



Treatment patterns and outcomes in patients with Pancoast tumors: a national cancer database analysis

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Background: Pancoast tumors represent 5% of non-small cell lung cancers. Complete surgical resection and no lymph node involvement are important positive prognostic factors. Previous literature has identified neoadjuvant chemoradiation treatment, followed by surgical resection, as the standard of care. But many institutions choose upfront surgery. Our goal was to identify the treatment patterns and outcomes in patients with node-negative Pancoast tumors using the National Cancer Database (NCDB).

Methods: The NCDB was queried from 2004 through 2017 to identify all patients who had undergone surgery for a Pancoast tumor. Treatment patterns, including the percentage of patients who received neoadjuvant treatment, were recorded. Logistic regression and survival analyses were used to determine outcomes based on different treatment patterns. Secondary analyses were performed on the cohort who received upfront surgery.

Results: A total of 2,910 patients were included in the study. Overall 30- and 90-day mortality were 3% and 7% respectively. Only 25% (717/2,910) of the group received neoadjuvant chemoradiation treatment prior to surgery. Patients who received neoadjuvant chemoradiation treatment experienced significantly improved 90-day survival ($P < 0.01$) and overall survival ($P < 0.01$). When analyzing the cohort who received upfront surgery, there was a statistically significant difference in survival based on adjuvant treatment pattern ($P < 0.01$). Patients in this group who received adjuvant chemoradiation had the best survival, whereas patients who received adjuvant radiation only or no treatment had the worst outcomes.

Conclusions: Patients with Pancoast tumors receive neoadjuvant chemoradiation treatment in only a quarter of cases nationally. Patients who received neoadjuvant chemoradiation treatment had improved survival compared to patients who had upfront surgery. Similarly, when surgery is performed first, adjuvant chemoradiation treatment improved survival compared to other adjuvant strategies. These results suggest underutilization of neoadjuvant treatment for patients with node-negative Pancoast tumors. Future studies with a more clearly defined cohort are needed to assess the treatment patterns being utilized on patients with node-negative Pancoast tumors. It will be beneficial to see whether neoadjuvant treatment for Pancoast tumors has increased in recent years.

Keywords: Pancoast tumor; neoadjuvant; adjuvant; trimodality

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Introduction

Pancoast tumors account for nearly 5% of lung tumors encompassing the apex of the lung. These tumors commonly involve the ribs, periosteum, brachial plexus or subclavian vessels (1). Also known as superior pulmonary sulcus tumors, most of these tumors are non-small-cell lung cancers (NSCLCs) (2). Surgery can be technically challenging at times, with mortality and complication rate higher than standard lobectomy (3-5).

Over the last several decades, advancements in treatment options have improved the outcomes in patients with Pancoast tumors (6). Resection with negative margins and complete pathologic response are positive prognostic indicators (7). Positive lymph node status, brachial plexus invasion and great vessel involvement worsen overall prognosis (8-10). Neoadjuvant chemoradiation treatment followed by surgery has emerged as the standard of care in patients without lymph node involvement (11-15). With tri-modality treatment, five-year survival ranges from 55% to 70% (12).

Although tri-modality therapy is standard of care, many patients are offered alternative treatment plans for various reasons. Previous literature has not focused on the percentage of patients who receive standard of care compared to other approaches. As such, our goals were to identify treatment patterns and outcomes in patients with node-negative Pancoast tumors. The National Cancer Database (NCDB) was utilized over a 13-year period to perform this study. We present the following article in accordance with the STROBE reporting checklist (available

at <https://jtd.amegroups.com/article/view/10.21037/jtd-22-1077/rc>).

Methods

Patients

The NCDB was developed as a joint project of the Commission on Cancer of the American College of Surgeons and the American Cancer Society as a comprehensive database of cancer cases in the United States (16). The NCDB is a clinical oncology database which acquires hospital registry data from over 15,000 Commission on Cancer-accredited facilities. The NCDB contains over 70% of all newly diagnosed cancer cases and has more than 34 million records overall. The NCDB was queried for all cases of Pancoast tumors from 2004 to 2017. Although there is no strict delineation for Pancoast tumor in the NCDB, all patients with upper lobe tumors who underwent chest wall resection were included in the analysis. This is consistent with the definition of Pancoast tumors being those of the apex of the lung invading surrounding structures including nerve roots, rib bone and periosteum, subclavian vessels, and chest wall (17). Only patients with node-negative disease were included in the analysis to reduce confounding from more advanced disease. The data used in the study were derived from a de-identified NCDB file. The American College of Surgeons and the Commission on Cancer have not verified and are not responsible for the analytic or statistical methodology employed, or the conclusions drawn from these data by the investigators. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the University of Texas Medical Branch institutional review board (IRB# 19-0168) and individual consent for this retrospective analysis was waived as the database we received was de-identified prior to us receiving it.

Variables

The following variables were collected for each patient: age, gender, race/ethnicity, medical insurance status, income level, Charlson-Deyo comorbidity score, distance from the patient's residence to the treating institution, urban *vs.* rural location of patient residence, year of diagnosis, clinical stage, pathologic stage, type of treating institution, high-volume *vs.* low-volume lobectomy institution, histology, type of treatment given (surgery, chemotherapy, radiation), time from diagnosis to start of treatment and to mortality.

Highlight box

Key findings

- Patients with Pancoast tumors receive chemoradiation ahead of surgery in only 25% of cases.

What is known and what is new?

- Neoadjuvant chemoradiation is standard of care for patients with Pancoast tumors.
- Most patients do not get neoadjuvant treatment. Patients who get neoadjuvant treatment had improved survival compared to patients who received upfront surgery. When surgery is done first, patients who received adjuvant treatment experienced improved survival.

What is the implication, and what should change now?

- More standardization toward neoadjuvant treatment would benefit patients. Future studies can assess whether there is an increased rate of neoadjuvant treatment for patients with Pancoast tumors.

Income was measured as the median income of the zip code in which the patient lived. A center was considered to be high-volume if it performed more than an average of 40 or more lobectomies per year, as 40 was the guideline by the Leapfrog Group during the midpoint of the study (18). To calculate yearly volume, we divided the total number of cases at each institution by the number of years of the study. The primary endpoint was the receipt of neoadjuvant chemoradiation. The secondary endpoints were overall survival in both the neoadjuvant and upfront surgery groups.

Statistical methods

Demographics, cancer characteristics, facility characteristics and treatment patterns were presented as means, standard deviation, median, and quartile 1 and 3 for continuous variables, and as frequencies and percentage for categorical variables. A logistic regression model was used to compare treatment patterns and outcomes. The logistic regression model was adjusted for demographics and facility characteristics. To examine the effect of treatment pattern on survival, unadjusted survival rates were estimated by using Kaplan-Meier method and compared with the log-rank test. Multivariate Cox proportional hazard models were used to estimate hazard ratios adjusted for demographics and facility characteristics. All patients were censored at the last contact date or at the end of study (December 31, 2019). The proportional hazard assumption was evaluated first by visual inspection of the Kaplan-Meier curve and then by adding the interaction between race and log (time) to the model and checking for significance. Race was reported as Caucasian, African American and “other” since the “other” category was only 2.9% of the cohort. The “other” category consisted of Hispanic, Asian, Pacific Islander and Native American. In both the Kaplan-Meier analysis and the Cox proportional hazards model, patients diagnosed in 2017 were excluded due to not having follow-up information. All analyses were conducted using SAS 9.4 (Cary, NC, USA). Patients who received (I) chemotherapy only or (II) radiation treatment only before surgery were excluded from the analysis. When subdividing the upfront surgery group, a patient was considered to have received adjuvant treatment if it was received within 3 months of the date of surgery.

Results

Demographics

After exclusion of patients with missing data and those

that did not fit the above criteria, a total of 2,910 patients were identified to have Pancoast tumors and no positive lymph nodes. Demographic data for this cohort is displayed in *Table 1*. Mean age was 63.7 ± 10.5 years. Approximately 34% of the cohort was between the ages of 60 and 70. The majority of the cohort was Caucasian, male and lived in metropolitan areas. In the cohort there were 25% (717/2,910) of patients who underwent neoadjuvant chemoradiation prior to surgery. *Table 2* shows patients who underwent neoadjuvant chemoradiation treatment compared to the rest of the cohort. When comparing patients who had neoadjuvant chemoradiation treatment versus the rest of the cohort, patients who received surgery first were older, less likely to have private insurance and were more likely to be treated at low-volume centers. There were no significant differences in racial distribution, income or distance from home to the treating facility. *Table S1* shows the multivariate logistic regression analyses of these results. In this supplemental table we have included the results of the multivariate analyses with corresponding 95% confidence intervals.

Survival

Overall 30-day mortality for the cohort was 3.3%, while overall 90-day mortality was 7.5%. When analyzing the entire group, the only variable which was associated with improved survival was facility volume, as high-volume centers had an improved overall survival both at 30 days (hazard ratio 0.57, 95% CI: 0.35–0.93) and 90 days (hazard ratio 0.71, 95% CI: 0.52–0.98).

Figures 1-3 shows Kaplan-Meier analyses for patients who underwent neoadjuvant chemoradiation treatment versus upfront surgery at 30 days, 90 days and 14 years. Patients who received neoadjuvant chemoradiation had similar survival when compared to the upfront surgery group at 30 days ($P=0.27$), but experienced a significantly improved survival at 90 days ($P<0.01$). At the 14-year period, survival estimates were worse for the upfront surgery group compared to the neoadjuvant group ($P<0.01$).

Survival in upfront surgery group

Figure 4 demonstrates overall survival in the upfront surgery group only. Patients in this group were subdivided into surgery only, surgery followed by chemoradiation treatment, surgery followed by chemotherapy only and surgery followed by radiation only. There was a statistically significant difference in survival among these 4 groups.

Table 1 Patient demographics

Variables	Number (%)
All	2,910
Age at diagnosis, years	
Mean \pm SD	63.7 \pm 10.5
Median, Mean [Q1–Q3]	65 [55–72]
<50	308 (10.6)
50–59	708 (24.3)
60–69	983 (33.8)
70–79	911 (31.3)
Gender	
Male	1,753 (60.2)
Female	1,157 (39.8)
Race	
Caucasian	2,561 (88.0)
African American	266 (9.1)
Other	83 (2.9)
Metropolitan/rural	
Metropolitan	2,307 (79.3)
Urban	603 (20.7)
Primary payor	
Not insured	114 (3.9)
Private	1,176 (40.4)
Medicaid	227 (7.8)
Medicare	1,393 (47.9)
Income	
Q1	523 (18.0)
Q2	687 (23.6)
Q3	815 (28.0)
Q4	885 (30.4)
Charlson–Deyo Score	
0	1,549 (53.2)
1	983 (33.8)
2+	378 (13.0)

Table 1 (continued)**Table 1** (continued)

Variables	Number (%)
Region	
Midwest	859 (29.5)
Northeast	582 (20)
South	1,137 (39.1)
West	332 (11.4)
Distance from home to facility (miles)	
Median, Mean [Q1–Q3]	13 [5.5–31.9]
Facility type	
Community Cancer Program	203 (7.0)
Comprehensive Community Cancer Program	1,205 (41.4)
Academic/Research	1,106 (38.0)
Integrated Network Cancer Program	396 (13.6)
Facility volume (surgeries per year)	
<40 per year	1,287 (44.2)
40+ per year	1,623 (55.8)
Histology	
Squamous cell carcinoma	1,548 (53.2)
Adenocarcinoma	937 (32.2)
Other	425 (14.6)
T category	
T3	2,306 (79.2)
T4	604 (20.8)
Vital status	
Dead	1047 (36.0)
Alive	1863 (64.0)
30-day mortality	
Alive	2,822 (97.0)
Dead	88 (3.0)
90-day mortality	
Alive	2,705 (93.0)
Dead	205 (7.0)

SD, standard deviation; Q1, first quarter; Q2, second quarter; Q3, third quarter; Q4, fourth quarter.

Table 2 Neoadjuvant chemoradiation group versus rest of cohort

Variables	Upfront surgery	Neoadjuvant chemoradiation	P value
N	2,193	717	
Age at diagnosis, years	65.0	59.0	<0.001
Male	60.2% (1,320/2,193)	60.4% (433/717)	0.925
Race			0.330
White	88.5% (1,941/2,193)	86.5% (620/717)	
Black	8.7% (191/2,193)	10.5% (75/717)	
Other	2.8% (61/2,193)	3.1% (22/717)	
Metropolitan	78.4% (1,720/2,193)	81.9% (587/717)	0.049
Primary payor			<0.001
Uninsured	3.4% (74/2,193)	5.6% (40/717)	
Private	37.2 (816/2,193)	50.2% (360/717)	
Medicaid	7.4% (162/2,193)	9.1% (65/717)	
Medicare	52.0% (1,141/2,193)	35.2% (252/717)	
Income			0.116
Q1	18.9% (415/2,193)	15.1% (108/717)	
Q2	23.1% (507/2,193)	25.1% (180/717)	
Q3	27.6% (605/2,193)	29.3% (210/717)	
Q4	30.4% (666/2,193)	30.5% (219/717)	
Charlson-Deyo Score			<0.001
0	50.0% (1,097/2,193)	63.0% (452/717)	
1	354 (777/2,193)	28.7% (206/717)	
2+	14.6% (319/2,193)	8.2% (59/717)	
Region			0.025
Midwest	28.6% (626/2,193)	32.5% (233/717)	
Northeast	19.4% (425/2,193)	21.9% (157/717)	
South	40.1% (880/2,193)	35.8% (257/717)	
West	12.0% (262/2,193)	9.8% (70/717)	
Great circle distance, mean (miles)	29.3	34.6	0.370
Facility type			0.002
Community Cancer Program	7.3% (161/2,193)	5.9% (42/717)	
Comprehensive Community Cancer Program	42.5% (932/2,193)	38.1% (273/717)	
Academic/Research	37.3% (817/2,193)	40.3% (289/717)	
Integrated Network Cancer Program	12.9% (283/2,193)	15.8% (113/717)	
Facility volume (surgeries per year)			<0.001
<40 per year	45.8% (1,005/2,193)	39.3% (282/717)	
40+ per year	54.2% (1,188/2,193)	60.7% (435/717)	

Q1, first quarter; Q2, second quarter; Q3, third quarter; Q4, fourth quarter.

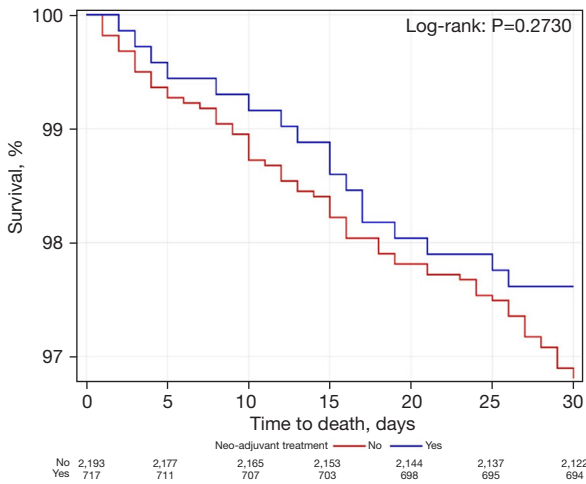


Figure 1 The 30-day Kaplan-Meier survival curves of neoadjuvant chemoradiation group compared to upfront surgery group; y-axis represents percent alive.

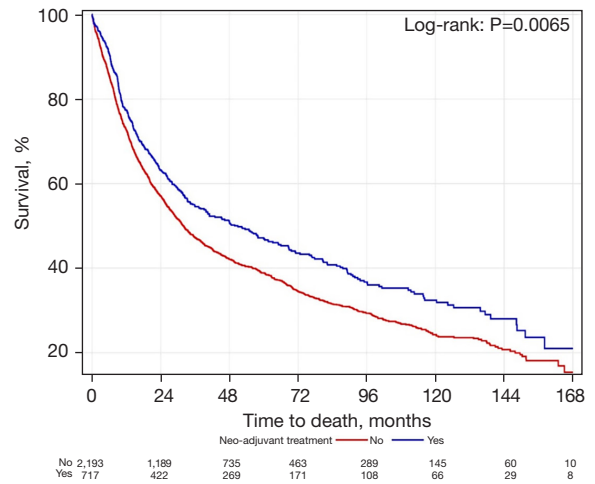


Figure 3 The 14-year Kaplan-Meier survival curves of neoadjuvant chemoradiation group compared to upfront surgery group; y-axis represents percent alive.

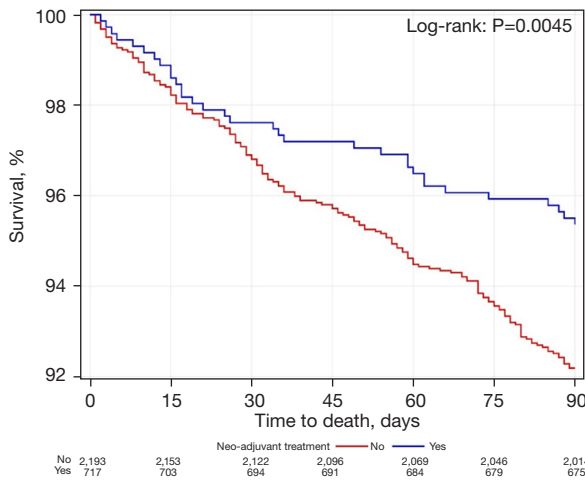


Figure 2 The 90-day Kaplan-Meier survival curves of neoadjuvant chemoradiation group compared to upfront surgery group; y-axis represents percent alive.

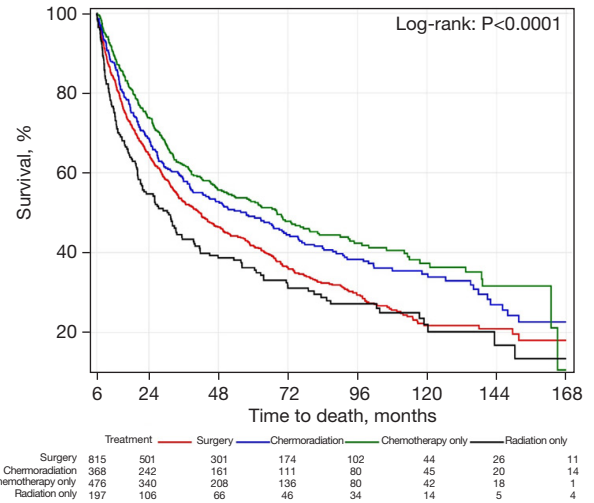


Figure 4 The overall survival of the upfront surgery group subdivided into surgery only, surgery followed by chemoradiation treatment, surgery followed by chemotherapy only and surgery followed by radiation only after 14 year followup. The “surgery” group represents patients who had surgery alone without adjuvant treatment. The numbers below the curves represent the remaining patients at risk. The y-axis represents the percent of each group alive.

Patients in the upfront surgery group who underwent adjuvant chemoradiation had the best survival, followed by patients who underwent adjuvant chemotherapy alone. Patients who underwent adjuvant radiation alone and patients who received no adjuvant treatment had similar survival rates and the worst rates in the upfront surgery group.

Discussion

In our study we examined trends in treatment patterns for

Pancoast tumors over a 13-year period using the NCDB. Standard of care treatment for Pancoast tumors has changed from upfront surgical resection followed by adjuvant therapy to a trimodality approach with neoadjuvant chemoradiation followed by surgical resection (1,19). This trimodality

approach has been associated with improved outcomes and longer disease free and overall survival (20-22). Given that trimodality treatment is considered standard of care for Pancoast tumors, we wanted to investigate how often this is being applied to patients nationally. We queried the NCDB starting in 2004 when this trimodality approach was accepted as standard of care. The NCDB does not specifically identify tumors as Pancoast tumors. As such, we used upper lobe tumors which required chest wall resections as a surrogate for Pancoast tumors. Due to this limitation, we may have not captured every patient with a Pancoast tumor during this study time, and additionally may have included some upper lobe tumors that were not Pancoast tumors. But the fact that (I) the majority of tumors were squamous cell cancer and (II) there was overall improvement in survival with neoadjuvant treatment suggests that the majority of patients did have Pancoast tumors. Furthermore, the categorization of Pancoast tumors is relatively subjective in clinical practice. Although these tumors are labeled as superior sulcus tumors, most clinicians categorize these tumors based on their initial surgical resectability and distance from critical structures such as the brachial plexus and the great vessels (23,24). But there is no absolute distance that can be measured or recorded which will define a Pancoast tumor absolutely. As such, we feel that this study and use of the NCDB can have useful results to guide treating providers.

When examining the treatment patterns in the United States over our study period, we observed that patients who received neoadjuvant chemoradiation followed by surgical resection had the best survival. This supports the body of literature that has demonstrated that neoadjuvant therapy contributes to improved survival in patients with Pancoast tumors (25). We were surprised, however, with the low adherence to this standard of care treatment in our cohort. Of the 2,910 unique patients in the cohort, less than 25% received neoadjuvant chemoradiation. Although this trend suggests that the majority of patients are receiving surgery upfront, further multi-institutional studies should be performed prospectively to get a more precise idea about the percentage of patients with Pancoast tumors who receive neoadjuvant chemoradiation treatment.

Our study also revealed that high-volume institutions were more likely to offer neoadjuvant treatment compared to low-volume institutions. We chose 40 pulmonary resections as the cutoff because this number was adopted by the Leapfrog Group (18). We hypothesize that high-volume institutions may be more accustomed to utilizing multi-

modality treatment plans for patients and thus may be more likely to offer neoadjuvant treatment ahead of surgery.

When examining the upfront surgery group only, patients who received adjuvant chemoradiation had the best survival overall when compared to those who received chemotherapy alone, radiation alone, or no adjuvant therapy. This pattern suggests that a multidisciplinary treatment plan is beneficial even if surgery is performed upfront. Our study did progress over a long time period. During this time, there were significant advancements in neoadjuvant regimens and surgical conduct (26). We feel that this study may prompt future studies to examine whether practice patterns have changed in the last few years as the database is updated.

In the future, our group would like to further understand why certain patients are offered standard of care treatment for Pancoast tumors while the majority in our study were offered treatment below the standard of care. We would like to obtain information directly from cancer centers as to their practice patterns for treatment of Pancoast tumors in the node negative patient population. We hope these future studies will help us determine how to better serve patients and promote standard of care treatment for all node negative Pancoast tumor patients.

Conclusions

In a query of the NCDB over a period of 13 years, we observed that only 24% of patients with Pancoast tumors are offered standard of care treatment with a trimodal treatment approach. Patients who received standard of care treatment had improved overall survival compared to those who received other treatment patterns. In patients who received upfront surgical resection, adjuvant chemoradiation was associated with improved survival compared to adjuvant chemotherapy, radiation therapy or no adjuvant therapy. Future studies to examine why certain patients are offered standard of care treatment while most are not needed to understand how to promote widespread acceptance of standard of care for all Pancoast tumor patients.

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Footnote

Reporting Checklist: The authors have completed the

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the University of Texas Medical Branch institutional review board (IRB# 19-0168) and individual consent for this retrospective analysis was waived as the database we received was de-identified prior to us receiving it.

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