

Commentary: Return to intended radiation therapy— Criteria for resection?



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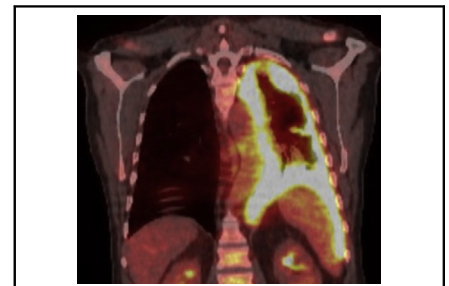
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Positron emission tomographic scan demonstrating malignant pleural mesothelioma.

Central Message

Rational combinations of existing and emerging therapies should be investigated in the management of malignant pleural mesothelioma.

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Malignant pleural mesothelioma (MPM) is a locoregionally aggressive malignancy with dismal outcomes. Trimodality therapy including neoadjuvant chemotherapy, surgical resection, and adjuvant radiotherapy (RT) is associated with a survival benefit in selected patients.^{1,2} However, 50% to 60% of patients are unable to complete trimodality treatment—resection is deferred because of disease progression during chemotherapy, and RT is deferred because of postoperative complications.³ In their article in this issue of the *Journal*, Nelson and colleagues⁴ explore factors affecting the likelihood of returning to RT after surgical resection for MPM.

Nelson and colleagues⁴ reviewed the medical records of patients with MPM completing surgical resection and the reasons that they did not receive RT. Sixty-five percent of patients completed RT, which is consistent with published results.⁵ On multivariate analysis, smoking history and American Society of Anesthesiologists (ASA) score greater than 3 were associated with decreased probability of RT completion (odds ratios, 0.42 and 0.27, respectively). More than two-thirds of patients had ASA scores greater than 3, which, if accurate, should identify patients with severe systemic disease.⁶ Although ASA score is used by anesthesiologists in the preoperative assessment, it is unlikely that patients with severe systemic disease were selected for aggressive resection by this experienced group, which demonstrates the limitations of ASA score. Preoperative comorbidities and performance status measures, such as Karnofsky and Eastern Cooperative Oncology Group measures, which can help to stratify patients, were not included in the study. On univariate analysis, cardiovascular or pulmonary complications were associated with a 50% decreased likelihood of RT completion.

Type of resection did not translate into significant differences in likelihood of RT completion. The limited prognostic value of resection type is consistent with previous findings from meta-analyses that, although early

postoperative mortality is higher with extrapleural pneumonectomy, there is no difference in long-term survival.⁷ Whether patients with higher rates of comorbidities were selected for pleurectomy decortication rather than extrapleural pneumonectomy and whether this influenced results should be considered. Nevertheless, because resection type is not prognostic for completion of trimodal therapy, Nelson and colleagues⁴ do not suggest changes to the standard of care regarding choice of resection type.

Nelson and colleagues⁴ suggest that patients with higher baseline rates of comorbidities should not be considered for cytoreduction. Respiratory complications are common after resection for MPM and can account for delay or avoidance of RT. These patients, however, may also be at risk for significant respiratory complications after RT.⁸ Furthermore, 13% of patients did not complete RT because of bulky remaining or recurrent tumor, perhaps as a result of tumor location; it is unlikely that these patients would benefit from RT without surgery. As the authors' group previously demonstrated, multimodality therapy including surgery is superior to medical management alone.⁹ Failure to complete RT thus does not justify forgoing surgery.

Patients who have a lower likelihood of RT completion or are at risk of surgical complications might benefit from emerging therapies such as immunotherapy to augment or replace the trifecta. RT may boost antitumor immune responses, especially when given at or in a rationally based

dose or regimen.¹⁰ Rational combinations of existing and emerging therapies should be investigated in the management of MPM.

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