



Editorial

Prognostic Factors in Stage I Lung Cancer[☆]

Cáncer de pulmón en estadio I y factores pronósticos

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Lung cancer (LC) still has a very poor prognosis, with overall 5-year survival rates of 10%–20% in most countries.¹ Nevertheless, the life expectancy of individual patients ranges widely, depending on specific circumstances: in non-small cell lung cancer (NSCLC), 5-year survival in stage IV disease is 2%–3%, but can be as high as 70% in stage I patients with fully resected disease.²

With regard to TNM classification of stage I disease, a minor change in the latest edition means that patients are subdivided into 2 subgroups according to tumor size: ≤ 2 cm (Ia) and > 2 cm (Ib).³ However, we have been aware for some time of other tumor characteristics, in addition to size, that might play a part in prognosis.^{4,5} Detailed characterization of the features that might identify tumors with poor prognoses that are, as such, candidates for adjuvant treatment with chemotherapy (CT), has attracted great interest and been the subject of much recent research. For example, great expectations have arisen from the detection of certain mutation profiles in some groups of genes (“genomic signatures”) that may differentiate tumors with altered biological conduct and metastatic potential. In this respect, promising results⁶ have been published by several groups, although the incorporation and translation of these techniques into clinical practice has been curtailed to date by problems, such as: (a) different researchers studying different genes, (b) difficulties in validating and standardizing procedures and outcomes or in clearly separating their prognostic value from that of other more simple parameters, and (c) the need for expensive, complex technology that is not usually available in general clinical practice.⁷

In addition to the tumor’s genomic profile, other anatomical or morphological features which also seem to have prognostic significance must be taken into account. Cell line and the degree of cellular differentiation, vascular or lymphatic infiltration or infiltration of the visceral pleura by the tumor in surgical specimens have been examined by researchers who have underlined their prognostic value.^{4,5} So, while many guidelines only refer to the TNM staging system as a criterion for selecting candidates for adjuvant CT (and NSCLC stage I is excluded from this indication), the National Cancer Comprehensive Network defines stage I patients with the

following features as high risk: poorly differentiated tumors; vascular invasion; wedge resection; minimal resection margins; visceral pleural invasion and unknown lymph node status.⁸ Peñalver et al.,⁹ in their study published in this edition of the journal, analyze in detail the influence of these features in a series of stage I NSCLC patients. They used multivariate analysis to demonstrate the independent prognostic value of vascular invasion and visceral pleural involvement. These features emerged as the most relevant parameters, and on this basis 3 subgroups with different life expectancies were established. Of special interest in this report is the long follow-up period, with particular emphasis on the detection of relapses and/or appearance of second tumors or other potentially fatal diseases. The authors note that, after 6.3 years, the probability of dying of cancer is less than that of dying from another cause. Andrade et al. reported a very similar outcome in their series of patients undergoing LC resection: 7 years after resection, the risk of death from cardiovascular disease was greater than death from cancer.¹⁰ These conclusions can only be drawn from studies with a lengthy, meticulous follow-up examining the patient’s full medical progress and cause or causes of death, something that is often difficult to establish. To enhance their results, Peñalver et al. used statistical methods that included competitive risk of death (or other outcomes of interest), giving a more accurate picture of mortality specifically due to LC, and how this influenced the prognostic factors under study. These parameters may have been less clear-cut if only overall survival had been examined.

Along these same lines, it is interesting to note that, in preparation for the next edition of the TNM classification, the case report form of the IASLC international prospective study includes details on the morphopathological variables examined in this project. Hopefully, the analysis of these data from a very large series of patients will help ascertain and confirm their prognostic value. Finally, as the authors suggest, the inclusion of these variables (vascular and visceral pleural invasion) should be taken into consideration for weighting the results of future trials assessing the role of CT or other adjuvant treatment in stage I resected patients.

[☆] Please cite this article as: Sánchez de Cos-Escuín J. Cáncer de pulmón en estadio I y factores pronósticos. Arch Bronconeumol. 2015;51:427–428.

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