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Controversies Over UICC-TNM Classification of Non-small Cell Lung Cancer : Model for a Diagnostic Path

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Model for a Diagnostic Path

To the Editor:

The evaluation of a patient with a lung tumor cannot be made separately from the molecular biology of the tumor itself, the presence of growth factors, the presence of inhibitors of tissue invasion, and the development of metastases, tumor suppressor genes, and the presence of dominant oncogenes.[1] Currently, the therapeutic program is based on the rigid staging rules imposed by the TNM classification,[2] which contrast with the plasticity and singularity of tumors found in individual patients. In the face of this criticism, an increasing number of reports[3,4] and clinical evidence regard these staging criteria as penalizing patients who are, for example, in advanced stages of disease such as IIIB and IV. Some authors in fact maintain that the TNM classification underestimates the real long-term survival potential in patients with stage T4, resectable lung tumors (*ie*, in the vertebra, superior vena cava, and atrium),[5,6] stage T4 for double neoplasm in the same lobe,[7] stage M1 for double intrathoracic ipsilateral or contralateral synchronous neoplasms,[8] and also for stage M1 disease resulting from sole brain[9,10] or adrenal metastases.[11]

From a purely practical point of view, what needs to be established is the most useful diagnostic and therapeutic path for optimizing the available resources and guaranteeing that each individual patient receives the highest diagnostic efficiency as well as the maximum therapeutic efficacy, even in the long term. The current staging proposal, in our opinion, does not reflect these needs, particularly the real long-term survival prospects of patients with advanced-stage lung tumors. Some authors have suggested modifying the International Union Against Cancer (UICC) model by bringing both interesting and useful changes to the interpretation of stage N2 and by introducing the concept of operable stage T4 disease.[12] However, once more the biological behavior of the disease has to be considered, and the problem of the synchronous tumor has not been dealt with. Obviously, the primary objective is "personalized" biological staging in the near future; this is not possible as yet, however, and consequently we must make an effort to create a diagnostic model that reflects as accurately as possible the progress of the lung tumor disease of the patient in question in order to arrive at a histologic definition of stages T, N2, and N3, as well as M, whatever is required and is technically feasible, before imposing a definitive therapeutic program.

After an initial evaluation with chest radiograph and CT scan, we propose carrying out tests that help to reach a histologic diagnosis of a suspect pulmonary neoplasia, including bronchoscopy with brushing and, if necessary, an endoscopic biopsy, transbronchial biopsy, an ultrasound-guided transbronchial biopsy, transthoracic biopsy (ultrasonically or CT-guided), and ultrasound-guided transesophageal biopsy. On completion of the clinical staging, a whole-body positron emission tomography (PET) scan (which has greater sensitivity compared to bone scintigraphy in osteolytic lesions and greater sensitivity compared to CT and ultrasound scanning in secondary hepatic and adrenal lesions[13,14]) and a CT scan of the brain (because of the low accuracy of PET with 2-[18F]fluoro-2-deoxy-D-glucose in this zone) should be performed.

On the basis of the data supplied by the PET and CT scans of the brain, the following order of staging classification can be made: stage N2, N3, M-negative patients for whom surgical intervention is suggested, subject to a functional evaluation; stage N2 or N3-positive; stage M-negative patients who need to undergo the necessary procedures (*ie*, mediastinoscopy, mediastinotomy, videothoracoscopy, transtracheal biopsy, transbronchial biopsy, ultrasound-guided transbronchial biopsy, and ultrasound-guided transesophageal biopsy) for the histologic definition of stage N; stage N2 and N3-negative; stage M-positive patients for whom, where possible, a histologic definition of stage M is necessary; stage N2 and M-positive patients in whom tests need to be carried out to obtain a histologic definition of stage M first, wherever possible, and then of stage N2; and, finally, stage N3 and M-positive patients for whom the histologic definition is needed of the most easily obtainable site of stage N3 or M disease. In our opinion, this approach guarantees the reduction of the current overtreatment of patients with stage N3 or M-positive disease, without removing the possibility of increasing the survival of selected patients who are in advanced stages of disease.

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