patients had 1 or more postoperative complication(s). In third and fourth quartile centers (>53), prolonged ICU stay rates were significantly lower than in first and second quartile hospitals (≤53) (Table 4). No statistical differences in failure to rescue, prolonged hospital stay, readmissions, and reinterventions were identified.

Sensitivity Analyses

Supplemental Digital Content Table 2, http://links.lww.com/SLA/D190 shows the results of multivariable logistic regression analyses investigating the impact of hospital volume as a continuous variable on the outcome measures. Results were largely comparable with the general analyses: technical complication, anastomotic leakage, and prolonged ICU stay rates were inversely correlated with rising hospital volume and lymph node yield and textbook outcome rates rose with increasing hospital volume.

DISCUSSION

This population-based cohort study investigated the volume-outcome trends in esophageal cancer surgery in the Netherlands,

TABLE 1. Baseline and Treatment Characteristics of Esophageal Cancer Patients in 1st + 2nd Volume Quartile Hospitals (≤53 Annual Resections) and 3rd + 4th Volume Quartile Hospitals (>53 Annual Resections)

	Total	≤53 Annual Resections (N = 1583)	>53 Annual Resections (N = 1552)	
	N (%)	N (%)	N (%)	*P* value*
Sex				0.253
Male	2422 (77.3)	1236 (78.1)	1186 (76.4)	
Female	712 (22.7)	346 (21.9)	366 (23.6)	
Missing	1 (0)	1 (0.1)	0 (0)	
Age				0.307
<65 yr	1230 (39.2)	619 (39.1)	611 (39.4)	
65–75 yr	1532 (48.9)	762 (48.1)	770 (49.6)	
>75 yr	373 (11.9)	202 (12.8)	171 (11.0)	
Preoperative weight loss				0.009
None	1016 (32.4)	526 (33.2)	490 (31.6)	
1-5 kg	926 (29.5)	464 (29.3)	462 (29.8)	
6–10 kg	706 (22.5)	357 (22.6)	349 (22.5)	
>10 kg	352 (11.2)	146 (9.2)	206 (13.3)	
Missing	135 (4.3)	90 (5.7)	45 (2.9)	
BMI				0.436
<20	194 (6.2)	94 (5.9)	100 (6.4)	
20–25	1465 (46.7)	746 (47.1)	719 (46.3)	
26–30	1087 (34.7)	561 (35.4)	526 (33.9)	
>30	376 (12.0)	177 (11.2)	199 (12.8)	
Missing	13 (0.4)	5 (0.3)	8 (0.5)	
CCI†				0.356
0	1422 (45.4)	701 (44.3)	721 (46.5)	
1	766 (24.4)	400 (25.3)	366 (23.6)	
2+	936 (29.9)	482 (30.4)	454 (29.3)	
Missing	11 (0.4)	0 (0)	11 (0.7)	
ASA score‡				0.225
1–2	2298 (73.3)	1145 (72.3)	1153 (74.3)	
3+	834 (26.6)	436 (27.5)	398 (25.6)	
Missing	3 (0.1)	2 (0.1)	1 (0.1)	
Previous esophageal or gastric surgery				0.289
No	3058 (97.5)	1548 (97.8)	1510 (97.3)	
Yes	68 (2.2)	30 (1.9)	38 (2.4)	
Unknown/missing	9 (0.3)	5 (0.3)	4 (0.3)	
Tumor location				0.065
Intrathoracic	2452 (78.2)	1257 (79.4)	1195 (77.0)	
Gastro-esophageal junction	669 (21.3)	316 (20.0)	353 (22.7)	
Unknown/missing	14 (0.4)	10 (0.6)	4 (0.3)	
Histology				0.257
Adenocarcinoma	2480 (79.1)	1255 (79.3)	1225 (78.9)	
Squamous cell	548 (17.5)	261 (16.5)	287 (18.5)	
Unknown/other	69 (2.2)	39 (2.5)	30 (1.9)	
Missing	38 (1.2)	28 (1.8)	10 (0.6)	
Clinical tumor stage				0.042
T0–2	683 (21.8)	345 (21.8)	338 (21.8)	
T3–4	2341 (74.7)	1169 (73.8)	1172 (75.5)	
Tx	111 (3.5)	69 (4.4)	42 (2.7)	
Clinical node stage				<0.001
N0	1156 (36.9)	590 (37.3)	566 (36.5)	
N+	1875 (59.8)	918 (58.0)	957 (61.7)	
Nx	104 (3.3)	75 (4.7)	29 (1.9)	
Salvage surgery				0.019
No	2930 (93.5)	1453 (91.8)	1477 (95.2)	
Yes	96 (3.1)	36 (2.3)	60 (3.9)	
Missing	109 (3.5)	94 (5.9)	15 (1.0)	
Neoadjuvant therapy				<0.001
Chemoradiotherapy	2645 (84.4)	1394 (88.1)	1251 (80.6)	
None	221 (7.0)	99 (6.3)	122 (7.9)	
Chemotherapy	262 (8.4)	84 (5.3)	178 (11.5)	
Other/missing	7 (0.2)	6 (0.4)	1 (0.1)	
Type of surgery				<0.001
Transhiatal esophagectomy	409 (13.0)	273 (17.2)	136 (8.8)	
Transthoracic esophagectomy	2557 (81.6)	1238 (78.2)	1319 (85.0)	
Other	169 (5.4)	72 (4.5)	97 (6.2)	
Anastomotic location				<0.001
Intrathoracic	1651 (52.7)	660 (41.7)	991 (63.9)	
Cervical	1284 (41.0)	820 (51.8)	464 (29.9)	
None/other/unknown	68 (2.2)	32 (2.0)	36 (2.3)	
Missing	132 (4.2)	71 (4.5)	61 (3.9)	
Minimally invasive surgery				0.758
No	302 (9.6)	150 (9.5)	152 (9.8)	
Yes	2832 (90.3)	1433 (90.5)	1399 (90.1)	
Missing	1 (0.0)	0 (0)	1 (0.1)	

**P* value based on χ^2 statistic.
†Charlson Comorbidity Index.
‡American Society of Anesthesiologists score.
ASA indicates American Society of Anesthesiologists

TABLE 2. Multivariable Logistic Regression Analyses of Short-term Surgical Outcomes After Esophageal Cancer Surgery – Comparison Between 1st Volume Quartile Hospitals (<40 Annual Resections) and 2nd + 3rd + 4th Volume Quartile Hospitals (≥40 Annual Resections)

	Annual Esophagectomy Hospital Volume	Outcome Incidence (%)	aOR*	95% CI†	*P* value
Overall postoperative complications (yes)					
	<40	523 (66.8%)	1		
	≥40	1287 (62.8%)	0.83	0.69–0.99	**0.036**
Severe complications‡ (yes)	<40	255 (32.5%)	1		
	≥40	585 (28.6%)	0.81	0.68–0.98	**0.027**
Anastomotic leakage (yes)	<40	176 (22.5%)	1		
	≥40	336 (16.4%)	0.66	0.53–0.81	**<0.001**
Pulmonary complications (yes)	<40	227 (29.0%)	1		
	≥40	665 (32.5%)	1.17	0.97–1.41	0.095
Technical complications§ (yes)	<40	302 (38.5%)	1		
	≥40	603 (29.4%)	0.65	0.54–0.78	**<0.001**
30-d/in-hospital mortality (yes)	<40	22 (2.8%)	1		
	≥40	54 (2.6%)	0.93	0.57–1.58	0.793
Surgical radicality (R0) (yes)	<40	735 (95.6%)	1		
	≥40	1892 (95.5%)	0.97	0.64–1.44	0.892
Lymph node yield (≥15)	<40	627 (81.3%)	1		
	≥40	1854 (93.1%)	3.12	2.41–4.04	**<0.001**
Prolonged length of hospital stay (>11 d)	<40	386 (49.2%)	1		
	≥40	874 (42.7%)	0.76	0.64–0.90	**0.002**
Prolonged length of ICU stay (>1 d)	<40	464 (59.3%)	1		
	≥40	907 (44.3%)	0.53	0.45–0.63	**<0.001**
Textbook outcome‖ (yes)	<40	321 (42.6%)	1		
	≥40	1009 (51.8%)	1.48	1.24–1.76	**<0.001**

*Adjusted odds ratio. Corrected for: sex, age, preoperative weight loss, BMI, Charlson Comorbidity Index, ASA score, previous esophageal or gastric surgery, tumor location, histology, clinical tumor stage, clinical node stage, and salvage surgery. When degrees of freedom were insufficient for correction for all possible confounders, only confounders leading to a 10% change in OR were included for analyses.

†95% Confidence interval.

‡Clavien-Dindo grade III or higher.

§Includes: postoperative bleeding (excluding intraluminal), recurrent nerve injury, iatrogenic intestinal injury, gastric tube necrosis, iatrogenic tracheal or bronchial injury, persistent air leakage requiring drainage >10 d postoperatively, Chyle leakage, anastomotic leakage, intraoperative complications.

‖R0 resection, ≥15 lymph nodes, length of hospital stay ≤21 d and no intra- or severe postoperative complication, readmission (to either hospital or ICU) or mortality.

BMI indicates body mass index; ICU, intensive care unit.

where all hospitals reached the volume-threshold of 20 annual resections. This study showed that surgery performed in the lowest volume quartile (ie, <40 annual esophagectomies) was associated with higher postoperative complication, severe complication, technical complication, and anastomotic leakage rates, longer hospital and ICU stay, lower textbook outcome rates and lower lymph node yield. When raising the cut-off from 40 to 53 annual resections (ie, from the first to the second volume quartile), the technical complication, and anastomotic leakage rates were higher, ICU stay was longer and textbook outcome and lymph node yield were lower in the lower-volume quartiles (≤53 annual resections). For textbook outcome, technical complications, and length of ICU stay the volume trend eventually plateaued around 60 resections. However, anastomotic leakage and lymph node yield continued to improve with increasing volumes above 60 cases annually.

The volume-outcome relationship in esophageal cancer surgery has been studied extensively, with several studies reporting favorable outcomes in higher-volume centers. A well-conducted meta-analysis including 16 studies found lower short-term mortality rates and prolonged long-term survival rates after esophageal cancer surgery in high-volume centers.[8] However, in this meta-analysis, the high-volume category ranged from 2.33 to 87 annual esophagectomies. The Leapfrog initiative was one of the first to set a standard volume cut-off at 7 annual esophagectomies.[25] Another study verified this Leapfrog threshold but concluded that setting the volume standard higher would improve results.[26] Several studies found inferior results in low-volume centers when applying 20 as a volume threshold.[7,27,28] These publications provoked the introduction of a volume threshold of 10 annual resections in 2006 and 20 in 2011 in the Netherlands. However, it remains unclear whether the volume-outcome relationship eventually reaches a plateau. A previous Dutch population-based study investigated whether such a plateau existed and concluded that reduced postoperative mortality and 2-year overall survival rates were correlated with rising hospital volumes but this relationship plateaued at 60 annual resections.[11] Another nationwide study endorsed the conclusion that the volume-outcome relationship might eventually reach a plateau as it found that mortality rates leveled out at approximately 30 to 40

TABLE 3. Multivariable Logistic Regression Analyses of Short-term Surgical Outcomes After Esophageal Cancer Surgery – Comparison Between 1st + 2nd Volume Quartile Hospitals (≤53 Annual Resections) and 3rd + 4th Volume Quartile Hospitals (>53 Annual Resections)

Annual Esophagectomy Hospital Volume		Outcome Incidence (%)	aOR*	95% CI†	*P* value
Overall postoperative complications (yes)					
	≤53	890 (64.7%)	1		
	>53	920 (63.2%)	0.95	0.81–1.11	0.524
Severe complications‡					
(yes)	≤53	413 (30.0%)	1		
	>53	427 (29.3%)	0.98	0.83–1.15	0.798
Anastomotic leakage					
(yes)	≤53	273 (19.8%)	1		
	>53	239 (16.4%)	0.80	0.66–0.97	**0.026**
Pulmonary complication					
(yes)	≤53	432 (31.4%)	1		
	>53	460 (31.6%)	1.02	0.87–1.20	0.825
Technical complications§					
(yes)	≤53	472 (34.3%)	1		
	>53	433 (29.8%)	0.82	0.70–0.96	**0.014**
30-d/in-hospital mortality					
(yes)	≤53	36 (2.6%)	1		
	>53	40 (2.8%)	1.02	0.67–1.56	0.930
Surgical radicality (R0)					
(yes)	≤53	1291 (95.3%)	1		
	>53	1336 (95.6%)	1.05	0.74–1.50	0.772
Lymph node yield					
(≥15)	≤53	1,147 (84.5%)	1		
	>53	1334 (95.0%)	3.56	2.68–4.77	**<0.001**
Prolonged length of hospital stay					
(>11 d)	≤53	612 (44.4%)	1		
	>53	648 (44.5%)	1.01	0.87–1.18	0.900
Prolonged length of ICU stay					
(>1 d)	≤53	706 (51.3%)	1		
	>53	665 (45.7%)	0.80	0.69–0.93	**0.004**
Textbook outcome‖					
(yes)	≤53	618 (46.4%)	1		
	>53	712 (51.2%)	1.25	1.07–1.46	**0.005**

*Adjusted odds ratio. Corrected for: sex, age, preoperative weight loss, BMI, Charlson Comorbidity Index, ASA score, previous esophageal or gastric surgery, tumor location, histology, clinical tumor stage, clinical node stage, and salvage surgery. When degrees of freedom were insufficient for correction for all possible confounders, only confounders leading to a 10% change in OR were included for analyses.

†95% Confidence interval.

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‖R0 resection, ≥15 lymph nodes, length of hospital stay ≤21 d and no intra- or severe postoperative complication, readmission (to either hospital or ICU) or mortality.

BMI indicates body mass index; ICU, intensive care unit.

esophagectomies per year.[29] This is in line with the results of the current study, which also shows a plateau of the volume-outcome trend at around 50–60 annual resection for most outcomes. However, for other outcomes (like postoperative mortality and surgical radicality) no volume-outcome trend was identified.

Most of the studies referred to above, found improved outcomes in "high-volume" centers compared to very low-volume hospitals (ie, 1–20 annual esophagectomies). In 2019, all Dutch hospitals still performing esophageal cancer surgery reached the volume threshold of 20 annual esophagectomies. Even though only these hospitals were included (meaning that the annual median volume is relatively high compared to existing literature from other Western countries where esophageal surgery has not been centralized), the current study revealed a volume-outcome trend. In contrast with existing literature including really low-volume hospitals (<20 annual resections), the current study did not show higher short-term mortality or failure-to-rescue rates in lower-volume centers. This might suggest that short-term mortality would only be higher in really low-volume hospitals (ie, <20 esophagectomies per year), and that earlier waves of centralization have reduced mortality rates. However, a recent DUCA study investigating time trends showed that joint efforts by all Dutch upper gastrointestinal surgeons in annual best practice meetings also resulted in improvement: mortality rates decreased from 4.2% in 2011/2012 to 2.5% in 2017/2018.[10]

In the light of hospital anonymity, this study pooled data into hospital volume quartiles, it did not provide information on the quality of care provided by individual hospitals. Certain lower-volume centers have excellent short-term outcomes (eg, 1 lowest volume-quartile hospital showed an annual leakage rate of 4.2%) and the higher-volume centers in this study do not invariably provide high-quality care [eg, one quartile four hospital had an annual anastomotic leakage rate of 28.4% (data not shown because of hospital anonymity)]. Therefore, this study does not plea for a higher volume threshold in the Netherlands. It rather pleas for better regional and national cooperation between (lower and higher-volume) hospitals. In addition, in the light of outcome differences between hospitals (irrespective of volume), the role of openly showing, comparing, and discussing differences in outcome data

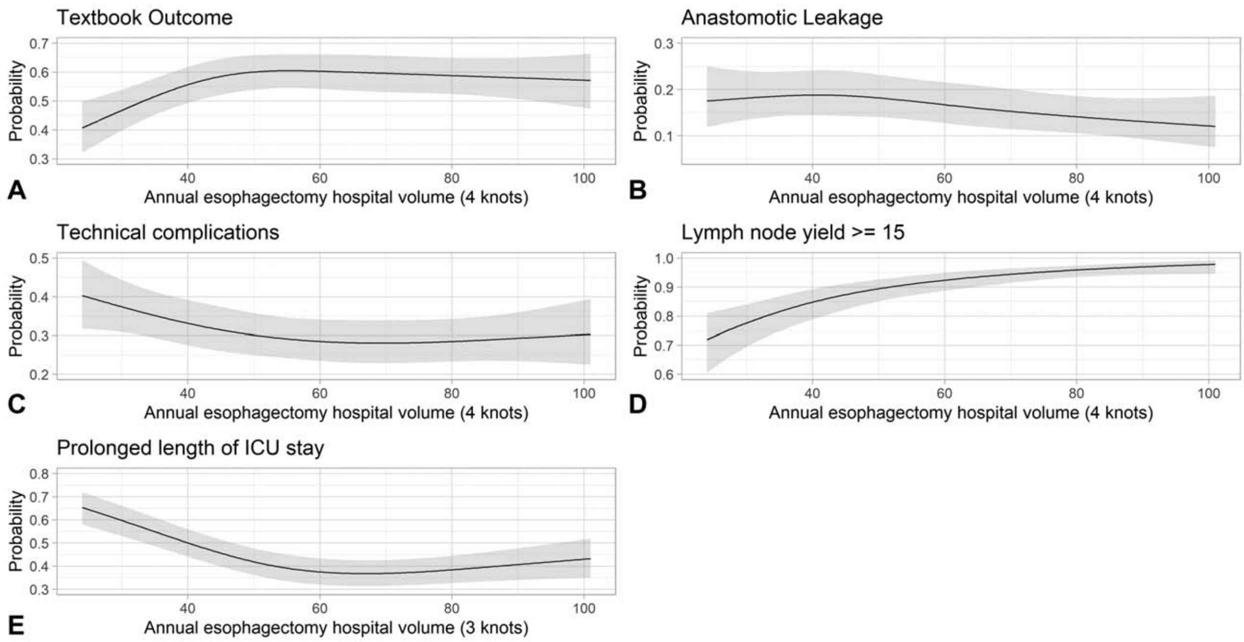

FIGURE 3. Restricted cubic splines analyses of the association between esophagectomy hospital volume and clinical outcomes.

is vital. Especially since the anastomotic leakage and technical complication rates reported in the Netherlands are relatively high compared to other European countries.[30–32] Therefore, to reduce hospital variation and improve leakage rates on a national level, the Dutch Task Force Upper GI Surgery organizes annual best practice meetings.[33] At these meetings, anastomotic leakage rates of individual hospitals are openly discussed. Best-practice hospitals are identified and present their techniques. Underperforming centers can learn from the informative discussion that follows and are given the opportunity to visit outperforming centers to learn and improve in clinical practice. Dutch leakage rates are relatively high due to the historical preference for a transhiatal approach with a cervical anastomosis (associated with higher leakage rates than intrathoracic anastomoses) and the transition in recent years towards minimally invasive surgery (31% in 2011 to 93% in 2019), transthoracic surgery (43% in 2011 to 83% in 2019), and intrathoracic anastomosis (11% in 2011 to 58% in 2019).[10] As shown by a recent Dutch study, implementation of such new techniques and the associated proficiency gain curves are correlated with an increase in complications.[34]

TABLE 4. Complicated Esophageal Cancer Surgery: Multivariable Logistic Regression Analyses of Short-term Surgical Outcomes – Comparison Between 1st + 2nd Volume Quartile Hospitals (≤53 Annual Resections) and 3rd + 4th Volume Quartile Hospitals (>53 Annual Resections)

	Annual Esophagectomy Hospital Volume	Outcome Incidence (%)	aOR*	95% CI†	*P* value
Failure to rescue (30-d/in-hospital mortality)					
(yes)	≤53	35 (3.9%)	1		
	>53	36 (3.9%)	0.97	0.62–1.51	0.901
Prolonged length of hospital stay					
(>14 d)	≤53	409 (46.0%	1		
	>53	447 (48.6%)	1.13	0.93–1.36	0.212
Prolonged length of ICU stay					
(>2 d)	≤53	384 (43.2%)	1		
	>53	345 (37.5%)	0.79	0.65–0.96	**0.018**
30-d readmission					
(yes)	≤53	185 (21.1%)	1		
	>53	162 (17.9%)	0.84	0.66–1.06	0.144
Reintervention					
(yes)	≤53	337 (37.9%)	1		
	>53	379 (41.2%)	1.15	0.95–1.39	0.162

*Adjusted odds ratio. Corrected for: sex, age, preoperative weight loss, BMI, Charlson Comorbidity Index, ASA score, previous esophageal or gastric surgery, tumor location, histology, clinical tumor stage, clinical node stage, and salvage surgery. When degrees of freedom were insufficient for correction for all possible confounders, only confounders leading to a 10% change in OR were included for analyses.

†95% Confidence interval.

BMI indicates body mass index; ICU, intensive care unit.

The current study showed lower (severe) postoperative complication, technical complication, and anastomotic leakage rates in centers with an annual esophagectomy volume over 40. Surgeons in lower-volume centers more often performed a cervical anastomosis, which is associated with higher leakage rates.[35] However, when analyzed separately, both intrathoracic and cervical leakage rates were lower in higher-volume centers. In the current study, high-volume hospital surgeons more often chose a transthoracic surgical approach. Even though transthoracic surgery is associated with increased pulmonary and cardiac complication and Chyle leakage rates, high-volume hospitals did not have increased pulmonary complication rates and had lower overall complication rates.[36] In addition, high-volume centers more often performed salvage surgery without this negatively impacting their results. The lower complication rates might be caused by more efficient clinical care pathways or by differences in experience at various levels (ICU staffing, hospital ward personnel, surgeons, operation room staffing, residents). Transparently discussing treatment decisions, surgical techniques and best practices (not necessarily of high-volume centers) with other hospitals might induce nationwide improvement.

In the Netherlands, neoadjuvant chemoradiotherapy therapy has been administered in over 80% of patients in recent years.[37] This study showed a more differentiated use of neoadjuvant therapy, with a higher percentage of neoadjuvant chemotherapy but lower chemoradiotherapy rates in higher-volume centers. This might be related to the slightly higher rate of gastro-esophageal junction tumors treated in higher-volume centers. The more differentiated use of neoadjuvant therapy might also implicate that higher-volume centers more often deviate from the standard of care.

Multiple previous studies hypothesized that prompt recognition of complications in high-volume hospitals leads to more timely and adequate treatment of complications compared to low-volume centers.[38–40] These studies hypothesized that nurses, residents, and intensive care or other hospital ward personnel are better trained in recognizing complications when exposed to a higher caseload. The additional analyses of the current study could not confirm this hypothesis.

The present study has several limitations. The current study could not investigate the impact of hospital volume on long-term survival as the DUCA database does currently not contain long-term follow-up data and because this study included a recent cohort of patients. At the set-up, it was decided not to add long-term data to the DUCA registry as providing short-loop feedback is essential for a clinical audit. However, the DUCA database used to feature long-term follow-up and survival data via a link with Dutch insurers data. Unfortunately, due to tightened privacy legislation, this link is not possible anymore. The DUCA scientific committee is currently working on a collaboration with the Netherlands Cancer Registry to regain access to long-term follow-up data. On the other hand, this study showed that in higher-volume centers textbook outcome rates and lymph node yield were higher and complication rates were lower. From previous literature it emerged that these outcomes are associated with improved survival and better prognostication.[18,41–43] Another limitation is the retrospective nature of this study, which might introduce residual confounding. In addition, this study did not investigate outcomes at a hospital level. Therefore, this study cannot reflect on individual hospital quality and its conclusions cannot be used as arguments for raising the volume threshold.

CONCLUSIONS

This population-based cohort study showed that, after the introduction of an annual volume threshold of 20 esophageal cancer resections, a volume trend in multiple short-term outcomes of esophageal cancer surgery exists in the Netherlands. The volume trends of most outcomes reached a plateau at 50 or 60 annual resections but anastomotic leakage and lymph node yield continued to improve with rising volumes despite intercenter variation. Although this study does not reflect on individual hospital quality, there appears to be a volume trend towards better outcomes in high-volume centers. Projects have been initiated to improve national quality of care by reducing hospital variation (irrespective of volume) in outcomes in The Netherlands.

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DISCUSSANT

Dr. Valerie W. Rusch

Good afternoon and thank you for the opportunity to comment on this excellent presentation and manuscript from the Dutch Upper Gastrointestinal Audit Group. The current analyses extend their prior work in correlating institutional case volumes with *short-term* surgical outcomes after esophagogastrectomy for cancer, and now lead to a recommendation for continued centralization of care. Starting from a standard of 10 cases established in 2006 and increased to 20 cases in 2011, the authors' data now suggest that an annual institutional volume of at least 50 cases is associated with optimal surgical outcomes. Importantly, this work, while facilitated by the geographically small size of the Netherlands and a universal healthcare system, again demonstrates how a national database incorporating clinically meaningful individual and composite endpoints, and providing benchmarked feedback to clinicians and hospitals can lead to continuous improvement in surgical and oncologic outcomes.

I have 2 questions for the authors:

(1) Although institutional case volumes are clearly associated with morbidity and mortality, variations in surgical approach and the frequency of severe complications, technical complications, and anastomotic leaks, even in high volume institutions, remain relatively high at roughly 29%, 30%, and 16%, respectively. Has consideration been given to potential methods to reduce these further in order to improve outcomes?

(2) The impact of short-term surgical outcomes on disease-free and overall survival cannot be assessed through this audit. Is there a way either to extend data acquisition to include survival information or, alternatively, to link these data with a national cancer registry to assess the correlation with long-term outcomes?

Response Prof van Berge Henegouwen

Thank you very much for your kind words and opportunity to present our work. We agree that the audit has great potential in improving care at a national level as it provides clinicians with benchmarked feedback. It is true that reported anastomotic leakage rates in the Netherlands are comparatively high, just as they have been in other nationwide collaborative studies (eg, the CROSS study). This is partially caused by a historical nationwide preference for cervical anastomosis as standard procedure in many centers. Cervical anastomosis is traditionally associated with higher leakage rates than the Ivor Lewis procedure. Another important development during the past decade was the adoption of new techniques in many centers in the Netherlands. This is illustrated by the increase in transthoracic procedures from around 50% to 85% and an increase in minimally invasive procedures to 90%. There has been an overall trend towards minimally invasive Ivor Lewis procedures. These implementations, and especially the proficiency gain curves of these procedures have been shown to be accompanied by higher complication rates.

Improving anastomotic leakage rates is, however, one of the core focuses of the audit. Based on DUCA data, the Upper GI Surgery taskforce of the Association of Surgeons of the Netherlands organizes yearly best practice meetings. All hospitals show their anastomotic leakage rates and all centers show their operative techniques. A discussion follows which is very informative and we try to help the underperforming centers to improve. Also, based on these meetings, underperforming centers visit high-performance centers to learn techniques in clinical practice. At our last meeting we also discussed that the best practice centers would create a ‘‘best practice’’ document regarding anastomotic leakage. All underperforming centers will draw up improvement plans.

Regarding your second question; this is a very good point. Adding long-term survival data would significantly enhance the value of the DUCA. In the past, the DUCA had access to long-term survival data through a link with healthcare insurance survival data. However, due to restrictions in privacy legislation, this link is no longer possible. We are working on a new link with the Netherlands Cancer Registry. We expect to add this long-term data to the DUCA shortly.

In addition, we performed studies with DUCA data (published recently in Annals of Surgery) that showed a strong correlation between short-term outcomes and survival. Especially complications show a decreased survival. On the other hand, textbook outcome (a composite outcome which includes many parameters like radicality, lymph node yield, complications, and others) shows a better survival; this implies that these short-term outcomes are very important in long-term outcomes as well.