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Commentary: Is surgery better than chemoradiation for T3N1M0 non–small cell lung cancer?

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Currently, there are few guidelines on how to treat clinical T3N1M0 stage IIIA non–small-cell lung cancer (NSCLC). The recommendations on locally advanced lung cancer from the American College of Chest Physicians¹ and the European Society for Medical Oncology² do not specifically detail algorithms for T3N1M0 NSCLC. The National Comprehensive Cancer Network (NCCN) does provide treatment recommendations for T3N1M0 NSCLC,³ but perhaps because T3N1M0 NSCLC is relatively uncommon (especially compared with T3N0 NSCLC or T3N2 NSCLC),⁴ data supporting the NCCN treatment guidelines for T3N1M0 NSCLC are limited. Until now, there have been no randomized trials or prospective or retrospective studies specifically comparing definitive chemoradiation and surgery for T3N1M0 NSCLC.

In this issue of the *Journal*, Rahouma and colleagues⁵ provide much-needed data on outcomes of surgery versus definitive chemoradiation for patients with T3N1M0 NSCLC. The authors evaluated 1937 patients who underwent surgery (with induction and/or adjuvant chemotherapy with or without radiation) and 1844 patients who underwent definitive chemoradiation for clinical T3N1M0 NSCLC

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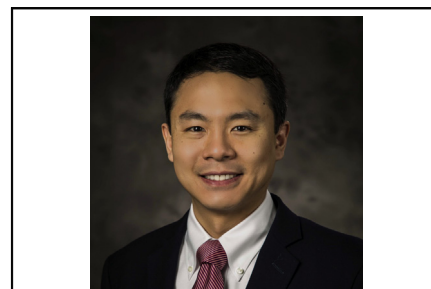
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CENTRAL MESSAGE

In appropriately selected patients, surgery for T3N1M0 lung cancer is likely associated with improved survival compared with definitive chemoradiation, but further research evaluating different types of T3 tumors is needed.

between 2004 and 2014. They found that in the surgery group, among patients who did not receive preoperative chemotherapy or radiation (n = 1518), 19% had pathological N0 disease and 9.5% had pN2 disease. The surgery group had better survival than the definitive chemoradiation group in unadjusted and multivariable analyses. The authors also performed a propensity score–matched analysis in which they created a cohort of 1081 patients with cT3N1M0 NSCLC who underwent surgery (with induction and/or adjuvant chemotherapy with or without radiation) with similar baseline characteristics as 1081 patients who underwent definitive chemoradiation. Five-year overall survival was significantly greater for the surgery group when compared with the definitive chemoradiation group (35.7% vs 19.0%).

The study has several strengths. By using the National Cancer Data Base, the authors were able to include a large

number of patients with cT3N1M0 NSCLC and specifically evaluate the outcomes of this particular subset of stage IIIA disease. The follow-up time of around 52 months was relatively long. The authors also used included propensity score matching and multivariable Cox proportional hazards modeling to minimize confounding and bias. The authors properly acknowledged the limitations of their study—that are related to the limitations of the NCDB—which notably include lack of detail regarding the designation of T3 and details regarding the N1 (eg, hilar, interlobar and intersegmental lymph nodes) lymph nodes. It is also important to note that the definition of T3 itself has changed over time. The authors included T3 tumors that had been staged according to the 6th and 7th editions, and there have been some subtle but important changes in the 8th edition (eg, T3 tumors no longer include those greater than 7 cm in size but rather those between 5 and 7 cm).⁶

There are key takeaways from the study that can be used to guide practice. First, for T3 N1 tumors, clinical staging can have significant inaccuracies. In their cohort, Rahouma and colleagues found that 19% of patients were overstaged clinically and actually had pN0 disease. This highlights the importance of comprehensive pathological staging. Second, nationally in the United States, nearly one-half of the patients received chemoradiation as opposed to surgery, suggesting underutilization of surgery. Third, given how much better survival was in the surgery group compared with the definitive chemoradiation group, there probably is a survival benefit associated with surgery, although this finding requires further investigation in a randomized setting or at least in prospective or retrospective studies that not only evaluate T3N1M0

disease, but also specifically examine outcomes for the different types of T3 tumors that exist. Owing to the length of time it takes to design a randomized trial and the need for data now to guide clinical practice, further investigation of the other type of T3N1 tumors will probably rely on prospective or retrospective multi-institutional data that capture specifics about the T3 tumor and the N1 lymph node.

In the meantime, as we await findings from future analyses, this study by Rahouma and colleagues is a welcome addition to the literature and provides evidence to recommend surgery for operable T3N1 NSCLC for carefully selected patients whose care and treatment plans are discussed in a multidisciplinary setting.

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