MPM Nodal Status: Where are We at?

Subjects: Health Care Sciences & Services | Surgery
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Definition

Due to the lack of both prospective trial and high-volume retrospective studies, the management of clinical N+ malignant pleural mesothelioma (MPM) patients remain highly debated. Node positive patients show poor survival compared with node-negative ones; thus, lymph node staging appears crucial in determining treatment strategy. Notwithstanding the improvement in pre-treatment staging and the update on lymph node classification in the 8th edition of TNM, several open controversies remain on N parameter.

How should people stage suspected N+ patients?

How should people treat node positive patients?

Which is the definition of “resectable patient”?

Is the site or the number the main prognostic factor for node positive patients?

The aim of the entry is to analyse the existing relevant literature on lymph node status in MPM.

1. Introduction

Several open controversies remain on N parameter of Malignant Pleural Mesothelioma (MPM). Nodal involvement is recognised as a poor prognostic factor, but several weaknesses of nodal staging persist despite the improvement in the 8th edition of TNM classification [1]. N+ patients present poor survival compared to N− patients, therefore accurate lymph node staging is mandatory to plan a treatment strategy [2][3]. Besides, regarding both topography and extent, the N+ group is extremely heterogeneous [4]. According to ERS/ESTS/EACTS/ESTRO 2020 task force member, the use of non-invasive imaging is inaccurate in the assessment of nodal status, and even in case of direct biopsy, the presence of occult nodal metastasis cannot be excluded [5]. Moreover, endobronchial ultrasound (EBUS) and mediastinoscopy, useful techniques in clinical staging, are not able to detect nodal involvement in extra-mediastinal stations (e.g., internal mammary), peri-diaphragmatic or intercostal areas, frequently site of metastases in MPM. In absence of prospective randomized control trial, evidence-based approach including surgical therapy is debated. Based on data of high-volume centres, the N+ MPM disease has not been considered a contraindication to surgery. However, surgery alone seems not appropriate in node positive patients, and a multimodality approach, preferably in a context of a clinical trial, should be considered [6]. Multimodal treatment, including at least macroscopic complete resection and chemotherapy, is better than single modality in selected patients regarding OS, but it increases treatment-related morbidity and mortality [7]. Hence, clinicians should be conscious of the implications of the staging and treatment knowledge limitations when discussing with patients the pre-treatment prognosis.

2. Focused on

- The Role of N Parameter

- MPM Nodal Drainage Pattern

- How to Stage N?

- Clinical versus Pathological Staging

- The Role of Imaging Tests
- The Role of Invasive Mediastinal Staging

- How to treat N+?

- Does the Number of Involved Nodes Matter?

- How to predict Tumour Response?

3. Conclusion

Several open questions on staging and management of node positive MPM patients still exist.

Nodal status is a strong prognostic factor for median survival, however if the location or the number of positive nodes is the main prognosticator is still debating.

Clinical staging alone, including total body CT and PET scan , it’s clear to be not sufficient to identify surgically treatable patients. However even invasive staging with cervical mediastinoscopy and/or endobronchial ultrasound, has shown several limits in MPM. The role of surgery in N+ MPM is highly debated: there is no level I evidence to support surgery for MPM, but these patients are not considered un-resectable. Several patients seem to benefit from a surgery-based approach, particularly those with epithelioid histology, lower-volume disease, and minimal nodal involvement. Anyway, surgery alone seems to be not appropriate and a multimodality approach, preferably as part of a clinical trial, should be considered.

The future debate about the “perfect management of N+ MPM” will be focused more deeply on the open questions that still remain unanswered. Large prospective randomized trials are mandatory to establish an evidence-based approach in order to better stage and treat node positive MPM patients [7].

4. Area for Further Research

- Investigate the prognostic value of LNR and number of involved nodes, in N+ patients;
- Analyse tumour volumetry and assessing its role in staging, treatment response, and as a predictor of OS;
- Investigate the clinical routine applicability of the proposed circulating biomarkers in diagnosis and as prognosticator;
- Clarify the definition of “resectable disease” in N+ MPM;
- Define a prognostic score helping patient allocation for surgery;
- Determine the role of immunotherapy, new targeted therapies and cancer vaccines in MPM treatment.

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Keywords

malignant pleura mesothelioma;surgery;prognostic factors;node positive MPM;staging