



## How Old is Too Old to Operate for Mesothelioma?

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Malignant pleural mesothelioma (MPM) is a highly lethal cancer which, to date, has seen few improvements in overall survival despite best practices. Owing in part to the rarity of the disease, there is a paucity of evidence-based data from adequately powered randomized trials, and no consensus regarding optimal multimodal treatment. Surgical management strategies, including extrapleural pneumonectomy and pleurectomy decortication, have been widely employed as part of this treatment paradigm. While surgery has been demonstrated (in nonrandomized series) to provide a survival benefit in highly selected patients, the data suffer from the lack of standardized surgical techniques and expertise.<sup>1–3</sup> As such, careful patient selection remains at the center of our treatment algorithm and is a critical determinant of overall patient outcome.

In the current issue of *Annals of Surgical Oncology*, Verma et al.<sup>4</sup> utilize the National Cancer Database to assess national practice patterns and postoperative/survival outcomes in 4526 geriatric patients ( $\geq 80$  years of age) with MPM. They report that 63% of patients were observed without treatment, 22% received chemotherapy alone, 13% received surgery alone, and 2% underwent both surgery and chemotherapy. Postoperative 30- and 90-day mortality was found to be 11% and 28.5%, respectively. A propensity matched analysis of surgery/chemotherapy versus chemotherapy alone demonstrated a survival benefit of 13.4 months versus 6.5 months ( $p = 0.002$ ) in favor of the combined treatment approach.

While these results underscore the importance of patient selection, one major limitation is the lack of granularity into the ‘functional age’ of the patients selected for various

treatments. As the authors discuss, unknown clinical factors, including performance status, nutrition status, and other comorbidities, likely leads to biased survival statistics, and may account for the high postoperative mortality rates.

Of critical importance is that of the 663 patients who received surgery, 85% ( $n = 566$ ) did not receive adjuvant treatment. As surgery alone is not a recognized treatment option for MPM, we do not know the potential negative effect on survival in patients who were unable to receive/tolerate adjuvant therapy as a result of the surgery itself. This must be taken into account when considering the inclusion of surgery into the management algorithm of patients with mesothelioma.

While surgical strategies for mesothelioma continue to be refined, and intraoperative cytoreductive strategies explored (i.e. photodynamic therapy and chemotherapy lavage, among others), it is uncertain what role surgery will ultimately have in the management of MPM.<sup>5</sup> However, it is reasonable to suspect that future advances in mesothelioma therapy will be derived from breakthroughs in adjuvant and/or neoadjuvant treatment regimens. Much ongoing translational research is dedicated to such novel therapeutic strategies, including immune checkpoint inhibition, angiogenesis inhibition, tyrosine kinase inhibition, and viral therapy, as well as novel radiation strategies.<sup>6–8</sup> When selecting patients with mesothelioma for surgery, it is paramount to consider the ability to offer adjuvant treatment. In this regard, the present study is informative when managing geriatric patients with MPM.

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