JCS Journal of Chest Surgery
https://doi.org/10.5090/jcs.22.037
pISSN: 2765-1606 eISSN: 2765-1614
J Chest Surg. 2022;55(5):405-412

Clinical Research

# Survival Effect of Complete Multimodal Therapy in Malignant Pleural Mesothelioma

Muhammet Sayan, M.D.[1], Aynur Bas, M.D.[2], Merve Satir Turk, M.D.[1], Dilvin Ozkan, M.D.[1], Ali Celik, M.D.[1], İsmail Cuneyt Kurul, M.D.[1], Abdullah Irfan Tastepe, M.D.[1]

[1]Department of Thoracic Surgery, Gazi University, Ankara; [2]Division of Thoracic Surgery, Basaksehir Cam Sakura City Hospital, Istanbul, Turkey

**ARTICLE INFO**
**Received** May 18, 2022
**Revised** July 8, 2022
**Accepted** July 28, 2022

**Corresponding author**
Muhammet Sayan
**Tel** 90-5071927600
**Fax** 90-3122025890
**E-mail** muhammets@gazi.edu.tr
**ORCID**
https://orcid.org/0000-0002-5402-9031

**Background:** Malignant pleural mesothelioma (MPM) is an aggressive pleural malignancy, and despite all multimodal treatment modalities, the 5-year overall survival rate of patients with MPM is less than 20%. In the present study, we aimed to analyze the surgical and prognostic outcomes of patients with MPM who received multimodal treatment.
**Methods:** In this retrospective, single-center study, the records of patients who underwent surgery for MPM between January 2010 and December 2020 at our department were reviewed retrospectively.
**Results:** Sixty-four patients were included in the study, of whom 23 (35.9%) were women and 41 (64.1%) were men. Extrapleural pneumonectomy, pleurectomy/decortication, and extended pleurectomy/decortication procedures were performed in 34.4%, 45.3%, and 20.3% of patients, respectively. The median survival of patients was 21 months, and the 5-year survival rate was 20.2%. Advanced tumor stage (hazard ratio [HR], 1.8; p=0.04), right-sided extrapleural pneumonectomy (HR, 3.1; p=0.02), lymph node metastasis (HR, 1.8; p=0.04), and incomplete multimodal therapy (HR, 1.9; p=0.03) were poor prognostic factors. There was no significant survival difference according to surgical type or histopathological subtype.
**Conclusion:** Multimodal therapy can offer an acceptable survival rate in patients with MPM. Despite its poor reputation in the literature, the survival rate after extrapleural pneumonectomy, especially left-sided, was not as poor as might be expected.

**Keywords:** Mesothelioma, Pneumonectomy, Pleura, Extrapleural pneumonectomy

## Introduction

Malignant pleural mesothelioma (MPM), which arises from pleural mesothelial cells, is a rare and fatal tumor. The incidence of MPM has been reported to be 3–17 per million [1]. Although asbestos exposure is the most widely known etiological factor, exposure to erionite, which is specific to Turkey and the western United States, has also been reported in the literature [2-4]. Related guidelines have emphasized the importance of multimodal therapy (MMT) for patients with MPM in suitable conditions. Surgery is the principal component of MMT, and the main goal of surgery for MPM is maximal cytoreduction [1]. There are 2 types of surgical treatment of MPM, called pleurectomy/decortication (PD) and extrapleural pneumonectomy (EPP), depending on whether the entire ipsilateral lung is included in the excision. Additionally, a variation of the PD procedure including pericardiectomy and/or diaphragm resection is called extended pleurectomy/decortication (EPD) in various references [5,6].

The eighth tumor-mode-metastasis (TNM) system, which has been used since 2018, is the current staging system of MPM, and many patients with MPM are clinically candidates for surgery except for those with T4 and M1 tumors [7]. Nonetheless, despite all treatment efforts, MPM has a poor prognosis. Various references have reported that the median survival of MPM was 18–22 months, and the 5-year overall survival (OS) rate was less than 20% [8-10]. Researchers and clinicians from various departments, including thoracic surgery, medical oncology, and radiation

https://doi.org/10.5090/jcs.22.037

oncology, are trying to contribute to the literature by publishing their experiences on the survival outcomes and prognostic factors of this rare and fatal tumor. In the present study, we also aimed to analyze the prognostic factors and surgical outcomes of patients with MPM who underwent MMT including surgery in this single-center study.

# Methods

## Inclusion criteria

This study was approved by the Institutional Review Board of Gazi University (IRB approval no., 2021-789). The patients provided written informed consent for the publication of clinical details and images. The record of patients who underwent surgery for MPM between January 2010 and December 2020 at our department was reviewed retrospectively. Patients who underwent EPP, PD, or EPD with or without induction chemotherapy were included in the study. Patients whose medical follow-up records were not obtained, those without mediastinal lymph node sampling or dissection, and those who underwent only diagnostic surgery were not included in the study. The pathological staging of patients was conducted according to the eighth TNM system.

## Preoperative evaluation

Since our department is a surgical clinic, most of the patients included in the study were referred after the histopathological diagnosis of MPM. Endobronchial ultrasound-guided transbronchial needle aspiration in patients who had lymph nodes with a short axis larger than 1 cm on thoracic computed tomography (CT) and/or mediastinal lymph node involvement on positron emission tomography–CT. Surgery, direct or after induction chemotherapy, was planned in patients with an early clinical stage after a multidisciplinary evaluation. Additionally, those who had mediastinal lymph node invasion or severe chest pain (suspected chest wall invasion) were referred for induction therapy. Some patients included in the study had also received induction chemotherapy at another center.

A detailed preoperative evaluation and preparation were performed for patients scheduled for surgery. A complete blood count (CBC), biochemical tests, coagulation tests, pulmonary function tests including the diffusing capacity for carbon monoxide, a cardiac evaluation, the 6-minute walk test and when necessary, ventilation/perfusion scintigraphy and $VO_2$-max calculations were performed. Patients with bilateral involvement, peritoneal invasion, and contralateral hilar-mediastinal or supraclavicular lymph node metastases, those who were medically inoperable, and those who refused surgery were referred for definitive chemo-radiotherapy.

## Surgical approach

To the extent possible, we preferred PD and EPD, which are lung-protective methods were preferred. However, EPP was planned when maximal cytoreduction could not be achieved with lung-sparing methods. The decision to perform EPP was made intraoperatively in some patients. The indications for EPP were as follows: (1) radiologically diffuse parenchymal involvement and the presence of intense visceral pleural thickening; (2) inability to achieve maximal intraoperative cytoreduction with PD and EPD; (3) concern about excessive air leakage due to excessive lung damage after pleurectomy; (4) a suitable patient for pneumonectomy in terms of cardiopulmonary function and medical performance; and (5) no mediastinal lymph node metastasis in clinical staging.

## Postoperative management

Patients who underwent surgery directly without induction therapy were referred for adjuvant therapy. Adjuvant treatment was planned as sequential chemotherapy followed by radiotherapy, or combined chemoradiotherapy. Those who underwent surgery after induction therapy were referred to adjuvant radiotherapy. EPP patients received adjuvant radiotherapy in the form of high-dose whole hemithorax irradiation, while hemi-thoracic pleural intensity-modulated radiation therapy was performed in those who underwent lung-sparing surgery. Post-treatment follow-up examinations included thoracic/abdominal CT, CBC, liver function tests, kidney function tests at 3-month intervals.

## Statistical analysis

All analyses were performed with IBM SPSS ver. 20.0 (IBM Corp., Armonk, NY, USA) software. The normality of the distribution of numeric data was investigated using the Kolmogorov-Smirnov test and histograms. The mean and standard deviation were used for parameters with a normal distribution and the median with minimum-maximum was used for those with a skewed distribution. The chi-square and log-rank tests were used for categorical and continuous variables, respectively. OS time was calculated as the interval from the date of surgery to the date of the study for living patients and the date of death for dead patients. The OS was calculated using the Kaplan-Meier method. Survival differences between the groups were investigated by log-rank and Cox regression analyses. Early postoperative mortality referred to deaths from any cause occurring within the first 30 days after surgery. All analyses were performed with 95% confidence intervals (CIs). Two-sided p-values were calculated, and a p-value less than 0.05 was considered to indicate statistical significance.

## Results

Sixty-four patients who met the inclusion criteria were included in the study. There were 23 (35.9%) women and 41 (64.1%) men. The median age of the patients was 58 years (range, 32–76 years). The general characteristics of patients are given in Tables 1 and 2. The most common surgical procedure performed was PD (45.3%) and the most common tumor stage was IB (51.6%) according to the eighth TNM system. The epithelioid histopathology rate was 82.8%. Induction chemotherapy with the cisplatin-pemetrexed protocol was administered in 32 patients (50%) between 3 and 6 cycles. MMT was not completed in 10 patients (15.6%) due to various factors such as patient rejection or poor medical performance. The medical oncology team did not approve adjuvant chemotherapy in patients with cardiomyopathy, advanced age, renal failure, and cachexia.

The mean follow-up time of our study was 29.6 months (SD, 3.8 months). The median survival was 21 months (95% CI, 11.3–30.6 months), and the 3- and 5-year OS rates were 39.2% and 20.2%, respectively (Fig. 1). Early postoperative mortality occurred only in 1 patient who underwent EPD surgery due to an air leak followed by pneumonia and respiratory failure. Ninety-day mortality occurred in 4 patients (6.25 %) in our study: 2 of them were in the EPD group, 1 was in the EPP group, and 1 was in the PD group. One patient who underwent right EPP died on the 86th

**Table 1.** Characteristics of patients included in the study (n=64)

| Characteristic | Category | Value |
|---|---|---|
| Age (yr) | | 58 (32–76) |
| Length of stay (day) | | 9 (4–25) |
| Length of intensive care unit (day) | | 1 (1–7) |
| Sex | Female | 23 (35.9) |
| | Male | 41 (64.1) |
| T stage | I | 17 (26.6) |
| | II | 27 (42.2) |
| | III | 20 (31.2) |
| N stage | 0 | 45 (70.3) |
| | I | 19 (29.7) |
| Surgery | Extrapleural pneumonectomy | 22 (34.4) |
| | Right | 10 (15.6) |
| | Left | 12 (18.8) |
| | PD | 29 (45.3) |
| | Extended PD | 13 (20.3) |
| Stage (eighth TNM) | IA | 12 (18.8) |
| | IB | 33 (51.6) |
| | II | 10 (15.6) |
| | IIIA | 9 (14.0) |
| Histopathology | Epithelioid | 53 (82.8) |
| | Biphasic | 9 (14.1) |
| | Sarcomatoid | 2 (3.1) |
| Induction chemotherapy | Yes | 32 (50.0) |
| | No | 32 (50.0) |
| Completed multimodal therapy | No | 10 (15.6) |
| | Yes | 54 (84.4) |

Values are presented as median (range) or number (%).
PD, pleurectomy/decortication; TNM, tumor-node-metastasis staging system.

**Table 2.** Clinicopathological features of patients according to the side of malignant pleural mesothelioma (n=64)

| Variable | Category | Right | Left |
|---|---|---|---|
| Sex | Female | 8 (12.5) | 24 (37.5) |
| | Male | 15 (23.4) | 17 (26.6) |
| Surgery | EPP[a)] | 10 (15.6) | 12 (18.7) |
| | PD | 17 (26.6) | 12 (18.7) |
| | EPD | 5 (7.8) | 8 (12.5) |
| Age (yr) | ≥65 | 20 (31.3) | 23 (35.9) |
| | <65 | 10 (15.6) | 11 (17.2) |
| Stage | I–II | 23 (35.9) | 19 (29.6) |
| | III | 9 (14.1) | 13 (20.4) |
| T category | I | 10 (15.6) | 7 (10.9) |
| | II | 13 (20.4) | 14 (21.8) |
| | IIII | 9 (14.1) | 11 (17.2) |
| N stage | 0 | 25 (39.1) | 20 (31.3) |
| | I | 7 (10.9) | 12 (18.7) |
| Histopathology | Epithelioid | 26 (40.6) | 27 (42.2) |
| | Biphasic | 4 (6.3) | 5 (7.8) |
| | Sarcomatoid | 2 (3.1) | 0 |
| Induction therapy | Yes | 17 (26.6) | 15 (23.4) |
| | No | 15 (23.4) | 17 (26.6) |
| MMT | Incomplete | 3 (4.6) | 7 (10.9) |
| | Complete | 29 (45.4) | 25 (39.1) |

Values are presented as number (%).
EPP, extrapleural pneumonectomy; PD, pleurectomy/decortication; EPD, extended pleurectomy/decortication; MMT, multimodal therapy.
[a)]There was a significant survival difference between right- and left-sided EPP (hazard ratio, 3.1; 95% confidence interval, 1.1–9.6; p=0.02).

https://doi.org/10.5090/jcs.22.037

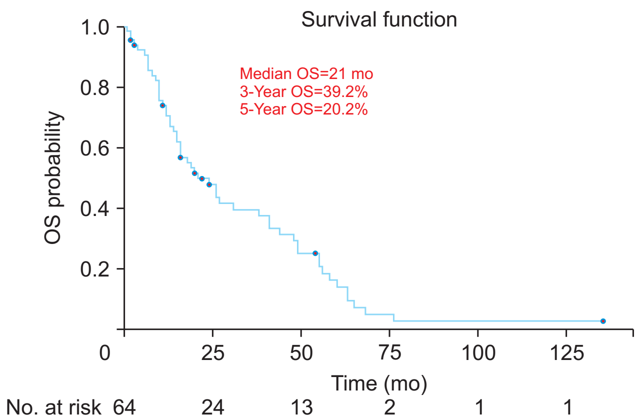


**Fig. 1.** Median and 5-year survival of patients shown using a Kaplan-Meier curve. The median survival was 21 months (95% confidence interval, 11.3–30.6 months), and the 3- and 5-year overall survival (OS) rates were 39.2% and 20.2%, respectively.

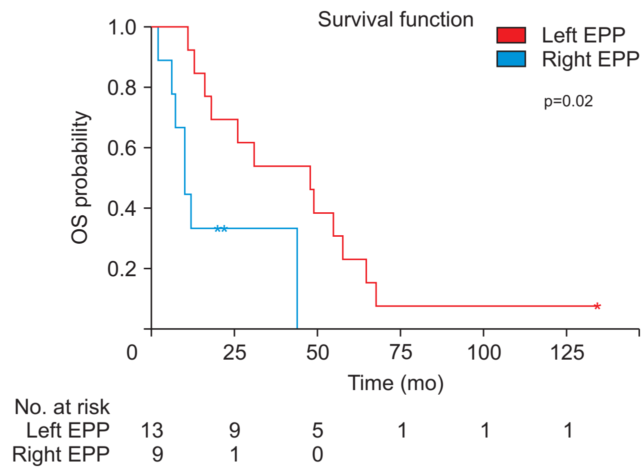


**Fig. 3.** Survival curves according to the extrapleural pneumonectomy (EPP) side.

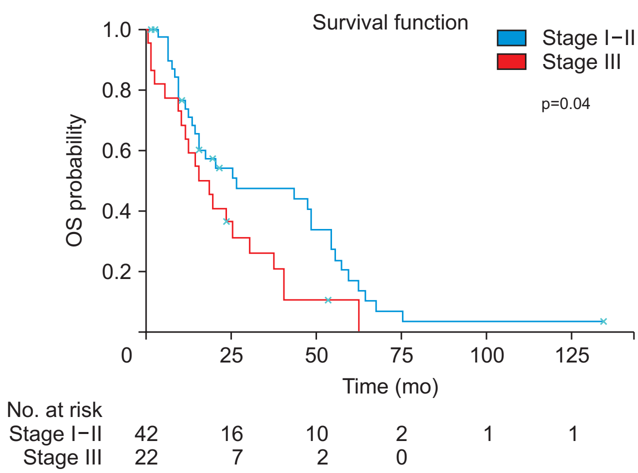


**Fig. 2.** Survival curves showing a significant difference between early and advanced tumor stages.

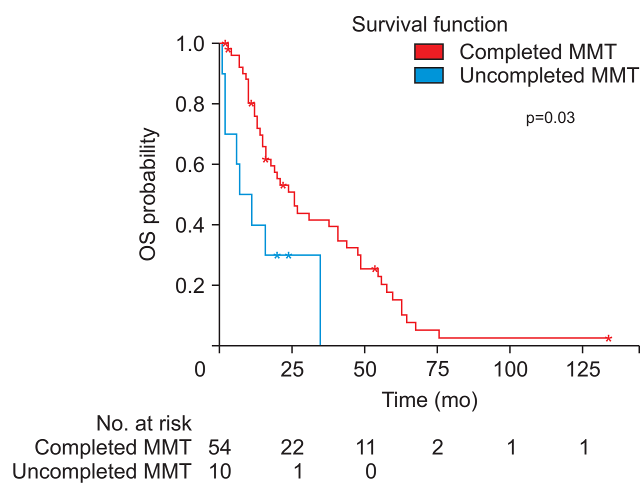


**Fig. 4.** Survival curves showing better median survival in patients who had completed multimodal therapy (MMT).

day due to bronchopleural fistula. The causes of mortality of the other patients were acute coronary syndrome and neutropenia resulting from chemotherapy. Advanced tumor stage (hazard ratio [HR], 1.8; p=0.04), right-sided EPP (HR, 3.1; p=0.02), the presence of lymph node metastasis (HR, 1.8; p=0.04) and incomplete MMT (HR, 1.9; p=0.03) were statistically significant poor prognostic factors (Figs. 2–4, Table 2). Induction chemotherapy, age, sex, the surgical procedure performed, and the histopathological subtype had no significant effect on survival (Table 3).

The most common postoperative morbidities were air leak and atelectasis in the pulmonary-sparing group. Atrial fibrillation occurred at similar frequencies in the EPD and EPP groups. Severe bacterial pneumonia was detected in a patient who underwent EPD surgery, and he died on postoperative day 26. Four patients had minor wound site problems. Chylothorax, which was treated medically, occurred in 2 patients in the right EPP group. Bronchopleural fistula occurred in 1 patient who underwent EPP surgery.

## Discussion

In this study, we aimed to demonstrate the surgical outcomes and prognostic factors of patients with MPM who underwent MMT at our department. Studies have reported that MPM is more common in male patients. Klotz et al. [11] reported that the mean age was 63.2 years and the proportion of male patients was 82.9%. Baas et al. [12] demonstrated that the median age was 75 years, most patients

**Table 3.** Comparison of survival according to demographic and clinicopathological variables

| Variable | Category | Median survival (mo) | 95% CI | p-value | HR (95% CI) |
|---|---|---|---|---|---|
| Sex | Female | 14 | 7.7–20.2 | 0.2 | 0.7 (0.3–1.2) |
| | Male | 26 | 19.9–32.0 | | |
| Age (yr) | <65 | 26 | 13.6–38.3 | 0.7 | 1.1 (0.4–2.8) |
| | >65 | 20 | 13.3–26.7 | | |
| Surgery | EPP | 16 | 2.0–49 | | |
| | PD | 24 | 13.3–34.6 | 0.9 | 0.9 (0.5–1.7) |
| | EPD | 22 | 13.6–30.3 | | |
| T category | TI–II | 26 | 2.5–49.4 | 0.04 | 1.8 (1.1–3.4) |
| | TIII | 15 | 11.0–18.9 | | |
| N stage | N0 | 27 | 18.8–35.1 | 0.04 | 1.8 (1.1–3.3) |
| | N1 | 16 | 10.3–21.6 | | |
| Histopathology | Epithelioid | 26 | 18.6–33.3 | | |
| | Biphasic | 11 | 4.07–17.9 | 0.5 | 0.7 (0.1–5.8) |
| | Sarcomatoid | 19 | - | | |
| EPP side | Right | 10 | 5.6–14.3 | 0.02 | 3.1 (1.1–9.6) |
| | Left | 48 | 9.2–86.7 | | |
| Induction CT | Yes | 22 | 12.7–31.2 | 0.2 | 1.4 (0.7–2.5) |
| | No | 18 | 5.4–30.5 | | |
| Completed MMT | Yes | 24 | 15.5–32.4 | 0.03 | 1.9 (1.1–4.2) |
| | No | 11 | 1.0–24.9 | | |

CI, confidence interval; HR, hazard ratio; EPP, extrapleural pneumonectomy; PD, pleurectomy/decortication; EPD, extended pleurectomy/decortication; CT, chemotherapy; MMT, multimodal therapy.

were men, and young age and female sex were good prognostic factors. Similarly, Bovolato et al. [13] found that the median age was 67 years, 68.1% of patients were men, and advanced age was a poor prognostic factor. Although most patients were men in our study, which was compatible with the literature, the prognosis was worse in female patients than in male patients. A reason for this may be that about half of female patients underwent EPP surgery, which had a worse prognosis than other types of surgical procedures. Another possible cause of the worse survival among female patients may have been that 9 of 23 (approximately 39%) female patients were diagnosed at an advanced tumor stage. In addition, unlike the literature, no significant correlation between age and survival was found in our series.

The early postoperative mortality rate after MPM surgery has been reported as 0%–12.5% in the literature [14]. Bovolato et al. [13] reported that the operative mortality rates of PD and EPP surgery were 2.6% and 4.1%, respectively. Lang-Lazdunski et al. [15] found that the operative mortality rate of EPP was 4.5%, but there was no early postoperative mortality in patients who underwent PD in their study. In a review published by Bueno et al. [6], operative mortality was reported as 0%–17.6%. To summarize, the operative mortality of EPP was reported to be prominently higher than that of lung-sparing MPM surgery in all papers mentioned above. On the contrary, in our study, early operative mortality occurred in 1 patient who underwent EPD, but in none who underwent EPP.

Since the surgical approach is traditionally recommended for non-sarcomatoid MPM, the most common histopathological subtypes in surgical series are epithelioid and biphasic MPM [15,16]. Bovolato et al. [13] reported that the most common histopathological subtype was epithelioid MPM, and the survival of sarcomatoid MPM was significantly worse. Similarly, Lewis et al. [17] demonstrated that survival was significantly worse in biphasic and sarcomatoid subtypes than in epithelioid MPM. In 2 other series, the predominant histopathological subtype was epithelioid MPM, and there was no survival difference between histopathological groups [9,15]. Similarly, the predominant histopathological type was the pure epithelioid type in our study, and there was no significant survival difference between histopathological subgroups. In our study, only 2 patients had the sarcomatoid type, and those patients underwent PD surgery. Due to the small number of patients, it would not seem realistic to claim that histopathological type does not affect survival. However, if that result is interpreted together with the other results of our study (in particular, the identification of advanced T stage and lymph node metastasis as poor prognostic factors), it can be tentatively said that TNM staging is more important for survival than the histopathological subtype of MPM.

Generally, related publications in the literature reported that lung-sparing surgery (PD and EPD) for MPM was superior to EPP in terms of mortality, morbidity, and OS. The Mesothelioma and Radical Surgery 1 (MARS-1) study, which was the first and only randomized prospective study related to this topic, revealed the negative aspects of EPP and recommended lung-sparing surgery [18]. Two retrospective studies reported that, while the operative mortality rate was significantly higher in the EPP group, there was no difference in terms of median survival between the EPP and lung-sparing groups [9,19]. According to a large database obtained from the International Association for the Study of Lung Cancer Mesothelioma Staging Project, the survival of patients who underwent EPP, especially for stage 1 MPM, was reported to be significantly better than those who underwent PD [8]. Bovalato et al. [13] demonstrated there was no significant difference between EPP and other surgical groups in terms of operative mortality and median survival. As we mentioned before, no early postoperative mortality was detected in the EPP group in our study. Moreover, EPP was mainly performed in patients with early-stage MPM, and we did not detect significant survival differences between the surgical groups.

In contrast to the poor prognostic effect of right pneumonectomy in non-small cell lung cancer, sufficient data do not exist in the English-language literature regarding a potential correlation between the side of EPP and survival in patients with MPM. A large EPP series including 529 cases published by Sugarbaker et al. [20] found no survival differences according to the side of surgery. Two other retrospective studies of EPP for MPM also reported that both sides had similar survival [21,22]. Unlike the literature, right-sided EPP was associated with significantly poorer survival than left-sided EPP in our study. However, we could not conclusively interpret the reason for this result because we could not fully demonstrate that the deaths were directly related to cancer.

There are different opinions about the effect of adjuvant treatment for MPM on survival in the literature. A guideline published by the American Society of Clinical Oncology suggested that adjuvant radiotherapy had positive effects on local control and OS [23]. A database study performed by Lewis et al. [17] reported there was a significant correlation between OS and adjuvant therapy. Another current guideline published by the European Society of Medical Oncology stated that while adjuvant radiotherapy diminished local recurrence, there was not a sufficient level of evidence for adjuvant radiotherapy as standard treatment [1]. In our study, adjuvant treatment was applied as sequential chemo-radiotherapy in patients who did not receive induction chemotherapy, while radiotherapy was applied in those who received induction chemotherapy. Patients who completed all treatment procedures were included in the completed MMT group. The median survival and 5-year OS were significantly better in patients who completed the MMT in our study. Another result of our study was that induction chemotherapy did not have a significant effect on survival. When these results are interpreted together, it can be inferred that local control of the tumor with a combination of surgery and radiotherapy and systemic control of the tumor with chemotherapy is effective for survival in patients with MPM.

The primary limitations of our study were that it was retrospective and included a small number of patients. It is very difficult to conduct a prospective randomized study of surgery for MPM, which is a rare and fatal malignancy; even in the MARS-1 trial, which is the only prospective randomized trial on this topic, only approximately 20 patients in each arm could be provided. As another limitation, this was a single-center study. However, single-center studies may have the advantage of ensuring homogeneity because the technique of cytoreductive surgery performed for MPM may differ from center to center. Another major limitation was the use of OS for survival analysis instead of disease-free survival (DFS). Although the survival outcomes in MPM can be best determined using DFS, as with other cancers, studies have emphasized that it is difficult to calculate DFS in MPM patients, so studies have generally evaluated OS [8]. Additionally, the time interval of our study was relatively long, and variability in both treatment strategies and the quality of perioperative management during that long span could bias the outcomes.

As a result, despite all treatment strategies, MPM continues to have a very high mortality rate. Nonetheless, acceptable survival results can be achieved with MMT. Advanced tumor stage, incomplete MMT and right-sided EPP were identified as poor prognostic factors. The results of our study may be encouraging to surgeons regarding the performance of left-sided EPP.

## Article information

### ORCID

Muhammet Sayan: https://orcid.org/0000-0002-5402-9031
Aynur Bas: https://orcid.org/0000-0001-5754-2677

Merve Satir Turk: https://orcid.org/0000-0003-4873-3281
Dilvin Ozkan: https://orcid.org/0000-0002-7149-5982
Ali Celik: https://orcid.org/0000-0001-5385-6492
İsmail Cuneyt Kurul: https://orcid.org/0000-0002-9480-010X
Abdullah Irfan Tastepe: https://orcid.org/0000-0002-2032-7444

## Author contributions

Conceptualization: MS, AB, MST, DO, AC, ICK, AIT. Design: MS, AB, MST, DO, AC, ICK, AIT. Supervision: MS, AB, MST, DO, AC, ICK, AIT. Data curation: MS, AB. Formal analysis: MS, AB, AC. Methodology: MS, AC, AIT. Project administration: MS, AB, AC, AIT. Visualization: MS, AC. Writing–original draft: MS, AB, AC, AIT. Writing–review & editing: MS, AB, MST, DO, AC, ICK, AIT. Final approval of the manuscript: all authors.

## Conflict of interest

No potential conflict of interest relevant to this article was reported.

## Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

# References

1. Popat S, Baas P, Faivre-Finn C, et al. *Malignant pleural mesothelioma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up*. Ann Oncol 2022;33:129-42.
2. Opitz I, Furrer K. *Preoperative identification of benefit from surgery for malignant pleural mesothelioma*. Thorac Surg Clin 2020;30:435-49.
3. Selcuk ZT, Coplu L, Emri S, Kalyoncu AF, Sahin AA, Baris YI. *Malignant pleural mesothelioma due to environmental mineral fiber exposure in Turkey: analysis of 135 cases*. Chest 1992;102:790-6.
4. Beaucham C, King B, Feldmann K, Harper M, Dozier A. *Assessing occupational erionite and respirable crystalline silica exposure among outdoor workers in Wyoming, South Dakota, and Montana*. J Occup Environ Hyg 2018;15:455-65.
5. Bertoglio P, Garelli E, Brandolini J, et al. *Surgical management and reconstruction of diaphragm, pericardium and chest wall in mesothelioma surgery: a review*. J Clin Med 2021;10:2330.
6. Bueno R, Opitz I; IASLC Mesothelioma Taskforce. *Surgery in malignant pleural mesothelioma*. J Thorac Oncol 2018;13:1638-54.
7. Berzenji L, Van Schil PE, Carp L. *The eighth TNM classification for malignant pleural mesothelioma*. Transl Lung Cancer Res 2018;7:543-9.
8. Opitz I, Weder W. *A nuanced view of extrapleural pneumonectomy for malignant pleural mesothelioma*. Ann Transl Med 2017;5:237.
9. Zhou N, Rice DC, Tsao AS, et al. *Extrapleural pneumonectomy versus pleurectomy/decortication for malignant pleural mesothelioma*. Ann Thorac Surg 2022;113:200-8.
10. Kang SR, Bok JS, Lee GD, et al. *Surgical options for malignant mesothelioma: a single-center experience*. Korean J Thorac Cardiovasc Surg 2018;51:195-201.
11. Klotz LV, Gruenewald C, Bulut EL, et al. *Cytoreductive thoracic surgery combined with hyperthermic chemoperfusion for pleural malignancies: a single-center experience*. Respiration 2021;100:1165-73.
12. Baas P, Daumont MJ, Lacoin L, et al. *Treatment patterns and outcomes for patients with malignant pleural mesothelioma in England in 2013-2017: a nationwide CAS registry analysis from the I-O Optimise initiative*. Lung Cancer 2021;162:185-93.
13. Bovolato P, Casadio C, Bille A, et al. *Does surgery improve survival of patients with malignant pleural mesothelioma?: a multicenter retrospective analysis of 1365 consecutive patients*. J Thorac Oncol 2014;9:390-6.
14. Abdel-Rahman O, Elsayed Z, Mohamed H, Eltobgy M. *Radical multimodality therapy for malignant pleural mesothelioma*. Cochrane Database Syst Rev 2018;1:CD012605.
15. Lang-Lazdunski L, Bille A, Lal R, et al. *Pleurectomy/decortication is superior to extrapleural pneumonectomy in the multimodality management of patients with malignant pleural mesothelioma*. J Thorac Oncol 2012;7:737-43.
16. Mangiameli G, Bottoni E, Cariboni U, et al. *Single-center 20-year experience in surgical treatment of malignant pleural mesothelioma*. J Clin Med 2022;11:4537.
17. Lewis GD, Dalwadi SM, Farach A, Brian Butler E, Teh BS. *The role of adjuvant radiotherapy in the treatment of pleural mesothelioma*. Ann Surg Oncol 2019;26:1879-85.
18. Treasure T, Lang-Lazdunski L, Waller D, et al. *Extra-pleural pneumonectomy versus no extra-pleural pneumonectomy for patients with malignant pleural mesothelioma: clinical outcomes of the Mesothelioma and Radical Surgery (MARS) randomised feasibility study*. Lancet Oncol 2011;12:763-72.
19. Ichiki Y, Goto H, Fukuyama T, Nakanishi K. *Should lung-sparing surgery be the standard procedure for malignant pleural mesothelioma?* J Clin Med 2020;9:2153.
20. Sugarbaker DJ, Richards WG, Bueno R. *Extrapleural pneumonectomy in the treatment of epithelioid malignant pleural mesothelioma: novel prognostic implications of combined N1 and N2 nodal involvement based on experience in 529 patients*. Ann Surg 2014;260:577-82.
21. Cao C, Yan TD, Bannon PG, McCaughan BC. *Summary of prognostic factors and patient selection for extrapleural pneumonectomy in*

*the treatment of malignant pleural mesothelioma*. Ann Surg Oncol 2011;18:2973-9.
22. Bedirhan MA, Cansever L, Demir A, et al. *Which type of surgery should become the preferred procedure for malignant pleural mesothelioma: extrapleural pneumonectomy or extended pleurectomy?* J Thorac Dis 2013;5:446-54.
23. Kindler HL, Ismaila N, Armato SG 3rd, et al. *Treatment of malignant pleural mesothelioma: American Society of Clinical Oncology Clinical Practice Guideline*. J Clin Oncol 2018;36:1343-73.