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Postoperative Complications Do Not Affect Long-Term Outcome in Esophageal Cancer Patients

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Abstract
Background As esophagectomy is associated with a considerable complication rate, the aim of this study was to assess the impact of postoperative complications and neoadjuvant treatment on long-term outcome of adenocarcinoma (EAC) and squamous cell carcinoma (SCC) patients.
Methods Altogether, 134 patients undergoing transthoracic esophagectomy between 2005 and 2010 with intrathoracic stapler anastomosis were included in the study. Postoperative complications were allocated into three main categories: overall complications, acute anastomotic insufficiency, and pulmonary complications. Data were collected prospectively and reviewed retrospectively for the purpose of this study.
Results SCC patients suffered significantly more often from overall and pulmonary complications (SCC vs. EAC: overall complications 67 vs. 45 %, $p = 0.044$; pulmonary complications 56 vs. 34 %, $p = 0.049$). The anastomotic insufficiency rates did not differ significantly (SCC 11%, EAC 15%, $p = 0.69$). Long-term survival of EAC and SCC patients was not affected by perioperative (overall/pulmonary) complications or by the occurrence of anastomotic insufficiency. Also, neoadjuvant treatment did not influence the incidence of complications or long-term survival.
Conclusions This is the first time the patient population of a center experienced with esophageal cancer surgery was assessed for the occurrence of general and esophageal cancer surgery-specific perioperative complications. Our results indicated that these complications did not affect long-term survival of EAC and SCC patients. Our data support the hypothesis that neoadjuvant treatment might not affect the incidence of perioperative complications or long-term survival after treatment of these tumor subtypes.

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Introduction

The prognoses of adenocarcinoma (EAC) and squamous cell carcinoma (SCC) of the esophagus are poor, with an overall 5-year survival rate of 10–13 % [1]. Surgery remains the most important treatment option for patients with early or locally advanced but not metastasized disease. The 5-year survival rate following esophagectomy is approximately 15–40 % [2–4].

Owing to improvements in the management of esophageal cancer patients, the early postoperative mortality and morbidity has decreased in recent years [5, 6], but surgical complications still occur in approximately 10–27 % of cases [7]. Although most authors agree that postoperative complications affect perioperative mortality, the possible long-term impact on overall survival remains unclear [8–12]. Furthermore, the impact of neoadjuvant treatment—which was only recently demonstrated to improve survival in case of a major response [13–18]—on perioperative morbidity is still controversial [9, 10, 14, 19, 20]. However, even as many recent publications included major histologic entities (EAC and SCC) [8, 11, 12, 21, 22] or different surgical approaches [10, 23, 24] in their analysis, proper comparison between complications and evaluation of a potential impact of perioperative complications on long-term outcome remains difficult.

The aim of the current study was to contribute to the discussion regarding the impact of postoperative complications on long-term outcomes by providing a detailed

comparison of (overall/pulmonary) complications and anastomotic insufficiency for both tumor types (separately) while comparing only transthoracic esophagectomy with intrathoracic stapler anastomosis at a single, experienced, high-volume center.

Material and methods

Patient selection

Between January 2005 and December 2010, a total of 176 esophageal resections had been performed at our Department of General and Visceral Surgery at the University of Muenster. Among that group, 134 consecutive patients were included in this study who underwent Ivor-Lewis esophagectomy for esophageal EAC ($n = 89$, 6 %) or SCC ($n = 45$, 3 %). Patients with other surgical approaches or diagnoses were excluded from the study to provide a study population that was as homogeneous as possible. Furthermore, patients who died during the hospital stay (in-hospital death) were also excluded as we intended to analyze the effect of complications on long-term outcome.

Clinical data were collected prospectively and then reviewed retrospectively for the current study. In all, 58 % of patients (SCC vs. EAC: 62 vs. 56 %) underwent neoadjuvant treatment consisting of combined radiochemotherapy (5-fluorouracil/cisplatin 50.4 Gy) (SCC) or chemotherapy alone (EAC). Based on the initial clinical and postoperative tumor stage, neoadjuvant-treated patients were allocated into three responder groups: complete responders (cR): ypT0 and ypN0; partial responders (pR): tumor or nodal down-staging in the histologic examination compared to the initial tumor stage; and nonresponders (NR): no change in, or even increased, tumor stage according to the histologic examination compared to the initial tumor stage.

Preoperative staging and evaluation of operability

The preoperative workup included a detailed medical history; physical examination; blood tests for renal/liver function and infection parameters; radiography of the chest; electrocardiography; and anesthesiology consultation. Further examinations were conducted as required (pulmonary function tests in 76 %, cardiac workup in 23 %). The preoperative tumor staging consisted routinely of upper endoscopy/biopsy, ultrasonography, and computed tomography/positron emission tomography (CT/PET-CT) of the chest/abdomen/pelvis to rule out distant metastases. In addition, bronchoscopy/eye-nose-throat consultations were held for 7 % to exclude bronchial invasion or involvement of the recurrent laryngeal nerve.

Standard surgical procedure and postoperative course

An Ivor-Lewis esophagectomy was performed in all 134 patients with en bloc two-field lymphadenectomy via a right transthoracic and abdominal approach. To restore intestinal continuity, a gastric conduit was formed. An end-to-side anastomosis was formed using a circular stapler and placed in the chest (posterior mediastinum). A gastric tube was inserted. The height of the anastomosis resulted from the tumor location (approximately 5 cm above the oral tumor margin). The chest was drained via a tube parallel to the gastric tube ending close to the anastomosis. Duration of surgery and the occurrence of intraoperative complications such as splenic laceration, bleeding from liver veins, left-sided pneumothorax, and lung tissue injury were assessed.

Postoperatively, patients were extubated immediately or at least within the first 12 h and transferred to the intensive care unit. Epidural analgesia was placed preoperatively and continued for the first days. At postoperative day (POD 1), the gastric tube was removed, and enteral nutrition (initially 400 ml drinking) was started with adaptation according to the clinical situation. Patients also received total parenteral nutrition until enteral nutrition was sufficient. The chest tube was removed with decreasing output after approximately 5–7 days. The anastomosis was not checked routinely. If anastomotic leakage was suspected, endoscopy was performed [25].

Postoperative complications

Postoperative complications were subdivided into two subgroups: overall complications and esophageal cancer surgery-specific complications. Overall complications were divided into major, minor, or no overall complications. For details regarding the respective complications that were included in the various categories see Table 1.

Esophageal cancer surgery-specific complications were assessed separately by establishing two additional categories: acute anastomotic insufficiency and pulmonary complications. The acute anastomotic insufficiency group included patients who presented with clinical deterioration, and examinations revealed anastomotic insufficiency with leakage. Allocation to this complication group was based on the clinical aspect—not on the need for operative re-intervention as both surgically and conservatively treated anastomotic insufficiencies were included. Patients with other anastomotic complications (e.g. later diagnosed fistula or minor mucosal necrosis of conduit without leakage) were excluded from this category of complications.

Pulmonary complications were divided into no, minor, and major pulmonary complications. For details regarding the respective complications that were included in these

Table 1 Postoperative complications

Complications	Overall ($n = 134$)		EAC ($n = 89$)		SCC ($n = 45$)	
	No.	%	No.	%	No.	%
Overall complications						
No complications	64	47.8	49	55.1	15	33.3
Minor complications	50	37.3	27	30.3	23	51.1
Pulmonary complications[a]	52	38.8	28	31.5	24	53.3
Cardiac arrhythmia (excluding MI)	23	17.2	13	14.6	10	22.2
Delirium	3	2.2	2	2.3	1	2.2
Surgical side infection/dehiscence	7	5.2	4	4.5	3	6.6
Postop. nerve palsy (plexus)	2	1.5	2	2.3	0	0
Postop. cholecystitis/hydrops	1	0.7	1	1.1	0	0
Deep vein thrombosis	1	0.7	0	0	1	2.2
Paresis of recurrent nerve (one-sided)	1	0.7	0	0	1	2.2
Major complications	21	15.7	14	15.7	7	15.6
Septic MOF[b]	5	3.7	2	2.3	3	6.6
Anastomotic bleeding	2	1.5	1	1.1	1	2.2
Overall anastomotic insufficiency/ fistula/necrosis	18	13.4	13	14.6	5	11.1
Myocardial infarction	4	2.9	1	1.1	3	6.6
Pulmonary embolism	2	1.5	1	1.1	1	2.2
Mediastinitis	1	0.7	0	0	1	2.2
Pleural empyema	1	0.7	0	0	1	2.2
ARDS (without MOF)	1	0.7	1	1.1	0	0
Anastomotic insufficiency	19	14.2	14	15.7	5	11.1
Pulmonary complications						
No complications	36	26.9	21	23.6	15	33.3
Minor complications	64	47.8	52	58.4	12	26.7
Pleural effusion	27	20.1	13	14.7	14	31.1
Respiratory depletion/insufficiency	13	9.7	7	7.9	6	13.3
Atelectasis	2	1.5	1	1.1	1	2.2
Bronchitis	3	2.2	1	1.1	2	4.4
Chylous leakage (no intervention)	3	2.2	1	1.1	2	4.4
Serothorax	1	0.7	0	0	1	2.2
Major complications	17	12.7	8	8.9	9	20.0
Pneumonia	8	5.9	6	6.7	2	4.4
Pneumothorax (with/without need of intervention)	10	5.6	5	5.6	5	11.1
Hematothorax	4	2.9	2	2.3	2	4.4
Fistula (e.g., bronchoesophageal, mediastinal)	5	3.7	1	1.1	4	8.8
Lung edema	4	3.4	3	3.4	1	2.2
Pulmonary embolism	0	0	0	0	1	2.2
Mediastinitis	0	0	0	0	2	4.4
Pleural empyema	0	0	0	0	0	0
ARDS (with/without MOF	2	2.3	2	2.3	0	0

Multiple answers per patient were permitted in this table. In these cases, patients were allocated into the "overall complication" and "pulmonary complication" groups according to the most severe complication

EAC esophageal adenocarcinoma, *SCC* esophageal squamous cell carcinoma, *ARDS* acute respiratory distress syndrome, *MI* myocardial infarction, *Postop.* postoperatively, *MOF* multiple organ failure

[a] Except pulmonary embolism, mediastinitis, pleural empyema, and ARDS (without MOF)

[b] Including septic ARDS

categories see Table 1. Respiratory complications were diagnosed by clinical suspicion in combination with adequate radiological examinations and laboratory tests. Additional bronchoscopy was performed to exclude or confirm the presence of a bronchopulmonary fistula.

In case of multiple complications, patients were allocated into an overall complication group or the pulmonary complication group according to the most severe complication. To meet concerns about the clinical relevance of our complicated classification system, we further compared

Table 2 Patients' characteristics in our study population

Characteristic	Overall ($n = 134$)		EAC ($n = 89$)		SCC ($n = 45$)	
	No.	%	No.	%	No.	%
Age (years), median and range	63 (38–89)	82.8	62 (38–89)	87.6	65 (39–76)	73.3
Male sex	111		78		33	24.4
Postop. staging					11	28.9
(y)pT0	23	17.2	12	13.5	13	11.1
(y)pT1	37	27.6	24	27.0	5	35.6
(y)pT2	33	24.6	28	31.5	16	0
(y)pT3	40	29.9	24	27.0	0	55.6
(y)pT4	1	0.7	1	1.1	25	42.2
(y)pN0	75	55.9	50	56.2	19	2.2
(y)pN1	51	38.1	32	36.0	1	0
(y)pN2	5	3.7	4	4.5	0	
(y)pN3	3	2.2	3	3.4	1.9 ± 3.2	
No. of positive LNs (mean ± STDEV)	1.9 ± 3.2		1.8 ± 2.9	5.6	19.2 ± 8.3	
No. of LNs examined (mean ± STDEV)	19.5 ± 9.2		19.8 ± 10.9			
M0	128	95.5	84	94.4	44	97.8
M1	6	4.5	5	5.6	1	2.2
R0	124	92.5	83	93.2	41	91.1
R1	8	6.0	6	6.7	2	4.4
R2	2	1.5	0	0	2	4.4
G1 or G1-2	4	3	2	2.2	2	4.4
G2 or G2-3	55	41	36	40.4	19	42.2
G3	52	38.8	39	43.8	13	28.9
Missing G stage	23	17.2	12	13.4	11	24.4
Duration of surgery (min) (median with range)	275 (149-502)		269 (149–502		286 (186–385)	
Intraoperative complications						
No	121	90.3	81	91.0	40	88.9
Yes	13	9.7	8	9.0	5	11.1
Neoadjuvant therapy	78	58.2	50	56.2		
Non-responder	20	25.6	13	26	5	25.0
Partial responder	42	53.8	28	56	28	62.2
Complete responder	16	20.5	9	18	7	25
In-hospital stay (median with range)	21 (10–86)		20 (11–86)		20 (10–72)	50 25

No. positive LNs number of positive lymph nodes in the resection specimen, *No. LN examined* number of lymph nodes examined in the resection specimen, *STDEV* standard deviation

our overall complication categories to the standardized classification of postoperative complications according to the Clavien–Dindo system [26].

Statistical analysis

All data were presented as means with standard deviations unless otherwise stated. Statistical analysis was performed by using χ^2/Fisher's exact test for categoric variables, Pearson's correlation for numeric variables, and one-way analysis of variance/Wilcoxon/Kruskal–Wallis test for comparison between numeric and categoric variables as appropriate. Survival rates were estimated using the Kaplan–Meier method. Statistical comparisons between groups were performed using the log-rank test. The Cox regression was used for survival analysis of numeric variables. Multivariate analysis (Cox procedure) was performed to prove independence of investigated variables. A value of $p \leq 0.05$ was considered statistically significant. All analyses were performed using SPSS 21.0 (SPSS, Chicago, IL, USA).

Table 3 Comparison between "overall complications" and the Clavien–Dindo classification (I–IV) for the entire patient population

		%			
Overall complications	0	I	II	III	IV
None ($n = 63$)	98.4	1.6	0	0	0
Minor ($n = 50$)	12	48	30	10	0
Major ($n = 21$)	0	0	0	52.4	47.6

Clavien–Dindo classification. *grade 0* no complication, *grade I* any deviation from the normal postoperative course without any particular therapy; *grade II* complications that require medical therapy, blood transfusion, parenteral nutrition, *grade III* complications that require surgical, endoscopic or radiological intervention, *grade IV* life-threatening complications that require intensive care therapy

Results

Patient characteristics

In total, 176 patients underwent esophageal resection in our center during the study period. The overall 30-day-mortality after esophagectomy was 6.8 %. After excluding patients who did not meet the inclusion criteria, we finally enrolled 134 patients in the study. Detailed characteristics of these 134 patients are shown in Table 2. Regarding the presented data, there were no significant differences between the two tumor entities.

Clinical significance of the "overall complication" classification

To evaluate whether the complication classification as established in our study has clinical significance, we compared our "overall complications" to the standardized classification of postoperative complications according to the Clavien–Dindo system [26]. We found a highly significant correlation between the distribution of overall complications and Clavien–Dindo complications grades 0 to IV for our entire patient population as well as for both histologic subtypes ($p < 0.001$) (Table 3).

Incidence of postoperative complications

Table 1 presents an overview of the postoperative complications in the entire patient population and the EAC and SCC subgroups. The incidence of anastomotic insufficiency did not differ significantly between the two histologic tumor types. However, SCC patients suffered significantly more often from overall and pulmonary complications ($p = 0.044$ and $p = 0.049$, respectively).

Impact of patients' characteristics on complications

For the entire patient population, the hospital length of stay (LOS) was positively correlated with overall complications ($p < 0.001$), pulmonary complications ($p = 0.003$), and occurrence of anastomotic insufficiency ($p < 0.001$). Additionally, a correlation between hospital LOS and the severity of the overall complications could be demonstrated. Female patients presented significantly fewer pulmonary complications ($p = 0.011$), and the number of positive lymph nodes was positively associated with increasing incidence of pulmonary complications ($p = 0.005$). All other patient characteristics did not correlate with the incidence of complications.

In EAC patients, the hospital LOS was again positively correlated with overall complications ($p < 0.001$), pulmonary complications ($p = 0.040$), and occurrence of anastomotic insufficiency ($p < 0.001$). Also, the number of positive lymph nodes was associated with increasing pulmonary complications ($p = 0.005$). None of the other factors correlated with the incidence of complications.

In SCC patients, postoperative hospital LOS was positively associated with overall complications ($p < 0.001$) and the appearance of anastomotic insufficiency ($p < 0.001$). The incidence of complications was not associated with any of the other factors, except for pulmonary complications, which t occurred significantly more often in female patients ($p = 0.013$).

Impact of patients' characteristics on survival

To evaluate the impact of demographics on survival, subgroups with fewer than three subjects were excluded from the analysis.

In the entire population, increasing T stage [(y)pT3 vs. (y)pT0: $p < 0.001$, (y)pT3 vs. (y)pT2: $p < 0.001$] and N stage [(y)pN2 vs. (y)pN0: $p < 0.001$, (y)pN2 vs. (y)pN1: $p = 0.035$] and a positive M stage ($p < 0.001$) negatively affected long-term overall survival. Also, increasing grades of differentiation were associated with worse short- and long-term survival ($p = 0.005$). Also, the number of positive lymph nodes was negatively correlated with survival ($p < 0.001$). Although neoadjuvant treatment (yes or no) did not affect survival ($p = 0.389$), complete responders showed a significantly better survival (no response vs. complete response cR: $p = 0.005$).

For EAC patients, T stage [(y)pT3 vs. (y)pT0: $p = 0.016$, (y)pT3 vs. (y)pT2: $p = 0.040$], N stage [(y)pN2 vs. (y)pN0: $p = 0.001$, (y)pN2 vs. (y)pN1: $p = 0.010$], and positive M stage ($p < 0.001$) negatively affected long-term survival. Also, the number of positive lymph nodes was negatively correlated with survival ($p = 0.001$). Neither neoadjuvant treatment nor a complete response had an effect on survival ($p = 0.606$, $p = 0.546$, respectively).

Table 4 Median survival after esophageal cancer surgery with respect to complications and treatment (months with range)

Complication category	Median overall survival [months]
Total population	38.1 (1.4–95.3)
Adenocarcinoma	
All patients	41.1 (2.6–95.3)
Primary surgery	55.4 (2.6–95.3)
Neoadjuvant therapy	34.2 (4.2–91.9)
Nonresponders	31.1 (14.6–73.0)
Partial responders	37.9 (4.2–91.9)
Complete responders	49.8 (13.1–76.6)
Overall, major	29.9 (3.3–91.9)
Overall, minor	51.2 (9.1–95.3)
Overall, none	33.2 (2.6–91.9)
Anastomotic insufficiency	33.7 (3.3–91.9)
No anastomotic insufficiency	42.8 (2.6–95.3)
Pulmonary, major	43.8 (9.1–81.2)
Pulmonary, minor	49.8 (13.3–95.3)
Pulmonary, none	32.9 (2.6–91.9)
Squamous cell carcinoma	
All patients	32.5 (1.4–85.2)
Primary surgery	30.6 (7.5–82.0)
Neoadjuvant therapy	33.8 (1.4–85.2)
Nonresponders	22.4 (4.5–73-0)
Partial responders	37.8 (1.4–91.9)
Complete responders	50.5 (13.1–83.6)
Overall, major	42.6 (3.4–51.8)
Overall, minor	26.2 (1.4–83.6)
Overall, none	30.6 (9.4–85.2)
Anastomotic insufficiency	40.04 (3.4–51.8)
No anastomotic insufficiency	30.0 (1.4–5.2)
Pulmonary, major	42.4 (3.4–83.6)
Pulmonary, minor	37.9 (1.4–82.0)
Pulmonary, none	29.4 (3.0–85.2)

For the SCC patients, higher T stage [(y)pT3 vs. (y)pT0: $p = 0.035$ (y)pT3 vs. (y)pT2: $p = 0.030$] and N stage [(y)pN2 vs. (y)pN0: $p = 0.035$, (y)pN2 vs. (y)pN1: $p = 0.030$], and lower tumor differentiation ($p = 0.21$) were associated with a worse long-term survival. Also, the number of positive nodes had a negative impact on survival ($p = 0.014$). Complete responders to neoadjuvant treatment had a significantly better survival ($p < 0.001$).

Impact of complications on survival

Table 4 shows the median survival after esophageal cancer surgery with respect to complications and treatment. Figure 1 shows the cumulative survival of EAC and SCC patients. Figure 2 (EAC) and Figure 3 (SCC) present the cumulative survival of patients with regard to overall complications. Survival was not different between the EAC and SCC patients. Furthermore, neither overall complications nor pulmonary complications or anastomotic insufficiency significantly affected survival in the entire patient population or in the two subgroups (EAC and SCC).

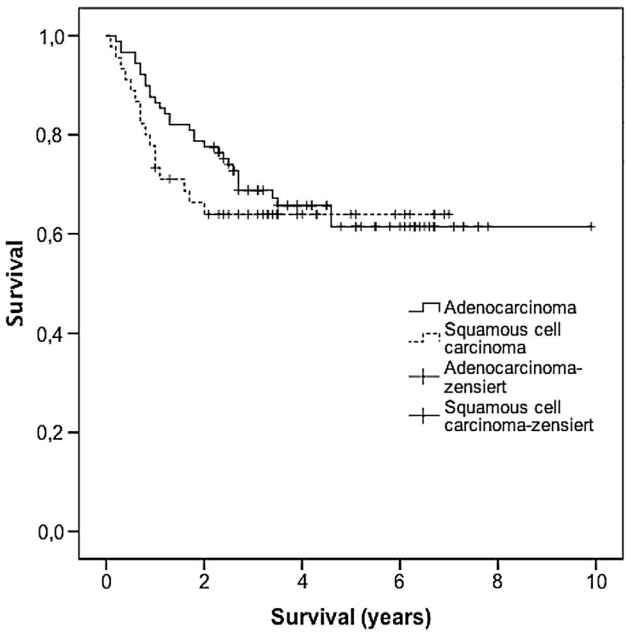

Fig. 1 Cumulative overall survival for esophageal adenocarcinoma and squamous cell carcinoma patients. Log-rank test: $p = 0.532$

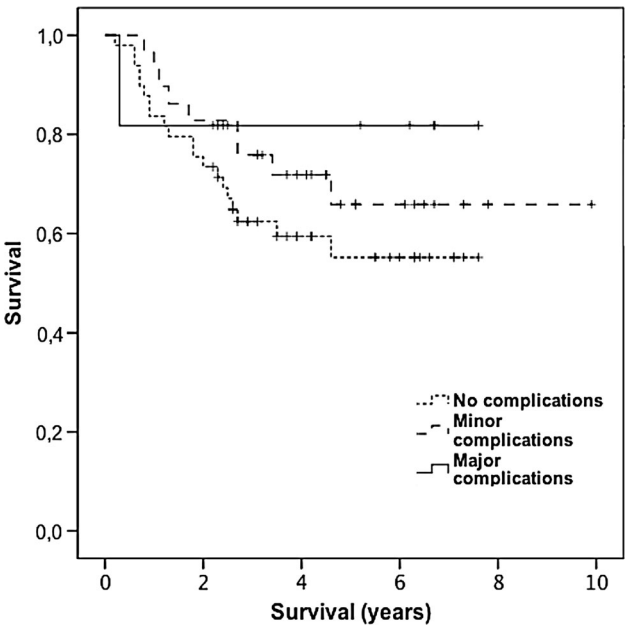

Fig. 2 Impact of (minor/major) overall complications on cumulative survival of adenocarcinoma patients. Major versus minor overall complications: $p = 0.660$; major versus no overall complications: $p = 0.287$

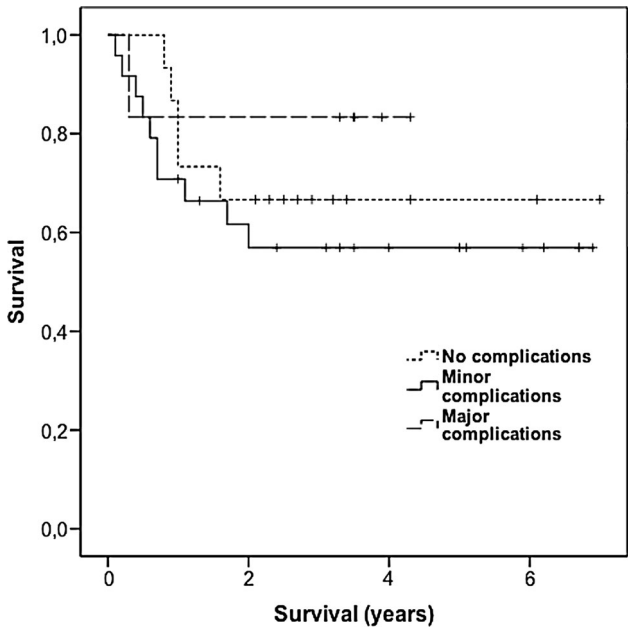

Fig. 3 Impact of (minor/major) overall complications on cumulative survival of squamous cell carcinoma patients. Major versus minor overall complications: $p = 0.305$; major versus no overall complications: $p = 0.534$

Table 5 Multivariate analysis of independent predictors of survival

Stage	Significance	RR	95 % CI (for RR)	
			Lower1	Upper
pT	0.154			
(y)pT1	0.865	82697.029	0.000	2.575E + 061
(y)pT2	0.874	38644.769	0.000	1.191E + 061
(y)pT3	0.871	48261.624	0.000	1.486E + 061
(y)pT4	0.861	110065.214	0.000	3.379E + 061
(y)pN	0.280			
(y)pN1	0.451	2.404	0.246	23.508
(y)pN2	0.302	3.023	0.370	24.674
(y)pN3	0.102	6.500	0.690	61.259
Npos	0.183	1.069	0.969	1.179
(y)pM	**0.000**	**0.060**	**0.017**	**0.210**
G	0.314			
G(1)	0.148	0.211	0.026	1.735
G(2)	0.833	0.001	0.000	2.102E + 27
G(3)	0.154	0.601	0.299	1.211

Significant predictors are given in bold

For multivariate analysis via Cox regression, we included only variables having a statistically significant impact on survival in the univariate analysis and pooled subgroups as appropriate (minimal subgroup size: $n = 9$). A subgroup analysis of patients undergoing neoadjuvant therapy was not conducted

RR relative risk; *CI* confidence interval

Multivariate analysis

For multivariate analysis, we included only variables having a statistically significant impact on survival in the univariate analysis and pooled subgroups as appropriate (minimum subgroup size: $n = 9$). Only the M stage was proven to predict survival independently (Table 5). A subgroup analysis of patients undergoing neoadjuvant therapy was not conducted.

Discussion

The reported overall morbidity and the rates of pulmonary complications and anastomotic insufficiency after esophagectomy vary widely (3–84 %, 2–100 %, and 2–25 %, respectively) [8–10, 21–23, 27–30]. Several factors could contribute to this wide range. Several authors did not analyze different histologic subtypes separately [7, 8, 21, 22, 28, 29] or included different surgical approaches (transhiatal versus abdominothoracic versus minimally invasive [8, 10, 12, 23, 24, 29, 31, 32], stapler versus hand-sewn, cervical versus thoracic anastomoses [10, 23]). These factors might affect to varying degrees the complications and outcomes [7, 12, 27, 31–44].

We aimed to create a homogeneous study population by selecting only patients who underwent transthoracic resection with intrathoracic stapler anastomosis. Analyses were performed separately for both tumor types, and complications were assessed using detailed complication categories. The clinical significance of our complication categories was proven by comparing them to the standardized Clavien–Dindo classification [26].

With this approach, we were able to draw four major conclusions from our study: (1) Although, in general, the complication rates of our patients were comparable to those in the current literature, SCC patients experienced pulmonary and overall complications significantly more often than did the EAC patients. (2) Postoperative complications were basically not affected by the patients' characteristics. Only pulmonary complications were affected by the number of positive lymph nodes (EAC) and the patient's sex (SCC). (3) We showed that long-term survival was not influenced by overall or pulmonary complications or by anastomotic insufficiency. (4) Neoadjuvant treatment did not have any impact on the incidence of complications or long-term survival (despite the fact that complete responders presented a significantly better outcome than nonresponders).

The most reasonable explanation for the higher complication rate of our SCC patients might lie in the location and aggressiveness of these tumors. As SCC presents with earlier lymphatic spread, a higher location in the esophagus, and a worse prognosis [45], radical resection might be

more complicated. Furthermore, classic SCC patient-related factors such as nicotine abuse increase perioperative mortality/morbidity [29, 46].

To date, there is no final agreement as to whether perioperative complications affect long-term outcomes. Whereas some authors found a negative impact of complications on survival in EAC and SCC populations [7, 8, 11, 23], others could not confirm these observations [22, 29, 30]. However, the only two articles investigating only either EAC or SCC patients reported survival to be negatively influenced by perioperative complications in the EAC patients [9] but not in the SCC patients [10]. Our current study assessed for the first time EAC and SCC patients separately in a single experienced high-volume center for treating esophageal cancer surgery. We demonstrated that neither EAC nor SCC patients experienced a negative impact of perioperative complications on long-term outcome. We further found that esophageal cancer surgery-specific complications (anastomotic insufficiency, pulmonary complications) did not affect long-term outcome in our patients, although both factors have been reported to influence outcome to varying degrees [27, 28, 47–49].

Some authors have reported outcomes after neoadjuvant treatment to be strongly affected by an increase in perioperative morbidity/mortality [14, 20, 24] as it might trigger postoperative acute lung injury, cardiac events, or anastomotic leakage or might complicate postoperative weaning or surgical resections due to fibrosis, esophagitis. or infection arising from treatment-related toxicity [19, 30, 50–52]. In contrast, others could not confirm these observations [10, 36, 53]. One study reported that quality of life appeared to be improved after neoadjuvant therapy [54]. Our data seem to support the idea that there is no significantly increased risk for perioperative complications after neoadjuvant therapy. This seems especially important as recent studies suggested that a major response to neoadjuvant treatment positively influenced survival [13–18]. However, based on the limitation of the retrospective design of our study, the final answer to this question needs further evaluation in prospective randomized controlled trials.

The most important limitation of our study is the small sample size, especially in the SCC group. This sample size was caused by the strict patient selection. We believe that this selection resulted in a homogeneous study population, which can avoid the impact of aspects such as histologic tumor type or surgical approach on complications. Another limitation is the exclusion of patients from the analysis who died during their early postoperative course. Perioperative complications affect the early postoperative course and finally determine disease- or treatment-specific mortality. Early postoperative mortality affects the general outcome. However, we did not intend to analyze the effect of perioperative complications on short-term outcomes, as recent studies have already demonstrated a negative impact of surgical [7, 20] and medical [30] complications. We aimed to assess the impact of perioperative complications on long-term outcome. Therefore, we used a common approach as described in the literature [55–57] and excluded in-hospital deaths from our analysis.

Conclusions

Our study contributes to the discussion as to whether perioperative complications affect outcome after esophageal cancer surgery. Our data support the hypothesis that perioperative complications do not influence long-term survival of esophageal cancer patients as, for the first time, we separately assessed EAC and SCC patients. Moreover, our data support the hypothesis that neoadjuvant treatment does not affect perioperative complications or long-term survival.

Conflict of interest There are no potential or real conflicts of interest for any of the authors.

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