Management and prognosis of malignant pleural effusions managed with indwelling pleural catheters

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TO THE EDITOR:

Malignant pleural effusion (MPE) affects 15% of cancer patients, and the incidence of MPE is likely to rise as the global incidence of cancer increases and the overall survival improves.[1,2] Most patients with MPE are symptomatic, with dyspnea being the most common symptom. As MPE represents advanced or metastatic disease, survival is generally poor, ranging from a median of 3 months to 12 months depending on underlying patient factors and tumor-related factors.[1] An overall survival of 3 months has recently been reported in patients with MPE, regardless of lung expandability.[3] Indwelling pleural catheters (IPCs) are the primary modality of treatment in MPE patients with nonexpandable lung (NEL) and symptomatic recurrence. Multiple studies have established the effectiveness of IPCs in achieving the palliation of symptoms.[4]

We conducted a retrospective analysis of a cohort of adult patients with MPE managed with IPCs between August of 2014 and August of 2022 at a university hospital. The main objective of the analysis was to validate the PROMISE score in patients with MPE undergoing drainage with an IPC. The PROMISE score was developed and validated by Psallidas et al.[5] and is the first prognostic score for MPE to combine biological markers and clinical parameters to estimate 3-month mortality. Patients were assigned a 3-month mortality rate on the basis of their PROMISE scores, calculated at the time of IPC placement. The patients were divided into four groups: group 1 (a PROMISE score of 0-20)—a mortality rate of < 25%; group 2 (a PROMISE score of 21-27)—a mortality rate of 25-50%; group 3 (a PROMISE score of 28-35)—a mortality rate of 50-75%; and group 4 (a PROMISE score > 35)—a mortality rate > 75%. The PROMISE score includes parameters such as previous chemotherapy, previous radiation therapy, hemoglobin, serum white blood cell count, C-reactive protein, Eastern Cooperative Oncology Group (ECOG) performance status, cancer type, and tissue inhibitor of metalloproteinases 1 (an optional protein biomarker, used for calculating the biological PROMISE score).

Survival curves were generated by the Kaplan-Meier method and compared by the log-rank test. An independent sample t-test was used in order to evaluate differences between continuous variables with normal distribution, and Mann-Whitney U tests were used in order to evaluate differences between continuous variables with skewed distribution. Patient data were entirely anonymized, and the study protocol complied with the ethical principles of the Declaration of Helsinki. The study was approved by the Research Ethics Committee of the *Centro Hospitalar Universitário de São João*, located in the city of Porto, Portugal.

Of the 45 patients included in the present analysis, 68.9% were male (n = 31). The median age was 68 years (IQR, 60.5-74.5), and most (55.5%) of the patients were current or former smokers (n = 25). MPEs were mostly located on the right side (in 53.3% of the patients; n = 24), and the most common etiologies were lung adenocarcinoma (in 48.9% of the patients; n = 22), breast cancer (in 11.1%; n = 5), and pancreatic adenocarcinoma (in 8.9%; n = 4). Indications for IPC placement included NEL (in 44.4% of the patients; n = 20) and talc slurry pleurodesis failure (in 31.1%; n = 14). Most (73.3%) of the patients were hospitalized at the moment of IPC placement (n = 33). Thoracentesis had been performed a median of 59 days before IPC placement (IQR, 35.0-109.0), and immediate complications of IPC placement (subcutaneous emphysema and hemothorax) were observed in two cases. Pleural infection occurred in 22.2% of the patients (n = 10). Of those, 40% (n = 4) were identified within one week of IPC placement. Chemotherapy did not correlate with an increased risk of complications (p = 0.177), namely, pleural infection. In accordance with a protocol established in August of 2016, we shifted from Tenckhoff catheters to Rocket® catheters (Rocket Medical plc., Watford, UK), and the frequency of complications associated with IPCs decreased. IPCs were removed early in 24.4% of the patients (n = 11), because of pleural infection (in 36.4%; n = 4), because of spontaneous pleurodesis (in 36.4%; n = 4), or accidently (in 27.3%; n = 3).

The pleural fluid **l**actate dehydrogenase, **E**COG performance status, **n**eutrophil-to-lymphocyte ratio, and **t**umor type (LENT) score has been reported to be an easy-to-use, accessible tool to predict the survival of patients with MPE quite accurately. The LENT score can be useful in palliating the symptoms of advanced malignancies by modifying treatment strategies.[6] According to Psallidas et al.,[5] "the PROMISE score is the first prospectively validated prognostic model for MPE that combines biological and clinical parameters to accurately estimate 3-month mortality. It is a robust, clinically relevant prognostic score that can be applied immediately, provide important information on patient prognosis, and guide the selection of appropriate management strategies." In a recent study comparing

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the LENT and PROMISE scores, the latter was found to be more accurate in predicting survival.[7]

Approximately 30% of the 45 patients included in the present analysis (n = 13) were receiving palliative care at the time of IPC placement. Sixteen patients were later referred for symptom relief. The median waiting time until the first palliative care appointment was 53.5 days (IQR, 17.5-108.0). The patients were divided into four groups on the basis of their PROMISE scores (not including tissue inhibitor of metalloproteinases 1): group 1 (n = 21); group 2 (n = 18); group 3 (n = 6); and group 4 (n = 0). Half (51.1%) of the patients had an ECOG performance status > 2 (n = 23). Median survival was 63.0 days (IQR, 22.25-190.5), being significantly different among the groups ($p < 0.001$): 87.5 days (IQR, 20.5-184.5) in group 1; 76 days (IQR, 30.5-268.0) in group 2; and 22.5 days (IQR, 3.5-40.5) in group 3 (Figure 1). There was no significant difference among the groups regarding the frequency of pleural infection ($p = 0.171$).

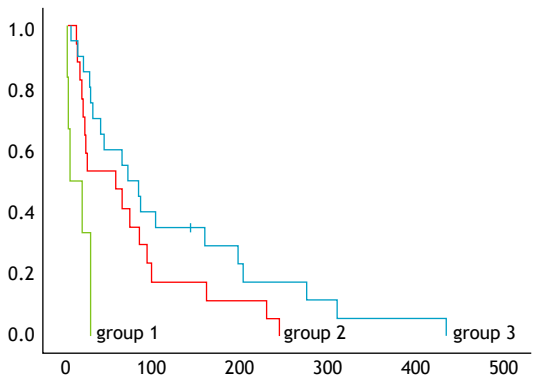

Figure 1. Kaplan-Meier survival curves based on the PROMISE score in individuals with malignant pleural effusion (MPE) requiring placement of an indwelling pleural catheter ($p < 0.001$). NOTE: group 1—MPE patients with a PROMISE score of 0-20; group 2—MPE patients with a PROMISE score of 21-27; and group 3—MPE patients with a PROMISE score of 28-35.

Although IPC can be a suitable first-line treatment option in patients with MPE, it is not exempt from adverse effects such as pleural infection, which, in our population, did not correlate with previous chemotherapy. The PROMISE score was found to be a valuable tool for predicting 3-month mortality in MPE patients undergoing IPC placement. The PROMISE score allows clinicians to reassess prognosis in this subset of patients and might have clinical implications as to whether or not to proceed with IPC placement, even in MPE patients without NEL. Furthermore, it is important to acknowledge that IPC placement is a treatment option that should be carefully discussed in frail patients. Application of the PROMISE score before IPC placement can identify those who are more likely to benefit from supportive measures alone rather than definitive treatment options such as IPC placement, which is not a risk-free therapeutic strategy. Thus, the PROMISE score is important in the decision-making regarding the use of IPCs in this population. We do not recommend IPC placement in group 3 and 4 patients and recommend a personalized evaluation in group 1 and 2 patients. Some of the limitations of the present analysis include its retrospective nature and limited sample size.

AUTHOR CONTRIBUTIONS

MM: conceptualization; methodology; investigation; data curation; software; resources; formal analysis; visualization; and writing, reviewing, and editing of the manuscript. MS and FVM: methodology; investigation; data curation; resources; formal analysis; and writing, reviewing, and editing of the manuscript. HNB: conceptualization; methodology; investigation; data curation; software; resources; formal analysis; visualization; writing, reviewing, and editing of the manuscript; and supervision. All authors read and approved the final manuscript.

CONFLICTS OF INTEREST

None declared.

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