Korean J Thorac Cardiovasc Surg 2018;51:195-201 □ CLINICAL RESEARCH □
ISSN: 2233-601X (Print) ISSN: 2093-6516 (Online) https://doi.org/10.5090/kjtcs.2018.51.3.195

Surgical Options for Malignant Mesothelioma: A Single-Center Experience

Seung Ri Kang, M.D., Jin San Bok, M.D., Geun Dong Lee, M.D., Ph.D., Se Hoon Choi, M.D., Ph.D., Hyeong Ryul Kim, M.D., Ph.D., Dong Kwan Kim, M.D., Ph.D., Seung-Il Park, M.D., Ph.D., Yong-Hee Kim, M.D., Ph.D.

Department of Thoracic and Cardiovascular Surgery, Asan Medical Center, University of Ulsan College of Medicine

Background: We investigated the surgical outcomes of patients who underwent therapeutic surgery for malignant pleural mesothelioma (MPM) at a single center. **Methods:** A retrospective review of 21 patients who underwent therapeutic surgery for MPM from January 2001 to June 2015 was conducted to assess their outcomes. The patients' characteristics and postoperative course, including complications, mortality, overall survival, and recurrence-free survival, were analyzed. **Results:** Of the 21 patients who underwent therapeutic surgery, 15 (71.4%) underwent extrapleural pneumonectomy, 2 pleurectomy (9.5%), and 4 excision (19.1%). The median age was 57 years (range, 32–79 years) and 15 were men (71.4%). The mean hospital stay was 16 days (range, 1–63 days). Median survival was 14.3 months. The survival rate was 54.2%, 35.6%, and 21.3% at 1, 3, and 5 years, respectively. In patients' postoperative course, heart failure was a major complication, occurring in 3 patients (14.3%). The in-hospital mortality rate was 2 of 21 (9.5%) due to a case of severe pneumonia and a case of acute heart failure. **Conclusion:** A fair 5-year survival rate of 21.3% was observed after surgical treatment. Heart failure was a major complication in our cohort. Various surgical methods can be utilized with MPM, each with its own benefits, taking into consideration the severity of the disease and the comorbidities of the patient. Patients with local recurrence may be candidates for surgical intervention, with possible satisfying results.

Key words: 1. Malignant mesothelioma
2. Pneumonectomy

Introduction

Malignant pleural mesothelioma (MPM) is an uncommon type of malignancy with an aggressive nature. It is difficult to diagnose and its outcome is usually fatal, with a median survival of <12 months, a number that has shown little change according to the Surveillance, Epidemiology, and End-Results (SEER) database [1]. MPM is known to show little response to chemotherapy and radiotherapy. Many studies have been conducted regarding the appropriate therapeutic modality for this disease, but its proper management is still a matter of debate. However, in patients with localized tumors without distant metastasis and the medical tolerance to undergo general anesthesia and surgery, complete surgical resection can be considered in order to achieve macroscopic cytoreduction, although the exact role of surgery has been a matter for debate [2].

The International Association for the Study of Lung

Received: September 7, 2017, Revised: December 13, 2017, Accepted: December 28, 2017, Published online: June 5, 2018
Corresponding author: Yong-Hee Kim, Department of Thoracic and Cardiovascular Surgery, Asan Medical Center, 88 Olympic-ro 43-gil, Songpa-gu, Seoul 05505, Korea
(Tel) 82-2-3010-3580 (Fax) 82-2-3010-6966 (E-mail) kimyh67md@hotmail.com

Table 1. Demographic, perioperative, and survival data for the cohort (n=21)

Characteristic	Value
Gender	
Male	15
Female	6
Mean age (yr)	55 (32–79)
Smoking	16 (76.1)
Exposure to asbestos	6 (28.6)
Mean forced expiratory volume in 1 second (L)	70.4 (41–100)
Mean diffusing capacity of the lungs for carbon monoxide (ml/min/mm Hg)	70.8 (42–116)
Chief complaint	
Pleuritic pain	8 (38.1)
Dyspnea	7 (33.3)
Cough	2 (19.1)
Comorbidities (Charlson comorbidity index)	
Mean (range)	1.29 (0–3)
Median	1
Side	
Right	15 (71)
Left	6 (29)
Neoadjuvant treatment	
Chemotherapy	1 (4.8)
Radiotherapy	1 (4.8)
Types of surgical procedures	
Extrapleural pneumonectomy	15 (71.4)
Pleurectomy	2 (9.5)
Chest wall excision	4 (19.1)
Stage	
II	5 (23.8)
III	15 (71.4)
IV	1 (4.8)
Lymph node metastasis	
N0	12 (57.1)
N1	2 (9.5)
N2	5 (23.8)
Nx	2 (9.5)
Histologic type	
Epithelioid	13 (61.9)
Sarcomatoid	2 (9.5)
Biphasic	1 (4.8)
Others[a]	5 (23.8)
Adjuvant therapy	
Chemotherapy	5 (23.8)
Radiotherapy	7 (33.8)
Chemotherapy and radiotherapy	1 (4.8)
None	8 (42.9)

Values are presented as number, mean (range), or number (%).
[a]Undifferentiated (n=1), desmoplastic (n=1), and unclassified (n=3).

Table 2. Postoperative data for the cohort

Variable	Value
Mean hospital stay (day)	16 (1–63)
Median follow-up (mo)	5.33 (0–75.3)
Postoperative complication	7/21 (33.3)
Heart failure	3/21 (14.3)
Pneumonia	1/21 (4.8)
Vocal cord palsy	2/21 (9.5)
Wound complication	1/21 (4.8)
In-hospital mortality	2/21 (9.5)
Cause of death	
Heart failure	1/21 (4.8)
Pneumonia	1/21 (4.8)
90-day mortality	2/21 (9.5)
Cause of death	
Heart failure	1/21 (4.8)
Recurrence	1/21 (4.8)
Survival rate (%)	
1 yr	54.2
3 yr	35.6
5 yr	21.3
Median survival duration (mo)	14.3 (0–75.3)
Cause of death	
Recurrence	8 (42.9)
Acute renal failure	1 (4.8)
Acute respiratory distress syndrome	1 (4.8)
Heart failure	2 (4.8)
Pneumonia	1 (4.8)
Sepsis (empyema)	1 (4.8)

Values are presented as mean (range), number (%), or %.

Cancer currently defines the procedures for gross tumor reduction as extrapleural pneumonectomy (EPP), pleurectomy/decortication (P/D), and extended pleurectomy/decortication (e-P/D) [3]. EPP, which is the more aggressive, lung-sacrificing procedure, entails surgical removal of the ipsilateral lung, diaphragm, pleura, and the pericardium. In contrast, P/D spares the lung of the MPM-affected side, with removal of all gross tumors and pleura. The P/D procedure spares the pericardium and diaphragm, while the e-P/D procedure entails resection of the ipsilateral pericardium and diaphragm.

The Mesothelioma and Radical Surgery (MARS) trial in 2011 stated that EPP, in the context of trimodal therapy, was of no benefit and was harmful enough that further study was not warranted [4]. However, that study has been criticized for the factors it analyzed, its design, and the high rate of mortality fol-

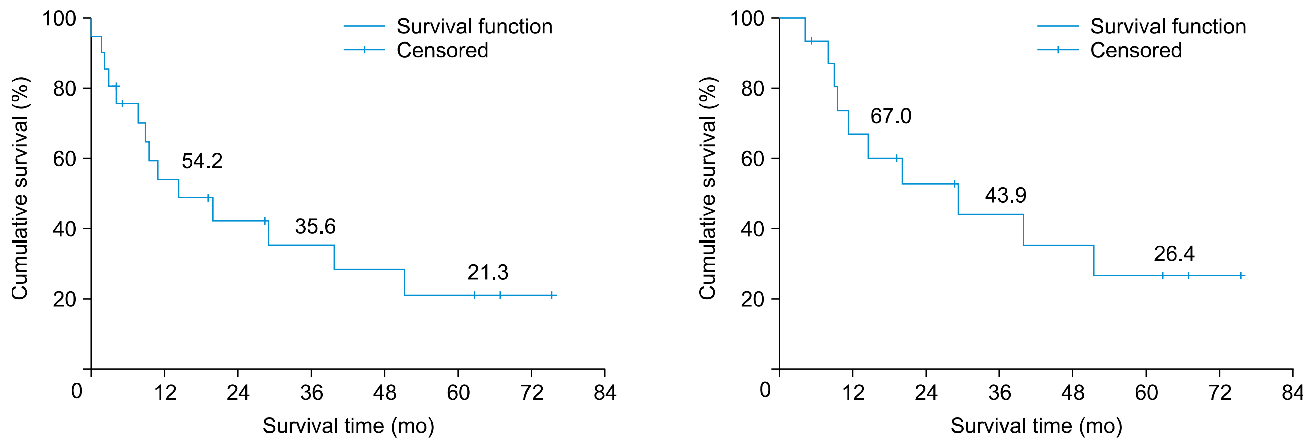

Fig. 1. (A) Overall survival of 21 patients. The overall median survival was 14.3 months. (B) Overall survival excluding 90-day mortality. The overall median survival was 29.0 months.

lowing EPP, and to some, has been regarded as a study that can "lead research regarding MPM into a wrong direction" [5,6]. To support this, most current studies in the literature support surgery as part of multimodal therapy [7-10]. In the SEER analysis of 13,734 MPM patients between 1973 and 2009, surgery was a predictive factor for longer survival [11].

In this context, we sought to analyze our single-institution experience with the surgical treatment of MPM by assessing patients' preoperative characteristics and their postoperative course, including complications, mortality, overall survival, and recurrence-free survival.

Methods

This was a retrospective review of 21 patients who underwent surgical treatment for MPM at a single institution from January 2001 to June 2015. Patients' preoperative profiles and postoperative data were reviewed from medical records. Patients who presented with possible MPM were initially evaluated to obtain a histologic confirmation via thoracoscopic or needle biopsy. Staging following tissue confirmation was performed using computed tomography (CT), positron emission tomography scans to investigate possible metastasis, and magnetic resonance imaging. When the patient was deemed fit for surgical resection, preoperative echocardiography and a pulmonary function test including the diffusing capacity of the lungs for carbon monoxide were evaluated. Detailed demographics and preoperative data are shown in Table 1. The preoperative risk factors were classified according to the Charlson comorbidity index. The type of surgery was defined as EPP; pleurectomy if the whole parietal pleura, diaphragm, and pericardium were excised; and chest wall excision if only the affected portion of the chest wall was resected. The patient's final pathology and staging were classified postoperatively. Local recurrence was defined as metastasis in the ipsilateral hemithorax. All patients were staged as according to the seventh American Joint Committee on Cancer TNM staging system. The cohort's postoperative complications, mortality, overall survival, and recurrence rate were analyzed.

Table 3. Recurrence-free survival

Variable	Value
Recurrence pattern	
Local (ipsilateral mediastinal lymph node, chest wall)	8 (38.6)
Distant (liver, bone, peritoneum)	2 (9.5)
Mixed (local+distant)	2 (9.5)
Recurrence-free survival (%)	
1 yr	41.8
3 yr	33.4
5 yr	11.1
Median recurrence-free survival for different types of surgery (mo)	
Extrapleural pneumonectomy	7.5
Pleurectomy	2.5
Excision	38.3
Median recurrence-free survival	11.8

Values are presented as number (%), %, or median.

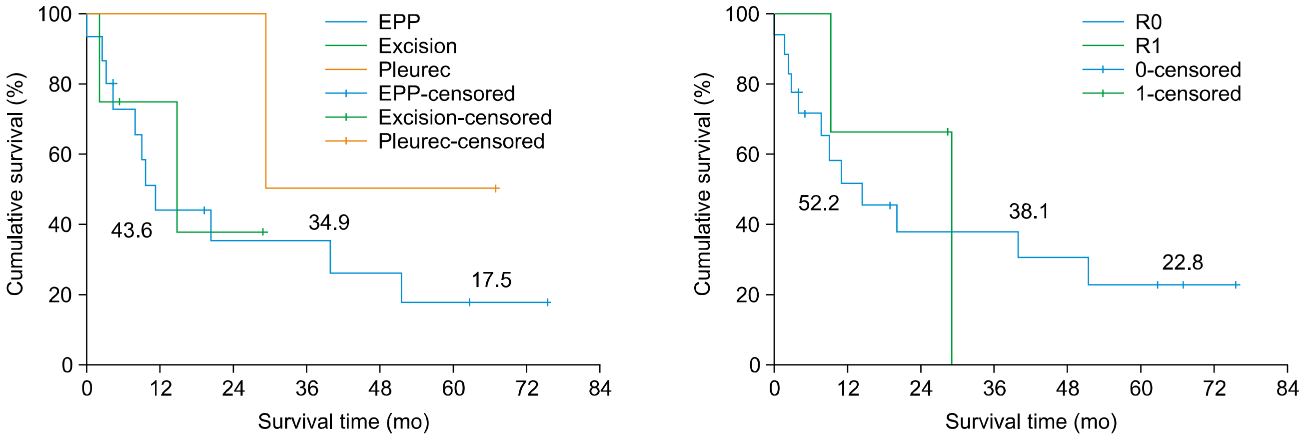

Fig. 2. (A) Survival by operation type (p=0.595). (B) Survival by whether the resection was complete (p=0.826). EPP, extrapleural pneumonectomy.

Results

Patients' postoperative course, including complications, mortality, survival rate, and cause of death, is shown in Table 2. The most common histologic type was epithelioid (13 of 21, 61.8%), followed by sarcomatoid (2 of 21, 9.5%), biphasic (1 of 21, 4.8%), undifferentiated (1 of 21, 4.8%), and desmoplastic (1 of 21, 4.8%), and 5 cases were unclassified. The median hospital stay was 12 days (range, 1–63 days). The overall incidence of postoperative complications was 33.3%. Heart failure was the most common complication (n=3, 14.3%), followed by vocal cord palsy (n=2, 9.5%), pneumonia (n=1, 4.8%), and wound complications (n=1, 4.8%). In-hospital mortality occurred in 2 patients, one patient due to sudden cardiac arrest on postoperative day 0, owing to acute right ventricular failure, and the other due to postoperative bacterial pneumonia. Two patients died within 90 days after surgery: 1 due to aggravated heart failure, and 1 due to extensive systemic metastasis. The survival rate at 1 year, 3 years, and 5 years was 54.2%, 35.6%, and 21.3%, respectively, with a median survival duration of 14.3 months (range, 0–75.3 months) (Fig. 1A). Overall, tumor recurrence was the most common cause of death (8 of 21), followed by heart failure (2 of 21) and severe acute renal failure, acute respiratory distress syndrome, pneumonia, and sepsis empyema, all with 1 occurrence each.

The median recurrence-free survival was 11.8 months in the total cohort, as shown in Table 3. The 1-year, 3-year, and 5-year recurrence-free survival rate was 41.8%, 33.4%, and 11.1%, retrospectively. In the 12 cases of recurrence, 8 patients showed local recurrence (defined as metastasis to the ipsilateral hemithorax) in the lung, rib, peritoneum, pleura, thoracic spine, and intrathoracic lymph node; 2 patients showed distant metastasis in the liver and retroperitoneum; and 2 patients showed both local and distant metastasis.

The patients who underwent pleurectomy showed the highest rate of survival at 43.6%, followed by the excision group at 34.9% and the EPP group at 17.5%, although this pattern was statistically non-significant (p=0.595) (Fig. 2A). All but 3 patients (19 of 22) had a complete resection with negative resection margins, while the remaining 3 patients showed R1 resection and had a worse outcome (Fig. 2B).

One patient of note is #15 in Table 4. A 53-year old man without any other medical history other than diabetes mellitus was initially diagnosed with MPM. Neoadjuvant radiotherapy was done (60 Gy in 30 fractions) and the patient underwent pleurectomy with chest wall resection (8th–11th rib) and reconstruction, as well as wedge resection of the affected right lower lobe of the lung. All resection margins were negative for malignancy. However, 3 months later, a CT scan revealed an enlargement of the right costophrenic angle lymph node. He again underwent excision of the mass, which was consistent with metastasis of MPM. He then underwent 9 cycles of cisplatin and pemetrexed. After 7 years, he is still receiving outpatient follow-up without any symptoms or signs of recurrence.

Table 4. Individual profiles of the entire cohort

No.	Age (yr)	Sex	Operation type	Side	Comorbidity (Charlson index)	Resection margin	Histology	Staging	Stage	Neoadjuvant therapy	Adjuvant therapy	Regimen	Survival time (mo)	Recurrence site	Recurrence-free survival (mo)	Cause of death
1	57	M	Lobectomy, RLL, partial resection of 8th–9th ribs	Rt.	1	R0	Undifferentiated	T3N0	3	-	-	-	1.8	-	1.8	Pneumonia
2	49	M	EPP	Rt.	0	R0	Sarcomatoid	T2N0	2	-	-	-	2.8	-	26.8	Heart failure
3	47	M	EPP	Rt.	0	R0	NA	T2N0	2	CTx	RTx	Cisplatin, pemetrexed	9	Liver	29.0	Recurrence
4	45	F	EPP	Rt.	0	R0	NA	T3N0	3	-	CTx+RTx	Cisplatin, pemetrexed	10.9	Chest wall, liver	2.8	Recurrence
5	59	M	EPP	Lt.	1	R0	Epithelial	T2N0	2	-	RTx	-	39.7	T12	4.0	Recurrence
6	65	M	EPP	Rt.	2	R0	Epithelial	T3N0	3	-	-	-	0.1	-	1.9	Heart failure
7	57	M	EPP	Rt.	0	R0	Epithelial	T3N2	3	-	RTx	-	4	-	0.5	ARDS
8	57	M	EPP	Rt.	3	R0	Epithelial	T3N2	3	-	CTx	Cisplatin, pemetrexed	20	Retroperitoneal LN	75.3	Recurrence
9	52	M	EPP	Lt.	1	R0	Epithelial	T2N2	3	-	CTx	Cisplatin, pemetrexed	7.7	Liver, rib	3.0	ARF
10	61	F	EPP	Lt.	2	R1	Epithelial	T2N1	3	-	RTx	-	9.2	-	36.4	Sepsis
11	53	M	EPP	Rt.	1	R0	Epithelial	T3N0	3	-	RTx	-	51.2	RTx. rib	7.3	Recurrence
12	79	M	Chest wall resection	Rt.	3	R0	Epithelial	T3N1	3	-	-	-	14.3	Lung	5.7	Recurrence
13	63	M	EPP	Lt.	2	R0	Desmoplastic	T2N0	2	-	CTx	Cisplatin, pemetrexed	2.3	Chest wall	9.2	Recurrence
14	64	M	Pleurectomy	Rt.	2	R1	Biphasic	T3Nx	3	-	-	-	29	Pleura	28.4	Recurrence
15	53	M	Pleurectomy with chest wall resection	Rt.	2	R0	Sarcomatoid	T4Nx	4	RTx	-	-	66.7	Cardiophrenic LN	2.7	-
16	61	F	EPP	Lt.	3	R0	NA	T2N0	2	-	-		75.3		7.9	-
17	39	F	EPP	Rt.	0	R0	Epithelial	T3N2	3	-	CTx	Cisplatin, pemetrexed	19	Peritoneum	11.8	-
18	60	M	EPP	Rt.	2	R0	Epithelial	T3N0	3	-	-	-	62.5	Chest wall	5.4	-
19	32	F	EPP	Rt.	0	R0	Epithelial	T2N2	3	-	CTx	Cisplatin, pemetrexed	3.8	-	4.9	-
20	50	M	Excision	Rt.	1	R1	Epithelial	T3N0	3	-	RTx	-	28.4	-	3.8	-
21	53	F	Chest wall resection	Lt.	1	R0	Epithelial	T3N0	3	-	RTx	-	4.9	-	0.1	-

M, male; F, female; RLL, right lower lobe; Rt., right; Lt., left; EPP, extrapleural pneumonectomy; NA, unclassified; CTx, chemotherapy; RTx, radiotherapy; ARDS, acute respiratory distress syndrome; LN, lymph node; ARF, acute renal failure.

Discussion

Mesothelioma is a rare type of malignancy that is known for its aggressiveness, with a median survival of approximately 1 year. [1] The National Comprehensive Cancer Network (NCCN) 2017 clinical practice guidelines for MPM present general steps that clinicians must take when treating patients with MPM. Treatment options may include radiotherapy, chemotherapy, and surgery, and select patients (clinical stages I–III, resectable tumor, and medical tolerance to undergo therapy) are candidates for multimodal therapy [12].

However, the role of surgery itself has always been a matter for debate. A dataset study from 1990 to 2004 found that patients who underwent surgery showed a median overall survival of 11 months, as compared to 7 months in patients who did not undergo surgery ($p < 0.0001$) [13]. In this light, most of the current literature incorporates surgery as part of a multimodal therapeutic plan for MPM.

The surgical procedure can be either EPP, which is defined as en bloc resection of the pleura, lung, ipsilateral diaphragm, and often the pericardium, or P/D, which entails complete removal of the pleura, all gross tumor, and/or en bloc resection of the pericardium and/or diaphragm with reconstruction. Due to the lack of surgical margins and diffuse growth pattern, complete resection is microscopically impossible. Thus, the goal of any surgical procedure for MPM is complete gross cytoreduction of the tumor, or in other words, a macroscopic complete resection. Thus, when multiple site involvement is suspected, surgery should not be considered.

The 2017 NCCN guidelines suggest that both EPP and P/D are feasible surgical options, but which surgical method is oncologically better remains unknown. Two meta-analyses reported that P/D, when compared to EPP, was associated with a greater than 50% reduction in postoperative morbidity, a 2.5-fold lower short-term mortality rate, and an equivalent, if not greater, median overall survival [14,15]. Support regarding P/D as the surgical method of choice over EPP is increasing, and the MARS-II trial comparing P/D to the best medical therapy is currently underway [16]. However, it must be pointed out that selection bias may play a part in the choice between EPP and P/D. As Flores et al. [17] pointed out in a 2008 study of 663 patients, many surgeons do not consider EPP and P/D to be exchangeable in terms of indications, and cases with bulky parenchymal involvement or involvement of the fissures may only be dealt with through EPP. It must also be pointed out that patients undergoing EPP have a higher tumor staging preoperatively than those undergoing P/D, which may affect postoperative mortality in terms of tumor recurrence. Moreover, patient comorbidities should also be considered, as those with a lower functional status or any other major underlying disease are probably unfit to undergo EPP. Clear guidelines regarding the surgical procedure of choice according to tumor staging and patient characteristics would be helpful for choosing the proper treatment.

In our series, except for patient #1, all in-hospital mortality and morbidity occurred in patients who underwent EPP, which support the general consensus that EPP is associated with higher preoperative and postoperative mortality and morbidity. Our study could not provide sufficient data as to which operative method is associated with the most oncologic benefits due to the insufficient number of patients. However, patient #15, as mentioned, underwent P/D as well as chest wall resection and another metastatectomy in the following years, and is still receiving follow-up with any sign of recurrence. This implies that P/D can also achieve complete resection of tumors, although the aggressiveness of MPM limits the percentages.

There is limited evidence regarding the best treatment option for cases of recurrent MPM, especially in terms of surgical intervention [18]. As shown by patient #15, we consider surgery to be a feasible option in cases of recurrence of a single tumor in the ipsilateral chest cavity, which is a local recurrence that can be excised. We plan to do so in the future for further cytoreduction of MPM, although its efficacy must be demonstrated in a study with a larger group of cases of recurrent MPM.

A surgical lesson we recognized was that the inevitable sacrifice of the phrenic nerve must prompt the surgeon to preserve the integrity of the diaphragm, as elevation of the diaphragm and the underlying liver deterred a patient from undergoing postoperative adjuvant radiotherapy. We usually ‘peeled’ the outer layer of the diaphragm when preserving the diaphragm. However, the diaphragm lost integrity in terms of its function as time passed, and showed radiological signs of diaphragm elevation. Thus, when diaphragmatic involvement is suspected, total excision of the diaphragm and reconstruction with a non-native material may worth considering in light of possible future plans for radiotherapy and postoperative respiratory function.

In conclusion, although our data did not yield conclusive outcomes due to the small number of cases, we have illustrated the various forms of surgical management used in various cases of MPM. A further study is warranted with a larger patient cohort, which may lead to clear surgical guidelines regarding MPM.

Conflict of interest

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

Acknowledgments

This study was supported by a Grant of the Samsung Vein Clinic Network (Daejeon, Anyang, Cheongju, Cheonan; Fund no. KTCS04-102).

References

1. Taioli E, Wolf AS, Camacho-Rivera M, et al. *Determinants of survival in malignant pleural mesothelioma: a Surveillance, Epidemiology, and End Results (SEER) study of 14,228 patients*. PLoS One 2015;10:e0145039.
2. Burt BM, Cameron RB, Mollberg NM, et al. *Malignant pleural mesothelioma and the Society of Thoracic Surgeons Database: an analysis of surgical morbidity and mortality*. J Thorac Cardiovasc Surg 2014;148:30-5.
3. Rice D, Rusch V, Pass H, et al. *Recommendations for uniform definitions of surgical techniques for malignant pleural mesothelioma: a consensus report of the international association for the study of Lung Cancer International Staging Committee and the International Mesothelioma Interest Group*. J Thorac Oncol 2011;6:1304-12.
4. 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.
5. Weder W, Stahel RA, Baas P, et al. *The MARS feasibility trial: conclusions not supported by data*. Lancet Oncol 2011;12:1093-4.
6. Bliss JM, Coombes G, Darlison L, et al. *The MARS feasibility trial: conclusions not supported by data: authors' reply*. Lancet Oncol 2011;12:1094-5.
7. Wolf AS, Richards WG, Tilleman TR, et al. *Characteristics of malignant pleural mesothelioma in women*. Ann Thorac Surg 2010;90:949-56.
8. Sugarbaker DJ, Wolf AS. *Surgery for malignant pleural mesothelioma*. Expert Rev Respir Med 2010;4:363-72.
9. Taioli E, Wolf AS, Camacho-Rivera M, Flores RM. *Women with malignant pleural mesothelioma have a threefold better survival rate than men*. Ann Thorac Surg 2014;98:1020-4.
10. Sugarbaker DJ, Wolf AS, Chirieac LR, et al. *Clinical and pathological features of three-year survivors of malignant pleural mesothelioma following extrapleural pneumonectomy*. Eur J Cardiothorac Surg 2011;40:298-303.
11. Taioli E, Wolf AS, Moline JM, Camacho-Rivera M, Flores RM. *Frequency of surgery in black patients with malignant pleural mesothelioma*. Dis Markers 2015;2015:282145.
12. De Perrot M, Feld R, Cho BC, et al. *Trimodality therapy with induction chemotherapy followed by extrapleural pneumonectomy and adjuvant high-dose hemithoracic radiation for malignant pleural mesothelioma*. J Clin Oncol 2009;27:1413-8.
13. Flores RM, Riedel E, Donington JS, et al. *Frequency of use and predictors of cancer-directed surgery in the management of malignant pleural mesothelioma in a community-based (Surveillance, Epidemiology, and End Results [SEER]) population*. J Thorac Oncol 2010;5:1649-54.
14. Taioli E, Wolf AS, Flores RM. *Meta-analysis of survival after pleurectomy decortication versus extrapleural pneumonectomy in mesothelioma*. Ann Thorac Surg 2015;99:472-80.
15. Cao C, Tian D, Park J, Allan J, Pataky KA, Yan TD. *A systematic review and meta-analysis of surgical treatments for malignant pleural mesothelioma*. Lung Cancer 2014;83:240-5.
16. Lim E. *MARS 2: a feasibility study comparing (extended) pleurectomy decortication versus no pleurectomy decortication in patients with malignant pleural mesothelioma (MARS2)* [Internet]. Bethesda (MD): U.S. National Library of Medicine; 2015 [cited 2017 Sep 1]. Available from: http://www.clinicaltrials.gov/show/NCT02040272.
17. Flores RM, Pass HI, Seshan VE, et al. *Extrapleural pneumonectomy versus pleurectomy/decortication in the surgical management of malignant pleural mesothelioma: results in 663 patients*. J Thorac Cardiovasc Surg 2008;135:620-6.
18. Politi L, Borzellino G. *Second surgery for recurrence of malignant pleural mesothelioma after extrapleural pneumonectomy*. Ann Thorac Surg 2010;89:207-10.