Editorial

International trends in the clinical epidemiology of malignant pleural mesothelioma

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The role of surgical treatment for malignant pleural mesothelioma (MPM) is still subject to debate. A recent paper in the Annals of Thoracic Surgery explored treatment patterns for patients with MPM in the United States, based on information from the National Cancer Database (NCDB) (1). The patient series comprised 19,134 cases of MPM, diagnosed from 2004 to 2013, and 26% were treated by surgical intervention. The NCDB captures approximately 70% of all cancer cases in the USA and is increasingly used for comparative effectiveness research. An update study including 2014 data reported no change in the use of trimodality treatment over time, while median overall survival improved from 8 to 11 months (2). A third paper that was based on the same NCDB data used propensity score matching to assess prognostic factors and reported that cancer-directed surgery was associated with improved survival (hazard ratio 0.78) (3).

Nevertheless, it is generally known that the evaluation of treatment effects in observational research is hampered by multiple types of bias. Especially selection bias and immortal time bias—also called guarantee time bias—can confound the benefits of surgery for mesothelioma (4). An Italian retrospective multicenter analysis of 1,365 consecutive patients suggested that patients with good prognostic factors had a similar survival whether they received medical therapy only, or combined with surgery (5). A British modeling exercise elegantly confirmed that the selection criteria for surgery could by itself explain the favorable results in surgical series (6). Moreover, patients treated by neoadjuvant chemotherapy will receive a 'survival head start', whenever survival is calculated from the day of diagnosis or the day of starting chemotherapy. Also, the trimodality subgroup, receiving additional radiotherapy, will not contain patients who died in the postoperative phase. Propensity score matching is a powerful tool to control for confounding by indication but it is less effective in the evaluation of sequential treatment combinations. Intention-to-treat analysis is extremely difficult in retrospective series, but analyses with the landmark method or time-dependent covariates can be applied to attenuate the impact of immortal time bias. The flawed results from retrospective studies and the absence of evidence from randomized trials ultimately leave us with marginal information regarding the benefits of surgical treatment.

The NCDB studies suggest that surgery is more common in the USA than in European countries (*Table 1*). This, however, reflects variation in definitions. Surgery comprises cytoreductive operations such as pleurectomy/decortication and extrapleural pneumonectomy, but even procedures like palliative pleurectomy and minor debulking may have been coded as surgery. Postoperative morbidity and mortality is an important concern in patients with a limited life expectancy. NCDB data revealed a 30- and 90-day postoperative mortality of 6.3% and 15.5%, respectively (3), corroborating recommendations that MPM surgery should be performed in dedicated centers. While cancer registries

Table 1 Selected review of population-based studies reporting treatment patterns for MPM

Reference	Data source	Period	N	Surgery (%)	Surgery + chemotherapy (%)	Median survival (months)
(1)	NCDB	2004–2013	19,134	26	15	–
(2,3)	NCDB*	2004–2014	20,561	17	11	8–11
(7)	SEER-Medicare**	2005–2009	1,625	30	15	8
(8)	England	2007–2011	5,808	8	2	9.5
(8)	Netherlands	2007–2011	2,306	3	2	9.2
(8)	Belgium	2007–2010	900	16	11	10.7

*, stricter definition of surgery; **, aged 65 years and older, including 6% peritoneal mesothelioma. MPM, malignant pleural mesothelioma.

may not be able to assess the efficacy of surgical treatment, they can monitor patterns of care and supply real-world information about 30- and 90-day postoperative mortality. Adequate coding of the surgical procedures will be required to allow international comparisons.

The controversial role of surgical treatment is reflected in two recent guidelines. Whereas the ASCO guideline recommends maximal surgical cytoreduction in selected patients with early stage disease (9), the BTS guideline recommends against extrapleural pneumonectomy for disease control and calls the role of pleurectomy/decortication controversial (10). With the advent of novel therapeutics such as targeted medication and immuno-enhancing treatment, selection criteria for surgery may change in the near future, but for now, recruitment into trials is the best option to secure progress.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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