Therapeutic R2 resection for pleural mesothelioma

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Central Message

Macroscopic complete resection in MPM, although an R1 resection, remains the objective of curative-intent surgery for this disease.

See Article page 2724.

Why would resection of the majority of a pleural tumor that spreads dominantly by local invasion not extend the time required for it to take the life of its host? In this issue of the *Journal*, Batirel¹ presents his single institution experience with resection-based multimodal therapy for malignant pleural mesothelioma (MPM). In an unadjusted retrospective comparison of 75 patients undergoing macroscopic complete resection (MCR) for MPM with 57 patients undergoing partial (incomplete) resection, there was no difference in overall survival, a finding supported by a propensity-matched analysis.¹ Perhaps these results should not be surprising because MPM behaves biologically similar to advanced thymic epithelial tumors for which subtotal (R2) resection is associated with extension of life.^{2,3}

To the extent that any surgical principle can be established in MPM, MCR is considered a central tenet of mesothelioma surgery.⁴ The foundation of MCR in mesothelioma is based on a variety of single institution datasets, well cited in the accompanying article, that independently associated MCR with improved overall survival. Similar support for MCR is evidenced by the International Association for the Study of Lung Cancer Mesothelioma Database in which 1493 patients undergoing curative-intent surgery had longer overall survival than the 732 patients undergoing palliative procedures, including partial pleurectomy.⁵ Whereas each of these datasets is retrospective and limited, the reader will speculate as to why survival was not improved by MCR in the current study. The series by Batirel¹ represents a commendable effort in MPM surgery, and the author appropriately acknowledges the shortcomings that temper its interpretation. Specifically, the MCR and non-MCR groups were disproportionate with respect to T stage, unexplored nodal status, and receipt of adjuvant therapy, and propensity matching resulted in comparator groups consisting of only 23 patients per group. Most important, the authors humbly admit that the study is underpowered; 355 subjects would be required to

demonstrate a 10% difference in overall survival between MCR and non-MCR cohorts. Thus, a definitive relationship between completeness of resection and survival could not be established.

What is obvious from this and other contemporary reports is that progress in the treatment of MPM is slow and measured generally against historical controls. In the current study, propensity-matched patients undergoing MCR survived for a median of only 13.3 months, and only 15% were alive at 5 years. It can be rationally stated that the predominant reason for our continual reporting of such dismal survival statistics in surgically treated MPM is an inability to overcome local recurrence, which affects approximately three quarters of patients.⁶ Our readers should understand that MCR remains the objective of surgery for MPM; however, by its inability to eliminate microscopic disease, MCR is an R1 resection. Although it is reasonable to hypothesize that the long-term outcomes after R1 resection and R2 resection with minimal residual macroscopic disease may not be substantial, additional data are required to make such a conclusion. Taken together, advances in surgical technique, although important, are capped in their ability to affect survival in MPM, and the greatest unmet need remains the development of improved measures to locally and systemically control micrometastatic disease.

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