

# Timing of surgery after neoadjuvant chemoradiation in stage IIIA NSCLC impacts overall survival

6 October 2016, by Jacinta Wiens, PhD

The timing of surgery after neoadjuvant chemoradiation in patients with stage IIIA non-small cell lung cancer (NSCLC) affects the overall survival of patients receiving trimodality therapy.

Approximately one third of all NSCLC patients have locally advanced (stage III, subtypes IIIA and IIIB) disease at the time of diagnosis, with a five-year survival ranging from 7 to 19%. Patients with stage III NSCLC represent a significant clinical challenge due to the poor prognosis associated with this stage of the disease. Trimodality therapy involving the use of radiation concurrently with chemotherapy, otherwise known as neoadjuvant chemoradiation therapy (NCRT), followed by surgery is an acceptable treatment strategy for stage IIIA patients with resectable tumors and limited mediastinal node (N2) involvement. However, trimodality therapy has not been shown to have significant survival advantage over definitive chemoradiation therapy and the optimal interval to surgery (ITS) after completion of NCRT has not been well explored.

A group of investigators conducted a retrospective analysis to examine whether the ITS after completion of NCRT correlates with survival outcomes in clinical stage IIIA, T1-3 N2 NSCLC patients using patient records between 2004 and 2013 from the National Cancer Database (NCDB). Patients were categorized based on the interval between chemoradiation and surgery (0 - ?3 weeks, 3 - ?6 weeks, 6 - ?9 weeks, and 9 - ?12 weeks). Patients with stage IIIB and other clinical stages were excluded from this study. Overall survival (OS) was examined using Kaplan-Meier method and log-rank tests and bootstrapped Cox proportional hazards model was used to determine significant contributors to OS.

The results of the study published in the *Journal of*

*Thoracic Oncology*, the official journal of the International Association for the Study of Lung Cancer (IASLC), showed that of the 1,623 NSCLC patients identified with clinical stage IIIA, T1-3 N2 disease, 7.9% underwent surgery at 0 – ?3 weeks, 50.5% underwent surgery 3 – ?6 weeks, 31.9% underwent surgery 6 - ?9 weeks, and 9.6% underwent surgery 9 - ?12 weeks after NCRT. In the univariate analysis, there was no significant difference in OS between the patients that underwent surgery at 0 – ?3 weeks or 3 – ?6 weeks. Decreasing OS was observed in patients that underwent surgery at 6 - ?9 weeks and patients that underwent surgery 9 - ?12 weeks fared significantly worse than those patients that had surgery at 0 – ?3 weeks after NCRT. Multivariate analysis, which accounted for patients receiving lobectomy versus pneumonectomy, showed no significant difference in OS for patients who underwent surgery within 6 weeks of NCRT. However, a significant decrease in OS was observed in patients who had surgery 6 - ?9 weeks (HR: 1.33, 95% CI: 1.01-1.76, P=0.043) and 9 - ?12 weeks (HR: 1.44, 95% CI: 1.04-2.01, P=0.030) after NCRT.

The authors comment that, "The results of our study suggest that waiting greater than 6 weeks to have surgery after NCRT may negatively impact both perioperative mortality and OS. This finding concurs with prior data that recommend an ITS following NCRT of less than 8 weeks. Minimizing the time between NCRT and surgery is thought to improve outcomes because it reduces the risks associated with operating in the presence of radiation pneumonitis. Although radiation may affect surgical outcomes anywhere between 3 and 12 weeks, it is particularly troublesome at the tail end of that interval when a patient is at highest risk for the development of fibrosis, narrowing of the pulmonary vessels, microvascular thrombosis, and

collagen deposition by fibroblasts into the interstitium, increasing the risk for postoperative complications."

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