

SOME CONTROVERSIES IN THE PRESENT INTERNATIONAL TNM STAGING SYSTEM FOR LUNG CANCER

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The rationale for dividing cancer patients into groups according to the so-called T (tumor), N (node) and M (metastasis) stages was based on the finding that survival rates are higher for patients with localized disease compared to those in patients with tumor extending beyond the organ of origin. The international TNM classification proposed by the Union Internationale Congre le Cancer (UICC) has been widely used in the investigation and treatment of cancers of various organs. The UICC believes the TNM staging system serves a number of related objectives, namely (1) aiding the clinician in planning treatment, (2) giving some indication of prognosis, (3) assisting the evaluating treatment results, (4) facilitating the exchange of information between treatment centers and (5) contributing to the continuing investigation of human cancer [1].

In the 1997 version (5th edition) [1], the new international TNM classification system for lung tumors underwent an extensive revision which corrected many of the deficiencies of the old staging system. Major revisions in the new TNM staging system for lung cancer were as follows: (1) Stage I was subdivided into IA and IB, and stage II was subdivided into IIA and IIB. (2) T3N0M0 was upgraded to IIB. (3) Staging for intrapulmonary separate nodule either in the primary lobe or in another lobe was changed. As a result, the new international staging system appeared to be a great improvement over the 4th edition. There are, however, still some controversies arising in daily diagnoses and treatments for lung cancer patients, even when the new staging system is applied. In fact, since the revision of the 5th edition, 109 articles or abstracts were published concerning controversies in staging system for lung cancer. From Japan, there were 29 abstracts at the related society and 32 articles in Japanese. There were 48 English publications and 15 of them were published from Japan. There appear to be two main problems. One concerns the interpretation of the terminology describing the T, N and M criteria, while the other involves the classification itself, mainly with regard

to survival rates, when each stage is further subdivided according to T, N and M factors.

“T “ CATEGORY PROBLEMS

In the new staging system, stage I was divided into stages IA (T1N0M0) and IB (T2N0M0), because most of the reports showed a significant difference between the two groups. This seems to be a reasonable revision. However, by multivariate analysis, tumor size was found to be the most significant factor associated with the prognosis of stage I patients. When the survival rate of the patients with T2N0M0 (tumor more than 3 cm in maximal dimension) were analyzed, patients showed a further difference in survival with respect to tumor size. There was a significant difference in the survival rate between the patients with 3.1-5.0 cm tumor and those with >5.1 cm tumor. Patients having tumors >5.1 cm showed a similar survival to patient with T3 lesions. Therefore, T2N0M0 with tumor diameter more than 5.1 cm should be categorized as T3. It would thus seem reasonable to subdivide T disease further by size of tumor, as already done in the TNM classification of breast, thyroid, salivary gland, skin and pharyngeal cancer.

There exist heterogeneity of T3 classification regarding Pancoast tumor, chest wall invasion with rib destruction and diaphragmatic invasion of the muscle layer or deeper, all of which show poorer prognoses compared with other T3 lesions. These lesions should be categorized into T4 lesions.

What is the difference between mediastinal pleural invasion (defined as T3) and mediastinum (defined as T4) ?

“N” CATEGORY PROBLEMS

To date, there are three kinds of maps, i.e. Japan Lung cancer Society (JLCS) map (so-called Naruke's map) [2], American Thoracic Society (ATS) map [3], and the recently proposed Mountain's map [4]. After the proposal of Mountain's map, there was great confusion regarding N category, especially concerning the boundary between #7 (subcarinal) and #10 (hilar) lymph nodes. In the JLCS map, the #7 lymph node is defined as the lymph node in contact with the subcarina. However, on the other hand, Mountain's map defines all subcarinal area nodes within pleural reflection as #7 nodes, including part of the nodes designated as #10 nodes in JLCS map. Lymph node metastasis to the #7 lymph node is an N₂ lesion, whereas metastasis to #10 is an N₁ lesion. This confusion apparently affects the survival rates of N₁ and N₂ lesions.

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There are also differences in nomenclature for nodal stations of nodes #3, #7, and #1 between the JLCS map and the ATS map. In the ATS map nodal involvements is divided strictly at the midline and #7 node involvement is bilateral involvement. Furthermore the ATS map includes #3 node with #2 (paratracheal), #4 (tracheobronchial), #6 (paraaortic), and node #3p with node #8. Accordingly, where lymphadenopathy in these node groups extends beyond the midline, it is defined as bilateral nodal involvement (N₃ lesion). Consequently, there is great confusion as well as some controversy over the definitions of N₂ and N₃ disease, which may lead to difficulties in interpreting results for such patients. If metastases to nodes #3, #3p and #3a are included in N₃ disease, the survival of stage IIIA patients is moderately improved; furthermore, if the involvement of node #7 is excluded from N₂ disease, survival in stage IIIA is even more markedly improved. As the survival rate of patients having c-N₂ disease shows a poor prognosis, there are some reports that this group should be categorized into stage IIIB [5,6].

“M” CATEGORY PROBLEMS

The greatest controversy regarding the definition of M1 disease arises when ipsilateral satellite lesions (separate tumor nodule, STN) are present [7,8,9]. In the 5th edition, STN in the same lobe is defined as T4 and STN in a different lobe is M1. As a result, patients with stages IIIB and IV show favorable prognoses because a moderate number of patients with STN of T4 or M1 lesions are included. From these fact, there are some proposals (including ours), that STS in the same lobe should be T3 or an upgrade of one T number (T1 to T2, T2 ro T3,and T3 to T4).

PROBLEMS IN STAGING

There are no objections to dividing stage I into IA and IB. However, most of the reports indicate that there are no differences between stage IB and IIA, and stage IIA and IIB. There is little meaning in separating stage IIA and IIB. In the present classification, T3N0M0 was upgraded to IIB, but T3N1M0 shows a similar survival rate . Therefore, T3N1M0 may also need to be upgraded to IIB. As T3N₂M0 shows a poor prognosis, it may appropriate to classify such cases IIIB. The heterogeneity of the stage IIIB has been pointed out and a new revision of the staging system has been proposed [6].

Furthermore, there are proposals that the biological parameters should be also calculated in the staging of lung cancer [10].

The international TNM staging system is the "international language" of cancer diagnosis and treatment. Although moderate revisions of the classification have already been made, several problems still exist. There are also still a number of differences between nations [even between institutes] regarding the interpretation of definitions in the TNM staging system. As a result, reported results from around the world are not based on a common standard, in contrast to the original purpose of the international TNM classification. We must prepare for the next revision of TNM staging system which will take place in 2007.

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