ORIGINAL ARTICLE

Trends in Management and Prognosis for Esophageal Cancer Surgery

Twenty-five Years of Experience at a Single Institution

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Objective: To investigate trends in results of esophagectomies to treat esophageal cancer at a single high-volume institution during the past 25 years.

Design and Setting: Retrospective cohort study in a university tertiary referral center.

Patients and Methods: Patients with cancer of the thoracic esophagus or esophagogastric junction seen from 1980 through 2004 were included (N=3493). Three time periods were defined: 1980-1987, 1988-1995, and 1996-2004.

Main Outcome Measures: Clinical presentation, tumor characteristics, and morbidity, mortality, and survival rates among patients with esophageal cancer undergoing esophagectomy.

Results: The ratio of squamous cell carcinoma to adenocarcinoma decreased from 3.3 to 1.7 ($P<.001$) during the study period, in parallel with an increase in the number of patients with tumors in the lower esophagus/esophagogastric junction. An increasing proportion of patients who underwent resection received neoadjuvant treatment (chemotherapy/chemoradiotherapy), and 1978 patients underwent esophagectomy. The R0 resection rate increased from 74.5% to 90.1% ($P<.001$). In addition, an increasing proportion of patients had early-stage tumor in the resected specimen. In-hospital postoperative mortality decreased from 8.2% to 2.6% ($P<.001$), and the 5-year survival rate significantly improved from 18.8% to 42.3% ($P<.001$) for all patients who underwent resection. Pathological tumor stage, completeness of the resection, time period, sex, tumor histological type, and tumor location influenced the prognosis of patients with esophageal cancer undergoing esophagectomy.

Conclusions: A change in location and histological type of esophageal cancer has occurred during the past 25 years. Earlier diagnosis, a multidisciplinary approach, and refinements in surgical technique and perioperative care have led to a significant reduction in postoperative mortality rate and improved long-term survival among patients with cancer of the thoracic esophagus or esophagogastric junction.

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THE EPIDEMIOLOGICAL CHARacteristics of esophageal cancer have changed dramatically in recent years as the incidence of adenocarcinoma has risen.[1,2] Parallel changes in treatment strategies, such as refinements in surgical technique, creation of referral centers for esophageal diseases throughout the world, and a more extensive use of chemoradiotherapy, have contributed to a reduction in perioperative mortality and improved long-term survival after esophagectomies in patients with esophageal cancer.

See Invited Critique at end of article

During a 25-year period, clinical and treatment-related data from more than 4000 patients seen at a single university tertiary referral center were prospectively collected in a database. This provides a unique opportunity to evaluate trends in short- and long-term outcomes after esophagectomies to treat cancer.

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METHODS

We evaluated all patients with cancer of the thoracic esophagus or esophagogastric junction (EGJ)—Siewert type I and II tumors—seeking treatment at the University of Padova between January 1, 1980, and December 31, 2004. Three time periods were defined: 1980-1987, 1988-1995, and 1996-2004. Patients with tumors of the cervical esophagus were excluded from the study because, during the past 25 years, the therapeutic strategy shifted from immediate surgical treatment, often a mutilating laryngectomy, to first-line chemoradiotherapy with salvage op-

Table 1. Demographic Characteristics and Clinical Presentation for Patients With Esophageal and EGJ Cancer

	No. (%) of Patients			
	1980-1987 (n=1438)	1988-1995 (n=1178)	1996-2004 (n=877)	*P* Value
Sex				
Male	1199 (83.4)	1003 (85.1)	722 (82.3)	.21
Female	239 (16.6)	175 (14.9)	155 (17.7)	
Age, median (interquartile range), y	61.0 (54-69)	61.7 (54-68)	64.3 (56-71)	<.001
Tumor site[a]				
Upper thoracic	298 (20.7)	285 (24.2)	210 (24.0)	<.001
Midthoracic	550 (38.3)	380 (32.3)	231 (26.4)	
Lower thoracic/EGJ (Siewert type I and II)	590 (41.0)	513 (43.5)	435 (49.6)	
Tumor histological type[b]				
Squamous cell	1003 (73.1)	823 (71.4)	530 (60.9)	<.001[c]
Adenocarcinoma	301 (21.9)	278 (24.1)	306 (35.1)	
Other	69 (5.0)	52 (4.5)	35 (4.0)	
Clinical TNM stage[d]				
0	15 (1.0)	21 (1.8)	25 (2.9)	<.001
I	98 (6.8)	112 (9.5)	80 (9.2)	
II	868 (60.4)	486 (41.4)	249 (28.7)	
III	271 (28.9)	381 (32.5)	367 (42.2)	
IV	185 (12.9)	174 (14.8)	148 (17.0)	
Treatment strategy				
Resection	785 (54.6)	659 (55.9)	534 (60.9)	.01
Chemoradiotherapy[e]	147 (10.2)	400 (34.1)	411 (46.9)	<.001

Abbreviation: EGJ, esophagogastric junction.
[a] Data were not available for 1 patient.
[b] Data were not available for 96 patients.
[c] Squamous cell carcinoma vs adenocarcinoma.
[d] Data were not available for 13 patients.
[e] First-line chemotherapy or chemoradiotherapy with or without subsequent surgical treatment.

erations reserved only to treat nonresponding or recurrent cancers. Patients with Siewert type III tumors were considered to have gastric tumors and were also excluded from our study. The study was approved by the Ethics Committee of the University of Padova Medical School. Because individual patients could not be identified, the need for patients' consent was waived.

The preoperative workup included physical examination, standard laboratory tests, lung function tests, and anesthesiological assessment. In selected cases, noninvasive cardiac evaluation (echocardiogram and/or dynamic tests to estimate patients' ventricular function) were also performed. The American Society of Anesthesiology classification system was used to assess the operative risk. Barium swallow study and upper gastrointestinal endoscopy were performed to assess the features of the tumor; flexible bronchoscopy and otolaryngologic evaluation were also performed for tumors of the cervical, upper, and middle esophagus. To rule out any metastatic disease, computed tomographic scans of the chest and abdomen (as well as the neck in selected cases) were obtained for all patients seen after 1986. Endoscopic ultrasonography was used from 2000 onward to provide additional information about tumor depth and lymph node status. From 1992 onward, the treatment strategy for patients with esophageal and esophagogastric cancer was based on disease-oriented multidisciplinary team decisions. A tailored therapeutic approach was defined: surgical procedure as the first treatment for localized cancer in fit patients; neoadjuvant chemotherapy or chemoradiotherapy, if feasible, for locally advanced cancer (ie, T3N+M0 or T4 any NM0); and endoscopic palliation or best supportive care for patients with metastatic disease or unfit patients with high American Society of Anesthesiology scores.

The esophageal TNM staging system was used for esophageal carcinoma, and gastric TNM staging was used for tumors at the esophagogastric junction (EGJ). Complete tumor resection was defined as R0, and incomplete resections with microscopic or macroscopic residual disease were defined as R1 and R2, respectively.

Both in-hospital (all deaths occurring at the hospital) and 30-day (all deaths occurring within 30 days of surgical treatment) perioperative mortality rates were calculated. Postoperative morbidity included any minor or major medical or surgical complication. Anastomotic complications (ie, necrosis of the esophageal substitute and anastomotic leaks) were recorded, including symptomatic and small asymptomatic leaks detected on routine postoperative radiological examination.

SURGICAL TREATMENT

Esophagectomy was performed using an Ivor-Lewis procedure, via a laparotomy and right thoracotomy, for tumors of the mid-lower esophagus and EGJ. A 3-incision McKeown procedure, with an additional left cervical incision, was reserved for tumors in the upper third of the thoracic esophagus. Transhiatal esophagectomy was mainly performed in selected patients with poor respiratory function or contraindications for thoracotomy. At least 6 to 8 cm of healthy esophagus were resected above the proximal edge of the tumor to avoid neoplastic involvement of the resection margins. Over the years, we have adopted a more radical lymphadenectomy for patients undergoing resection with a curative intent: en bloc lymph node dissection was performed, including the periesophageal, infracarinal, posterior mediastinal, and paracardial lymph nodes, as well as those located along the lesser gastric curvature, the origin of the left gastric artery, the celiac trunk, the common hepatic artery, and the splenic artery (with the cervical, recur-

Table 2. Demographic and Tumor Characteristics in Patients Who Underwent Resection

	No. (%) of Patients				
	1980-1987 (n=785)	1988-1995 (n=659)	1996-2004 (n=534)	Total (N=1978)	*P* Value
Male sex	655 (83.4)	563 (85.4)	426 (79.9)	**1644** (83.1)	.03
Age, median (interquartile range), y	59.1 (52-65)	60.6 (53-66)	64.0 (56-70)	60.9 (54-67)	<.001
Tumor site[a]					
Upper thoracic	133 (16.9)	422 (18.5)	89 (16.7)	**344** (17.4)	<.001
Midthoracic	305 (38.9)	202 (30.7)	147 (27.6)	**654** (33.1)	
Lower thoracic/EGJ (Siewert type I and II)	347 (44.2)	335 (50.8)	297 (55.7)	**979** (49.5)	
Tumor histological type[b]					
Squamous cell carcinoma	550 (70.0)	443 (67.5)	293 (55.0)	**1286** (65.2)	<.001[c]
Adenocarcinoma	188 (24.0)	180 (27.5)	219 (41.1)	**587** (29.7)	
Other	47 (6.0)	33 (5.0)	21 (3.9)	**101** (5.1)	
History of Barrett esophagus[d]	23 (12.2)	38 (21.1)	64 (29.2)	**125** (6.3)	<.001

Abbreviation: EGJ, esophagogastric junction.
[a] Data were not available for 1 patient.
[b] Data were not available for 4 patients.
[c] Squamous cell carcinoma vs adenocarcinoma.
[d] Analysis limited to patients with adenocarcinoma.

rent laryngeal chains and paratracheal nodes also resected for cancers of the cervical and upper thoracic esophagus). The alimentary tract was reconstructed immediately, preferably using the gastric pull-up technique; if the stomach was unavailable, either a Roux-en-Y jejunal loop or the left colon interposition technique was used. Anastomoses were performed using a circular stapling device in the thoracic cavity and a hand-sewn suture in the neck.

In addition, over the years we have adopted a more aggressive surgical approach, reserving transhiatal esophagectomy only for patients in whom thoracotomy was formally contraindicated.

Postoperative patient care was refined to include early extubation (preferably in the operating room), aggressive respiratory care with frequent bronchoscopic suctioning, pain control (epidural analgesia along with patient-controlled analgesia), respiratory exercise, early mobilization, and deambulation. Food intake was allowed, provided that results of a postoperative diatrizoate meglumine swallow study (Gastrografin; Schering, Berlin, Germany) showed no evidence of leakage, on the 7th and 10th postoperative days for stapled and hand-sewn anastomoses, respectively.

Patients were routinely seen by their surgeons and oncologists for follow-up 1, 3, 6, and 12 months after their operation and every 6 to 12 months thereafter. We selected patients who underwent the procedure before December 2004 to allow for at least 2 years of follow-up.

STATISTICAL ANALYSIS

Data are expressed as medians and interquartile ranges. Proportions were compared using the χ^2 or Fisher exact tests. Continuous variables were compared using the Mann-Whitney test. Survival estimates were calculated by the Kaplan-Meier method, and survival comparisons were performed using the log-rank test. Cox proportional hazard models were used to identify independent predictors of survival. $P<.05$ was considered significant.

RESULTS

From 1980-2004, 4105 patients were referred to our department with cancer of the esophagus or EGJ (Siewert type I, II, and III tumors), and 3493 patients (85.1%) with cancer of the thoracic esophagus or EGJ (Siewert type I and II tumors) were selected for the study. Of 3493 patients, 1978 (56.6%) underwent resection. Temporal trends of patients' clinical presentation and treatment strategies are shown in **Table 1**.

CLINICOPATHOLOGICAL CHARACTERISTICS

Demographic information and tumor characteristics for the 3 study groups are summarized in **Table 2**. Histological type, tumor location, and prevalence of Barrett esophagus differed over time, with a higher proportion of adenocarcinoma, lower tumor location, and Barrett esophagus among patients seen from 1996-2004. **Table 3** summarizes the treatment details and pathological findings for inpatients who underwent resection. Of these, 389 (19.7%) had undergone preoperative chemotherapy or chemoradiotherapy (1980-1987, 5.7%; 1988-1995, 25.3%; 1996-2004, 33.2%; $P<.001$). There was a significant trend toward lower pathological stage of disease, with no differences in the degree of tumor differentiation during the study period. A growing proportion of patients were considered curatively resected (R0) (1980-1987, 585 of 785 [74.5%]; 1996-2004, 481 of 534 [90.1%]; $P<.001$). During the study period, an increasing proportion of patients underwent transthoracic rather than transhiatal esophagectomy ($P<.001$), had intrathoracic rather than cervical anastomosis ($P<.001$), and had extended rather than limited lymph node dissection ($P<.001$) (Table 3).

MORBIDITY AND MORTALITY

Overall, the in-hospital mortality was 6.1% (120 of 1978), which decreased significantly during the study period (1980-1987, 64 of 785 [8.2%]; 1988-1995, 42 of 659 [6.4%]; 1996-2004, 14 of 534 (2.6%); $P<.001$) (**Table 4**). From the 1996-2004 study period, the in-

Table 3. Surgical Treatment and Pathological Findings

	No. (%) of Patients				
	1980-1987 (n=785)	1988-1995 (n=659)	1996-2004 (n=534)	Total (N=1978)	*P* Value
Had neoadjuvant therapy	45 (5.7)	167 (25.3)	177 (33.2)	**389** (19.7)	<.001
Access					
Laparotomy and thoracotomy (R)	428 (54.5)	343 (52.1)	378 (70.8)	**1149** (58.1)	<.001[a]
Thoracotomy (R), laparotomy, and cervicotomy (L)	206 (26.2)	157 (23.8)	101 (18.9)	**464** (23.5)	
Laparotomy and cervicotomy (L)	116 (14.8)	135 (20.5)	29 (5.4)	**280** (14.1)	
Other	35 (4.5)	24 (3.6)	26 (4.9)	**85** (4.3)	
Reconstruction					
Stomach	652 (83.1)	575 (87.3)	478 (89.5)	**1705** (86.2)	<.001[b]
Colon	62 (7.9)	83 (5.8)	26 (4.9)	**126** (6.4)	
Other	71 (9.0)	46 (6.9)	30 (5.6)	**147** (7.4)	
Pathological TNM stage[c]					
0	14 (1.8)	36 (5.5)	60 (11.3)	**110** (5.6)	<.001
I	68 (8.7)	62 (9.4)	89 (16.8)	**219** (11.1)	
II	219 (27.9)	182 (27.6)	147 (27.7)	**548** (27.8)	
III	266 (33.9)	267 (40.5)	181 (34.2)	**714** (36.2)	
IV	218 (27.8)	112 (17.0)	53 (10.0)	**383** (19.4)	
Resected lymph nodes[d]	70.2	71.2	83.3	74.9	<.001
Tumor differentiation[e]					
Well or moderately differentiated	554 (75.1)	478 (77.0)	381 (74.6)	**1413** (75.6)	.59
Poorly differentiated	184 (24.9)	143 (23.0)	130 (25.4)	**457** (24.4)	
Resection					
R0	585 (74.5)	502 (76.2)	481 (90.1)	**1568** (79.3)	<.001
R1-2	200 (25.5)	157 (23.8)	53 (9.9)	**410** (20.7)	

Abbreviations: L, left; R, right.
[a] Transthoracic vs nontransthoracic access.
[b] Stomach vs colon.
[c] Data were not available for 4 patients.
[d] Data are given as percentage of patients with 15 or more resected lymph nodes.
[e] Patients with squamous cell carcinoma or adenocarcinoma (n = 1870).

Table 4. Morbidity and Mortality

	No. (%) of Patients				
	1980-1987 (n=785)	1988-1995 (n=659)	1996-2004 (n=534)	Total (N=1978)	*P* Value
Mortality					
In hospital	64 (8.2)	42 (6.4)	14 (2.6)	**120** (6.1)	<.001
30 d	54 (6.5)	28 (4.3)	7 (1.3)	**89** (4.5)	<.001
Complications					
Overall	361 (46.0)	306 (46.4)	243 (45.5)	**910** (46.0)	.95
Fatal[a]	17.2	13.7	5.7	13.0	.002
Pulmonary[b]	85 (10.8)	85 (12.9)	66 (12.4)	**236** (11.9)	.45
Cardiovascular[c]	41 (5.2)	27 (4.1)	39 (7.3)	**107** (5.4)	.05
Anastomotic[d]	93 (11.6)	85 (12.9)	30 (5.6)	**208** (10.5)	<.001
Fatal anastomotic[e]	22.6	18.8	6.7	18.7	<.001
Chylothorax	3 (0.4)	6 (0.9)	6 (1.1)	**15** (0.8)	.27
Laryngeal nerve palsy	40 (5.1)	31 (4.7)	38 (7.1)	**109** (5.5)	.16
Hemorrhage	17 (2.2)	17 (2.6)	5 (0.9)	**39** (2.0)	.11
Renal failure	19 (2.4)	7 (1.1)	1 (0.2)	**27** (1.4)	.002
Wound infection	56 (7.1)	37 (5.6)	5 (0.9)	**98** (4.6)	<.001
Reoperation	34 (4.3)	32 (4.9)	16 (3.0)	**82** (4.2)	.26

[a] Data are expressed as percentage of all complications that were fatal.
[b] Pneumonia, atelectasis, or lung failure.
[c] Myocardial infarction, severe arrhythmia, pulmonary edema, or pulmonary embolism.
[d] Including anastomotic leakage (clinical or radiological) and necrosis of the esophageal substitute.
[e] Data are expressed as percentage of anastomotic complications that were fatal.

hospital mortality was 1.4% (7 of 495) among patients undergoing esophagectomy with cervical or intrathoracic gastric pull-up.

Overall, postoperative morbidity did not change significantly over time, and the most common complications remained pulmonary and cardiovascular (Table 4).

However, we observed a reduction in potentially fatal postoperative complications, such as anastomotic complications (1980-1987, 11.6%; 1996-2004, 5.6%; $P<.001$).

SURVIVAL

The median duration of survival for all patients in the 1980-1987, 1988-1995, and 1996-2004 study periods was 7.8, 11.5, and 16.8 months, respectively (**Figure 1**). Median duration of survival was 19 months (interquartile range, 9.3-47.3) for all patients who underwent resection with curative intent. The 5-year survival rate for the entire series was 25.9%, and it significantly improved from 18.8% in 1980-1987 to 42.3% in 1996-2004 ($P<.001$) (**Figure 2**). Survival curves by stage and histological type from study period 1996-2004 are shown in **Figure 3**A and B. Among patients with R0 curative resection, 5-year survival rates were 23.6%, 29.5%, and 46.1% for 1980-1987, 1988-1995, and 1996-2004, respectively ($P<.001$). There was a significant difference in survival rates between men and women overall and in the first 2 time periods but not in the last period. The 5-year survival rate was higher for patients with adenocarcinoma than for patients with squamous cell carcinoma (30.9% vs 23.8%; $P<.001$).

Details of univariate analysis of prognostic factors of survival are shown in **Table 5**. Cox multivariate analysis identified lower pathological tumor stage, R0 resection, more recent study period, female sex, adenocarcinoma histological type, and lower tumor location as independent predictors of long-term survival (**Table 6**).

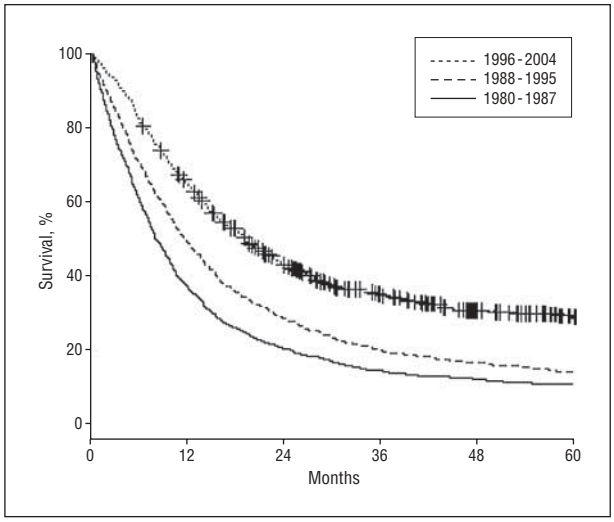

Figure 1. Kaplan-Meier survival curves (including postoperative deaths) plotted for all patients by period subgroup, independent of type of treatment.

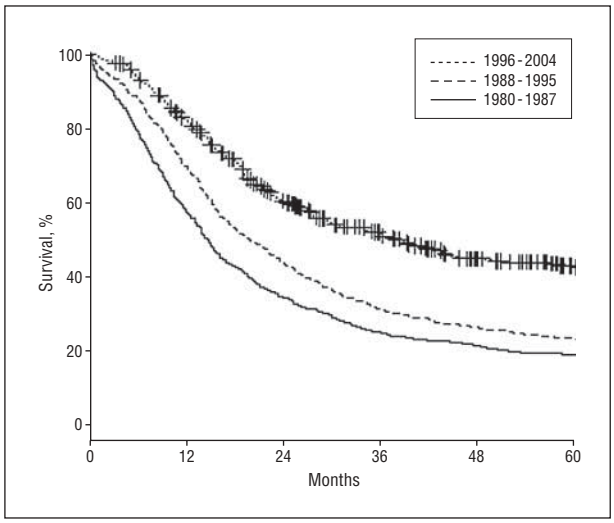

Figure 2. Kaplan-Meier survival curves (including postoperative deaths) plotted for patients who underwent resection by period subgroup.

COMMENT

In the past 2 decades we have observed a significant change in epidemiological characteristics and treatment approach for esophageal cancer. The goal of treatment has moved from palliation of dysphagia to cure of disease.[3-5] Although the prognosis for patients with esophageal cancer is still poor, there are reports from specialized high-volume centers throughout the world suggesting that a 5-year survival rate of greater than 40% can be attained.[6-10]

Improvement in diagnostic tools (computed tomography, endoscopic ultrasonography, and positron emission tomography) has allowed for more accurate staging of patients with esophageal cancer. However, despite all efforts for early diagnosis and accurate clinical assessment, less than 50% of patients have lesions amenable to surgical resection with curative intent at the time of diagnosis. A tailored approach has been defined for patients with esophageal cancer: neoadjuvant treatment is, to date, preferred for patients with locally advanced disease. A partial or complete response can be achieved in an average of 50% of cases, resulting in a significant improvement in the number of R0 resections. Surgical treatment remains the standard of care for fit patients with localized cancer of the esophagus and EGJ.[11]

Despite the lack of definite data and consensus among oncologists and surgeons on the efficacy of therapies before and after esophagectomy, a multimodal approach is still preferred by many centers that specialize in treating patients with locally advanced esophageal cancer.[12-21] This has certainly contributed to the improved long-term survival rate reported in a growing number of patients with esophageal cancer.

Advances in surgical treatment, with standardization of techniques and improvement in perioperative care, have resulted in a significant drop in perioperative mortality rates in referral centers in the West and East. Law et al[22] reported a median duration of survival of 16 months for patients with esophageal cancer operated on in Hong Kong between 1990 and 1995 and survival of 26 months for those undergoing esophagectomy between 1995 and 2000, with no mortality in the last 5 years of the study. Similarly, in a US series, Hofstetter et al[23] documented an improvement in median duration of survival from 17 to 34 months in the last 30 years; the mortality dropped from 12% to 6%. Similar results have been reported by Ellis et al[24] and Bouvier et al.[25] Our results from 1978 esophagectomies to treat cancer of the esophagus and EGJ from study period 1980-2004 are in line with those reported previously: postop-

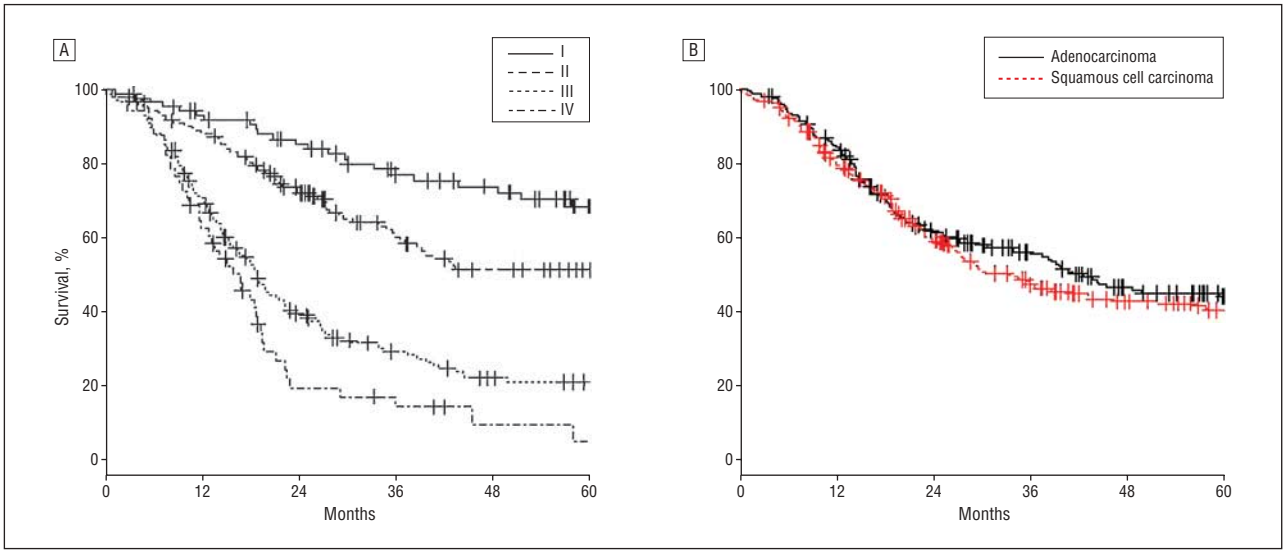

Figure 3. Kaplan-Meier survival curves (including postoperative deaths) in the last time period plotted by tumor stage (A) and histological type (B).

Table 5. Univariate Analysis of Survival

	5-Year Survival, %	*P* Value
Age, y		
<70	25.7	.42
≥70	27.2	
Sex		
Male	24.2	<.001
Female	34.5	
Tumor location		
Upper-midthoracic	22.6	<.001
Lower thoracic, EGJ (Siewert type I-II)	29.3	
Tumor histological type		
Squamous cell carcinoma	23.8	<.001
Adenocarcinoma	30.9	
Tumor differentiation		
Well or moderately differentiated	27.2	.01
Poorly differentiated	22.2	
Neoadjuvant therapy		
Yes	29.8	.02
No	25.0	
Type of resection		
R0	31.6	<.001
R1-2	4.6	
Pathological TNM stage		
0-I-II	45.9	<.001
III-IV	10.0	
Time period		
1980-1987	18.8	<.001
1988-1995	23.2	
1996-2004	42.3	

Abbreviation: EGJ, esophagogastric junction.

Table 6. Multivariate Analysis of Predictors of Worse Survival

	χ^2 Test	*P* Value
Male sex	32.82	<.001
Upper tumor location[a]	5.28	.02
Squamous cell carcinoma histological type	5.51	.02
Poor degree of tumor differentiation	2.78	.10
No neoadjuvant therapy	0.45	.50
R1-2 resection	84.68	<.001
Tumor stage III-IV	214.75	<.001
1980-1987 Time period	43.41	<.001

[a] Includes upper thoracic and midthoracic tumors.

erative mortality dropped from 8.2% from study period 1980-1987 to 2.6% from study period 1996-2004. Comparing the same 2 periods, the 5-year survival rate increased from 18.8% to 42.3%.

A decreasing number of patients have been referred to our department during the study period. This can be explained, in part, by the development of several new referral centers specialized in esophageal surgery in Northern Italy. In parallel with a decrease in the number of patients with esophageal cancer, we have observed an increase in difficult cases (ie, advanced stage of disease, preoperative chemotherapy or chemoradiotherapy, elderly patients, patients with several comorbidities, etc). Despite this, a more careful preoperative risk assessment has allowed a more accurate selection of patients for esophagectomy and tailored perioperative care. Therefore, an increasing number of patients have been offered surgical treatment over the years. The use of intraoperative and postoperative fluid restriction and epidural analgesia—allowing for lower dosage, better pain control, and less interference with pulmonary mechanics—early extubation, respiratory exercise (both preoperatively and postoperatively to improve lung activity), and early patient mobilization are among the factors that have contributed to a significant reduction in the postoperative mortality rate.[26,27] Of interest, because decreasing the risk of a treatment expands its indications, to elderly patients or to patients with severe or multiple comorbidities, the consequence was that the postoperative morbidity rate—including all major and minor complications both surgical and medical—did not change significantly during the study period. In addition, expertise gained by a dedicated interdisciplinary team has made

possible early diagnosis and treatment of complications once considered fatal if left untreated or treated too late.

Several reports in the literature suggest that at high-volume centers patients are treated by surgeons with greater experience in preoperative evaluation, are more carefully selected as candidates for surgical treatment, and experience better outcomes after the operation. Patient volume has been shown to be not just a predictive factor for short-term survival (ie, postoperative mortality)—18% postoperative mortality in low-volume centers compared with 5% in high-volume center (>20 esophagectomies per year)—but also for long-term survival.[28-30]

In the past 2 decades, in the Western world, there has been a shift from a predominance of squamous cell carcinoma to adenocarcinoma, in parallel with an increase in esophageal carcinoma of the distal esophagus and EGJ compared with a more proximal location.[1,2] In several centers in Europe and the United States, adenocarcinoma is now the prevalent histological type of esophageal cancer. This is particularly important because having the histological type adenocarcinoma itself is considered a prognostic factor for survival following esophagectomy.[31] This might be explained in part by differing biological behavior and in part by the fact that more effective en bloc tumor resection and more complete lymphadenectomy are possible in tumors mostly located in the lower esophagus and EGJ. Furthermore, the recognition of the metaplasia-dysplasia-adenocarcinoma sequence in patients with Barrett esophagus has prompted worldwide endoscopic surveillance programs to detect early-stage, curable lesions.[32]

As the population of elderly people increases, there has been a growing number of septuagenarian and octogenarian patients seeking treatment for esophageal cancer and searching for a cure, not just palliation. Recent studies report much the same morbidity and mortality rates among elderly patients undergoing esophageal resection as in their younger counterparts, both with and without neoadjuvant treatments.[33,34] These data have prompted a reassessment of the true effect of age on the outcome of esophagectomy to treat esophageal cancer and have identified a greater proportion of patients with esophageal cancer as amenable to curative surgical resection. In our experience, both short- and long-term outcomes after esophagectomy to treat carcinoma in patients older than 70 years were comparable with those of younger patients.[35]

In conclusion, from 1980-2004, a multidisciplinary approach increased team experience, and refinements both in surgical technique and perioperative care have led to a significant reduction in postoperative mortality rates and improved long-term survival rates among patients with esophageal cancer.

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INVITED CRITIQUE

The review by Ruol et al of data from nearly 3500 patients with esophageal cancer treated at the University of Padova during a 25-year period confirms much of our current understanding of esophageal cancer. There have been changes in tumor location (proximal to distal) and histological type (squamous cell carcinoma to adenocarcinoma), enhanced multidisciplinary treatment algorithms, and improved surgical mortality and overall survival rates. According to Ruol et al, most of their patients, even in the most recent time period from 1996-2004, had squamous cell carcinoma. In addition, most patients were treated with thoracotomy-based resections, and, enviably, more than 70% of patients had 15 or more lymph nodes resected. Increasing use of preoperative chemoradiotherapy was temporally associated with increased R0 resection and long-term survival rates. The authors comment that a history of Barrett esophagus was disclosed in less than 30% of patients with adenocarcinoma, data that may lead to improved use of screening endoscopy in their population. They do not comment on the presence of Barrett epithelium in the resected specimens.

As in many large, retrospective cohort studies conducted at university tertiary referral centers, this study offers a large sample of patients and powerful statistics to inform, or confirm suppositions, about esophageal carcinoma. The continued preponderance of squamous cell carcinoma, the rare use of transhiatal esophagectomy, and the variable use of neoadjuvant therapy make this article less applicable to the United States' patient population. Furthermore, the lack of odds ratio analyses, a fundamental aspect of retrospective studies, is a critical weakness of this study.

In summary, the authors should be congratulated for contributing such an impressive series to the esophageal cancer literature. Although their data and conclusions are more confirmatory than innovative, the surgical results are noteworthy.

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