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EDITORIAL COMMENT

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Precision follow-up for resected non-small-cell lung cancer: is it ready for prime time?

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Lung cancer remains the leading cause of cancer deaths in 2020 as stated by the World Health Organization with 1.80 million deaths. Early-stage non-small-cell lung cancer may benefit from curative-intent surgical resection with a cumulative 5-year survival of 70%. However, even patients with the most favourable prognosis who underwent the most efficient treatment could experience disease recurrence within 5 years. This fact is the justification for a systematic postoperative follow-up protocol after the resection of early-stage non-small-cell lung cancer (NSCLC). Precision medicine has made tremendous progress in advanced stage NSCLC with the development of targeted therapies and immunotherapies [1]. Therapeutic developments were correlated to better understand tumour drivers and biological behaviours [2]. Efforts have been made to translate these advances to early-stage NSCLC by investigating the field of induction and adjuvant therapies with already encouraging results [3]. However, we still lack evidence regarding the efficacy of perioperative precision medicine, which holds the promise of reducing the rate of recurrence after complete resection. Usually, postoperative follow-up protocols do not differ according to pTNM stage but conversely may differ among institutions and sometimes even from one physician to another. Deng *et al.* [4] reported that their scoring system was able to predict the timing and the site of lung adenocarcinoma recurrence after curative-intent surgery. They developed their score on a population of >1500 Chinese patients who underwent lung resection for NSCLC and validated its predictive value in a cohort of 465 additional Chinese patients. Their work suggests that metastatic recurrences occurred earlier than local recurrences and that the site and timing (> or <2 years) of recurrences could be predicted based on selected genetic and clinicopathological analyses of the phenotype of the tumour. It seems to be the first step towards personalized follow-up and perioperative precision medicine, meaning that we could imagine targeting the at-risk population with adapted therapies in future clinical studies. Surgeons have so far developed postoperative scores to predict early mortality and morbidity, thereby highlighting their primary goal of reducing the early impact of surgical lung resection seen during previous decades [5]. Improvement of surgical techniques with minimally invasive procedures and enhanced recovery after surgery dramatically improved postoperative early outcomes. Clinical prediction models of short-term results such as the Eurolung risk model [6] substantially helped in clinical practice evaluation and improvements. The needed next step is to improve long-term outcomes after lung cancer resection because local and distant recurrences remain a matter of concern. Brunelli *et al.* [6] recently reported that the Eurolung risk score could predict long-term survival after curative resection and may be useful to stratify patients for personalized follow-up or adjuvant treatment. Deng *et al.* went a step further in predicting the timing of recurrence (early <2 years or late >2 years) and the recurrence site, which will definitely help in designing future surgical oncology trials. However, even if this is a step in the right direction, the presented prediction model certainly needs improvement and adaptation to become a worldwide recognized stratification tool for follow-up and multimodal therapy strategy decision. First, the authors calculated their score from a highly selected population with lung adenocarcinoma, which is the most prevalent but not unique NSCLC subtype. In addition, at the time of the deep sequencing of tumours in research studies [7], they already incorporated clinically available partial tumour sequencing. It is highly likely that future predictive scores will be implemented by next-generation complete sequencing data. One should emphasize that patients would benefit from a careful analysis of the large surgical specimen rather than from small pieces from a tumour biopsy to determine optimal follow-up and multimodal approach strategies. The Shanghai Cancer Center score has been developed including only Chinese patients, which represents a barrier to its dissemination. Further validation studies using non-Chinese populations are needed before we can hope to develop personalized follow-up and perioperative therapies based on such scores. Finally, in addition to developing prognostic scores, the availability of predictive scores (e.g. a molecular alteration that predicts the risk of recurrence but also the efficacy of a therapeutic

intervention) that could be prospectively monitored represents the main objective to be collectively reached.

With their results, Deng *et al.* made us look in the right direction of personalized perioperative management, which may be the solution for improvements in long-term outcomes in curative intent NSCLC resection. They shed light on the need for changes in perioperative management and showed what remains to be done!

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