

Letter to the Editor

Clinical Implications of Postoperative Radiotherapy on Patient Survival in Stage IIIA Resected Lung Cancer: More Variables Should Be Considered

Re: Gao F, Li N, Xu Y, et al. Effects of postoperative radiotherapy on survival of patients with stage IIIA resected non-small cell lung cancer: analysis of the SEER database. *J Natl Compr Canc Netw* 2020;18(6):718–727.

We would like to comment on the recent article by Gao et al,¹ titled “Effects of Postoperative Radiotherapy on Survival of Patients With Stage IIIA Resected Non-Small Cell Lung Cancer: Analysis of the SEER Database.” The authors found that postoperative radiotherapy (PORT) significantly improved overall survival and decreased lung cancer-related mortality in patients with stage IIIA, N2 disease with ≥ 6 positive lymph node metastases. The authors should be commended on their efforts to address an important question in thoracic oncology. However, we have some concerns.

First, as shown in Tables 1 and 2, the authors listed the information on postoperative chemotherapy, which was a significant parameter in patients with stage IIIA non-small cell lung cancer (NSCLC). However, the sequence of radiotherapy and surgery could be obtained in the SEER database, but the sequence and details of chemotherapy regimens was not provided.^{2,3} How could the authors ensure that the chemotherapy was not given before surgery given that neoadjuvant chemotherapy might be administered to patients with suspected stage IIIA-N2 disease?

Second, given that the authors provided the number of positive lymph nodes in the tables, why was the total number of harvested nodes, which possibly affected decisions regarding PORT, not available? More specifically, patients with a lower lymph node yield along with metastatic mediastinal lymph nodes were more likely to receive PORT to improve local control. Meanwhile, it has been reported that a greater lymph node yield was associated with a greater number of positive lymph nodes and could correlate with a lower probability of stage migration.⁴ Therefore, the data on examined lymph nodes in each cohort are important and should have been displayed.

Finally, the SEER database is not an ideal tool for assessing the role of PORT in resected NSCLC because it does not include information on surgical margin. As shown in Figure 2, is it inspiring to show patients with resected N0 and N1 disease undergoing PORT who have worse survival compared with those undergoing non-PORT? A major source of potential bias is that surgeons and radiation therapists might have identified adverse prognostic factors during or after surgery, which led to referring patients for radiation therapy consultation. An important prognosticator is the quality of surgical resection, including surgical margin status and adequacy of nodal staging. Therefore, R1/R2 resection and inadequate lymph node sampling probably accounted for

the significantly poorer survival in patients with N0/N1 disease receiving PORT. These points should be addressed before the results can be interpreted into clinical practice.

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Authors' Reply

to Letter to the Editor by Chen et al

We thank Chen et al for their thoughtful comments on our article, “Effects of Postoperative Radiotherapy on Survival of Patients With Stage IIIA Resected Non-Small Cell Lung Cancer: Analysis of the SEER Database.”¹ We appreciate their interesting points.

According to the inclusion criteria in our study, we selected patients pathologically diagnosed with stage IIIA non-small cell lung cancer (NSCLC) in 2010 through 2015. According to the NCCN Guidelines, adjuvant chemotherapy is strongly recommended for patients with resected stage IIIA disease, including those with resected stage IIIA-N2 disease who can tolerate chemotherapy.² It is undeniable that preoperative

neoadjuvant chemotherapy is applied to patients with IIIA-N2 disease, but in the real world, the number of people who received neoadjuvant chemotherapy is smaller than the number who received adjuvant chemotherapy for all patients with IIIA NSCLC. However, in light of Chen et al's comments, use of the word *chemotherapy* would be more accurate.

At present, there is no clear standard for postoperative radiotherapy (PORT) use in accordance with the total number of harvested nodes. As previously reported,^{3,4} the number of positive lymph node metastases is an independent prognostic factor for survival and prognosis in NSCLC.

Additionally, in our study, the numbers of lymph nodes dissected in a sizable portion of patients with IIIA disease were unknown. Therefore, in order to reduce the selection bias of retrospective study, we did not analyze the impact of PORT on prognosis from dissected nodes. Thus, our study focused on the effect of PORT on the prognosis of patients with different numbers of positive lymph nodes.

It is notable that the SEER database, as an important large-scale retrospective database, collected information from a large number of patients, including chemoradiotherapy and prognosis data, which provides valuable reference for clinical