Ideal prognostic model in lung squamous cell carcinoma

Tomonari Kinoshita

Department of Thoracic Surgery, Tokyo Metropolitan Cancer and Infectious Diseases Center Komagome Hospital, Tokyo, Japan
Correspondence to: Tomonari Kinoshita. Department of Thoracic Surgery, Tokyo Metropolitan Cancer and Infectious Diseases Center Komagome Hospital, 3-18-22, Honkomagome, Bunkyo-ku, Tokyo 113-8677, Japan. Email: kinotomo0415@gmail.com.

Thus far, many researchers have identified prognostic clinicopathological factors that can potentially predict postoperative survival in non-small cell lung cancer (NSCLC) (1-4). However, few papers have paid attention to the histological subtypes of NSCLC. The occurrence of lung adenocarcinoma is generally not related to patients' smoking habits whereas lung non-adenocarcinomas, such as squamous cell cancer and high-grade neuroendocrine carcinomas, are broadly known to be strongly associated with smoking (5). For treatment, molecular targeted therapies including epidermal growth factor tyrosine kinase inhibitors are usually used in patients with adenocarcinoma. Conversely, immune checkpoint inhibition has shown particular efficacy in squamous cell carcinoma, confirming its place alongside surgery, chemotherapy, and radiotherapy as a primary treatment for NSCLC (6). In order to realize personalized medicine, histological subtype should be considered both for the clinical treatment of and basic research into NSCLC.

Sun *et al.* proposed a novel prognostic model based on circular RNA pyruvate dehydrogenases kinase 1 (circPDK1) expression and multiple clinicopathological factors for predicting survival/recurrence resected lung squamous cell carcinoma (7). Although several groups have described prognostic models that combine some clinicopathological parameters with TNM staging to predict post-treatment survival (8-10), models that integrate genetic information are novel and interesting. By adding an appropriate biomarker to a model using 'conventional' factors, more precise predictions of postoperative survival for any type of cancer could be realized. A critical limitation of such models, however, is the cost and complexity associated with genetic testing. The success of TNM staging has been its reliance of more readily obtainable clinical and pathological data; such data should continue to form the foundation of our basic prognostic models until genetic testing becomes more widely available.

Furthermore, it is likely difficult to identify appropriate prognostic markers in lung squamous cell carcinoma as such patients usually have a smoking history that is often correlated with other pulmonary diseases (e.g., including chronic obstructive pulmonary disease) and other malignancies (11). It is well known that patients with idiopathic pulmonary fibrosis also develop lung squamous cell carcinoma more frequently (12). Sun and co-authors combined clinicopathological and genetic information to predict overall and recurrence-free survival. In order to exclude the influence of death from other diseases on postoperative survival analysis, disease-specific survival should be evaluated. As Sun and co-workers, I tried to identify prognostic clinicopathological factors that could supplement TNM staging among pathological stage I squamous cell carcinoma cases to better predict overall, recurrence-free, and disease-specific survival (8). Vascular invasion and tumor makers were chosen based on survival analyses. Although our proposed model predicted overall and recurrence-free survival accurately, no difference in disease-specific survival was detected between patients with and without the identified risk factors. Pilotto *et al.* created a risk classification model for resected lung squamous cell cancer based on a combination of clinicopathological predictors to provide a practical tool to evaluate patients' prognoses, evaluating disease-free and cancer-specific survival (9).

Several forms of circular RNAs have been reported to be associated with prognosis in lung cancer patients (13). Sun *et al.* focused on the expression of circPDK1. The relationship between circPDK1 expression and other pulmonary concomitant diseases should be analyzed to validate the the mechanism that the circular RNA plays in SCC pathogenesis. Understanding the distribution of circPDK1 expression within squamous cell carcinoma tumors would be interesting.

Despite concerns for its generalizability to global lung cancer care, the combination of conventional factors and genetic information, especially circular RNA, is of interest and promising. I wish to congratulate the authors on their novel work. Further investigation into a more appropriate prognostic model should continue with a balanced approach.

Footnote

Conflicts of Interest: The author has completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/tlcr.2020.03.22). The author has no conflicts of interest to declare.

Ethical Statement: The author is accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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