Evaluation of International Contemporary Operative Outcomes and Management Trends Associated With Esophagectomy

A 4-Year Study of >6000 Patients Using ECCG Definitions and the Online Esodata Database

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Objective: This study aims to verify the utility of international online datasets to benchmark and monitor treatment and outcomes in major oncologic procedures.

Background: The Esophageal Complication Consensus Group (ECCG) has standardized the reporting of complications after esophagectomy within the web-based Esodata.org database. This study will utilize the Esodata dataset to update contemporary outcomes and to monitor trends in practice in an era of rapid technical change.

Methods: This observational study, based on a prospectively developed specific database, updates esophagectomy outcomes collected between 2015 and 2018. Evolution in patient and operative demographics, treatment, complications, and quality outcome measures were compared between patients undergoing surgery in 2015 to 2016 and 2017 to 2018.

Results: Between 2015 and 2018, 6022 esophagectomies from 39 centers were entered into Esodata. Most patients were male (78.3%) with median age 63. Patients having minimally invasive esophagectomy constituted 3177 (52.8%), a chest anastomosis 3838 (63.7%), neoadjuvant chemoradiotherapy 2834 (48.7%), and R0 resections 5441 (93.5%). For quality measures, 30- and 90-day mortality was 2.0% and 4.5%, readmissions 9.7%, transfusions 12%, escalation in care 22.1%, and discharge home 89.4%. Trends in quality measures between 2015 and 2016 (2407 patients) and 2017 and 2018 (3318 patients) demonstrated significant ($P < 0.05$) improvements in readmissions 11.1% to 8.5%, blood transfusions 14.3% to 10.2%, and escalation in care from 24.5% to 20% A significantly ($P < 0.05$) reduced incidence in pneumonia (15.3%–12.8%) and renal failure (1.0%–0.4%) was observed. Anastomotic leak rates increased from 11.7% to 13.1%, whereas leaks requiring surgery decreased 3.3% and 3.0%, respectively.

Conclusions: The Esodata database provides a valuable resource for assessing contemporary international outcomes. This study highlights an increased application of minimally invasive approaches, a high percentage of complications, improvements in pneumonia and key quality metrics, but with anastomotic leak rates still >10%.

Keywords: Esodata online oncologic database, Esophagectomy, complications, surgical and quality outcomes measures

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Major complications following esophageal cancer surgery are associated with increased operative mortality,[1–3] cancer recurrence, diminished long-term survival,[4–8] longer hospital stay,[8–10] more readmissions,[11–14] greater hospital costs,[15,16] and worse long-term health-related quality of life (HRQL).[17,18] Mortality rates are best in high-volume centers, but 90-day mortality remains between 2.5% and 7%, and, even in a minimally invasive era, morbidity rates are high.[3,19,20]

Until standardized and generally accepted definitions were developed by the Esophageal Complications Consensus Group (ECCG) in 2015, it was impossible to make comparisons between studies. The first internet-based international oncologic dataset (Esodata.org), has previously provided a contemporary benchmark for the incidence of perioperative esophageal outcomes including complications.[19] This has provided a validated methodology for

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institutions,[20] a tool for systematic reviews,[9] a secondary outcome data set used within international randomized clinical trials (RCTs),[21] and national datasets[22] as well as an infrastructure for comparative national and international audits, thereby supporting the development of quality improvement programs.

An ECCG publication on benchmarks comprehensively documented all perioperative complications as well as 30- and 90-day mortality in 2704 resections from 24 high-volume centers representing 14 countries collected over a 2-year period between January 2015 and December 2016.[19] The report herein expands this dataset to >6000 patients, with the primary aim of the present study to compare outcomes, including rates of four specific complications (anastomotic leak, conduit necrosis, recurrent laryngeal nerve injury, chyle leak) between the original ECCG dataset (January 2015–December 2016) to a more recent 2-year period (January 2017–December 2018). Secondary goals included reporting on recommended quality improvement measures developed by the ECCG[23] [90-day mortality rate, 30-day readmission rates, requirement for documenting change/escalation in level of care, blood product utilization (quantity and timing) and documentation of discharge location]. This study will also assess the utility of an internet-based high-volume international standardized dataset to document short-term evolution in patient and tumor demographics, operative technique, mandatory quality measures, as well as individual complication incidence and overall complication severity.

METHODS

The Esodata dataset, based on the standardized platform developed by the ECCG,[23] was initiated as a secure, web-based database in March 2015. The original 24 centers of the ECCG committed to entering all esophageal resections done at their institution starting in January 2015 (see Membership Agreement Supp1). Data were collected from these 24 centers until December 2016 when the preliminary benchmark of complications was published.[19]

Over the subsequent year, 15 additional high-volume international esophagectomy centers applied and were admitted to the International Esodata Study Group (IESG), so currently there are 39 centers representing 19 countries (Table 1). All centers were responsible for complying with institutional and national ethics and IRB requirements and the dataset remained in a format where all patient information within the database was anonymized to comply with international data privacy agreements.

The original Esodata dataset was designed using the consensus-based data fields and definitions agreed by the ECCG, and only registered contributors from participating institutions could enter patients into the database. The data collection process via a secure web interface was constructed using a standardized ‘‘user-friendly’’ online database platform to encourage not only compliance with entering all esophageal resections but also encouraging data completeness and integrity. In the context of the wide variation in computer systems between the 39 participating centers, the integrity and security of the dataset was guaranteed by utilizing a modern web browser-based interface using encrypted network communications. In addition, preexisting computer systems did not require institutional IT support or the downloading of complex software systems onto individual institutional hard drives. The dataset is available to surgeons, data managers, and cancer coordinators through a secure sign-on at any location that they had internet connections allowing encrypted network communications. The dataset was constructed with a database interface using multiple-level data validation algorithms that allowed only targeted data to be submitted.

The database and web portal were hosted, as previously described,[19] in a private dedicated web server and database interface that was accessible only through an authenticated and encrypted secure network connection (SSL Client and Server Certificate with Extended Validation issued by Symantec Corporation, Mountain View, CA). Open-source database server package (MariaDB V10.1.21 by MariaDB Foundation, Redwood City, CA) with regular encrypted backup system arrangements in combination with Drupal Content Management System (Distributed under the terms of GNU General Public License) was used for user and data access management. The system as originally designed provided portability, dynamic live data analytics, modularity and flexibility in content access management. The registered data contributors from each institution were authenticated individually to access the database interface in the members-only area of the Esodata.org web portal. Importantly, registered contributors had instant access to their own institutional results on the Esodata website that was available to them anywhere in the world where secure internet access was available.

TABLE 1. Esodata Contributing Centers 2015–2018

Countries: 19	Institutions: 39
Australia	Princess Alexandra Hospital, University of Queensland
Belgium	Katholieke Universiteit Leuven
Brazil	University of São Paulo School of Medicine
Canada	Toronto General Hospital
China	Queen Mary Hospital, The University of Hong Kong
	Sichuan Cancer Hospital & Institute
Denmark	Odense University Hospital
France	Claude Huriez University Hospital
	Hôpital Nord, Aix-Marseille Université
Germany	Agaplesion Markus Krankenhaus
	University Hospital of Cologne
India	Tata Memorial Centre
Ireland	St. James’s Hospital Trinity College
Italy	University of Verona
	Vita-Salute San Raffaele University
Japan	Keio University
The Netherlands	Amsterdam UMC, University of Amsterdam
	Erasmus Medical Center
	University Medical Center
Singapore	National University Hospital
Spain	Hospital Universitario del Mar
Sweden	Karolinska Institutet and Karolinska University Hospital
Switzerland	Hirslanden Medical Center
United Kingdom	Cambridge Oesophago-Gastric Centre, Addenbrookes Hospital
	Nottingham University Hospitals NHS Trust
	Oxford University Hospitals NHS Foundation Trust
	Queen Elizabeth Hospital University of Birmingham
	Royal Victoria Hospital
	Guy’s & St Thomas’ NHS Foundation Trust
	Northern Oesophagogastric Cancer Unit, Royal Victoria Infirmary
	University Hospital Southampton NHS Foundation Trust
USA	Esophageal and Lung Institute, Allegheny Health Network
	Massachusetts General Hospital
	MD Anderson Cancer Center
	Memorial Sloan Kettering Cancer Center
	Oregon Health and Science University
	The University of Chicago Medicine
	University of Michigan Health System
	Virginia Mason Medical Center

Statistical Methods

The cohort was stratified according to time period of inclusion. Comparisons between the groups were done using Chi-square test. Quantile regression model was used to analyze the association between grade of anastomotic leak, conduit necrosis, recurrent laryngeal nerve injury, and chyle leak to Clavien-Dindo score and length of hospital stay. Significance level was set at 0.05. Analyses were performed using STATA version 13 software (StataCorp LP, College Station, TX).

RESULTS

Outcome Analysis of Entire Study Population (2015–2018)

The present study population includes 6022 patients entered into the Esodata dataset between January 2015 and December 2018. Patient demographics are shown in Table 2. The majority were male (78.3%), with a mean age of 63.2 years. Patients presented with a body mass index (BMI) >30 in 20.5% of cases, and 5.4% had a BMI <18.5. ASA II was most common, reported in 44.3%, with ASA III at 40.0% and ECOG 0/1 in 93.9%. Most tumors were located in the distal esophagus (54.4%) or at the esophagogastric junction (33.8%). Minimally invasive esophagectomy (MIE) surpassed open cases, at 52.8% versus 47.2% cases, respectively, and 53.1% of MIE cases were accomplished with MI approaches in both abdomen and thorax (Table 3). A transhiatal esophagectomy represented 21.5% of open cases. Neoadjuvant chemoradiation was the more common approach at 63.5% of patients undergoing neoadjuvant therapy.

For key complications (Table 4), anastomotic leak was observed in 12.5%, pneumonia in 13.9%, atrial dysrhythmia in 14.7%, chyle leak in 4.6%, delirium in 3.7%, and generalized sepsis in 2.2%. Thirty-day mortality was 2.2%, and 90-day mortality 4.5%; 39.5% of patients had no complications, and 32.3% had ≥2 complications (Table 5). For severity of complications as per Clavien-Dindo (Table 5), Grade III/IV was 30.2%, and IIIB/IV was 15.0%.

TABLE 2. Patient Demographics

N (%)	2015–2016	2017–2018	All Patients	P
Sex				0.088
Female	614 (22.7%)	693 (20.9)	1307 (21.7%)	
Male	2090 (77.3%)	2625 (79.1)	4715 (78.3%)	
Mean age, y	63.0	63.5	63.2	0.035
Age group, y				0.015
≤40	66 (2.4%)	89 (2.7%)	155 (2.6%)	
41–50	230 (8.5%)	266 (8.0%)	496 (8.2)	
51–60	706 (26.1%)	787 (23.7%)	1493 (24.8)	
61–70	1091 (40.4%)	1313 (39.6%)	2404 (39.9)	
71–80	540 (20.0%)	785 (23.7%)	1325 (22.0)	
>80	71 (2.6%)	78 (2.4%)	149 (2.5)	
BMI group				<0.001
<18.5	184 (6.8%)	140 (4.2%)	324 (5.4%)	<0.001
18.5–25	1027 (38.0%)	1290 (38.9%)	2317 (38.5)	
25–30	929 (34.4%)	1214 (36.6%)	2143 (35.6%)	
30-35	395 (14.6%)	462 (13.9%)	857 (14.2%)	
>35	169 (6.3%)	212 (6.4)	381 (6.3%)	
ACCI score groups				0.571
0–3	751 (27.8%)	884 (26.6%)	1635 (27.2)	
4–7	1872 (69.2%)	2321 (70.0%)	4193 (69.9)	
8–11	74 (2.7%)	106 (3.2%)	180 (3.0)	
≥12	7 (0.3%)	7 (0.2%)	14 (0.2)	
ASA status score				<0.001
1	428 (15.8%)	373 (11.2%)	801 (13.3%)	
2	1256 (46.5%)	1410 (42.5%)	2666 (44.3%)	
3	947 (35.0%)	1459 (44.0%)	2406 (40.0)	<0.001
4	69 (2.6%)	75 (2.3%)	144 (2.4%)	
5	4 (0.2%)	1 (0.0%)	5 (0.1%)	
WHO/ECOG performance				<0.001
0	1503 (55.6%)	1515 (45.7%)	3018 (50.1%)	<0.001
1	1054 (39.0%)	1583 (47.7%)	2637 (43.8%)	
2	133 (4.9%)	158 (4.8%)	291 (4.8%)	
3	11 (0.4%)	56 (1.7%)	67 (1.1%)	
4	3 (0.1%)	6 (0.2%)	9 (0.2%)	

Comparison of 2015–2016 with 2017–2018

Demographic changes from Period 1 (2015–2016) to Period 2 (2017–2018) included increases in ASA III, 35% to 44% and decreases in BMI >30, 20.9% to 20.3% and BMI <18.5, 6.8% to 4.2%. In Period 2, MIE had increased significantly at 56.7% compared with 48.0% in Period 1 ($P < 0.001$). A surgery-first approach decreased from 22.4% to 19.7%, and neoadjuvant chemoradiation as a percentage of the total having neoadjuvant therapy increased from 60% to 68.6% (Table 3).

Table 4 provides a comprehensive review of overall incidence of complications in the entire study group and an assessment of changes in complication incidence between the 2 study periods. Anastomotic leaks increased from 11.7% to 13.1% ($P = 0.121$). Pneumonia decreased from 15.3% to 12.8% ($P = 0.005$), and atrial dysrhythmia was 14.8% and 14.7%, respectively. Ninety-day mortality was 4.4% and 4.6% in Period 1 and 2, respectively. Acute renal failure requiring dialysis decreased from 1.0% to 0.4% ($P = 0.004$). Grade IIIb/IV complication was 14.9% versus 15.09%.

Table 5 demonstrates that the overall incidence of complications increased from 59% to 61.1%. There was a significant decrease in the number of patients sustaining >3 complications from 18.0% to 15.3%. Table 5 also demonstrates changes in Clavien-Dindo severity scores with the incidence of Grade I and Grade II complications increasing, however without a significant change in the incidence of complications graded IIIb or higher. Length of hospital stay decreased slightly between the 2 study periods 17.3 to 16.7 days.

Quality Metrics

ECCG Quality Measures are documented in Table 6. There was no significant change in 30- or 90-day mortality between the 2 study periods. Readmissions within 30 days of discharge was 9.7% overall, decreased from 11.1% to 8.5%, ($P < 0.05$). Blood transfusion rates decreased from 14.3% to 10.2% ($P < 0.001$). Escalation in level of care defined as a change in patient location due to the need for a higher level of monitoring of care, for example, Ward to ICU, decreased from 24.5% to 20% ($P < 0.001$). Patients requiring escalation in care most commonly had pneumonia (25.9%) and atrial dysthymia (21.2%). Conversely, 41.1% of patients with pneumonia and 31.8% who had atrial dysrhythmia required an escalation of their care during their hospitalization. The percentage of patients who were discharged home decreased from 91.4% to 87.8% ($P < 0.001$).

The specific definitions, incidence, severity stratification, and trends over time of the 4 major complications of anastomotic leak, conduit necrosis, recurrent laryngeal nerve injury, and chyle leak are shown in Table 7. Although anastomotic leak rate increased, patients requiring surgical interventions decreased from 3.3% to 3.0% in these successive periods ($P = 0.087$). The incidence of conduit necrosis remained stable throughout the study period at 1.2%. The incidence of recurrent nerve injury was unchanged with Type IIIa and IIIb being rare at 0.1% and 0.2%, respectively. The incidence of chyle leak decreased from 5.1% to 4.3% but most of this decrease was seen in patients with Type I leaks that required only dietary modifications. A significant increase was noted in Type IIIb leaks, involving high output (>1 L) and surgical treatment, from 0.6% to 1.2% ($P = 0.026$).

TABLE 3. Demographics—Pathology and Operative Approach

N (%)	2015–2016	2017–2018	All Patients	P
Pathology (indication for surgery)				0.058
Benign	90 (3.3%)	77 (2.3%)	167 (2.8%)	
Malignant	2597 (96.0%)	3222 (97.1%)	5819 (96.6)	
Others, including perforations	17 (0.6%)	19 (0.6%)	36 (0.6%)	
Tumor location				<0.001
At the GE junction	758 (29.2%)	1211 (37.6%)	1969 (33.8%)	
Proximal 1/2 of esophagus	311 (12.0%)	374 (11.6%)	685 (11.8%)	
Distal 1/2 of esophagus	1528 (58.8%)	1637 (50.8%)	3165 (54.4%)	
Surgical approach				<0.001
Minimally invasive	1297 (48.0%)	1880 (56.7%)	3177 (52.8%)	
Open	1407 (52.0%)	1438 (43.3%)	2845 (47.2%)	
Open esophagectomy				0.256
Transhiatal	290 (20.6%)	322 (22.4%)	612 (21.5%)	
Transthoracic	1117 (79.4%)	1118 (77.6%)	2235 (78.5%)	
Minimally invasive esophagectomy				<0.001
Abdomen only	485 (37.4%)	752 (40.0%)	1237 (38.9%)	
Chest only	135 (10.4%)	119 (6.3%)	254 (8.0%)	
Abdomen and chest	677 (52.2%)	1009 (53.7%)	1686 (53.1%)	
Site of anastomosis				0.003
Chest	1661 (61.4%)	2177 (65.6%)	3838 (63.7%)	
Neck	1010 (37.4%)	1108 (33.4%)	2118 (35.2%)	
Others/none	33 (1.2%)	33 (1.0%)	66 (1.1%)	
Esophageal conduit				0.695
Stomach	2581 (95.5%)	3185 (96.0%)	5766 (95.8%)	
Colon	34 (1.3%)	34 (1.0%)	68 (1.1%)	
Small bowel	64 (2.4%)	68 (2.1%)	132 (2.2%)	
Others/None	25 (0.9%)	31 (0.9%)	56 (0.9%)	
Lymphadenectomy neck				0.296
No	2295 (91.6%)	2552 (92.4%)	4847 (92.0%)	
Yes	211 (8.4%)	211 (7.6%)	422 (8.0%)	
Resection margins				0.380
R0—negative	2417 (93.1%)	3024 (93.9%)	5441 (93.5%)	
R1—microscopic positive	163 (6.3%)	175 (5.4%)	338 (5.8%)	
R2 – Macroscopic positive	17 (0.7%)	23 (0.7%)	40 (0.7%)	
Neoadjuvant treatment				<0.001
None	581 (22.4)	633 (19.7)	1214 (20.9%)	
Neoadjuvant chemotherapy	833 (32.1)	792 (24.6)	1625 (27.9%)	
Neoadjuvant chemoradiotherapy	1099 (42.3)	1735 (53.9)	2834 (48.7%)	
Definitive chemoradiotherapy	80 (3.1)	56 (1.7)	136 (2.3%)	
Hospital stay, days	17.3	16.7	17.0	0.138

DISCUSSION

This study has demonstrated that a secure online standardized dataset provides a viable method for not only benchmarking esophagectomy outcomes, but also monitoring the evolution in technical approach, perioperative outcomes, and quality measures.

The last 2 decades have witnessed increased utilization of national administrative datasets across a wide range of diseases. However, the utilization of these datasets for answering specific clinical questions has limitations, specifically in the area of directing or grading quality of performance improvement projects, and benchmarking.[24–26] Participation in national disease or procedure nonspecific outcomes datasets has not routinely been associated with improving institutional clinical outcomes over time.[24] It is likely, however, that institutional improvements are better facilitated in "made for purpose" voluntary datasets. The ECCG dataset within Esodata.org may represent one such exemplar with standardized reporting platforms, specific outcome definitions, and quality measures which can be monitored over time and compared to published benchmarks.[19]

One objective of this study was to provide a real-time contemporaneous report from >6000 cases, assembled from predominantly high-volume academic medical centers globally. It highlights that 90-day mortality remains between 4% and 5%, and that pneumonia, atrial fibrillation, and anastomotic leak are the most common index complications. However, the main object of this study was to compare 2 consecutive study periods. This assessment demonstrates that the complexity of patients is increasing, reflected by higher ASA and ECOG scores. Obesity levels in a global network were 20%, and undernutrition, with a BMI <18.5, has significantly decreased, perhaps a reflection of a greater focus as per ERAS[27] and NCCN Guidelines.[28]

The study confirms that MIE has established itself globally, now surpassing open approaches, and where MIE is undertaken it is completely minimally invasive in >50% of cases. Pneumonia occurring in association with esophageal resection has been a particularly important outcome measure and has been directly related to increased costs,[15] increased incidence of perioperative mortality,[29] and readmissions[11,12,28,30] as well as a decrease in overall 5-year survival rates.[7,29] Pneumonia rates significantly decreased between the 2 study periods. Whether this relates to the increasing application of MIE is not yet clear and requires further analysis, although a reduction in pneumonia and major respiratory complications was seen in the TIME, MIRO, and

TABLE 4. ECCG Complication Outcomes: Entire Study Group and Trends in Complications Over Time

N, % (95% CI)	2015–2016	2017–2018	All Patients	*P*
Gastrointestinal—Overall Incidence	**610 (22.6%)**	**815 (24.6%)**	**1425 (23.7%)**	**0.069**
Esophagoenteric leak from anastomosis, staple line, or localized conduit necrosis	317, 11.7% (10.2–12.6)	433 (13.1)	750, 12.5% (11.6–13.3)	0.121
Conduit necrosis/failure requiring surgery	33 (1.2%)	41 (1.2%)	74, 1.2% (1.0–1.5)	0.957
Ileus defined as small bowel dysfunction preventing or delaying enteral feeding	49, (1.8%)	36 (1.1%)	85, 1.4% (1.1–1.7)	0.017
Small bowel obstruction	15 (0.6%)	12 (0.4%)	27, 0.5% (0.3–0.7)	0.265
Feeding J-tube complication	33 (1.2%)	70 (2.1%)	103, 1.7% (1.4–2.1)	0.008
Pyloromyotomy/pyloroplasty complication	4 (0.2%)	5 (0.2%)	9, 0.2% (0.1–0.3)	0.978
Clostridium difficile infection	27 (1.0%)	29 (0.9%)	56, 0.9% (0.7–1.2)	0.617
Pancreatitis	9 (0.3%)	5 (0.2%)	14, 0.2% (0.1–0.4)	0.144
GI bleeding requiring intervention or transfusion	28 (1.0%)	16 (0.5%)	44, 0.7% (0.5–1.0)	0.012
Liver dysfunction	7 (0.3%)	14 (0.4%)	21, 0.4% (0.2–0.5)	0.286
Delayed conduit emptying requiring intervention or delaying discharge or requiring maintenance of NG drainage >7 days post-op	159 (5.9%)	221 (6.7%)	380, 6.3% (5.7–7.0)	0.215
Pulmonary	**784 (29.0%)**	**838 (25.3%)**	**1622 (26.9%)**	**0.001**
Pneumonia	414 (15.3%)	424 (12.8%)	838 (13.9%)	0.005
Pleural effusion requiring additional drainage procedure	264 (9.8%)	263 (7.9%)	527 (8.8%)	0.012
Pneumothorax requiring intervention	92 (3.4%)	85 (2.6%)	177 (2.9%)	0.055
Atelectasis mucous plugging requiring bronchoscopy	86 (3.2%)	74 (2.2%)	160 (2.7%)	0.023
Respiratory failure requiring reintubation	190 (7.0%)	214 (6.5%)	404 (6.7%)	0.373
Acute respiratory distress syndrome	57 (2.1%)	69 (2.1%)	126 (2.1%)	0.939
Acute aspiration	22 (0.8%)	40 (1.2%)	62 (1.0%)	0.134
Tracheobronchial injury	13 (0.5%)	6 (0.2)	19 (0.3%)	0.039
Chest drain requirement for air leak for >10 days post-op	12 (0.4%)	17 (0.5%)	29 (0.5%)	0.702
Cardiac	**459 (17.0%)**		**1013 (16.8%)**	
Cardiac arrest requiring CPR	24, 0.9% (0.6–1.3)	24 (0.7%)	48 (0.8%)	0.476
Myocardial infarction	15 (0.6%)	16 (0.5%)	31 (0.5%)	0.696
Atrial dysrhythmia requiring intervention	400 (14.8%)	487 (14.7%)	887 (14.7%)	0.900
Ventricular dysrhythmia requiring intervention	23 (0.9%)	32 (1.0%)	55 (0.9%)	0.644
Congestive heart failure requiring intervention	11 (0.4%)	15 (0.5%)	26 (0.4%)	0.790
Pericarditis requiring intervention	3 (0.1%)	9 (0.3%)	12 (0.2%)	0.165
Thromboembolic	67 (2.5%)	94 (2.8%)	161 (2.7%)	0.395
DVT	26 (0.0%)	31 (0.9%)	57 (1.0%)	0.914
PE	33 (1.2%)	55 (1.7)	88 (1.5%)	0.160
Stroke	4 (0.2%)	8 (0.2%)	12 (0.2%)	0.420
Peripheral thrombophlebitis	5 (0.2%)	9 (0.3%)	14 (0.2%)	0.489
Urologic	**234 (8.7%)**		**421 (7.0%)**	
Acute renal insufficiency (defined as doubling of baseline creatinine)	40 (1.5%)	45 (1.4%)	85 (1.4%)	0.687
Acute renal failure requiring dialysis	26 (1.0%)	13 (0.4%)	39 (0.7%)	0.006
Urinary tract infection	78 (2.9%)	51 (1.5%)	129 (2.1%)	<0.001
Urinary retention requiring reinsertion of urinary catheter, delaying discharge, or discharge w/urinary catheter	102 (3.8%)	86 (2.6%)	188 (3.1%)	0.009
Infection	172 (6.4%) 14.2%	297 (9.0%)	469 (7.8%)	<0.001
Wound infection requiring opening wound or antibiotics	9 (0.3%)	153 (4.6%)	162, 2.7%	<0.001
Central IV line infection requiring removal or antibiotics	52 (1.9%)	34 (1.0%)	86 (1.4%)	0.003
Intrathoracic/intra-abdominal abscess	64 (2.4%)	56 (1.7%)	120 (2.0%)	0.061
Generalized sepsis	59 (2.2%)	76 (2.3%)	135 (2.2%)	0.777
Other infections requiring antibiotics	212 (7.8%)	202 (6.1%)	414 (6.9%)	0.008
Neurologic/Psychiatric	**275 (10.2%%)**	**258 (7.8%)**	**533 (8.9%)**	**0.001**
Recurrent nerve injury	131 (4.8%)	133 (4.0%)	264, 4.4%	0.115
Other neurologic injury	38 (1.4%)	6 (0.2%)	44 (0.7%)	<0.001
Acute delirium	105 (3.9%)	118 (3.6%)	223 (3.7%)	0.504
Delirium tremens	15 (0.6%)	6 (0.2%)	21 (0.4%)	0.014
Wound/Diaphragm	**82 (3.0%)**	**58 (1.8%)**	**140 (2.3%)**	**0.001**
Thoracic wound dehiscence	43 (1.6%)	27 (0.8%)	70 (1.2%)	0.005
Acute abdominal wall dehiscence/hernia	34 (1.3%)	25 (0.8%)	59 (1.0%)	0.048
Acute diaphragmatic hernia	8 (0.3%)	8 (0.2%)	16 (0.3%)	0.681
Other Complications	**194 (7.2%)**	**212 (6.4%)**	**406 (6.7%)**	**0.227**
Chyle leak	137 (5.1%)	141 (4.3%)	278 (4.6%)	0.133
Reoperation for reasons other than anastomotic leak or conduit necrosis	40 (1.5%)	46 (1.4%)	100 (1.7%)	0.762
Multiple organ dysfunction syndrome	26 (1.0%)	19 (0.6%)	45 (0.8%)	0.081

TABLE 5. Complications: Overall Incidence and Incidence of Multiple Complications

N, N% (95% CI)	2015–2016	2017–2018	All Patients	P
Complications				0.320
No	1087 40.2% (38.4–42.1)	1292 38.9% (37.3–40.6)	2379 39.5% (38.2–40.7)	
Yes	1617 59.8% (57.9–61.6)	2026 61.1% (59.4–62.7)	3643 60.5% (59.3–61.7)	
No. of complications in each patient				<0.001
0	1087 (40.2%)	1292 (38.9%)	2379 39.5% (38.2–40.7)	
1	704 (26.0%)	1019 (30.7%)	1723 28.6% (27.5–29.8)	
2	426 (15.8%)	500 (15.1%)	926 15.4% (14.5–16.3)	
3	229 (8.5%)	264 (8.0%)	493 8.2% (7.5–8.9)	
≥4	258 (9.5%)	243 (7.3%)	501 8.3% (7.6–9.0)	
Clavien-Dindo score				<0.001
Grade I	259 (9.6%%)	222 (6.7%)	481 (8.0%)	
Grade II	611 (22.6%)	805 (24.3%)	1416 (23.5%)	
Grade IIIa	375 (13.9%)	542 (16.3%)	917 (15.2%)	
Grade IIIb	195 (7.2%)	237 (7.1%)	432 (7.2%)	
Grade IVa	170 (6.3%)	225 (6.8%)	395 (6.6%)	
Grade IVb	39 (1.4%)	35 (1.1%)	74 (1.2%)	
Grade V	69 (2.6%)	74 (2.2%)	143 (2.4%)	
Grade ≥IIIb	473 (17.5%)	571 (17.2%)	1044 (17.3)	0.773

ROBOT RCTs.[31–33] Other factors may include increased application of early mobilization programs within ERAS, as well as targeted prehabilitation and postoperative care pathways to prevent respiratory complications.[27]

In contrast to decreasing pneumonia rates, atrial fibrillation rates remained stable, whereas anastomotic leaks demonstrated an increase from 11.7% to 13.1%. These results are consistent with a recent meta-analysis,[34] and also published trends associated with MIE.[35] Despite this increase, the most severe leaks requiring surgery were unchanged, an important quality metric as the severity of leaks is a major determinant of operative mortality.[1,36] The continued documentation of anastomotic leak rates over time remains a critical issue, particularly as MIE is increasingly adopted and in light of evidence associating leaks with overall survival.[35] The study also highlights that when comprehensively documented, that complication rates remain high, at approximately 60% and severe complications, Clavien-Dindo ≥ IIIb, occur in approximately 1 in 7 patients.

TABLE 6. Quality Measure Outcomes: Entire Study Group and Trends Over Time

N, N% (95% CI)	2015–2016	2017–2018	All Patients	P
Readmission within 30 days of discharge				<0.001
No readmission	2266 (86.0%)	2836 (87.6%)	5102 (86.9%)	
Readmission related to esophagectomy	292 (11.1%)	275 (8.5%)	567 (9.7%)	
Unrelated readmission	31 (1.2%)	31 (1.0%)	62 (1.1%)	
Readmissions status not known	46 (1.8%)	94 (2.9%)	140 (2.4%)	
Not discharged at 30 days or died inpatient	71 (2.6%)	82 (2.5%)	153 (2.5%)	
Perioperative mortality				
Alive after 30 days post-op but died before 90 days	56 (2.1%)	68 (2.1%)	128 (2.1%)	0.650
Alive after 90 days post-op	2574 (95.7%)	2773 (95.4%)	5347 (88.8%)	0.679
Died within 30 days post-op	65 (2.4%)	65 (2.0%)	122 (2.0%)	0.683
90-day mortality	117 (4.4%)	133 (4.6%)	250 (4.5%)	0.679
Status not known/lost to follow-up after 30 days post discharge	2 (0.1%)	27 (0.8%)	29 (0.5%)	<0.001
Blood utilization				<0.001
No transfusions	2320 (85.8%)	2979 (89.8%)	5299 (89.0%)	
Intraoperative transfusion	53 (2.0%)	45 (1.4%)	98 (1.6%)	
Postoperative transfusion	297 (11.0%)	273 (8.2%)	570 (9.5%)	
Intra- and postoperative transfusion	34 (1.3%)	21 (0.6%)	55 (0.9%)	
Readmissions				
No readmission	2266 (83.8%)	2836 (85.5%)	5102 (84.7%)	
Readmission related to esophagectomy	292 (10.8%)	275 (8.3%)	567 (9.4%)	
Unrelated readmission	31 (1.2%)	31 (0.9%)	62 (1.0%)	
Unknown	115 (4.3%)	176 (5.3%)	291 (4.8%)	
Level of care escalation				<0.001
Yes	663 (24.5%)	665 (20.0%)	1328 (22.1%)	
No	2041 (75.5%)	2653 (80.0%)	4694 (78.0%)	
Discharged home				<0.001
No	234 (8.7%)	405 (12.2%)	639 (10.6%)	
Yes	2470 (91.4%)	2913 (87.8%)	5383 (89.4%)	

P s comparing 2015–2016 cohort to 2017–2018.

TABLE 7. Outcomes of ECCG Complications

N (%)	2015–2016	2017–2018	All Patients	P
Anastomotic leak				
No anastomotic leak	2387 (88.3%)	2885 (87.0%)	5272 (87.6%)	0.121
Type of leak				0.003
Type I:	99 (3.7%)	109 (3.3%)	208 (3.5%)	
Type II:	120 (4.4%)	223 (6.7%)	343 (5.7%)	
Type III:	89 (3.3%)	101 (3.0)	190 (3.2%)	
Unknown type of leak	9 (0.3%)	0 (0%)	9 (0.2%)	
Conduit necrosis				
No conduit necrosis	2671 (98.8%)	3277 (98.8)	5948 (98.8%)	0.957
Type of conduit necrosis				0.576
Type I:	2 (0.1%)	5 (0.2%)	7 (0.1%)	
Type II:	6 (0.2%)	10 (0.3%)	16 (0.3%)	
Type III:	23 (0.9%)	26 (0.8%)	49 (0.8%)	
Unknown type of conduit necrosis	2 (0.1%)	0 (0%)	2 (0.0%)	
Recurrent laryngeal nerve injury				
No injury	2573 (95.2%)	3185 (96.0%)	5758 (95.6%)	0.115
Type of injury				0.797
Type Ia:	88 (3.3%)	99 (3.0%)	187 (3.1%)	
Type Ib:	8 (0.3%)	6 (0.2%)	14 (0.2%)	
Type IIa:	14 (0.5%)	19 (0.6%)	33 (0.6%)	
Type IIb:	4 (0.2%)	3 (0.1%)	7 (0.1%)	
Type IIIa:	3 (0.1%)	1 (0.0%)	4 (0.1%)	
Type IIIb:	5 (0.2%)	5 (0.2%)	9 (0.2%)	
Unknown type of nerve injury	9 (0.3%)	0	9	
Chyle leak				
No chyle leak	2567 (94.9%)	3177 (95.8%)	5744 (95.4%)	0.133
Type of chyle leak				0.043
Type Ia:	74 (2.7%)	64 (1.9%)	138 (2.3%)	
Type Ib:	7 (0.3%)	6 (0.2%)	13 (0.2%)	
Type IIa:	13 (0.5%)	10 (0.3%)	23 (0.4%)	
Type IIb:	8 (0.3%)	10 (0.3%)	18 (0.3%)	
Type IIIa:	16 (0.6%)	12 (0.4%)	28 (0.5%)	
Type IIIb:	16 (0.6%)	39 (1.2%)	55 (0.9%)	
Unknown type of chyle leak	3 (0.1%)	0 (0%)	3	

Definitions

Anastomotic leak: Full thickness GI defect involving esophagus, anastomosis, staple line, or conduit irrespective of presentation or method of identification

Grade I	Local defect requiring no change in therapy or treated medically or with dietary modification
Grade II	Localized defect requiring interventional but not surgical therapy, for example, IR drain, stent, or bedside opening and packing of incision
Grade III	Localized defect requiring surgical therapy

Conduit necrosis: Full thickness GI defect involving esophagus, anastomosis, staple line, or conduit irrespective of presentation or method of identification

Grade I	Conduit necrosis focal; identified endoscopically Treatment—additional monitoring or nonsurgical therapy
Grade II	Conduit necrosis focal; identified endoscopically and not associated with free anastomotic or conduit leak Treatment—surgical therapy not involving esophageal diversion
Grade III	Conduit necrosis extensive Treatment—treated with conduit resection with diversion

Recurrent laryngeal nerve injury: Vocal cord dysfunction post-resection. Confirmation and assessment should be by direct examination

Grade I	Transient injury requiring no therapy; dietary modification allowed
Grade II	Injury requiring elective surgical procedure, eg, thyroplasty or medialization procedure
Grade III	Injury requiring acute surgical intervention (due to aspiration or respiratory issues), eg, thyroplasty or medialization procedure
Severity	a) Unilateral
Level	b) Bilateral

Eg, a unilateral vocal cord injury requiring elective medialization procedure. Final Grade IIA

Chyle leak: Milky discharge upon initiation of enteric feeds and/or pleural fluid analysis demonstrating triglyceride level >100 mg/dL and/or chylomicrons in pleural fluid

Grade I	Treatment—enteric dietary modifications
Grade II	Treatment—total parenteral nutrition
Grade III	Treatment—interventional or surgical therapy*
Severity	a) <1 L output/day
Level	b) > 1 L output/day

For example,, a chyle leak initially producing 1200 mL/day and successfully treated by stopping enteric feeds and initiating TPN. Final Grade IIB.

*NOTE: Does not include elective insertion of additional surgical or interventional chest drains.

Complications are linked to short-term (2 years)[32] and long-term (10 years) HRQL,[17] and costs,[15] as well as individual surgeon wellbeing.[37] Trends in individual complication incidence over time can in some cases be explained by paralleling evolutions in perioperative management. An example would be the significant decrease in urinary tract infections seen in the present study which may be related to evolving enhanced recovery protocols recommending early removal of urinary catheters, whereas at the same, this same process evolution could also partially explain the increased incidence in urinary retention over the study period.

Quality measures are embedded within the Esodata Database Platform.[23] Readmission rates have historically been inaccurately or incompletely reported. The readmission rate post esophagectomy reported by NSQIP in 2015 was 10.7%,[12] whereas the same year, the SEER database documented an incidence of 18.6%.[38] During the period of 2010 and 2014, the Nationwide Readmissions Database indicated that 19.4% of patients undergoing esophageal resection in the United States required readmission.[15] Readmissions have been most commonly related to the incidence of pneumonia,[11,30] anastomotic leak[39] and have also been associated with documented decreases in overall survival[38] and increased 90-day perioperative mortality.[40] The importance of accurately documenting and following trends in readmissions over time is important as it has been recognized as a key quality indicator which is reflected in the Centers for Medicare and Medicaid Services Readmission Reduction Program linking the occurrence of readmissions to overall reimbursement in the United States.[41] Accordingly, the reduction in readmission rates from 12% in Period 1 to 9% in Period 2 is encouraging.

The need for blood transfusion is also an important quality measure, being directly linked to long-term survival,[42–45] tumor recurrence,[43] anastomotic leak,[36] readmissions,[30] and perioperative mortality.[43,46,47] It is now generally accepted that blood loss is a quality indicator in major oncologic procedures,[48] and both medical and technical complications have been clearly linked to intraoperative blood loss.[49] The present study documented a significant increase in the incidence of patients undergoing esophagectomy without requiring a blood transfusion at any time, from 85.8% to 89.8% in successive periods. This may be an expression of raising thresholds for transfusion or improved surgical performance.

Escalation in level of care is rarely reported.[8] In the present study, this quality measure decreased from 24.5% to 20% over the 2 time periods. The 2 most common complications associated with escalation of care were pneumonia (25.9%) and atrial dysrhythmia (21.2%) with >40% of the patients with pneumonia requiring an escalation in care at some point in their postoperative recovery.

The discharge location for patients after esophageal resection is an important quality measure because it can directly affect other quality parameters such as length of stay and readmissions. However, previous reports demonstrate that the incidence of readmissions is higher in patients who are discharged to nursing facilities.[30] The complexity of reporting results of discharge location utilizing an international dataset involves the recognition that there is significant international disparity between post-surgical discharge resources and societal expectations. In some countries in Europe, there is an historical expectation and national funding allotted for patients to spend a time at a rehabilitation facility after major oncologic surgery. This suggests that continuing to monitor international trends in discharge location remains relevant, although it is likely more pertinent to monitor changes in discharge location on a national or regional basis.

This study has some limitations. The accuracy of the data submitted by the contributing institutions has not been evaluated, although all centers (Table 1) are high-volume cancer centers that have routinely led and contributed to national datasets as well as participating in institutional and national research projects on esophageal cancer. Every lead investigator from contributing institutions signed the membership agreement (see Supplement 1, http://links.lww.com/SLA/C409) which required the guarantee of submitting data on all esophagectomies done in their institution, and data integrity. The composition of contributing centers highlights the obvious limitation that the outcomes reflect that of the best centers internationally and may not be indicative of general practice outcomes associated with esophageal resection. This in itself underlines the importance of the data and the key points, that complications are common, that they can be severe, and that 4% to 5% of patients will die of complications, all of this in the best-performing hospitals internationally.

There are many strengths of the present study, principally the large volume of esophagectomies accumulated in a contemporary time period using standardized definitions; hence the outcomes are reflective of current international practice patterns and service delivery. The number of centers contributing to the current Esodata dataset continue to increase from the 24 international centers who contributed to the initial ECCG study in 2017[19] to 39 centers entering patients for the present study reporting on outcomes up to December 2018. The question which naturally arises regarding the present study is why the comparison of trends in outcomes was not limited to the original 24 ECCG centers. The answer includes the fact that all current contributing institutions are high-volume Centers of Excellence and that the number of centers entering data will continue to grow over time, which ultimately will make ongoing assessments of the entire dataset increasingly relevant from the international standpoint.

Since the completion of the present study, 18 additional centers have joined the International Esodata Study Group (IESG) bringing the current number of contributing centers to 57 institutions representing 19 countries with currently >10,000 resections recorded. Other advantages of the present study reside in the fact that not only does the database has the opportunity to efficiently benchmark perioperative outcomes at a specific period of time, but it clearly has the power to follow and assess trends in a wide variety of cancer-related and technical issues in addition to perioperative outcomes and quality measures. Other strengths include the secure, cloud-based series of dedicated servers, and the simplicity for data entry and the ability of institutional review from anywhere there is secure internet access.

In the future, an evolving Esodata database will enable the accurate monitoring of changes in technical trends and treatment outcomes over time, assess survival for future esophageal cancer staging systems, and ultimately collect biologic and genetic data to amalgamate research efforts regarding targeted oncologic therapy. In an era of change with MIE and robotic approaches, and a focus on ERAS, this dataset will provide a vehicle to monitor this evolution and underpin safety and quality assurance.

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