Received: 11 January 2021 | Revised: 23 April 2021 | Accepted: 27 May 2021

DOI: 10.1002/jso.26587

RESEARCH ARTICLE

Journal of SURGICAL ONCOLOGY WILEY

Impact of postoperative complications on long-term survival after esophagectomy in older adults: A SEER-Medicare analysis

Joanna Sesti MD[1] | Biruk Almaz MD[2] | Jaimie Bell NP, DNP[1] | Andrew Nguyen MD[2] | Zubin Bamboat MD[3] | Adam Lackey MD[1] | Russell C. Langan MD[2] | Amber L. Turner MPH[2] | Patrick Hilden DrPH[4] | Subroto Paul MD, MPH[1,2]

[1]Thoracic Surgical Services, RWJBarnabas Health, West Orange, New Jersey, USA

[2]Department of Surgery, RWJBarnabas Health, Saint Barnabas Medical Center, Livingston, New Jersey, USA

[3]Department of Surgery, Summit Medical Group, Summit, New Jersey, USA

[4]Department of Biostatistics, RWJBarnabas Health, Saint Barnabas Medical Center, Livingston, New Jersey, USA

Correspondence
Subroto Paul, MD, MPH, Thoracic Surgical Services, RWJBarnabas Health, 101 Old Short Hills Rd Ste. 302, West Orange, NJ 07052, USA.
Email: Subroto.Paul@rwjbh.org

Abstract

Background: Esophagectomy is a complex procedure associated with a high rate of postoperative complications. It is not clear whether postoperative complications effect long-term survival. Most studies report the results from single institutions.

Methods: We examined the Surveillance, Epidemiology and End Results (SEER)-Medicare database to assess whether long-term overall and cancer-specific mortality of patients undergoing esophagectomy for cancer is impacted by postoperative complications.

Results: Nine hundred and forty patients underwent esophagectomy from 2007 to 2014, of which 50 died, resulting in a cohort of 890 patients. Majority were males ($n = 764$, 85.8%) with adenocarcinoma of the lower esophagus. Almost 60% of the group had no neoadjuvant therapy. Four hundred and fifty-five patients had no major complications (51.1%), while 285 (32.0%) and 150 (16.9%) patients had one, two, or more major complications, respectively. Overall survival at 90 days was 93.1%. Multivariate analysis of patients followed up for a minimum of 90 days demonstrated that the number of complications was significantly associated with decreased overall survival but no impact on cancer-specific survival.

Conclusions: Our population-based analysis with its inherent limitations suggests that patients undergoing esophagectomy who experience complications have worse overall survival but not cancer-specific survival if they survive at least 90 days from the date of surgery.

KEYWORDS
complications, esophagectomy, outcomes, thoracic surgery

1 | INTRODUCTION

Esophageal cancer is the sixth leading cause of cancer mortality worldwide.[1] Esophageal resection remains a vital part of the treatment options for patients, often in conjunction with preoperative chemotherapy or chemoradiation. Despite advances in surgical technique and critical care, esophagectomy remains a complex procedure with high rates of morbidity and mortality. Postoperative complications include pneumonia, recurrent nerve injury, chylous effusions, tracheobronchial fistulas, as well as anastomotic leaks. Left untreated, many of these complications can lead to sepsis, organ failure, and death.[2] Even those patients whose complications are identified in a timely manner and properly treated can have considerable disabilities.

Several studies have examined whether postoperative complications after an esophagectomy can lead to decreased long-term survival.[3–6] Some of these analyses have demonstrated complications leading to a negative impact on survival, while some demonstrated no or minimal impact. These studies are largely limited to single institution series. In other complex oncologic operations, the impact of postoperative complications on survival are mixed.[7–9]

Hence, it remains unclear whether long-term outcomes are affected in these patients who have been "rescued" from postoperative complications. In this study, we examined the SEER-Medicare database, a large national database, to assess whether long-term overall and cancer- specific mortality (CSM) of patients undergoing esophagectomy for cancer is impacted by postoperative complications.

2 | METHODS

2.1 | Data source

The Surveillance, Epidemiology and End Results (SEER)–Medicare data set includes patient demographics, cancer diagnosis, and treatment-related information, and cause of death linked to Medicare data.[10] The Medicare linkage provides Medicare hospital, outpatient, physician, home health, and hospice claims. Medicare insures approximately 97% of people 65 and older in the United States, allowing approximately 93% of that population in the SEER registry to be linked to the Medicare enrolment file. The current release contains patients diagnosed from 2006 to 2013 linked to Medicare claims through 2014, with enrolment and survival data through 2015. The study was approved by the Saint Barnabas Medical Center institutional review board (IRB) (Protocol No. 17-67).

2.2 | Study cohort

Patients who underwent an esophagectomy within 6 months after diagnosis of a first esophageal cancer were eligible for inclusion in this study. Patients with a prior primary cancer diagnoses, upper esophageal carcinomas, as well as those whom died inpatient (n = 50) were excluded from analysis, consolidated standards of reporting trials (CONSORT) Diagram (Figure 1).

2.3 | Variables

We categorized patients by disease, site, demographic, and surgery-specific variables provided in the SEER registry, including pathological stage (Derived AJCC Stage Group, 6th edition), histology (Adenocarcinoma and Squamous), site (Middle and Lower), number of nodes examined, age on surgery date, year of procedure, sex, race (Black, White, and Other), marital status at diagnosis, metropolitan area (grouped as rural, urban), zip-code per-capita income (quartiles), and provider procedure volume based on the number of procedures in the cohort. We defined individual patient comorbidities using the Elixhauser approach, excluding the solid tumor comorbidity, given all patients had an esophageal cancer.[11] An overall risk score based on the total number of comorbidities noted was also determined. Raw data are provided in Appendix Table 2. Data from inpatient

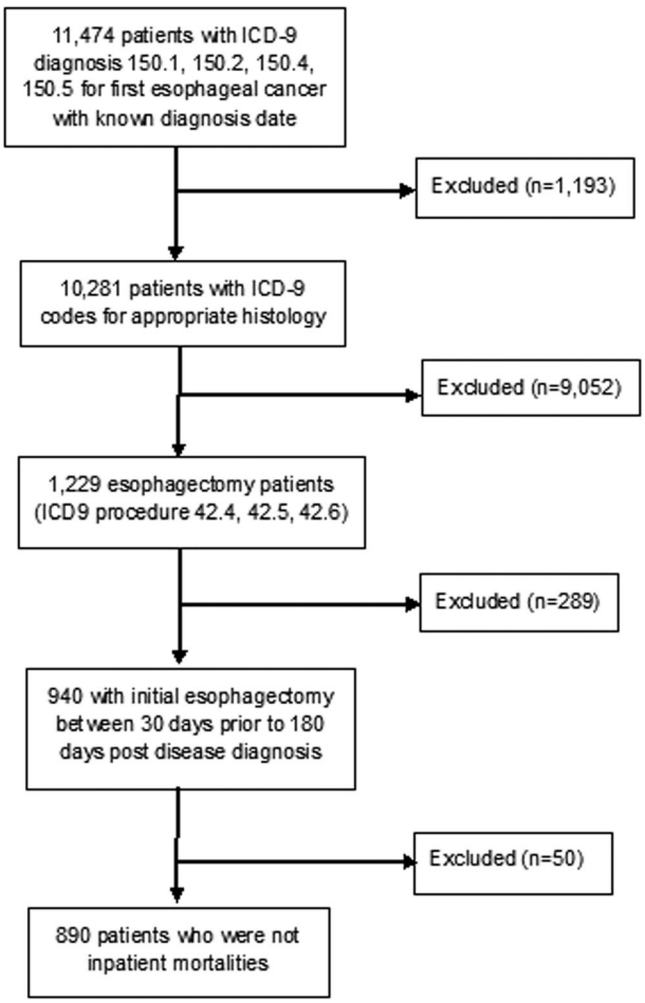

FIGURE 1 CONSORT diagram. CONSORT, consolidated standards of reporting trials

TABLE 1 Demographics of cohort

	Group	Overall	0 Complication	1 Complication	2+ Complications	*p*-value
Median (IQR), *n* (%)		890 (100%)	455 (51.1%)	285 (32.0%)	150 (16.9%)	
Variable						
Age		70 (67, 75)	70 (67, 74)	71 (67, 75)	70 (66, 76)	0.077
Age (group)						0.054
	<65	91 (10.2)	49 (10.8)	22 (7.7)	20 (13.3)	
	[65, 70)	321 (36.1)	178 (39.1)	95 (33.3)	48 (32.0)	
	[70, 75)	246 (27.6)	123 (27.0)	89 (31.2)	34 (22.7)	
	75+	232 (26.1)	105 (23.1)	79 (27.7)	48 (32.0)	
Sex						0.845
	Female	126 (14.2)	65 (14.3)	38 (13.3)	23 (15.3)	
	Male	764 (85.8)	390 (85.7)	247 (86.7)	127 (84.7)	
Race						0.399
	White	832 (93.5)	427 (93.8)	264 (92.6)	[a]	
	Black	33 (3.7)	[a]	[a]	[a]	
	Other	25 (2.8)	[a]	[a]	[a]	
Married						0.109
	No	236 (27.6)	128 (29.4)	63 (23.0)	[a]	
	Yes	619 (72.4)	308 (70.6)	211 (77.0)	100 (69.0)	
	(Missing)	35	19	[a]	[a]	
Median income (thousands, quartiles)						0.436
	[13.2,44.7]	[a]	[a]	[a]	46 (30.9)	
	(44.7,60.1]	221 (24.9)	109 (24.0)	73 (25.7)	39 (26.2)	
	(60.1,81.4]	227 (25.6)	118 (26.0)	76 (26.8)	33 (22.1)	
	(81.4,191]	223 (25.1)	121 (26.7)	71 (25.0)	[a]	
	(Missing)	[a]	[a]	[a]	[a]	
Location						0.606
	Metropolitan	755 (84.8)	382 (84.0)	242 (84.9)	131 (87.3)	
	Nonmetropolitan	135 (15.2)	73 (16.0)	43 (15.1)	19 (12.7)	
Year		2010 (2008, 2012)	2010 (2008, 2012)	2010 (2008, 2012)	2011 (2009, 2012)	0.001
Stage						0.690
	1	234 (27.1)	119 (27.2)	74 (26.9)	[a]	
	2	285 (33.1)	141 (32.2)	95 (34.5)	49 (32.9)	
	3	293 (34.0)	158 (36.1)	86 (31.3)	49 (32.9)	
	4	50 (5.8)	20 (4.6)	[a]	[a]	
	(Missing)	28	[a]	[a]	[a]	
Histology						0.331
	Adenocarcinoma	726 (81.6)	379 (83.3)	225 (78.9)	122 (81.3)	
	Squamous	164 (18.4)	76 (16.7)	60 (21.1)	28 (18.7)	

(Continues)

TABLE 1 (Continued)

	Group	Overall	0 Complication	1 Complication	2+ Complications	*p*-value
Site						0.008
	Lower	726 (81.6)	379 (83.3)	225 (78.9)	122 (81.3)	
	middle	164 (18.4)	76 (16.7)	60 (21.1)	28 (18.7)	
Nodes		726 (81.6)	379 (83.3)	225 (78.9)	122 (81.3)	0.660
Provider volume[b]						0.580
	[1, 3]	222 (24.9)	103 (22.6)	73 (25.6)	46 (30.7)	
	(3,8]	242 (27.2)	123 (27.0)	78 (27.4)	41 (27.3)	
	(8,16]	205 (23.0)	111 (24.4)	64 (22.5)	30 (20.0)	
	(16,35]	221 (24.8)	118 (25.9)	70 (24.6)	33 (22.0)	
Neoadjuvant therapy						0.663
	None	526 (59.1)	263 (57.8)	178 (62.5)	85 (56.7)	
	Chemo	33 (3.7)	[a]	[a]	[a]	
	Rad	22 (2.5)	[a]	[a]	[a]	
	Chemo/rad	309 (34.7)	161 (35.4)	90 (31.6)	[a]	
Adjuvant therapy						0.001
	None	681 (76.5)	325 (71.4)	223 (78.2)	133 (88.7)	
	Chemo	125 (14.0)	81 (17.8)	[a]	[a]	
	Rad	36 (4.0)	20 (4.4)	[a]	[a]	
	Chemo/rad	48 (5.4)	29 (6.4)	[a]	[a]	
Elixhauser score						<0.001
	0	116 (13.0)	88 (19.3)	15 (5.3)	13 (8.7)	
	1	203 (22.8)	132 (29.0)	44 (15.4)	27 (18.0)	
	2	219 (24.6)	115 (25.3)	75 (26.3)	29 (19.3)	
	3+	352 (39.6)	120 (26.4)	151 (53.0)	81 (54.0)	

Abbreviation: DUA, Data Use Agreement.

[a]Data not shown due to compliance with DUA restrictions.

[b]Total number of claims per provider.

(MEDPAR), outpatient, and carrier claims (NCH) files were used to identify neoadjuvant and adjuvant therapy, defined as treatment with chemotherapy, radiation, or a combination of the two within 180 days pre- or postesophagectomy, respectively, as well as anastomic leak (Appendix Table 1).[12,13] The first day of the month was used to define the date of diagnosis, given only the month and year are provided, and patients with an unknown month or year of diagnosis were excluded. Cell counts of 1–10 were coarsened in the data summaries in accordance with SEER-Medicare data use agreement (DUA).

2.4 | Outcomes

Overall survival (OS) was defined as time from surgery until death or loss to follow-up (12/31/2015). SEER provides information about disease-specific cause of death, allowing us to determine CSM. Utilizing a landmark analysis, we also determined OS and CSM for those patients who survived or were not lost to follow-up after 90 days postsurgery. We performed this analysis to exclude the impact of postoperative complications on the immediate postoperative period during which there impact would be the greatest. Postoperative complications were defined using International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes (Appendix Table 1) as previously described.[14,15] Current procedural terminology codes (CPT) were used along with ICD-9-CM codes (Appendix Table 1) to define major anastomotic leak, as done previously.[7] Major complications were defined as the following: anastomotic leak, pulmonary embolus, pneumonia, myocardial infarction, renal failure, sepsis, bleeding, arrhythmia, and stroke. The primary outcome measure examined was to compare OS and CSM between patients undergoing esophagectomy having none, one, or two or more major complications.

TABLE 2 Univariate and multivariate analysis of predictors of overall survival (d90 Landmark)

				Univariate		Multivariate	
Variable	**Term**	***n***	**events**	**HR (95% CI)**	***p*-value**	**HR (95% CI)**	***p*-value**
Age (10 years)		829	455	1.02 (0.88, 1.18)	0.774		
Sex					0.040		
	Female	116	51	Reference			
	Male	713	404	1.36 (1.01, 1.82)			
Race					0.335		
	White	772	424	Reference			
	Black	32	[a]	1.18 (0.75, 1.85)			
	Other	25	[a]	0.68 (0.37, 1.85)			
Married					0.997		
	No	216	118	Reference			
	Yes	619	363	1 (0.81, 1.24)			
Median income (thousands, quartiles)					0.374		
	[13.2,44.7]	202	120	Reference			
	(44.7,60.1]	200	106	0.93 (0.67, 1.13)			
	(60.1,81.4]	212	111	0.8 (0.61, 1.03)			
	(81.4,191]	212	115	0.87 (0.67, 1.12)			
Location					0.634		
	Metropolitan	705	392	Reference			
	Nonmetropolitan	124	63	0.94 (0.72, 1.22)			
Year		829	455	0.96 (0.92, 1.01)	0.132		
Stage					< 0.001		<0.001
	1	225	65	Reference		Reference	
	2	264	151	2.55 (1.9, 3.41)		2.83 (2.10, 3.81)	
	3	270	189	4.13 (3.11, 5.5)		4.59 (3.42, 6.14)	
	4	[a]	[a]	7.67 (5.09, 11.54)		9.21 (6.02, 14.11)	
Histology					0.714		
	Adenocarcinoma	676	372	Reference			
	Squamous	153	83	0.96 (0.75, 1.21)			
Site					0.925		
	Lower	696	383	reference			
	Middle	133	72	1.01 (0.79, 1.3)			
Nodes (per 10)		829	455	0.99 (0.85, 1)	0.050	0.84 (0.78, 0.92)	< 0.001
Provider volume[b]					0.003		
	[1, 3]	199	122	Reference			
	(3,8]	225	133	0.97 (0.76, 1.24)			
	(8,16]	193	107	0.92 (0.71, 1.2)			
	(16,35]	212	93	0.63 (0.48, 0.82)			

(Continues)

TABLE 2 (Continued)

Variable	Term	*n*	events	Univariate HR (95% CI)	*p*-value	Multivariate HR (95% CI)	*p*-value
Neoadjuvant therapy					< 0.001		
	None	492	244	Reference			
	Chemo	[a]	[a]	1.54 (0.99, 2.41)			
	Rad	[a]	[a]	1.54 (0.86, 2.75)			
	Chemo/rad	286	178	1.57 (1.29, 1.91)			
Elixhauser score					0.188		
	0	112	64	Reference			
	1	192	100	0.96 (0.7, 1.31)			
	2	197	109	1.04 (0.76, 1.42)			
	3+	328	182	1.23 (0.92, 1.63)			
Major complications					< 0.001		<0.001
	0	438	218	Reference		Reference	
	1	265	154	1.28 (1.04, 1.57)		1.37 (1.11, 1.70)	
	2+	126	83	1.74 (1.35, 2.24)		1.94 (1.50, 2.52)	

Abbreviation: DUA, Data Use Agreement.

[a]Data not shown due to compliance with DUA restrictions.

[b]Total number of claims per provider.

2.5 | Statistical analysis

Differences in patient and treatment characteristics across major complication groups were assessed using the Kruskall Wallis test for continuous characteristics and Fisher's Exact or χ^2 test for categorical characteristics as appropriate. CSM was assessed using a competing risks approach, with death not due to cancer considered to be a competing risk. Cox proportional hazards regression models were used to assess differences in OS and CSM across patient and treatment characteristics, with a cause-specific hazard model used for CSM. Estimates of OS and CSM over time were determined using the Kaplan–Meier and Cumulative Incidence methods, respectively. Multivariate models were built using a forward selection procedure, including all covariates with univariate $p < 0.05$ as candidate predictors, with a final inclusion criteria of $p < 0.05$ for the multivariate model. A landmark analyses was used to assess outcomes among patients followed up for at least 90 days. All analyses were completed in R 4.0.2.

3 | RESULTS

3.1 | Patient characteristics and postoperative complications

Table 1 summarizes the demographics of the analysis cohort ($n = 890$). The median age for the group was 70. The majority were males ($n = 764$, 85.8%) with adenocarcinoma of the lower esophagus. Almost 60% of the group had no neoadjuvant therapy. Chemoradiation was the predominant mode of neoadjuvant therapy ($n = 309$, 34.7%).

Four hundred fifty-five patients had no major complications (51.1%), while 285 (32.0%) and 150 (16.9%) patients had one or two or more major complications, respectively. Patients undergoing esophagectomy who had two or more complications were more likely to have mid esophageal tumors, higher Elixhauser comorbidity scores, and have their surgeries during later years.

The distribution of complications is provided in Appendix Table 3. Rates of major complications include the following: anastomotic leak $n = 77$ (8.7%), pulmonary embolus $n = 19$ (2.1%), pneumonia $n = 123$ (13.8%), myocardial infarction $n = 13$ (1.5%), renal failure $n = 30$ (3.4%), sepsis $n = 71$ (8.0%), bleeding $n = 42$ (4.7%), arrhythmia $n = 238$ (26.7%), and stroke $n = 16$ (1.8%). Thirty-day, 60-day, 90-day, and 1-year survival were as follows: 98.0% (96.8%–98.7%), 95.7% (94.2%–96.9%),93.1% (91.3%–94.6%), and 76.2% (73.2%–78.8%).

3.2 | Impact of complications on OS

Multivariate analysis of OS for the entire cohort demonstrated that higher pathologic stage and a higher number of complications were associated with worse survival. Higher number of nodes examined and higher provider claims (volume) were associated with improved survival. (Appendix Table 4).

TABLE 3 Univariate and multivariate analysis of predictors of cancer-specific mortality (d90 Landmark)

				Univariate			
Variable	**Term**	***n***	**Events**	**Estimate (95% CI)**	***p*-value**	**Multivariate**	
Age (10 years)		829	328	0.92 (0.78, 1.09)	0.347		
Sex					0.074		
	Female	116	37	Reference			
	Male	713	291	1.37 (0.97, 1.92)			
Race					0.689		
	White	772	303	Reference			
	Black	32	[a]	1.23 (0.73, 2.07)			
	Other	[a]	[a]	0.8 (0.48, 1.7)			
Married					0.727		
	No	216	88	Reference			
	Yes	579	237	1.05 (0.81, 1.34)			
Median income (thousands, quartiles)					0.043		0.026
	[13.2,44.7]	202	86	Reference		Reference	
	(44.7,60.1]	200	82	0.95 (0.7, 1.29)		1.23 (0.89, 1.68)	
	(60.1,81.4]	212	65	0.67 (0.48, 0.92)		0.74 (0.53, 1.03)	
	(81.4,191]	212	94	1 (0.75, 1.34)		1.00 (0.74, 1.35)	
Location					0.839		
	Metropolitan	705	281	Reference			
	Nonmetropolitan	124	47	0.97 (0.71, 1.32)			
Year		829	328	0.89 (0.84, 0.94)	< 0.001	0.88 (0.83, 0.93)	<0.001
Stage					< 0.001		<0.001
	1	225	36	Reference		Reference	
	2	264	104	3.05 (2.09, 4.46)		3.08 (2.10, 4.50)	
	3	270	153	5.56 (3.86, 8.01)		5.68 (3.94, 8.22)	
	4	43	27	8.96 (5.41, 14.82)		9.79 (5.87, 16.31)	
Histology					0.800		
	Adenocarcinoma	676	264	Reference			
	Squamous	153	64	1.04 (0.79, 1.36)			
Site					0.541		
	Lower	696	272	Reference			
	Middle	133	56	1.09 (0.82, 1.46)			
Nodes (per 10)		829	328	0.95 (0.86, 1.04)	0.037		
Provider volume[b]					0.008		0.019
	[1, 3]	199	86	Reference		Reference	
	(3,8]	225	92	0.96 (0.72, 1.29)		0.85 (0.63, 1.15)	
	(8,16]	193	86	1.06 (0.79, 1.43)		1.01 (0.75, 1.38)	
	(16,35]	212	64	0.63 (0.46, 0.87)		0.64 (0.46, 0.89)	

(Continues)

TABLE 3 (Continued)

Variable	Term	*n*	Events	Univariate Estimate (95% CI)	*p*-value	Multivariate
Neoadjuvant therapy					0.001	
	None	492	174	Reference		
	Chemo	32	17	1.66 (1.01, 2.74)		
	Rad	[a]	[a]	2.04 (1.11, 3.75)		
	Chemo/rad	286	126	1.49 (1.19, 1.88)		
Elixhauser score					0.980	
	0	112	46	Reference		
	1	192	82	1.07 (0.75, 1.54)		
	2	197	82	1.08 (0.75, 1.54)		
	3+	328	118	1.05 (0.75, 1.45)		
Major complications					0.202	
	0	438	169	Reference		
	1	265	108	1.13 (0.89, 1.44)		
	2+	126	51	1.32 (0.96, 1.8)		

Abbreviation: DUA, Data Use Agreement.

[a]Data not shown due to compliance with DUA restrictions.

[b]Total number of claims per provider.

Within the day 90 landmark cohort, multivariate analysis of OS demonstrated that higher pathologic stage and a higher number of complications were associated with worse OS. Higher number of nodes examined were associated with improved survival. Of note, higher Elixhauser morbidity scores were not correlated with OS in univariate analysis (Table 2).

3.3 | Impact of complications on CSM

Multivariate analysis of CSM for the entire cohort demonstrated that higher pathologic stage, and the higher number of complications were associated with worse survival. Higher number of nodes examined, and surgery that is more recent were associated with improved CSM (Appendix Table 5).

In the day 90 landmark cohort, multivariate analysis of CSM demonstrated that higher pathologic stage were associated with worse CSM. Higher provider claims and those patients with income between $60,100 and $81,400 were associated with improved CSM (Table 3). The number of complications had no impact on CSM.

4 | DISCUSSION

Esophagectomy remains a mainstay of curative treatment modalities for esophageal cancer. Despite improvement in the toxicity of preoperative treatments, intraoperative surgical technique, and postoperative critical care medicine, esophagectomy remains a highly complex procedure with considerable morbidity and mortality. Our national study demonstrated an inpatient mortality of 5.3% ($n = 50$) with nearly 50% of surviving patients experiencing at least one major complication. These outcomes are in keeping with outcomes reported elsewhere.[16]

Whether the high rate of complications lead to decreased overall or cancer-specific survival is unclear. Most analyses are limited to institutional case series data. Table 4 summarizes the relevant studies evaluating long-term outcomes after esophagectomy complications, with most studies demonstrating a negative impact on survival from postoperative complications.[3–6,17–19] In other complex operations, such as pancreaticoduodenectomy, postoperative complications in one retrospective single institution study were not associated with OS.[9] In colorectal resections, anastomotic leaks were found to be associated with increased local recurrence and decreased cancer-specific survival.[7,8]

Our analysis of the SEER-Medicare Database shows that the number of major complications effect OS but not necessarily CSM. For those patients who followed up for at least 90 days, CSM is not impacted by the number of complications. The results of our study are consistent with the single institutional series reported by Lerut et al. and the meta-analysis of published by Booka et al.[4,6] The study is also in line with the report of Rizk et al. who reported technical but not medical complications leading to decreased survival.[5]

Our results show that OS is impacted by the number of complications in both the full cohort as well as those who survive or

TABLE 4 Summary of studies on effect of postoperative esophagectomy complications on survival

Author	Design	Cancer type	Sample size	Outcomes
Ancona et al.[3]	Retrospective	Esophageal cancer	522	Surgical complications have no negative impact on survival rates ($p = 0.9$).
Booka et al.[6]	Meta-analysis	Esophageal Cancer	11,368	Postoperative complications were associated with significantly decreased 5-year OS (hazard ratio [HR] 1.16, 95%, CI: 1.06 to 1.26; $p < 0.001$) and 5-year CSS (HR: 1.27, 1.09 to 1.47; $p = 0.002$).
Junemann-Ramirez et al.[17]	Retrospective	Esophageal cancer	276	30-day mortality rate was 35.7% for anastomotic leak compared with 4.2% for patients without leak ($p < 0.05$) however no difference in 5-year survival.
Lagarde et al.[18]	Retrospective	Esophageal cancer	351	Presence of surgical complications ($p < 0.030$), wound infections ($p < 0.033$) and sepsis ($p < 0.013$) was related to a shorter time to death due to recurrence of malignancy.
Lerut et al.[4]	Prospective	Esophageal cancer	150	−6.7% ($n = 10$) recurrence within 6 months, 19.3%($n = 29$) within 12 months, 26%($n = 39$) within 18 months, 28%($n = 42$) within 24 months, 31%($n = 47$) within 3 years, 90% of all recurrences occurring within 2 years -Recurrence was significantly higher for complication grades above with no significant mutual correlation among Grades 2, 3, and 4.
Rizk et al.[5]	Retrospective	Esophageal cancer	510	Postoperative complication is highly predictive of poor overall survival. Anastomotic leak worse overall survival compared with other complications.
Takeuchi et al.[19]	Prospective	Esophageal cancer	65	Postoperative survival rate with medical/surgical complications have lower short-term and long-term survival rate ($p = 0.042$; 0.023) in the salvage group.

Abbreviations: CI, confidence interval; CSS, cause-specific survival; HR, hazard ratio; OS, overall survival.

follow-up at 90 days. However, CSM is not impacted by the number of complications in those patients who make it past 90 days. Our data suggest that when early deaths, which are more likely related to complications, are removed from analysis, CSM is not impacted. As the number of early events are small in the 90-day period ($n = 61$), the effect of complications may have an outsized impact on CSM.

Intuitively, the number of complications should not affect CSM. Rather, the biology and extent of disease influence cancer recurrence and CSM. The number, type, and extent of complications impact clearly affect short-term survival. However, long-term OS may also be affected as patients may be deconditioned by complications leading to poorer outcomes even if the complications resolve.

Our study also found that higher nodal harvests were associated with improved OS and CSM. Higher provider volume was also associated with improved OS and CSM in the multivariable analysis depending on the period examined. These findings are consistent with prior studies.[20,21] We also noted that those patients with higher income, specifically income between $60,100 and $81,400, had improved CSM if they followed up past 90 days. Although it is not unexpected that patients with increased means would do better than those without, it is not clear why this specific median income quartile has better cancer survival.[22]

Preventing complication at all stages of disease is the aim. However, particular attention should be paid for early stages of disease where postoperative complications may have a greater impact on survival. Meticulous attention to operative detail as well as vigilance for common complications should be the norm. Early identification of patients with complications can lead to the improved ability to "rescue" patients from additional morbidity. The Leapfrog Group and others have reported guidelines of minimal hospital and surgical volume. Volume outcome relationships for esophagectomy haven been well established.[20,23] Implementation of guidelines, however, has been less than stellar with the majority of esophagectomies occurring in low volume centers with less than 3% meeting Leapfrog Group Criteria.[24] Achieving these goals will require the collaboration of payers, providers, as well as patients.[25]

We recognize that there are several limitations to our analysis. First and foremost, the granularity of data available in SEER-Medicare is not as robust as that available in the records of institutions. As an example, SEER-Medicare does not record anastomotic leakage and the data are inferred from codes. The true rate may be higher or lower than the 9% found in our study. SEER-Medicare also as noted does not capture clinical staging data. Therefore, we are unable to evaluate pathologic upstaging data and can only include pathologic data in our multivariable models. SEER-Medicare also does not provide disease recurrence and hence we are unable to evaluate whether complications effect recurrence rates. Operative technique and postoperative care are not standardized either as SEER-Medicare data incorporates multiple institutions. We are also able to examine low and high volume institutions over a period of time. However in this lies the strength of our study as SEER-Medicare gives a more generalizable set of data to evaluate the impact of esophagectomy complications.

Our population-based analysis with its inherent limitations suggests that patients undergoing esophagectomy who experience complications have worse OS but not cancer-specific survival if they survive at least 90 days from the date of surgery.

CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

DATA AVAILABILITY STATEMENT

The data sets used for the current study are available from SEER-Medicare. This study used the linked SEER-Medicare database. The interpretation and reporting of these data are the sole responsibility of the authors. The authors acknowledge the efforts of the National Cancer Institute; the Office of Research, Development and Information, CMS; Information Management Services (IMS), Inc.; and the Surveillance, Epidemiology, and End Results (SEER) Program tumor registries in the creation of the SEER-Medicare database.

ORCID

Russell C. Langan http://orcid.org/0000-0002-0250-120X
Amber L. Turner http://orcid.org/0000-0003-0749-0527

REFERENCES

1. Fan J, Liu Z, Mao X, et al. Global trends in the incidence and mortality of esophageal cancer from 1990 to 2017. *Cancer Med*. 2020;9:e03338-e06887.
2. Paul S, Bueno R. Section VI: complications following esophagectomy: early detection, treatment, and prevention. *Semin Thorac Cardiovasc Surg*. 2003;15(2):210-215.
3. Ancona E, Cagol M, Epifani M, et al. Surgical complications do not affect longterm survival after esophagectomy for carcinoma of the thoracic esophagus and cardia. *J Am Coll Surg*. 2006;203(5):661-669.
4. Lerut T, Moons J, Coosemans W, et al. Postoperative complications after transthoracic esophagectomy for cancer of the esophagus and gastroesophageal junction are correlated with early cancer recurrence: role of systematic grading of complications using the modified Clavien classification. *Ann Surg*. 2009;250(5):798-807.
5. Rizk NP, Bach PB, Schrag D, et al. The impact of complications on outcomes after resection for esophageal and gastroesophageal junction carcinoma. *J Am Coll Surg*. 2004;198(1):42-50.
6. Booka E, Takeuchi H, Suda K, et al. Meta-analysis of the impact of postoperative complications on survival after oesophagectomy for cancer. *BJS Open*. 2018;2(5):276-284.
7. Walker KG, Bell SW, Rickard MJ, et al. Anastomotic leakage is predictive of diminished survival after potentially curative resection for colorectal cancer. *Ann Surg*. 2004;240(2):255-259.
8. Bell SW, Walker KG, Rickard MJ, et al. Anastomotic leakage after curative anterior resection results in a higher prevalence of local recurrence. *Br J Surg*. 2003;90(10):1261-1266.
9. Pugalenthi A, Protic M, Gonen M, et al. Postoperative complications and overall survival after pancreaticoduodenectomy for pancreatic ductal adenocarcinoma. *J Surg Oncol*. 2016;113(2):188-193.
10. Warren JL, Klabunde CN, Schrag D, Bach PB, Riley GF. Overview of the SEER-Medicare data: content, research applications, and generalizability to the United States elderly population. *Med Care*. 2002;40(8 Suppl):IV-3-18.
11. Quan H, Sundararajan V, Halfon P, et al. Coding algorithms for defining comorbidities in ICD-9-CM and ICD-10 administrative data. *Med Care*. 2005;43(11):1130-1139.
12. Hammond J, Lim S, Wan Y, Gao X, Patkar A. The burden of gastrointestinal anastomotic leaks: an evaluation of clinical and economic outcomes. *J Gastrointest Surg*. 2014;18(6):1176-1185.

13. Hong JC, Murphy JD, Wang SJ, Koong AC, Chang DT. Chemoradiotherapy before and after surgery for locally advanced esophageal cancer: a SEER-Medicare analysis. *Ann Surg Oncol*. 2013;20(12):3999-4007.
14. Paul S, Altorki NK, Sheng S, et al. Thoracoscopic lobectomy is avssociated with lower morbidity than open lobectomy: a propensity-matched analysis from the STS database. *J Thorac Cardiovasc Surg*. 2010;139(2):366-378.
15. Sesti J, Langan RC, Bell J, et al. A comparative analysis of long-term survival of robotic Versus thoracoscopic lobectomy. *Ann Thorac Surg*. 2020;110:1139-1146.
16. Varghese TK Jr, Wood DE, Farjah F, et al. Variation in esophagectomy outcomes in hospitals meeting Leapfrog volume outcome standards. *Ann Thorac Surg*. 2011;91(4):1003-1009. discussion 1009-10.
17. Junemann-Ramirez M, Awan MY, Khan ZM, Rahamim JS. Anastomotic leakage post-esophagogastrectomy for esophageal carcinoma: retrospective analysis of predictive factors, management and influence on longterm survival in a high volume centre. *Eur J Cardiothorac Surg*. 2005;27(1):3-7.
18. Lagarde SM, De Boer JD, Ten Kate FJ, Busch OR, Obertop H, Van Lanschot JJ. Postoperative complications after esophagectomy for adenocarcinoma of the esophagus are related to timing of death due to recurrence. *Ann Surg*. 2008;247(1):71-76.
19. Takeuchi H, Saikawa Y, Oyama T, et al. Factors influencing the long-term survival in patients with esophageal cancer who underwent esophagectomy after chemoradiotherapy. *World J Surg*. 2010;34(2):277-284.
20. Chang AC, Birkmeyer JD. The volume-performance relationship in esophagectomy. *Thorac Surg Clin*. 2006;16(1):87-94.
21. Altorki NK, Zhou XK, Stiles B, et al. Total number of resected lymph nodes predicts survival in esophageal cancer. *Ann Surg*. 2008;248(2):221-226.
22. Erhunmwunsee L, Gulack BC, Rushing C, Niedzwiecki D, Berry MF, Hartwig MG. Socioeconomic status, not race, is associated with reduced survival in esophagectomy patients. *Ann Thorac Surg*. 2017;104(1):234-244.
23. Birkmeyer JD, Siewers AE, Finlayson EV, et al. Hospital volume and surgical mortality in the United States. *N Engl J Med*. 2002;346(15):1128-1137.
24. Group, TL. 2019. Majority of U.S. Hospitals Not Meeting Surgical Safety Standards. https://www.leapfroggroup.org/news-events/majority-us-hospitals-not-meeting-surgical-safety-standards. Accessed January 17, 2020.
25. Birkmeyer JD, Skinner JS, Wennberg DE. Will volume-based referral strategies reduce costs or just save lives? *Health Aff*. 2002;21(5):234-241.

How to cite this article: Sesti J, Almaz B, Bell J, et al. Impact of postoperative complications on long-term survival after esophagectomy in older adults: a SEER-Medicare analysis. *J Surg Oncol*. 2021;124:751-766.
https://doi.org/10.1002/jso.26587

APPENDIX A

TABLE A1 Codes used for cohort identification, procedures type, comorbidities, and complications

Aspect	Source	Code
Diagnosis		
Site	ICD-10-CM[a]	Esophagus: 150.1, 150.2, 150.4, 150.5
Histologic type	ICD-O-3	Squamous cell carcinoma, adenocarcinoma, other
Procedure		
Esophagectomy	ICD-9-CM	42.4, 42.5, 42.6
Major complications		
Arrhythmia	ICD-9-CM	427.31, 427.32, 427.0
Myocardial infarction		410.00-410.92, 411.81, 413.0-413.9
Postoperative stroke		997.02, 430-436
Pneumonia		481-486, 997.31, 997.32
Renal insufficiency/failure		585.1-585.9
Sepsis/shock		038.0-038.9, 995.91, 995.92, 998.0-998.09, 999.31, 999.32
Accidental puncture or laceration, complicating surgery		998.2
Bleeding complicating procedure		998.11
Major anastomotic leak		43266, 43212, 75989, 10060, 10061, 10160, 10180, 32556, 32557, 32554, 32555, 49405, 32651, 32652, 3220, 32225, 32320, 32310, 35800, + ICD9 997.4
Pulmonary embolus		415.1, 415.11, 415.12, 415.19

(Continues)

TABLE A1 (Continued)

Aspect	Source	Code
Chemotherapy		
	ICD-9-CM	V58.1, V66.2, V67.2, 99.25
	HCPCS	96400-96549, Q0083-Q0085, 51720, CY2005, J9000-J9999
Radiation		
	ICD-9-CM	V58.0, V66.1, V67.1, 92.21-92.29
	HCPCS	77401-77499, 77520, 77523, 77750-77799, G0256, G0261
	Revenue Center	0330, 0333

Note: For all codes listed above, a dash (-) indicates all codes (including subcodes) between the given values.
[a]Recoded from ICD-O-3.

TABLE A2 Individual comorbidities of group

Variable	Group	Summary, *n* (%)
elix_aids		
	No	[a]
	Yes	[a]
elix_alcohol		
	No	901 (95.9)
	Yes	39 (4.1)
elix_blane		
	No	928 (98.7)
	Yes	12 (1.3)
elix_carit		
	No	620 (66.0)
	Yes	320 (34.0)
elix_chf		
	No	895 (95.2)
	Yes	45 (4.8)
elix_coag		
	No	903 (96.1)
	Yes	37 (3.9)
elix_cpd		
	No	775 (82.4)
	Yes	165 (17.6)
elix_dane		
	No	926 (98.5)
	Yes	14 (1.5)

TABLE A2 (Continued)

Variable	Group	Summary, *n* (%)
elix_depre		
	No	894 (95.1)
	Yes	46 (4.9)
elix_diabc		
	No	912 (97.0)
	Yes	28 (3.0)
elix_diabunc		
	No	785 (83.5)
	Yes	155 (16.5)
elix_drug		
	No	921 (98.0)
	Yes	19 (2.0)
elix_fed		
	No	666 (70.9)
	Yes	274 (29.1)
elix_hypc		
	No	912 (97.0)
	Yes	28 (3.0)
elix_hypothy		
	No	882 (93.8)
	Yes	58 (6.2)
elix_hypunc		
	No	520 (55.3)
	Yes	420 (44.7)

TABLE A2 (Continued)

Variable	Group	Summary, *n* (%)
elix_ld		
	No	894 (95.1)
	Yes	46 (4.9)
elix_lymph		
	No	939 (99.9)
	Yes	<11
elix_metacanc		
	No	737 (78.4)
	Yes	203 (21.6)
elix_obes		
	No	882 (93.8)
	Yes	58 (6.2)
elix_ond		
	No	904 (96.2)
	Yes	36 (3.8)
elix_para		
	No	[a]
	Yes	[a]
elix_pcd		
	No	916 (97.4)
	Yes	24 (2.6)
elix_psycho		
	No	924 (98.3)
	Yes	16 (1.7)
elix_pud		
	No	[a]
	Yes	[a]
elix_pvd		
	no	895 (95.2)
	yes	45 (4.8)
elix_rf		
	No	904 (96.2)
	Yes	36 (3.8)
elix_rheumd		
	No	919 (97.8)
	Yes	21 (2.2)
elix_valv		
	No	907 (96.5)
	Yes	33 (3.5)

(Continues)

TABLE A2 (Continued)

Variable	Group	Summary, *n* (%)
elix_wloss		
	No	770 (81.9)
	Yes	170 (18.1)

Abbreviation: DUA, Data Use Agreement.

[a]Data not shown due to compliance with DUA restrictions.

TABLE A3 Individual major complications of group

Variable	Group	Summary, *n* = 890 (%)
comp_arrhythmia		
	No	652 (73.3)
	Yes	238 (26.7)
comp_leak		
	No	813 (91.3)
	Yes	77 (8.7)
comp_myo_inf		
	No	877 (98.5)
	Yes	13 (1.5)
comp_pneumonia		
	No	767 (86.2)
	Yes	123 (13.8)
comp_pulm_emb		
	No	871 (97.9)
	Yes	19 (2.1)
comp_renal_failure		
	No	860 (96.6)
	Yes	30 (3.4)
comp_sepsis		
	No	819 (92.0)
	Yes	71 (8.0)
comp_stroke		
	No	874 (98.2)
	Yes	16 (1.8)

TABLE A4 Univariate and multivariate analysis of predictors of overall survival

Variable	Term	*N*	Events	Univariate HR (95% CI)	*p*-value	Multivariate HR (95% CI)	*p*-value
Age (10 years)		890	516	1.04 (0.91, 1.2)	0.529		
Sex					0.079		
	Female	126	61	Reference			
	Male	764	455	1.27 (0.97, 1.66)			
Race					0.245		
	White	832	484	Reference			
	black	33	[a]	1.09 (0.7, 1.68)			
	other	25	[b]	0.61 (0.33, 1.11)			
Married					0.721		
	no	236	138	Reference			
	yes	619	363	0.96 (0.79, 1.17)			
Median income (thousands, quartiles)					0.386		
	[13.2,44.7]	216	134	Reference			
	(44.7,60.1]	221	127	0.93 (0.73, 1.19)			
	(60.1,81.4]	227	126	0.82 (0.64, 1.04)			
	(81.4,191]	223	126	0.86 (0.67, 1.1)			
Location					0.823		
	metropolitan	755	442	Reference			
	nonmetropolitan	135	74	0.97 (0.76, 1.24)			
Year		890	516	0.96 (0.92, 1.01)	0.121		
Stage					< 0.001		<0.001
	1	234	74	Reference		Reference	
	2	285	172	2.48 (1.89, 3.26)		2.74 (2.07, 3.63)	
	3	293	212	3.83 (2.93, 5.01)		4.23 (3.21, 5.58)	
	4	[a]	[a]	7.04 (4.82, 10.28)		8.63 (5.82, 12.79)	
Histology					0.716		
	Adenocarcinoma	726	422	Reference			
	Squamous	164	94	0.96 (0.77, 1.2)			
Site					0.991		
	Lower	748	435	Reference			
	Middle	142	81	1 (0.79, 1.27)			
Nodes (per 10)		890	516	0.99 (0.98, 1)	0.005	0.85 (0.78, 0.93)	< 0.001
Provider volume[b]					< 0.001		0.037
	[1, 3]	222	145	Reference		Reference	
	(3,8]	242	150	0.92 (0.73, 1.16)		0.88 (0.70, 1.12)	
	(8,16]	205	119	0.87 (0.68, 1.1)		0.86 (0.67, 1.11)	
	(16,35]	221	102	0.59 (0.46, 0.76)		0.67 (0.51, 0.88)	

TABLE A4 (Continued)

Variable	Term	N	Events	Univariate HR (95% CI)	p-value	Multivariate HR (95% CI)	p-value
Neoadjuvant therapy					< 0.001		
	None	526	278	Reference			
	Chemo	[a]	[a]	1.4 (0.91, 2.16)			
	Rad	[a]	[a]	1.64 (0.98, 2.76)			
	chemo/rad	309	201	1.52 (1.26, 1.82)			
Elixhauser score					0.139		
	0	116	68	Reference			
	1	203	111	1 (0.74, 1.35)			
	2	219	131	1.16 (0.87, 1.56)			
	3+	352	206	1.27 (0.96, 1.67)			
Major complications					<0.001		<0.001
	0	455	235	Reference		Reference	
	1	285	174	1.32 (1.09, 1.61)		1.41 (1.15, 1.73)	
	2+	150	107	1.99 (1.58, 2.51)		2.18 (1.72, 2.76)	

Abbreviation: DUA, Data Use Agreement.

[a]Data not shown due to compliance with DUA restrictions.

[b]Total number of claims per provider.

TABLE A5 Univariate and multivariate analysis of predictors of cancer-specific mortality

Variable	Term	n	Events	Univariate Estimate (95% CI)	p-value	Multivariate
Age (10 years)		890	374	0.96 (0.82, 1.13)	0.639	
Sex					0.145	
	Female	126	45	Reference		
	Male	764	329	1.26 (0.92, 1.72)		
Race					0.676	
	White	832	348	Reference		
	Black	33	[a]	1.14 (0.69, 1.89)		
	Other	25	[a]	0.8 (0.43, 1.5)		
Married					0.993	
	No	236	98	Reference		
	Yes	619	267	1 (0.79, 1.26)		
Median income (thousands, quartiles)					0.057	
	[13.2,44.7]	216	96	Reference		
	(44.7,60.1]	221	98	1.02 (0.77, 1.35)		
	(60.1,81.4]	227	76	0.7 (0.52, 0.95)		
	(81.4,191]	223	103	0.99 (0.75, 1.3)		
Location					0.913	
	Metropolitan	755	318	Reference		
	Nonmetropolitan	135	56	1.02 (0.76, 1.35)		

(Continues)

TABLE A5 (Continued)

Variable	Term	*n*	Events	Univariate Estimate (95% CI)	*p*-value	Multivariate	
Year		890	374	0.9 (0.85, 0.94)	<0.001	0.89 (0.84, 0.94)	<0.001
Stage					<0.001		<0.001
	1	234	42	Reference		Reference	
	2	285	122	3 (2.11, 4.26)		3.37 (2.34, 4.86)	
	3	293	169	4.99 (3.55, 7)		5.81 (4.08, 8.28)	
	4	50	33	8.35 (5.27, 13.23)		11.16 (6.94, 17.97)	
Histology					0.754		
	Adenocarcinoma	726	301	Reference			
	Squamous	164	73	1.04 (0.81, 1.35)			
Site					0.414		
	Lower	748	309	Reference			
	Middle	142	65	1.12 (0.86, 1.46)			
Nodes (per 10)		890	374	0.99 (0.98, 1)	0.037	0.84 (0.76, 0.92)	<0.001
Provider volume[b]					0.003		
	[1, 3]	222	102	Reference			
	(3,8]	242	106	0.93 (0.71, 1.23)			
	(8,16]	205	95	0.99 (0.75, 1.31)			
	(16,35]	221	71	0.6 (0.44, 0.81)			
Neoadjuvant therapy					0.001		
	None	526	200	Reference			
	Chemo	33	[a]	1.52 (0.94, 2.46)			
	Rad	22	[a]	2.18 (1.27, 3.75)			
	chemo/rad	309	142	1.43 (1.15, 1.78)			
Elixhauser score					0.748		
	0	116	49	Reference			
	1	203	91	1.11 (0.79, 1.57)			
	2	219	99	1.21 (0.86, 1.7)			
	3+	352	135	1.1 (0.79, 1.53)			
Major complications					0.008		0.001
	0	455	184	Reference		Reference	
	1	285	122	1.16 (0.93, 1.46)		1.26 (0.99, 1.60)	
	2+	150	68	1.55 (1.17, 2.05)		1.77 (1.33, 2.36)	

Abbreviation: DUA, Data Use Agreement.

[a]Data not shown due to compliance with DUA restrictions.

[b]Total number of claims per provider.