ORIGINAL ARTICLE

The IASLC Lung Cancer Staging Project: External Validation of the Revision of the TNM Stage Groupings in the Eighth Edition of the TNM Classification of Lung Cancer

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ABSTRACT

Introduction: Revisions to the TNM stage classifications for lung cancer, informed by the international database (N = 94,708) of the International Association for the Study of Lung Cancer (IASLC) Staging and Prognostic Factors Committee, need external validation. The objective was to externally validate the revisions by using the National Cancer Data Base (NCDB) of the American College of Surgeons.

Methods: Cases presenting from 2000 through 2012 were drawn from the NCDB and reclassified according to the eighth edition stage classification. Clinically and pathologically staged subsets of NSCLC were analyzed separately. The T, N, and overall TNM classifications were evaluated according to clinical, pathologic, and "best" stage (N = 780,294). Multivariate analyses were carried out to adjust for various confounding factors. A combined analysis of the NSCLC cases from both databases was performed to explore differences in overall survival prognosis between the two databases.

Results: The databases differed in terms of key factors related to data source. Survival was greater in the IASLC database for all stage categories. However, the eighth edition TNM stage classification system demonstrated consistent ability to discriminate TNM categories and stage groups for clinical and pathologic stage.

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**See Appendix for members of the IASLC Staging and Prognostic Factors Committee, Advisory Boards, and Participating Institutions.

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Conclusions: The IASLC revisions made for the eighth edition of lung cancer staging are validated by this analysis of the NCDB database by the ordering, statistical differences, and homogeneity within stage groups and by the consistency within analyses of specific cohorts.

Keywords: Lung cancer; Staging; National Cancer Database; AJCC; UICC; Validation

Introduction

Proposals to revise the staging criteria for lung cancer were published in 2015 by the Staging and Prognostic Factors Committee of the International Association for the Study of Lung Cancer (IASLC).[1–5] The proposals take effect on January 1, 2017, in the staging guidelines for the Union for International Cancer Control (UICC) and on January 1, 2018, for the American Joint Committee on Cancer (AJCC). Changes to the T component included subclassification of T1 and T2 by size in 1-cm increments and reclassification of tumors larger than 5 cm as T3 and tumors larger than 7 cm as T4. *Diaphragm invasion* became a T4 descriptor. Lung atelectasis, whether partial or total, and all cases of main bronchus invasion regardless of the distance from the carina were classified as T2. Tumors with extrathoracic metastases were subdivided into M1b for a single distant metastasis and M1c for multiple distant metastatic lesions. No changes were made to the N component for the eighth edition. Following the proposed revisions to the T and M components, the TNM stage grouping scheme was revised accordingly. All of these revisions were informed by the analyses of an international database, with participants submitting data from 46 sites from 19 countries.[6]

Internal validation of the proposed revisions has been described in a separate publication.[7] However, recommendations based on a single database, regardless of the size, geographic representation, and heterogeneity of data sources, should also be validated externally, through one or more separate databases. The National Cancer Data Base (NCDB) provides an excellent opportunity for external validation of the TNM staging recommendations. The NCDB is a large and inclusive North American database, with broad representation from all treatment modalities for lung cancer and the entire range of institution types, from community hospitals to university research institutions. The eighth edition TNM staging criteria were evaluated against this large and detailed database.

Methods

The NCDB is a hospital-based registry jointly produced by the Commission on Cancer of the American College of Surgeons (ACoS) and the American Cancer Society. The NCDB asserts that "the National Cancer Data Base (NCDB) is a joint project of the Commission on Cancer (CoC) of the American College of Surgeons and the American Cancer Society. CoC's NCDB and the hospitals participating in the CoC NCDB are the source of the de-identified data used herein; they have not verified and are not responsible for the statistical validity of the data analysis or the conclusions derived by the authors." The de-identified cases, which were originally entered by participating institutions with appropriate human subjects' approval, were received and analyzed in the Division of Thoracic Surgery at the Swedish Cancer Institute, Seattle, Washington, which is an ACoS member hospital. Institutional review board review of the analysis of the de-identified data set at the Swedish Cancer Institute was not required.

Cases entered into the registry with invasive NSCLC or SCLC presenting from January 2000 to December 2012 were used for analyses. Cases that were classified as a second primary tumor, or without sufficient anatomical information to be able to classify them according to eighth edition stage were excluded. To maintain consistency with the analyses of the IASLC database, cases with yp staging (stage based on pathologic evidence after neoadjuvant therapy [approximately 2% of NCDB cases]) were excluded from analyses of pathologic stage. Most of these yp cases were also effectively excluded from analyses of clinical stage as well, because the tumor descriptors were based on surgical findings after neoadjuvant therapy. Cases were also excluded if the TNM descriptors were in conflict with the recorded stage. Surgical cases from both databases were included regardless of margin status after surgery.

TNM components for the NCDB cases were entered by the participating registrars according to sixth or seventh edition AJCC criteria, depending on the period during which they were registered. Pathologic TNM stage was provided in surgical cases, and clinical stage was provided in both surgical and nonsurgical cases. Anatomic T descriptors were provided following the AJCC Collaborative Stage guidelines, with only the "highest" T descriptor given for each case. For each case, there is a field indicating the source of the recorded T descriptor information, either surgical/pathologic staging or pretreatment radiologic/clinical. Information about the NCDB and its data elements resides at the website of the ACoS.[8]

Cases were reclassified according to the eighth edition stage groupings after translation of the T and M categories using the descriptors provided with each case. In cases originally entered under the fifth or sixth edition, particular care was taken to ensure that cases