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Prognostic Significance of the Non–Size-Based AJCC T2 Descriptors*

Visceral Pleura Invasion, Hilar Atelectasis, or Obstructive Pneumonitis in Stage IB Non-small Cell Lung Cancer Is Dependent on Tumor Size

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Background: **The T2 descriptor for staging non-small cell lung cancer (NSCLC) contains several non–size-based criteria. It remains unknown whether the prognostic significance of these non–size-based criteria is dependent on tumor size.**

Methods: **A total of 10,545 patients with stage IB NSCLC from the California Cancer Registry between 1989 to 2003 were categorized into the following three nonoverlapping criteria: (1) tumor size (T2S); (2) visceral pleura invasion, hilar atelectasis, or obstructive pneumonitis (T2P); and (3) main bronchus involvement ≥ 2 cm from the carina (T2C). Univariate survival analyses were performed using the Kaplan-Meier method. Multivariate survival analyses were performed using Cox proportional hazards ratios.**

Results: **A total of 51.1% of patients with stage IB NSCLC were staged by T2S, 43.2% by T2P, and 5.7% by T2C; 2,224 stage IB patients (total, 21.1%; 18.9% T2P + 2.2% T2C) had tumors ≤ 3 cm in size. The 5-year survival rate and the median survival time of these stage IB patients with tumors ≤ 3 cm in size were as follows: T2P, 51.2% and 64 months, respectively; T2C, 49.0% and 58 months, respectively. These values were similar to the 53.2% 5-year survival rate and 67-month median survival time for patients with stage IA NSCLC (p = 0.40). Cox proportional hazards model revealed T2P of > 3 cm was a poor prognostic factor for survival (vs T2S; hazard ratio [HR], 1.16; 95% confidence interval [CI], 1.08 to 1.24). Conversely, T2P ≤ 3 cm was a favorable prognostic factor for survival (vs T2S; HR, 0.89; 95% CI, 0.82 to 0.96). T2C was not an independent prognostic factor for survival.**

Conclusions: **Prognostic significance of the non–size-based T2 descriptor T2P is dependent on tumor size.** ***(CHEST 2008; 133:662–669)***

Key words: hilar atelectasis; obstructive pneumonitis; stage I lung cancer; T2 descriptor; visceral pleura invasion

Abbreviations: AJCC = American Joint Committee on Cancer; CCR = California Cancer Registry; CI = confidence interval; EOD = extent of disease; HR = hazard ratio; NSCLC = non-small cell lung cancer; SEER = Surveillance, Epidemiology and End Results; SES = socioeconomic status; T2C = T2 descriptor with main bronchus tumor involvement ≥ 2 cm from the carina; T2P = T2 descriptor with visceral pleura invasion, hilar atelectasis, or obstructive pneumonitis involving less than the entire lung; T2S = T2 descriptor using tumor size alone; VPI = visceral pleura invasion

The American Joint Committee on Cancer (AJCC) and the Union Internationale Contre le Cancer first applied the TNM staging system,[1] which underwent its most recent revision in 1997, to lung cancer in 1974.[2] The most recent major revision to the AJCC/Union Internationale Contre le Cancer TNM staging system for lung cancer was to subdivide stage I lung cancer into stage IA (T1N0M0) and stage IB (T2N0M0), and was based on significant survival time difference between patients with T1 tumors (*ie*, ≤ 3 cm in size) and T2 tumors (*ie*, > 3 cm in size).[2] However, the T staging system defines a primary tumor not only by size but also by airway location and extent of local invasion. In addition to tumor size of

> 3 cm, the current AJCC T2 descriptor also includes the following three non–size-based criteria: tumor involves the main bronchus ≥ 2 cm distal to the carina; visceral pleura invasion (VPI); and tumor

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resulting in atelectasis or obstructive pneumonitis that extends to the hilar region but does not involve the entire lung radiographically.[2] For example, a tumor 2.0 cm in size with VPI and no lymph node involvement or distant metastasis will be staged as stage IB (T2N0M0). Tumor size has been a classic factor in determining survival in patients with non-small cell lung cancer (NSCLC), but the prognostic significance of non–size-based T descriptors such as VPI, hilar atelectasis, or obstructive pneumonitis, or main bronchus involvement ≥ 2 cm from the carina is less well known. The current T2 descriptor has remained unchanged since 1974, and stage IB NSCLC has been shown to be a heterogeneous group of diseases that can be subdivided into different risk groups.[3] With the next revision to the TNM staging system for NSCLC scheduled to be released in 2009, proposed revisions to the T descriptor in early-stage NSCLC have been primarily based on a finer subdivision of tumor size.[4–9] However, proposed changes to the non–size-based T2 descriptors for early-stage NSCLC are less clear, given the relatively unknown frequency and prognostic significance of these non–size-based criteria. We set out to determine whether there is a difference in survival between stage IB NSCLC patients with tumors ≤ 3 cm, but staged as T2 due to non–size-based descriptors, and stage IA patients. Furthermore, we investigated whether there are differences in prognostic significance between stage IB NSCLC patients classified by the T2 descriptor based solely on the size criterion alone (*ie*, > 3 cm) and stage IB NSCLC patients classified based also on non–size-based criteria.

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Materials and Methods

Study Cohort and Diagnostic Codes

Data were obtained on 101,844 incident NSCLC cases from the California Cancer Registry (CCR) in which patients had received diagnoses between 1989 and 2003 with complete TNM staging data and complete follow-up data available. A total of 9,157 stage IA NSCLC cases and 10,545 stage IB NSCLC cases were identified. Data were abstracted from medical and laboratory records by trained tumor registrars according to the California Tumor Registry.[10]

Tumor site and histology were abstracted as previously described.[11] Only histologically or cytologically confirmed NSCLC cases were included in the analysis. Non-small cell histologies were categorized as undifferentiated NSCLC if they were not coded as adenocarcinoma, squamous cell carcinoma, large cell carcinoma, bronchioloalveolar carcinoma, or metastatic lung lesion from a separate primary tumor, as previously described.[12] Ethnicities, marital status, histologic grade, tumor lobe location, and tumor size were abstracted using Surveillance, Epidemiology and End Results (SEER) codes. The measurement of socioeconomic status (SES) used in this analysis was a composite measure using CCR and census data as previously described.[13,14] Standardized component scores for the SES index for the 20,919 census block groups were sorted and categorized into quintiles, with a value of 1 representing the lowest SES level and a value of 5 representing the highest SES level.[13,14]

The SEER extent of disease (EOD) codes for the lung and bronchus were used to identify the various T2 descriptors. EOD code 10 identified T2 tumors classified by size criterion only (> 3 cm). EOD code 20 identified tumors involving the mainstem bronchus that were ≥ 2 cm from the carina. EOD code 40 identified tumors invading the visceral pleura, hilar atelectasis, or obstructive pneumonitis involving less than the entire lung. The EOD codes are hierarchically ranked such that patients with T2 tumors containing two or more criteria satisfying more than one EOD code will be coded only with the highest EOD code. For patients with T2 tumors, by the current T2 descriptor definition they will be coded as one of the three EOD codes (EOD10, EOD20, or EOD40) depending on the presence of the coding criteria.

The radiation and surgical techniques used (*ie*, local treatment, wedge/segmentectomy, lobectomy, and pneumonectomy) were abstracted using SEER codes. Chemotherapy given during the first course of therapy was ascertained using CCR codes. The last date of follow-up was either the date of death or the last date the patient was contacted.

Statistical Analysis

The Pearson χ^2 test or Fisher exact test were used to compare categoric and dichotomous variables. Analysis of variance with

Tukey *post hoc* test was used for multiple comparisons of continuous variables. Life tables and Kaplan-Meier curves were generated for overall survival analysis. Comparisons between groups were analyzed with the log-rank test. Multivariate Cox regression analyses were used to determine the factors significantly associated with survival. Statistical significance was assumed for a two-tailed p value of < 0.05. All statistical analyses were performed using a statistical software package (SAS, version 9.1; SAS Institute; Cary, NC).

Ethical Considerations

This research study involved the analysis of existing data from the CCR database with no subject intervention and no identifiers linked to subjects. Therefore, this study was approved by the University of California Irvine Institutional Review Board under the category "exempt" status (Institutional Review Board No. 2004–3971).

Results

Patient Characteristics

From 1989 to 2003, a total of 9,157 stage IA NSCLC cases and 10,545 stage IB NSCLC cases were identified from the 101,844 incident NSCLC cases. The mean age of patients at diagnosis was 68 years for those with stage IA NSCLC, and 69 years for those with stage IB NSCLC. The median follow-up time of all patients with stage I NSCLC was 53 months.

T2 Descriptors

Among the patients with stage IB NSCLC, 5,385 patients (51.1%) were classified by tumor size alone (*ie*, > 3 cm) [T2S], 4,557 patients (43.2%) were classified as having VPI, hilar atelectasis, or obstructive pneumonitis involving less than the entire lung (T2P), and 603 patients (5.7%) were classified as having a tumor involving the mainstem bronchus ≥ 2 cm from the carina (T2C). All 10,545 patients with stage IB NSCLC were coded by one of these three T2 descriptors. The clinicopathologic characteristics of these stage IB patients stratified by the three T2 descriptors are shown in Table 1.

Tumor Size

None of the stage IB patients identified by size alone (EOD code 10) had tumors ≤ 3 cm. For T2C patients, 234 of the 603 patients (38.8%) had tumors ≤ 3 cm; they accounted for 2.2% of the total number of patients with stage IB NSCLC. For T2P patients, 1,990 of 4,557 patients (43.7%) had tumors ≤ 3 cm; they accounted for 18.9% of the total number of patients with stage IB NSCLC.

Univariate Survival Analysis

Survival of Stage IA and IB Patients With Tumor Size of ≤ 3 cm: The 5-year survival rate and the median overall survival time for all patients with stage IA NSCLC (n = 9,157) were 53.2% and 67 months, respectively; 40.2% and 42 months, respectively, for all patients with stage IB NSCLC (n = 10,545; $p < 0.0001$). The 5-year survival rate and the median survival time for patients with stage IB NSCLC whose tumor size was ≤ 3 cm but were coded as having stage IB NSCLC due to tumor involving the main bronchus ≥ 2 cm from the carina (*ie*, T2C) were 49.0% and 58 months, respectively. For T2P patients with stage IB NSCLC, the 5-year and median survival time was 51.2% and 64 months, respectively (Fig 1). The survival differences were not statistically significant in comparison with patients with stage IA disease ($p = 0.40$) [Table 2].

Survival of Stage IB Patients With Tumor Size of > 3 cm: The 5-year overall survival rate and the median overall survival time for stage IB NSCLC patients identified by size alone (T2S) were 38.6% and 39 months, respectively; for patients identified as having a tumor involving the mainstem bronchus ≥ 2 cm from the carina (T2C), 40.8% and 39 months, respectively; and for patients with VPI, hilar atelectasis, or obstructive pneumonitis (T2P), 37.2% and 37 months, respectively. The survival differences were not statistically significant in comparison to those with stage IB patients coded by size alone (T2S) ($p = 0.70$) [Table 2].

Multivariate Survival Analysis

Since the survival of the non–size-based IB patients appear to depend on the primary size of the tumor (Table 2), we subdivided the non–size-based T2 descriptors using the AJCC 3-cm size cutoff for T1 and T2 descriptors (*ie*, ≤ 3 cm vs > 3 cm). The prognostic significance of the non–size-based T2 descriptors (T2C ≤ 3 cm; T2C > 3 cm; T2P ≤ 3 cm; T2P > 3 cm) was then evaluated in the Cox proportional hazards model using the T2S descriptor as the referent. Important prognostic factors such as age at diagnosis, gender, ethnicity, SES, marital status, histology, histologic grade, tumor lobar location, and surgical treatment were also incorporated into the Cox proportional hazards model.[15] Using the T2S descriptor as the referent, patients with a non–size-based T2 descriptor (*ie*, T2P > 3 cm) carried an independent increased risk of mortality (vs T2S patients; hazard ratio [HR], 1.16; 95% confidence interval [CI], 1.08 to 1.24). Conversely, patients whose tumors were characterized as T2P ≤ 3 cm carried an independent decreased risk of mortality (vs T2S patients; HR, 0.89; 95% CI, 0.82 to 0.96). For T2C patients with stage IB NSCLC, there was no increased or decreased risk of mortality for either

Table 1—*Clinicopathologic Characteristics of Stage IB NSCLC Patients (n = 10,545) Stratified by T2 Descriptors***

Variables	T2 Descriptor		
	T2S (With Tumor Size of > 3 cm) [n = 5,385]	T2C (n = 603)	T2P (n = 4,557)
Race			
White	4,238 (78.7)	471 (78.1)	3,563 (78.2)
African-American	414 (7.7)	53 (8.8)	293 (6.4)
Hispanic	365 (6.8)	43 (7.1)	301 (6.6)
Chinese	91 (1.7)	15 (2.5)	126 (2.8)
Non-Chinese	254 (4.7)	18 (3.0)	267 (5.9)
Other	23 (0.4)	3 (0.5)	7 (0.2)
Sex			
Male	3,089 (57.4)	366 (60.8)	2,437 (53.5)
Female	2,295 (42.6)	236 (39.2)	2,119 (45.6)
Age, yr			
0–29	9 (0.2)	5 (1.0)	14 (0.3)
30–39	65 (1.2)	17 (2.8)	58 (1.3)
40–49	376 (7.0)	51 (8.5)	379 (8.3)
50–59	1,151 (21.4)	146 (24.2)	962 (2.1)
60–69	2,056 (38.2)	254 (42.1)	1,816 (39.9)
70–79	1,505 (27.9)	119 (19.7)	1,164 (25.5)
80+	223 (4.1)	12 (2.0)	164 (3.6)
Marital status			
Married	2,181 (40.5)	233 (38.6)	1,835 (40.3)
Unmarried†	3,100 (57.6)	357 (59.2)	2,659 (58.4)
Unknown	104 (1.9)	13 (2.2)	63 (1.4)
SES			
Quintile 1 (SES1-lowest)	773 (14.4)	105 (17.4)	649 (14.2)
Quintile 2 (SES2)	1,034 (19.2)	96 (15.9)	821 (18.0)
Quintile 3 (SES3)	1,217 (22.6)	137 (22.7)	996 (21.9)
Quintile 4 (SES4)	1,188 (22.1)	124 (20.6)	1,026 (22.5)
Quintile 5 (SES5-highest)	1,173 (21.8)	141 (23.4)	1,064 (23.4)
Histology			
Adenocarcinoma	1,891 (35.1)	204 (33.8)	2,023 (44.4)
Squamous cell carcinoma	1,936 (36.0)	248 (41.1)	1,268 (27.8)
Large cell carcinoma	406 (7.5)	42 (7.0)	281 (6.2)
Bronchioloalveolar carcinoma	441 (8.2)	48 (8.0)	532 (11.7)
Undifferentiated	711 (13.2)	61 (10.1)	453 (9.9)
Histologic grade			
Well-differentiated	432 (8.0)	52 (8.6)	431 (9.5)
Moderately differentiated	1,477 (27.4)	172 (28.5)	1,499 (32.9)
Poorly differentiated	2,203 (40.9)	245 (40.6)	1,755 (38.5)
Undifferentiated	381 (7.1)	31 (5.1)	233 (5.1)
Unknown	892 (16.6)	103 (17.1)	639 (14.0)
Lobar location			
Right upper lobe	1,709 (31.7)	176 (29.2)	1,544 (33.9)
Left upper lobe	1,289 (23.9)	124 (20.6)	1,210 (26.6)
Right middle lobe	225 (4.2)	21 (3.5)	218 (4.8)
Right lower lobe	1,063 (19.7)	82 (13.6)	693 (15.2)
Left lower lobe	853 (15.8)	73 (12.1)	616 (13.5)
Right and left main bronchus/carina/hilar	54 (1.0)	98 (16.3)	51 (1.1)
NOS	191 (3.5)	29 (4.8)	224 (4.9)
Tumor size			
≤ 3 cm	0 (0)	234 (38.8)	1,990 (43.7)
> 3 cm	5,385 (100)	299 (49.6)	2,274 (49.9)
Unknown	0 (0)	70 (11.6)	293 (6.4)
Surgery			
None	1,278 (23.7)	148 (24.5)	764 (16.8)
Local	9 (0.2)	6 (1.0)	8 (0.2)
Segmentectomy/wedge	251 (4.7)	48 (8.0)	452 (9.9)
Lobectomy	3,477 (64.6)	317 (52.6)	3,052 (70.0)
Pneumonectomy	358 (6.7)	84 (13.9)	269 (5.9)
NOS	11 (0.2)	0 (0)	10 (0.2)
Unknown	1 (0.02)	0 (0)	2 (0.04)

Table 1—*Continued*

Variables	T2 Descriptor: T2S (With Tumor Size of > 3 cm) [n = 5,385]	T2C (n = 603)	T2P (n = 4,557)
Radiation			
Yes	956 (17.8)	129 (21.4)	760 (16.7)
No	4,429 (82.3)	474 (78.6)	3,797 (83.3)
Chemotherapy			
Yes	444 (8.2)	76 (12.6)	363 (8.0)
No	4,897 (90.9)	519 (86.1)	4,133 (90.7)
Unknown	44 (0.8)	8 (1.3)	61 (1.3)

*Values are given as No. (%). NOS = not otherwise specified.
†Single, separated, divorced, or widowed.

T2C > 3 cm (vs T2S patients; HR, 0.97; 95% CI, 0.82 to 1.14) or T2C patients with tumor ≤ 3 cm in size (vs T2S patients; HR, 0.90; 95% CI, 0.75 to 1.09) [Table 3].

Discussion

The T2 descriptor in AJCC staging for NSCLC has remained unchanged since 1974 and contains several non–size-based criteria, thus allowing some NSCLC patients with tumors ≤ 3 cm in size to be staged as IB. Controversy exists over whether these stage IB NSCLC patients with tumors ≤ 3 cm have poorer survival than stage IA NSCLC patients. Furthermore, there is a paucity of published literature on how many stage IB NSCLC patients are staged solely due to these non–size-based T2 criteria, and the prognostic significance of these non–size-based T2 criteria is not well established. The proposed changes to T2 staging generally emphasize a finer subdivision of tumor size into three categories (*ie*, 2 cm as T1; 2 to 4 to 5 cm as T2; and > 4 to 5 cm as T3)[4–9] but generally have not addressed in detail whether and/or how to reclassify the non–size-based T2 criteria.

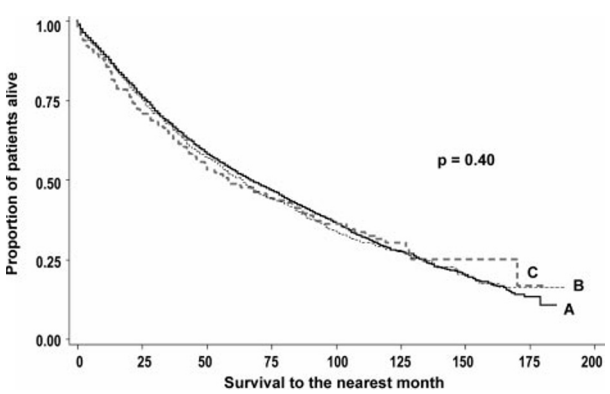

Figure 1. Kaplan-Meier survival curves of stage IA patients and stage IB patients whose tumors were ≤ 3 cm stratified by non–size-based T2 descriptors. A = stage IA; B = T2P (tumor size, ≤ 3 cm); C = T2C (tumor size, ≤ 3 cm).

In this report using the CCR database, 21.1% of the stage IB patients (2,224 of 10,545 patients) had tumors ≤ 3 cm because they were staged solely by non–size-based T2 descriptor criteria. However, despite being staged as stage IB NSCLC, the 5-year survival rate and median overall survival time of these 2,224 patients were similar to those of the 9,157 stage IA patients during the same period in the CCR (Fig 1). In addition, we found that only 5.7% of stage IB patients (603 of 10,545 patients) had features of the T2C descriptor, and only 2.2% of the stage IB patients were staged solely due to the T2C descriptor. Only 18.9% of stage IB patients (1,990 of 10,545 patients) were staged solely due to the T2P descriptor. The relatively small percentage of patients staged solely by the non–size-based criteria were in agreement with the study by Jones et al,[16] in which, of the 119 T2N0M0 patients analyzed, none were classified as having a T2 lesion on the basis of hilar atelectasis, lobar collapse, or proximity to the carina in the absence of other criteria. Osaki et al[17] also reported that only 4 patients of 483 T1-2N0M0 patients were categorized as T2C. Furthermore, in our report, there was no difference in the prognostic significance between T2C patients with stage IB NSCLC independent of tumor size compared to that in T2S patients. This lack of prognostic significance of T2C may be due to the small numbers of patients in this report. However, our findings highlighted the very low frequency of T2C being used as a sole descriptor in stage IB patients. Our findings, in addition to those of other investigators[16,17] call into question the utility of the T2C descriptor and whether it should be retained in the future staging system, as has been discussed by others.[16,17]

One relatively common non–size-based T2 descriptor is VPI, which has been shown generally to be

Table 2—*Survival of Stage IA and IB NSCLC Patients According to Size and T2 Descriptors*

AJCC Stage	Patients, No.	5-Year Survival Rate, %	Median Survival Time, mo	p Value
IA	9,157	53.2	67	
IB	10,545	40.2	42	< 0.0001
IA	9,157	53.2	67	
IB (T2C with tumor size ≤ 3 cm)	234	49.0	58	
IB (T2P with tumor size ≤ 3 cm)	1,990	51.2	64	0.40
IB (T2S)	5,385	38.6	39	
IB (T2C with tumor size > 3 cm)	299	40.8	39	
IB (T2P with tumor size > 3 cm)	2,274	37.2	37	0.70

a poor prognostic factor for survival,[8,17–26] although a few reports have not shown VPI to be a poor prognostic factor.[16,18] It has been shown that VPI portends more frequent mediastinal metastasis and poorer histologic grade and thus poorer survival in univariate analysis when compared to tumors with no VPI.[26] However, whether the survival outcome of stage IB NSCLC patients with VPI whose tumors are ≤ 3 cm is similar to or worse than that of patients with stage IA NSCLC has remained controversial, especially in the absence of hilar or mediastinal lymph node metastasis. While VPI has been shown to be a poor independent prognostic factor regardless of size,[17,23–26] when the prognostic significance of VPI was stratified by tumor size of 3 cm, several reports[3,20–22] found that for tumors ≤ 3 cm in size with VPI prognosis was not adversely affected. Padilla et al[20] analyzed 158 stage I (T1-2N0M0) NSCLC patients with tumor size ≤ 3 cm and found that tumor size was the only significant determinant of outcome. The authors extended their observation with 637 patients and found that patients with VPI whose tumors were ≤ 3 cm had survival similar to patients with stage IA disease, which is similar to the conclusion of our report.[3] Monac'h et al[21] reported the 5-year survival rate and median survival time of patients with VPI whose tumors were ≤ 3 cm were 58.9% and 93 months, respectively, which compared favorably to the 5-year survival rate of 56.5% and the 81-month median survival time of patients without VPI whose tumors were ≤ 3 cm in size. One caveat was that this univariate analysis did not take nodal status into account. In the same study,[21] patients with VPI whose tumors were > 3 cm had significantly poorer survival. Inoue et al[22] reported that VPI was not a prognostic variable for survival in patients with tumors were < 2 cm, but only 12 of 143 patients analyzed were in this group. Although Martini et al[18] did not find that VPI affects overall survival in a series of 598 stage 1 NSCLC patients, they did find that VPI was a contributing adverse factor in patients with larger (T2) tumors. In the present study, the 53.3% 5-year survival rate and the 67-month median survival time of the 1,597 T2P patients with tumors ≤ 3 cm in size were almost identical to the 53.2% 5-year survival rate and 67-month median survival time of the 9,157 stage IA patients. On multivariate analysis, we were able to show that T2P with tumor size of > 3 cm is an independent poor prognostic factor for survival in NSCLC patients, while T2P with tumor size of ≤ 3 cm is an independent favorable prognostic factor for survival when compared to patients with stage IB NSCLC staged solely by tumor size alone. Our study agrees with reports[3,20–22] that VPI carried an increased mortality risk, but this mortality risk is dependent on the size of the tumor.

An advantage of our report is that we restricted our analysis to stage I NSCLC patients so that the prognostic significance of the various T2 descriptors was not confounded by hilar or mediastinal nodal involvement. Many of the prognostic studies in VPI included patients with nodal metastasis, which may have confounded the analysis.[19,21,24,26] Significantly, there was excellent internal validity of the data since none of the stage IB NSCLC patients staged by size alone had tumor sizes of ≤ 3 cm or tumor size that was unknown. There was also no overlap of the three EOD codes, indicating excellent hierarchical coding of the EOD codes in the CCR. Our study is one of the largest studies to analyze stage IB NSCLC patients, and we made adjustments for many known prognostic factors such as age at diagnosis, gender, histology, histologic grade, tumor lobar location, SES, marital status, race, and surgical treatment.[15] Our results thus indicated that tumor size plays an important role in determining survival outcome even when patients were staged by non–size-based criteria. One of the limitations of our study is that it is retrospective in nature and without central pathology findings to standardize the reporting of VPI. There was also no central radiology review to standardize the interpretation of main bronchus involvement ≥ 2 cm from the carina, hilar atelectasis, or obstructive pneumonitis. We were not able to ascertain how many of the stage I patients were staged by medias-

Table 3—*Cox Proportional Hazards Model for Stage IB NSCLC Patients*

Variables	HR	95% CI	p Value
Ethnic origin			
White	1.00		
African-American	0.969	0.867–1.083	0.5741
Hispanic	1.025	0.913–1.150	0.6773
Chinese	0.823	0.681–0.996	0.0451
Non-Chinese Asian	0.792	0.692–0.907	0.0007
Other	0.834	0.455–1.418	0.5137
Age at diagnosis*	1.029	1.026–1.033	< 0.0001
Sex			
Male	1.00		
Female	0.757	0.713–0.803	< 0.0001
Marital status			
Married	1.00		
Unmarried	1.185	1.117–1.258	< 0.0001
Unknown	1.131	0.904–1.415	0.2801
SES			
Quintile 1 (SES1-lowest)	1.00		
Quintile 2 (SES2)	0.910	0.828–1.001	0.0519
Quintile 3 (SES3)	0.902	0.822–0.989	0.0281
Quintile 4 (SES4)	0.863	0.786–0.947	0.0019
Quintile 5 (SES5-highest)	0.758	0.689–0.833	< 0.0001
Histology			
Adenocarcinoma	1.00		
Squamous cell carcinoma	1.076	1.009–1.148	0.0261
Large cell carcinoma	0.995	0.882–1.123	0.9328
Bronchioloalveolar carcinoma	0.872	0.773–0.983	0.0249
Undifferentiated	0.976	0.879–1.083	0.6425
Histologic grade*	1.106	1.060–1.154	< 0.0001
Location of tumor			
Left lower lobe	1.00		
Left upper lobe	0.826	0.763–0.895	< 0.0001
Right upper lobe	0.842	0.780–0.909	< 0.0001
Right middle lobe	0.927	0.804–1.068	0.2927
Right lower lobe	0.947	0.868–1.034	0.2287
T2 descriptor			
T2S	1.00		
T2P (with tumor size > 3 cm)	1.155	1.079–1.236	< 0.0001
T2P (with tumor size ≤ 3 cm)	0.890	0.822–0.963	0.0039
T2C (with tumor size > 3 cm)	0.967	0.823–1.136	0.6815
T2C (with tumor size ≤ 3 cm)	0.903	0.750–1.088	0.2856
Surgery			
No	1.00		
Local	0.599	0.345–1.039	0.0683
Wedge/segmentectomy	0.364	0.319–0.414	< 0.0001
Lobectomy	0.277	0.252–0.304	< 0.0001
Pneumonectomy	0.343	0.300–0.393	< 0.0001
NOS	0.409	0.231–0.723	0.0021
Radiation			
No	1.00		
Yes	1.020	0.933–1.116	0.3372
Chemotherapy			
No	1.00		
Yes	1.036	0.931–1.153	0.5174

*Analyzed as a continuous variable. See Table 1 for expansion of abbreviation.

tinoscopy. Furthermore, we were not able to separate VPI from hilar atelectasis or obstructive pneumonitis within the T2P category (EOD code 40). However, we expect that the majority of the patients within the T2P category had VPI as studies[16,17] have shown that the incidence of hilar atelectasis or obstructive pneumonitis was relatively low.

In summary, in future considerations to the changes in the T2 descriptor in the AJCC staging system for NSCLC the non–size-based criteria should be linked to size criteria rather than remaining as independent criteria. This report shows that as many as 21.1% of the stage IB patients may be unnecessarily upstaged from stage IA to stage IB as their survival was no different from that of stage IA patients. Patients with VPI with a tumor size of > 3 cm may be considered to be upgraded to T3 in the next AJCC staging system revision, as proposed by others.[8,24] Finally, future considerations should also be given to whether the T2C criterion should be retained, as only a small minority (5.7%) of stage IB NSCLC patients had this feature of main bronchus involvement ≥ 2 cm from the carina and only 2.2% of stage IB patients were staged solely according to this criterion. Because of the low number of T2C patients due to the low frequency of this criterion, T2C is not an independent variable to be used in prognosticating the survival outcome of stage IB NSCLC patients in this report.

The International Association for the Study of Lung Cancer lung cancer staging project recently published[27,28] proposed changes for staging lung cancer. The T descriptor and stage-grouping assignment of the non–size-based criteria described in this report (*ie*, T2C and T2P) remained the same as those in the current staging system due to a small number of patients and a lack of validation.[27,28] This report may provide information for future studies to critically assess the prognostic significance of these non–size-based descriptors for the next staging changes.

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