Editorial

Malignant pleural mesothelioma—the impact of globalization on rare diseases

M. Alireza Hoda, Till Ploenes, Clemens Aigner

Mesothelioma Program, Department of Thoracic Surgery and Thoracic Endoscopy, University Medicine Essen-Ruhrlandklinik, Essen, Germany
Correspondence to: Clemens Aigner, MD, MBA. Prof. of Thoracic Surgery, University Medicine Essen-Ruhrlandklinik, Essen, Germany. Email: clemens.aigner@uk-essen.de.

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Staging in malignant pleural mesothelioma (MPM) still remains a huge challenge. Accurate staging is the basis of a more customized treatment approach for MPM patients. In this review all relevant steps towards the current staging system based on the International Association for the Study of Lung Cancer (IASLC) mesothelioma database are pointed out (1). The effects of international cooperation and the contribution towards global databases are particularly important in rare diseases where even national databases fail to provide sufficient evidence for diagnostic or therapeutic algorithms.

In the past 40 years, numerous efforts have been undertaken to establish and improve staging of MPM patients with internationally accepted staging systems. Early efforts by Butchart (2) or Tammilehto's (3) classification proposals have been an attempt for staging, however both have lacked important issues such as detailed TNM descriptors.

The TNM-based staging system in MPM has been created 23 years ago through an international collaboration, when the IASLC and the International Mesothelioma Interest Group (IMIG) joined forces and analyzed surgical databases and available clinical trial data in MPM. They created a staging system which was able to identify patient subgroups with early stage of MPM according to the extent of disease spread on the pleural cavity and degree of invasion of surrounding tissue (4). Consequently, early stage MPM was diagnosed more often compared to the past. However, although validated in surgical series and used in retrospective as well as in prospective clinical trials, this first widely accepted IMIG staging system had some important limitations. Especially it's applicability to non-surgical patients, the judgment of nodal involvement and the influence of type of surgery were questioned. Subsequently, to improve these shortcomings of the first IMIG staging system, an alternative Brigham Staging System was proposed based on tumor, resectability and nodal status (5). Since there were many differences in the T and N factor in a large series of patients in comparison to the IMIG staging system, a new approach was warranted to improve staging in MPM.

By establishing a large international staging database, the IASLC in collaboration with members of the IMIG, went on a quest 8 years ago to improve staging in MPM. In this retrospective database, data were collected from 15 centers on four continents, analyzed and finally published 5 years ago (6). The key findings of this effort were: the poor correlation of clinical and pathological TNM staging, the lack of detailed data to revise more effectively T and N staging categories, the impact of MPM histological subtypes on outcome, the influence of the intent of surgical procedure and the use of adjuvant treatment on survival, and the better outcome of stage I patients treated by extrapleural pneumonectomy (EPP) in comparison with pleurectomy/decortication (P/D), both in curative intent. Interestingly, multivariable analyses could

not identify a significant difference in survival between stages I and II. This finding made it quite clear, that the amount of clinicopathologic data available in this large registry was not sufficient to define patients with early stage mesothelioma and identifying those individuals with the very best outcome.

The first IASLC MPM database provided also interesting additional analyses on prognostic variables for MPM, including variables such as use of other treatment modalities than surgery, patient's history (smoking, asbestos exposure, weight loss), performance status, clinical symptoms and laboratory parameters (7). These variables served to develop prognostic models for patients in three different scenarios but the main limitation for these analyses were missing data for key clinical parameters. However, the prognostic importance of laboratory data, already discovered by previous studies, was validated.

Four years ago, to address these shortcomings and controversies raised by the first IASLC MPM database, the second IASLC MPM database was initiated. One of the main goals of this second effort was the improvement of available information with regard to the T, N, and M descriptors analyses. Furthermore, the improved data acquisition should lead to changes in the T and N categories and stage grouping of the existing first IASLC database. Twenty-nine centers from four continents submitted data from patients mostly diagnosed between 2000 and 2013 to this second MPM registry.

Detailed analyses of this second MPM IASLC database served as the main source for the proposed changes in the 8th edition of the American Joint Commission of Cancer (AJCC) and the Union for International Cancer Control (UICC) staging systems (8-10).

However, besides these tremendous international efforts, the goal of an accurate staging of MPM has not been reached. The quest for this Holy Grale will have to continue, since even the improved second database of the IASLC shows still some limitations. In general, clinical databases in MPM will always have limitations since these registries, include mainly (I) data from patients who have been treated surgically, (II) data on clinical staging of MPM patients by non-surgical means is not always fully available (III) lack analyses of regional differences of MPM outcome.

Only through international collaboration and more awareness for detailed data acquisition, especially in non-surgical MPM patients and staging procedures, these databases can be optimized and serve as sources of more accurate TNM based staging systems.

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Footnote

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

References

1. Pass H, Giroux D, Kennedy C, et al. The IASLC Mesothelioma Staging Project: Improving Staging of a Rare Disease Through International Participation. J Thorac Oncol 2016;11:2082-8.
2. Butchart EG, Ashcroft T, Barnsley WC, et al. Pleuropneumonectomy in the management of diffuse malignant mesothelioma of the pleura. Experience with 29 patients. Thorax 1976;31:15-24.
3. Tammilehto L, Kivisaari L, Salminen US, et al. Evaluation of the clinical TNM staging system for malignant pleural mesothelioma: an assessment in 88 patients. Lung Cancer 1995;12:25-34.
4. Rusch VW. A proposed new international TNM staging system for malignant pleural mesothelioma. From the International Mesothelioma Interest Group. Chest 1995;108:1122-8.
5. Sugarbaker DJ, Flores RM, Jaklitsch MT, et al. Resection margins, extrapleural nodal status, and cell type determine postoperative long-term survival in trimodality therapy of malignant pleural mesothelioma: results in 183 patients. J Thorac Cardiovasc Surg 1999;117:54-63; discussion 63-5.
6. Rusch VW, Giroux D, Kennedy C, et al. Initial analysis of the international association for the study of lung cancer mesothelioma database. J Thorac Oncol 2012;7:1631-9.
7. Pass HI, Giroux D, Kennedy C, et al. Supplementary prognostic variables for pleural mesothelioma: a report from the IASLC staging committee. J Thorac Oncol 2014;9:856-64.
8. Nowak AK, Chansky K, Rice DC, et al. The IASLC Mesothelioma Staging Project: Proposals for Revisions of the T Descriptors in the Forthcoming Eighth Edition of the TNM Classification for Pleural Mesothelioma. J Thorac Oncol 2016;11:2089-99.
9. Rice D, Chansky K, Nowak A, et al. The IASLC Mesothelioma Staging Project: Proposals for Revisions of the N Descriptors in the Forthcoming Eighth Edition of the TNM Classification for Pleural Mesothelioma. J

Thorac Oncol 2016;11:2100-11.
10. Rusch VW, Chansky K, Kindler HL, et al. The IASLC Mesothelioma Staging Project: Proposals for the M Descriptors and for Revision of the TNM Stage Groupings in the Forthcoming (Eighth) Edition of the TNM Classification for Mesothelioma. J Thorac Oncol 2016;11:2112-9.

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