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Long-Term Survival Following Endoscopic and Surgical Treatment of High-Grade Dysplasia in Barrett's Esophagus

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Abstract

Background & Aims—Photodynamic therapy (PDT) for high-grade dysplasia (HGD) in Barrett's esophagus is a Food and Drug Administration–approved alternative to esophagectomy. Critical information regarding overall survival of patients followed up long-term after these therapies is lacking. Our aim was to compare the long-term survival of patients treated with PDT with patients treated with esophagectomy.

Methods—We reviewed records of patients with HGD seen at our institution between 1994 and 2004. PDT was performed 48 hours following the intravenous administration of a photosensitizer using light at 630 nm. Esophagectomy was performed by either transhiatal or transthoracic approaches by experienced surgeons. We excluded all patients with evidence of cancer on biopsy specimens. Vital status and death date information was queried using an institutionally approved Internet research and location service. Statistical analysis was performed using Kaplan–Meier curves and Cox proportional hazards ratios.

Results—A total of 199 patients were identified. A total of 129 patients (65%) were treated with PDT and 70 (35%) with esophagectomy. Overall mortality in the PDT group was 9% (11/129) and in the surgery group was 8.5% (6/70) over a median follow-up period of 59 ± 2.7 months for the PDT group and 61 ± 5.8 months for the surgery group. Overall survival was similar between the 2 groups (Wilcoxon test = 0.0924; $P = .76$). Treatment modality was not a significant predictor of mortality on multivariate analysis.

Conclusions—Overall mortality and long-term survival in patients with HGD treated with PDT appears to be comparable to that of patients treated with esophagectomy.

Barrett's esophagus (BE) is a complication of gastroesophageal reflux disease in which the normal squamous lining of the esophagus is replaced by specialized columnar epithelium.¹ Approximately 5%–10% of patients diagnosed with BE are believed to be at risk for developing esophageal adenocarcinoma.² Patients with high-grade dysplasia (HGD) on biopsy are at the greatest risk for cancer and are generally referred for treatment.^{3–12} The conventional treatment for most patients with HGD has been esophagectomy. Despite recent studies indicating ablative therapies might be efficacious in the control of HGD, esophagectomy

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continues to be recommended, primarily because of concerns of malignancy occurring during long-term follow up.^{5,7,8,13–19} Esophagectomy is a very invasive intervention associated with a 1.8%–10% mortality rate.^{5,7,8,13–20} In this study, we aimed to compare the overall survival of a cohort of patients treated with photodynamic therapy (PDT) with a cohort treated with esophagectomy to define long-term outcomes, including risks and causes of death as well as rates of occurrence of esophageal cancer.

Patients and Methods

Study Design

This was a retrospective cohort study. Patients were referred for evaluation for PDT to the BE Unit by physicians. All patients seen in the BE Unit for endoscopic therapy had received consultation with thoracic surgeons at the Mayo Clinic or in their local hospitals. Patients referred for esophagectomy were usually referred directly by their physicians.

PDT Cohort

Data from a prospectively maintained database were obtained on consecutive patients with BE and HGD who underwent PDT from September 1994 to July 2004 at the BE Unit at the Mayo Clinic (Rochester, MN). Patients with evidence of carcinoma on pretreatment histopathologic analysis (from either mucosal biopsy specimens and/or endoscopic mucosal resection²¹ specimens) were excluded. All patients underwent 4-quadrant biopsies every centimeter of the involved esophagus. Patients had their diagnosis of HGD confirmed by 2 experienced gastrointestinal pathologists. Baseline assessments also included endoscopic ultrasonography and endoscopic mucosal resection (EMR) for any mucosal abnormalities. Computed tomographic scans of the chest and upper abdomen were obtained in patients who had any suspicion of malignant disease. PDT was delayed a minimum of 4 weeks if an EMR was performed to allow healing of the EMR site(s).

Photosensitizing drugs used included hematoporphyrin derivative (4 mg/kg) in 26 patients (20%) or the commercially available equivalent porfimer sodium (Photofrin; Axcan Pharma, Mont-Saint-Hilaire, Quebec, Canada) at a similar dose of 2 mg/kg in the remainder. Both were administered intravenously 48 hours before photoradiation. Photoradiation was performed using either centering balloons or with a bare cylindrical diffusing fiber. The cylindrical diffusing fibers were either 2.5- or 5.0-cm-long fibers (Fibers Direct, Andover, MA). The cylindrical diffusing fiber was passed through the accessory channel of the endoscope and placed in the center of the esophageal lumen. The light was delivered from a laser (Lambda Plus [Coherent, Palo Alto, CA] or Diomed [Diomed Inc., Andover, MA]) producing 630 nm light with an adjusted power output of 400 mW/cm fiber, delivering a total energy of 200 J/cm fiber energy to the mucosa. Twelve patients received PDT via centering balloons with 5- to 7-cm windows and 7- to 9-cm fibers (for a total of 22 treatments). The deflated balloon was passed into the esophagus over a “spring-tipped” guide wire, the balloon was then endoscopically positioned such that the window of the photoradiating balloon was adjacent to the targeted area of Barrett’s mucosa, and the balloon was inflated to a pressure of 30 mm Hg with air. A pediatric gastroscope was positioned above the centering balloon to verify its position. The light dose applied for balloon photoradiation was 130 J/cm fiber. A second-look endoscopy was performed from 1992 to 1998 in 24–48 hours to assess the adequacy of treatment, and additional photoradiation (50 J/cm) was administered if untreated areas were seen. In 1999, this practice was discontinued because it did not appear that there was any increase in efficacy with the additional treatment. Patients were subsequently evaluated at 3 months after the index PDT treatment.

Focal endoscopically visible lesions underwent EMR for diagnostic purposes to determine histology and exclude carcinoma. EMR was performed by initially injecting 5–10 mL of diluted epinephrine (1:100,000) solution into the submucosa underneath the lesion. The initial technique was a variceal ligation method in which a Bard Six-Shooter (Bard Interventional Products, Billerica, MA) and suction were used to retract the lesion of interest and had a band placed over it to create a pseudopolyp, which was then resected. Beginning in April 2000, EMR was performed using a commercially available EMR cap (EMR-001; Olympus America Inc., Center Valley, PA). Mucosal resection was performed by suctioning the lesion into the cap after positioning of a crescent snare. The snare was then closed with application of cautery current removing the tissue.²²

All patients were placed on proton pump inhibitor therapy twice daily following PDT at the standard dose of the proton pump inhibitor. Patients were carefully educated regarding PDT and its complications, especially dysphagia and photosensitivity, by the physicians, nurse practitioner, and clinical coordinators. Follow-up included endoscopic surveillance with biopsies and EMR if indicated, performed every 3 months for 2 years and then every 6 months for 1–2 years if HGD was eliminated. If HGD persisted, patients were followed up at 3-month intervals. If low-grade dysplasia was present, then patients were followed up every 6 months. If only nondysplastic Barrett's mucosa or normal squamous mucosa was present at 2 years, patients were followed up annually. Data on photosensitivity and stricture formation were prospectively collected.

Surgical Cohort

Patients were identified by a retrospective review of all patients with HGD in the Mayo Clinic pathology database who underwent esophagectomy at the Mayo Clinic between 1994 and 2004. All patients underwent esophagectomy performed by experienced thoracic surgeons using either the transthoracic or the transhiatal route. Data extracted by chart review included postoperative course, days to discharge, complications, and follow-up data.

Survival (vital status and death date) information for both groups was assessed by using an institutionally approved Internet research and location service (www accurint.com). Cause of death was obtained from either the medical records and/or the prospective BE Unit database.

Statistical Analysis

Data management and statistical analysis were performed using JMP software (version 6.0; SAS Institute Inc, Cary, NC). Baseline continuous data were compared using the 2-sample *t* test or the Wilcoxon rank sum tests depending on the data normality. Baseline categorical data were compared using the χ^2 test (or Fisher exact test when necessary because of small sample size). Overall survival was analyzed with the Kaplan–Meier product limit method. The log-rank statistic was used to compare overall survival between patients treated with PDT and esophagectomy for HGD. Baseline variables (age, sex, length of BE segment, age-adjusted Charlson comorbidity index score, and propensity score) were analyzed as factors affecting overall survival using Cox proportional hazards modeling. (Propensity score is the predicted probability of being in the PDT group based on age, sex, length of BE, and the age-adjusted Charlson comorbidity index. The propensity score was obtained using logistic regression.²³) Estimates of hazard rates and 95% confidence intervals were determined.

Results

A total of 199 patients were included in the study, of whom 129 were in the PDT group and 70 were in the surgical group. Patients in the PDT group and the surgical group were followed up for a mean duration of 59 and 61 months, respectively. Patients in the PDT group were older

than those in the surgical group, although the sex distribution was similar (Table 1). Patients in the surgical group had a longer BE segment than those in the PDT group. The frequency of associated medical illnesses was comparable between the 2 groups (Table 1) except for cardiac disease, which was more frequent in the PDT group. We compared the baseline surgical risk and functional status of the groups using the American Society of Anesthesiologists (ASA) classification for preoperative risk assessment²⁴ and the Eastern Cooperative Oncology Group (ECOG)/Zubrod performance score. We also calculated the age-adjusted Charlson comorbidity index for all patients in both cohorts using an electronic calculator.^{25,26} Although the proportion of patients in the PDT group with a higher ASA score was numerically greater, this difference did not meet statistical significance. Notably, patients in the PDT group had a significantly lower functional status (higher ECOG score) compared with those in the surgical group. The distribution of the age-adjusted Charlson comorbidity index scores in the 2 groups is shown in Figure 1. The median age-adjusted Charlson index also was significantly higher in the PDT group compared with the surgical group (Table 1).

After the administration of PDT, patients were followed up by serial endoscopic surveillance as described previously. At 1 year, HGD was eliminated in 88% of patients; at 3 years, HGD was eliminated in 86% of patients. We classified failure of PDT as the detection of HGD within 12 months of the initial PDT session; this occurred in 33 patients who were then re-treated with PDT and/or EMR, which led to the eradication of HGD in most of the patients (70%) who failed initial therapy. Recurrence of HGD, defined as HGD detected after 12 months free of HGD, occurred in 10 patients who were subsequently re-treated with EMR and/or multipolar electrocoagulation, resulting in the eradication of HGD in 60% of patients with recurrence. PDT was performed as an outpatient procedure at our institution, with no procedure-related mortality in this cohort of patients. We recently reported the prevalence and predictive factors for stricture formation following PDT at our institution.²⁷ Stricture formation occurred in 27% of 131 patients (with rates of stricture formation being similar in patients receiving hematoporphyrin derivative and porfimer sodium). Patients required a median of 4 endoscopic dilations for sustained symptomatic relief. All patients were successfully treated endoscopically, except for one patient who developed a perforation following dilation and underwent partial esophagectomy at an outside institution. No patients were readmitted following PDT for related complications within 90 days. Photosensitivity following PDT occurred in 77 patients (60%), of whom 70 patients (91%) had transient mild erythema that responded to conservative measures, 6 patients had localized blistering that responded to topical therapy, and one patient needed oral corticosteroids.

During follow-up, 8 patients (6.2%) in the PDT group developed carcinoma. Five patients had intramucosal carcinoma (cancer confined to the mucosa), of whom 4 elected to have esophagectomy and one had EMR and has not had a recurrence to date. Three patients had submucosal cancer detected during surveillance, and all underwent esophagectomy. None of these patients had metastatic lymphadenopathy detected at surgery. Of these 8 cancers, 6 were detected within 12 months and 2 were detected within 18 months of PDT. All 8 patients were alive at the date of last follow-up (June 2005). Two of 26 patients (7.7%) treated with hematoporphyrin derivative developed recurrent cancer compared with 6 of 103 patients (5.8%) treated with porfimer sodium ($P = .68$).

In the surgical group, 9 of 70 patients (12.8%) had evidence of carcinoma within the resected surgical specimen despite preoperative surveillance described previously. Forty-three patients (60%) in the surgical group underwent endoscopic ultrasonography and 11 patients (15%) underwent EMR before surgery. Additionally, endoscopic ultrasonography had been performed in 8 of the 9 patients with cancer on surgical pathology. Four patients had intramucosal cancer, and 5 had submucosal cancer. None of the 9 patients had metastatic lymphadenopathy, and all were alive at last follow-up (June 2005). Median length of

hospitalization for esophagectomy was 10 days (interquartile range, 8–13; range, 4–74). Following esophagectomy, one patient died, yielding an operative mortality of 1.4%. The postoperative morbidity rate was 38%. Nine patients (12.6%) were readmitted within 90 days for medical/surgical complications. Nine patients (12.6%) developed anastomotic strictures requiring endoscopic dilation.

The overall mortality in the 2 groups was comparable over the mean follow-up period of approximately 5 years (Table 2). Total mortality in the hematoporphyrin derivative–treated group was 19% (5 of 26 patients), compared with 5.8% (6 of 103 patients) in the porfimer sodium group ($P = .04$). Causes of death in the 2 groups are described in Table 2. Figure 1 compares the overall survival of the 2 groups using the Kaplan–Meier curve. As is evident, the 2 curves overlap, with the log-rank test showing the absence of a significant difference. Figure 2 compares the cancer-free survival of patients in both cohorts. Although cancer-free survival is lower in the PDT group, there is no statistically significant difference between the 2 cohorts (Wilcoxon test = 0.0924, $P = .76$). Using Cox proportional hazards modeling, overall survival was comparable (Table 3) after adjusting for age, sex, length of BE, the age-adjusted Charlson comorbidity index, treatment modality (PDT or surgery), and propensity scores for patients in the 2 groups.

We also calculated the ECOG/Zubrod performance score of patients in both groups at the end of follow-up. Six percent of patients in the surgical group had an ECOG score of ≥ 2 compared with 27% in the PDT group. This was similar to the pretreatment proportions.

Discussion

This is the first study that reports long-term (5-year) results following the treatment of HGD in BE with endoscopic therapy (PDT and/or EMR) and esophagectomy in terms of overall survival in a large cohort of patients. We found that overall survival in the 2 groups was comparable despite HGD occurring in 30% of PDT-treated patients and progression to cancer in 5.4% of patients in the PDT group. The majority of HGD recurrences were successfully treated endoscopically. Additionally, overall survival between the groups was similar despite 12.7% of the surgical group having cancer ultimately discovered in the resected surgical specimen. Long-term survival remained comparable even though patients in the PDT group had a significantly lower performance status than those in the surgical group after adjusting for multiple baseline variables. None of the patients in this large cohort of patients treated either with surgery or endoscopic means died from esophageal cancer over a mean follow-up of almost 5 years.

A recent population-based study from Scandinavia reported the prevalence of BE in a white population to be 1.6%.²⁸ It is estimated that 10%–20% of patients with BE may have some degree of dysplasia at initial diagnosis, and progression to carcinoma may occur almost exclusively in this subgroup.^{29,30} Initial reports of the risk of progression to cancer in patients with BE were believed to be overestimates,^{31–33} with the current consensus being an annual incidence of progression to cancer of 0.5% per year.³³ As a result of the appearance of studies with conflicting conclusions, controversy continues on the effect of BE on overall survival.³⁴ Eckardt et al³⁵ followed up 60 consecutive patients with long-segment BE (excluding patients with prevalent dysplasia or cancer) and 2 control groups (patients with achalasia and Schatzki's ring) over a mean of 10 years with endoscopy every 2 years. They found that the life expectancy of patients with BE was comparable to age- and sex-matched German population controls. Two patients with BE (3%) developed esophageal cancer. Eleven patients with BE died (overall mortality rate of 16.6% over 10 years), with no patient dying of esophageal cancer. This prospective study suggested that BE rarely produces esophageal malignancy leading to increased mortality. These findings were echoed by another population-

based study from Northern Ireland.³⁶ However, a recent large prospective population-based study from the United Kingdom³⁷ reported an increase in the overall mortality rate in patients with BE (42/1000 patient-years) compared with those with reflux esophagitis (37/1000 patient-years) and gastroesophageal reflux (32/1000 patient-years). Only a minority (12%) of deaths in the Barrett's cohort were due to esophageal cancer.

Headrick et al²⁰ reported outcomes in 54 patients with HGD who underwent esophagectomy with a median follow-up of 63 months. Overall 5-year survival was 86% and did not differ significantly from a population matched for age and sex. Five-year survival for patients with only HGD was 96% but decreased to 68% when cancer was identified in the resected specimen ($P = .017$). Overall morbidity in this series was 57%. They also measured quality of life by a 2-part survey utilizing a 4-page digestive questionnaire and the Medical Outcomes Study 36-Item Short-Form Health Survey. Despite the significant perioperative morbidity, esophagectomy for HGD resulted in acceptable gastrointestinal functional outcomes and a positive quality of life. Reed et al³⁸ recently reported outcomes in 47 patients with HGD who underwent esophagectomy with similar survival results. In the series by Headrick et al and Reed et al, invasive cancer was found in the resected surgical specimen in 35% and 37% of the patients, respectively. This contrasts with the present study, where only 13% of patients in the surgical group had invasive cancer (all with early-stage disease). This raises the question of the intensity and accuracy of endoscopic surveillance before esophagectomy. None of the patients in the series from Headrick et al and only 10% of patients in the series from Reed et al underwent EMR, as opposed to 80% in our current series. EMR at our institution is performed for diagnosis, staging, and therapy of neoplasia arising in BE. Hence, visible lesions are targeted for EMR as well as areas of "flat dysplasia" (areas where mucosal biopsy specimens have shown HGD). This probably accounts for the higher rate of EMR compared with what would be expected from the prevalence of visible lesions in other studies (ranging from 10%³⁹ to 33%⁴⁰). We have previously shown that EMR in patients with BE leads to a change in grading of dysplasia/neoplasia in as many as 40% of patients,⁴¹ and hence EMR is performed in a large proportion of our patients. Overall survival in the surgical group in our study is comparable to that reported by Headrick et al and Reed et al. Furthermore, our results are similar to those of Eckardt et al in that esophageal cancer was not a cause of death in any patient who was treated with PDT or esophagectomy.

Esophagectomy is currently recommended for patients with HGD and BE due to the risk of coexistent carcinoma, as shown in initial reports of patients who underwent esophagectomy for HGD (10%–40%), as well as the risk of progression to invasive cancer (with poor survival) with endoscopic surveillance (12%–56%). However, endoscopic therapy for HGD in BE has been gaining acceptance due to the mortality (2%–10%) and morbidity (40%–50%) associated with esophagectomy (even in high-volume centers, defined as those performing more than 18 esophagectomies in a year).⁴² PDT for HGD has also been shown to be cost-effective in modeling studies.⁹ Studies showing that a majority of patients with HGD do not progress to invasive cancer have also provided strength to the argument against performing surgery associated with complications in a significant proportion of patients.¹⁰

A number of investigators have reported the successful elimination of HGD following endoscopic therapy using either ablative therapy (PDT, multipolar electrocoagulation, argon plasma coagulation) and/or mucosal resection techniques (focal and/or widespread EMR). Most studies, however, have provided relatively short follow-up. Few investigators have reported outcomes beyond 24 months following PDT for HGD. The international randomized multicenter trial of PDT plus omeprazole versus omeprazole in patients with HGD⁴⁰ reported that after 24 months of follow-up, 77% of patients in the PDT plus omeprazole group had HGD ablated versus 39% in the omeprazole-only group ($P < .001$). A statistically significant decline in the rate of progression to cancer was also seen in the PDT plus omeprazole group (13%)

compared with the omeprazole group (28%). Overholt et al⁴³ followed up 80 patients with HGD who were treated with PDT (using porfimer sodium as a photosensitizer) and Nd:YAG laser for a mean of 50 months. Dysplasia was eradicated in 79% of patients. Two patients (2.5%) had persistent HGD, 6 (7.5%) developed cancer (3 in subsquamous epithelium at 6, 46, and 52 months following PDT), and 7 patients underwent surgery. One patient who developed cancer following PDT died of metastatic adenocarcinoma, 2 were treated successfully with endoscopic therapy, one developed recurrence following radiation, and one underwent surgery and was found to have metastatic lymphadenopathy. Pech et al³⁹ followed up 35 patients treated for HGD with PDT (using aminolevulinic acid as a photosensitizer) for a median of 37 months. They defined complete remission as 2 successive endoscopies being negative for dysplasia or cancer. Complete remission was achieved in 34 of the 35 patients, with a median of 1 (interquartile range, 1–3) treatment. Three patients were also treated with EMR. Six patients (18%) developed metachronous lesions, of which 5 were successfully treated endoscopically. No deaths were reported. The rates of eradication of HGD reported by these investigators are comparable to our results in the PDT group. In contrast, however, patients who developed cancer despite PDT/EMR in our study were all diagnosed at early stages, without metastatic lymphadenopathy, presumably due to the more intensive and aggressive endoscopic follow-up protocol (including EMR of suspicious nodules) at our institution. None of the patients in our group developed cancer in subsquamous epithelium, also probably due to the intensive use of EMR in surveillance at our center. Mortality rates in patients treated with hematoporphyrin derivative were higher than those treated with porfimer sodium, whereas rates of cancer recurrence and stricture formation were comparable. Patients treated before 2000 received hematoporphyrin derivative, and those treated subsequently received porfimer sodium. This probably reflects the use of endoscopic therapy only for patients who were poor surgical candidates with multiple comorbidities before 2000, with subsequent greater use of PDT in patients who had better performance status.

Although results between the 2 groups appear to be comparable, this study is susceptible to some biases because patient assignment to the 2 groups was not randomized. Patients in the PDT group were either believed to be poor surgical candidates or did not wish to undergo radical surgery. Patients who underwent surgery were referred by either gastroenterologists or primary caregivers for surgery. It is possible to speculate that patients who underwent PDT were more likely to be motivated, because they had gathered information on available non-surgical modalities leading to improved outcomes. This factor cannot be excluded, because patients who elected to undergo endoscopic therapy did so with the understanding that long-term endoscopic surveillance would be required with this strategy. Patients who underwent surgery had less intensive preoperative surveillance (60% underwent endoscopic ultrasonography and 15% underwent EMR) compared with the PDT group; however, despite this difference, only 12.7% of patients in the surgical group had an undetected cancer, which is lower than figures reported in the literature (as high as 43% in some studies^{7,8}). Data on outcomes were obtained retrospectively for patients in the surgical group; while this may lead to ascertainment bias, the primary outcome of this study, overall mortality, is an objective end point that is less susceptible to bias and was moreover assessed by the same technique for both cohorts. Other parameters, such as complications and recurrent Barrett's/esophageal cancer in the surgical group, are admittedly susceptible to bias (possibly an underestimate) because the data were collected retrospectively. With the use of robust statistical techniques such as multivariable analysis, with adjustment for propensity scores and comorbidities, we hope to have minimized bias. Finally, the relatively small number of events (deaths, used as the primary outcome in this study) may have led to a type II error, preventing the identification of potentially significant predictor variables.

In conclusion, this single-center, retrospective, cohort study shows that overall survival at 5 years of patients following treatment of HGD in BE with PDT and EMR is comparable to that

of patients treated with esophagectomy. A small proportion of patients in the PDT subgroup do progress to develop cancer; however, in this study, development of cancer did not appear to affect overall survival, possibly due to the early stage of detection of these cancers, which may be attributed to our use of endoscopic mucosal resection.

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Abbreviations used in this paper

ASA	American Society of Anesthesiologists
BE	Barrett's esophagus
ECOG	Eastern Cooperative Oncology Group
EMR	endoscopic mucosal resection
HGD	high-grade dysplasia
PDT	photodynamic therapy

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Figure 1.
Overall survival in the PDT and surgical groups.

Figure 2.
Cancer-free survival in the PDT and surgical groups.

Table 1

Comparison of Baseline Variables

	PDT group (n = 129)	Surgical group (n = 70)	P value
Age (y), mean (SEM)	64.5 (0.9)	60.3 (1.3)	.008
Male (%)	94	87	NS
BE length (cm), median (interquartile range)	5 (3–8.5)	7 (5–10.5)	.003
Hypertension (%)	33	36	NS
Diabetes mellitus (%)	14	5	NS
Cardiac disease (%)	30	14	.015
Pulmonary disease (%)	12	7	NS
Malignancy (%)	5	3	NS
ASA score 3 and 4 (%)	24	14	NS ^a
ECOG score 2 or more	27	8.5	.001 ^a
Age-adjusted Charlson comorbidity index, median (IQR)	2 (0–4)	0 (0–0)	3.0001 ^b

NOTE. Cardiac diseases include coronary artery disease, valvular heart disease, and congestive heart failure; pulmonary diseases include chronic obstructive pulmonary disease and restrictive lung diseases; and previous malignancy (in remission) includes lung cancer, breast cancer, prostate cancer, and colon cancer.

^aObtained using Fisher exact test.

^bObtained using Wilcoxon test.

Table 2

Comparison of Overall Mortality and Causes of Death

	PDT group	Surgical group
Follow-up (<i>mo</i>), mean ($\pm$ SEM)	59 ($\pm$ 2.7)	61 ($\pm$ 5.8)
Overall mortality (%)	11/129 (9)	6/70 (8.5)
Causes of death	Lung cancer, 7	Pneumonia, 3
	Congestive heart failure, 3	Postoperative complications, 1
	Pulmonary embolism, 1	Malignant astrocytoma, 1
		Metastatic transitional cell cancer, 1

Table 3

Overall and Cancer-free Survival in the PDT and Surgical Groups

Variable	Hazard ratio (95% confidence interval)	<i>P</i> value
Overall patient survival adjusting for covariates	1.31 (0.41–4.17)	.653
Overall patient survival adjusting for propensity score	1.25 (0.38–4.10)	.714
Cancer-free survival adjusting for all covariates	2.45 (0.85–7.12)	.099
Cancer-free survival adjusting for propensity score	2.49 (0.84–7.41)	.102