Benchmarking Complications Associated With Esophagectomy

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ABSTRACT

OBJECTIVE**:** Utilizing a standardized dataset with specific definitions to prospectively collect international data to provide a benchmark for complications and outcomes associated with esophagectomy.

BACKGROUND: Outcome reporting in oncologic surgery has suffered from the lack of a standardized system for reporting operative results particularly complications. This is particularly the case for esophagectomy affecting the accuracy and relevance of international outcome assessments, clinical trial results and quality improvement projects.

METHODS: The Esophageal Complications Consensus Group (ECCG) involving 24 high volume esophageal surgical centers in 14 countries developed a standardized platform for recording complications and quality measures associated with esophagectomy. Using a secure online database (ESODATA.org), ECCG centers prospectively recorded data on all resections according to the ECCG platform from these centers over a two-year period.

RESULTS: Between January 2015 and December 2016, 2704 resections were entered into the database. All demographic and follow-up data fields were 100% complete. The majority of operations were for cancer (95.6%) and typically located in the distal esophagus (56.2%). Some, 1192 patients received neoadjuvant chemoradiation (46.1%) and 763 neoadjuvant chemotherapy (29.5%). Surgical approach involved open procedures in 52.1% and minimally invasive operations in 47.9%. Chest anastomoses were done most commonly (60.7%) and R0 resections were accomplished in 93.4% of patients. The overall incidence of complications was 59% with the most common individual complications being pneumonia (14.6%) and atrial dysrhythmia (14.5%). Anastomotic leak, conduit necrosis, chyle leaks, recurrent nerve injury occurred in 11.4%, 1.3%, 4.7% and 4.2% of cases, respectively. Clavien-Dindo complications ≥ IIIb

occurred in 17.2% of patients. Readmissions occurred in 11.2% of cases and 30- and 90-day mortality was 2.4% and 4.5%, respectively.

CONCLUSIONS: Standardized methods provide contemporary international benchmarks for reporting outcomes after esophagectomy.

INTRODUCTION

Esophagectomy retains an important role in the management of many patients with locally advanced esophageal cancer, often in conjunction with neoadjuvant therapy.

Reviews of national datasets from North America confirm that esophagectomy 30-day mortality remains above 5%.[1] National audits and meta-analyses have demonstrated that in-hospital and 90-day mortality, more accurately reflect actual mortality associated with esophagectomy with in-hospital mortality being approximately 7-8% and 90-day mortality as high as 13% when assessed from all centers performing any annual volume of esophageal resections[2-4].

The incidence of complications associated with esophagectomy has been previously reported between 17% and 74%[5,6]. Irrespective of whether these outcomes originate from national audits or databases from single centers, all of these results have suffered from the absence of a standardized system for documenting and reporting operative outcomes including complications. Previous meta-analyses have documented considerable heterogeneity in the methodology of defining and reporting esophagectomy complications[7]. The absence of a standardized method of reporting perioperative outcomes means that there is no reliable method to compare reports from different institutions or assess the effect of quality improvement initiatives on mortality and perioperative complications. It has also resulted in the failure of the surgical community to generate a truly representative reflection of contemporary short-term outcomes associated with esophagectomy.

The Esophageal Complications Consensus Group (ECCG) was formed in 2011 and included 21 esophageal surgeons from high volume centers representing 14 countries. Through a series of Delphi surveys and face-to-face meetings, the ECCG developed a standardized platform for reporting mortality, complications and quality measures associated with esophagectomy which was published in 2015[8].

Having produced a system for reporting outcomes associated with esophagectomy, the ECCG agreed to test the system. The hypothesis was that a web-based dataset could be used to document outcomes according to the ECCG platform in international high-volume esophagectomy centers and that this would disclose less variation in complication rates than previously reported. The inclusion of all esophagectomies done over a two-year period within the ECCG centers should provide a contemporary benchmark of morbidity and mortality associated with esophageal resection.

METHODS

A web-based dataset incorporating all of the data items and definitions published previously was developed to facilitate contemporary data collection[8]. In March 2015, the ECCG reached a consensus regarding additional demographic, surgical and outcomes data fields that were considered critical to collect in addition to the complications platform, definitions and quality measures. Nineteen original ECCG centers and 5 new high volume esophagectomy units agreed to submit patients. (Figure 1) A study protocol was distributed to the study centers. All centers signed the membership agreement (see Supplement 1) and agreed to fulfill all institutional and

national ethics and IRB requirements in order to supply anonymized patient information to the database. All participating centers agreed to enroll all esophagectomies at their institutions during the study period.

After arriving at a consensus for determining the data fields, face-to-face ECCG meetings were held to review the specific issues involved in the implementation of a web-based international data collection project. Consensus-based data fields and definitions mandated a consistent and "user-friendly" platform to encourage participation while maintaining data integrity and completeness. To overcome variations in computer systems and capabilities between participating centers, a database was developed with secure access that offered a web browser-based interface using existing computer systems without the requirement for additional local resource utilization or IT support other than internet connection involving both desktop and mobile devices. Validation algorithms were built into the database interface to ensure that only validated data was entered.

The database and the web portal were hosted in a high performance, dedicated private web server and the database interface was accessible only via authenticated and encrypted secure network connections (SSL Client and Server Certificate with Extended Validation—Issued by Symantec Corporation). Open-sourced database server package (Maria DB V10.1.21 by Maria DB FOUNDATION) with appropriate backup system arrangements in combination with Drupal content management software (distributed under the terms of the GNU General Public License) was used. This system provided data portability, analytics, modularity and flexibility in content access management. Participating institutes' data-contributing members were authenticated

individually by the ECCG to access the database's interface and members-only area of the ESODATA.org web portal. Authenticated contributors had instant access to their own institutional results on the ESODATA website that was available to them whenever they had secure internet web access. Contributors received regular email communications every three to four months updating them on patient accrual and intermediate term results.

It was agreed that the study period should run between January of 2015 and December 2016. Data entry began at the time each institution adopted the ECCG platform within their institutional datasets. It was agreed that the study population should yield at least 1200 resections with the goal being to record complications associated with both benign and malignant resections. No formalized system of audit was available for the study although all centers signed and agreed to adhere to the Members Agreement (see Supplement 1). From September 2016, the International Society for Diseases of the Esophagus (ISDE) Executive acted as an external body to provide oversight of the ESODATA website and database.

STATISTICAL METHODS

The characteristics of the patient population are reported using frequency and percentage for categorical variables and 95% confidence limits for non-normally distributed continuous variables. The incidence of complications associated with each patient subgroup were also described using frequency and percentage with 95% confidence limits. Statistical analyses of the present study were performed using SPSS software (version 23.0; IBM Corp., Armonk, NY, USA).

RESULTS

From January 2015 to December 2016, 2704 esophagectomies were enrolled in the ESODATA database website. All esophagectomies done at each institution during the study period from the time of the initiation of the ECCG complications platform were included. Data was 100% complete in all demographic and outcome data fields. Patient demographics and data regarding surgical technique are shown on Table 1. Over 99% of esophagectomies were elective and 95.6% of resections were for malignant disease with the most common tumor location being the distal esophagus (56.2%).

Within the study population of 2704, 2585 patients underwent esophagectomy for malignant disease. Among the patients undergoing resection for cancer, 1722 patients presented with cT3 disease (66.6%) and 1395 patients presented with findings of cN+ (53.9%) All data for both clinical and pathologic staging are shown in Supplement 2. Of these 2585 patients undergoing esophageal resections for cancer, 1192 patients (46.1%) received neoadjuvant chemoradiotherapy, 763 patients (29.5%) neoadjuvant chemotherapy and 3.1% had esophagectomy as a salvage operation after definitive chemotherapy. Of the 3.1% of patients undergoing a salvage resection, 47.5% underwent their resection more than 12 months after completing chemoradiotherapy. Some 545 patients (21.1%) underwent surgery alone.

Data relating to surgical technique are outlined in Table 1. Open operations were more common (52.1%), with transthoracic (79.9%) being more frequently utilized than transhiatal operations (20.1%). Minimally invasive procedures were done in 47.9% with 48.7% of those operations

being done with a totally minimally invasive approach. Of the 51.3% of hybrid procedures, minimally invasive abdominal operations comprised 40.2% with minimally invasive thoracic procedures comprising 11.1%.

Chest anastomoses were most commonly utilized (60.7%) and reconstructions utilizing stomach were done in 94.9% of cases. Two-field lymphadenectomy was reported in 93% with three-field procedures occurring in 7%. An R0 resection margin was achieved in 93.4% of operations.

The overall incidence of complications was 59.0%. In the 1595 patients who sustained complications, 905 (56.7%) experienced multiple complications (Table 2). Table 3 demonstrates the incidence of individual complications along with the variation (95% confidence limit) of the incidences of complication within the data contributing ECCG centers. The most common complications were pneumonia (14.6%) and atrial dysrhythmias (14.5%). The actual number of complications in each complication groups and variations in individual complication rates among the data contributing ECCG centers is shown in Table 3. Overall, the incidence of anastomotic leak was 11.4%, conduit necrosis 1.3%, chyle leak 4.7% with recurrent nerve injury in 4.2%. Specific outcomes according to ECCG definitions[8] are shown in Table 4**.** Complications graded by the Clavien-Dindo Classification are shown in Table 5 with 17.2% of patients sustaining complications ≥ Clavien-Dindo IIIb.

Mortality was 2.4% at 30 days and 4.5% at 90 days (Table 6). Follow-up of 30day mortality and readmissions is 100% complete. Ninety-day mortality was available in 99.6% of the study population with eleven out of 2704 patients lost to follow-up between 30 and 90 days of post

post-op. Readmissions were recorded if they occurred within 30 days of discharge. These occurred for any reason in 11.2% of patients (Table 6). Of the 275 patients who required readmission related to their esophagectomy, 214 (77.6%) had experienced post-operative complications. Some 62 (22.4%) patients required readmission without experiencing inpatient complications.

DISCUSSION

Esophagectomy has historically been recognized as one of the most complex major oncologic operations. A meta-analysis of 122 publications including 17 randomized controlled clinical trials and 105 observational studies involving over 57,000 esophagectomies indicated that no complication appeared in all reports and more than 67% of studies contained no definitions. In addition, 115 reports utilized 10 different methods for reporting mortality[7]. This variability in reporting makes it impossible to make comparisons between national audits or clinical trials or to assess results in response to quality improvement initiatives between institutions.

Accuracy and consistency in reporting complications is critically important. Complications have been directly associated with every other critical outcome parameter associated with the surgical treatment of esophageal cancer. The incidence of complications has been directly linked to operative mortality[7,9,10], cancer recurrence[11,12], cancer survival[10,13], hospital length of stay[10,13-15], readmissions[16-18], hospital costs[19-21], hospital profit margin[21] as well as health-related quality of life[22-24]. Generating an accurate reflection of contemporary morbidity and mortality is particularly important as the role of surgery in the treatment of a variety of stages of esophageal malignancy is undergoing continuous assessment.

The ECCG complications platform was not intended to represent every potential problem which may occur following esophagectomy, but developed as a standardized system for reporting the common and relevant aspects of morbidity and mortality associated with esophageal resection. The system utilizes internationally recognized definitions when appropriate, as well as

definitions previously developed by the ECCG membership notably for anastomotic leak, conduit necrosis, chyle leak and recurrent nerve injury[8]. These specific definitions were considered a critical component as a previous report documented no less than 56 different definitions for anastomotic leak in 97 publications reporting surgical adverse events[25]. The specific definitions enable comprehensive reporting of these important complications reflecting the severity and treatment requirements in all instances, not necessarily represented in either the Accordion[26] or the Clavien-Dindo[27] severity stratification systems that report only the most severe complication.

The overall incidence of complications was 59.0%. This incidence of complications is twice that reported in some comprehensive national audits of esophagectomy[28] , and other analyses have demonstrated that complication rates vary enormously between cohorts in different studies[5,6]. When a standardized approach has been applied, as in the present study, this high incidence of complications showed remarkably little variation between the 24 contributing centers (Table 3). This suggests that 59% is more likely to be the true rate of complications after esophagectomy and that previous explanations for variations, reflecting different patient demographics, are no longer tenable.

In some instances, the incidence of individual complications was lower than that seen in previous reports, such as pneumonia with an overall incidence of 14.6%. This may be due to the fact that this report is based on very recent data and modern practice, potentially reflecting the use of standardized clinical pathways, ERAS protocols and a decreased likelihood of failure to rescue[29,30] in high volume esophagectomy centers. The quality of the contributing centers is

reflected in a 30-day mortality rate of 2.4%, 90-day mortality of 4.5% an R0 resection rate of 93.4% and a readmission rate of 11.2%. These results can be compared to reports of national audits but drawing conclusions will be difficult due to the lack of the focused and standardized system applied in the current study. For example the STS database, although a very well established dataset focuses on staging and procedure specific outcome measures, it does not currently contain the granularity necessary for providing a comprehensive report on short term complications.

The use of a secure online database was designed to improve accessibility while standardizing data input and providing instantaneous reporting of individual institutional data that could be assessed anywhere with internet access along with a format for center-specific internal audit. No center reported difficulties with data entry or access to the system during the course of the study. Ease of access and data entry were likely major contributors to data completeness.

The strengths of the present study include the use of a protocol and dataset specifically aimed to facilitate data collection related to patient demographics and complications associated with esophagectomy. The centers were all high volume units with a history of institutional data collection and previous publications of esophagectomy outcomes. In addition, all individuals entering data were registered and authenticated. All demographic, outcome and complications data entry fields were complete. Follow-up outcomes including 30-day mortality and readmissions data complete in 100% and 90-day mortality data was complete in 99.6% of patients. The dataset is large involving over 2700 patients accrued in a short time period and gathered internationally, making outcomes relevant to current practice at a global level.

Data entry was simplified using dropdown boxes utilizing modern web browser interface and data entry could take place anywhere that had internet access via HTTPS (Hyper Text Transfer Protocol Secure) network communication.

The present study does have limitations. Other than the signed Members Agreement (Supplement 1), there was no method in place for auditing individual institutional data. The study was not designed, and did not include data on patient quality of life or cancer survival.

These outcomes provide a contemporary benchmark for morbidity and mortality associated with esophagectomy. They reflect current international practice and probably represent the most reliable estimates of esophagectomy outcomes presently available. Secure online data collection has been demonstrated to be a very efficient methodology for carrying out this multi-institution international clinical trial. We predict that this methodology will be utilized regularly in national and international datasets moving forward.

The ECCG system, now overseen by the Research and Database Committee of the International Society for Diseases of the Esophagus (ISDE), should be considered for routine international application in audits and clinical trials as a means of standardizing esophagectomy outcomes. Information on the ESODATA dataset is available at the project web portal (https://esodata.org).

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FIGURE 1.

Esophageal Complications Consensus Group (ECCG) Data Contributing Center

FIGURE 1

Esophageal Complications Consensus Group (ECCG) Data Contributing Centers

AUSTRALIA	Brisbane	The University of Queensland	Mark Smithers Iain Thomson
BELGIUM	Leuven	Katholieke Universiteit Leuven	Toni Lerut Philippe Nafteux
BRAZIL	São Paulo	University of São Paulo	Ivan Cecconello Ulysses Ribeiro, Jr.
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GERMANY	Cologne	University of Cologne	Wolfgang Schroeder Marc Bludau
	Frankfurt	Agaplesion Markus Krankenhaus	Arnulf Hoelscher
INDIA	Mumbai	Tata Memorial Hospital	C. S. Pramesh
IRELAND	Dublin	Trinity College Dublin	John V. Reynolds
JAPAN	Tokyo	Keio University	Yuko Kitagawa
NETHERLANDS	Amsterdam	Academic Medical Center	Suzanne Gibertz Mark van Berge Henegouwen
	Rotterdam	Erasmus Medical Center	Jan van Lanschot Bas Wijnhoven
SPAIN	Barcelona	Hospital Universitario del Mar	Manuel Pera
UNITED KINGDOM	Oxford	Oxford OesophaoGastric Centre	Nick Maynard
	Birmingham	Queen Elizabeth Hospital	Derek Alderson Sonia Puig John Whiting
	London	St. Thomas' Hospital	Andrew Davies
	Newcastle	University of Newcastle upon Tyne	Michael Griffin
UNITED STATES	Boston	Massachusetts General Hospital	Christopher Morse
	Houston	MD Anderson Cancer Center	Wayne Hofstetter
	Pittsburgh	Allegheny Health System	Blair Jobe
	Ann Arbor	University of Michigan Health System	Andrew C. Chang
	Seattle	Virginia Mason Medical Center	Donald E. Low MadhanKumar Kuppusamy

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RECOGNITION MUST BE GIVEN TO THE DATA MANAGERS AT THE VARIOUS ECCG CENTERS FOR THEIR ADVICE AND PERSONAL CONTRIBUTIONS TO THE ESODATA DATASET

Name	Institution
Janine Thomas	The University of Queensland, Brisbane, Australia
Johnny Moons	Katholieke Universiteit Leuven, Leuven, Belgium
Emma Small	Toronto General Hospital, Toronto, Canada
Jeannette Kwok	Queen Mary Hospital, Hong Kong SAR, China
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One of the most important members of the ECCG passed away in July 2017.
Professor Dr. Christophe Mariette, Head of the Department of Digestive and Oncologic Surgery, CHRU de Lille, France, was an internationally recognized surgeon and academic. He was a friend and counsellor throughout the ECCG project. He will be greatly missed and the Members of the ECCG respectfully dedicate this paper to his memory.

Table 1 – Patient's Demographics & Surgical data

Total patients = 2704

Gender	N	N %
Female	607	22.4%
Male	2096	77.5%
Age group		
40 or less	66	2.4%
41 – 50	217	8.0%
51 – 60	721	26.7%
61 – 70	1100	40.7%
71 – 80	532	19.7%
More than 80	67	2.5%
BMI group		
< 18.5	184	6.8%
18.5 – 25	1085	40.1%
25 – 30	908	33.6%
> 30	526	19.5%
ACCI score groups		
0 – 3	325	12.0%
4 – 7	2201	81.4%
8 – 11	165	6.1%
12 and above	12	0.4%
ASA status score		
1	412	15.2%
2	1249	46.2%
3	992	36.7%
4	49	1.8%
5	1	0.0%
WHO / ECOG performance		
0	1514	56.0%
1	996	36.8%
2	136	5.0%
3	51	1.9%
4	6	0.2%
Comorbidities		
Myocardial Infarction	146	5.4%
Congestive Heart Failure	124	4.6%
Chronic Pulmonary Disease	285	10.5%
Peripheral Vascular Disease	185	6.8%
Diabetes Mellitus (uncomplicated)	348	12.9%
Diabetes Mellitus (end organ damage)	16	0.6%
Moderate to Severe Renal Disease	35	1.3%

Timing of surgery	N	N %
Elective	2680	99.1%
Emergency	23	0.9%
Pathology (indication for surgery)		
Benign	97	3.6%
Malignant	2585	95.6%
Others, including perforations	21	0.8%
Tumor location		
At the GE Junction	762	28.2%
Proximal ⅓ of esophagus	304	11.2%
Distal ⅓ of esophagus	1519	56.2%
Surgical approach		
Minimally Invasive	1296	47.9%
Open	1407	52.1%
Open esophagectomy		
Trans Hiatal	283	20.1%
Trans Thoracic	1124	79.9%
Minimally invasive esophagectomy		
Abdomen only	521	40.2%
Chest only	144	11.1%
Abdomen and chest	631	48.7%
Site of anastomosis		
Chest	1641	60.7%
Neck	1025	37.9%
Others/None	37	1.4%
Esophageal conduit		
Stomach	2564	94.9%
Colon	34	1.3%
Small bowel	72	2.7%
Others/None	33	1.2%
Lymphadenectomy neck		
No	2403	93.0%
Yes	182	7.0%
Resection margins		
R0 - Negative	2414	93.4%
R1 - Microscopic positive	157	6.1%
R2 - Macroscopic positive	14	0.5%

ACCI – Age-Related Charlson Comorbidity Index; WHO – World Health Organization; ECOG – Eastern Cooperative Oncology Group; ASA – American Society of Anesthesiology; BMI – Body Mass Index

Table 2 – Occurrence of ECCG Complications

Total patients = 2704

Complications*	N	N%	95% Lower CL for N%	95% Upper CL for N%	Standard Error of N%
No	1109	41.0%	39.2%	42.9%	0.9%
Yes	1595	59.0%	57.1%	60.8%	0.9%
Number of Complications Occurring in Each Patient					
0	1109	41.0%	39.2%	42.9%	0.9%
1	690	25.5%	23.9%	27.2%	0.8%
2	406	15.0%	13.7%	16.4%	0.7%
3	238	8.8%	7.8%	9.9%	0.5%
4 or more	261	9.7%	8.6%	10.8%	0.6%

CL – Confidence Limit; ECCG – Esophagectomy Complications Consensus Group
** - Incidence of complication as per ECCG complication platform definitions*

Table 3. Incidence of Complications and Variation between Centers According to the ECCG Definitions

Complication Groups*	N	N%	95% Lower CL of N %	95% Upper CL of N %	Stand Error of N %
Gastrointestinal	**606**	**22.4%**	**20.9%**	**24.0%**	**0.8%**
Esophagoenteric leak from anastomosis, staple line, or localized conduit necrosis	307	**11.4%**	10.2%	12.6%	0.6%
Conduit necrosis/failure requiring surgery	34	**1.3%**	0.9%	1.7%	0.2%
Ileus defined as small bowel dysfunction preventing or delaying enteral feeding	46	**1.7%**	1.3%	2.2%	0.2%
Small bowel obstruction	12	**0.4%**	0.2%	0.8%	0.1%
Feeding J-tube complication	27	**1.0%**	0.7%	1.4%	0.2%
Pyloromyotomy/Pyloroplasty complication	5	**0.2%**	0.1%	0.4%	0.1%
Clostridium Difficile infection	23	**0.9%**	0.6%	1.3%	0.2%
Pancreatitis	8	**0.3%**	0.1%	0.6%	0.1%
GI bleeding requiring intervention or transfusion	21	**0.8%**	0.5%	1.2%	0.2%
Liver dysfunction	6	**0.2%**	0.1%	0.5%	0.1%
Delayed conduit emptying requiring intervention or delaying discharge or requiring maintenance of NG drainage >7 days post-op	180	**6.7%**	5.8%	7.6%	0.5%
Pulmonary	**752**	**27.8%**	**26.1%**	**29.5%**	**0.9%**
Pneumonia	396	**14.6%**	13.4%	16.0%	0.7%
Pleural effusion requiring additional drainage procedure	267	**9.9%**	8.8%	11.0%	0.6%
Pneumothorax requiring intervention	91	**3.4%**	2.7%	4.1%	0.3%
Atelectasis mucous plugging requiring bronchoscopy	85	**3.1%**	2.5%	3.9%	0.3%
Respiratory failure requiring reintubation	189	**7.0%**	6.1%	8.0%	0.5%
Acute respiratory distress syndrome	50	**1.8%**	1.4%	2.4%	0.3%
Acute aspiration	27	**1.0%**	0.7%	1.4%	0.2%
Tracheobronchial injury	11	**0.4%**	0.2%	0.7%	0.1%
Chest drain requirement for air leak for >10 days post-op	13	**0.5%**	0.3%	0.8%	0.1%
Cardiac	**455**	**16.8%**	**15.5%**	**18.3%**	**0.7%**
Cardiac arrest requiring CPR	28	**1.0%**	0.7%	1.5%	0.2%
Myocardial infarction	15	**0.6%**	0.3%	0.9%	0.1%
Atrial dysrhythmia requiring intervention	393	**14.5%**	13.2%	15.9%	0.7%
Ventricular dysrhythmia requiring intervention	25	**0.9%**	0.6%	1.3%	0.2%
Congestive heart failure requiring intervention	12	**0.4%**	0.2%	0.8%	0.1%
Pericarditis requiring intervention	2	**0.1%**	0.0%	0.2%	0.1%

Complication Groups*	N	N%	95% Lower CL of N %	95% Upper CL of N %	Stand Error of N %
Thromboembolic	**141**	**5.1%**	**4.3%**	**5.9%**	**0.4%**
DVT	25	**0.9%**	0.6%	1.3%	0.2%
PE	33	**1.2%**	0.9%	1.7%	0.2%
Stroke	4	**0.1%**	0.0%	0.4%	0.1%
Peripheral thrombophlebitis	79	**2.9%**	2.3%	3.6%	0.3%
Urologic	**224**	**8.3%**	**7.3%**	**9.4%**	**0.5%**
Acute renal insufficiency (defined as: doubling of baseline creatinine)	39	**1.4%**	1.0%	1.9%	0.2%
Acute renal failure requiring dialysis	24	**0.9%**	0.6%	1.3%	0.2%
Urinary tract infection	68	**2.5%**	2.0%	3.2%	0.3%
Urinary retention requiring reinsertion of urinary catheter, delaying discharge, or discharge with urinary catheter	104	**3.8%**	3.2%	4.6%	0.4%
Infection	**383**	**14.2%**	**12.9%**	**15.5%**	**0.7%**
Wound infection requiring opening wound or antibiotics	20	**0.7%**	0.5%	1.1%	0.2%
Central IV line infection requiring removal or antibiotics	55	**2.0%**	1.6%	2.6%	0.3%
Intrathoracic/Intra-abdominal abscess	65	**2.4%**	1.9%	3.0%	0.3%
Generalized sepsis	52	**1.9%**	1.5%	2.5%	0.3%
Other infections requiring antibiotics	227	**8.4%**	7.4%	9.5%	0.5%
Neurologic / Psychiatric	**254**	**9.4%**	**8.3%**	**10.5%**	**0.6%**
Recurrent nerve injury	114	**4.2%**	3.5%	5.0%	0.4%
Other neurologic injury	33	**1.2%**	0.9%	1.7%	0.2%
Acute delirium	105	**3.9%**	3.2%	4.7%	0.4%
Delirium tremens	16	**0.6%**	0.4%	0.9%	0.1%
Wound/Diaphragm	**78**	**2.9%**	**2.3%**	**3.6%**	**0.3%**
Thoracic wound dehiscence	40	**1.5%**	1.1%	2.0%	0.2%
Acute abdominal wall dehiscence/hernia	33	**1.2%**	0.9%	1.7%	0.2%
Acute diaphragmatic hernia	8	**0.3%**	0.1%	0.6%	0.1%
Other complications	**185**	**6.8%**	**5.9%**	**7.8%**	**0.5%**
Chyle leak	128	**4.7%**	4.0%	5.6%	0.4%
Reoperation for reasons other than anastomotic leak or conduit necrosis	39	**1.4%**	1.0%	2.3%	0.2%
Multiple organ dysfunction syndrome	27	**1.0%**	0.7%	1.4%	0.2%

*CL – Confidence Limit; ECCG – Esophagectomy Complications Consensus Group; DVT – Deep Venous Thrombosis; PE – Pulmonary Embolus; CVA – Cerebrovascular Accident; CPR – Cardiopulmonary Resuscitation. * Complication group items include patients with more than one complications.*

Table 4. Complications Definitions Summary

Total patients = 2704

Anastomotic leak			N	N %
DEFINITION: Full thickness GI defect involving esophagus, anastomosis, staple line, or conduit irrespective of presentation or method of identification	No Leak		2403	88.9%
	Type I:	Local defect requiring no change in therapy or treated medically or with dietary modification	90	3.3%
	Type II:	Localized defect requiring interventional but not surgical therapy, for example, interventional radiology drain, stent or bedside opening, and packing of incision	131	4.8%
	Type III:	Localized defect requiring surgical therapy	80	3.0%
Conduit necrosis / failure				
DEFINITION: Postoperative identification of conduit necrosis.	No Conduit necrosis		2672	98.8%
	Type I:	Conduit necrosis focal Identified endoscopically (Treatment—Additional monitoring or non-surgical therapy)	2	0.1%
	Type II:	Conduit necrosis focal Identified endoscopically and not associated with free anastomotic or conduit leak (Treatment—Surgical therapy not involving esophageal diversion)	7	0.3%
	Type III:	Conduit necrosis extensive (Treatment—Treated with conduit resection with diversion)	23	0.9%
Recurrent laryngeal nerve injury involvement				
DEFINITION: Vocal cord dysfunction post-resection. Confirmation and assessment should be by direct examination.	No Recurrent laryngeal nerve injury		2595	96.0%
	Type Ia:	Unilateral transient injury requiring no therapy (Dietary modification allowed)	81	3.0%
	Type Ib:	Bilateral transient injury requiring no therapy (Dietary modification allowed)	6	0.2%
	Type IIa:	Unilateral Injury requiring elective surgical procedure, for example, thyroplasty or medialization procedure	12	0.4%
	Type IIb:	Bilateral Injury requiring elective surgical procedure, for example, thyroplasty or medialization procedure	4	0.1%
	Type IIIa:	Unilateral Injury requiring acute surgical intervention (due to aspiration or respiratory issues), for example, thyroplasty or medialization procedure	2	0.1%
	Type IIIb:	Bilateral Injury requiring acute surgical intervention (due to aspiration or respiratory issues), for example, thyroplasty or medialization procedure	4	0.1%
Chyle leak severity				
DEFINITION: Milky discharge upon initiation of enteric feeds and/or pleural fluid analysis demonstrating triglyceride level >100 mg/dl and/or chylomicrons in pleural fluid	No Chyle leak		2578	95.3%
	Type Ia:	<1 liter output/day Treatment—enteric dietary modifications	67	2.5%
	Type Ib:	>1 liter output/day Treatment—enteric dietary modifications	10	0.4%
	Type IIa:	<1 liter output/day Treatment—total parenteral nutrition	11	0.4%
	Type IIb:	>1 liter output/day Treatment—total parenteral nutrition	6	0.2%
	Type IIIa:	<1 liter output/day Treatment—interventional or surgical therapy	12	0.4%
	Type IIIb:	>1 liter output/day Treatment—interventional or surgical therapy	20	0.7%

Table 5 – Clavien-Dindo Classification of Surgical Complications

Total patients = 2704

Complication severity	N	N %	95% Lower CL for N%	95% Lower CL for N%	Standard Error of N%
No Complications*	1109	41.0%	39.2%	42.9%	0.9%
Grade I	204	7.5%	6.6%	8.6%	0.5%
Grade II	551	20.4%	18.9%	21.9%	0.8%
Grade IIIa	385	14.2%	13.0%	15.6%	0.7%
Grade IIIb	178	6.6%	5.7%	7.6%	0.5%
Grade IVa	173	6.4%	5.5%	7.4%	0.5%
Grade IVb	35	1.3%	0.9%	1.8%	0.2%
Grade V	69	2.6%	2.0%	3.2%	0.3%

* *No complications as per Esophageal Complication Consensus Group definitions, CL – Confidence Limit*

Grades	Clavien-Dindo Complication severity definitions
Grade I:	Any deviation from the normal postoperative course without the need for pharmacological treatment or surgical, endoscopic and radiological interventions (Allowed therapeutic regimens are: drugs as antiemetics, antipyretics, analgesics, diuretics and electrolytes and physiotherapy. This grade also includes wound infections opened at the bedside)
Grade II:	Requiring pharmacological treatment with drugs other than such allowed for grade I complications. Blood transfusions and total parenteral nutrition are also included
Grade IIIa:	Requiring surgical, endoscopic or radiological intervention – Not under general anesthesia
Grade IIIb:	Requiring surgical, endoscopic or radiological intervention – Under general anesthesia
Grade IVa:	Single organ dysfunction (including dialysis)
Grade IVb:	Multi-organ dysfunction
Grade V:	Death of a patient

Table 6. Readmissions and Mortality status outcomes

Total patients = 2704

Readmission within 30 days of discharge	**N**	**N%**
No readmission	2280	84.3%
Readmission related to esophagectomy	275	10.2%
Unrelated readmission	28	1.0%
Readmissions status not known	47	1.8%
Not discharged at 30 days or died inpatient	74	2.7%
Perioperative mortality		
Alive after 30 days post-op but died before 90 days	56	2.1%
Alive after 90 days post-op	2572	95.1%
Died within 30 days post-op	65	2.4%
Status not known / lost to follow-up after 30days post discharge	11	0.4%

SUPPLEMENT 1

Membership Agreement Signed at the Time of Registration on the ESODATA Website Documenting the Responsibility of Contributing Institutions

ESODATA.org
Membership Agreement

I WILL take part in the analysis and production of manuscripts based on the results of the ESODATA.org data collection.

I WILL NOT share the results of the interim reports sent from esodata.org until formally reviewed for publication by the ISDE-appointed Research and Database Committee.

I WILL comply and fulfill all institutional and national criteria for participation in this study.

I WILL record all patients undergoing esophageal resection at my institution that fulfill the criteria for inclusion during the study period.

I WILL record information accurately, completely and in a timely fashion on the www.esodata.org data collection I will promptly respond to email/correspondence requests for information, data update or opinion to maintain consensus during the study period.

I WILL ensure that data entered is fully anonymized and no identifiable patient information is entered in esodata.org database.

BY SIGNING THIS DOCUMENT, I accept ESODATA.org membership and agree to adhere to all the responsibilities of the Membership Agreement.

_____
Signature

Supplement 2 – Clinical & Pathological staging data

Total patients with malignant pathology = 2585

Clinical Stage		N	N %
cT stage	T0	4	0.2%
	Tx	83	3.2%
	Tis	21	0.8%
	T1	263	10.2%
	T2	411	15.9%
	T3	1722	66.6%
	T4	81	3.1%
cN stage	Nx	297	11.5%
	N0	893	34.5%
	N1	1030	39.8%
	N2	314	12.1%
	N3	51	2.0%
cM stage	Mx	200	7.7%
	M0	2349	90.9%
	M1	36	1.4%

Pathologic Stage		N	N %
pT stage	pT0	429	16.6%
	pTx	24	0.9%
	pTis	30	1.2%
	pT1	584	22.6%
	pT2	365	14.1%
	pT3	1075	41.6%
	pT4	78	3.0%
pN stage	pNx	7	0.3%
	pN0	1477	57.1%
	pN1	550	21.3%
	pN2	359	13.9%
	pN3	192	7.4%
pM stage	pMx	369	14.3%
	pM0	2170	83.9%
	pM1	46	1.8%