Role of surgery in the multidisciplinary treatment of malignant pleural mesothelioma

Interview with Federico Rea[1] and Paolo Andrea Zucali[2] *by* Lorenzo D'Ambrosio[3]

In favor:
Federico Rea[1]
Against:
Paolo Andrea Zucali[2]

Introduction

Malignant pleural mesothelioma (MPM) is a malignancy that is hard to diagnose and treat successfully. Over the years, the optimal treatment of MPM has been, and continues to be, controversial. There are three main components to the treatment of MPM: surgery, chemotherapy, and radiation therapy. Radical surgery alone (extrapleural pneumonectomy or pleurectomy/decortication) is a maximal cytoreductive procedure but an R0 resection is rarely achieved and the risk of local recurrence remains high due to the location and the relation to surrounding normal tissues. Currently available chemotherapies are associated with an objective response rate of only 30–40%, and complete responses are extremely rare. Moreover, full-dose radiotherapy (RT) to the entire hemi-thorax as a treatment for controlling tumor growth, although effective, may cause life-threatening pulmonary toxicity in the absence of lung removal. To date, the best survival data have been reported with multimodality treatment strategies including surgical resection. However, there is still a lot of debate in the literature regarding both the necessity and timing of each treatment approach. Improving outcomes for patients with MPM is an unmet need, especially because the number of cases of MPM is expected to continue to rapidly increase in the coming years. Without any treatment, the median expected overall survival for a patient with MPM is less than 12 months. In this interview, two experts in the field discuss several MPM treatment strategies that involve surgery in combination with different adjuvant and neoadjuvant therapies to provide some insight into the best multimodality treatment approach for patients with MPM.

[1]Department of Cardiac, Thoracic and Vascular Sciences, Thoracic Surgery Division, University of Padova, Padova, Italy.
[2]Division of Oncology and Hematology, Humanitas Cancer Center Istituto Clinico Humanitas-IRCCS, Rozzano (Milano), Italy.
[3]Division of Medical Oncology, Candiolo Cancer Center, IRCCS, Candiolo, Italy.
Correspondence to: Lorenzo D'Ambrosio, MD, Oncologia Medica, Candiolo Cancer Center, IRCCS, Strada Provinciale 142, 10060 Candiolo (Torino), Italy.
Phone: +39 011 99333623 – Fax: +39 011 9933290
E-mail: lorenzo.dambrosio@ircc.it
CANCER BREAKING NEWS 2016;4(1):11-16
DOI: 10.19156/cbn.2016.0003

1. Which is, in your opinion, the best upfront treatment in medically operable malignant pleural mesothelioma: surgery or induction chemotherapy ± radiotherapy?

Pro induction chemotherapy

The obvious limitations of current treatment options have prompted the exploration of combination therapies. Over recent years, various combinations of multimodality therapies have been evaluated and this approach seemed to reduce both local and distant recurrences improving the overall survival of MPM patients. Nevertheless, the best treatment combination still remains a matter of debate. Indeed, the optimal treatment sequence is not clearly defined and, in particular, the role of surgery in combination with adjuvant or neoadjuvant chemotherapy and/or postoperative radiotherapy has not yet been studied in a randomized controlled trial (RCT). However, the administration of both chemotherapy and postoperative RT for most MPM patients prompted many groups to introduce a trimodal approach based on preoperative chemotherapy, surgery and postoperative RT with the goal of improving treatment compliance. This strategy had shown the best results in terms of both overall and progression-free survival [1-10]. Indeed, median survival for all patients included in these studies (intention-to-treat analyses) ranged from 13 to 26 months. Moreover, the patients who completed all three phases of therapy had a median survival of 29-59 months compared with 9-14 months for those who were unable to complete the planned regimen. To address the question of the best timing of chemotherapy, the European Organization for Research and Treatment of Cancer (EORTC) is starting a randomized phase II trial that compares induction chemotherapy followed by extended (radical)

pleurectomy decortication (EPD) with upfront EPD followed by adjuvant chemotherapy.
Over the years, standard chemotherapy regimens for systemic treatment of MPM have changed. Pemetrexed plus platinum derivatives represent the best front-line treatment option to date for MPM patients. The pemetrexed-cisplatin combination has been associated with median time to progression and overall survival of 5.7 and 12.1 months, respectively [11]. In patients unfit to receive a cisplatin-based chemotherapy, pemetrexed alone or in combination with carboplatin has been proposed as a strategy that reduces toxicity while maintaining the same survival outcomes [12, 13].
The optimal induction chemotherapy regimen has not yet been defined, and prospective randomized studies assessing toxicity and survival data for the different protocols are required. In a retrospective analysis, Pasello et al. observed that both carboplatin plus pemetrexed (CA) and cisplatin plus pemetrexed (CP) combinations were active and feasible neoadjuvant regimens with similar outcomes in terms of progression-free survival, response rate, disease control and resection rate [14]. However, the lower tolerability of the CP combination might reduce the clinical condition of patients who are about to undergo surgery. As a result, several institutions currently prefer the CA combination in the neoadjuvant setting.

Against induction chemotherapy

Several published trials [7-9] have reporting the results of multimodality treatment for MPM, including neoadjuvant chemotherapy. The rationale and the potential advantages of this approach are to: a) facilitate better patient tolerance of chemotherapy to allow the complete course to be administered; b) prevent distant relapses; c) facilitate surgical resection by reducing disease burden; and d) increase tolerance to high-dose RT. A recent review [15] compared several series of MPM patients treated with trimodality therapy and showed a median survival for all intention–to–treat patients that ranged from 13–26 months. A further analysis showed that patients able to complete all three phases of the treatment protocol achieved a median survival of 29–59 months, compared with a median survival of 9–14 months for patients who were unable to complete the protocol. Despite these encouraging data, it has to be noted that 25–28% of the patients showed disease progression during chemotherapy and only a few cases demonstrated a complete pathological response on the resected specimen. Most importantly, fewer than 50% of patients (range 33–71%, with the lower percentage rates observed in studies using extrapleural pneumonectomy [EPP] as surgical option) were able to complete the full trimodality scheme (induction chemotherapy, surgery, hemi-thoracic radiation) [1, 7-9]. Disease progression, toxicity, and renal failure were the main causes of chemotherapy dose reduction or withdrawal. Induction chemotherapy-related adverse events and toxicities might also be responsible for delay in surgery and radiotherapy administration (especially when chemotherapy is not effective) and could decrease a patient's performance status at the time of surgery. Indeed, some authors reported the impairment of cardiorespiratory function as a relevant detrimental effect of induction chemotherapy that could lead to increased risk of perioperative morbidity and mortality [16]. This uncertainty points out the importance of multidisciplinary management so as to improve patient selection to each strategy.

2. If your patient has been judged "resectable", do you suggest extrapleural pneumonectomy (EPP) or pleurectomy/decortication (P/D)? In this context, when do you perform pleurodesis?

Pro pleurectomy/decortication

Surgical resection has a controversial role in the management of MPM and it is essentially based on two different procedures: EPP that involves an en bloc resection of the lung, pleura, pericardium and diaphragm, and P/D that involves resection of the parietal and visceral pleurae, pericardium, and diaphragm (when necessary), but spares the lung. The goal of surgery is to remove all gross disease, but a complete resection (R0) with surgery alone is theoretically unobtainable given the substantial difficulty of eradicating residual microscopic disease regardless of whether an EPP or P/D procedure is performed.
Given the current focus on surgery in combination with chemotherapy and/or radiation in a multimodality strategy, the decision to perform either EPP or P/D in this setting is based more on surgeon preference rather than scientific data. Debate between EPP and P/D focuses on their relative merits with respect to operative risk, ability to remove all gross tumor and available options for adjuvant therapy. In a field that completely lacks randomized clinical trials comparing these two surgical approaches, published data suggest significantly lower perioperative mortality and a trend towards longer survival after P/D compared with EPP [17-19]. In particular, analysis of a large number of studies comparing P/D and EPP suggested that P/D was associated with a 2.5-fold lower short-term mortality (peri-operatively and within 30 days) than EPP [19]. Another analysis comparing data for extended P/D (n=513) *versus* EPP (n=632) showed similar results, with

significantly lower peri-operative mortality (2.9% *vs* 6.8%, p=0.02) and morbidity (27.9% *vs* 62.0%, p<0.0001) in patients who underwent extended P/D compared to EPP. Moreover, the median overall survival was 13–29 months for extended P/D and 12–22 months for EPP, with a non-statistically significant trend favoring extended P/D. Notably, if performed in specialized centers, P/D is considered an effective part of a multimodality treatment program in conjunction with systemic chemotherapy and intensity-modulated radiation therapy, a technique able to deliver high doses of radiation to the hemi-thorax of MPM patients with the intact lung with an acceptable safety profile [20, 21]. Therefore, it is this author's opinion that P/D should be preferred over EPP when technically feasible.

In the context of a trimodality approach, the role of pleurodesis is not yet established. Current clinical practice for the management of MPM effusions is derived from general studies of malignant pleural effusions mainly based on patients with metastatic carcinomas (lung, breast, gynecological and gastro-intestinal). Dedicated studies on pleurodesis in MPM have been retrospective, underpowered and employed different pleurodesis methods and definitions of success [22]. Despite the lack of randomized trials to confirm the benefit of this procedure, in our clinical practice we usually perform talc pleurodesis at the time of diagnostic video-assisted thoracoscopy (VAT) in all MPM patients presenting pleural effusion with the goal of preventing the recurrence of dyspnea.

Against pleurectomy/decortication (pro extrapleural pneumonectomy)

Even if the standard of care for MPM treatment has not yet been established, surgery still plays an important role. The performance of two surgical procedures are associated with maximal cytoreductive intent: radical P/D and EPP. EPP involves en bloc resection of the parietal pleura, lung, ipsilateral hemi-diaphragm, and ipsilateral pericardium; its aim is to achieve "radical" cytoreduction and facilitate maximal delivery of postoperative RT. EPP was first described by Sarot [23] for the treatment of tuberculous empyema in 1949; in 1976 Butchart et al. [24] performed the first EPP for patients with MPM reporting a prohibitively high perioperative mortality rate of 31% and a median survival of only 10 months. Since these early reports, advances in patient selection, surgical technique, and perioperative care have enabled improvements in the surgical outcomes of patients undergoing EPP. Studies involving adjuvant and neoadjuvant therapies such as systemic chemotherapy, intrapleural chemotherapy, RT, and photodynamic therapy associated with EPP have reported varying degrees of success.

In a recent review [18], median overall survival in patients undergoing EPP for MPM was reported to range from 9.4 to 27.5 months [2, 5, 7, 8, 17, 25-29], with 1-, 2-, 3-, and 5-year survival rates of 36–83%, 5–59%, 0–41%, and 0–24%, respectively; median disease-free survival was 7–19 months. Overall perioperative mortality rates were 0–11.8% (interquartile range 3.7–7.6%), and overall rates for perioperative morbidity and major morbidity of 22–82% and 12.5–48%, respectively. According to one of the largest series published to date involving 385 patients who underwent EPP, the most common morbidities included atrial arrhythmia, respiratory failure, respiratory infections, pulmonary embolus, and myocardial infarction [17]. Unfortunately, due to the aggressive nature of the disease, treatment failure after EPP alone still remains high and is characterized by both local and distant relapses.

More recently, Rusch et al. [30] collected the largest international database with 3101 cases from 15 centers as part of the revision process for the International Union Against Cancer (UICC) TNM staging system. Among 1494 patients undergoing surgery with curative intent, the best outcome was achieved in patients with stage I disease who underwent EPP. Other studies have compared EPP and P/D and reported slightly lower short-term mortality with P/D [19]. However, these were not randomized studies, and are therefore subject to biases. The only RCT of MPM surgery to date compared EPP with no surgery. In this study the authors concluded that there was no evidence to support the use of EPP in the treatment of MPM [31]. However, this study has been widely criticized because of the small sample size and the unusually high operative mortality. In conclusion, even in the absence of an RCT, in our opinion there is enough evidence to support the use of EPP in well selected patients and at high-volume centers, with good results possible (in terms of both survival and relapse rates), with morbidity comparable to that with other surgical techniques performed with cytoreductive intent (P/D).

3. Is there a role for chemotherapy ± radiotherapy after induction chemotherapy and surgery?

Pro chemotherapy ± radiotherapy

Given the difficulty in delivering adjuvant treatments after surgery, several studies have been conducted to investigate the effects of neoadjuvant chemotherapy in MPM patients. The main advantages of treating patients with systemic chemotherapy before surgery include improved tolerance of chemotherapy without altering the surgical morbidity and mortality rates in the majority of the cases, and potential improvement in objective response at the time of definitive treatment. Therefore, postoperative chemotherapy with or without RT could be seen as difficult to tolerate after induction chemotherapy and radical surgery. However, in selected fit patients who have achieved tumor shrinkage during neoadjuvant chemotherapy, postoperative treatment could be considered an interesting option. Theoretically, the combination of chemotherapy with RT in these patients might have a greater potential to reduce not only the local recurrence rate but also the distant recurrence rate. However, there is currently no published data to define the feasibility, tolerability and safety of this strategy. At this stage, it is our opinion that this strategy should be considered only in the context of a clinical trial.

Against chemotherapy ± radiotherapy

The use of adjuvant therapies (chemo- and/or radiotherapy) in MPM patients is intended to improve both local control and distant relapses. However, in a study that analyzed a large cohort of patients [26] who received an aggressive treatment encompassing cytoreductive EPP, adjuvant chemotherapy and consolidative RT, half of the patients experienced recurrence, with the ipsilateral hemithorax the predominant site of first failure (67% of all recurrences). A significant obstacle to the delivery of high dose RT after surgery was the concurrent administration of adjuvant chemotherapy. Furthermore, several patients may not tolerate the full dose of chemotherapy after aggressive surgical intervention, or treatment delivery may be significantly limited in these patients due to side effects, toxicities, decreased cardio-pulmonary reserve, and worsening of quality of life. Finally, the option of using adjuvant chemotherapy alone is limited by the difficult evaluation of its real effectiveness after the disease has already been resected. A promising perspective comes from intraoperative adjuvant chemotherapy, such as heated intraoperative chemotherapy (HIOC), that may represent an effective paradigm to enhance local control in the context of minimal residual disease [32].

4. Do you foresee a role, if any, for new radiotherapy techniques (e.g. tomotherapy) in the management of medically operable MPM or limited relapses?

Pro new radiotherapy techniques

The role of RT in the management of medically operable MPM has not been well defined and it is still under evaluation in a randomized study run by the Swiss Group for Clinical Cancer Research (NCT00334594). Many studies have evaluated the use of RT as part of multimodality treatment in addition to surgery and/or chemotherapy in an attempt to improve local control and reduce local failure. More recently, a novel modality of irradiation, known as "Intensity-Modulated Radiation Therapy" (IMRT), has been developed for the treatment of several tumors. IMRT allows delivery of dose distributions that conform to complicated convex and concave target volumes. This represents a potential advantage for large, irregular targets in close proximity to critical structures, as is the case in MPM. IMRT overcomes some limitations of classical RT techniques, providing more conformal high-dose RT and improving coverage of the at-risk hemi-thorax area). Preliminary results with IMRT in the adjuvant setting after EPP appear particularly promising [7, 9, 33, 34]. Indeed, at least 63% of patients were able to complete IMRT after EPP and most patients achieved excellent local control after hemithoracic radiation treatment. Moreover, radical IMRT was associated with promising survival outcomes with an acceptable toxicity profile, including after lung-sparing surgery and chemotherapy [20, 21]. However, it is strongly recommended that this type of RT be carried out in highly specialized centers.

The absence of a significant pathologic response after induction chemotherapy led several centers to develop new RT-containing strategies. A group of Canadian researchers hypothesized that induction RT before EPP would potentially represent a more efficient approach. Preoperative radiation aims to provide optimal local control, keeping the administration of systemic therapy for patients with a higher risk of distant recurrence, such as in presence of pN2 disease. With this aim, they developed a new Surgery for Mesothelioma After Radiation Therapy (SMART) protocol consisting of induction-accelerated hemithoracic radiation followed by EPP. The rationale behind this approach was to maximize both the tumoricidal and immunogenic potential of RT while minimizing radiation toxicity to the ipsilateral lung. A preliminary trial demonstrated the feasibility of this approach and showed encouraging results in patients with epithelial histology [35].

In the presence of small tumor volume, the use of IMRT instead of radical surgery, in MPM patients who are potentially resectable but unfit or unwilling to receive surgery, could represent an intriguing option. However, this approach in MPM patients with intact lung should be considered very carefully and preferably in the context of a clinical trial.

Against new radiotherapy techniques

RT has evolved as an important component of treatment for MPM. From the first study by Rusch et al. [33] showing a potential benefit for patients undergoing adjuvant high-dose hemi-thoracic radiation after EPP, further studies have demonstrated a survival benefit of adjuvant intensity-modulated RT (IMRT) after EPP [7, 9, 34]. The down side is that this sequence of treatments exposes patients to the risk of radiation-induced pneumonitis in the contralateral lung (in the case of EPP) or in both lungs (in the case of P/D). However, only conflicting data are currently available. Indeed, in the experience published by Allen et al. [36], the authors reported a 46% rate of grade 5 pneumonitis using IMRT after EPP, while other centers did not report any grade 3 to 5 pneumonitis in the same setting of post-surgical radiotherapy [7, 34]. Thus, there are not yet enough data to make recommendations on the use of new RT techniques for MPM patients.

Acknowledgments

The authors thank Nicola Ryan, an independent medical writer, who provided native English editing and journal styling on behalf of HPS. This editorial assistance was funded by PharmaMar, Spain.

Conflicts of Interest

The Authors declare there are no conflicts of interest in relation to this article.

References

1. Weder W, Kestenholz P, Taverna C, et al. Neoadjuvant chemotherapy followed by extrapleural pneumonectomy in malignant pleural mesothelioma. J Clin Oncol 2004; 22(17):3451-7.
2. Opitz I, Kestenholz P, Lardinois D, et al. Incidence and management of complications after neoadjuvant chemotherapy followed by extrapleural pneumonectomy for malignant pleural mesothelioma. Eur J Cardiothorac Surg 2006;29(4):579-84.
3. Flores RM, Krug LM, Rosenzweig KE, et al. Induction chemotherapy, extrapleural pneumonectomy, and postoperative high-dose radiotherapy for locallyadvanced malignant pleural mesothelioma: a phase II trial. J Thorac Oncol 2006;1(4):289-95.
4. Weder W, Stahel RA, Bernahrd J, et al. Multicenter trial of neo-adjuvant chemotherapy followed by extrapleural pneumonectomy in malignant pleural mesothelioma. Ann Oncol 2007;18(7):1196-202.
5. Rea F, Marulli G, Bortolotti L, et al. Induction chemotherapy, extrapleural pneumonectomy (EPP) and adjuvant hemi-thoracic radiation in malignant pleural mesothelioma (MPM): feasibility and results. Lung Cancer 2007;57(1):87-95.
6. Buduhan G, Menon S, Aye R, et al. Trimodality therapy for malignant pleural mesothelioma. Ann Thorac Surg 2009; 8(3):870-6.
7. de Perrot M, Feld R, Cho BCJ, et al. Trimodality therapy with induction chemotherapy followed by extrapleural pneumonectomy and adjuvant highdose hemithoracic radiation for malignant pleural mesothelioma. J Clin Oncol 2009;27(9):1413-8.
8. Krug LM, Pass HI, Rusch VW, et al. Multicenter phase II trial of neoadjuvant pemetrexed plus cisplatin followed by extrapleural pneumonectomy and radiation for malignant pleural mesothelioma. J Clin Oncol 2009;27(18): 3007-13.
9. Van Schil PE, Bass P, Gaafar R, et al. Trimodality therapy for malignant pleural mesothelioma: results from an EORTC phase II multicentre trial. Eur Resp J 2010;36(6):1362-9.
10. Rea F, Favaretto AG, Marulli G, et al. Phase II trial of neoadjuvant pemetrexed plus cisplatin followed by surgery and radiation in the treatment of malignant pleural mesothelioma (MPM). J Clin Oncol 2011;29(23):3120-5.
11. Vogelzang NJ, Rusthoven JJ, Symanowski J, et al. Phase III study of pemetrexed in combination with cisplatin versus cisplatin alone in patients with malignant pleural mesothelioma. J Clin Oncol 2003;21(14):2636-44.
12. Ceresoli GL, Zucali PA, Favaretto AG, et al. Phase II study of pemetrexed plus carboplatin in malignant pleural mesothelioma. J Clin Oncol 2006;24(9):1443-8.
13. Santoro A, O'Brien ME, Stahel RA, et al. Pemetrexed plus cisplatin or pemetrexed plus carbolatin for chemonaive patients with malignant pleural mesothelioma: results of the International Expanded Access Program. J Thorac Oncol 2008;3(7):756-63.
14. Pasello G, Marulli G, Polo V, et al. Pemetrexed plus carboplatin or cisplatin as neoadjuvant treatment of operable malignant pleural mesothelioma (MPM). Anticancer Res 2012;32(12):5393-400.
15. Donahoe L, Cho J, de Perrot M. Novel induction therapies for pleural mesothelioma. Semin Thorac Cardiovasc Surg 2014;26(3):192-200.
16. Stewart DJ, Martin-Ucar AE, Edwards JG, et al. Extra-pleural pneumonectomy for malignant pleural mesothelioma: the risks of induction chemotherapy, right-sided procedures and prolonged operations. Eur J Cardio-Thorac Surg 2005;27(3):373-8.
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(3):620-6.
18. Cao C, Tian D, Park J, et al. A systematic review and meta-analysis of surgical treatments for malignant pleural mesothelioma. Lung Cancer 2014;83(2):240-5.
19. Taioli E, Wolf AS, Flores RM. Meta-Analysis of survival after pleurectomy decortication versus extrapleural pneumonectomy in mesothelioma. Ann Thorac Surg 2015;99(2):472-80.
20. Chance WW, Rice DC, Allen PK, et al. Hemithoracic intensity modulated radiation therapy after pleurectomy/decortication for malignant pleural mesothelioma: toxicity, pat-

terns of failure, and a matched survival analysis. Int J Radiat Oncol Biol Phys 2015;91(1):149-56.
21. Minatel E, Trovo M, Bearz A, et al. Radical radiation therapy after lung-sparing surgery for malignant pleural mesothelioma: survival, pattern of failure, and prognostic factors. Int J Radiat Oncol Biol Phys 2015;93(3):606-13.
22. Fysh ET, Tan SK, Read CA, et al. Pleurodesis outcome in malignant pleural mesothelioma. Thorax 2013;68(6):594-6.
23. Sarot IA. Extrapleural pneumonectomy and pleurectomy in pulmonary tuberculosis. Thorax 1949;4(4):173-223.
24. 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(1):15-24.
25. Sugarbaker DJ, Flores RM, Jaklitsch MT, et al. Resection margins, extrapleural nodal status, and cell type determine postoperative longterm survival in trimodality therapy of malignant pleural mesothelioma: results in 183 patients. J Thorac Cardiovasc Surg 1999;117(1):54-63; discussion 63-5.
26. Baldini EH, Recht A, Strauss GM, et al. Patterns of failure after trimodality therapy for malignant pleural mesothelioma. Ann Thorac Surg 1997;63(2):334-8.
27. Sugarbaker DJ, Garcia JP, Richards WG, et al. Extrapleural pneumonectomy in the multimodality therapy of malignant pleural mesothelioma. Results in 120 consecutive patients. Ann Surg 1996;224(3):288-94; discussion 294-6.
28. Maggi G, Casadio C, Cianci R, et al. Trimodality management of malignant pleural mesothelioma. Eur J Cardiothorac Surg 2001;19(3):346-50.
29. Maziak DE, Gagliardi A, Haynes AE, et al. Surgical management of malignant pleural mesothelioma: a systematic review and evidence summary. Lung Cancer 2005;48(2):157-69.
30. 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;7:1631-39.
31. 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) randomized feasibility study. Lancet Oncol 2011;12(8):763-72.
32. Sugarbaker DJ, Gill RR, Yeap BY, et al. Hyperthermic intraoperative pleural cisplatin chemotherapy extends interval to recurrence and survival among low-risk patients with malignant pleural mesothelioma undergoing surgical macroscopic complete resection. J Thorac Cardiovasc Surg 2013;145(4):955-63.
33. Rusch VW, Rosenzweig K, Venkatraman E, et al. A phase II trial of surgical resection and adjuvant high-dose hemithoracic radiation for malignant pleural mesothelioma. J Thorac Cardiovasc Surg 2001;122(4):788-95.
34. Rice DC, Stevens CW, Correa AM, et al. Outcomes after extrapleural pneumonectomy and intensity-modulated radiation therapy for malignant pleural mesothelioma. Ann Thorac Surg 2007;84(5):1685-92.
35. Cho BCJ, Feld R, Leighl N, et al. A feasibility study evaluating surgery for mesothelioma after radiation therapy: The "SMART" approach for resectable malignant pleural mesothelioma. J Thorac Oncol 2014;9(3):397-402.
36. Allen AM, Czerminska M, Jänne PA, et al. Fatal pneumonitis associated with intensity-modulated radiation therapy for mesothelioma. Int J Radiat Oncol Biol Phys 2006;65(3):640-5.