Second primary non-small-cell lung cancer: implications of the new adenocarcinoma classification in the challenging decision of the best surgical strategy

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Zuin et al. [1] have recently reported an interesting retrospective analysis on a relative large series of second primary non-small-cell lung cancers (NSCLCs), comparing the long-term outcomes between patients treated with a lobectomy and those where a sub-lobar resection was performed, which prompted a series of reflections by us, discussed here.

The best therapeutic strategy for synchronous/metachronous primary NSCLCs remains an open subject of discussion in the scientific community, particularly regarding the surgical approach. By commenting on the paper by Zuin et al. [1], we wish to contribute to this debate.

The International Association for the Study of Lung Cancer (IASLC) has issued a revised adenocarcinoma classification [2] jointly with the American Thoracic Society (ATS) and the European Respiratory Society (ERS). Briefly, the confusing term 'bronchioalveolar carcinoma' has been discontinued and the entire category of pulmonary adenocarcinomas has been reclassified into three different subgroups: adenocarcinoma in situ (AIS), minimally invasive adenocarcinoma (MIA) and invasive adenocarcinomas (IA). As remarked in detail by Van Schil et al. [3], this new classification has profound implications for thoracic surgeons in the management of 'early-stage' adenocarcinomas; indeed the 'early-stages' AIS and MIA should have 100% or near 100% disease-specific survival after sub-lobar resection and mediastinal sampling, respectively, where the oncological need to perform a lobar resection and mediastinal lymph nodal systematic resection is reserved for IAs only. By extreme simplification we may infer that such relevant new evidence deserves focal attention when planning the best surgical strategy in second primary NSCLCs.

First, we would like to encourage the authors to abandon the 'old' histopathological classification when matching data with the most updated TNM framework (7th). In particular, it would be extremely helpful to reclassify the vast amount of precious data according to the new classification to get significant clues (albeit with the limitations of a retrospective analysis exercise) for further prospective evaluations.

Secondly and more generally, when an 'early-stage' adenocarcinoma is detected and rightfully classified as a synchronous or metachronous primary lung tumour, the decision-making process and the best strategy of treatment should mandatorily take into the account the new IASLC/ATS/ERS classification. Indeed, the same profound implications in the management of 'early-stage' adenocarcinomas (summarized above) may have a crucial value (or even more) in the management of 'early-stage' second adenocarcinomas too. Basically, the different surgical outcomes between lobar vs sub-lobar resections in a 'second adenocarcinoma' may be potentially influenced by the different prognostic pattern at the base of the new categories (AIS, MIA and IA).

Thirdly and finally, as correctly remarked by the authors, ‘…the possibility that some cases of solitary pulmonary metastasis always exist within the group of patients with synchronous and early metachronous lung cancers could be included.’ In this context, although the IASLC/ATS/ERS classification recommended testing only patients with advanced adenocarcinomas for epidermal growth factor receptor (EGFR) mutations, we strongly advocate the assessment of EGFR mutations also in patients with synchronous/metachronous primary adenocarcinomas, because the eventual differences in clonality may indeed be a helpful tool for the differential diagnosis of pulmonary metastases vs secondary lung neoplasms [4]. We would greatly appreciate the authors reflections and reactions to the points raised.

Conflict of interest: none declared.

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LETTER TO THE EDITOR RESPONSE

Reply to Lococo et al.

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We have read and appreciated the comments of Lococo et al. [1] regarding our recently published article ‘Is lobectomy really more effective than sublobar resection in the surgical treatment of second primary lung cancer?’ [2], and it is our pleasure to reply.

The new and revised adenocarcinoma classification issued by the International Association for the Study of Lung Cancer, the American Thoracic Society and the European Respiratory Society [3] should help the thoracic surgical community to update and focus the therapeutic strategy, particularly in the field of early stage disease, but also for second primary lung cancer, where the debate between lobar and sublobar resection is still alive and controversial [4].

Although most of our adenocarcinoma patients had an invasive pattern, we agree with the suggestion of Lococo et al. about the opportunity to reclassify all adenocarcinoma.

After the publication of the classification by Travis et al. [1], a complete review of all our adenocarcinoma histopathological blocks is currently being undertaken, and epidermal growth factor receptor mutations are regularly being assessed in all new diagnoses of adenocarcinoma, regardless the stage; we hope this will help us to better understand our surgical results, even more accurately plan the therapeutic strategy and to contribute with further experience to the application and introduction of this new classification.

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