Intramucosal esophageal adenocarcinoma: Primum non nocere

Zhigang Li, MD, PhD,[a] Thomas W. Rice, MD,[a] Xiuli Liu, MD, PhD,[b] John R. Goldblum, MD,[b] Sarah J. Williams, MS,[c] Lisa A. Rybicki, MS,[c] Sudish C. Murthy, MD, PhD,[a] David P. Mason, MD,[a] Daniel P. Raymond, MD,[a] and Eugene H. Blackstone, MD[a,c]

Objectives: Intramucosal esophageal cancer treatment is evolving. Less-invasive therapies have emerged, necessitating review of safety, effectiveness, and determinants of long-term outcome after esophagectomy to clarify the role of this traditional, maximally invasive, and potentially harmful therapy.

Methods: From January 1983 to January 2011, 164 patients underwent esophagectomy alone for intramucosal adenocarcinoma. Cancers were subdivided by depth of invasion: lamina propria 50 (30%) and muscularis mucosa 114 (70%; inner 42 [26%], middle 16 [10%], and outer 56 [34%]). We assessed complications and esophagectomy-related mortality (safety) and cancer recurrence (effectiveness), and identified determinants of long-term outcomes.

Results: Barrett esophagus ($P = .005$), larger cancers ($P < .001$), worse histologic grade ($P < .001$), lymphovascular invasion ($P < .001$), and overstaging ($P = .02$) were associated with deeper cancers. One patient had regional lymph node metastases (0.6%). Seventy-five patients (46%) had complications. Seven of 9 deaths within 6 months were esophagectomy related, 6 from respiratory failure. Seven patients had recurrence, all within 4 years. Five-, 10-, and 15-year survivals were 82%, 69%, and 60%, respectively, which were similar to those of a matched general population. Determinants of late mortality were older age ($P = .004$), poorer lung function ($P < .0001$), longer cancer ($P = .04$), postoperative pneumonia ($P = .06$), cancer recurrence ($P < .0001$), and second cancers ($P < .0001$).

Conclusions: Survival after esophagectomy for intramucosal adenocarcinoma is excellent, determined more by patient than cancer characteristics. Patient selection and respiratory function are crucial to minimize harm. Considering the outcome of emerging therapies, esophagectomy should be reserved for patients with a long intramucosal adenocarcinoma or those in whom endoscopic therapies fail or are inappropriate. (J Thorac Cardiovasc Surg 2013;145:1519-24)

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Supplemental material is available online.

Intramucosal esophageal adenocarcinoma treatment is evolving. Less invasive therapies have emerged, necessitating reexamination of esophagectomy. To clarify the role of this traditional, maximally invasive, and potentially harmful procedure, we assessed its safety and effectiveness, and identified patient and cancer determinants of long-term outcome.

From the Department of Thoracic and Cardiovascular Surgery,[a] Heart and Vascular Institute, Department of Anatomic Pathology,[b] Pathology and Laboratory Medicine Institute, and Department of Quantitative Health Sciences,[c] Research Institute, Cleveland Clinic, Cleveland, Ohio.

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Address for reprints: Thomas W. Rice, MD, Department of Thoracic and Cardiovascular Surgery, Cleveland Clinic, 9500 Euclid Ave/Desk J4-1, Cleveland, OH 44195 (E-mail: ricet@ccf.org).

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PATIENTS AND METHODS

Patients

From January 1983 to January 2011, 1357 patients underwent esophagectomy for cancer at Cleveland Clinic (Appendix E1). Of these patients, 164 had a pathologic diagnosis of adenocarcinoma invading the mucosae but not beyond (pT1a). All patients had esophagectomy alone without induction therapy. The esophagectomy database used for this study was approved for use in research by the institutional review board, with patient consent waived.

Patients were predominantly elderly white men with hiatal hernia (87%) and Barrett esophagus (92%) (Table 1); 38% were in a Barrett surveillance program. Lung function varied widely, and 13% of patients had a prior nonesophageal malignancy.

Cancer Characteristics

Clinical stage was determined by biopsy at esophagogastroduodenoscopy in 164 patients, with additional esophageal ultrasound staging in 88 patients (54%). Clinical stage was clinical high-grade dysplasia (HGD) in 28 patients (17%), cT1aN0 in 115 patients (70%), and greater than cT1N0 in 21 patients (13%) (Table 1). Ninety-eight percent of cancers (n = 161) were located in the lower thoracic esophagus. Cancers were small, with a median length at esophagogastroduodenoscopy of 0.8 cm and width of 0.4 cm. Pathologic re-review was performed by 2

Abbreviation and Acronym
HGD = high-grade dysplasia

gastrointestinal pathologists. Cancer length, depth of invasion, histologic grade, presence of lymphovascular invasion, and number of positive nodes were assessed. One patient was found to have 6 positive nodes (pN2). However, 14% of patients had definite or possible lymphovascular invasion. No patient had distant metastasis. The majority of cancers were moderate or well differentiated (85%).

Esophagectomy

Sixty-eight percent of patients (n = 111) underwent a transhiatal esophagectomy, and 32% underwent a thoracotomy.[1] All cancer margins were R0, except in 1 patient who had Barrett esophagus without dysplasia at the proximal margin. The median number of lymph nodes sampled was 12.

Outcomes

Safety was assessed by the combination of postoperative complications (Table 2), operative mortality (deaths in hospital or within 30 days of esophagectomy), and deaths in the first 6 months attributed to esophagectomy (esophagectomy related). *Effectiveness* was assessed by esophageal cancer recurrence and all-cause mortality referenced to an age-, race-, and sex-matched US population. *Determinants of long-term outcome* were based on cancer recurrence, all-cause mortality, and second nonesophageal cancer.

Active follow-up for vital status, cancer recurrence, and second cancers was complete to January 2010 in 156 patients (95%) and to January 2011 in 104 patients (63%). Median follow-up was 85 months, and 10% of patients were followed more than 14 years. For survival, time relatedness of cancer recurrence, all-cause mortality, and second cancers were estimated by the nonparametric time-related Kaplan–Meier method and parametrically using multiphase hazard modeling.[2] (For additional details, see http://my.clevelandclinic.org/professionals/software/hazard/default.aspx.) Overall survival was referenced to an age-, race-, and sex-specific US population.

Determinants of long-term outcomes were identified for cancer recurrence, all-cause mortality, and second cancers, and for each hazard phase simultaneously using variables listed in Table 1 and detailed in Appendix E2. Variable selection used bagging.[3,4] Briefly, automated stepwise variable selection was performed on 1000 bootstrap samples, and frequency of occurrence of variables related to procedure performed was ascertained by the median rule.[3] For all-cause mortality, analysis proceeded sequentially. First, only preoperative patient and cancer characteristics were entered into the analysis. This was followed by these plus details of the operation and then of postoperative complications. Finally, esophageal cancer recurrence and second cancer, and time to their diagnosis, were entered as time-varying covariables.

Presentation

Continuous variables are summarized as mean ± 1 standard deviation for normally distributed variables and as equivalent median, 15th, and 85th percentiles when values are skewed. Categoric variables are summarized as frequency and percentage. Time-related estimates are accompanied by 68% confidence limits equivalent to ±1 standard error.

RESULTS

Safety

Mortality. Three patients (1.8%) died in hospital, and 2 patients (1.2%) died within 30 days of esophagectomy. Nine deaths occurred within 6 months, 7 of which were esophagectomy related, resulting in an actuarial survival of 95% at 6 months. These deaths were from respiratory failure in 6 patients and accompanied by renal failure in 3. The seventh patient died of superior mesenteric artery thrombosis.

Complications. Seventy-five patients (46%) experienced 125 complications (Table 3). The most common were wound (22%), cardiovascular (21%), and respiratory (20%).

Effectiveness

Cancer recurrence. Seven patients had esophageal cancer recurrence, all within 4 years of esophagectomy (Figure 1), 3 locoregional and 4 distant. One patient is alive 43 months after esophagectomy, and 6 patients died 13 to 58 months after esophagectomy (4-44 months after recurrence).

All-cause mortality. Five-, 10-, and 15-year survivals were 82%, 69%, and 60%, respectively (Figure 2). These cancer patients had a higher risk of death after esophagectomy than a matched US population (Figure 2), but after 9 months, risk was similar.

Determinants of Long-Term Outcome

Preoperative. No predictors of early mortality were identified because of the small number of postoperative events. Operative mortality was similar across the experience. Patient characteristics associated with mortality included older age at esophagectomy and poorer lung function (Table 4 and Figure E1). The only cancer characteristic associated with mortality was length. However, there was interplay among cancer characteristics. Barrett esophagus, deeper invasion of the mucosa, worse histologic grade, lymphovascular invasion, and overstaging were associated with larger cancers (Table E1 and Figure E2).

Operative details. No operative feature was a risk factor.

Postoperative. Respiratory complications, particularly pneumonia, increased the risk of mortality (Table 4).

Time-related factors. Cancer recurrence and second nonesophageal cancers (Figure 3) were risk factors for late mortality (Table 4). The following cancers developed in 20 patients: 23 second nonesophageal malignancies, 10 genitourinary (6 prostate, 3 kidney, 1 bladder), 3 lung, 3 colorectal, 3 skin, and 1 each head and neck, brain, pancreas, and duodenum. Eight patients have died—6 with second nonesophageal malignancies, 1 with pre-esophagectomy melanoma, and 1 of a non–cancer-related cause.

DISCUSSION

Intramucosal esophageal adenocarcinoma is truly an early cancer because it is locally confined and rarely metastasizes to lymph nodes. Esophagectomy cures 95% of patients. However, risk of cancer recurrence is approximately equal to risk of death from esophagectomy. Therefore, it is critical to do no harm in treating patients with this good prognosis, but this maximally invasive procedure

TABLE 1. Patient and cancer characteristics (n = 164)

Characteristics	n*	Value
Patient		
Age (y)	164	
Mean ± SD		63 ± 10
Median (range)		64 (35-82)
Gender	164	
Male		142 (87)
Female		22 (13)
Race	164	
White		161 (98)
Black		2 (1.2)
Hispanic		1 (0.6)
FEV_1 (% of predicted)	149	
Mean ± SD		92 ± 18
Median (range)		92 (35-136)
FVC (% of predicted)	148	
Mean ± SD		98 ± 16
Median (range)		96 (57-158)
Pathologic Barrett esophagus	164	
Yes		151 (92)
No		13 (7.9)
Pathologic Barrett length (cm)	115	
Mean ± SD		4.6 ± 3.1
Median (range)		4.5 (0-12)
Hiatal hernia	164	
Yes		143 (87)
No		21 (13)
Hiatal hernia length (cm)	164	
Mean ± SD		3.0 ± 2.0
Median (range)		3.0 (0-11)
Cancer		
Clinical stage†	164	
cHGD		28 (17)
cT1N0		115 (70)
>cT1N0		21 (13)
Depth of invasion	164	
LP		50 (30)
MM1 (inner)		42 (26)
MM2 (between)		16 (9.8)
MM3 (outer)		56 (34)
Tumor length on pathology (cm)	156	
Median (range)		0.70 (0.10-5.9)
Histologic grade	164	
G1		55 (34)
G2		83 (51)
G3		26 (16)
Lymphovascular invasion	154	
Yes		6 (3.9)
Possible		15 (9.7)
No		133 (86)
No. of lymph nodes sampled	164	
Median (range)		12 (0-56)
No. of positive nodes	164	
0		163 (99)
6		1 (0.60)

SD, Standard deviation; *FEV_1*, forced expiratory volume in 1 second; *FVC,* forced vital capacity; *cHGD,* clinical high-grade dysplasia; *LP,* lamina propria; *MM,* muscularis mucosa. *Patients with data available. †Endoscopic ultrasound and preoperative biopsy.

TABLE 2. Definition of complications

Wound

Anastomotic leak: Detection of saliva, ingested material, gastric secretions, or bile in the drain or wound. Radiographic confirmation was not required.

Infection: Local findings of erythema, drainage, subcutaneous emphysema, or tenderness requiring wound opening with positive wound culture.

Pulmonary

Pneumonia: Radiographic confirmation with positive respiratory tract culture.

Respiratory failure: Reintubation or tracheostomy for weaning failure.

Vocal cord paralysis: Laryngoscopy confirmation required.

Pneumothorax: Radiographic confirmation requiring chest tube reinsertion.

Pleural effusion: Pleural effusion after chest tube removal requiring chest tube reinsertion or thoracentesis.

Cardiovascular

Electrocardiographic confirmation of atrial arrhythmia.

Ultrasound confirmation of deep venous thrombosis.

Neurologic

Delirium: Transient confusion confirmed by disturbances in consciousness, cognition, and perception.

is associated with postoperative complications in nearly 50% of patients, and these contribute to the death of 5% of patients in the first 6 months after surgery. Endoscopic therapy also may do harm because it is not totally safe and is not as effective in curing cancer. This has led us to examine the technical success, safety, and clinical effectiveness of these treatment options.

Success

Technical success is the ability to locally eliminate cancer and precursor intestinal metaplasia. In this series of 164 patients, all had R0 resections for cancer and 163 had R0 resections for Barrett metaplasia. Intestinal metaplasia

TABLE 3. Postoperative complications

Type	No. of complications	No. of patients	% of 164
Wound	36	36	22
Anastomotic leak	9	9	5.5
Infection	27	27	16
Respiratory	42	32	20
Pneumonia	6	6	3.7
Respiratory failure	20	20	12
Vocal cord paralysis	5	5	3.0
Pneumothorax	1	1	0.6
Pleural effusion	10	10	6.1
Cardiovascular	36	35	21
Atrial arrhythmia	26		16
Deep vein thrombosis	10		6.1
Neurologic			
Delirium	11	11	6.7
Total	125	75*	

*Many patients had multiple complications.

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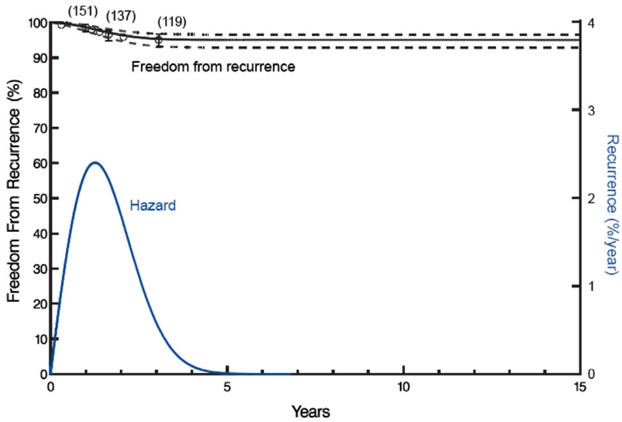

FIGURE 1. Recurrence of cancer after esophagectomy for intramucosal cancer. Each *circle* represents a recurrence, *vertical bars* represent 68% confidence limits, and *numbers in parentheses* represent patients remaining at risk. *Solid line* enclosed within *dashed 68% confidence band* represents parametric estimate. Instantaneous risk of recurrence (hazard function) peaks at 15 months. There was no recurrence after 37 months.

after a cervical esophagogastrostomy develops in few patients (16% at 5 years), and dysplasia and cancer are rare.[1] Inflammatory changes at the anastomosis can be lessened by construction of a high anastomosis and proton-pump inhibitor therapy.

Endoscopic mucosal resection or ablative therapy is less likely to be technically successful than esophagectomy. In a study by Pech and colleagues[5] of 486 patients with clinical HGD or intramucosal cancer, 279 underwent endoscopic mucosal resection, 55 received photodynamic ablative therapy, and 13 received both.[5] Ninety-six percent of patients had a "complete response," but 3.6% required esophagectomy for technical failures. At a median of 15 months (25th percentile 12 months, 75th percentile 24 months), 22% of

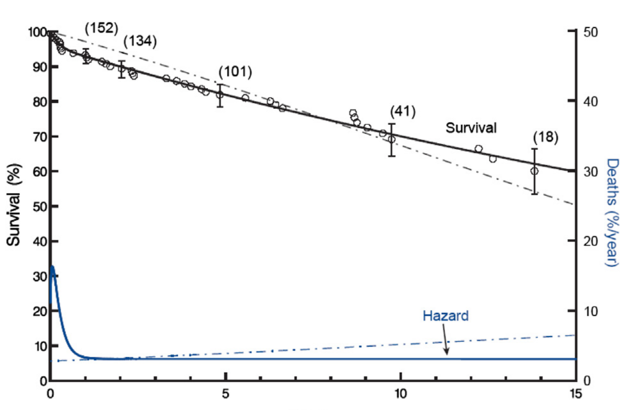

FIGURE 2. Survival after esophagectomy for intramucosal cancer. Format is as in Figure 1 except that the age-, race-, and sex-matched US population life table is superimposed (*dash-dot-dash line*). Instantaneous risk of death (hazard function) peaks early after operation and then decreases to a constant level similar to that of the general population.

TABLE 4. Incremental risk factors for mortality after esophagectomy for intramucosal cancer: Sequential analysis

Risk factor	Coefficient ± SD	*P*	Reliability (%)*
1. Patient and cancer characteristics, operative details			
Older age (y)†	0.75 ± 0.24	.002	80
Lower FVC (% of predicted)‡	3.2 ± 0.52	<.0001	96
Longer cancer (cm)§	0.060 ± 0.024	.01	89
2. Add postoperative complications			
Older age (y)†	0.76 ± 0.24	.001	76
Lower FVC (% of predicted)‡	3.3 ± 0.52	<.0001	94
Longer cancer (cm)§	0.062 ± 0.023	.008	88
Postoperative pneumonia	1.3 ± 0.67	.05	55
3. Add recurrence and second cancers			
Older age (y)†	0.58 ± 0.20	.004	59
Lower FVC (% of predicted)‡	3.2 ± 0.51	<.0001	94
Longer cancer (cm)§	0.051 ± 0.025	.04	90
Postoperative pneumonia	1.1 ± 0.58	.06	67
Cancer recurrence	2.5 ± 0.46	<.0001	99.6
Longer interval to second cancer (y)	0.27 ± 0.048	<.0001	98.9

No risk factors were identified in the early hazard phase. *SD*, Standard deviation; *FVC*, forced vital capacity. *Percent of times factor appeared in 1000 bootstrap models. †Exp (age/50), exponential transformation. ‡$(81/FVC)^2$, inversed squared transformation. §$Length^2$, squared transformation.

patients had HGD or cancer. Predictors of recurrence were piecemeal resection, long-segment Barrett esophagus, no ablative therapy after complete response, more than 10 months required to achieve complete response, and multifocal neoplasia. Among 341 patients studied by Pouw and colleagues,[6] 169 underwent endoscopic resection of early Barrett neoplasia at 4 centers. At the end of treatment, 98% had eradication of neoplasia and 85% had eradication of metaplasia. Two patients (2.4%) required surgery for immediate technical failures or complications. At a median of 32 months (interquartile range, 19-49 months), 95% of

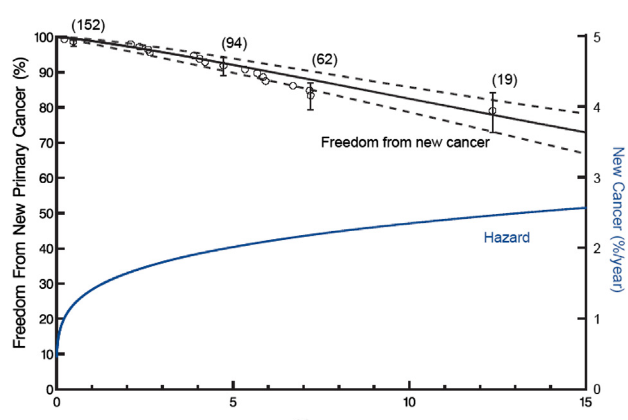

FIGURE 3. Freedom from second nonesophageal cancer after esophagectomy for intramucosal cancer. Depiction is as in Figure 1.

patients had eradication of neoplasia and 80% had eradication of metaplasia, with 9 patients (5.3%) requiring retreatment during follow-up.

Ablative therapy has been reported typically for Barrett metaplasia and dysplasia but not for intramucosal cancer. Unlike esophagectomy, but like endoscopic resection, ablative therapy is less likely to eradicate Barrett metaplasia and dysplasia. Lyday and colleagues[7] studied 429 treated patients who had Barrett metaplasia with or without dysplasia. In 1 cohort, 338 patients had at least 1 biopsy session after ablation, with 72% free of Barrett metaplasia and 89% free of dysplasia. In another cohort of 137 patients with at least 1 session a year or more after therapy, 77% were free of metaplasia and 100% were free of dysplasia.[7] Among 50 patients with nondysplastic Barrett esophagus reported by Fleischer and colleagues,[8] freedom from metaplasia after radiofrequency ablation was 91% (95% confidence interval, 77%-97%) at 4 years. Shaheen and colleagues[9] reported that 77% of patients had eradication of metaplasia and 81% had eradication of dysplasia 12 months after ablation of dysplastic Barrett esophagus.

Safety

Safety is freedom from risk and can be assessed by complications and death after treatment. Although esophagectomy can be performed with a 30-day in-hospital mortality of approximately 1%, longer follow-up demonstrates that it is associated with late death. It can be expected that approximately 50% of patients will experience a complication after esophagectomy.

Treatment mortality is rarely reported after endoscopic therapy, and complications are less frequent than after esophagectomy by approximately half.[10] Pech and colleagues[5] reported complications in 17% of patients after endoscopic mucosal resection. In other studies, complications occurred in 3.6%[7] and 2.3%[9] of patients receiving ablation, with strictures reported in 6%[9] and 2.1%.[7]

Clinical Effectiveness

Clinical effectiveness is the ability to cure cancer. Although overall survival is generally similar after esophagectomy or endoscopic therapy,[11-13] cancer-free survival is worse after endoscopic therapy. Recurrence after esophagectomy is uncommon, and if it occurs, it does so early after surgery, whereas after ablative therapy, recurrence is a later and continuing problem. Prasad and colleagues[12] reported 5-year cancer-free survival of 97% after esophagectomy and 80% after endoscopic therapy ($P = .01$). Schembre and colleagues[13] reported no cancer recurrences after a median follow-up of 48 months in 32 patients undergoing esophagectomy, despite identifying previously unrecognized cancer in 25% of the resection specimens; cancer recurrence developed at a median of 20 months of follow-up in 6% of 62 patients receiving endoscopic therapy.[13]

Strengths and Limitations

A limitation of this study is that it is a large, single-institution experience covering more than 25 years. However, this is also a strength because of availability of a large volume of long-term data on intramucosal esophageal adenocarcinoma. The patients represent a highly selected referral population. The only outcomes studied were survival, cancer recurrence, and second primary cancer; quality of life was not assessed. This analysis does not include a direct comparison group of patients treated endoscopically.

CONCLUSIONS

Both esophagectomy and endoscopic therapy may inadvertently harm patients with intramucosal esophageal adenocarcinoma, requiring concerted attempts to improve the safety of both therapies. Esophagectomy is more successful and effective in this setting than endoscopic therapies, but it is not as safe. Treatment decisions require balancing harm with ineffective cancer treatment. It is critical to carefully prescribe therapy on the basis of treatment goals, cancer characteristics, and patient characteristics. Esophagectomy is best for patients in whom complete and durable eradication of the cancer is paramount and in whom esophagectomy is a low-risk procedure. Endoscopic therapy is best for patients in whom the risk of esophagectomy outweighs the need for freedom from cancer. Choice of endoscopic therapy requires adequate esophageal function, that is, is the esophagus worth saving? Choice of esophagectomy requires meticulous patient preparation and fastidious surgical technique. Unfortunately, it has been reported that a major determinant of therapy in patients with these cancers is who performs the first evaluation: a surgeon or a gastroenterologist.[14]

> *I will prescribe regimens for the good of my patients according to my ability and my judgment and never do harm to anyone.*
>
> —Hippocratic Oath

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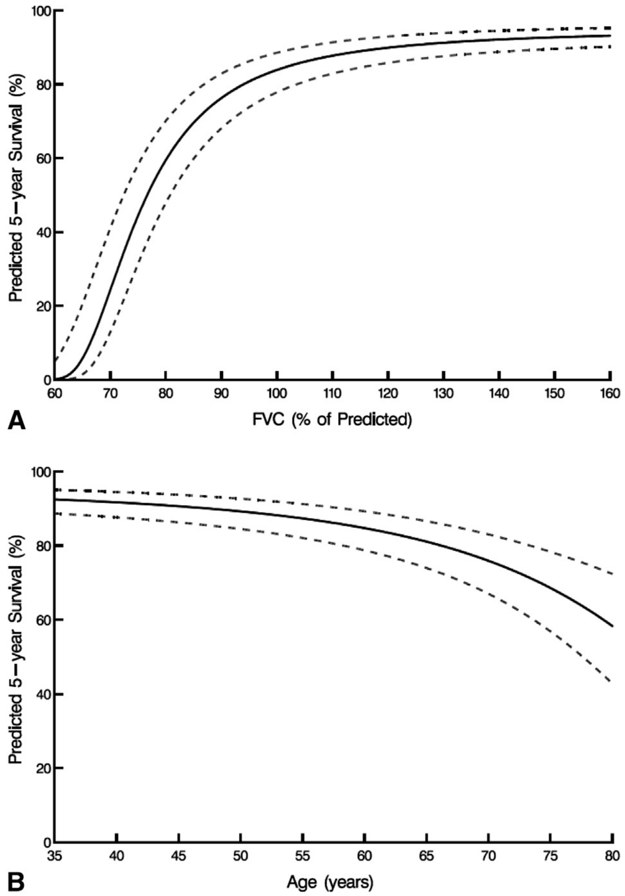

FIGURE E1. Nomogram of 5-year survival after esophagectomy for intramucosal esophageal adenocarcinoma according to lung function and age at operation based on model 1 in Table 4. *Dashed lines* are equivalent to ±1 standard error of the predicted value. A, Lung function. Values for other risk factors were set as follows: age = 65 years and length of cancer = 1.4 mm. B, Age. Values for other risk factors were set as follows: forced vital capacity (percent of predicted) = 95 and length of cancer = 1.4 mm. *FVC,* Forced vital capacity.

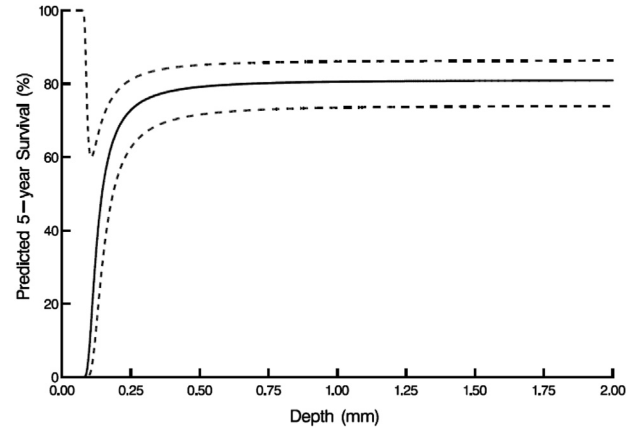

FIGURE E2. Nomogram for multivariable equation in Table 4. Predicted mortality at 5 years by pathologic tumor depth. Values for other risk factors were set as follows: age = 65 years, forced vital capacity (percent of predicted) = 95, no hiatal hernia, no esophageal cancer recurrence, no new primary cancer. *Dashed lines* are equivalent to ±1 standard error of the predicted value.

TABLE E1. Interplay among cancer characteristics

Characteristic	Depth of invasion				P
	LP (n = 50) no. (%)	MM1 (n = 42) no. (%)	MM2 (n = 16) no. (%)	MM3 (n = 56) no. (%)	
Barrett esophagus	43 (86)	37 (88)	15 (94)	56 (100)	.005
Cancer size on EGD					
Length (cm), median (range)	0.3 (0-4.5)	0.4 (0-4)	0.8 (0-5.5)	1 (0-10)	.002
Width (cm), median (range)*	0.3 (0-7.5)	0.1 (0-7.5)	0.6 (0-2.5)	0.6 (0-4.6)	.01
Area (cm^2), median (range)*	0.1 (0-30)	0 (0-30)	0.4 (0-14)	0.5 (0-32)	.008
Cancer size on pathology					
Length (cm), median (range)†	0.4 (0.1-2.0)	0.7 (0.1-2.0)	0.6 (0.1-5.5)	1.2 (0.3-5.9)	<.001
Depth (mm), median (range)‡	0.5 (0.2-2.0)	1.0 (0.4-4.0)	1.0 (0.5-4.5)	1.8 (0.1-9.0)	<.001
Clinical stage					.02
cHGD	12 (24)	8 (19)	1 (6.2)	7 (12)	
cT1	33 (66)	31 (74)	14 (88)	37 (66)	
>cT1	5 (10)	3 (7.1)	1 (6.2)	12 (21)	
Pathologic stage					<.001
IA	48 (96)	38 (90)	14 (88)	38 (68)	
IB	2 (4.0)	4 (9.5)	2 (12)	17 (30)	
IIIA	0 (0)	0 (0)	0 (0)	1 (1.8)	
Histologic grade					<.001
G1	24 (48)	16 (38)	3 (19)	12 (21)	
G2	24 (48)	22 (52)	11 (69)	26 (46)	
G3	2 (4.0)	4 (9.5)	2 (12)	18 (32)	
Lymphovascular invasion					<.001
Yes	0 (0)	0 (0)	0 (0)	6 (11)	
Possible	0 (0)	3 (7.3)	3 (19)	9 (17)	
No	43 (100)	38 (93)	13 (81)	39 (72)	

LP, Lamina propria, *MM*, muscularis mucosa; *MM1*, inner; *MM2*, between; *MM3*, outer; *EGD*, esophagogastroduodenoscopy; *cHGD*, clinical high-grade dysplasia. *n = 50, 40, 15, and 50, respectively. †n = 43, 42, 16, and 55, respectively. ‡n = 42, 42, 16, and 55, respectively.

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APPENDIX E1. Clinical and pathologic stage

Pathologic stage	Clinical stage	
	cT1N0*	cT1bxN0†
<pT1N0M0	12	17
pT1aN0M0	65	48
pT1aN+M0‡	0	0
pT1bN0M0	43	14
pT1bN+M0	7	3
>pT1N0M0	6	21
>pT1N+M0	4	82
>pT1N0M1	0	1
>pT1N+M1	0	5
Total	137	191

Of 1357 esophagectomies between January 1983 and January 2010, 1149 were for adenocarcinoma; 722 patients had no induction therapy. Distribution of pathologic stage cT1N0 patients is shown. *cT1 includes both intramucosal (cT1a) and submucosal cancers (cT1b). †Endoscopic ultrasound was noninformative, so preoperative biopsy was used to determine clinical stage. ‡N+ indicates regional lymph node metastases.

APPENDIX E2. Variables considered in multivariable analyses

Demographic	Age (y), sex
Pulmonary function	FEV_1 (percent of predicted), FVC (percent of predicted)
Esophagus	Barrett esophagus, Barrett surveillance, hiatal hernia, hiatal hernia length (cm)
Cancer	Prior cancer; pathologic tumor length (cm), depth (cm), and location (LP, MM1, MM2, MM3); histologic grade (G1, G2, G3); site of anastomosis (neck, chest); pathologic staging (LP, MM1, MM2, MM3, G1, G2, G3); cHGD; total number of nodes sampled
Surgical approach	Thoracotomy, transhiatal
Postoperative complications	Anastomotic leak, respiratory failure, vocal cord paralysis, wound infection, deep vein thrombosis, atrial fibrillation, pleural effusion, pneumothorax, pneumonia
Future complications	New primary cancer, time to new primary cancer, recurrence of esophageal cancer, time to recurrence of esophageal cancer
Experience	Years since January 1, 1983

FEV_1, Forced expiratory volume in 1 second; *FVC,* forced vital capacity, *LP*, lamina propria, *MM,* muscularis mucosa; *MM1*, inner; *MM2*, between; *MM3*, outer; *cHGD,* clinical high-grade dysplasia.

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