Short Report

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Treatment with Multiple Modalities for T4 N2 Non-Small Cell Lung Cancer Including Ipsilateral Pulmonary Nodules

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ABSTRACT

Background : It is difficult to determine the best course of action for T4 non-small cell lung cancer (NSCLC) with extra intrapulmonary nodules in a different ipsilateral lobe (T4-Add) across clinical N stages. In contrast to contemporaneous chemoradiation, this study assessed the long-term survival of patients with T4-Add N2 NSCLC who had multimodal therapy, which included chemotherapy and surgical resection.

Methods : The National Cancer Database's T4-Add N2 M0 NSCLC patients from 2010 to 2015 were included.Using Kaplan-Meier analysis and Cox proportional hazards, long-term survival was assessed and compared between patients who underwent main site surgical resection with chemotherapy and those who received concomitant chemoradiation.propensity score matching and modeling on nine common prognostic factors, including comorbidities.

Results : Out of the 499 patients who met the trial eligibility requirements and had a diagnosis of T4-Add N2 M0 NSCLC, 220 (44.1%) underwent chemotherapy-assisted primary site surgical resection, while 279 (55.1%) underwent chemoradiation. Better long-term outcomes were linked to surgical resection with chemotherapy after multivariable adjusted Cox proportional hazards models.more resilient to chemoradiation. Patients who underwent surgical resection along with chemotherapy had a higher 5-year overall survival rate than patients who underwent chemoradiation, according to a propensity score-matched analysis of 100 patients receiving surgical resection and 100 patients receiving chemotherapy.

Conclusions : According to the findings of this nationwide study of individuals with T4 N2 NSCLC who also had extra nodules in an ipsilateral lobe, multimodal therapy, which includes surgery, may improve survival over chemotherapy alone. These results encourage more research on surgical resection for carefully chosen individuals with T4-Add N2 illness as part of multimodal therapy.

INTRODUCTION

Owing to the disease's heterogeneity, many treatment plans are available for stage IIIB, T4 N2 non-small cell lung cancer (NSCLC).demonstration. As the primary treatment, definitive chemotherapy and radiation are advised for most T4 N2 NSCLC cases, as per the current National Comprehensive Cancer Network treatment guidelines.1. The 5-year overall survival (OS) with surgical resection (44%) was comparable to concomitant chemoradiotherapy (40%) in the phase 3 randomized trial ESPATUE for possiblyresectable NSCLC in stages IIIA–B, including a subset of T4 N2 tumors.2. However, only T4 N2 illness, which manifests as an invasion of the surroundingstructures, without concentrating on other T4 characteristics, such as tumors larger than 7 cm and tumors having extra intrapulmonary nodules in an ipsilateral lobe (T4-Add). The clinical N status specifically determines how to treat T4-Add cancers. The best course of treatment for T4-Add N2 tumors is not well defined, with the majority of patients receiving chemotherapy and radiation without surgical resection, in accordance with guidelines for all T4 N2 disease, even though surgical resection of the primary tumor and any additional nodules is advised for T4-Add N0-1 disease1.This study aimed to assess the long-term survival of patients with T4-Add N2 NSCLC who had multimodal therapy, such as chemotherapy and primary site surgical resection, with concomitant chemotherapy and radiation therapy in the absence of surgical resection, in a national analysis that hasn't been published before. We investigated the idea that, in patients with T4-Add N2 tumors, primary site surgical resection and chemotherapy would be linked to a better overall survival rate when compared to concomitant chemoradiation.

METHODS AND PATIENTS

Data supply

The Massachusetts General Hospital's institutional review board gave its approval for this study. Data from the National Cancer Database's (NCDB) deidentified Participant User File were examined. A collaborative effort between the American According to estimates from the American Cancer Society and the College of Surgeons Commission on Cancer, 80% of newly diagnosed cases of lung cancer in the US and Puerto Rico are included in this statistic.3.

design of study

Individuals having synchronous extra intrapulmonary nodules in a separate ipsilateral lobe (T4-Add) at the time of diagnosis with T4 N2 M0 NSCLC.The diagnoses were made using the Third Edition International Classification of Diseases for Oncology topography and histology codes, as well as the Eighth Edition AJCC TNM Staging Manual. Intrapulmonary metastases in the NCDB require the patient's medical records to list them as "tumor nodules of the same histologic type as the primary tumor."3 Patients with additional T4 tumors, such as those larger than 7 cm or those that invaded nearby structures, were not accepted. Nonmalignant disease, a history of associated malignant disease in the past, and lacking treatment or survival data were additional exclusion factors. Patient diagnoses made between 2010 and 2015 were taken into consideration due to the availability of data on particular T4 staging characteristics.Patients were categorized based on the final treatment modality: Chemoradiation: simultaneous chemoradiation, defined as radiation doses of less than 60 Gy administered 30 days prior to or following chemotherapy, in the absence of surgical resection; or (2)Thoracic surgery: multimodal therapy that may involve radiation therapy or chemotherapy, as well as main site surgical excision performed six months before to or following the latter. OS, which was determined by timing the diagnosis to the moment of death or the last follow-up, was the main result.

a statistical examination

Baseline characteristics were compared between the chemoradiation and thoracic surgery groups by the Wilcoxon rank sum test for continuous variables and Pearson c2 test for discrete variables. OS was compared by Kaplan-Meier analysis and multivariable adjusted Cox proportional hazards modeling, adjusting for 9 prognostic factors including age, sex, race,Charlson-Deyo comorbidity score, median census tract income, facility type, distance to facility, tumor location,and tumor histologic type. Propensity score matching was performed with a logistic regression model based on the same 9 factors determined a priori to most likely act as confounders. The most appropriately matched pairs were identified by a greedy nearest neighbor matching algorithm without replacement and caliper of 0.045 (20%standard deviation of the logit of propensity scores).Balance was assessed using standardized differences. Adoubly robust estimator of OS using Cox proportional hazards modeling was calculated after propensity score weighting.4 A case complete analysis was used to address any potential missing data.Two more sensitivity analyses were carried out using multivariable adjusted Cox proportional hazards models that were restricted to: comparing OS following thoracic surgery vs chemoradiation Patients with primary tumors and those without comorbidities make up the first group. About 3 cmsize, taking into consideration individuals with "bulky" or severe N2 illness. Notably, prior research has indicated that less extensive nodal illness is likely to be linked to smaller tumors.5.Model balance and diagnostics were evaluated, and no significant assumptions were broken. Stata Statistical Software: Release 13.0 (StataCorp LP) was used for all statistical analyses. Significance was determined using a 2-sided P value of.05.

RESULTS

study cohort

The 499 patients with T4-Add N2 M0 NSCLC who met the criteria included extra intrapulmonary nodules in a separate ipsilateral lobe.study inclusion standards, Two hundred and twenty-one (44.1%) patients underwent multimodal treatment, which included primary site surgery, while 279 (55.9%) patients received concurrent chemoradiation without surgical resection.Thoracic surgical procedures include resection and chemotherapy (Supplemental Figure). The overall cohort's median follow-up period was 27.3 months (interquartile range: 13.1–54.6).months), and the 5-year OS was 32.6% (28.3–36.9%, 95% CI).

Comparison between chemotherapy and orthopedic surgery

Supplemental Table 1 displays baseline characteristics of individuals who underwent thoracic surgery or received chemotherapy and radiation. Of the 279 individuals who were given Chemoradiation, external beam radiation (145/52.0%), 3-dimensional conformal therapy (15.1%), intensity-modulated radiation therapy (32.3%), and stereotactic body radiation (0.7%) were the treatments administered to the patients. Thoracic surgery patients had a better overall survival (OS) than chemotherapy-radiation patients in both multivariable adjusted Cox proportional hazards modeling (hazard ratio [HR], 0.56; 95% CI, 0.41-0.76; P <.001; Supplemental Table 2) and Kaplan-Meier analysis of 5-year OS (P <.001; Figure A).These patient cohorts were subjected to a propensity score-matched analysis, which produced two groups of 100 patients

each that had thoracic surgery and chemotherapy/radiation. fairly balanced in terms of the fundamental attributes (Supplemental Table 3). When using the Kaplan-Meier method, thoracic surgery was Compared to chemoradiation, correlated with an improved 5-year OS (P ¼.01; Figure B). Propensity score weighting was taken into account in a Cox proportional hazards analysis, which was conducted as a doubly robust estimator of OS and was consistent with the unweighted analysis (HR, 0.58; 95% CI, 0.47-0.71; P <.001).

sensitivity analysis. patients with no comorbidities

A sensitivity analysis was conducted, focusing on patients without any co-occurring conditions. Specifically, patients with a Charlson-Deyo comorbidity score greater than 0 were excluded.individuals in the chemotherapy-radiation group who, due to contraindicating risk factors (such as highly concomitant illnesses, old age, or tumor progression prior to scheduled surgical resection), did not receive surgical resection. Thoracic surgery was still linked to a greater overall survival (OS) than chemoradiation after multivariable adjusted Cox proportional hazards modeling (HR, 0.54; 95% CI, 0.35-0.83; P ¼.005).

individuals with £3 cm tumors

An additional multivariable adjusted Cox proportional hazards model limited to individuals with tumors less than 3 cm in size was run in order to account for patients who might have had more widespread or "bulky" N2 nodal disease.indicate tumors that have "nonbulky" nodal disease, which is less widespread. Previous research has shown a correlation between less extensive nodal disease and a smaller original tumor size.5. Patients who underwent thoracic surgery in this analysis showed improved overall survival compared to those who underwent chemotherapy and radiation (HR, 0.53; 95% CI, 0.31-0.90; P ¼.019).

COMMENT

Patients who completed multimodal therapy were included in this nationwide analysis of T4 N2 M0 NSCLC patients with extra nodules in a separate ipsilateral lobe (T4-Add).Patients who had concurrent chemoradiation without surgical resection (chemoradiation) had a worse overall survival than those who got therapy that included main site surgical resection plus chemotherapy (thoracic surgery). Following Cox proportional hazards modeling and propensity score matching, these results held true in both unadjusted and multivariable adjusted analyses. They also held true in sensitivity analyses involving patients without comorbidities and those with initial tumors less than 3 cm in size.This study's capacity to assess the long-term survival of patients with T4-Add N2 was one of its advantages.NSCLC divided into therapy groups. For every patient in this trial, the 5-year OS was 32.6%. Prior research using extensive databases examined the 5-year OS of individuals found, irrespective of treatment strategy, between 8% to 33% with T4-Add malignancies.6–10 The 5-year overall survival (OS) for patients with T4-Add N2 disease who underwent surgical resection was reported to be 10.2% only by Nagai and colleagues9, who used data from the Japanese Joint Committee of Lung Cancer Registry. However, this study evaluated data from 1994 without providing specific details on the use of multimodal treatment regimens.The therapy and prognosis of T4-Add N2 NSCLC were also explored in this study, with a focus on whether these tumors should be treated differently from other T4 N2 diseases or other T4-Add diseases. Surgical resection is advised in the current National Comprehensive Cancer Network treatment guidelines for T4-Add N0-1 NSCLC.of the main tumor as well as any other nodules, however they don't offer any particular advice for T4-Add N2 NSCLC.1 The few clinical trials that assessed surgical resection for T4 N2 disease that may be resectable typically only included tumors that invaded neighboring structures; tumors with extra ipsilateral intrapulmonary nodules were not included in these trials.2. This study examined a large sample of patients with T4-Add N2 NSCLC utilizing the NCDB to answer this question. It included comprehensive information about each patient's unique treatment plan, with a focus on comparing chemotherapy and surgery.There are various restrictions on this study. First, even with the use of propensity score matching and multivariable adjusted approaches, there may be unobserved confounding and selection bias due to the retrospective character of the study. Second, because to the NCDB's constraints, we were unable to identify the precise number or location of extra intrapulmonary nodules. intervention targeted at the extra nodules. Tumor nodules in a patient's medical records have to be marked as "of the same histologic type as the primary tumor" in order for the NCDB to classify them as further intrapulmonary metastases.3. Data regarding the existence of Only from 2010 to 2015, when immunotherapy was routinely incorporated into multimodal treatment regimens, were new intrapulmonary nodules available.Lastly, there are no data on recurrence, disease-free, or disease-specific survival in the NCDB.The findings of this nationwide study of individuals with T4 N2 M0 NSCLC because of the existence of extra intrapulmonary nodules in an alternative ipsilateral lung.After multivariable adjusted analysis and propensity score matching, findings show that multimodality therapy, which includes main site surgical resection and chemotherapy, was linked with improved OS than concurrent chemotherapy and radiation without surgical resection. These results demonstrate the heterogeneity of stage IIIB NSCLC and provide credence to the idea that T4-Add tumors represent a distinct, potentially curable subset of T4 N2 illness.

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