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Defining Benchmarks for Transthoracic Esophagectomy: A Multicenter Analysis of Total Minimally Invasive Esophagectomy in Low Risk Patients. — Source link

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Abstract: Objective: To define "best possible" outcomes in total minimally invasive transthoracic esophagectomy (ttMIE). Background: TtMIE, performed by experts in patients with low comorbidity, may serve as a benchmark procedure for esophagectomy. Patients and Methods: From a cohort of 1057 ttMIE, performed over a 5-year period in 13 high-volume centers for esophageal surgery, we selected a study group of 334 patients (31.6%) that fulfilled criteria of low comorbidity (American Society of Anesthesiologists score 2, WHO/ECOG score 1, age 65 years, body mass index 19–29 kg/m2). Endpoints included postoperative morbidity measured by the Clavien-Dindo classification and the comprehensive complication index. Benchmark values were defined as the 75th percentile of the median outcome parameters of the participating centers to represent best achievable results. Results: Benchmark patients were predominantly male (82.9%) with a median age of 58 years (53–62). High intrathoracic (Ivor Lewis) and cervical esophagogastrostomy (McKeown) were performed in 188 (56.3%) and 146 (43.7%) patients, respectively. Median (IQR) ICU and hospital stay was 0 (0–2) and 12 (9–18) days, respectively. 56.0% of patients developed at least 1 complication, and 26.9% experienced major morbidity (grade III), mostly related to pulmonary complications (25.7%), anastomotic leakage (15.9%), and cardiac events (13.5%). Benchmark values at 30 days after hospital discharge were 55.7% and 30.8% for overall and major complications, 18.0% for readmission, 3.1% for positive resection margins, and 23 for lymph node yield. Benchmarks at 30 and 90 days were 1.0% and 4.6% for mortality, and 40.8 and 42.8 for the comprehensive complication index, respectively. Conclusion: This outcome analysis of patients with low comorbidity undergoing ttMIE may serve as a reference to evaluate surgical performance in major esophageal resection.

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Defining Benchmarks for Transthoracic Esophagectomy

A Multicenter Analysis of Total Minimally Invasive Esophagectomy in Low Risk Patients

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Background: TtMIE, performed by experts in patients with low comorbidity, may serve as a benchmark procedure for esophagectomy.

Patients and Methods: From a cohort of 1057 ttMIE, performed over a 5-year period in 13 high-volume centers for esophageal surgery, we selected a study group of 334 patients (31.6%) that fulfilled criteria of low comorbidity (American Society of Anesthesiologists score $\leq$2, WHO/ECOG score $\leq$1, age $\leq$65 years, body mass index 19–29 kg/m^2). Endpoints included postoperative morbidity measured by the Clavien-Dindo classification and the comprehensive complication index. Benchmark values were defined as the 75th percentile of the median outcome parameters of the participating centers to represent best achievable results.

Results: Benchmark patients were predominantly male (82.9%) with a median age of 58 years (53–62). High intrathoracic (Ivor Lewis) and cervical esophagogastrostomy (McKeown) were performed in 188 (56.3%) and 146 (43.7%) patients, respectively. Median (IQR) ICU and hospital stay was 0 (0–2) and 12 (9–18) days, respectively. 56.0% of patients developed at least 1 complication, and 26.9% experienced major morbidity ($\geq$grade III), mostly related to pulmonary complications (25.7%), anastomotic leakage (15.9%), and cardiac events (13.5%). Benchmark values at 30 days after hospital discharge were $\leq$55.7% and $\leq$30.8% for overall and major complications, $\leq$18.0% for readmission, $\leq$3.1% for positive resection margins, and $\geq$23 for lymph node yield. Benchmarks at 30 and 90 days were $\leq$0.0% and $\leq$4.6% for mortality, and $\leq$40.8 and $\leq$42.8 for the comprehensive complication index, respectively.

Conclusion: This outcome analysis of patients with low comorbidity undergoing ttMIE may serve as a reference to evaluate surgical performance in major esophageal resection.

Keywords: benchmark values, comprehensive complication index, minimally invasive esophagectomy, outcome

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Benchmarking may be defined as a method to find a point of reference – the benchmark – against which the results of others can be compared. Usually, a benchmark describes a ''best possible'' outcome under ideal circumstances. Benchmarking is a standard tool to assess industrial productivity and efficacy, and represents an integral part of management concepts such as continuous quality improvement.[1] With the growing need to monitor performance within healthcare systems, the concept of benchmarking is gaining considerable weight in the field of surgery, particularly with the aim to evaluate complex and cost-intensive procedures.[2]

In this context, we conceived this multicenter analysis of total minimally invasive transthoracic esophagectomy (ttMIE). Minimal invasive surgery for esophageal cancer was introduced around 25 years ago, with the aim to reduce procedure-related morbidity.[3,4] Hybrid approaches, that combine either laparoscopy with thoracotomy or thoracoscopy with laparotomy, have become common procedures in many centers around the world. In contrast, the technically more complex and even less invasive total (laparoscopic-thoracoscopic) MIE has been adopted by a minority of esophageal surgeons only.[5,6] TtMIE was pioneered by James Luketich, who, in 2012, published an impressive series of more than 1000 consecutive patients with excellent outcomes.[7] As this study depicts a unique and since then unparalleled experience of a single dedicated surgeon, it may not adequately reflect the results of many centers that started total MIE during the course of recent years. In this regard, our aim was to create a realistic snapshot of the actual state of this procedure in international expert centers for esophageal surgery by means of a benchmark analysis.

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Parallel to other recent outcome research on esophageal cancer surgery,[8,9] we implemented the comprehensive complication index (CCI). The CCI is a novel scoring system that permits to integrate all complications into a single value on a scale from 0 (no complication) to 100 (death).[10] The fundamentally new aspect of this parameter is that it takes all types and grades of complications into account. Consequently, the patient's own perception of morbidity is reproduced more adequately.[11,12] We are convinced that the CCI is both clinically relevant and easy to understand and therefore, will be rapidly accepted within the surgical community.

METHODS

Data Collection

Thirteen surgical departments (Amsterdam, Cologne, Eindhoven, Gent, Helsinki, Leuven, Mainz, Milano, Philadelphia, Portsmouth, Rotterdam, Stockholm, Zurich) participated in this study. Hospital inclusion criteria were a caseload of more than 20 esophagectomies per year (minimally-invasive and other procedures), the availability of a prospective database, and a special commitment to esophageal surgery as documented by recent publications. Patients that underwent ttMIE [Ivor Lewis (I.L.) or McKeown (M.K.) procedures] over a 5-year period (June 1, 2011–May 31, 2016) for malignant or benign indications were eligible; conversions to open surgery, hybrid, and transhiatal procedures were excluded. Data were collected via a secure online platform (https://www.esobenchmark.org/) provided by the University Hospital of Zurich. We used a data entry management system to meet international standards for online databases including fully anonymized data. In agreement with each participating center, no data are reported with patient or hospital identifiers. The information collected per patient included basic demographics, American Society of Anesthesiologists (ASA)- and WHO/ECOG-scores, tumor-specific parameters, technical details of the surgical procedure, and postoperative complications. Time-endpoints for analysis of postoperative events were at 30 and 90 days after hospital discharge. The complications basic platform published by the Esophagectomy Complications Consensus Group (ECCG)[13] was used to classify all adverse events, which were then graded according to the Clavien-Dindo (CD) classification.[14] Approval from the ethical committee of the Canton of Zurich (BASEC-No. 2016–01430) and from the institutional review boards of each respective center was obtained before analysis.

Study Cohort and Inclusion Criteria of Low Comorbidity

The basic dataset included 1057 patients after ttMIE with a median (IQR) age of 64 (57–70) and a median (IQR) body mass index (BMI) of 25.6 kg/m^2 (22.8–28.4); 80.5% were men. From this basic dataset, 334 patients (31.6%) with a low risk profile (ECOG grade $\leq$1 and ASA score $\leq$2, age $\leq$65 years, and BMI 19–29 kg/m^2) were selected to form the study group for benchmark analysis (Fig. 1). Criteria of low comorbidity were derived from statistical analysis (Fisher exact test of proportions) of the whole patient cohort. Age >65 years and BMI >30 kg/m^2 were significantly associated with higher 90-day mortality ($P < 0.05$). These cutoff parameters are consistent with the results of a recent publication that identified an ECOG score >1, age >65 years, and obesity as predictors of major morbidity after esophagectomy.[15]

Performance Metrics of Benchmarking

Primary outcome measures for benchmark analysis were overall and major (CD $\geq$3a) morbidity, readmissions, anastomotic, and pulmonary complications; all at 30 days after hospital discharge. In addition, positive resection margins, the number of examined lymph nodes (LN), the 30- and 90-day CCI of patients that developed at least 1 CD grade II complication, and 30- and 90-day mortality rates were calculated.

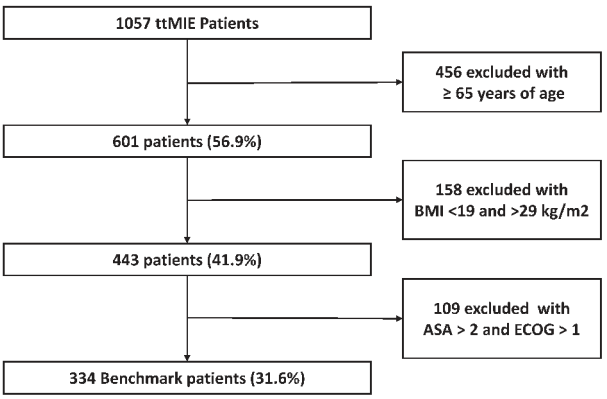

FIGURE 1. Flowchart depicting the basic dataset, exclusion criteria, and benchmark cohort.

Statistical Analysis

Data are reported as median and IQR for continuous variables or number and proportions (%) for categorical variables. For subgroup analyses (ie, comparison of the surgical technique or benchmark vs non-benchmark groups), continuous variables were compared using the Mann-Whitney U test. Categorical variables were compared using the Fischer exact or the Pearson χ^2 tests, where appropriate. Overall survival rates were calculated according to the Kaplan-Meier function. All P values were 2-sided and considered statistically significant if $P \leq 0.05$.

Benchmark values were exclusively derived from the study cohort with low comorbidity (n = 334). As previously described,[2] benchmarks were defined as the 75th percentile of the median outcome parameters of the participating centers representing best achievable results. Briefly, to adjust for variability in outcomes across centers,[2] we first calculated the median values of continuous parameters and the proportions of categorical variables for each participating center. After calculating the median and IQR of the center specific values, the 75th percentile was chosen as the benchmark value for all outcomes indicated above, with the exception of the number of lymph nodes examined, where the 25th percentile was chosen indicating the higher number the better. The reported 30- and 90-day CCI was derived from patients with available data for both 30 as well as 90 days of follow up developing at least 1 CD grade II complication.[2]

Statistical analysis was performed using R version 3.3.2 (R Core Team, GNU GPL v2 License), R Studio version 1.0.44 (RStudio, Inc. GNU Affero General Public License v3, Boston, MA, 2016) with the graphical user interface (GUI) rBiostatistics.com alpha version (rBiostatistics.com, Zurich, Canton of Zurich, Switzerland, 2016).

RESULTS

Basic Characteristics of Benchmark Patients

The 334 patients (31.6%) patients comprising the benchmark group were predominantly male (82.9%) with a median age of 58 years (IQR 53–62) (Table 1). Except for 2 patients, the indication for esophagectomy was esophageal cancer, with adenocarcinoma (77.2%) being the most common histological entity. Accordingly, most tumors were located in the distal esophagus (63.5%) or at the

TABLE 1. Patient Characteristics

	All Patients n = 1057 (100%)	Non-benchmark patients n = 723 (68.4%)	Benchmark patients n = 334 (31.6%)	*P*
Age yrs (median, IQR)	64 (57–70)	67 (61–72)	58 (53–62)	<0.01
BMI kg/m^2 (median, IQR)	25.6 (22.8–28.4)	25.8 (22.6–29.7)	25.3 (23.3–27.5)	<0.01
Male, n (%)	851 (79.4)	574 (79.4)	277 (82.9)	ns
WHO/ECOG performance status, n (%)				
Grade 0	630 (59.6)	407 (56.3)	223 (66.8)	<0.01
Grade I	387 (36.6)	276 (38.2)	111 (33.2)	–
Grade II	40 (3.8)	40 (5.5)	–	–
ASA status, n (%)				
Grade I	226 (21.4)	118 (16.3)	108 (32.3)	<0.01
Grade II	539 (51)	313 (43.3)	226 (67.7)	–
Grade III	288 (27.2)	288 (39.8)	–	–
Grade IV	4 (0.4)	4 (0.6)	–	–
Histology, n (%)				
AC	813 (76.9)	555 (76.8)	258 (77.2)	ns
SCC	224 (21.2)	155 (21.4)	69 (20.7)	–
Other type of malignancy	13 (1.2)	8 (1.1)	5 (1.5)	–
Benign	7 (0.7)	5 (0.7)	2 (0.6)	–
Tumor location, n (%)				
Proximal half of esophagus	47 (4.4)	26 (3.6)	21 (6.3)	ns
Distal half of esophagus	655 (62)	443 (61.3)	212 (63.5)	–
Esophagogastric junction	355 (33.6)	254 (35.1)	101 (30.2)	–
Preoperative therapy, n (%)				
None	291 (27.5)	219 (30.3)	72 (21.6)	0.02
Chemotherapy	125 (11.9)	74 (10.2)	51 (15.3)	–
Radiotherapy	4 (0.4)	3 (0.4)	1 (0.3)	–
Radiochemotherapy	635 (60.1)	426 (58.9)	209 (62.6)	–
Definitive radiohemotherapy	2 (0.2)	1 (0.1)	1 (0.3)	–
Surgical approach				
McKeown	482 (45.6)	336 (46.5)	146 (43.7)	ns
Ivor Lewis	575 (54.4)	387 (53.5)	188 (56.3)	–
UICC Stages, n (%)				
IA	395 (37.5)	279 (38.8)	116 (34.7)	ns
IB	103 (9.8)	71 (9.9)	32 (9.6)	–
IIA	150 (14.3)	101 (14)	49 (14.7)	–
IIB	96 (9.1)	64 (8.9)	32 (9.6)	–
IIIA	151 (14.4)	99 (13.8)	52 (15.6)	–
IIIB	76 (7.2)	47 (6.5)	29 (8.7)	–
IIIC	67 (6.4)	51 (7.1)	16 (4.8)	–
IV	14 (1.3)	8 (1.1)	6 (1.8)	–

ECOG indicates Eastern Cooperative Oncology Group; IQR, interquartile range; ns, not significant; UICC, Union internationale contre le cancer TNM classification for esophageal cancer 7Th edition; –, Pearson chi-square; WHO, World Health Organization.

esophagogastric junction (30.1%). Furthermore, the majority of patients received neoadjuvant treatment, either chemotherapy alone (15.3%) or chemoradiation (62.6%). Seventy-two patients (21.6%) underwent esophagectomy without neoadjuvant treatment.

Postoperative Outcome in Benchmark Patients

Overall morbidity at 30 days after discharge was 56.0%, with 90 patients (26.9%) experiencing major complications (CD grade ≥IIIa) (Table 2, Fig. 2). Although some variation was observed, overall and major morbidity was not statistically different comparing the different surgical centers (Fig. 2). Thirty- and ninety-day mortality rates were 0.9% and 2.4%, respectively. Most common complications were pulmonary (25.7%; CD grades I, II, IIIA, IIIb, IVa, IVb, and V in 13, 29, 9, 4, 23, 4, and 4 patients, respectively), followed by anastomotic leaks (15.9%; CD grades I, II, IIIA, IIIb, IVa, IVb, and V in 7, 11, 8, 15, 9, 2, and 1 patients, respectively), and cardiac events (13.5%; CD grades I, II, IIIA, IIIb, IVa, IVb, and V in 6, 30, 1, 1, 4, 0, and 3 patients, respectively). Fatal outcomes (CD grade V, n = 8) were highly associated with anastomotic leakage (6 patients); only 1 patient suffered a cardiac arrest without any other documented complication. The median CCI was 8.7 (IQR 0.0–30.8) including morbidity leading to readmission. Median intensive care unit (ICU) stay was 0 days (IQR 0–2) and median hospital stay was 12 days (IQR 9–18). Forty-eight patients (14.4%) with complicated postoperative course needed higher level of care with readmission to ICU. Blood transfusions were administered intraoperatively in 2 patients (0.6%) and postoperatively in 25 patients (7.5%). Twenty-four patients (7.2%) required rehospitalization within 30 days of discharge. Readmission was most commonly related to delayed gastric emptying (3 patients), anastomotic stricture (3 patients), and overeating or dumping syndrome (9 patients). Three patients were readmitted with late anastomotic leaks, 1 of whom developed a gastro-tracheal fistula. Another readmission was due to an abscess adjacent to the pancreas. The majority of cases were treated conservatively (eg, antibiotics, drainage, nil per mouth) or endoscopically (pyloric dilation, stent placement, tracheostomy). One patient underwent redo-surgery for a positive resection margin and was reconstructed with colon interposition.

Intrathoracic and Cervical Anastomosis

In the benchmark group, high intrathoracic (IL procedure) and cervical esophagogastrostomy (MK procedure) were performed in

TABLE 2. Postoperative Outcomes

	All Patients n = 1057 (100%)	Non-benchmark Patients n = 723 (68.4%)	Benchmark Patients n = 334 (31.6%)	*P*
LN examined, median (IQR)	25 (18–33)	24 (17–32)	27 (20–34)	<0.01
Pos. resection margins, n (%)	35 (3.4)	25 (3.5)	10 (3.0)	ns
Complications, n (%)				
Any type	629 (59.5)	442 (61.1)	187 (56)	0.04
Minor (CDC Grade I–II)	288 (27.2)	191 (26.4)	97 (29)	–
Major (CDC Grade IIIa–V)	341 (32.3)	251 (34.7)	90 (26.9)	0.01
Anastomotic leak	170 (16.1)	117 (16.2)	53 (15.9)	ns
Conduit necrosis	21 (2)	16 (2.2)	5 (1.5)	ns
Chyle leak	58 (5.5)	43 (5.9)	15 (4.5)	ns
Gastrointestinal event	85 (8)	53 (7.3)	32 (9.6)	ns
Pulmonary event	328 (31)	242 (33.5)	86 (25.7)	0.01
Cardiac event	199 (18.8)	154 (21.3)	45 (13.5)	<0.01
Thrombembolic event	27 (2.6)	18 (2.5)	9 (2.7)	ns
Urologic event	34 (3.2)	29 (4)	5 (1.5)	0.04
Infection	162 (15.3)	115 (15.9)	47 (14.1)	ns
Neurologic event	72 (6.8)	57 (7.9)	15 (4.5)	0.04
Wound infection	28 (2.6)	22 (3)	6 (1.8)	ns
Change in level of care, n (%)	162 (15.4)	114 (15.8)	48 (14.4)	ns
Blood product utilization, n (%)				
Intraoperative	9 (1)	7 (1.1)	2 (0.6)	ns
Postoperative	91 (9.8)	66 (10.2)	25 (7.5)	–
Intra- and postoperative	7 (0.8)	7 (1.1)	–	
ICU stay, median (IQR)	1 (2–5.25)	2 (1–6)	2 (1–5.25)	<0.01
Hospital stay, median (IQR)	13 (10–21)	13 (10–22)	13 (10–21)	ns
Readmission rate within 30 days of discharge, n (%)				
Related to esophagectomy	69 (6.7)	49 (7)	20 (6)	ns
Unrelated to esophagectomy	9 (0.9)	5 (0.7)	4 (1.2)	–
CCI, median (IQR)				
30-day	20.9 (0–33.7)	20.9 (0–36.2)	8.7 (0–30.8)	0.01
90-day	20.9 (0–39.2)	26 (0–40)	20.9 (0–34)	<0.01
Mortality, n (%)				
30-day	22 (2.1)	19 (2.6)	3 (0.9)	ns
90-day	55 (5.2)	47 (6.5)	8 (2.4)	<0.01

CCI indicates comprehensive complication index; CDC, Clavien-Dindo Classification; IQR, interquartile range, –, Pearson chi-square; LN, lymph node, ns, not significant.

188 (56.3%) and 146 (43.7%) patients, respectively. Basic patient characteristics, WHO/ECOG status, and UICC stages were similar, but ASA grades were significantly higher in MK patients. Also, squamous cell carcinoma and proximal esophageal localization of the tumor were significantly more common in MK patients. No statistically significant differences were found for overall (52.7% and 60.3%) and major (28.2% and 25.3%) morbidity, the median CCI [8.7 (IQR 0–26.2) and 20.9 (IQR 0–33.7)], anastomotic leakage rates (14.9% and 17.1%), pulmonary (25.5% and 26.0%), and cardiac complications (11.2% and 16.4%) in both groups, respectively. Likewise, positive resection margins (2.2% and 4.2%), hospital readmission rates (6.6% and 5.7%), and 30- (0.5% and 1.4%) and

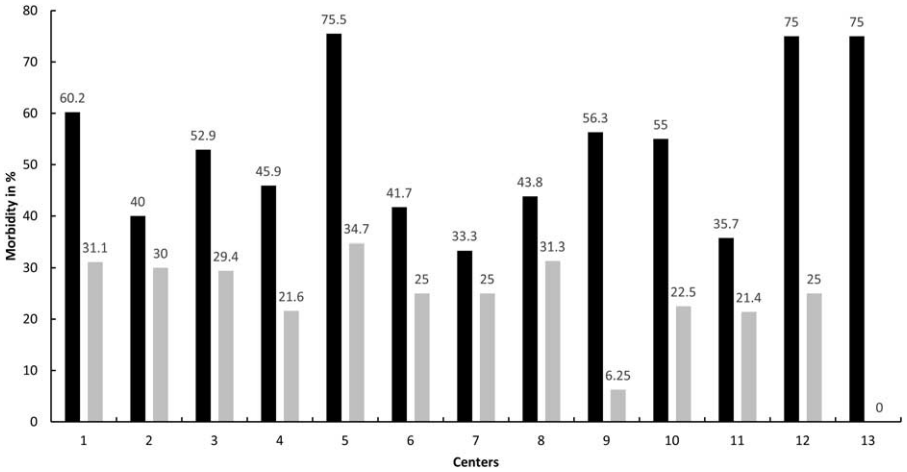

FIGURE 2. Overall (black columns) and major (CD ≥III, grey columns) complication rates at 30 days after discharge in benchmark patients (n = 334) of all 13 surgical centers included.

90-day (1.6% and 3.4%) mortality were comparable. In contrast, a shorter postoperative ICU stay [1 (IQR 0–4) and 1 (IQR 1–4)] ($P = 0.05$) and a lower yield of harvested lymph nodes [26 (IQR 19–33) and 29 (IQR 22–35)] ($P = 0.02$) was documented in IL patients.

Benchmark- and Non-benchmark Patients

Benchmark- and non-benchmark cohorts were significantly different for most basic patient characteristics (ASA score, WHO/ECOG score, BMI, age). In contrast, both groups were similar regarding oncological parameters (type of histology, tumor location, UICC stage) and the type of surgical intervention performed (Table 1). Considering postoperative outcome, overall and major morbidity was significantly higher in the non-benchmark cohort. This was caused by a significantly higher rate of pulmonary, cardiac, urological, and neurological complications, which also translated into a higher CCI ($P = 0.01$) and an almost 3-fold increase in 30- and 90-day mortality. In contrast, surgical complications (anastomotic leakage rate, conduit necrosis, lymphatic leak), and also readmission rates were similar in both groups (Table 2).

Oncological Outcome in Benchmark- and Non-benchmark Patients

Oncological results were calculated for patients with either squamous cell- or adenocarcinoma (AC) only (n = 1037); benign diseases and other malignancies (n = 20) were excluded. Median LN yield in the whole population of ttMIE patients was 25 (IQR 18–33). The number of harvested LN was significantly higher in the benchmark cohort compared with non-benchmark patients (Table 2). In contrast, positive resection margins (overall 3.4%) were similar in benchmark- and non-benchmark patients (Table 2). Overall survival (OAS) of the whole cohort, and of benchmark- and non-benchmark patients was 82.3% and 85.5%, 80.8% (1 year), 60.1%, 62.2%, and 58.2% (3 years), and 54.5%, 59.7%, and 52.0% (5 years), respectively.

Benchmark Values ()

Thirty-day benchmark values were based on 326 patients (97.6%) from 11 centers (2 centers with <10 patients excluded), and 90-day benchmarks were derived from 218 patients (65.3%) from 10 centers (2 centers with <10 patients and 1 center with incomplete 90-day morbidity data reporting excluded) (Table 3).

Benchmark cutoff values 30 days after discharge were ≤55.7% and ≤30.8% for overall and major (CD grade ≥III) morbidity, ≤20.0% and ≤31.6% for anastomotic leakage and pulmonary complications, ≤3.1% and ≥23 for positive resection margins and LN yield, and ≤18.0% for hospital readmission rate. Benchmarks for the CCI at 30 and 90 days were ≤40.8 and ≤42.8 in patients, and ≤0.0% and ≤4.6% for 30- and 90-day mortality, respectively.

TABLE 3. Benchmark Results

Benchmark Parameters	Benchmark Values
Complications of any severity	≤55.7%
Major complications (CD Grade ≥IIIa)	≤30.8%
Anastomotic leak	≤20%
Pulmonary complication	≤31.6%
Lymph nodes examined	≥23¥
Positive resection margins	≤3.1%
Hospital readmission	≤18.0%
30-day CCI	≤40.8
90-day CCI	≤42.8
30-day mortality	0%
90-day mortality	≤4.6%

Benchmark values are the 75th percentile of the median proportions, except ¥ is the 25th percentile of the median proportion indicating the high number of lymph nodes yielded the better.

DISCUSSION

In recent years, outcome assessment has become an important part of surgical patient care in many developed countries. Hospitals, departments, and even individual surgeons are increasingly obliged to measure the quality they deliver and to make this data available to the public. This information is then often used to rank performance among competitors with the goal to achieve better transparency and improved patient autonomy.[16] Consequently, Medicare and private payors, policymakers, the media, physicians, and also patients increasingly tend to guide their decisions based on such datasets, a mechanism that strongly impacts on the economic interests of healthcare providers. Indeed, quality assessment of patient care has become a powerful public relation tool of the healthcare industry.

On the other hand, there are concerns that the evidence provided by large national databases, audits, and meta-analyses may be biased by the heterogeneity of target populations and procedures performed.[17,18] Often, the spectrum of inclusion criteria is kept rather large to increase sample sizes and no risk adjustment of cases is performed. For example, a profiling algorithm may ascribe a superior performance rank to surgeon A due to an inferior mortality rate compared with surgeon B. However, if the scheme does not consider the case-mix of patients, this ranking system will be wrong and cause misunderstanding. Moreover, this may lead to risk-aversion, as healthcare providers may adopt avoidance strategies for highly morbid or complex cases.[19] Other potential weaknesses of traditional databases are the absence of uniform datasets, the nonexistence of consistent validation methods, and the focus on single outcome parameters only, like ''30-day mortality.''[2]

Our present study may overcome these drawbacks as it provides benchmarks for several clinically relevant endpoints, ready to be implemented by third-party institutions. Our study complies with the proposal for standardized reporting of benchmarking as suggested in a previous study on major hepatectomy,[2] with the exception that we were able to include expert centers from only 2 (instead of 3) continents. A particular strength of our work is that data were derived from a highly-selected ''optimal'' group of patients with low comorbidity that underwent a clearly defined, minimally-invasive surgical procedure in expert institutions only. This unique approach allows for the first time to define benchmark parameters, or ''best achievable results'' for ttMIE. Benchmarking is a novel concept for the evaluation of surgical procedures and, to our best knowledge, has not been performed in esophageal surgery cohorts before. In this context, an interesting novel application of the benchmark concept may be to directly compare morbidity – and consequently – its related cost among different types of major surgery. Thus, the 30-day benchmark values for overall and major complications in our ttMIE cohort (≤55.7% and ≤30.8%, respectively) are considerably higher than those reported after major hepatectomy[2] (≤26.9% and ≤6.0%, respectively), but substantially lower compared with those found in patients undergoing liver transplantation (≤80.0% and ≤42.0%, respectively) (unpublished data). This further illustrates the potential of benchmarking to provide elaborate points of reference for use in studies comparing the impact of morbidity – even across different surgical specialties.

We chose ttMIE as benchmark procedure, because it is one of the least invasive surgical approaches for esophageal cancer, but permits a strictly curative approach including systematic lymphadenectomy in both the thoracic and the abdominal body cavity. Accordingly, there is increasing evidence that this operation results in equivalent oncological outcome[20] and less postoperative

complications compared with the conventional open approach.[21,22] Other techniques, although equally labeled ''minimally invasive'' – such as laparoscopically or thoracoscopically assisted, hybrid or transhiatal esophagectomy – were strictly excluded from this analysis to keep our cohort as homogeneous as possible.

Furthermore, we restricted this data collection to recognized experts in the field of esophageal surgery. Only centers with a case load of more than 20 esophagectomies per year, maintaining a prospective database, and with a documented special interest in esophageal surgery were included. Also, we insisted on careful retrospective review of patient files by our coinvestigators in the event of incompletely submitted case report forms. This stringent policy resulted in a remarkably high quality of the final dataset with no missing parameters for primary endpoints at 30 days after discharge. In order to further enhance the quality of our database, postoperative complications were assessed according to the systematic classification and definitions published by the ECCG.[13] This strategy translated into a high plausibility of our data: key indicators such as leakage rate and 30- or 90-day mortality are well within the range of other data collections.[23–26]

Patient survival in this dataset was superior to that reported by others for open[26] and minimally invasive esophageal cancer surgery.[7,23] One the one hand, this relatively high OAS in our series reflects a technically adequate oncological resection. On the other, it can be explained by a large proportion of UICC stage 1a carcinoma (37.5%) in our cohort, which in turn may be caused by the high rate (72.5%) of induction therapy – in particular radiochemotherapy – a treatment leading to downstaging in a relevant proportion of patients. Also, an effect of patient selection cannot be excluded, as some centers may have not performed ttMIE in advanced carcinoma when starting their program.

Undeniably, there are some limitations to our study. First, we found substantial variability in the number of cases submitted per center. Indeed, 5 centers included more than 100 cases, and 8 centers less than 50 cases. Although we believe that this diversity should rather be regarded as a strength than a weakness and might better reflect reality than a single high-volume experience, it may also mirror a different degree of experience with this specific procedure and suggests that learning curve related morbidity may play a role in our dataset. However, statistical analysis did not reveal higher morbidity in institutions with less than 50 cases included. In particular, there was no significant difference for surgical complications such as anastomotic and conduit leakage. The ''smaller'' centers, although still working on their learning curve for ttMIE, invariably had vast experience in open and hybrid esophagectomy and complication management, which may explain the similar outcomes compared with the ''larger'' contributors.

We were not able to perform an intention to treat analysis, because the conversion rate to open or hybrid access surgery was not included in our database – this may be considered as a weakness of the study design. However, our work was strictly focused on postoperative morbidity of completed ttMIE, and therefore, conversions, open, and hybrid approaches were strictly excluded.

In our dataset, the anastomotic leakage rate was 15.9%, which is in the upper range compared with other outcome research.[20] On the one hand, we may attribute this to the strict adoption of the definitions for this specific complication as published by the ECCG.[13] In contrast to other studies,[7] even minor and clinically unapparent events were recorded and taken into account. On the other hand, it should be noted that some of the larger (>50 cases) centers changed their standard technique from MK to IL ttMIE during the study period, and learning curve-associated effects during the transition phase cannot be excluded. This might also explain the lack of correlation between a center's ttMIE experience level and the leakage rate. Therefore, at the present stage, it cannot be excluded that the relatively high leakage rate may be related to the total minimally invasive approach itself. Nevertheless, the low 30- and 90-day mortality rates in our benchmark cohort (0.9% and 2.4%, respectively) reflect a remarkable quality of postoperative care and consequent management in case of complications. In fact, only 6 deaths (1.8%) in the study group were actually associated with anastomotic leaks.

Another limitation of our paper is that we cannot exclude that some adverse events may have been misclassified or even not documented at all. In particular, CD grade 1 complications were not equally distributed between centers. From earlier research, we know that minor morbidity, such as urinary tract infections or nonstandard lab results, is frequently underreported.[2] However, CD grade 1 complications only have an insignificant impact on the CCI, and therefore, are not expected to bias the message of the paper.

In summary, our study is the first to present benchmark values for outcome parameters after major esophageal surgery. Our database was derived from a large cohort of patients that exclusively underwent ttMIE performed by an international group of experts for esophageal surgery. By restricting our analysis to a subgroup of ''ideal'' patients with low comorbidity, ''best possible'' results for ttMIE were obtained. However, we should keep in mind that our results represent a snapshot of the actual situation – benchmark values will presumably improve with time. TtMIE is a very complex and new procedure with a steep learning curve. With growing experience, morbidity might shift and this benchmark analysis will need an update.

Nevertheless, we are confident that our results may soon be implemented as a reference for other institutions or surgical procedures owing to the novelty of the benchmark concept, the up-to-dateness of ttMIE, and the lack of comparable outcome values in the current literature.

REFERENCES

1. Ettorchi-Tardy A, Levif M, Michel P. Benchmarking: a method for continuous quality improvement in health. *Healthc Policy*. 2012;7:e101–e119.
2. Rossler F, Sapisochin G, Song G, et al. Defining benchmarks for major liver surgery: a multicenter analysis of 5202 living liver donors. *Ann Surg*. 2016;264:492–500.
3. Giugliano DN, Berger AC, Rosato EL, et al. Total minimally invasive esophagectomy for esophageal cancer: approaches and outcomes. *Langenbecks Arch Surg*. 2016;401:747–756.
4. Cuschieri A, Shimi S, Banting S. Endoscopic oesophagectomy through a right thoracoscopic approach. *J R Coll Surg Edinb*. 1992;37:7–11.
5. Haverkamp L, Seesing MF, Ruurda JP, et al. Worldwide trends in surgical techniques in the treatment of esophageal and gastroesophageal junction cancer. *Dis Esophagus*. 2016;30:1–7.
6. Lazzarino AI, Nagpal K, Bottle A, et al. Open versus minimally invasive esophagectomy: trends of utilization and associated outcomes in England. *Ann Surg*. 2010;252:292–298.
7. Luketich JD, Pennathur A, Awais O, et al. Outcomes after minimally invasive esophagectomy: review of over 1000 patients. *Ann Surg*. 2012;256:95–103.
8. Nederlof N, Slaman AE, van Hagen P, et al. Using the comprehensive complication index to assess the impact of neoadjuvant chemoradiotherapy on complication severity after esophagectomy for cancer. *Ann Surg Oncol*. 2016;23:3964–3971.
9. Eberhard KE, Achiam MP, Rolff HC, et al. Comparison of ''Nil by Mouth'' Versus Early Oral Intake in Three Different Diet Regimens Following Esophagectomy. *World J Surg*. 2017;41:1575–1583.
10. Slankamenac K, Graf R, Barkun J, et al. The comprehensive complication index: a novel continuous scale to measure surgical morbidity. *Ann Surg*. 2013;258:1–7.
11. Slankamenac K, Nederlof N, Pessaux P, et al. The comprehensive complication index: a novel and more sensitive endpoint for assessing outcome and reducing sample size in randomized controlled trials. *Ann Surg*. 2014;260:757–762. discussion 762–3.

12. Clavien PA, Vetter D, Staiger RD, et al. The comprehensive complication index (CCI). Added value and clinical perspectives 3 years ''Down the Line''. *Ann Surg*. 2017;265:1045–1050.
13. Low DE, Alderson D, Cecconello I, et al. International consensus on standardization of data collection for complications associated with esophagectomy: Esophagectomy complications consensus group (ECCG). *Ann Surg*. 2015;262:286–294.
14. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Ann Surg*. 2004;240:205–213.
15. Raymond DP, Seder CW, Wright CD, et al. Predictors of major morbidity or mortality after resection for esophageal cancer: a Society of Thoracic Surgeons General Thoracic Surgery Database Risk Adjustment Model. *Ann Thorac Surg*. 2016;102:207–214.
16. Lane-Fall MB, Neuman MD. Outcomes measures and risk adjustment. *Int Anesthesiol Clin*. 2013;51:10–21.
17. Hemkens LG, Benchimol EI, Langan SM, et al. The reporting of studies using routinely collected health data was often insufficient. *J Clin Epidemiol*. 2016;79:104–111.
18. Langan SM, Benchimol EI. The need to improve reporting of routinely collected dermatology data for patient benefit. *Br J Dermatol*. 2016;174:477–480.
19. Spray TL, Gaynor JW. A word of caution in public reporting. *Semin Thorac Cardiovasc Surg Pediatr Card Surg Annu*. 2017;20:49–55.
20. Palazzo F, Rosato EL, Chaudhary A, et al. Minimally invasive esophagectomy provides significant survival advantage compared with open or hybrid esophagectomy for patients with cancers of the esophagus and gastroesophageal junction. *J Am Coll Surg*. 2015;220:672–679.
21. Biere SSAY, van Berge Henegouwen MI, Maas KW, et al. Minimally invasive versus open oesophagectomy for patients with oesophageal cancer: a multicentre, open-label, randomised controlled trial. *Lancet*. 2012;379:1887–1892.
22. Straatman J, van der Wielen N, Cuesta MA, et al. Minimally invasive versus open esophageal resection: three-year follow-up of the previously reported randomized controlled trial: the TIME Trial. *Ann Surg*. 2017;266:232–236.
23. Ben-David K, Tuttle R, Kukar M, et al. Minimally invasive esophagectomy utilizing a stapled side-to-side anastomosis is safe in the western patient population. *Ann Surg Oncol*. 2016;23:3056–3062.
24. Markar SR, Arya S, Karthikesalingam A, et al. Technical factors that affect anastomotic integrity following esophagectomy: systematic review and meta-analysis. *Ann Surg Oncol*. 2013;20:4274–4281.
25. van Hagen P, Hulshof MC, van Lanschot JJ, et al. Preoperative chemoradiotherapy for esophageal or junctional cancer. *N Engl J Med*. 2012;366:2074–2084.
26. Messager M, Pasquer A, Duhamel A, et al. Laparoscopic gastric mobilization reduces postoperative mortality after esophageal cancer surgery: A French Nationwide Study. *Ann Surg*. 2015;262:817–822. discussion 822–3.

DISCUSSANTS

Antonio J. Torres (Madrid, Spain):

In my opinion, this paper is dealing with a very important matter at present time. It tries to identify the best possible outcomes in minimally invasive surgery for esophageal cancer. We can discuss about the inclusion criteria for considering the low comorbidity group (specially the age: <65). Also, BMI <30 and benign cases could be controversial. It would be important to have more information about the decision process for selecting the Ivor-Lewis (56.3%) or the McKeown (43.7%) surgical approach in the benchmark group, taking into account that 93.7% of the tumors were located at the distal part of esophagus (63.5%) or at the esophago-gastric junction (30.2%). The same issue happens in the non-benchmark group, with similar numbers. It also would be interesting to know if there is any relationship between the transthoracoscopic anastomosis and the postoperative fistula.

So, my questions are: First, why to include the 20 non-malignant cases in this bench marking study? Is it not adding any bias? Second, if the McKeown's approach is most frequently performed in squamous cell carcinoma and/or esophageal cancers located proximally, why Ivor Lewis's technique was performed only in 56.3% of the patients? Third, do you consider that performed a thoracoscopic anastomosis can influence the high rate of anastomotic leak? Finally, do you have any information about the conversion rate from laparoscopic and/or thoracoscopic approach to open?

Response from Christian A. Gutschow (Zurich, Switzerland):

Professor Torres, thank you very much for your questions. You first asked why we also included non-malignant cases. When we conceived our study, we decided to include those cases, because the focus was strictly on postoperative morbidity of ttMIE – independent of the indications. We agree that the majority of patients undergoes esophagectomy for esophageal carcinoma. However, with the intention to picture clinical reality as close as possible, we chose to include benign indications as well as other malignant and semimalignant esophageal diseases, like GIST. One could assume that tubular esophagectomy without lymphadenectomy might possibly influence postoperative morbidity; however, due to their very small number in our cohort, these cases only have an insignificant impact on results, and therefore, are not expected to bias the message of the paper.

Your second question referred to the high rate of McKeown procedures in our study cohort. Unfortunately, we have no data on the decision process for McKeown and Ivor Lewis esophagectomy, because this was not included in our database. However, there was no distinct pattern of preferred techniques among the centers: some performed both types of procedure, while others almost exclusively performed either IL or MK. However, some of the larger centers started with MK – probably to avoid an intrathoracic anastomosis during the initial experience – and later moved on to IL.

This also relates to your third question about the potentially higher leakage rate of thoracoscopic esophago-gastrostomy. The scientific evidence comparing minimally invasive with open intrathoracic anastomosis is still very limited; thus, we cannot generally exclude a higher risk for anastomotic fistula in the thoracoscopic approach. Your last question referred to conversion rates. Again, this was not included in our database. We agree that this may be considered as a potential limitation of our study; however, when we planned our study design, we did not consider this a problem because the focus was strictly on postoperative morbidity of the benchmark procedure: a completed total minimally invasive transthoracic esophagectomy.

Christophe Mariette (Lille, France):

Congratulations for the very interesting presentation. I have some concerns regarding the paper and the methodology used. The first point is that you mentioned that the ideal circumstance for studying esophagectomy on a benchmarking point of view is transthoracic esophagectomy. You cite also low postoperative morbidity rate, surgical expert teams, and minimally invasive esophectomy. However, I'm not in agreement with the last issue, since no guidelines recommending minimally invasive esophagectomy has been published to date. So, do you think it can be considered as a standard?

The second point is about the McKeown esophagectomy procedure with first a thoracotomy and then a gastric pull up through the abdominal and cervical compartments. You mentioned that it's an ideal procedure, whereas some others have shown that placing the anastomotis in the neck is not the optimal way, leading to an increased rate of postoperative mortality, especially for low or middle third esophageal adenocarcinomas. Please comment. Third, some continents are missing here. Normally, for benchmarking you have to have various continents represented. Here you have European centers and only 1 American center. Please comment. Finally, the dimensions usually to be considered in such business process are quality, time and cost. In the paper, nothing about the costs is reported.

Response from Christian A. Gutschow (Zurich, Switzerland):

Prof. Mariette, thank you for your remarks. I am aware that ttMIE is not recommended as a standard procedure in the actual guidelines. However, morbidity after ttMIE has been shown to be lower compared with the conventional approach in a number of meta-analyses and oncologic outcome was equivalent in the randomized TIME trial. I fully agree that the evidence published so far does not allow for definite conclusions, but we are convinced that ttMIE, if performed by experts, has the potential for a benchmark procedure.

Concerning your second question about potential superiority of the McKeown approach, I assume that there must have been some misunderstanding. In our benchmark patients, there were no statistically significant differences for most parameters analyzed except for a statistically higher number of resected lymph nodes in the McKeown group. However, this difference was not clinically relevant.

Your third question relates to the contributing centers originating from 2 continents only. I fully agree: unfortunately, we were not successful in recruiting Asian, African, or Australian centers. This may be due to the fact that ttMIE is a relatively young procedure and many surgeons are still in their ''experimental'' phase. Therefore, it will be necessary to update this analysis relatively soon, and we are confident to be able to convince more centers from overseas to participate.

Your last question related to cost-effectiveness of ttMIE. When we conceived our study, we did not include this because the focus was clearly on morbidity of ttMIE. Also, we expected difficulties to analyze cost-effectiveness in a multinational study.

Olivier Farges (Clichy, France):

Thank you very much for your presentation. Two short questions: First, have you observed differences in outcome between the 13 centers? If not, does it suggest that your proposed benchmark values cannot discriminate quality of care between high-volume centers? Second, is an expert center only defined by its annual caseload?

Response from Christian A. Gutschow (Zurich, Switzerland):

Prof. Farges, thank you for your questions. Indeed, we did not find significant differences among the contributing centers for standard morbidity parameters in the benchmark cohort. In our opinion, this mirrors the high level of care in the centers that contributed to this study. Referring to your second question, I truly think that a high case load – it was at least 20 esophagectomies per year in our study – is necessary to achieve a certain level of expertise and quality. This has been shown in a number of studies: center and surgeon volumes correlate well with outcome in esophageal surgery. In our study, besides case load, hospital inclusion criteria were also the availability of a prospective database and a special commitment to esophageal surgery as documented by recent publications.

Editorial Comment by Christophe Mariette (Lille, France):

Defining a point of reference – the benchmark – against which the results of others can be compared with define a best possible outcome under ideal circumstances is emerging and of interest in the surgical field. Definition of the ideal circumstances in the present paper is debatable since totally minimally invasive esophagectomy has not been demonstrated as a standard approach and patients included represent a highly selected group operated on in high volume centers, including their learning curve. Reporting on long-term outcomes and cost-effectiveness would offer strength to the concept.