Impact of the New Lung Cancer Staging System for a Predominantly Advanced-Disease Patient Population

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Introduction: To investigate the feasibility and clinical impact of the 7th edition of the “Tumor, Node, Metastasis” (TNM) classification scheme in lung cancer as proposed by the International Association for the Study of Lung Cancer (IASLC) for non-small cell lung cancer.

Methods: We evaluated the feasibility of the new staging system in our routine biweekly multidisciplinary lung cancer staging conference compared with the 6th TNM staging in a prospective manner from April 2008 to June 2009. The impact of IASLC staging versus the 6th TNM staging was observed at three levels: change in substaging, staging, and clinical management (based on the discussion within the staging conference).

Results: From 348 patients discussed during these conferences, 226 eligible non-small cell lung cancer patients newly diagnosed within the study period were reviewed and clinically staged. The majority were elderly (median age, 67 years) and men (58%). Of these, 23 patients had different staging, and four patients had different substaging in the IASLC staging compared with the 6th TNM staging. An impact on clinical management was seen in 2.7% (6 of 226) of these patients because of coding ipsilateral different-lobe metastasis as T4 instead of M1.

Conclusions: The new staging system was clinically feasible and resulted in some (27 of 226, 12%) differences in staging. An impact on clinical decision making was occasionally seen within our institutional practice. Further studies are needed to investigate the comprehensive and long-term impact of the new staging system.

Key Words: IASLC, Non-small cell lung cancer, Staging.

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Lung cancer is a leading cause of cancer mortality around the world, and non-small cell lung cancer (NSCLC) comprises the majority of lung cancers. Staging is important for prognosis and treatment decision making, and some debate has occurred about the 1997 “tumor, node, metastasis” (TNM) staging system.1-3

The 7th edition of TNM in lung cancer was published by the International Union Against Cancer and the American Joint Committee on Cancer, with changes based primarily on proposals from the International Staging Project of the International Association for the Study of Lung Cancer (IASLC).4,5

This new staging system has been introduced in many medical journals among different medical specialties.6-9 Part of the new staging system has also been externally validated in terms of prognosis in surgical cases of NSCLC or patients with advanced nonbronchioalveolar carcinoma NSCLC.10-12

Some impact may also be observed in pathologic specimen processing due to this new staging system.13 However, to our knowledge, no study related to the clinical implementation, and impact of the new staging system has been reported. Thus, the objective of this study was to investigate the feasibility and clinical impact of this new staging system for NSCLC in a prospective manner.

PATIENTS AND METHODS

Study Setting

As a major tertiary medical center in central Taiwan with about 2000 beds, routine multidisciplinary lung cancer staging conferences have been held in our institute since 2001. All “new” and “treated” patients with lung cancer recorded by the lung cancer case manager (H.H.W.) are reviewed in this biweekly meeting. The “treated” patients list consisted of those patients whose treatment decision making had largely been made. The “new” patients list consisted of
those patients whose main treatment had not yet been decided. Generally, the “new” list reflected those diagnosed shortly before the date of the meeting, and the “treated” list reflected those diagnosed shortly after the date of previous meeting. Since April 2008, the feasibility and impact of the new staging system for “new” lung cancer patients were evaluated in a prospective manner in addition to the 6th TNM classification, and feasibility was evaluated based on whether consensus on IASLC staging could be achieved in this meeting. The data we collected and report in this study were the result of our routine records of lung cancer team meeting discussions, which were conducted by department/team head (T.-C.H.).

Data Collected

Demographic (gender and age), tumor (primary site and histology), and patient characteristics (Eastern Cooperative Oncology Group performance status) were collected. Histology was categorized as adenocarcinoma, squamous cell carcinoma, or other. Both 6th TNM and IASLC staging were based on discussion within this meeting, as was suggested treatment. Treatment was categorized as operation or not, systemic anticancer treatment or not, and radiotherapy or not. The staging workup was categorized into (A) conventional (primarily chest computed tomography based), (B) positron emission tomography included, or (C) cytopathological examination other than primary sites, which was primarily decided by the treating physician. The impact of IASLC staging in addition to the 6th TNM staging was observed at three levels: change in substaging (such as from IIA to IIB), change in staging (such as from III to IV), or change in clinical management, which was based on discussions within this conference.

Statistical Analysis

The results were tabulated and described by descriptive analyses. The $\chi^2$ test was used for comparisons among different groups. All analyses were done using the Statistical Analysis Software system for Windows, version 9.00 (Statistical Analysis Software Institute, Cary, NC).

RESULTS

Patients

Between April 2008 and June 2009, 537 newly diagnosed patients with lung cancer were added, according to institutional cancer registry, including 462 patients with histology-proven NSCLC. During the same period, 348 patient-visits were discussed as “new” patients for further decision making in our biweekly meetings, where “patient-visits” indicates that one patient might be discussed several times over the course. Among these “new” patient-visits reviewed and clinically staged in these conference ($n = 348$), those with no tissue diagnosis yet ($n = 66$), histology other than NSCLC ($n = 24$), history of previous treatment ($n = 12$), further workup needed ($n = 15$), and double cancer ($n = 5$) were excluded from our analysis. These exclusion criteria were decided during the first month (April 2008) when we began the study. The remaining 226 newly diagnosed patients with NSCLC constituted our study population (Table 1). Consensus for both 6th TNM and IASLC staging was achieved for these 226 patients at these meetings. Most of these patients were elderly males with adenocarcinomas.

Staging Results

The staging workups were 133 (59%), 50 (22%), and 43 (19%) for workups A, B, and C, respectively. The stage distribution was 14, 8, 56, and 148 for stages I, II, III, and IV, respectively, by the 6th TNM staging. The corresponding numbers were 12, 9, 53, and 152 by the new staging system (Table 2). In total, 23 patients had different staging, and four patients had different substaging using IASLC versus the 6th TNM staging. The reasons for these changes in staging and substaging are shown in Table 3. The predominant reasons for these differences (11 of 27, 41%) were due to coding of malignant effusion as M1 instead of T4, followed by coding of ipsilateral different-lobe nodules as T4 instead of M1 (7 of 27, 26%). Operations were indicated for 38 patients, whereas systemic treatment and radiotherapy were suggested for 156.

### TABLE 1. Characteristics of the Study Group ($n = 226$)

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>Median: 67 Range: 33–87</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>132 (58)</td>
</tr>
<tr>
<td>Female</td>
<td>94 (42)</td>
</tr>
<tr>
<td>Primary site</td>
<td></td>
</tr>
<tr>
<td>RUL</td>
<td>53 (23)</td>
</tr>
<tr>
<td>RML</td>
<td>13 (6)</td>
</tr>
<tr>
<td>RLL</td>
<td>42 (19)</td>
</tr>
<tr>
<td>LUL</td>
<td>33 (15)</td>
</tr>
<tr>
<td>LLL</td>
<td>49 (22)</td>
</tr>
<tr>
<td>NA</td>
<td>36 (16)</td>
</tr>
<tr>
<td>Histology</td>
<td></td>
</tr>
<tr>
<td>Adenocarcinoma</td>
<td>144 (64)</td>
</tr>
<tr>
<td>SCC</td>
<td>54 (24)</td>
</tr>
<tr>
<td>Others</td>
<td>28 (12)</td>
</tr>
<tr>
<td>PS</td>
<td></td>
</tr>
<tr>
<td>0–2</td>
<td>184 (81)</td>
</tr>
<tr>
<td>3–4</td>
<td>38 (17)</td>
</tr>
<tr>
<td>Missing</td>
<td>4 (2)</td>
</tr>
</tbody>
</table>

* Rounded.

### TABLE 2. Staging Distribution for 6th TNM versus IASLC ($n = 226$)

<table>
<thead>
<tr>
<th>Stage I, No. (%)</th>
<th>Stage II, No. (%)</th>
<th>Stage III, No. (%)</th>
<th>Stage IV, No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>6th TNM</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>14 (6)</td>
<td>8 (4)</td>
<td>36 (25)</td>
<td>148 (65)</td>
</tr>
<tr>
<td>IASLC</td>
<td>12 (5)</td>
<td>9 (4)</td>
<td>53 (23)</td>
</tr>
</tbody>
</table>

* Rounded.

IASLC, International Association for the Study of Lung Cancer; TNM, tumor, node, metastasis.
and 47 patients, respectively. An impact in clinical management was seen in 2.7% (6 of 226) of these patients, including a consideration of operation and radical thoracic radiotherapy for three patients each, in addition to chemotherapy alone. All were due to coding an ipsilateral different-lobe metastasis as T4 instead of M1. The number (percentage) of patients with differences in staging or substaging was 10 (8%), eight (16%), and nine (21%) for work-up methods A, B, and C, respectively (p = 0.038). Use of an advanced staging procedure (work-up B or C) was associated with changes between 6th TNM staging and IASLC staging/substaging (17 of 93 versus 10 of 133; p = 0.014).

DISCUSSION

The long-awaited new staging system for lung cancer has finally been published. Our study revealed that adoption of the 7th TNM staging of lung cancer, as proposed by IASLC, was feasible for newly diagnosed NSCLC in our routine multidisciplinary lung cancer staging conferences. The objectives of the staging system are to aid clinicians and investigators in planning treatment, assessing prognosis stratification, and facilitating communication. There is no doubt that the new staging system, as proposed by IASLC, is a major advance, as revealed by the superior prognostic stratification. This achievement was validated by retrospective studies and was further supported by this study evaluating its clinical feasibility and potential clinical impact. In our study, this clinical impact was seen primarily in patients with ipsilateral different-lobe nodules. Although the justification that we proposed to treat selected patients with ipsilateral different-lobe nodules aggressively as stage III, instead of stage IV, patients deserve further prospective studies; this concept was compatible with the present National Comprehensive Cancer Network guidelines.

Although this new staging system may also be applied to small-cell lung cancer, it was originally based on a database of patients with NSCLC only. Thus, only patients with NSCLC were included in our study. This study has some limitations. First, not all newly diagnosed patients with lung cancer during the study period were included in our analysis; in particular, some early-stage patients might not be included due to the unavailability of a tissue diagnosis before operation. This was also the number one cause (n = 66) of exclusion from our study. Thus, the impact of the new staging system on early-stage NSCLC might not be fully captured by our study. However, because changes in staging primarily occurred in IASLC stages II to IV patients, underrepresentation of patients with early-stage NSCLC in our study population might not lead to any significant change in staging result or clinical impact. Additionally, only “new” patients, and not “treated” patients, were included in our study. However, because these two groups only reflected patients diagnosed at times before and after the routine meetings, the omission of “treated” patients should only lead to a reduction in sample size not to limited representation.

Second, our study population was not staged uniformly. However, this made our results more relevant to the real world, where wide variations exist in the pattern of care for staging procedures of lung cancer. As suggested by the American College of Chest Physicians, tissue biopsies for abnormalities are preferred for accurate staging, and positron emission tomography has better sensitivity and specificity than does computed tomography. Thus, staging workups were categorized in three levels in our study. Our results also revealed that the impact of the new staging system might be enhanced if the use of the advanced staging procedures is increased. On the other hand, our results also indicated that conventional investigation alone (work-up group A) might often be sufficient for staging, especially for a predominantly advanced disease patient population.

Another limitation of our study is the moderate sample size, based on data from a single institution. However, for the seven situations where T or M coding was different between the 6th TNM and IASLC staging, all seven happened in our study group (Table 3). Thus, we believe our study population was big enough to be representative for a single institution. However, multinational and multinstitutional experiences are needed for further evaluation of the comprehensive impact of the new staging system, though we believe our findings provide a good starting point.

The lung cancer staging system may be further improved in the future. N staging was not revised in this new staging system, although some subclassification has been suggested. Other nonanatomic prognostic factors may also be incorporated in the future. Currently, a prospective project is underway by IASLC.

In conclusion, the new staging system was clinically feasible and led to some (27 of 226, 12%) differences in staging. Most of the changes were due to coding of malignant effusion as M1 instead of T4. An impact on clinical decision making was occasionally seen (6 of 226, 2.7%) within our institutional practice. Further studies are needed to investigate the comprehensive and long-term impact of the new staging system.

ACKNOWLEDGMENTS

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REFERENCES