IIB or Not IIB: The Current Question in Staging Non-small Cell Lung Cancer*

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It has been suggested that T3/N0-1/M0 non-small cell lung cancer should be classified as stage IIB rather than IIIA. This is the result of a widespread perception that the survival of patients with T3/N0-1 lung cancers greatly exceeds that of patients with stage IIIA (N2) lung cancers. This perception is based primarily on the survival of T3/N0-1 patients who have chest wall involvement. However, the T3 classification also includes tumors that involve mediastinal structures, the main stem bronchus <2 cm from the carina, and the brachial plexus as seen in Pancoast tumors. Survival for each of these T3 categories is examined in this article and found to be somewhat different. The available data show that patients with T3/N0-1 tumors involving the chest wall have a good prognosis after resection, whereas patients with central T3/N0-1 tumors (mediastinal or main stem bronchial involvement) have a prognosis similar to that of patients with resected IIIA (N2) tumors. If a new classification of T3/N0-1 tumors as stage IIB is to be adopted, it will be important for future studies to document which type of T3 tumor is being discussed.

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Key words: non-small cell lung cancer; staging; T3 tumors

Abbreviations: NSCLC=non-small cell lung cancer

Non-small cell lung cancer (NSCLC) remains the leading cause of cancer mortality in the United States. Approximately 140,000 new cases of NSCLC will be diagnosed in 1996. Earlier stages of disease enjoy favorable survival rates following surgery; 5-year actuarial survival is 65% for stage I and 41% for stage II.2 However, most cases are of an advanced stage that is not amenable to a surgical approach, which remains the most curative modality. Because of this, the current staging system for NSCLC attempts to identify those patients who are most appropriately treated by surgery. Accurate staging (clinical and pathologic) defines a group of patients with a more favorable prognosis and also assists in the selection of patients for surgical treatment. An appropriate staging system therefore defines both prognosis and therapy for a particular subset of disease.

In the 1986 American Joint Committee on Cancer staging system, lung cancers are classified as stage IIIA if there is involvement of ipsilateral mediastinal lymph nodes (“N2 disease”) or because of local tumor extension into extraparenchymal, yet still potentially resectable, structures (“T3 disease”).3 Only about 20% of all N2 patients undergo surgical resection, and these are primarily patients who were not suspected to have N2 nodal involvement preoperatively.4-7 However, the 5-year survival, even in this select group of patients with resected N2 disease, is only approximately 20%.4-5 Therefore, initial surgical resection for IIIA (N2) patients is not considered standard, and the optimal management of N2 disease remains controversial.9

The survival after resection of T3/N0-1 disease in patients is reported to be much better than that of patients with N2 disease, and there is a general consensus that these patients should undergo surgery as the primary treatment.8,10 Given the difference in both the accepted therapy and overall prognosis of these two groups (T3/N0-1 vs T1-3/N2), Green and Lilienbaum11 have suggested that these T3/N0-1 tumors be classified separately as stage IIB, rather than stage IIIA, thereby creating a new subset of disease. This perceived difference in the prognosis of T3/N0-1 vs T1-3/N2 is based primarily on the survival of T3/N0-1 patients who have chest wall involvement. However, the T3 classification includes tumors that involve other structures within the chest.

Tumors are classified as T3 because of the following: (1) peripheral extension into the chest wall or diaphragm; (2) extension centrally into mediastinal...
structures (mediastinal pleura, pericardium, phrenic nerve, azygous vein, or extrapericardial segments of the right or left pulmonary artery); (3) tumor involvement of a main stem bronchus within 2 cm of the carina; or (4) involvement of the brachial plexus at the apex of the chest (Pancoast tumors). These structures are generally resectable without requiring major reconstruction. This is in contrast to T4 tumors, which invade more vital structures, such as the aorta, heart, great vessels, trachea, esophagus, or vertebral bodies. This article critically reviews the published data regarding the surgical curability of T3 tumors divided into the following categories of disease: (1) extension into the chest wall; (2) extension into the mediastinum; (3) proximity to the carina and involving the main stem bronchus; and (4) Pancoast tumors. Survival for each of these T3 categories is found to be variable, making the question of reclassifying all T3 categories as IIB a complex issue.

**INCIDENCE**

A number of large series have reported that T3/N0-1 patients comprise about 5% of all NSCLC patients and about 10% of patients with resected NSCLC. It is not clear how many patients with T3 tumors also have N2 nodal involvement. Among surgical series, which have generally excluded patients who had clinical N2 disease, approximately 30% of the T3 primary tumors were nevertheless found to have N2 involvement histologically. These T3/N2 patients are not the focus of this article. In surgical series involving patients with T3 disease who are found to be pathologically N0-1, approximately two thirds of the patients have N0 disease and one third have N1 disease (Table 1). Thus, it appears that T3/N0-1 patients comprise a relatively small group, with most of these patients having N0 disease.

The distribution of the type of T3 tumor is shown in Table 1. The two largest groups are tumors invading the chest wall and those invading mediastinal structures. Although patients with chest wall involvement (excluding Pancoast tumor) are a large group, they make up less than half of all patients with T3 disease. Therefore, it is important to consider the long-term survival for each category of T3 disease.

**CHEST WALL INVOLVEMENT**

A number of series of patients with chest wall involvement have been reported. All series since 1980 reporting actuarial survival of at least 20 patients with resections with NSCLC invading the chest wall only are listed in Table 2. The average survival for all patients (including some T3/N2 patients) is 33%. The average survival of T3/N0 patients is 42%, whereas that of T3/N1 patients drops quite dramatically to 19%. It is difficult to compare the series because the inclusion criteria, as well as the method of reporting, are not consistent. However, it is worth noting that the lowest survival reported was 23%. This was from a series that included many incomplete resections. However, the survival of T3/N0 (chest wall) patients undergoing complete resections has been consistently reported to be 50 to 60%.

Thus, patients with resected T3 tumors involving the chest wall exhibit a much better survival than patients with resected stage IIIA (N2) tumors. Patients with stage IIIA (N2) tumors who have undergone resection represent only approximately 20% of all N2 patients, and 5-year survival of this selected subgroup is approximately 20%. The better survival of T3/N0-1 patients with chest wall involvement is seen both for the entire group and, more dramatically, for the T3/N0 patients undergoing complete resection. To our knowledge, no data are available on the survival after resection of T3 tumors invading the diaphragm. However, one might speculate that survival rates would be similar to those for chest wall lesions, because they are also peripheral tumors in which a wide margin can be easily achieved.

**TUMORS INVADING THE MEDIASTINUM**

The results of studies reporting survival of patients with tumors invading the mediastinum are shown in

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**Table 1—Distribution of T3 Lesions (Surgical Series)**

<table>
<thead>
<tr>
<th>Study, First Author</th>
<th>n</th>
<th>pN0, %</th>
<th>pN1, %</th>
<th>Chest Wall, %</th>
<th>Pancoast, %</th>
<th>Mediastinum, %</th>
<th>Main Stem Bronchus, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Watanabe15</td>
<td>102</td>
<td>69</td>
<td>31</td>
<td>681</td>
<td>201</td>
<td>461</td>
<td>12</td>
</tr>
<tr>
<td>Mountain10</td>
<td>80</td>
<td>90</td>
<td>20</td>
<td>39</td>
<td>15</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Izbicki16</td>
<td>77</td>
<td>44</td>
<td>56</td>
<td>46</td>
<td>0</td>
<td>48</td>
<td>6</td>
</tr>
</tbody>
</table>

*a pN2 patients have been excluded; p = pathologic staging.

1 P= Pancoast + chest wall.

1 Pericardium only.

1 Mediastinum and main stem bronchus.
Table 2—Survival of T3 Patients With Resections of Chest Wall Involvement

<table>
<thead>
<tr>
<th>Study, First Author</th>
<th>All T3</th>
<th>T3/N0</th>
<th>T3/N1</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>5-yr, %</td>
<td>n</td>
</tr>
<tr>
<td>Pitz1814</td>
<td>86</td>
<td>29</td>
<td>52</td>
</tr>
<tr>
<td>Piekler1911</td>
<td>66</td>
<td>33</td>
<td>31</td>
</tr>
<tr>
<td>Trastek201</td>
<td>73</td>
<td>40</td>
<td>28</td>
</tr>
<tr>
<td>McCaughan21**</td>
<td>77</td>
<td>40</td>
<td>45</td>
</tr>
<tr>
<td>Bato22</td>
<td>—</td>
<td>—</td>
<td>14</td>
</tr>
<tr>
<td>Albertucci23</td>
<td>37</td>
<td>30</td>
<td>21</td>
</tr>
<tr>
<td>Faione81</td>
<td>32</td>
<td>35</td>
<td>26</td>
</tr>
<tr>
<td>Mountain10</td>
<td>31</td>
<td>39</td>
<td>—</td>
</tr>
<tr>
<td>Watanabe15a§</td>
<td>24</td>
<td>43</td>
<td>—</td>
</tr>
<tr>
<td>Casillas21A</td>
<td>97</td>
<td>23</td>
<td>58</td>
</tr>
<tr>
<td>Allen20</td>
<td>52</td>
<td>26</td>
<td>43</td>
</tr>
<tr>
<td>Total</td>
<td>575</td>
<td>33</td>
<td>318</td>
</tr>
</tbody>
</table>

*Only completely resected.
1Excludes operative mortality.
1Includes 3% small cell.
1N1 + N2.
1Four-year survival.
1All N0-1.
1Eighteen percent incompletely resected and 10% wedge.
1Averages are weighted by number of patients.

Table 3,15,18,27,28 As is immediately apparent, the overall number of studies and patients is limited. The average 5-year survival in these series is 23%. The largest series involving only patients who underwent complete resection shows an average survival of only 9%27. The highest survival was found in the smallest series (17 patients).15 However, this series excluded operative mortality and also reported only on patients with pericardial involvement. The only data available on the influence of nodal status come from the Memorial Sloan-Kettering series and involve patients with both complete and incomplete resections. There was no difference in survival between the entire group (including N2 disease) and those with only N0 or N1 disease.27 Thus, patients with T3 lung cancers due to mediastinal invasion appear to have a poorer prognosis as compared to patients with primary chest wall invasion. It is also a group for which there are only limited data, making definitive conclusions somewhat more difficult.

**Main Stem Bronchus Involvement**

The data on 5-year survival in patients with involvement of the main stem bronchus within 2 cm of the carina are shown in Table 4.15,18,29,30 The largest series shows a 5-year survival of only 12%,30 whereas another series that excluded operative mortality reports a 5-year survival of 40%.18 The series with the best survival involved a select group of only 11 patients who underwent complete resection and excluded operative mortality.15 Once again, the limited data and variability in the patients included and the way the data are reported make definitive conclusions difficult. Nevertheless, the available data (Table 4) show an average 5-year survival of 24%, which is very similar to that seen in patients with mediastinal involvement. No data are available to analyze the influence of nodal status, resection margin, or other factors that may be related to survival, despite the fact that a number of studies involving sleeve resections have been published. These series have likely included some T2 and some T3 patients. However, because these studies have not staged patients according to T and N status, they are not useful in this analysis.
Table 4—Survival of T3 Patients With Resections of Involvement of the Main Stem Bronchus

<table>
<thead>
<tr>
<th>Study, First Author</th>
<th>n</th>
<th>5-yr, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vogt-Moykopf\textsuperscript{58}</td>
<td>97</td>
<td>12</td>
</tr>
<tr>
<td>Deslauriers\textsuperscript{30}</td>
<td>31</td>
<td>14</td>
</tr>
<tr>
<td>Pitz\textsuperscript{51}</td>
<td>75</td>
<td>40</td>
</tr>
<tr>
<td>Watanabe\textsuperscript{15,1}</td>
<td>11</td>
<td>46</td>
</tr>
<tr>
<td>Total</td>
<td>214</td>
<td></td>
</tr>
<tr>
<td>Average\textsuperscript{1}</td>
<td></td>
<td>24</td>
</tr>
</tbody>
</table>

\textsuperscript{1} Small cell in 15%.
\textsuperscript{1} Excludes operative mortality.
\textsuperscript{1} Only completely resected.
\textsuperscript{1} Weighted by number of patients.

Table 5—Survival of T3 Patients With Resections of Pancoast Tumors

<table>
<thead>
<tr>
<th>Study, First Author</th>
<th>n</th>
<th>5-yr, %</th>
<th>n</th>
<th>5-yr, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ginsberg\textsuperscript{32}</td>
<td>100</td>
<td>30</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Paulson\textsuperscript{33}</td>
<td>78</td>
<td>31</td>
<td>56</td>
<td>44</td>
</tr>
<tr>
<td>Maggi\textsuperscript{34}</td>
<td>60</td>
<td>17</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sartori\textsuperscript{35}</td>
<td>42</td>
<td>25</td>
<td>37</td>
<td>28</td>
</tr>
<tr>
<td>Wright\textsuperscript{36}</td>
<td>21</td>
<td>27</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stanford\textsuperscript{37}</td>
<td>16</td>
<td>50</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anderson\textsuperscript{38}</td>
<td>28</td>
<td>34</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>308</td>
<td></td>
<td>130</td>
<td></td>
</tr>
<tr>
<td>Average\textsuperscript{3}</td>
<td></td>
<td>27</td>
<td>37</td>
<td></td>
</tr>
</tbody>
</table>

\textsuperscript{1} Includes T4, proportion not reported.
\textsuperscript{1} Twenty-five to 30% T4.
\textsuperscript{1} Forty-three percent T4.
\textsuperscript{3} Weighted by number of patients.

**PANCOAST TUMORS**

Tumors arising in the apex of the chest and involving the brachial plexus are also classified as T3 tumors. These tumors also occasionally involve the subclavian vessels or the vertebral bodies, which classifies them as T4 tumors. In most surgical series of Pancoast tumors, approximately 30% of patients have T4 lesions. These series have generally employed radiation (either preoperatively, postoperatively, or both) in addition to resection. The average 5-year survival for a large number of patients with resection, including some patients with T4 and some patients with N2 disease, is 30%.\textsuperscript{31} Those series that contain the highest number of patients with T3/N0-1 tumors are shown in Table 5.\textsuperscript{32-38} The average 5-year survival in these series is 27%, which is intermediate between central T3 tumors (with mediastinal or main stem bronchial involvement) and chest wall tumors. It should be pointed out that with Pancoast tumors, a complete resection is achieved in only two thirds of patients.\textsuperscript{31} In patients with T3/N0-1 Pancoast tumors in whom a complete resection with negative margins is achieved, the 5-year survival has been reported to be 41%.\textsuperscript{32}

**DISCUSSION**

Primary tumors are classified as T3 on the basis of a number of different criteria. Although chest wall involvement is one of the largest categories, it accounts for <50% of patients with T3 disease. T3 tumors involving the chest wall are widely considered to be best treated by surgery. Indeed, the 5-year survival of patients with T3/N0 tumors who have undergone a complete resection is >50%.\textsuperscript{19,21-23} and is clearly better than survival of those IIIA patients with N2 disease who undergo surgical resection. From a stand point of cancer biology, it also makes intuitive sense to consider IIIA (T3) chest wall tumors separately from IIIA (N2) tumors.

The available published data suggest that tumors involving mediastinal structures or the main stem bronchus do not fare as well after surgical resection. The 5-year survival for each of these groups is quite similar to that of the select subgroup of IIIA (N2) patients who undergo resection. Pancoast tumors are a bit more difficult to interpret. However, the 5-year survival of patients with reasonably well-staged T3/N0-1 Pancoast tumors appears to be intermediate between that of IIIA (N2) tumors and IIIA (T3 chest wall) tumors.

Green and Lilenbaum\textsuperscript{11} suggested that T3/N0-1 tumors should be classified as stage IIB. However, they did not extensively consider the different subtypes of T3 classification. Their data were taken primarily from two references,\textsuperscript{10,15} which included the smallest number of reported patients in a variety of T3 categories. The more detailed analysis involving all available series since 1980 presented here shows that the reported survival of patients with T3 chest wall tumors is better than that of patients with central T3 (mediastinal or main stem bronchial) tumors.

Why should there be a difference in the survival of patients with these tumors? One could speculate that it may be the result of the biological behavior of these tumors. The usual pattern of spread of lung cancers appears to be via the lymphatic channels through the lung, then to the mediastinum, and finally distant hematogenous dissemination. By this hypothesis, peripheral T3 tumors may be less likely to involve mediastinal nodes or to have undergone hematogenous dissemination at the time of diagnosis. This might be particularly true for those patients
who undergo resection and whose tumors are pathologically staged as T3/N0-1. However, central T3 tumors (mediastinum and main stem bronchus) may have a greater propensity for lymphatic spread.

Alternatively, the apparent differences in survival may be due to inaccurate staging. Central T3 tumors appear to have a higher rate of mediastinal node involvement. Daly et al.\(^{39}\) found that even in patients with radiographically normal mediastinal lymph nodes, 22% of those with central T3 and T4 tumors harbored microscopic mediastinal nodal metastases. This is in contrast to those involving central T1 or peripheral tumors, where the incidence of microscopic nodal metastases and radiographically normal lymph nodes was <10%.\(^{39}\) Therefore, if radiographic staging of central T3 tumors is particularly unreliable, it may be especially important to do accurate surgical staging. Unfortunately, details of the adequacy of surgical staging are not given in most reports. In a recent survey, 45% of thoracic surgeons in Great Britain reported that they did not routinely sample mediastinal lymph nodes at thoracotomy.\(^{40}\) Thus, the apparent differences in survival between patients with peripheral T3 and central T3 tumors could be due to inaccurate staging.

One might also speculate that the differences in survival are due to differences in the ability to achieve a complete surgical resection. One can easily obtain a wide margin around peripheral tumors involving the chest wall or diaphragm. However, the presence of many vital structures within the mediastinum limits the ability to get a wide margin around central T3 tumors. Similarly, it is difficult to achieve a wide margin when resecting Pancoast tumors. Unfortunately, there are few data either to substantiate or to refute this hypothesis. Certainly, those patients with chest wall tumors or Pancoast tumors who achieve a complete resection exhibit relatively good survival. Unfortunately, no data are available (to our knowledge) on the incidence of complete resections or the impact on survival in central T3 tumors.

It is easy to rationalize that peripheral T3 tumors might exhibit a different biological behavior from stage IIIA (N2) tumors. The reported 5-year survival for such tumors is markedly better than that for IIIA (N2) tumors and lends strong support to the argument that T3 tumors should be classified separately as stage IIB. However, central T3 tumors may not exhibit the same biology and, indeed, do not appear to have the same good survival as that of peripheral T3 tumors involving the chest wall. Classifying T3 chest wall tumors as stage IIB may be justified; however, classifying central T3 tumors as stage IIB may not be justified if the goal of staging is to accurately reflect appropriate therapy and prognosis.

If a new classification of T3/N0-1 tumors as stage IIB is to be adopted, it is important to realize that not all categories of T3 are necessarily created equal. We believe the data suggest a difference between peripheral T3 chest wall lesions and central T3 lesions with regard to surgical curability. It is important for future reports on survival of patients with T3 disease to provide data for each of these groups separately. It is also important in reporting results for this group in the future that adequate staging be done and carefully reported. Otherwise, the confusion that has existed by the inclusion of two different groups within stage IIIA (T3/N0-1 and T1-3/N2) will persist, despite the new classification of T3/N0-1 tumors as stage IIB.

**REFERENCES**