

Safety and efficacy of trimodality therapy in patients undergoing extrapleural pneumonectomy

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Malignant pleural mesothelioma (MPM) is a rare but rapidly deadly disease (1). Macroscopic complete resection (MCR) is the goal of surgery (2). MCR seems to have the most significant impact on survival in patients undergoing multimodality treatment for MPM. The role of surgical resection in the management of MPM remains controversial. The selection criterion to perform either extrapleural pneumonectomy (EPP) or extended/radical pleurectomy/decortication (PD) rely not only on the cardio-pulmonary status of the patient, tumor stage and intraoperative findings but is strongly dependent also on surgeons' decision and philosophy. This is reflected by a recent survey of opinions and beliefs among 802 thoracic surgeons, in which EPP was believed to be more effective than PD (3). Nonetheless, either surgery might achieve MCR.

There is no evidence-based consensus about the treatment of MPM due to its rarity and the lack of large prospective randomized trials in multicenter settings. Therefore, the authors have to be congratulated for a concise, succinct and very informative systematic review with regard to trimodality therapy (TMT) involving EPP with neoadjuvant or adjuvant chemotherapy and adjuvant radiotherapy (4). Primarily, the authors assessed the safety and efficacy of TMT in patients undergoing EPP as surgical treatment modality.

EPP is the most aggressive surgical procedure. It involves the en bloc resection of the visceral and parietal pleura, lung, pericardium, and diaphragm. Complex surgical procedures come with mortality and morbidity, respectively. In this systematic review, mortality and morbidity ranged between 0-12.5% and 50-82.5%, respectively. However, complications of surgery may cause delay or refusal of chemotherapy and/or radiation which might be linked

directly to inferior outcomes in terms of survival. This is reflected by the fact that only approximately 50-60% of the patients completed the TMT in recent large prospective studies (5,6). As recommended by the NCCN Guidelines, EPP should be performed by board certified thoracic surgeons on highly selected patients (7). Thus, surgical expertise and patient selection play a major role to define EPP as a safe procedure.

Recurrence of disease occurs locally and distantly irrespective of the aggressiveness of surgery. The present study demonstrated that treatment failure in terms of overall disease recurrence was as high as up to 84%. The progression-free-survival ranged between 10.1 and 16.3 months. There is no doubt about the recurrence of disease irrespective of the aggressiveness of surgery. But further treatment options after EPP remain difficult. In case of recurrence only about 25% of the patients receive additional chemotherapy after EPP and TMT (5). Generally, approximately 85% of the patients die within the first 3 months in event of recurrence (8). On the other hand, EPP is associated with prolonged survival. Overall median survival ranged from 12.8-46.9 months. Non-surgical treatment options have to be compared to EPP outcomes. Best supportive care as the baseline therapy results in overall survival of 4.5 months, whereas early palliative chemotherapy is associated with overall survival of 14 months (9). Chemoradiation using the pleural IMRT technique results in promising median survival of 17 months (10). Thus, the role EPP within TMT remains controversial with regard to the efficacy of EPP but EPP offers long-term survival in highly selected patients.

The take home message of this systematic review

is that EPP within TMT is associated with acceptable perioperative outcomes and long-term survival in highly selected patients treated in specialized centers. But, the philosophy of limiting the surgery related morbidity and mortality as well as maintaining physiological reserve, while overall not compromising the oncological aggressiveness, might be a key component of long-term survival for MPM patients. There are several multimodality treatment studies using lung-sparing PD (11-13). These studies were associated with safety and efficacy as well. Lung-sparing procedures lead to significant improvement of pulmonary function and quality of life (14,15). Maybe less could be more for MPM patients. I hope that Cao and colleagues investigate the safety and efficacy of lung-sparing PD within multimodality treatments in a forthcoming systematic review.

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