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Title: Late radiation injury in preoperative chemoradiotherapy

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Body: Background: Preoperative chemoradiotherapy (CRT) seems to increase survival rates in advanced non-small cell lung cancer. In the evaluation of this strategy, overall survival (OS) and early complications are generally referred. However, the influence of induction CRT remains controversial. Therefore, the aim of this study is to investigate late radiation injury. Methods: From 1996 to 2010, 167 patients treated with major lung resections after CRT (139 lobectomy, 24 pneumonectomy, 3 wedge resection, and 1 segmentectomy) were enrolled. They were treated with platinum-based regimens and had 40 Gy delivered to the primary tumors, hilum and mediastinum. The postoperative condition of residual lungs was assessed in 142 cases. Results: 72 patients died. Of 72, 49 died of lung cancer, 17 died of other disease, and 5 died of postoperative complications (operative mortality was 3.0%). Of other disease death, 3 aspergillosis and 2 idiopathic pulmonary fibrosis were related to induction therapies. The 5-year OS rates of p-stage 0, 1a, 1b, 2a, 2b, 3a and 3b/4 were 72.0%, 80.5%, 68.2%, 55.6%, 46.9%, 30.5% and 0%, respectively. The 5-year OS rates of p-N0, N1, and N2 were 69.5%, 50.7% and 22.0%, respectively. In 142 cases assessed postoperative condition of residual lungs, 27(19.0%) mild fibrosis, 5(3.5%) severe fibrosis, 37(26.1%) shrinkage, and 9(6.3%) cavity/dead space formation occurred. Radiation injury appeared when residual normal lung was irradiated. Conclusions: Preoperative CRT increased survival rate in patients who achieved p-N0, but was associated with higher rates of pneumonectomy and operative mortality. Radiation might affect postoperative devastation in residual lungs. This therapy should be performed cautiously.