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Survival in the Elderly after Pneumonectomy for Early Stage Non-Small Cell Lung Cancer: A Comparison with Non-Operative Management

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Abstract

Background—Short-term outcomes of morbidity, mortality, and quality of life after pneumonectomy worsen with increasing age. The impact of age on long-term outcomes is not well-described. The purpose of this study was to quantify the impact of patient age on long-term survival after pneumonectomy for early-stage non-small cell lung cancer (NSCLC).

Study Design—Overall survival (OS) of patients who had a pneumonectomy for stage I-II NSCLC in the Surveillance Epidemiology and End Results (SEER) registry from 1988-2010 was evaluated using multivariable and propensity score adjusted Cox proportional-hazard models. Age was stratified as <50, 50-69, 70-79, and ≥ 80. Pneumonectomy patients' OS was compared to matched patients who refused surgery and underwent radiation therapy (RT).

Results—Pneumonectomies comprised 10.8% of NSCLC resections in 1988 but only 2.9% in 2010. Overall, 5-year OS of 5,701 pneumonectomy patients was 49.8% (95% CI 45.3-54.8%) for patients <50, 40.5% (38.8-42.2%) for patients 50-69, 28.9% (26.6-31.5%) for patients 70-79, and 18.8% (14.2-24.8%) for patients ≥ 80 ($p < 0.001$). Increasing patient age was the most important predictor of worse OS (HR 1.34/decade, $p < 0.001$). For patients <70, 5-year OS was 46.3% (36.2-59.2%) after pneumonectomy versus 18.4% (11.9-28.3%) for matched RT patients ($p < 0.001$). In matched-groups of patients ≥ 70, 5-year OS for pneumonectomy was 25.8% (20.8-32.0%) versus 12.2% for RT (8.6-17.4%), $p = 0.02$.

Conclusions—Survival after pneumonectomy for stage I-II NSCLC decreases steadily with patient age. The incremental benefit of pneumonectomy versus RT in matched patients is less in patients older than 70 than in younger patients, although outcomes with pneumonectomy are superior to RT in all age groups. Patients should not be denied pneumonectomy based on age alone, but careful patient selection in elderly patients is essential to optimize survival.

INTRODUCTION

Current clinical guidelines for the treatment of non-small cell lung cancer (NSCLC) recommend anatomic pulmonary resection with lobectomy if technically possible as the

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initial treatment of choice in patients with Stage I-II disease. When pneumonectomy is the only surgical option, the decision of whether to pursue surgery versus definitive radiation therapy (RT) depends on numerous factors, including stage, pulmonary function, patient comorbidities, and age.

Pneumonectomy is associated with notably higher rates of morbidity and mortality than less extensive resections, even for patients judged to be acceptable surgical candidates.[1-6] Perioperative morbidity is of particular concern in the elderly patient population, as age alone is known to be an important risk factor after lung resection.[7-10] Beyond the short-term perioperative risks, pneumonectomy is also associated with significantly decreased quality of life. In fact, having undergone a pneumonectomy has been termed a disease itself.[11-13] Multiple studies have shown that older patients have more significant deterioration in quality of life after pneumonectomy compared to younger patients, and even if they can tolerate a pneumonectomy, may not live long enough to realize the oncologic benefit of cancer resection due to other comorbidities.[12, 14-16]

Despite extensive literature demonstrating that age and pneumonectomy are associated with worse outcomes after surgery for NSCLC, quantitative data to support these difficult therapeutic decisions regarding when to offer pneumonectomy is lacking. Resources available to surgeons are often limited to their own subjective judgment of the potential benefits and risks of pneumonectomy. In this study, we seek to address this knowledge gap and better standardize care of elderly patients with NSCLC that requires a pneumonectomy for complete resection. The purpose of this study was to utilize a large, population-based database to quantify the impact of increasing patient age on both survival after pneumonectomy for early-stage NSCLC and the relative benefit of pneumonectomy compared to non-operative therapy.

METHODS

This analysis of the Surveillance Epidemiology and End Results (SEER) database was approved by the Institutional Review Board at Duke University. Patients included for study were those 18 years or older with early-stage NSCLC diagnosed between 1988 and 2010. Patients were identified using ICD-O-3 location codes for lung cancer (C34.0-C34.9) and appropriate SEER histology codes ranging from 8012 to 8576 for all possible non-small cell lung tumor histologies. Tumor-node-metastasis (TNM) stage was extracted directly from SEER for patients diagnosed in 2004 or later, and was manually recoded from available SEER variables using the 6th edition of the AJCC Cancer Staging Manual for patients diagnosed between 1988 and 2003.[17] Only patients with stage IA (T1N0M0), IB (T2N0M0), IIA (T1N1M0) and IIB (T2N1M0 or T3N0M0) NSCLC were kept for analysis. Only stages I and II were included because there is very good agreement in both guidelines and the thoracic oncology community that surgery when feasible is the appropriate treatment for these stages of disease. Patients with stage IIIA disease were not included because this stage encompasses a heterogeneous group of patients, and there is much less agreement that any surgical therapy, much less pneumonectomy, is appropriate in this setting. Patient age, sex, race, ethnicity, marital status, insurance status and time to last available reported survival time-point were also extracted. Patients living longer than seven years were right-censored.

Patients were stratified into subgroups based on age and SEER-recorded TNM stage. SEER tumor stage is based on pathological information when surgery was the initial cancer-directed therapy and clinical information if surgery was not performed or if patients had neoadjuvant therapy before pneumonectomy. Our primary analysis was to examine the effects of patient age strata and stage on both all-cause and disease-specific survival after

pneumonectomy. Comparisons of patient and treatment characteristics were performed using Pearson's chi-square test for categorical variables and Student's t-test for continuous variables. Unadjusted survival analyses for patients undergoing pneumonectomy, stratified by age and disease stage, were performed using the Kaplan-Meier method. A multivariable Cox proportional hazards model was created to estimate predictors of survival based on stage and age, adjusted for other patient and disease-related factors. Covariates included in the Cox models were: presence and timing of RT, extent of surgical resection, disease stage (AJCC 6th ed: IA, IB, IIA or IIB), laterality (right vs. left-sided primary), age, sex, race, and marital status. As age was our primary predictor of interest, the model was run both with age as a continuous variable and again with age categorized by strata: 18-49, 50-69, 70-79, and 80+ years.

To examine the role of pneumonectomy in the management of early-stage NSCLC, a non-operative control group was defined using the same SEER histology and staging information utilized to identify our primary pneumonectomy cohort. For this control group, we considered only patients with a reason for no cancer-directed surgery of "Patient or patient's guardian refused" recorded in SEER. The other reasons that can be recorded for this variable in SEER are "surgery not recommended", "surgery contraindicated due to other conditions", "patient died before surgery", and "unknown". In addition, we only included those patients who refused surgery but did receive RT. This strategy was based on the assumption that these patients were at least deemed potentially acceptable surgical candidates by their providers and received at least some RT. For this sub-analysis, patients in both the pneumonectomy and RT control groups were included only if they had stage IB, IIA, or IIB disease, to avoid comparisons to RT patients with small peripheral tumors for whom a pneumonectomy would not be indicated.

To attempt to control for likely nonrandom, fundamental differences between patients who did and did not have pneumonectomy, we performed a propensity-matched analysis. The purpose of this analysis was to create a cohort of non-operative patients who, based on known and possible confounders, would have a similar propensity to receive a pneumonectomy as the operative patients. In order to assess the impact of age on the potential benefits of pneumonectomy, patients were stratified into two groups: patients younger than 70 years old and patients 70 years or older. Variables chosen for the matching algorithm were those patient- and disease-related characteristics thought most likely to act as confounders.[18-20] These variables were entered into a logistic regression model to calculate propensity scores, and a nearest-neighbor algorithm was employed to find the most appropriate matched pairs. After propensity score matching, comparisons were made using Pearson's chi-square tests or Fisher's exact test for categorical variables, and Student's t-test for continuous variables. The Kaplan-Meier method was used to compare long-term disease-specific and all-cause survival across groups.

Model diagnostics were assessed, and no major model assumptions were violated. We made an affirmative decision to control for type I error at the level of the comparison. A p-value 0.05 was used to indicate statistical significance for all comparisons and analyses. Statistical analyses were performed using R version 3.0.1, Vienna, Austria.

RESULTS

A total of 5,701 patients who underwent pneumonectomy from 1988-2010 were identified for inclusion in this study. Baseline demographic, treatment and tumor characteristics of these patients are shown in Table 1. The majority of patients were male, white, and between the ages of 50 and 69 years. Left-sided pneumonectomy was more commonly performed, and adjuvant RT was used in a minority of patients.

Trends in the utilization of pneumonectomy for early-stage NSCLC cancer over the course of the study period are shown in Figure 1. Overall, use of pneumonectomy in patients with early stage NSCLC declined over time in this population, with 10.8% of surgical interventions recorded as pneumonectomies in 1988 compared to only 2.9% of operations in 2010. There was a similar decline in utilization of pneumonectomy for all patients (those treated either surgically or non-surgically), decreasing from 9.4% of patients in 1988 to 1.9% of patients in 2010.

Survival analyses

Older patient age was associated with progressively worse long-term outcomes after pneumonectomy. Overall 5-year survival for patients younger than 50 was 49.8% (95% CI: 45.3-54.8%), whereas for patients 50-69, 70-79, and 80+ it was 40.5% (95% CI: 38.8-42.2%), 28.9% (95% CI: 26.6-31.5%), and 18.8% (95% CI: 14.2-24.8%), respectively ($p < 0.001$). Kaplan-Meier survival curves, stratified by disease stage and patient age, are shown in Figure 2. Survival of stage I patients was better than survival for stage II patients. In analysis of all patients and patients stratified by stage, survival was progressively worse for each of the age strata that were studied. Specific 5-year all-cause and disease-specific survival estimates stratified by patient age and disease stage are shown in Table 2. Analysis of survival in patients with stage I and stage II disease, stratified by age (Figure 2c and 2d, respectively), revealed that younger patients had significantly improved long-term survival after pneumonectomy, although this difference was less pronounced in stage II disease.

The results of the Cox proportional hazards survival model, adjusted for available baseline characteristics, are shown in Table 3. Overall, patient age was the most important predictor of survival, with younger age associated with significantly improved survival (HR 1.34 per decade, $p < 0.001$). In addition, female sex, being married, left-sided tumors, and earlier stage disease all predicted improved survival after pneumonectomy. Patients undergoing RT had significantly worse survival. The survival analysis also revealed that a relatively large number of patients died within a year of undergoing pneumonectomy. One-year survival was 74.3% [95% CI 72.7-75.9] and 69.0% [67.3-70.7] after pneumonectomy for stage I and II disease, respectively. Overall, the one-year survival for the age strata studied was 82.7% [79.4-86.2] for patients younger than 50, and 74.5% [73.1-76.0], 63.8% [61.4-66.3], and 56.5% [50.5-63.1] for patients 50-69, 70-79, and 80+, respectively.

Propensity analysis

During the same time period, we identified 436 patients with stage IB, IIA, or IIB NSCLC who were deemed operative candidates but refused surgery and received RT instead. These patients were used as a non-operative control group. Of these RT control patients, 118 (27%) were younger than 70 and 318 (73%) were 70 or older. Comparison of baseline patient characteristics prior to propensity-matching between pneumonectomy and RT groups, stratified by age younger or older than 70 years, is shown in Table 4. Before matching, there were statistically significant differences with respect to most patient features. In both age strata, patients that refused surgery were older, more often non-white, more often had stage I disease, and were more often not married compared to patients that had a pneumonectomy.

After propensity matching, there were no statistically significant differences for any of the patient characteristics between the pneumonectomy and the RT groups (Table 5). Survival for these patients is shown in Figure 3. Pneumonectomy was associated with significantly better **overall** survival for both patients younger and older than 70 years. However, the survival improvement observed for pneumonectomy compared to RT treatment was much higher in the younger group of patients. In the matched-groups of patients less than 70 years

of age, 5-year survival for pneumonectomy was 46.3% (95% CI 36.2-59.2%) versus 18.4% in the RT group (95% CI 11.9-28.3%), $p < 0.001$. In the matched-groups of patients 70 years of age or older, 5-year overall survival for pneumonectomy was 25.8% (95% CI 20.8-32.0%) versus 12.2% in the RT group (95% CI 8.6-17.4%), $p = 0.02$. To confirm that the survival advantage was not simply due to the RT patients dying from other causes, disease-specific survival for the younger and older groups is shown in Figure 4. Disease-specific 5-year survival among patients younger than 70 was 55.6% after pneumonectomy compared to 27.1% in the RT group ($p=0.001$). Similarly, among older patients, disease-specific 5-year survival was 37.5% following pneumonectomy versus 21.6% in the RT group ($p=0.015$).

Kaplan-Meier analysis further revealed that in patients 70 and older, the survival benefit of pneumonectomy, while less pronounced, was also not established until approximately 15 months after diagnosis, where the survival curves of the pneumonectomy and RT groups crossed. For these older patients, the one-year survival was 60.2% (95% CI: 55.0-65.9%) after pneumonectomy and 65.8% (95% CI: 60.7-71.4%) after RT. A similar temporal delay in survival benefit was not observed in the younger groups of patients. For the younger patients, the one-year survival was 77.3% (95% CI: 69.8-85.6%) after pneumonectomy and 67.2% (95% CI: 59.0-76.5%) after RT.

DISCUSSION

Previous large series of resected stage I and stage II NSCLC have reported 5-year survival rates of 60-80% and 40-50%, respectively.[21] Long-term survival following pneumonectomy is generally accepted to be lower compared to less extensive resections, but has been reported as high as 53% for stage I disease.[22] In the current study, we found 5-year survival after pneumonectomy to be 42.1% for stage I NSCLC and 32.4% for stage II disease in a large, population-based study. The results of our propensity-based analysis suggest that while pneumonectomy confers a clear survival advantage over non-surgical treatment that includes RT in younger patients, this considerable effect is less pronounced but maintained in patients over the age of 70. In these older patients, the survival benefit of pneumonectomy over treatment that includes RT is not realized until after approximately one and a half years following surgery but does become substantial over the long term.

These findings can be used by clinicians in shared decision making with patients who would require a pneumonectomy for complete resection. Although pneumonectomy is associated with both short-term and long-term risks[1-3, 5, 6, 11-13], we show that both younger and older patients can have considerable long-term survival. Although each patient age strata had progressively lower one-year survival, figures 2B-D demonstrate that survival for the age groups essentially become parallel approximately one to two years after diagnosis. Despite the perioperative risks of pneumonectomy, we importantly also demonstrate improved survival after pneumonectomy compared to RT, for both all-cause and disease-specific survival estimates. Although quality of life issues are clearly important, many patients would likely accept some compromised quality of life to increase their chances of cure. It should also be noted that most long-term survivors after pneumonectomy for NSCLC can adjust to living with only one lung and are thus able to live fulfilling lives.[23]

Our finding that the benefits of pneumonectomy for early-stage lung cancer decrease somewhat with patient age is not unexpected. Clearly, older patients may have a limited expected lifespan compared to younger patients even in the absence of a lung cancer diagnosis. The overall and disease-specific survival estimates, however, suggest that while some of the patients included for analysis died of other causes, cancer-related deaths nonetheless account for the majority of deaths in this patient cohort regardless of treatment

approach. Notably, had those patients treated with RT been substantially less healthy and dying at higher rates from other causes related to comorbidities, we would expect to only see a survival advantage for pneumonectomy in overall survival, but not disease-specific survival as well. Nonetheless, at some point with advancing age, the potential oncologic benefits of treatment no longer outweigh the costs and associated morbidity and discomfort. This study does not endeavor to delineate exactly when that point is, but does provide robust estimates of the expected survival after pneumonectomy for early-stage NSCLC across different strata of patient age. This data can be used as a realistic estimate of the benefit of surgery to weigh against the potential risks for a particular patient.

Considering that lung cancer is generally a disease of older patients, patient age is clearly an important factor when choosing treatment of early stage cancer. Historically, patients older than 75 years have been offered curative surgery for lung cancer less often than younger patients.[24, 25] However, age alone should not be the sole determinant when considering surgery as a treatment option for lung cancer or other pulmonary diseases[26]. Carefully selected elderly patients can undergo lung resection with similar morbidity and mortality to younger patients.[27] Functional status, pulmonary function, and comorbid conditions should be considered with equal importance and in the context of chronologic age when considering patients for surgery, including potential pneumonectomy.[28] In addition, patient preferences should be carefully considered. This study does highlight that when considering therapy for older patients, the balance of risk and benefits may be significantly different from that of other patients groups, and must be weighed carefully.

Interestingly, we also show a steady decline in the frequency of pneumonectomy for early stage lung cancer. Pneumonectomy was used in approximately 11% of surgical resections for early stage NSCLC in 1988, but only 3% in 2010. One possible explanation for this trend is that surgeons are increasingly trying to perform parenchymal-sparing procedures whenever possible, and only utilize pneumonectomy when absolutely necessary. Another potential explanation is that tumors are now being diagnosed and treated when they are smaller or less locally advanced, allowing for a less extensive resection than pneumonectomy. However, surgical resection may have been avoided altogether in some patients when pneumonectomy was deemed necessary due to perceived hazards and a generalized overemphasis of the risks involved among traditional teaching. Radiation may also have been preferentially increasingly utilized in order to avoid performing a pneumonectomy. In light of the long-term survival demonstrated in this study, clinicians should be careful to not inappropriately eschew pneumonectomy based on the perceived risks, including the elderly patient population.

Advantages of using SEER data for this analysis include its population-based nature, with volume sufficient to enable subgroup analysis. However, the use of SEER does have inherent limitations. First, data regarding chemotherapy administration are lacking, and the impact on our results is not clear. Although surgical resection is the recommended initial treatment for the stages of NSCLC investigated in this study, adjuvant chemotherapy is recommended in some cases of stage I disease due to tumor size and in most cases of stage II disease due to either lymph node involvement or tumor size. However, the exact influence of chemotherapy in this patient cohort cannot be evaluated. Second, there is a lack of data regarding patient co-morbidities, baseline pulmonary function, and provider or center preferences and volumes. Third, the study results are not necessarily generalizable to all patients that may require pneumonectomy, in that the pneumonectomy cohort in this study were felt to have adequate pulmonary function, overall functional status and acceptable co-morbid conditions for surgery. Although our propensity analysis attempts to adjust for this bias, because these data are not available in the SEER dataset our analysis cannot fully

control for imbalance of these important variables. Fourth, treatment specifics of radiation therapy such as dose and method of treatment are also not available in SEER.

There are also some limitations to our analysis that compared pneumonectomy with RT. First, stage migration may have biased our results. SEER uses the “best available” staging for each patient, meaning that many of the RT patients were staged clinically, while the pneumonectomy patients were staged by pathology. A subgroup of patients undergoing pneumonectomy may have been clinical stage I or II but upstaged to stage III disease after surgery. These patients would therefore have been excluded from our analysis while similar patients who did not have surgery would have still been included in the non-surgical group, which could bias our survival results in favor of the pneumonectomy group. Second, to create the non-operative RT controls, we only included patients in the RT group who were recorded in SEER as having refused surgery, but it is possible that some of these patients refused even surgical consultation, and may not have actually been offered surgery had they undergone comprehensive evaluation by a surgeon. Other reasons for no surgery available in SEER, which were not included in our analysis, include: surgery not recommended, surgery contraindicated due to other conditions, patient died before surgery, and unknown. In addition, given the lack of SEER data regarding performance status and comorbid conditions, our operative and RT groups may have unmeasured differences in these characteristics that are not accounted for in our analyses. Given the lack of chemotherapy data available in SEER, we are also not able to provide any insight on how the strategy of definitive chemoradiation compares with pneumonectomy in terms of long-term outcomes. Finally, we included all patients with stage IB, IIA, and IIB who refused surgery in the control group. Many of these patients may not have required pneumonectomy for complete resection. However, if this were the case the control group patients may have had less extensive local disease than the pneumonectomy patients, leading us to underestimate the potential benefit of pneumonectomy over RT despite matching patients by overall stage.

CONCLUSION

Although its use for NSCLC has decreased with time, pneumonectomy plays an important role in the management of patients with early stage NSCLC that is not amenable to less extensive surgical resection, with five-year survival rates up to 60% depending on patient age and stage of disease at the time of resection. These outcomes are significantly better than outcomes for matched non-surgical patients, with pneumonectomy offering 2- to 3-fold higher 5-year survival across age groups. While younger patients derive more absolute survival benefits after pneumonectomy, pneumonectomy may also be indicated in older individuals after careful consideration of functional status, comorbidities, and expected remaining life span. Further research is necessary to determine the comorbidities and characteristics that are most important in both of these patient populations to optimize both perioperative outcomes and long-term survival. This study emphasizes the importance of multidisciplinary evaluations to determine optimal treatments for patients with NSCLC, and strongly suggests that patients should not be inappropriately denied surgery based on age alone.

REFERENCES

1. Alexiou C, Beggs D, Rogers ML, et al. Pneumonectomy for non-small cell lung cancer: predictors of operative mortality and survival. *Eur J Cardiothorac Surg.* 2001; 20:476–480.
2. Boffa DJ, Allen MS, Grab JD, et al. Data from The Society of Thoracic Surgeons General Thoracic Surgery database: the surgical management of primary lung tumors. *J Thorac Cardiovasc Surg.* 2008; 135:247–254.

3. Fernandez FG, Force SD, Pickens A, et al. Impact of laterality on early and late survival after pneumonectomy. *Ann Thorac Surg.* 2011; 92:244–249. [PubMed: 21718850]
4. Kozower BD, Sheng S, O'Brien SM, et al. STS database risk models: predictors of mortality and major morbidity for lung cancer resection. *Ann Thorac Surg.* 2010; 90:875–881. discussion 881–873. [PubMed: 20732512]
5. Ramnath N, Demmy TL, Antun A, et al. Pneumonectomy for bronchogenic carcinoma: analysis of factors predicting survival. *Ann Thorac Surg.* 2007; 83:1831–1836.
6. Shapiro M, Swanson SJ, Wright CD, et al. Predictors of major morbidity and mortality after pneumonectomy utilizing the Society for Thoracic Surgeons General Thoracic Surgery Database. *Ann Thorac Surg.* 2010; 90:927–934. discussion 934–925.
7. Deslauriers J, Ginsberg RJ, Piantadosi S, Fournier B. Prospective assessment of 30-day operative morbidity for surgical resections in lung cancer. *Chest.* 1994; 106:329S–330S. [PubMed: 7988256]
8. Fan J, Wang XJ, Jiang GN, et al. Survival and outcomes of surgical treatment of the elderly NSCLC in China: a retrospective matched cohort study. *Eur J Surg Oncol.* 2007; 33:639–643. [PubMed: 17386995]
9. Hanna N, Brooks JA, Fyffe J, Kesler K. A retrospective analysis comparing patients 70 years or older to patients younger than 70 years with non-small-cell lung cancer treated with surgery at Indiana university: 1989–1999. *Clin Lung Cancer.* 2002; 3:200–204. [PubMed: 14662043]
10. Harpole DH, DeCamp MM, Daley J, et al. Prognostic models of thirty-day mortality and morbidity after major pulmonary resection. *J Thorac Cardiovasc Surg.* 1999; 117:969–979.
11. Brunelli A, Socci L, Refai M, et al. Quality of life before and after major lung resection for lung cancer: a prospective follow-up analysis. *Ann Thorac Surg.* 2007; 84:410–416. [PubMed: 17643607]
12. Bryant AS, Cerfolio RJ, Minnich DJ. Survival and quality of life at least 1 year after pneumonectomy. *J Thorac Cardiovasc Surg.* 2012; 144:1139–1143. [PubMed: 23079008]
13. Sartipy U. Prospective population-based study comparing quality of life after pneumonectomy and lobectomy. *Eur J Cardiothorac Surg.* 2009; 36:1069–1074.
14. Birim O, Kappetein AP, Bogers AJJC. Charlson comorbidity index as a predictor of long-term outcome after surgery for nonsmall cell lung cancer. *Eur J Cardiothorac Surg.* 2005; 28:759–762.
15. Landreneau RJ, Sugarbaker DJ, Mack MJ, et al. Wedge resection versus lobectomy for stage I (T1 N0 M0) non-small-cell lung cancer. *J Thorac Cardiovasc Surg.* 1997; 113:691–698. discussion 698–700. [PubMed: 9104978]
16. Leo F, Scanagatta P, Vannucci F, et al. Impaired quality of life after pneumonectomy: who is at risk? *J Thorac Cardiovasc Surg.* 2010; 139:49–52. [PubMed: 19660279]
17. Greene, F.; Page, D.; Fleming, I. *AJCC cancer staging manual* 6th edition. Springer-Verlag; Berlin: 2003.
18. Arbogast, P.; Seeger, J. *Effective Health Care Program Research Report. AHRQ Publi*; 2012. Summary Variables in Observational Research: Propensity Scores and Disease Risk Scores.
19. Brookhart MA, Schneeweiss S, Rothman KJ, et al. Variable selection for propensity score models. *Am J Epidemiol.* 2006; 163:1149–1156. [PubMed: 16624967]
20. Pearl J. Causal inference in statistics: An overview. *Statistics Surveys.* 2009; 3:96–146.
21. Scott WJ, Howington J, Feigenberg S, et al. Treatment of non-small cell lung cancer stage I and stage II: ACCP evidence-based clinical practice guidelines (2nd edition). *Chest.* 2007; 132:234S–242S.
22. Thomas P, Doddoli C, Thirion X, et al. Stage I non-small cell lung cancer: a pragmatic approach to prognosis after complete resection. *Ann Thorac Surg.* 2002; 73:1065–1070.
23. Deslauriers J, Ugalde P, Miro S, et al. Long-term physiological consequences of pneumonectomy. *Sem Thorac Cardiovasc Surg.* 2011; 23:196–202.
24. Mery CM, Pappas AN, Bueno R, et al. Similar long-term survival of elderly patients with non-small cell lung cancer treated with lobectomy or wedge resection within the surveillance, epidemiology, and end results database. *Chest.* 2005; 128:237–245. [PubMed: 16002941]

25. Owonikoko TK, Ragin CC, Belani CP, et al. Lung cancer in elderly patients: an analysis of the surveillance, epidemiology, and end results database. *J Clin Oncol.* 2007; 25:5570–5577. [PubMed: 18065729]
26. Berry MF, Hanna J, Tong BC, et al. Risk factors for morbidity after lobectomy for lung cancer in elderly patients. *Ann Thorac Surg.* 2009; 88:1093–1099.
27. Cerfolio RJ, Bryant AS. Survival and outcomes of pulmonary resection for non-small cell lung cancer in the elderly: a nested case-control study. *Ann Thorac Surg.* 2006; 82:424–429. discussion 429-430. [PubMed: 16863740]
28. Bernard A, Ferrand L, Hagry O, et al. Identification of prognostic factors determining risk groups for lung resection. *Ann Thorac Surg.* 2000; 70:1161–1167. [PubMed: 11081862]

Figure 1.
Trends in the utilization of pneumonectomy for early-stage NSCLC over time, by year.

Figure 2. Kaplan-Meier survival after pneumonectomy for early-stage NSCLC, stratified by age and disease status. (A) Survival stratified by stage; (B) survival stratified by age; (C) survival for stage I, stratified by age; (D) survival for stage II, stratified by age.

Figure 3.
 (A) Kaplan-Meier overall survival in patients less than 70 years old, pneumonectomy versus no surgery; (B) Kaplan-Meier overall survival in patients 70 years and older, pneumonectomy versus no surgery.

Figure 4. (A) Kaplan-Meier disease-specific survival in patients less than 70 years old, pneumonectomy versus no surgery; (B) Kaplan-Meier disease-specific survival in patients 70 years and older, pneumonectomy versus no surgery.

Table 1
Preoperative Characteristics of Patients Undergoing Pneumonectomy

Patient characteristic	Total cohort, n = 5,701
Age, y, median(IQR)	65 (58,71)
Age groups, n (%)	
18-49 y	477 (8.4)
50-69 y	3474 (60.9)
70-79 y	1508 (26.5)
80+ y	242 (4.2)
Sex, n (%)	
Female	1792 (31.4)
Male	3909 (68.6)
Race, n (%)	
White	4,964 (87.1)
Black	484 (8.5)
Other	253 (4.4)
Laterality, n (%)	
Left	3189 (56)
Right	2506 (44)
Disease stage, n (%)	
Stage I	2844 (49.9)
Stage II	2857 (50.1)
Marital status, n (%)	
Married	3696 (64.8)
Not married	1845 (32.4)
Unknown	160 (2.8)
Radiation therapy, n (%)	1030 (18.5)

Table 2

Five-Year All-Cause and Disease-Specific Survival Estimates after Pneumonectomy, by Age And Stage

Patient age	Disease stage (AJCC 6th ed)	
	Stage I, % (95% CI)	Stage II, % (95% CI)
Five-year all-cause survival estimates after pneumonectomy, by age, y		
18-49	60.0 (53.5-67.4)	41.7 (35.9-48.5)
50-69	45.8 (43.4-48.4)	35.3 (33.0-37.8)
70-79	33.1 (29.8-36.7)	24.2 (21.0-27.8)
80+	21.3 (15.2-29.8)	15.3 (9.4-24.8)
Five-year disease-specific survival estimates after pneumonectomy, by age, y		
18-49	66.1 (59.5-73.6)	46.2 (39.9-53.4)
50-69	55.9 (53.1-58.9)	44.9 (42.2-47.9)
70-79	47.0 (42.5-52.1)	32.8 (28.6-37.8)
80+	36.3 (25.9-50.9)	27.8 (17.7-43.7)

Table 3

Risk of Death for Early-Stage Non-Small Cell Lung Cancer Patients Undergoing Pneumonectomy from 1988-2010

Predictor	Hazard Ratio	95% Confidence Interval		p Value
		Lower	Upper	
Age, y				
18-49	Ref	Ref	Ref	Ref
50-69	1.52	1.34	1.73	< 0.001
70-79	2.31	2.01	2.64	< 0.001
80+	2.97	2.47	3.57	< 0.001
Male sex	1.20	1.12	1.29	< 0.001
Race				
White	Ref	Ref	Ref	Ref
Black	1.03	0.92	1.16	0.57
Other	0.92	0.79	1.07	0.26
Marital status				
Married	Ref	Ref	Ref	Ref
Not married	1.17	1.09	1.25	< 0.001
Unknown	0.83	0.66	1.05	0.12
Laterality				
Left	Ref	Ref	Ref	Ref
Right	1.14	1.07	1.21	< 0.001
Clinical stage				
IA	Ref	Ref	Ref	Ref
IB	1.08	0.97	1.21	0.14
IIA	1.25	1.07	1.48	0.01
IIB	1.32	1.19	1.47	< 0.001
Radiation therapy	1.12	1.04	1.22	0.005

Cox proportional hazards model adjusting for age, disease stage, laterality, radiation therapy, race, sex, and marital status.

Table 4

Baseline Characteristics of Patients, Stratified by Age Group and Intervention

Characteristic	Patients < 70 y			Patients ≥ 70 y		
	Definitive radiation therapy (n = 118)	Pneumonectomy (n = 3,437)	p Value	Definitive radiation therapy (n = 318)	Pneumonectomy (n = 1,496)	p Value
Age, y	65 (60.67)	61 (54.65)	< 0.001	79 (74.82.8)	74 (72.77)	< 0.001
Sex, n (%)			0.140			< 0.001
Female	43 (36.4)	1020 (29.7)		141 (44.3)	456 (30.5)	
Male	75 (63.6)	2417 (70.3)		177 (55.7)	1040 (69.5)	
Race, n (%)			< 0.001			< 0.001
White	85 (72)	2940 (85.5)		251 (78.9)	1346 (90)	
Black	22 (18.6)	342 (10)		35 (11)	82 (5.5)	
Other	11 (9.3)	155 (4.5)		32 (10.1)	68 (4.5)	
Laterality, n (%)			0.360			< 0.001
Left	58 (49.2)	1908 (55.5)		144 (45.3)	858 (57.4)	
Right	60 (50.8)	1525 (44.4)		174 (54.7)	636 (42.5)	
Disease stage, n (%)			< 0.001			< 0.001
Stage I	80 (67.8)	1451 (42.2)		242 (76.1)	705 (47.1)	
Stage II	38 (32.2)	1986 (57.8)		76 (23.9)	791 (52.9)	
Marital status, n (%)			< 0.001			< 0.001
Married	52 (44.1)	2247 (65.4)		147 (46.2)	978 (65.4)	
Not married	65 (55.1)	1101 (32)		161 (50.6)	496 (33.2)	
Unknown	1 (0.8)	89 (2.6)		10 (3.1)	22 (1.5)	
Radiation therapy, n (%)	118 (100)	796 (23.2)	< 0.001	318 (100)	198 (13.2)	< 0.001

Table 5

Baseline Characteristics of Patients after Propensity Matching, Stratified by Age Group and Intervention

Characteristic	Patients < 70 y			Patients > 70 y		
	Definitive radiation therapy (n = 118)	Pneumonectomy (n = 3,437)	p Value	Definitive radiation therapy (n = 318)	Pneumonectomy (n = 1,496)	p Value
Age, y	65 (60.67)	64 (59.2,67)	0.58	79 (74,82.8)	78 (74,81)	0.09
Sex, n (%)			0.89			0.58
Female	43 (36.4)	41 (34.7)		141 (44.3)	133 (41.8)	
Male	75 (63.6)	77 (65.3)		177 (55.7)	185 (58.2)	
Race, n (%)			0.61			0.22
White	85 (72)	87 (73.7)		251 (78.9)	263 (82.7)	
Black	22 (18.6)	24 (20.3)		35 (11)	35 (11)	
Other	11 (9.3)	7 (5.9)		32 (10.1)	20 (6.3)	
Laterality, n (%)			0.43			1.00
Left	58 (49.2)	65 (55.1)		144 (45.3)	144 (45.3)	
Right	60 (50.8)	53 (44.9)		174 (54.7)	174 (54.7)	
Disease stage, n (%)			0.78			1.00
Stage I	80 (67.8)	83 (70.3)		242 (76.1)	243 (76.4)	
Stage II	38 (32.2)	35 (29.7)		76 (23.9)	75 (23.6)	
Marital status, n(%)			0.93			0.53
Married	52 (44.1)	55 (46.6)		147 (46.2)	159 (50)	
Not married	65 (55.1)	62 (52.5)		161 (50.6)	152 (47.8)	
Unknown	1 (0.8)	1 (0.8)		10 (3.1)	7 (2.2)	
Radiation therapy, n (%)	118 (100)	10 (8.5)	< 0.001	318 (100)	20 (6.3)	< 0.001