Creating a lung adenocarcinoma canvas, one brush stroke at a time

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Disclosures: Author has nothing to disclose with regard to commercial support.

Received for publication July 10, 2017; accepted for publication July 14, 2017; available ahead of print Aug 8, 2017.

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J Thorac Cardiovasc Surg 2017;154:1775-6

0022-5223/\$36.00

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<http://dx.doi.org/10.1016/j.jtcvs.2017.07.015>

In their carefully characterized large cohort of resected adenocarcinomas reported in this issue of the *Journal*, Takamochi and colleagues¹ demonstrate that epidermal growth factor receptor gene (*EGFR*) mutations are associated with better prognoses and that subtypes of mutations are not. With nearly 1000 patients analyzed, the study serves as an important guidepost as we navigate treatment courses, weighing the relative importance of each genetic change—particularly driver mutations in lung cancer, both adenocarcinomas and squamous cell carcinomas. Although Takamochi and colleagues¹ provide several important clinical characteristics, several elements are conspicuously absent. For example, it is well known that the proportion of the solid component and positron emission tomographic avidity have prognostic importance.² In addition, the new classification of adenocarcinoma has proved to be of great value in this regard.³ It would be useful to determine the added benefit of mutation testing beyond such routinely documented variables. In addition, the extent of surgery (whether a lobectomy or a segmentectomy was performed) is also relevant.

Takamochi and colleagues¹ then conclude that such a finding should be incorporated in the next iteration of the TNM staging system. This is where things get really difficult, for several reasons. First, the number of driver mutations discovered is constantly increasing.⁴ The proportions of each of these mutations are different in various ethnic origin groups, with Asians having the highest proportion.⁵ Second, several of these mutations are rare, thereby necessitating ever larger cohorts to evaluate their relative prognostic value. Third, several of these mutations may have incremental or synergistic effects, and histologic impressions may convey a summative meaning that may be easier to identify and interpret.⁶⁻¹⁰ Fourth, the results of genomic changes must be interpreted in light of changing treatment paradigms, such as increasing use of sublobar resections for the treatment of small lesions. The mathematical modeling and the cohort sizes required to accomplish this interpretation will be a challenge, one that surgeons, as an integral part of research groups,

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Central Message

The accumulation of a number of data points presented in this article, such as the prognostic impact of *EGFR* mutations, will, it is hoped, enable personalized surgical approaches to lung cancer.

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need to accomplish to create “personalized surgery” paradigms. It is tempting to consider that the current TNM staging could evolve into a “TNMG” staging, with *G* providing a genomic probability score independent of the TNM stage.

Despite these limitations, Takamochi and colleagues¹ are to be congratulated on a meticulous study of a large cohort. It is an important brush stroke for creating the canvas depicting lung adenocarcinoma.

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