Results of esophagectomy for esophageal cancer in elderly patients: Age has little influence on outcome and survival

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Objective: The aging of the population and a longer life expectancy have led to an increased number of elderly patients with esophageal cancer being referred for surgical treatment. The aim of this study was to assess the effects of age on the outcome of surgery for esophageal cancer at a single institution.

Methods: Perioperative outcome and long-term survival of patients at least 70 years old undergoing esophagectomy between 1992 and 2005 for cancer of the esophagus or esophagogastric junction were compared with findings in younger patients. Patients who underwent an abdominal procedure only were excluded from the analysis.

Results: The analysis considered 580 patients younger than 70 years and 159 at least 70 years old. Clinical presentation in the two groups was similar, as were postoperative morbidity and mortality, despite significant differences in perioperative risk factors. Irrespective of age, overall survival was 34% at 5 years for all patients and 37% for patients with R0 resection.

Conclusions: Increased experience and refinements in perioperative care explain the better results of esophagectomy in elderly patients in recent years. Short- and long-term outcomes after esophagectomy for carcinoma in patients older than 70 years are comparable with those of their younger counterparts. Advanced age per se thus should not be considered a contraindication to esophageal resection.

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The aging of the population and a longer life expectancy have led to more elderly patients with esophageal carcinoma being referred for surgical treatment. Controversies exist concerning the effect of advanced age on the outcome of esophagectomy. There is an apparent contradiction between reports in which the individual risk of mortality after esophagectomy is strongly related to the patient's age and performance status, with worse long-term survival among elderly patients,¹⁻³ and studies confirming improvements in the results of esophagectomy in patients 70 years old and older (mostly as a result of advances in perioperative care), with morbidity and mortality rates comparable to those in their younger counterparts.⁴⁻⁷ The aim of this study was to evaluate the effects of advanced age on the surgical outcome and long-term survival of patients undergoing esophagectomy for esophageal cancer at a single high-volume center.

Patients and Methods

We evaluated all patients with cancer of the esophagus or esophagogastric junction (Siewert type I-II) seen at our department between January 1992 and June 2005. Preoperative workup included physical examination, standard laboratory tests, lung function tests, and anesthesio-

logic assessment. In selected cases, noninvasive cardiac evaluation (echocardiogram or dynamic tests to estimate ventricular function) were also performed. The American Society of Anesthesiologists classification was used to assess the operative risk. Barium swallow study and upper gastrointestinal endoscopy were performed to assess the tumor's features; flexible bronchoscopy and otolaryngologic evaluation were added for tumors of the cervical, upper, and middle esophagus. Computed tomographic scans of the chest and abdomen (and neck in selected cases) were obtained in all cases to rule out any metastatic disease. Endoscopic ultrasonography was used from 2000 onward to provide additional information on tumor depth and lymph node status.

Complete tumor resection was defined as R0, and incomplete resection with microscopic or macroscopic residual disease was defined as R1 or R2, respectively. Perioperative mortality was classed as in-hospital mortality (all deaths occurring at the hospital) and 30-day mortality (all deaths occurring within 30 days of surgery). Postoperative morbidity included any minor or major medical or surgical complications. Anastomotic leaks were recorded, both symptomatic leaks and small asymptomatic leaks detected on radiologic examination.

Surgery

Esophagectomy was performed with an Ivor–Lewis procedure, through a laparotomy and right thoracotomy, for mid to lower esophageal and esophagogastric junction tumors. A 3-stage McKeown procedure, with an additional left cervical incision, was reserved for tumors in the upper third of the esophagus. At least 6 to 8 cm of healthy esophagus was resected above the proximal edge of the tumor to avoid neoplastic involvement of the resection margins. In 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, recurrent laryngeal chains, and paratracheal nodes also resected for cancers of the cervical and upper thoracic esophagus). The alimentary tract was reconstructed immediately, preferably with the gastric pull-up technique; if the stomach was unavailable, either a jejunal loop or the left colon was used. Anastomoses were performed with a circular stapling device in the thoracic cavity and a double layer of hand-sewn running suture in the neck. For patients with cancer of the cervical esophagus, a pharyngolaryngoesophagectomy was performed.

Postoperative patient care included early extubation (preferably in the operating room), aggressive respiratory care with frequent bronchoscopic suctioning, pain control (epidural analgesia along with patient-controlled analgesia), vigorous respiratory therapy, and early mobilization and ambulation. Food intake was allowed, provided a Gastrografin swallow showed no evidence of leakage, on postoperative days 7 and 10 for stapled and hand-sewn anastomoses, respectively.

Patients were followed up routinely by their surgeons 1, 3, 6, and 12 months after the operation and every 6 to 12 months thereafter.

TABLE 1. Treatment strategies by age group

	Surgical resection	No surgical resection*
All patients (n = 1400)	764 (54.6%)	636 (45.4%)
Patients <70 y (n = 1045)	599 (57.3%)	446 (42.7%)
Patients ≥70 y (n = 355)	165 (46.5%)	190 (53.5%)
P value†	.0004	

Data are expressed as numbers of patients with percentages in parentheses. *Including bypass operation, chemotherapy, radiotherapy, endoscopic dilation, endoscopic prosthesis placement, endoscopic laser therapy, feeding jejunostomy or gastrostomy, or any combination of these. †Surgical resection versus no surgical resection.

Statistical Analysis

Data are expressed as medians and interquartile ranges. Proportions were compared with the χ^2 or Fisher exact test. Continuous variables were compared with the Mann–Whitney test. Survival estimates were calculated by the Kaplan–Meier method, and survival comparisons were performed with the log–rank test. Cox proportional hazard models were used to identify independent predictors of survival.

Results

Of the 1400 patients with esophageal or esophagogastric junction cancer seen at our department between January 1992 and June 2005, a total of 764 (54.6%) underwent esophagectomy (Table 1). A significantly higher percentage of patients younger than 70 years underwent surgical resection relative to those at least 70 years old (57.3% vs 46.5%, $P = .0004$). We excluded from further analysis 25 patients who underwent a transabdominal procedure only ($n = 14$), free jejunal transplantation ($n = 1$), myocutaneous flap reconstruction ($n = 5$), or esophageal resection without reconstruction ($n = 5$). The remaining 739 patients formed the study population: 580 (78.5%) patients were younger than 70 years (group A) and 159 (21.5%) were at least 70 years old (group B). In the latter, elderly group, 107 (67.3%) patients were between 70 and 74 years old, 43 (27%) were aged 75 to 79 years, and 9 (5.7%) were in their 80s.

Clinicopathologic Characteristics

The demographic information and clinical characteristics of the patients in the two groups are summarized in Table 2. As expected, preoperative cardiovascular and respiratory risk factors were significantly more prevalent in group B. Tumor characteristics at presentation in the two groups are shown in Table 3. Tumor location and histologic type differed between the two groups, with a higher proportion of adenocarcinoma and a lower tumor location among the older patients. Table 4 summarizes the treatment details and pathologic findings at surgery. There were no significant differences in tumor stage or degree of differentiation between groups A and B. Overall, 90% of the patients were

TABLE 2. Demographic and clinical characteristics

	Patients <70 y (n = 580)	Patients ≥70 y (n = 159)	P value
Sex (male/female)	472/108	124/35	.365
Age (y, median with interquartile range)	59.5 (53.4–64.6)	73.1 (71.6–76.6)	
History of cardiac disease (No.)			<.0001
Yes	72 (12.4%)	47 (29.6%)	
No	508 (87.6%)	112 (70.4%)	
History of respiratory disease (No.)			.003
Yes	87 (15%)	40 (25.2%)	
No	493 (85%)	119 (74.8%)	
History of vascular disease (No.)			.0006
Yes	33 (5.7%)	23 (14.5%)	
No	547 (94.3%)	136 (85.5%)	
American Society of Anesthesiologists classification (No.)			<.0001
1-2	436 (77%)	91 (58.7%)	
3-4	130 (23%)	64 (41.3%)	
Data unavailable	14	4	
Weight loss (>10% body weight, No.)	121 (21.7%)	27 (17.4%)	.265

considered to have curative resection (R0): 514 (88.6%) of 580 in group A and 147 (92.5%) of 159 in group B ($P = .191$). The effects of neoadjuvant treatment in groups A and B are shown in [Table 5](#).

Morbidity and Mortality

Overall, the in-hospital mortality rate 2.6% (19/739): 2.7% (16/580) among patients younger than 70 years and 1.9% (3/159) among the older patients ($P = .778$). The overall 30-day mortality was 1.9% (14/739): 1.9% (11/580) in group A and 1.9% (3/159) in group B ($P > .999$). The

overall morbidity rate was 48.7% (360/739): 48.6% (282/580) in group A and 49.1% (78/159) in group B ($P = .929$). Details of the postoperative complications in the two groups are given in [Table 6](#). The most common complications were pulmonary and cardiovascular, and they were more prevalent among older patients.

Survival

The median survivals were 23.1 months (interquartile range 11.8–46.4 months) for patients younger than 70 years and 17.9 months (interquartile range 9.2–44.4

TABLE 3. Tumor characteristics

	Patients <70 y (n = 580)	Patients ≥70 y (n = 159)	P value
Histopathologic type			.0001*
Squamous cell carcinoma	372 (64.1%)	77 (48.4%)	
Adenocarcinoma	183 (31.6%)	77 (48.4%)	
Others	25 (4.3%)	5 (3.2%)	
History of Barrett esophagus†	50 (27.3%)	23 (29.9%)	.763
Tumor site			.001
Cervical	46 (7.9%)	4 (2.5%)	
Upper thoracic	110 (19%)	24 (15.1%)	
Mid thoracic	154 (26.5%)	37 (23.3%)	
Lower thoracic	110 (19%)	23 (14.5%)	
Esophagogastric junction (Siewert type I-II)	160 (27.6%)	71 (44.6%)	
Clinical TNM stage			.683
Stage 0	10 (1.7%)	5 (3.2%)	
Stage I	70 (12.1%)	20 (12.7%)	
Stage II	263 (45.6%)	71 (44.2%)	
Stage III	203 (35.2%)	50 (31.9%)	
Stage IV	31 (5.4%)	11 (7.0%)	
Data unavailable	3	2	

Data are expressed as numbers of patients with percentages in parentheses. *TNM*, Tumor-node-metastasis. *Squamous cell carcinoma versus adenocarcinoma. †Analysis limited to patients with adenocarcinoma only.

TABLE 4. Surgical treatment and pathologic findings

	Patients <70 y (n = 580)	Patients ≥70 y (n = 159)	P value
Neoadjuvant therapy	214 (36.9%)	28 (17.6%)	<.0001
Access			.608*
Laparotomy + thoracotomy (right)	373 (64.3%)	114 (71.7%)	
Thoracotomy (right) + laparotomy + cervicotomy (left)	128 (22.1%)	21 (13.2%)	
Laparotomy + cervicotomy (left)	79 (13.6%)	24 (15.1%)	
Reconstruction			.597†
Stomach	528 (91%)	147 (92.4%)	
Colon	41 (7.1%)	9 (5.7%)	
Other	11 (1.9%)	3 (1.9%)	
Pathologic TNM stage			.598
Stage 0	62 (10.7%)	13 (8.2%)	
Stage I	81 (14%)	25 (15.7%)	
Stage II	177 (30.6%)	41 (25.8%)	
Stage III	202 (35%)	62 (39%)	
Stage IV	56 (9.7%)	18 (11.3%)	
Data not available	2	0	
Degree of tumor differentiation‡			.831
Well or moderately differentiated	421 (76.3%)	115 (75.2%)	
Poorly differentiated	131 (23.7%)	38 (24.8%)	
Data not available	3	1	
Resection			.191
R0	514 (88.6%)	147 (92.5%)	
R1-2	66 (11.4%)	12 (7.5%)	

*Transthoracic versus nontransthoracic access. †Stomach versus colon. ‡Data refer to squamous cell carcinoma and adenocarcinoma only.

months) for those older. Five-year survival for the whole series was 34%: 33.6% in group A and 35.4% in group B ($P = .257$; Figure 1). When patients with R0 curative resection were considered alone, the 5-year survivals were 37% for group A and 39% for group B ($P = .279$; Figure 2). There was no significant difference in survival between male and female patients, either overall or in the age subgroups, but the 5-year survival in the older age group was higher for female patients than for male patients (48% vs 32%, difference not significant). When the older group was assessed separately, there was no significant difference

in 5-year survival between patients 70 to 74 years old and those at least 75 years of age.

Details of univariate analysis of survival are shown in Table 7. Cox multivariate analysis identified tumor stage, histologic type, and degree of differentiation as independent predictors of long-term survival (Table 8).

Discussion

Some important observations emerge from this study. First, with current advances in surgical management and perioperative care, elective esophagectomy can be safe even in elderly patients with medical risk factors if the tumor is amenable to surgical resection. Second, long-term survival for elderly patients is comparable with that of younger patients.

Worldwide increase in the elderly population in the last decades has made surgeons face the everyday dilemma of whether to perform major surgery on an elderly patient. The need for digestive tract surgery for patients at least 70 years old is becoming a serious and crucial health problem in Western countries. There have been advances in the multimodal management of many digestive tract cancers in the last 3 decades, but for many of them—esophageal cancer in particular—surgery remains the mainstay of treatment. Undoubtedly, esophagectomy is a major surgical procedure,

TABLE 5. Effect of neoadjuvant treatment

	Patients <70 y (n = 214)		Patients ≥70 y (n = 28)	
	Clinical stage*	Pathologic stage	Clinical stage†	Pathologic stage
Stage 0	0	49 (22.9%)	0	8 (28.6%)
Stage I	4 (1.9%)	19 (8.9%)	0	3 (10.7%)
Stage II	63 (29.7%)	72 (33.6%)	3 (11.1%)	10 (35.7%)
Stage III	120 (56.6%)	52 (24.3%)	18 (66.7%)	5 (17.9%)
Stage IV	25 (11.8%)	22 (10.3%)	6 (22.2%)	2 (7.1%)

Data are expressed as numbers of patients with percentages in parentheses. *Data not available for 2 patients. †Data not available for 1 patient.

TABLE 6. Morbidity and mortality

	Patients <70 y (n = 580)	Patients ≥70 y (n = 159)	P value
Mortality			
In hospital	16 (2.7%)	3 (1.9%)	.778
At 30 d	11 (1.9%)	3 (1.9%)	>.999
Complications			
Pulmonary (pneumonia, atelectasis, lung failure)	89 (15.3%)	27 (17%)	.623
Cardiovascular (myocardial infarction, severe arrhythmia, pulmonary edema, pulmonary embolism)	29 (5%)	15 (9.6%)	.056
Other			
Chylothorax	10 (1.7%)	0	.130
Laryngeal nerve palsy	46 (7.9%)	12 (7.5%)	>.999
Anastomotic leak or graft necrosis	53 (10.2%)	12 (7.5%)	.636
Hemorrhage	4 (0.7%)	3 (1.9%)	.174
Renal failure	5 (0.9%)	0	.59
Wound infection	10 (1.7%)	1 (0.6%)	.472
Reoperations	20 (3.4%)	4 (2.5%)	.800

Data are expressed as numbers of patients with percentages in parentheses.

and its high postoperative morbidity and mortality are well recognized. Nonetheless, improvements in perioperative care and recent studies reporting much the same morbidity and mortality rates among elderly patients undergoing esophageal resection as among their younger counterparts have prompted a reassessment of the true effect of age on the outcome of esophagectomy for esophageal cancer.

The idea that older age itself contraindicates major surgery such as esophagectomy seems to be a misconception. Of course, careful preoperative risk assessment is important in selecting patients for esophagectomy. A significant number of our elderly patients had preoperative cardiovascular or pulmonary dysfunction and similarly had cardiopulmonary complications in the postoperative period. Pulmonary complications were among the most frequent causes of morbidity among both younger and older patients, which

emphasizes the importance of frequent bronchoscopic suctioning and incentive spirometry before and after the operation, performed routinely by patients or preferably by a respiratory therapist.

The mortality did not differ significantly between our two age groups, and there are several factors responsible for this result. First is greater experience^{1,8} and refinement in surgical technique: all esophagectomies were performed by the same team of surgeons specializing in esophageal surgery. Improved perioperative patient care has also contributed to reduce related morbidity (especially pulmonary complications) and mortality. Most of all, postoperative epidural analgesia for better pain control and less interference with pulmonary mechanics has helped, along with incentive spirometry, to improve postoperative lung activity.⁹

Figure 1. Kaplan-Meier survival curves (including postoperative deaths) plotted for patients younger than 70 years versus patients 70 years old and older, all resections ($\chi^2 = 1.286$, $P = .257$).

Figure 2. Kaplan-Meier survival curves (including postoperative deaths) plotted for patients younger than 70 years versus patients 70 years old and older, R0 resections only ($\chi^2 = 1.169$, $P = .279$).

TABLE 7. Univariate analysis of survival

	5-y survival (%)	P value
Age (y)		.26
<70	33.6%	
≥70	35.4%	
Sex		.177
Male	33.3%	
Female	36.6%	
Tumor location		.52
Cervical, upper thoracic, mid thoracic	32.2%	
Lower thoracic, esophagogastric junction (Siewert type I-II)	36%	
Histologic type		.15
Squamous cell carcinoma	32.1%	
Adenocarcinoma	38%	
Neoadjuvant therapy		.38
Yes	36%	
No	33%	
Pathologic TNM stage		<.0001
Stage 0, I, or II	49.5%	
Stage III or IV	15.3%	
Degree of tumor differentiation		.004
Well or moderately differentiated	36.6%	
Poorly differentiated	26.7%	

Keeping in mind the previously mentioned results, we need to remember that they were obtained in a selected population of elderly patients. A significantly higher proportion of patients 70 years of age or older did not undergo surgery than their younger counterparts. When we analyzed the reasons for exclusion from surgery (data not shown), we found out that nearly 40% of elderly patients were excluded for comorbidity-related reasons; this cause accounted for fewer than 20% of exclusions of surgery among the younger subjects.

The reported 5-year survival after resection for esophageal carcinoma is in the 15% to 20% range,^{10,11} a fact that has raised concerns regarding the advisability of such an extensive procedure as esophagectomy in elderly patients.^{12,13} Palliative treatments have been advocated as the sole treatment option for such patients, although it is well known that the median survival after palliation is only 4 months. The overall 5-year survival in our series was more than 34%. What is more, there was no significant difference between older and younger patients. As shown previously,^{2,7,14-15} if elderly patients can survive the esophagectomy itself, then the 5-year survival is independent of age. When we analyzed the long-term results of our at least 75-year-old patients, they fared just as well as their younger counterparts, if not better.

Interestingly, we didn't find any significant difference in overall survival between male and female patients, and we interpreted the loss of prognostic effect of female sex as

TABLE 8. Multivariate analysis of predictors of survival

	χ^2	P value
Age group (≥70 y)	2.41	.12
Sex (male)	2.62	.11
Tumor location (upper site)*	0.7	.4
Neoadjuvant therapy (none)	0.09	.76
Histologic type (squamous)	7.89	.005
Degree of tumor differentiation (poor)	3.92	.048
Tumor stage (p III-IV)	97	<.0001

*Upper sites include cervical, upper thoracic, and mid-thoracic tumor locations.

probably the result of a higher percentage of esophageal squamous cell carcinoma among female patients than among male patients. This study was not designed to assess the relationship between sex, histologic type, and survival, however, and such will require further detailed analysis of our data.

Esophageal resection not only restores swallowing function, which means restoration of a decent quality of life, but it also gives patients a chance of cure. In other words, it is worthwhile. This study did not intend to assess the details of each single prognostic factor for survival among patients undergoing esophagectomy for esophageal cancer, but a review of the 739 esophagectomies included in this series, performed at our institution during the last 14 years, showed that older age did not affect long-term survival.

It is important to remember when discussing the results of this study that they were achieved in a specialized center for esophageal diseases. It is now widely recognized that certain high-risk surgical procedures have lower mortality and morbidity as well as better outcome when performed in high-volume centers.^{16,17} This is specifically true for esophageal cancer surgery, with individual surgeon experience, expert team assistance, and access to better infrastructure resources to manage critically ill patients all playing a determinant role.

In summary, increased surgical experience and refinements in perioperative care can explain the improved results achieved with esophagectomy in elderly patients in recent years. Short- and long-term outcomes after esophagectomy for carcinoma in patients 70 years old or older are equivalent to those of their younger counterparts. Advanced age per se thus should not be considered a contraindication to esophageal resection. For selected patients who are fit for surgery and have resectable lesions, esophagectomy is indicated and worthwhile, regardless of age. A careful selection of candidates for surgery is mandatory, however, to keep morbidity and mortality to acceptable levels and achieve much the same long-term survival for younger and older patients.

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