Time of modeling survival of patients with stage III-N2 non-small cell lung cancer: Before or after surgery makes a difference

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The study by Qixing and colleagues¹ is a retrospective analysis performed on the Surveillance, Epidemiology and End Results (SEER) database and includes 1765 patients with pathologic stage IIIA-N2 submitted to curative anatomic lung resections. The authors were able to develop a nomogram aimed at predicting postoperative survival. The model is based on 6 risk factors, which showed good discrimination and calibration in the training sample (SEER) and in another independent external validation set of patients who underwent operation in a Chinese Hospital. Although the prediction model shows fair discrimination, the survival curves cross, suggesting that critical survival variables are missing from the data. Indeed, the model is mostly composed by surgical and pathologic factors (ie, lymph node examined, positive lymph nodes, invasion of visceral pleural, and extent of resection), which are by definition unknown at the time of treatment selection. Unfortunately, factors such as comorbidities, forced expiratory volume in 1 second, and carbon monoxide lung diffusion capacity, which are known to influence survival in patients with lung cancer, are not included in this analysis because they are lacking in the SEER database.

The lack of preoperative variables in the nomogram limits its clinical use. This instrument cannot be used to inform the treatment selection given that it can be used only after all treatment decisions have been made (because it includes many variables that are available only after resection has been completed).

In addition, patients were included on the basis of their final pathologic stage. There is no indication of how many patients were diagnosed with N2 disease preoperatively versus those who were upstaged or downstaged during surgery. The construction of the model including all patients clinically staged with N2 disease (including those managed with nonsurgical treatment) would have produced a more realistic and clinically useful tool.

Another inherent limitation of the SEER database is the lack of information about induction or adjuvant

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Central Message

The inclusion of preoperative variables and precise information about chemotherapy is necessary to develop a model to inform treatment choice in patients with stage III-N2 lung cancer.

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chemotherapy, which is an integral part of the multimodality approach to locally advanced-stage non-small cell lung cancer. The inclusion of this factor in the model appears of paramount importance. SEER data cannot be used to separate the patients who received induction chemotherapy alone from the patients who received surgery alone, limiting the value of the nomogram, even as a post-treatment prognostic tool because it is not clear what the treatment algorithms were in the dataset used to develop the nomogram.

Taking into consideration all these limitations, I think Qixing and colleagues¹ did their best with the data available and the study presents an interesting approach, which may add to the current controversial literature. Qixing and colleagues¹ must be congratulated for their effort in developing a preliminary tool, which may assist in patient postoperative counseling. Future refinements of the model with the inclusion of specific preoperative variables and precise information about chemotherapy will be able to provide a more reliable treatment decision aid tool to assist the optimal treatment selection for these challenging patients during tumor board discussion.

Reference

1. Qixing M, Wenjie X, Gaochao D, Shuqi C, Anpeng W, Guangfu J, et al. A nomogram to predict the survival of stage IIIA-N2 non-small cell lung cancer after surgery. *J Thorac Cardiovasc Surg*. 2018;155:1784-92.