Patients Selected for Definitive Concurrent Chemoradiation at High-volume Facilities Achieve Improved Survival in Stage III Non–Small-Cell Lung Cancer

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Background: The relationship between provider experience and clinical outcomes is poorly defined in radiation oncology. This study examined the impact of facility case volume on overall survival in patients with stage III non–small cell lung cancer (NSCLC) treated with definitive concurrent chemoradiation therapy (CCRT).

Methods: Using the National Cancer Data Base, we identified clinical stage III NSCLC patients diagnosed in 2004 to 2006 who were treated with definitive CCRT to 59.4–74.0 Gy. High-volume facilities (HVF) were defined as those in the ninetieth percentile of annual CCRT volume (≥12 cases/year). Independent predictors of receiving CCRT at HVF were identified using multivariable logistic regression. Overall survival based on receiving CCRT at HVF was assessed using Kaplan–Meier analysis, Cox proportional hazards regression, and propensity score matching.

Results: Among 10,072 included patients, 1207 (12.0%) were treated at HVF. Patients in HVF were more likely to have a higher Charlson–Deyo comorbidity score, more advanced nodal stage, higher doses, and 3D-conformal or intensity-modulated radiotherapy. When controlling for demographic and clinical covariates including academic affiliation, treatment at HVF was independently associated with a significantly decreased risk of death (hazards ratio = 0.93; 95% confidence interval: 0.87–0.99; $p = 0.03$). Propensity score matching showed that these findings were robust (hazards ratio = 0.91; 95% confidence interval: 0.84–0.99; $p = 0.04$).

Conclusions: Our findings suggest that treatment at HVF is associated with improved overall survival among stage III NSCLC patients receiving definitive CCRT, independent of academic affiliation. Further research is needed to determine whether or not efforts supporting centralization of radiotherapy at HVF will improve population-based survival, toxicities, and costs.

Key Words: Radiation therapy, facility volume, case volume, non–small-cell lung cancer, survival.

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Lung cancer remains the leading cause of cancer mortality in the United States, with approximately 224,000 new diagnoses and 159,000 deaths estimated in 2014.[1] Approximately 87% of these patients have nonsmall-cell lung cancer (NSCLC), and survival for locoregionally advanced disease is approximately 26% at 5 years after diagnosis.[2] For patients with locally advanced stage III NSCLC, National Comprehensive Cancer Network guidelines support the use of definitive concurrent chemoradiation therapy (CCRT) as a standard-of-care treatment option.[3] Numerous studies have identified greater provider experience and higher hospital volume as predictors of improved outcomes, particularly for patients undergoing specialized oncologic surgeries, such as pancreaticoduodenectomy or lung lobectomy.[4–18] However, few studies have investigated the association between case volume and patient outcomes for radiotherapy (RT), especially in lung cancer.[19–22]

RT treatment planning and delivery for NSCLC can be quite complex and variable given the myriad choices of radiation modalities, CCRT regimens, and protocols currently available.[23–26] In addition, high-volume facilities (HVF) have been reported to have higher rates of protocol compliance, a factor shown to correlate with improved outcomes.[27,28] CCRT for NSCLC is also frequently complicated by acute and chronic toxicities, often requiring a network of experienced diagnostic, therapeutic, and support services to ensure optimal patient outcomes.[29–31] Because of the increasingly complex and multidisciplinary nature of locally advanced NSCLC treatment, we hypothesize that treatment at HVF with expertise in treating a large number of CCRT cases may be associated with improved overall survival.

In the current study, we used data from the National Cancer Data Base (NCDB) for patients who were treated with

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definitive CCRT for stage III NSCLC diagnosed and clinically staged between 2004 and 2006. Our primary objective was to investigate the relationship between RT facility volume and overall survival. We also assessed potential associations between various demographic and clinicopathologic characteristics and receipt of RT at HVF versus low-volume facilities (LVF). Finally, we sought to identify other factors associated with improved survival among patients with locally advanced NSCLC who received CCRT.

MATERIALS AND METHODS

National Cancer Data Base

We performed a retrospective analysis of United States national practice using the NCDB. The NCDB is a joint project of the Commission on Cancer (CoC) of the American College of Surgeons and the American Cancer Society. It contains de-identified information from approximately 70% of newly diagnosed cancers in the United States. NCDB contains information that is unavailable in the surveillance, epidemiology, and end results database, including treatment details pertaining to RT dose, technique, and target. The data used in this study are derived from a de-identified NCDB file. The American College of Surgeons and the CoC have not verified and are neither responsible for the analytic or statistical methodology employed nor the conclusions drawn from these data by the investigators. The Yale Human Investigations Committee determined that this study was exempt from review given that it used existing and de-identified data.

Patient Identification

We identified patients 18 years of age or older treated with definitive CCRT with clinical stage III NSCLC (cT1-4/cN2-3/cM0, cT3-4/cN1/cM0, or cT4/cN0/cM0, based on American Joint Committee on Cancer 6th edition classification) who were diagnosed and clinically staged in 2004 to 2006. Included International Classification of Diseases-*O*-3 histology codes are listed in Supplemental Table 1 (Supplemental Digital Content, http://links.lww.com/JTO/A819). CCRT was defined as (1) starting RT within 30 days of chemotherapy initiation or (2) starting chemotherapy before the end of the RT course. We excluded patients with unknown vital status or follow-up information and those with missing information on facility type. In addition, patients who underwent surgical resection as part of the first planned course of treatment, who had unknown or missing treatment data, or did not receive RT at the reporting facility were excluded (Fig. 1). We further restricted our study population to patients who received a total RT dose within the range of 59.4 to 74.0 Gy in 30 to 37 fractions to reduce the potential for misclassification due to miscoding during data submission to NCDB.

Statistical Methods

To estimate RT facility volume, we assigned an average annual volume to each facility appearing in the NCDB. This was achieved by dividing the total number of CCRT cases reported by each facility by the number of years of accreditation between 2004 and 2006. Because the number of

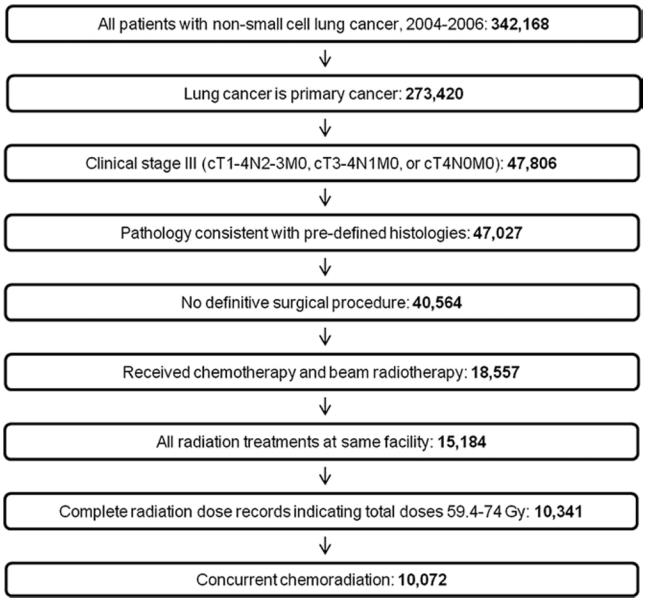

FIGURE 1. Exclusion criteria used to determine the final study cohort.

CoC-accredited cancer programs changes from one diagnosis year to the next, not all of the hospitals available in the NCDB were accredited for every one of the diagnosis years included over the study period. HVF were defined before analysis as those belonging in the ninetieth percentile of annual RT volume rounded to the nearest whole number, with the remainder aggregated as LVF.[32,33] We also performed a sensitivity analysis with alternative HVF definitions in an attempt to identify a threshold of facility case volume needed to achieve improved outcomes.

Demographic factors included in the analysis included age at diagnosis, race, 2000 census tract annual median income, insurance status, geographic region, patient location (rural, metro, and urban), travel distance to reporting facility, and Charlson/Deyo comorbidity score. Clinical characteristics, defined at the patient level, included RT modality (three-dimensional conformal RT, intensity-modulated RT, and nonconformal RT), total RT dose–fractionation, and year of diagnosis. Facility-level characteristics included hospital type and treatment volume. Classification of hospital academic status was made based on the cancer program category assigned by the CoC for each facility. Academic Comprehensive Cancer Program facilities (postgraduate medical education in at least four areas and more than 500 newly diagnosed cancer cases per year) were classified as academic, whereas Comprehensive Community Cancer Program (>500 newly diagnosed cancer cases per year), Community Cancer Program (100–500 newly diagnosed cancer cases per year), and other facilities were classified as nonacademic.

The NCDB requires hospital registries to update vital status and other information in 5-year cycles. At the time of the current study, overall survival was available for patients diagnosed up to 2006. Patients entered the study on their date of diagnosis and were followed until the most recent date of last contact, death, or the end of the study period. Our primary