The timing of chemotherapy in multimodality treatment of locally advanced lung cancer: One size does not fit all

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Central Message

The timing of chemotherapy with respect to surgery (neoadjuvant vs adjuvant) in locally advanced non-small cell lung cancer should be determined on the basis of the fitness of patients to increase compliance to treatment.

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In patients with large primary lung cancer or positive nodal disease, the timing of chemotherapy with respect to surgery remains a matter of debate. The study by Brandt and colleagues¹ is an elegant retrospective analysis on a specific subset of these patients, those with cT2-4 N0-1 non-small cell lung cancer. Although most of the studies focused on adjuvant chemotherapy in this setting, induction chemotherapy remains appealing for several reasons, including treatment of micrometastases and ability to assess treatment response, which may lead to modifying or stopping the therapy or informing appropriate selection of additional adjuvant therapies. This is becoming even more important with the increasing role of induction immunotherapy and the use of major pathologic response as the primary end point of efficacy studies.²

Brandt and colleagues¹ found a similar effect of neoadjuvant and adjuvant cisplatin-based chemotherapy on disease-free survival and overall survival.¹ This is not a completely new finding^{3,4}; however, it is based on robust single-institution data collected in a clinical database, which is one of the strengths of this analysis because it ensures standardization.

In my opinion, the most attractive feature of neoadjuvant chemotherapy is the increased compliance to systemic treatment. The only randomized trial directly comparing induction versus adjuvant treatment showed that only 67% of patients were able to complete all planned chemotherapy cycles after surgery versus 90% in the neoadjuvant arm. In addition, in the neoadjuvant group, only 5.5% of patients showed progressive disease during treatment.⁴

The results presented in the study by Brandt and colleagues¹ are reassuring because they show similar survival figures in the 2 groups. Unfortunately, the authors were

not able to perform an analysis including patients who were not able to receive chemotherapy after surgery or those who showed progressive disease during neoadjuvant chemotherapy and did not receive surgery. The inclusion of these 2 subsets of patients would have certainly added to the meaning of the analysis. In fact, based on previous data,⁴ it is probable that many more patients would have been included in the missed adjuvant group compared with the missed surgery/missed neoadjuvant chemotherapy group, likely increasing the survival benefit in the intention to neoadjuvant treatment group.

Fitness of the patient at the time of diagnosis should be taken into account when deciding the timing of chemotherapy. Previous studies have shown that pulmonary function and quality of life are at their lowest levels 4 weeks after surgery. This is the time when adjuvant chemotherapy is supposed to be started.

A young, fit patient would likely experience an uneventful postoperative course and be able to receive adjuvant chemotherapy. On the other hand, an 80-year-old patient with poor pulmonary function and other underlying comorbidities would probably not be able to tolerate full-dose and timely chemotherapy on top of lung resection. Knowing that the preoperative or postoperative administrations are at least equivalent is reassuring.

I want to congratulate Dr Brandt and colleagues at Memorial for their timely and important analysis.

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