

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

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Introduction: Extrapleural pneumonectomy has been well defined; however, surgeons vary regarding the surgical extent and goals of “pleurectomy/decortication” (P/D). We explored mesothelioma surgeons’ concepts of P/D with the aim of unifying surgical nomenclature.

Methods: A web-based survey was administered to surgeons who operated on malignant pleural mesothelioma (MPM) for diagnosis, staging, palliation, or cytoreduction. One hundred thirty surgeons from 59 medical centers were included. Surgeons who did not perform surgery for MPM within the last year were excluded.

Results: There were 62 (48%) respondents from 39 medical centers in 14 countries. The mean number of patients with MPM seen annually at each medical center was 46, and the mean annual number of cytoreductive procedures performed per surgeon was 8. Most (88%) agreed that the goal of cytoreductive surgery should be macroscopic complete

resection of tumor. P/D was defined as resection of parietal and visceral pleura with the aim of achieving macroscopic complete resection by 72% of respondents. If the diaphragm or pericardium required resection, 64% preferred the term “radical P/D,” whereas “P/D” (40%) or “total pleurectomy” (39%) was preferred if these structures were not removed. Most surgeons believed that extrapleural pneumonectomy (90%) or “radical P/D” (68%) could provide adequate cytoreduction, whereas only 23% thought that P/D could.

Conclusions: There was significant variation regarding surgical nomenclature for procedures for MPM. The International Staging Committee of the International Association for the Study of Lung Cancer and the International Mesothelioma Interest Group recommend that P/D should aim to remove all macroscopic tumor involving the parietal and visceral pleura and should be termed “extended” P/D when the diaphragm or pericardium is resected.

Key Words: Mesothelioma, Pleural neoplasm, nomenclature, Surgery.

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Surgery for malignant pleural mesothelioma (MPM) may include relatively minor procedures for diagnosis and staging, more involved debulking operations for palliation, and extensive cytoreductive procedures where the goal is to lengthen survival by reducing the intrathoracic tumor burden to microscopic levels. The latter is usually accomplished either by extrapleural pneumonectomy (EPP) or by a procedure that is presently classified as “pleurectomy/decortication” (P/D), generally as part of a multimodality treatment regimen. Although the surgical technique of EPP has been standardized, there is a variation among surgeons with respect to what is involved in P/D.^{1–5} For some mesothelioma surgeons, P/D refers to a surgical procedure that aims to remove all macroscopic tumor from the affected hemithorax.⁶ This typically includes resection of the entire parietal and

visceral pleura, with resection of portions of the pericardium and diaphragm if involved by tumor. Others refer to this extensive procedure as a “radical” P/D, reserving the term P/D for resection of only the parietal and visceral pleura.^{7,8} Still others use the term P/D to describe a palliative procedure where the intention is debulking of tumor to ameliorate pain and pleural effusion and improve respiratory mechanics.⁹ Occasionally, operative reports will describe P/D when little more than a thoracotomy and generous pleural biopsy has been performed.

In collaboration with the International Mesothelioma Interest Group (IMIG), the International Association for the Study of Lung Cancer (IASLC) recently formed a subcommittee of the International Staging Committee to improve the current staging system for MPM. The mesothelioma subcommittee “Mesothelioma Domain” of the International Staging Committee recently completed an analysis of a large retrospective database and is now developing an international, multidisciplinary, and multi-institutional cohort study that will collect information on extent of disease, personal and demographic characteristics, comorbid illness, treatment, and survival of newly diagnosed patients with MPM. Because there is considerable variation regarding the surgical management of mesothelioma, and in particular P/D, the mesothelioma subcommittee thought that it was important to arrive at definitions of surgical procedures for MPM that would be unambiguous and broadly acceptable to most thoracic surgeons. To arrive at a consensus regarding surgical definitions, a survey was conducted among surgeons who perform surgery for MPM.

METHODS

A web-based questionnaire was created by members of the IASLC mesothelioma subcommittee using a commercially available, online survey designer (www.surveymonkey.com). Unlike a recent survey of surgical opinion in mesothelioma, which included thoracic surgeons regardless of their level of experience with the disease, we polled only surgeons who had a clinical or research interest in MPM and who were presumed able to offer expert opinion.^{10,11} Surgeons were identified by having published on MPM during the past 5 years, by affiliation with a medical center known to specialize in MPM, by affiliation with the IMIG, or by peer reference. One hundred thirty surgeons from 59 centers worldwide were identified and asked to complete the electronic survey. The survey was designed to examine prevailing views about nomenclature for various surgical resections commonly performed for pleural mesothelioma and concepts regarding cytoreduction (Figures 1–4). In addition to multiple-choice options, most questions also offered respondents an opportunity to add text-based comments. We explored opinions regarding use of the terms “partial pleurectomy,” “pleurectomy/decortication,” “total pleurectomy,” and “radical pleurectomy/decortication.” Because EPP has been standardized from a procedural standpoint, we did not further explore terminology for this operation. The survey collected data over a 3-week period from October 11 through October 29, 2010. Two reminders were sent electronically to participants during this period. Responses from thoracic surgeons who did not perform any type of surgery for MPM (including either surgery for diagnosis,

staging, palliation, and/or cytoreduction) were censored from further analysis. Responses were analyzed according to the raw data, and results were reviewed with the members of the IASLC Mesothelioma Domain and the Advisory Board, and consensus achieved before the manuscript was prepared. It was then submitted to all members of the IASLC Staging Committee and to board members of the IMIG for approval before the manuscript and recommendations were finalized.

RESULTS

Respondents

The survey was sent through email to 130 thoracic surgeons, of which 62 (47.7%) responded. Respondents were affiliated with 39 different medical centers in 14 countries. Most were from centers in Europe (47%) or North America (42%) with only six (10%) responders from Asia and one from Australia (Table 1). Three participants did not perform any type of surgery for MPM and were censored from further analysis (Figure 1). One respondent provided incomplete data leaving a total of 58 respondents who provided analyzable data. The mean number of patients with MPM seen annually at participating centers was 40 (median, 32; range, 3–150), and the mean number of mesothelioma surgical cases annually performed by respondents ($n = 58$) was 20 (median, 16; range, 2–80). Ninety-eight percent of surgeons performed surgery for diagnosis, 82% for surgical staging, 85% performed cytoreductive surgery, and 71% performed surgery for palliation. Only 34 of 58 surgeons (59%) performed surgery for all four indications. Three (5%) surgeons performed palliative surgery but not cytoreductive surgery. Of surgeons who practiced cytoreductive surgery ($n = 49$), the mean number of cases performed within the 12-month period preceding the survey was 10.4 (range, 1–30).

Surgical Definitions

Most respondents (95%) felt that there was a need to refine surgical nomenclature to account for the procedural differences between P/D for palliation and P/D performed for macroscopic complete resection (MCR) or maximal cytoreduction (Figure 2). Thirty-nine of 58 (67%) respondents defined “partial pleurectomy” as a partial debulking of tumor for palliative purposes. Of these, 21 (36%) considered it to include resection of both parietal and visceral tumor, whereas the others considered it to include removal of only parietal tumor. Ten (17%) surgeons considered “partial pleurectomy” to be a subtotal removal of parietal and visceral tumor for palliation with the expectation of leaving gross residual disease behind, and another four (7%) defined the procedure as the removal of all gross parietal and visceral tumor with the intention of achieving an R0 or R1 resection without removal of the diaphragm or pericardium. Only three (5%) respondents felt that it should be defined as resection of parietal pleura for diagnostic purposes only. Forty-two of 58 (72%) respondents considered the term “P/D” to imply resection of all gross parietal and visceral tumor with the objective of achieving resection of all macroscopic disease. Of these, 18 (31%) considered the procedure to also include resection of the diaphragm and/or pericardium even if in-

Question 1. Please enter your name (optional), city and country:



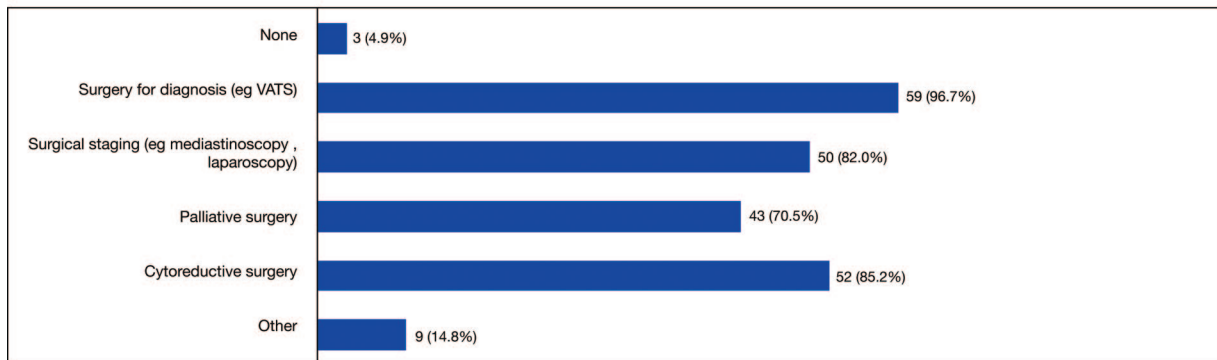
Answered question: 62
Skipped question: 0

Question 2. How many patients with malignant pleural mesothelioma were registered at your institution in the last 12 months?

Answer Options	Response Average	Response Total	Response Count
Number	40.4	2,381	60

Answered question: 62
Skipped question: 0

Question 3. I currently perform the following types of surgery for mesothelioma (answer all that apply):



Answered question: 61
Skipped question: 1

Question 4. How many patients with malignant pleural mesothelioma did you perform surgery on in the last 12 months (for diagnosis, staging, palliation or cytoreduction)?

Answer Options	Response Average	Response Total	Response Count
Number	20.0	1,158	58

Answered question: 58
Skipped question: 4

Question 5. How many patients with malignant pleural mesothelioma did you perform cytoreductive surgery on in the last 12 months?

Answer Options	Response Average	Response Total	Response Count
Number	8.8	512	58

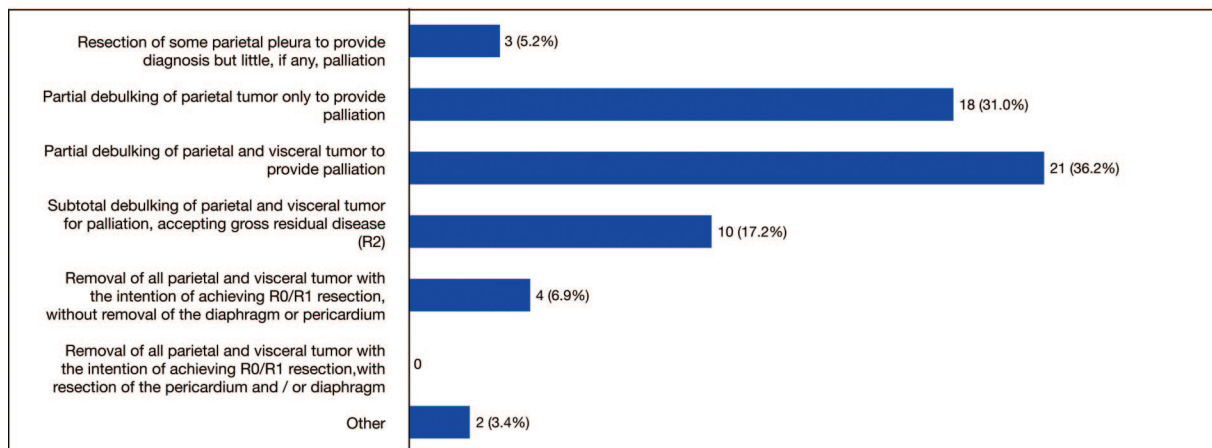
Answered question: 58
Skipped question: 0

FIGURE 1. Questions 1 to 5. Demographic and practice information of the respondents.

involved by tumor. Nevertheless, 15 (26%) surgeons considered “P/D” to be a subtotal removal of parietal and visceral tumor for palliation with the expectation of leaving gross

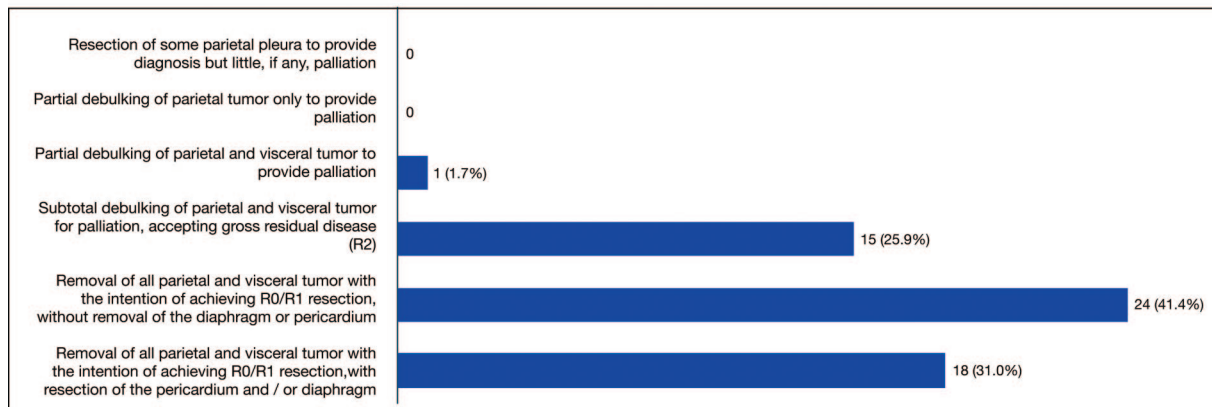
residual disease behind (R2), and one (2%) respondent defined the procedure as a partial debulking of parietal and visceral tumor for palliation.

Question 6. In your opinion which of the following procedures would describe a 'partial pleurectomy' the best?



Answered question: 58
Skipped question: 0

Question 7. In your opinion which of the following procedures would describe a 'pleurectomy / decortication' the best?



Answered question: 58
Skipped question: 0

Question 8. Do you think there is a need to develop terminology that would differentiate between the extent of resection associated with pleurectomy/decortication for palliation versus complete macroscopic resection (cytoreduction)?



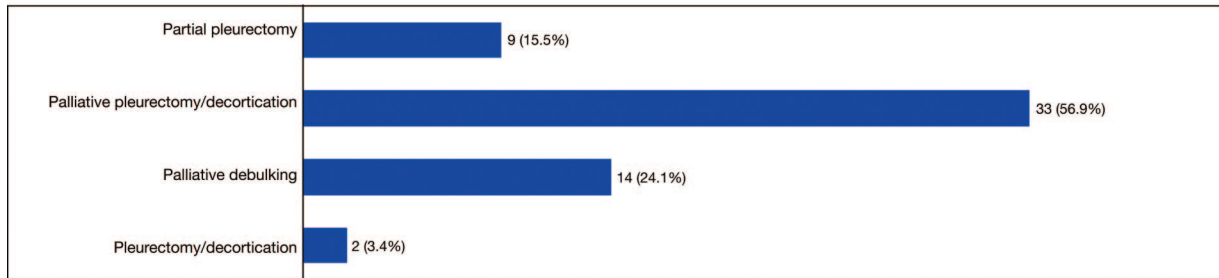
Answered question: 58
Skipped question: 0

FIGURE 2. Questions 6 to 8. Opinions regarding definition of partial pleurectomy and pleurectomy/decortication.

To further explore opinions regarding the extent of “P/D,” two scenarios were provided where the intent was to resect parietal and visceral tumor so that no residual macroscopic tumor remained (Figure 3). In one scenario, the diaphragm and pericardium were resected, and in the other scenario they were not. With regard to the first (diaphragm and/or pericardial resection), the majority

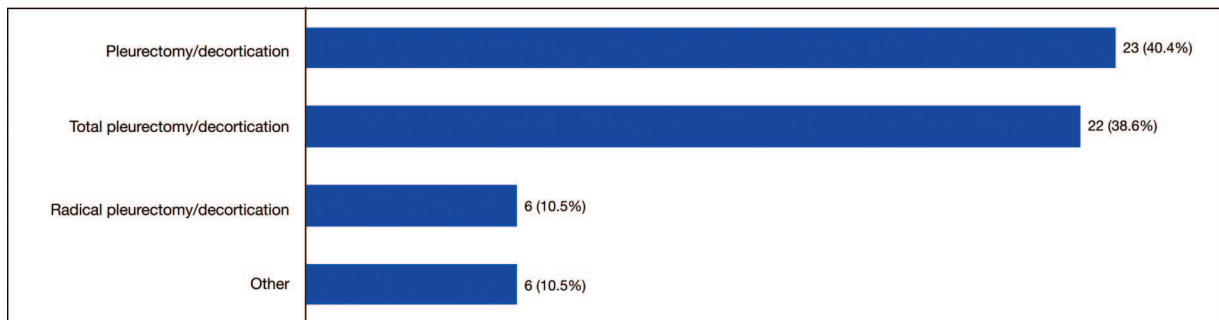
(64%) referred to the procedure as “radical P/D.” Eleven (19%) surgeons preferred the term “total pleurectomy” and only three (5%) used “P/D.” One surgeon considered this a “partial resection.” To describe the second scenario (no diaphragm or pericardial resection), 23 (40%) chose the term “P/D,” whereas 22 (39%) preferred “total pleurectomy.” Only six (10.5%) surgeons called this procedure a

Question 9. In a patient who undergoes parietal and visceral pleural resection for palliative purposes only, without the intention of achieving complete macroscopic resection, which of the following terms do you think is most appropriate?



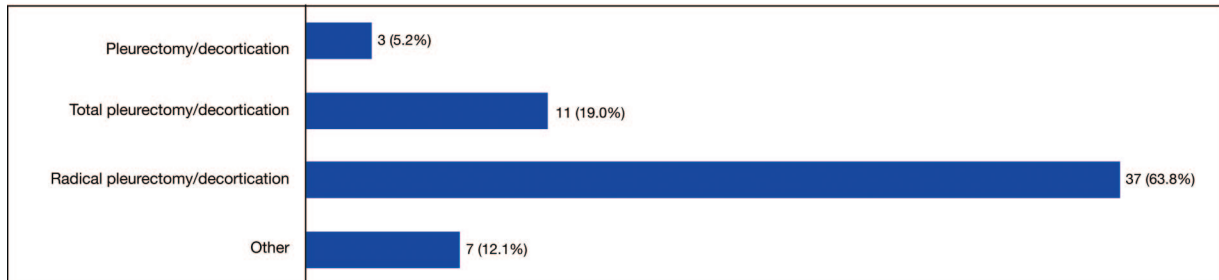
Answered question: 58
Skipped question: 0

Question 10. In a patient who undergoes parietal and visceral pleural resection (but not resection of the pericardium or diaphragm) with the intention of achieving macroscopic complete resection which of the following terms do you think is most appropriate?



Answered question: 57
Skipped question: 1

Question 11. In a patient who undergoes parietal and visceral pleural resection with the intention of achieving a macroscopic complete resection and the diaphragm and/or the pericardium is resected, which of the terms do you feel is most appropriate to use?



Answered question: 58
Skipped question: 0

FIGURE 3. Questions 9 to 11. Opinions regarding the surgical extent of pleurectomy/decortication.

“radical P/D.” Two (3.4%) respondents used the term “palliative debulking” and another two (3.4%) used “partial pleurectomy.” One (1.7%) respondent preferred the term “subtotal P/D.”

Cytoreduction

Fifty-one (88%) respondents agreed with the premise that the goal of cytoreductive surgery in MPM should be the removal of all visible or palpable tumor (R0 or R1) or a “macroscopic complete resection” (MCR) (Figure 4). When asked which cytoreductive procedure was capable of providing MCR, 51 (90%) chose EPP and 39 (68%) “radical P/D,”

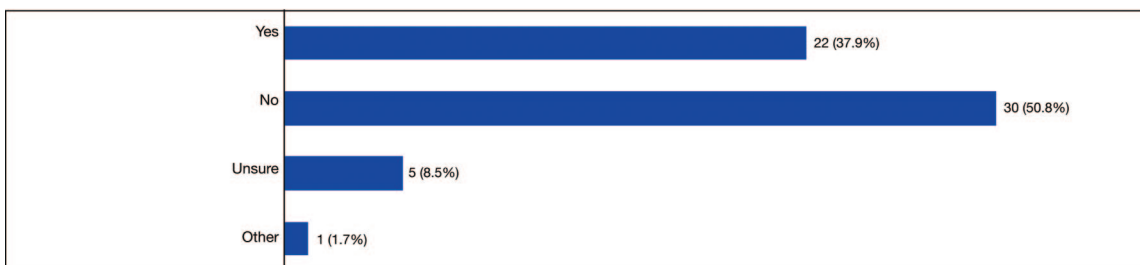
but only 13 (23%) thought that “P/D” could. One of the factors that influence performance of P/D versus EPP is whether tumor involves the fissures. Twenty-two (38%) respondents agreed that P/D could usually provide a MCR if tumor involved the fissure, however, 30 (51%) did not. In addition, the majority of respondents (86%) did not believe that video-assisted thoracoscopic surgery was capable of providing as complete a cytoreduction as an open procedure. Nevertheless, three (5%) respondents did, and another agreed that it could in patients with stage I disease. The remaining four respondents were uncertain.

Question 12. The goal of cytoreductive surgery for malignant pleural mesothelioma should be the removal of all visual and palpable tumor, in other words, a macroscopic complete resection (R0/R1):



Answered question: 58
Skipped question: 0

Question 13. In a patient with tumor involving the fissure(s) pleurectomy / decortication can usually achieve macroscopic complete resection:



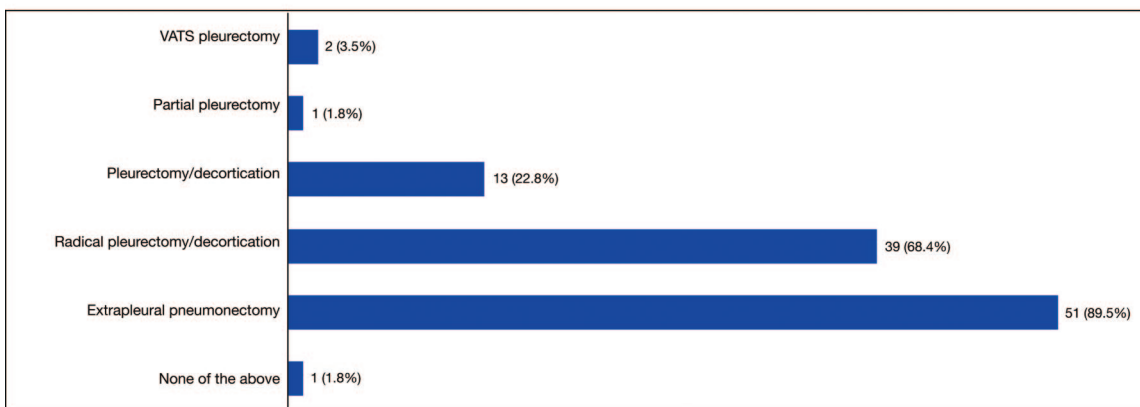
Answered question: 58
Skipped question: 0

Question 14. VATS pleurectomy / decortication can usually achieve as good a tumor cytoreduction as open pleurectomy / decortication:



Answered question: 58
Skipped question: 0

Question 15. Which of the following procedures do you consider capable of providing adequate cytoreduction (R0/R1)?



Answered question: 57
Skipped question: 1

FIGURE 4. Questions 12 to 15. Opinions regarding surgical goals and technical ability to achieve macroscopic complete resection.

TABLE 1. Geographic Distribution of Physicians Who Responded to the Online Survey

Country	No. of Responses	Percentage
United States	23	37.1
United Kingdom	10	16.1
Japan	6	9.7
Italy	5	8.1
Spain	3	4.8
Canada	3	4.8
Turkey	2	3.2
Switzerland	2	3.2
Germany	2	3.2
Belgium	2	3.2
Greece	1	1.6
Australia	1	1.6
Netherlands	1	1.6
France	1	1.6

DISCUSSION

The first description of P/D is attributed to Fowler¹² who reported the successful treatment of a man with chronic empyema and bronchopleural fistula in 1893. Nevertheless, it was not until 20 years later when four patients successfully underwent P/D at the Mayo Clinic that the procedure began to gain popularity and gradually superceded thoracoplasty as the preferred method for the initial treatment for chronic empyema and trapped lung.¹³ It is worth noting that “decortication” involved freeing of the fibrinous rind away from the visceral pleura and not resection of the visceral pleura itself. In the 1950s and 1960s, parietal pleurectomy was used for the treatment of spontaneous pneumothorax,^{14,15} and in 1963, Jensik et al.¹⁶ at the University of Chicago reported the use of parietal pleurectomy for treatment of malignant pleural effusions, showing a 96% freedom from recurrence in 50 patients. As meticulously described by Beattie,¹⁷ parietal pleurectomy began with creation of an extrapleural plane before insertion of a rib spreader, with continued dissection “up over the apex of the thoracic cavity, and down to and around the lung hilum.” Once the upper half of the parietal pleura had been freed, it was excised, and the lower half then dissected down to the costophrenic sulcus. It was noted that it was usually impossible to remove the diaphragmatic pleura which was left attached to the intact diaphragm.

The first report of pleural resection for MPM was by Martini et al.¹⁸ in 1975 who described outcomes of parietal pleurectomy in 83 patients with malignant pleural effusions, of which 14 had mesothelioma. At 1 year, 79% of patients were noted to have been alive, with little or no clinical limitation in pulmonary reserve, and the median survival of those with MPM was 16 months. A year later, this series was expanded to include 33 patients with MPM who had a median survival of 21 months. It should be noted that in these early descriptions of pleurectomy for mesothelioma “all pleura covering the rib cage and mediastinum (was) removed,” but attempts were not made to remove the visceral pleura or resection of the diaphragm or pericardium.¹⁹ The operation

became referred to as “subtotal parietal pleurectomy” as neither the visceral, diaphragmatic nor pericardial pleurae were removed.²⁰

Coincidentally, EPP (also termed pleuropneumonec-tomy) for MPM began to be performed, its proponents arguing that pleurectomy could not possibly achieve the same degree of tumor clearance as EPP, largely because with pleurectomy tumor frequently remained on the diaphragm, pericardium, and the visceral surfaces and fissures of the lung.^{21,22} Perhaps in response to this challenge, pleurectomy evolved in some surgeons’ hands into a more extensive procedure than had been described previously. In 1989, Rusch and Livingston^{23,24} described “radical decortication” in conjunction with intrapleural chemotherapy and, in the article that followed, P/D was defined as parietal pleurectomy with either partial or complete visceral pleurectomy according to the extent of tumor involvement. The diaphragm and/or pericardium were frequently resected and reconstructed but with preservation of the underlying peritoneum. Variations on this theme have been reported by others, the common thread being resection of tumor involved parietal and visceral pleurae.²⁵ In one of the larger and more recent series, Richards et al.⁴ from the Brigham and Women’s Hospital described P/D as resection of the parietal and visceral pleurae along with involved areas of the pericardium and diaphragm. As described by others, the intended goal was to obtain a MCR, arbitrarily defined as tumor residual less than 1.0 cm.^{3,5,26} The clear intent of these cytoreductive procedures is to resect all gross tumor while preserving underlying lung parenchyma. This has not gained unanimous acceptance however. For example, Butchart⁹ has referred to P/D as “debulking” surgery which did not include resection of the diaphragm. The term P/D is still frequently applied to procedures that remove some parietal and visceral pleural tumor and yet which are strictly palliative in intent leaving behind considerable amounts of gross tumor. Perhaps, this is why in an effort to differentiate the more intensive cytoreductive procedure from less extensive ones several authors have recently applied the qualifier “radical” when referring to a maximally cytoreductive P/D.^{7,8} Thus, 35 years after the initial description, there remains some ambiguity regarding the definition of P/D for MPM.

The overall response rate to our survey was less than 50% but is on a par with response rates of other recent web-based surgical surveys. The thoracic surgeons who completed the survey were experienced in MPM surgery—performing what would be considered a high volume of operations for this rare disease. Respondents were primarily from North America and Europe, so it can be argued that the findings may be biased toward Western practice, but this primarily reflects the incidence of MPM and the geographic location of centers involved in surgical and multimodality treatment for MPM. The survey confirmed significant variation among thoracic surgeons regarding the definition of P/D. When pleural resection was performed for palliative purposes, most respondents did not refer to the procedure as “P/D” but rather used terms such as partial pleurectomy, palliative debulking, or palliative P/D. Thus, based on the

findings of the survey, P/D seems to imply a level of completeness or thoroughness of tumor resection that did not apply to debulking or palliative procedures. Nevertheless, when the diaphragm or pericardium had to be resected to achieve MCR, most surgeons (64%) favored the term “radical” P/D.

Finally, we explored the opinion regarding completeness of resection achievable with surgery for mesothelioma. The majority of surgeons polled believed that MCR should be the goal of cytoreductive surgery, regardless of whether that involves EPP or a lung-preserving operation. This is certainly in line with the current surgical philosophy of high-volume centers.^{3,5,26} Furthermore, most agreed that either “radical P/D” or EPP could provide MCR in appropriately selected patients, but most responders did not consider that P/D (without diaphragm or pericardial resection) could do so. Nevertheless, this clearly depends on the extent of the disease.

RECOMMENDATION

On the basis of the survey data, which represented the opinions of experienced MPM surgeons from multiple centers in different geographical regions, the IASLC Mesothelioma Domain and the IMIG have recommended the following terminology to be used in the forthcoming Mesothelioma Staging Project:

- a. EPP: en bloc resection of the parietal and visceral pleura with the ipsilateral lung, pericardium, and diaphragm. In cases where the pericardium and/or diaphragm are not involved by tumor, these structures may be left intact.
- b. Extended P/D: parietal and visceral pleurectomy to remove all gross tumor with resection of the diaphragm and/or pericardium. The IASLC Mesothelioma Domain suggests use of the term “extended” rather than “radical” in this instance as the latter implies a completeness of resection with added therapeutic benefit. There is currently insufficient evidence that resection of the pericardium and diaphragm provides either.
- c. P/D: parietal and visceral pleurectomy to remove all gross tumor without diaphragm or pericardial resection.
- d. Partial pleurectomy: partial removal of parietal and/or visceral pleura for diagnostic or palliative purposes but leaving gross tumor behind.

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