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A National Cohort Study Evaluating the Association Between Short-term Outcomes and Long-term Survival After Esophageal and Gastric Cancer Surgery

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Objective: The aim of this study was to investigate the association between short-term outcome indicators and long-term survival after esophagogastric resections.

Summary Background Data: Short-term outcome indicators are often used to compare performance between care providers. Some short-term outcome indicators concern the direct quality of care, that is, complications, others are used because they are expected to be associated with long-term outcomes.

Method: For this national cohort study, all patients who underwent esophagectomy or gastrectomy for cancer with curative intent between 2011 and 2016 and were registered in the Dutch Upper gastrointestinal Cancer Audit were included. Primary outcome was conditional survival (under the condition of surviving the first postoperative 30 days and hospital admission). Cox regression modeling was used to study the independent association between ''textbook outcome'' with survival. ''Textbook outcome,'' a composite quality indicator, was defined as a pathological complete resection with at least 15 retrieved lymph nodes, an uneventful postoperative course, and no hospital readmission.

Results: In total, 4414 and 2943 patients with esophageal or gastric cancer, respectively, were included. The 1-, 2-, and 3-year overall survival rates were 76%, 62%, and 54%, and 71%, 56%, and 49% for esophageal and gastric cancer, respectively. Textbook outcome was achieved in 33% and 35% of patients respectively. ''Textbook outcome'' was independently associated with longer conditional survival [hazard ratio: 0.75 (95% confidence interval, 0.68–0.84) and 0.69 (0.60–0.79), respectively].

Conclusion: This study showed that the short-term outcome indicator textbook outcome is associated with long-term overall survival and therefore may accentuate the importance of using these indicators in clinical audits.

Keywords: clinical auditing, esophageal surgery, esophagectomy, esophagogastric cancer, esophagogastric surgery, gastrectomy, gastric surgery, hospital comparison, Outcome indicators, quality indicators, Quality of care, short, Short term indicators, term outcomes, upper gi surgery

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Society increasingly demands information on the quality of care in hospitals. One of the main principles of improving quality of care is monitoring and benchmarking performance of hospitals. To evaluate the quality of care, quality indicators for many diseases have been defined. These indicators can be subdivided into structure, process, and outcome indicators.[1]

To monitor the quality of esophageal and gastric cancer surgery, the Dutch Upper gastrointestinal Cancer Audit (DUCA)

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has developed a set of indicators. Benchmarked information on these indicators is weekly reported to all participating hospitals.[2] To limit registration burden, long-term follow-up including survival is not registered in most clinical audits. Short-term outcomes are currently used for feedback to facilitate continuous quality improvement in the hospitals.[3] Some of these short-term outcome indicators concern direct quality of care, for example, complications. Other short-term indicators are used because they are expected to be associated with long-term outcomes, for example, ''complete resection of the tumor.'' In clinical auditing, composite measures may help to ease the interpretation of outcomes, as it is not needed to evaluate all separate outcomes. In the DUCA, the composite measure ''a complicated postoperative course'' is used to evaluate outcomes on complications. This measure is defined as a postoperative complication in combination with a prolonged hospital stay (>21 days), reintervention, or death.[2] Another composite measure that is used in the DUCA is ''Textbook outcome.''[4] ''Textbook outcome'' consists of different parameters, all of which are short-term outcomes. It describes the number of patients in whom all desired outcomes are achieved, including a pathological complete tumor resection (pR0), retrieval of at least 15 lymph nodes, and no complicated postoperative course.

If outcomes on short-term quality indicators are associated with the ultimate goal of cancer treatment that is, long-term survival, this will accentuate the importance of using these outcome indicators in national audits. The aim of this study was to investigate the association of the short-term outcome indicators with long-term survival in a national cohort of patients with esophageal or gastric cancer who underwent resection with curative intent.

METHODS

For this national cohort study, data were retrieved from the DUCA. This surgical audit was initiated in 2011. It is mandatory for hospitals performing esophagogastric cancer surgery to register all patients with esophageal or gastric cancer undergoing surgery with the intent of resection. All hospitals in the Netherlands register data on the patient, tumor, and treatment characteristics, pathology, and 30-day morbidity, and 30-day/in-hospital mortality. Surgeons have the responsibility for completeness and validity of the data collection and registration. To limit the registration burden, registration of postoperative outcomes is limited to 30 days after surgery and/or the duration of hospital stay. Validation of completeness and accuracy of this data registration in the DUCA dataset has been performed by external data verification. The completeness of the DUCA database is estimated at 97.8% and 96.2% for all primary esophageal and gastric cancer resections, respectively. The accuracy of data was estimated to be 94% to 99.8% for morbidity and pathological outcomes.[2]

Patient Selection

Included in this study were all patients with esophageal or gastric cancer who underwent surgery with the intent of resection registered in the DUCA between January 2011 and December 2016. Patients were excluded if essential elements of the registration were unknown including the intent of surgery (curative/palliative/prophylactic), date of birth, survival status at 30 days after surgery, and date of discharge (in case of a hospital stay >30 days). Also, patients with a reported date of death in the Vektis dataset that lies before the date of surgery as reported in the DUCA dataset were excluded (n = 2). To identify best-performing hospitals and underperforming hospitals, patients operated between January 2015 and December 2018 were included because this composite measure was introduced in the DUCA in 2015.

Combined Datasets

To provide information regarding overall survival, the data of the DUCA were combined with a dataset provided by Vektis. Vektis is a national health care insurance database including all medical treatments paid for by Dutch insurance companies.[5] Date of death of all deceased patients is included in this database since health care insurance ends when the patient dies. Health care insurance is obligatory in the Netherlands and therefore almost all Dutch inhabitants (99%) are registered in the Vektis database.[6]

The combining of datasets was performed by a third trusted party to guarantee the privacy of patients: Medical Research Data Management (MRDM). MRDM is *NEN 7510:2011* and *ISO 27001:2013* certified and complies to privacy regulations in the Netherlands.[7] The combining of data was done in September 2017. As the Vektis dataset contains only deceased patients, it had to be assumed that all patients in the DUCA without a match were alive at the time that data were extracted from the Vektis database (date of the last follow-up: 1st of September 2017). For all patients, the interval (in months) from the date of surgery to the date of death or date of the last follow-up was calculated. The actual date-of-death-variable was deleted in the dataset to guarantee the privacy of all patients. It was not possible to differentiate between patients who did not match because they were not deceased and those that did not match because the matching was technically not possible. Therefore, validation tests of the survival information in the combined dataset were performed.

Validation of the Combined Dataset

The validation was performed with 2 patient cohorts. Validation cohort 1: 30-day mortality data: In the DUCA the 30-day mortality status is registered, including date of death if a patient died within 30 days or during hospital admission. All patients who had deceased within 30 days or during hospital admission were included in the primary validation cohort. A comparison was made between the date of death as registered by DUCA and by Vektis.

Validation cohort 2: Snapshot study. From a recent snapshot study with DUCA data, long-term outcomes of patients with additional pancreatic resection for gastric cancer were added to the DUCA dataset.[8] In this study, participating hospitals provided follow-up information regarding recurrence and survival of 54 patients. These data were compared with data registered by Vektis.

The main outcome in the validation was the percentage of patients with a discrepancy in survival status, that is, patients assumed to be alive in the combined dataset, whereas those have been registered deceased in the data of the validation cohort.

Primary Outcomes and Subgroups

The primary outcomes were overall survival and conditional survival (under the condition of surviving the first postoperative 30 days). To examine whether short-term outcomes were associated with long-term outcomes, stratified survival analyses were performed according to outcomes used in the DUCA: ''textbook outcome,'' ''complicated postoperative course,'' and ''pR0.'' For all survival analyses, only patients with curative intent of surgery, as preoperatively defined by the surgeon, were included.

To evaluate variation in hospital outcomes on ''textbook outcome,'' subgroups of patients treated in hospitals with different annual volumes were compared (0–19, 20–39, and ≥40 resections/year). Also, variation between individual hospitals was evaluated; to identify best-performing hospitals and underperforming hospitals, the percentage ''textbook outcome'' in every hospital was compared to the national mean. A hospital with a significantly higher percentage on textbook outcome was classified as ''best performer,'' and a

hospital with a significantly lower percentage on textbook outcome was classified as ''underperformer.''

Definitions

''Textbook outcome'' in the DUCA is defined as a radical resection according to the surgeon at the end of the operation, no intraoperative complications, a pR0 resection with at least 15 lymph nodes retrieved and examined, no severe postoperative complication, no reintervention, no readmission to the intensive care unit or medium-care unit, no prolonged hospital stay (21 days or less), no postoperative mortality, and no hospital readmission.[4] A ''complicated postoperative course'' in the DUCA is defined as a complication in combination with a hospital stay >21 days, any reintervention or death during hospitalization or within 30 days postoperative.[2] Pathological complete tumor resection (pR0) was defined as microscopic tumor-negative resection margins as reported by the pathologist. Incomplete resection was defined as tumor-positive resection margins as reported by the pathologist (pR1 or pR2).[9]

Statistical Analysis

In all analyses, patients with esophageal cancer (including gastroesophageal junction tumors) or gastric cancer were analyzed separately. Patient, tumor, and treatment characteristics were analyzed using descriptive statistics. Overall survival was reported using 1, 2, and 3-year survival rates and evaluated using the Kaplan–Meier method. To evaluate the independent association of ''textbook outcome,'' ''complicated postoperative course,'' ''pR0'' with overall survival and conditional survival, a multivariable Cox regression model was compiled. To assess confounding, the following factors were analyzed (based on the literature): sex, age, preoperative weight loss, body mass index, location of the tumor, American Society of Anesthesiologists score, Charlson comorbidity score,[10] pathological tumor stage according to the TNM-7 classifications, pathological T- and N-stage, clinical M-category, histological subtype of the tumor, differentiation grade, and, surgical procedure. All factors with a P value <0.10 in the univariable Cox regression analyses were included in the multivariable model to adjust for confounding.

Missing items were analyzed in a separate group if exceeding 5%. For all analyses, statistical significance was defined as $P < 0.05$. All analyses were performed with SPSS version 24 (for Mac, IBM, Armonk, NY) and R studio version 1.1.456 (for Mac, RStudio, Inc).

RESULTS

A total of 7357 patients were included, 4414 patients with esophageal cancer and 2943 patients with gastric cancer (Supplementary Fig. 1; http://links.lww.com/SLA/B783).

Validation of the Dataset

In the first validation cohort, in 15 of 249 patients (6.0%) a discrepancy in survival status was found between the combined dataset and data of the validation cohort (Supplementary Fig. 1; http://links.lww.com/SLA/B783). In the second validation cohort in 2 of 39 patients (5.1%) a discrepancy was found.

Patient Cohort

A curative intent of resection was registered for 4399 (99.7%) esophageal cancer patients and 2769 (94%) gastric cancer patients. Basic and treatment characteristics are shown in Tables 1 and 2. Of all patients with esophageal cancer who underwent resection with curative intent, 33% had a textbook outcome, 30% had a complicated postoperative course, and 93% had a pR0 resection. Of all patients with gastric cancer who underwent resection with curative intent, 35% had a textbook outcome, 19% had a complicated postoperative course, and 87% had a pR0 resection (Table 3).

Survival of Esophageal Cancer Patients

The 1-, 2-, and 3-year overall survival of patients who underwent a curative resection was 76%, 62%, and 54%, respectively (Fig. 1A). Patients with a textbook outcome had 1-, 2-, and 3-year overall survival rates of 85%, 70%, and 62%, respectively, versus 72%, 58%, and 50% for patients with no textbook outcome, respectively. The conditional survival curves are shown in Figure 1B. A textbook outcome was independently associated with longer overall survival {hazard ratio (HR): 0.68 [95% confidence interval (CI), 0.61–0.76]} and longer conditional survival {HR: 0.72 [95% CI, 0.65–0.81]} (Table 3). The conditional survival curves of patients with a pR0 versus pR1/pR2 resection are shown *in* supplementary Figure 2A, http://links.lww.com/SLA/B722. The association of a complicated postoperative course and pR0 resection with survival are shown in Table 3. A sensitivity analysis including only patients treated with neoadjuvant chemo radio therapy did not significantly change results.

Survival of Gastric Cancer Patients

The 1-, 2-, and 3-year overall survival of the patients who underwent a curative resection was 71%, 56%, and 49%, respectively (Fig. 1A). Patients with a textbook outcome had 1-, 2-, and 3-year overall survival rates of 85%, 70%, and 64%, respectively, versus 64%, 49%, and 42% for patients with no textbook outcome, respectively. The conditional survival curves are shown in Figure 1C. A textbook outcome was independently associated with longer overall survival {HR: 0.62 [95% CI, 0.54–0.71]} and longer conditional survival {HR: 0.69 [95% CI, 0.60–0.79]} (Table 3). The conditional survival curves of patients with pR0 versus pR1/pR2 are shown in supplementary Figure 2B, http://links.lww.com/SLA/B722. The association of a complicated postoperative course and pR0 resection with survival are shown in Table 3. A sensitivity analysis including only patients not treated with neoadjuvant therapy did not significantly change results.

Hospital Variation

''Textbook outcome'' was achieved in 15% of patients who underwent surgery in hospitals performing 0 to 19 esophagectomies per year [total number of patients (n) = 102], in 21% of patients in hospitals performing 20 to 39 esophagectomies per year (n = 938), and 37% of patients in hospitals performing >40 esophagectomies per year (n = 3374) ($P \leq 0.001$). For gastric cancer, ''textbook outcome'' was achieved in 23% of patients who underwent surgery in hospitals performing 0 to 19 gastrectomies per year (n = 483), 29% in hospitals performing 20 to 39 gastrectomies per year (n = 567), and 27% in hospitals performing >40 gastrectomies per year (n = 1896) ($P \leq 0.001$). In the time period 2015 to 2018, for esophagectomies, 4 hospitals could be identified as best performers and 4 hospitals as underperformers. Textbook outcome was achieved in 44% and 26% of patients in the best-performing and underperforming hospitals, respectively. For gastrectomies, 3 hospitals could be identified as best performers and 3 hospitals as underperformers. Textbook outcome was achieved in 48% and 32% of patients in the best-performing and underperforming hospitals, respectively.

DISCUSSION

This study was performed to assess the association between short-term outcomes and long-term survival in a national cohort of patients with esophageal or gastric cancer who underwent resection with curative intent. It was shown that the composite measure

TABLE 1. Basic Characteristics

	Esophageal Cancer		Gastric Cancer	
	n	%	n	%
Total	4414		2943	
Sex				
Male	3422	78%	1838	63%
Female	991	22%	1102	37%
Unknown	1	0%	3	0%
Age, y				
≤40	35	1%	69	2%
41–50	264	6%	171	6%
51–60	968	22%	418	14%
61–70	1927	44%	822	28%
71–80	1114	25%	1050	36%
>80	106	2%	413	14%
Body mass index				
<18.5	124	3%	116	4%
18.5–25	1848	42%	1367	46%
25–30	1695	38%	992	34%
30+	697	16%	371	13%
Unknown	50	1%	97	3%
ASA score				
I	737	17%	399	14%
II	2633	60%	1616	55%
III	994	23%	863	29%
IV	20	1%	39	1%
V	0	0%	1	0%
Unknown	23	1%	18	1%
Charlson Comorbidity score				
0	2098	48%	1282	44%
1	1124	26%	677	23%
2+	1192	27%	984	33%
Comorbidities				
Myocardial infarction	287	7%	231	8%
Congestive heart failure	47	1%	70	2%
Chronic pulmonary disease	820	19%	495	17%
Peripheral vascular disease	177	4%	130	4%
Diabetes mellitus (uncomplicated)	647	15%	474	16%
Diabetes mellitus (end-organ damage)	28	4%	14	3%
Moderate to severe renal disease	50	1%	103	4%
Timing of surgery				
Elective	4388	100%	2789	95%
Urgent	11	0%	111	4%
Emergency	9	0%	41	1%
Unknown	2	0%	1	0%
Neoadjuvant therapy				
No	419	10%	1368	47%
Chemotherapy	359	8%	1509	52%
Chemoradiotherapy	3612	82%	47	2%
Radiotherapy	11	0%	2	0%
Unknown	1	0%	2	0%
Location tumor: esophagus				
Cervical (C15.0)	9	0%	0	0%
Proximal (C15.3)	45	1%	0	0%
Mid (C15.4)	529	12%	0	0%
Distal (C15.5)	2681	61%	0	0%
Gastroesophageal junction (C16.0)	1120	25%	0	0%
Location tumor: stomach				
Fundus (C16.1)	0	0%	248	8%
Corpus (C16.2)	0	0%	870	30%
Antrum (C16.3)	0	0%	1133	39%
Pylorus (C16.4)	0	0%	260	9%
Total STOMACH	0	0%	184	6%
Rest stomach/anastomosis	0	0%	133	5%
Unknown (stomach)	28	1%	55	2%
Missing	2	0%	60	2%

ASA indicates American Society of Anesthesiologists.

TABLE 2. Treatment Characteristics

	Esophageal Cancer		Gastric Cancer	
	n	%	n	%
Total	4414		2943	
Pathological tumor stage				
pT0-2	2452	56%	937	32%
pT3	1561	35%	1005	34%
pT4	59	1%	608	21%
Missing	342	8%	393	13%
Pathological node stage				
pN−	2481	56%	1126	38%
pN+	1607	36%	1403	48%
pNx	16	0%	57	2%
Missing	310	7%	357	12%
Pathological metastases stage				
pM−	4071	97%	2248	88%
pM+	58	1%	183	7%
Not applicable	12	0%	46	2%
pMx	62	2%	66	3%
Surgical approach				
Open	1814	41%	1901	65%
MI	2595	59%	1037	35%
Type of procedure				
Transhiatal esophagectomy	1349	31%	21	1%
Transthoracic esophagectomy	2780	63%	19	1%
Total gastric resection	98	2%	1072	37%
Partial gastric resection	7	0%	1490	51%
Bypass (gastroenterostomy)	2	0%	110	4%
Exploratory only open	122	3%	192	7%
Exploratory only MI	38	1%	2	0%
Other	11	0%	33	1%
Site of anastomosis				
Intrathoracic	1401	32%	183	6%
Neck	2703	61%	23	1%
Abdomen	57	1%	2294	78%
Other/none	253	6%	443	15%
Conduit/reconstruction				
Stomach	4055	96%	54	2%
Colon	24	1%	4	0%
Small bowel	5	0%	40	2%
Esophagojejunostomy (Roux-Y)	90	2%	1054	41%
Gastroenterostomy (BII or Roux-Y)	12	0%	1365	53%
Other/none	24	1%	76	3%
Intent of resection preoperative				
Palliative	5	0%	120	4%
Prophylactic	5	0%	14	1%
Unknown	3	0%	39	1%
Curative	4399	100%	2769	94%
Intent end-of-surgery				
No resection	163		246	
Curative, macroscopic radical	4222		2445	
Palliative, tumor left behind	12		74	
Prophylactic	2		4	

''textbook outcome'' was associated with longer overall survival and conditional survival. Separately, an ''uncomplicated postoperative course'' and ''complete tumor resection (pR0)'' were also associated with longer overall and conditional survival. This study showed that it was possible to identify best-performing hospitals and underperforming hospitals based on ''textbook outcome.''

The results of this national cohort study are in line with findings of previous research. It is generally known that complete tumor resection (pR0) is associated with longer survival,[11–17] and recently, in a single-center cohort study, ''textbook outcome'' was found to be associated with longer survival.[18] This single center was a tertiary hospital, which might not represent the ''real world'' situation. In the present study, the association with long-term outcomes is confirmed with data of a ''real world'' cohort.

For patients with postoperative complications, it is known that these have worse short-term outcomes, that is, lower postoperative quality of life and higher costs.[19,20] However, there is inconclusive evidence that postoperative complications are associated with long-term survival. In the present study, the composite measure ''a postoperative complicated course'' was associated with worse long-term outcomes, even after adjustment for several confounding factors.

TABLE 3. Multivariable Cox Regression Analyses, Multiple Models Evaluating the Independent Association of Short-term Outcomes With Overall Survival and Conditional Survival (Under the Condition of Surviving the First Postoperative 30 Days

Esophageal cancer

Each outcome is adjusted for: sex, age, Charlson comorbidity score, American Society of Anesthesiologists, body mass index, weight loss preoperatively, location tumor, pTNM stage, pT-stage, pN-stage, cM-category, histological subtype, differentiation of the tumor, and surgical procedure.

	n	*P*	HR	95% CI	
Association short-term outcomes with overall survival	4110				
Textbook outcome	1443 (33%)	<0.001	0.68	0.61	0.76
Complicated postoperative course	1310 (30%)	<0.001	1.54	1.39	1.70
pR0	3933 (93%)	<0.001	0.75	0.63	0.89
Association short-term outcomes with conditional survival	4110				
Textbook outcome		<0.001	0.72	0.65	0.81
Complicated postoperative course		<0.001	1.36	1.22	1.51
pR0		0.003	0.77	0.64	0.92

Gastric cancer

Each outcome is adjusted for: sex, age, Charlson comorbidity score, American Society of Anesthesiologists, body mass index, weight loss preoperatively, location tumor, pTNM stage, pT-stage, pN-stage, cM-category, histological subtype, and differentiation of the tumor.

	n	*P*	HR	95% CI	
Association short-term outcomes with overall survival	2382				
Textbook outcome	975 (35%)	<0.001	0.62	0.54	0.71
Complicated postoperative course	533 (19%)	<0.001	1.91	1.67	2.20
pR0	2169 (87%)	<0.001	0.69	0.58	0.82
Association short-term outcomes with conditional survival	2276				
Textbook outcome		<0.001	0.67	0.59	0.77
Complicated postoperative course		<0.001	1.51	1.29	1.77
pR0		<0.001	0.67	0.56	0.80

In the Netherlands, the quality indicators evaluated in this study are currently used in the DUCA. ''Textbook outcome,'' ''complicated postoperative course,'' and ''pR0'' were already considered valuable by patient federations, healthcare insurance companies, and the scientific committee of the DUCA. The results of this study might accentuate the value of these indicators for use in clinical auditing.

The outcome indicators of the DUCA contain only information on the postoperative period until 30 days and during the initial hospital admission. There are 2 major reasons not to include long-term outcome indicators in the DUCA. A first reason for not using long-term outcomes in the DUCA is to limit the registration burden. The second reason for not using long-term outcomes may be even more important. For control and continuous improvement of processes, the Plan-Do-Check-Act cycle is often used.[21] For efficient quality improvement, a short feedback loop is essential. For long-term outcomes, the Plan-Do-Check-Act method is less effective and efficient as it may take up to 1 to 2 years to evaluate these long-term outcomes. For example, when the percentage of patients who experience anastomotic leakage is used as a quality indicator, a short feedback loop may help surgical teams noticing a high percentage of anastomotic leakage on time. Appropriate measures can be taken (eg, team evaluation, surgical training, or proctoring). Subsequently, the results of this intervention can then also be analyzed in the short term. When using long-term outcomes, deviating outcomes might be noticed too late, interventions might be started too late, and the results after an intervention might be announced too late. The present study provides additional evidence that short-term outcome indicators may be a proxy for long-term outcomes and this result may highlight the importance of the use of these outcomes.

Hospital outcomes on percentage ''complicated postoperative course'' and ''complete tumor resection'' are open to the public. The primary goal of transparency is to stimulate quality improvement initiatives in underperforming hospitals. Second, patients can use this information to choose between hospitals. Selecting good-performing hospitals by patients may improve outcomes on a nationwide basis. The national outcomes on the DUCA indicators suggest that performance on short-term indicators could be improved. This study showed that in patients that are operated on with curative intent, the percentage of patients with a ''textbook outcome'' in the DUCA cohort was only 33% for esophageal cancer and 35% for gastric cancer, respectively. A ''complicated postoperative course'' occurred in 30% of esophageal cancer patients and 19% of gastric cancer patients. Complete tumor resection was achieved in 93% of esophageal cancer patients and 87% of gastric cancer patients.

Because of the transparency of DUCA indicators, it was already known that the outcomes of ''complicated postoperative course'' and ''complete tumor resection'' varied between individual hospitals.[22] In this study also variety in hospital outcomes on ''textbook outcome'' was shown. High annual volume hospitals had higher percentages of ''textbook outcome'' after both esophagectomy and gastrectomy, and best-performing hospitals and underperforming hospitals could be identified. Taken together the variation between hospitals and the association of these outcomes with survival may underline the importance of the use of these indicators in national audits. These indicators might be an important instrument to improve the quality of care on a national level.

In previous studies, it has been suggested that the relationship between complications and survival may not be causal. Patients with comorbidities or more severe disease may be at higher risk for complications but may also die sooner because of comorbidities or more severe disease. However, some other studies suggest that secondary disturbance of the immune system owing to the presence of perioperative complications may lead to an early recurrence.[23–26] In this study, it was attempted to adjust for confounding with multivariable analysis. However, residual confounding could have been present. For more accurate assessment of causality, data on

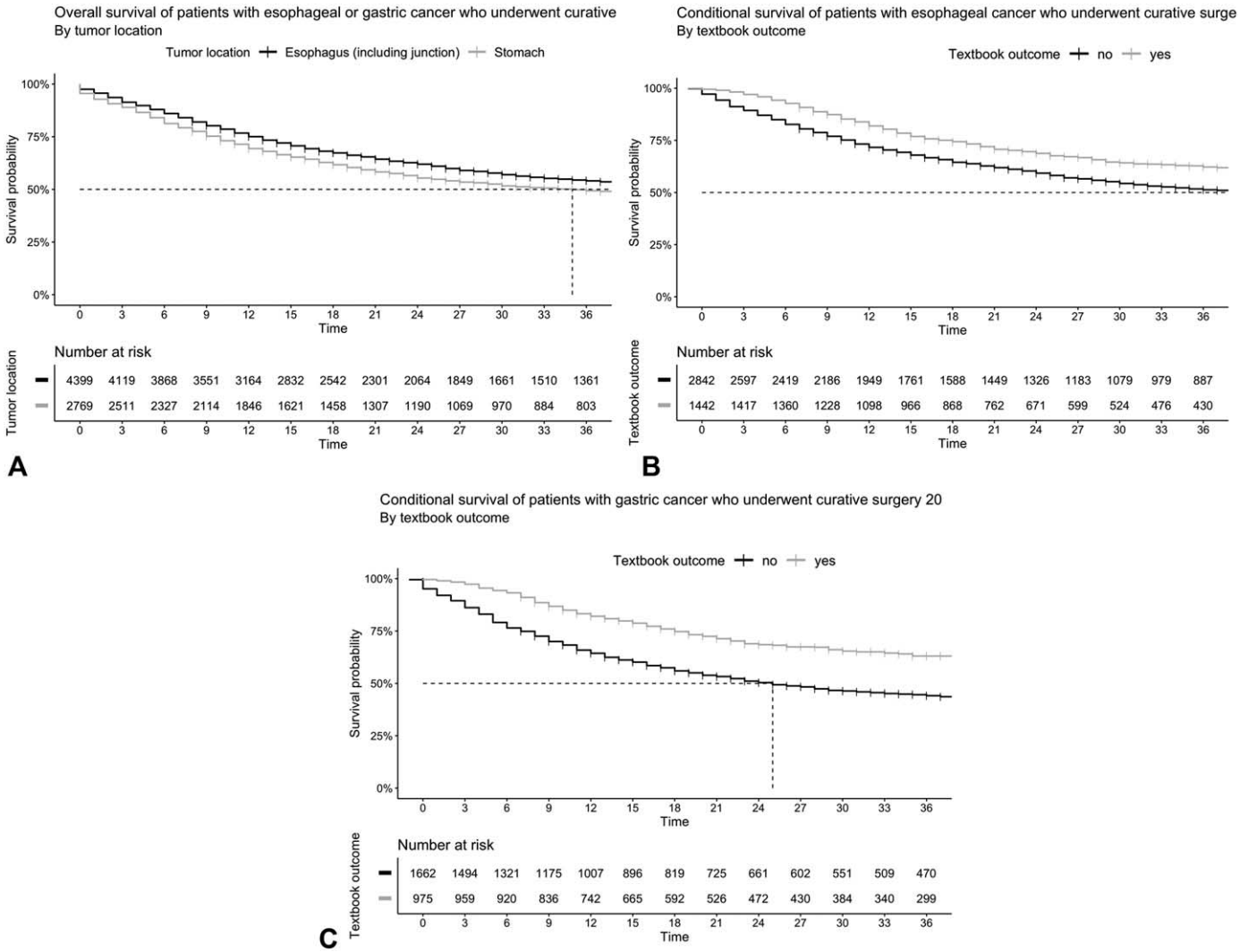

FIGURE 1. (A) Overall survival of esophageal and gastric cancer of patients who underwent curative surgery. (B) Conditional survival (under the condition of surviving the first postoperative 30 days) of patients who underwent curative surgery for esophageal cancer and whether or not had a 'textbook outcome. (C) Conditional survival (under the condition of surviving the first postoperative 30 days) of patients who underwent curative surgery for gastric cancer and whether or not had a ''textbook outcome.''

disease-specific survival are needed. Unfortunately, those were lacking in the used datasets.

A limitation of this study was the validity of the combined dataset. The survival information of a nationwide database was combined with the data of the DUCA. Based on the validation tests with 2 cohorts in this study, the accuracy of survival status in the combined dataset is estimated to be 94% to 95% based on discrepancies in 5.1% to 6.0% of patients in the test cohorts. The most likely reason for the discrepancy between test cohort data and the combined dataset is that matching of patients from both datasets failed. The citizen's service number (BSN) was used to match patients. However, when by accident an incorrect BSN was registered in the DUCA dataset, matching was not possible. Another reason for the discrepancy could be that patients were missing in the Vektis dataset, for example, because they had no health care insurance or because they have been migrated. In this study, it was assumed that patients with a discrepancy in survival status were randomly divided between the stratified analyses on outcomes executed in this study. However, registration of incorrect BSN might not be randomly divided between hospitals, and therefore it is not excluded that this dataset has influenced the analysis on association of hospital performance and survival.

Future Perspectives and Conclusions

This study showed an association of the composite measure ''a complicated postoperative course'' with long-term survival. Further research is needed to assess the association of different kinds of complications with long-term survival and to assess the association of complications with disease-specific survival. The DUCA group aims to create a dataset with fair survival information to also support hospital comparisons and more reliable survival rates.

With these findings, it can be concluded that the achievement of good short-term outcomes such as ''textbook outcome'' is valuable for long-term survival after surgery for both esophageal and

gastric cancer. These outcomes should be used in clinical auditing to improve outcomes of clinical care in these patients. With the Plan-Do-Check-Act cycle, the outcomes of every hospital need to be evaluated on a continuous base to improve the quality of care.

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DISCUSSANTS

John V. Reynolds (Dublin, Ireland):

Thank you, congratulations on a fine article and presentation. I have the following questions:

First, please, elaborate on what is novel? As you know there are publications, including some from DUCA, highlighting the predictive power of ''textbook outcome'' and ''postoperative complications,'' and we have known about the relevance of the R margin for years now. So, what is new in this study?

Second, your most recent article in the *Annals of Surgery*, which covers the period between 2016 and 2017, uses the Clavien-Dindo severity classification and Esophageal Complications Consensus Group definitions. Of course, this is a welcome addition to your datasets, but it begs the question of whether this present study is critically flawed from the lack of such strictly defined criteria for short-term outcomes and the use of composite, rather than specific, data points, in addition to survival data abstracted from the separate National Registry?

Third, in your opinion, why is there a clearer separation in outcomes for esophageal cancer and gastric cancer between low- and high-volume centers?

Fourth, how is audit data such as this applied toward quality improvement, standardization, or greater centralization within the Netherlands?

Finally, why do operative complications impact cancer outcomes? Are there biological mechanisms, or does it reflect disease and patient complexity?

Response From Leonie R. van der Werf (Rotterdam, The Netherlands):

Thank you very much for these important questions. Of course, it is important that this article further informs what we know already. You are right, in that there are 2 previous publications from the Netherlands describing textbook outcome. The first was Busweiler et al. She only described the outcome and the results within the Netherlands, but did not include survival rate because the combined dataset wasn't there when she wrote it. The second article described the association of textbook outcome with survival, but only from 1 center, which is a tertiary cancer care center. We believe that this does not reflect real world data. We believe that ours reflects real world data with the national dataset. We think that it's important to evaluate hospital outcome on the textbook outcome, and therefore, we compared outcomes of hospitals in the manuscript. There was hospital variation in the recent cohort. For esophageal cancer, there were 4 hospitals, which were best performers, and 4 hospitals, which were underperformers. For gastric cancer, the ratio was 3:3. When this outcome was introduced, it was considered to be new, as it was before the centralization of esophageal and gastric cancer care. We thought that this outcome was perhaps improved and that there weren't any outliers anymore; however, when we evaluated the data from 2015 and 2018, we saw outliers. So, that underlines the use of this outcome for clinical auditing in this national audit. This is what we believe to be new in this study.

Regarding your second question about the international standardized outcome set, I think it indeed improved the quality

of the national dataset, but we don't have the survival information. So, we couldn't answer the question in this study with the recent data. From 2016, we used the international definitions, and the Clavien-Dindo classification was scored in the previous cohort as well. However, we chose the complicated postoperative course because it includes the hospital stay, and we believe that the postoperative hospital stay may reflect a combination of several minor complications leading to a prolonged hospital stay. Since this affects patient' quality of life as well as the cost of care, we believe that this outcome may be more important for clinical auditing. However, for the quality of the dataset, the new dataset is better, as you said.

Third, we evaluated the percentages of textbook outcome for esophageal and gastric cancer between different hospital volumes. We compared groups of <20 resections a year, 20 to 40 resections a year, and ≥ 40 resections a year. For esophageal cancer, we noted percentages of textbook outcome as 15%, 21% and 37%, which is a big difference between volumes. For gastric cancer, we saw 23%, 29%, and 27%, which is less of a difference. We believe that this is because esophageal cancer care is more centralized and there are more very high-volume hospitals. Based on previous studies, we know that a high hospital volume is associated with more lymph node retrieval in esophageal cancer, which is one of the criteria. For gastric cancer, we know that a high hospital volume is associated with less R+ resections, which is also a criterion.

Sheraz R. Markar (London, United Kingdom):

Thank you very much. This was an excellent presentation, which was very elegantly described in a nice article. I just have 1 question with a point, which I think Prof. Reynolds was perhaps alluding to. Are you not, with your textbook outcome, overcomplicating the issue? If you look at your factors, resection margin status appears to be the greatest predictor of overall survival. By including your textbook outcomes, which comprises of all of these metrics, you're actually overcomplicating the issue.

Also, do you think that there was a wider implication to your study? You talked about the difference in hospital volume, but do you think that there is the potential to use some of these textbook outcomes as quality metrics before inclusion in trials, for example? I know that you do a lot of trials in the Netherlands. Is this something that is being thought about or considered?

Response From Leonie R. van der Werf (Rotterdam, The Netherlands):

I think that it's important to use textbook outcome as a composite measure for overall quality monitoring. However, if you want to improve your outcomes, as your hospital has a low percentage of textbook outcomes, then it's important to go through the specific outcomes, such as anastomotic leakage. In the Netherlands, there are national meetings to evaluate specific outcomes. Last year, we had the first one, and the second one was held last month. In these meetings, all of the surgeons publish their own results, and discuss and evaluate results of the whole country, with the aim of improving the specific outcomes, which then might lead to an improved textbook outcome in the long-term.

Lastly, it's not considered for trials. I think that it is important for policymakers and patients, but for trials, I think that specific outcomes are the best.

Peter A. Lodge (Leeds, United Kingdom):

Congratulations on a nice presentation. In colorectal metastases liver surgery, we've correlated infective complications with a much worse long-term outcome. You have a lot of patients. I was wondering whether you can look at specific complications like that, or do you not have the data available?

Response From Leonie R. van der Werf (Rotterdam, The Netherlands):

This is a very good suggestion. We didn't evaluate it in this study. However, we could do it with the data that we have.