Initial Analysis of the International Association For the Study of Lung Cancer Mesothelioma Database

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Background: The current staging system for malignant pleural mesothelioma (MPM) is controversial. To plan revisions of this system, the International Association for the Study of Lung Cancer Staging Committee developed an international database. Initial analyses focus on patients managed surgically.

Methods: Participation was solicited from centers known to have MPM registries. Common data elements were analyzed by the International Association for the Study of Lung Cancer Staging Committee Statistical Center. Survival was analyzed by the Kaplan–Meier method, prognostic factors by log rank and Cox regression model. *p* Value less than 0.05 was significant.

Results: Data included 3101 patients (15 centers, 4 continents). Demographics: median age 63 years, 79% men, 62.3% epithelioid tumor. Best tumor, node, metastasis (bTNM) stages were: I (11%), II, (21%), III (48%), and IV (20%). Curative-intent surgery was performed in 1494 patients (64.5%). Median survivals by clinical TNM and pathological TNM were similar: stage I, 21 months; stage II, 19 months; stage III,16 months; and stage IV, 12 months. Median survival by histology: epithelioid 19 months, biphasic 13 months, and sarcomatoid 8 months. By multivariable analyses, significant differences in overall survival were seen for: T4 versus T3 and T3 versus T2 but not T2 versus T1; N0 versus N1 and N2 but not N1 versus N2; stages III and IV versus I but not II versus I; epithelioid histology versus other; age of female versus age of male; and palliative versus curative-intent surgery.

Conclusions: This is the largest international database examining outcomes in surgically managed MPM patients. Survival differences reported from smaller databases are confirmed but suggest the need to revise tumor and node staging.

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Malignant pleural mesothelioma (MPM) is an uncommon and usually fatal malignancy. A well-validated and internationally accepted staging system is essential to evaluate new therapies for this difficult disease. Until the mid 1990s no such staging system existed. At least six staging paradigms had been proposed, none evidence-based, and few using a TNM (tumor, node, metastasis) system. In 1994, at a workshop sponsored by the International Association for the Study of Lung Cancer (IASLC) and the International Mesothelioma Interest Group (IMIG) MPM investigators analyzed existing surgical databases to develop a TNM-based staging system.[1] Subsequently, this proposed staging system was accepted by the *UICC* (International Union Against Cancer) and the *AJCC* (American Joint Commission on Cancer) as the international MPM staging system for the 6th and 7th editions of their staging manuals.[2,3] The IMIG staging system has since been widely used in both retrospective analyses and prospective clinical trials. However, widespread concerns exist about the validity of the current MPM staging system because it is derived from analyses of small, retrospective surgical series, can be difficult to apply to clinical staging, and uses descriptors for lymph node involvement, which may not be relevant to MPM. Therefore, in collaboration with IMIG, the IASLC has decided to update the staging system for MPM by developing a large international database, an effort modeled on the revisions that the IASLC proposed for lung cancer staging for the 7th editions of the *UICC* and *AJCC* manuals.[4] Here we report the initial analyses of the international IASLC/IMIG database for MPM, with the primary aim to identify areas in which the current staging system warrants modification.

METHODS

Data Acquisition

Participation in this database was solicited from investigators active in the IASLC and/or IMIG. The initial analyses planned to focus on MPM patients who had surgery as part of

their care and therefore, presumably had earlier-stage disease and better performance status than patients managed non-surgically. All data were retrospective, and by mutual agreement were transmitted to Cancer Research and Biostatistics in Seattle, Washington, as coded data without identifiable private information, with appropriate regulatory permission from the contributing sites. Common data elements were established after review of each institutional database at Cancer Research and Biostatistics. The timeframe chosen for data was from 1995 to 2009, which was considered a contemporary period providing information relevant to potential revisions of the MPM staging system.

Surgical procedures were classified as operations performed with either palliative or curative intent. The former included exploration, no resection, and *palliative* (i.e., partial) pleurectomy whereas the latter included extrapleural pneumonectomy (EPP), pleurectomy/decortication (P/D) for resection of all gross tumors, and P/D combined with anatomical lung resection other than pneumonectomy. Because of the diverse nature of the individual databases and the fact that they were amalgamated retrospectively, details of chemotherapy and radiation administered were not available and were thus simply recorded as modalities given or not given.

Statistical Methods

Survival was measured from the date of pathologic diagnosis to the date of last contact or death resulting from any cause. Median survival was estimated using the Kaplan–Meier regression method. Prognostic groups were assessed by Cox regression analysis of survival, using the SAS system for Windows version 9.2 PHREG method. Significance values from pairwise comparisons reflect the Wald test; those from joint model effects (e.g., comparing the full model to the null model) reflect the likelihood ratio test.

All covariates in regression analyses were modeled categorically using indicator variables, and the threshold for statistical significance was set at a p value of 0.05. Age was classified into three categories, with cutpoints at 50 and 65 years chosen based on graphical analysis of the data. The cutpoints at 50 and 65 years were confirmed as optimal split points (after rounding age to the nearest 5-year mark) by analysis of running log rank statistics. Covariates that met the criteria for statistical significance by univariate analysis were further evaluated for inclusion in multivariable regression models, using a stepwise algorithm with backward selection. Such models were considered *exploratory* in nature when 33% or more of the sample had to be excluded from analysis because of missing data for any of the covariates being explored.

Stage-related differences in the context of surgery with curative intent were identified a priori as of particular interest. Thus, type of operation (curative versus palliative) was included as a covariate in all analyses, and patterns were further explored in the subset of patients treated by surgery with curative intent.

RESULTS

Patient and tumor demographics are shown in Table 1. Data were submitted on 3101 patients from 15 centers in four continents, with 82.6% of the patients being from North America and Europe. Patients were predominantly men with a median age of 63 years. Asbestos exposure was recorded in nearly half the patients but data on this were lacking in 30.9% of the cases. Epithelioid histology was the most common MPM subtype reported and was seen in more than 60% of cases. Because of the heterogeneity of the individual databases, both clinical and pathological staging information was not available on all patients and thus clinical (cTNM) and pathological (pTNM) staging information were combined in 2316 patients to provide *best* staging (bTNM) in accordance with *AJCC* and *UICC* guidelines. Table 2 shows the surgical procedures performed. The majority of patients (64.5%) had curative-intent procedures with approximately half undergoing EPP.

Figure 1 shows the differences between clinical (cTNM) and pTNM staging in the 1056 patients for which such

TABLE 1. Patient Demographics

Source	No. of Patients	Percentage Total %	
United States of America	1151	37.1	
Italy	549	17.7	
Australia	392	12.6	
Turkey	236	7.6	
Japan	180	5.8	
Great Britain	177	5.7	
Switzerland	158	5.1	
Germany	97	3.1	
Canada	82	2.6	
EORTC (Europe)	59	1.9	
France	20	0.6	
Age (yrs)			
< 40	83	2.7	Min 13
40–60	1098	35.4	Max 94
60–80	1807	58.3	Mean 62.1
≥80 or older	110	3.5	Median 63
No data	3	0.1	
Sex			
Female	621	20.0	
Male	2451	79.0	
No data	1	0.0	
Histology			
Biphasic	483	15.6	
Epithelial	1933	62.3	
Sarcomatoid	253	8.2	
Other mesothelioma/NOS	432	13.9	
Asbestos exposure			
No	558	18.0	
Probable	91	2.9	
Yes	1495	48.2	
No data	957	30.9	

EORTC, European Organisation for Research and Treatment of Cancer; NOS, not otherwise specified.

TABLE 2. Information on Surgical Procedures Performed for all 3101 Submitted Cases That Met Initial Screening Requirements for Date of Diagnosis, Date of Last Follow-Up and Age

Procedure	Total	Staged Cases (Percentage Total, %)
Surgery—palliative	***1250***	***729 (31.5)***
Exploration	1172	669 (28.9)
Palliative pleurectomy	78	60 (2.6)
Surgery—curative	***1708***	***1494 (64.5)***
Pleurectomy/decortication	479	299 (12.9)
Extrapleural pneumonectomy	1225	1191 (51.4)
Therapeutic lung[a]	4	4 (0.2)
No surgery	***84***	***70 (3.0)***
No data	***59***	***20 (0.9)***
Total	**3101**	**2316**

[a]Cases in which lung resection other than pneumonectomy with or without chest-wall resection was performed with curative intent.

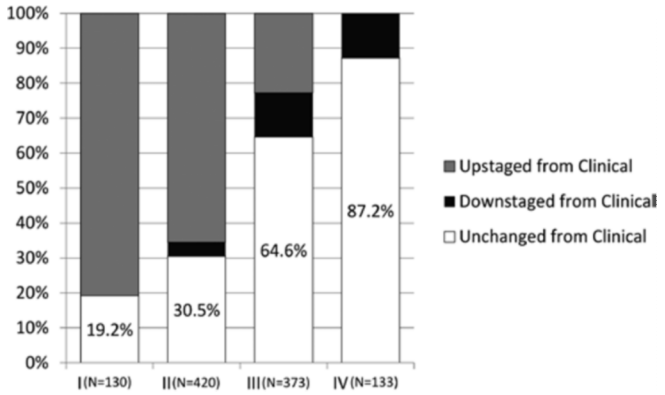

FIGURE 1. Differences between clinical and pathological staging in the 1056 patients for whom such information was available.

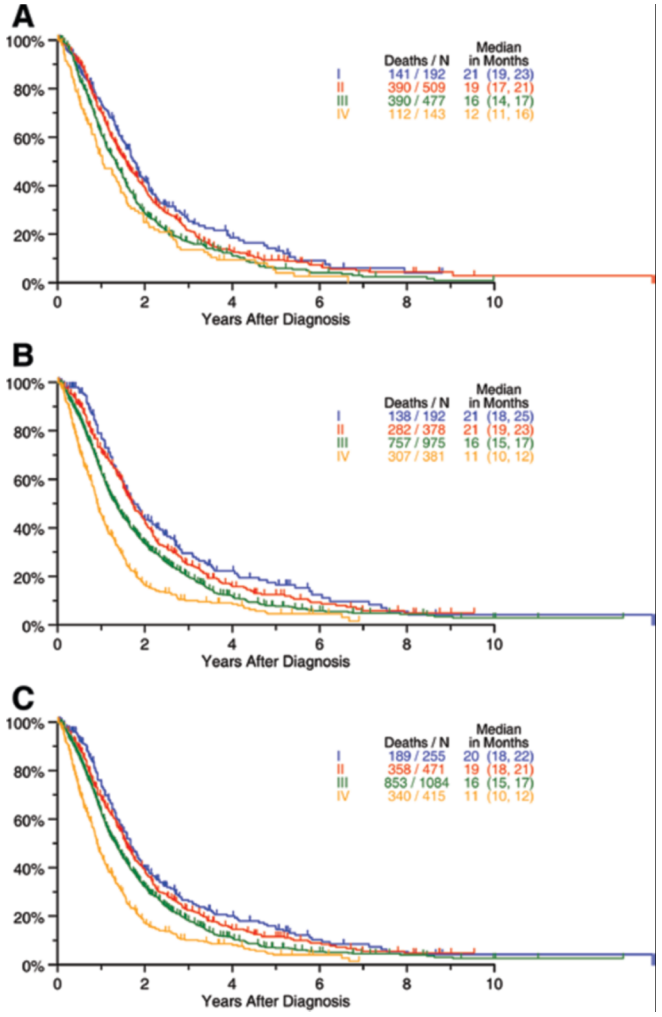

FIGURE 2. Survival for all patients undergoing any type of surgical procedure, according to clinical staging, pathologica staging, and best staging. The 95% confidence interval is shown in parentheses.

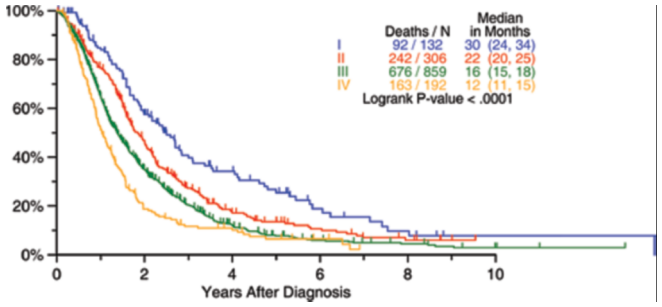

FIGURE 3. Overall survival by best staging for patients undergoing surgery with curative intent. The 95% confidence interval is shown in parentheses.

information was available. Upstaging based on final pTNM occurred in up to 80% of the patients considered to have cTNM stage I or II disease but only in 22.8% of the cTNM stage III tumors and not at all in stage IV disease.

More than 90% of the patients were followed until death or for a minimum of 1 year, and the median length of follow-up for all patients was 15 months. Survival cTNM, pTNM, and bTNM stages for all patients undergoing any type of surgical procedure are shown in Figure 2. Although these survival curves show separation by stage, the differences in median survival are least apparent between stages I and II. Overall survival by bTNM for the patients undergoing surgery with curative intent is shown in Figure 3 and demonstrates more obvious differences in median survival across all four tumor stages.

Survival by tumor T categories for all patients having nonmetastatic disease managed by any type of surgical procedure and for those undergoing operations with curative intent is shown in Figure 4. Separation is seen among the median survivals for all four T categories but this is least apparent between T2 and T3. Survivals by tumor N categories for patients undergoing any type of surgical procedure and for those having curative-intent operations are shown in Figure 5. Differences are seen for N0 versus N1 versus N2 but with the

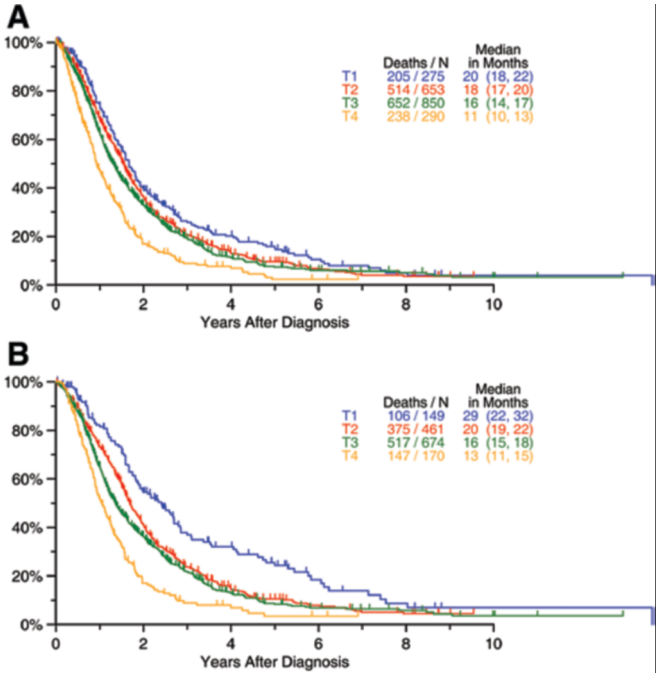

FIGURE 4. Survival by tumor T stage for (***A***) all patients with nonmetastatic disease having any type of surgical procedure, (***B***) those undergoing operations with curative intent. The 95% confidence interval is shown in parentheses.

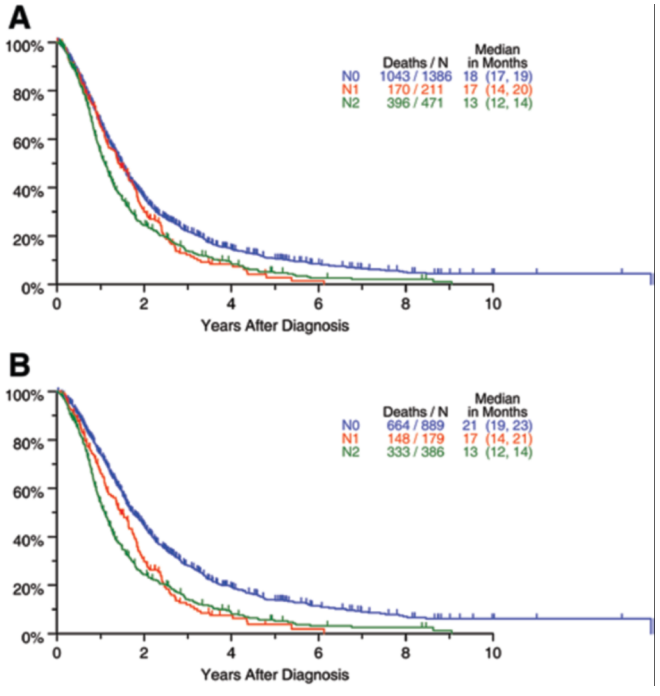

FIGURE 5. Survival by tumor N stage for patients undergoing any type of surgical procedure and for those having curative-intent operations. The 95% confidence interval is shown in parentheses.

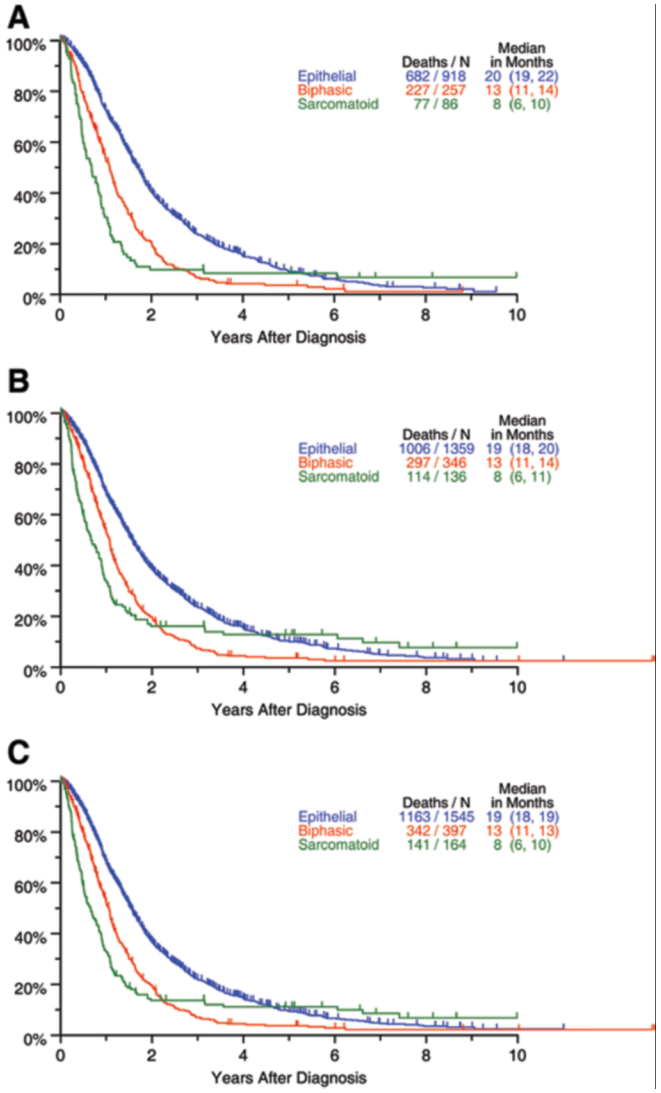

FIGURE 6. The relationship between histological subtype and survival according to clinical staging, pathological staging, and best staging for all patients undergoing surgery. The 95% confidence interval is shown in parentheses.

predominant difference being between N0 and N1/N2. Data on the number of lymph nodes showing metastatic disease were available in only 181 patients. In this small patient cohort, no difference in survival was seen according to the number of involved nodes (data not shown).

The relationship between histological subtype and survival for all patients undergoing surgery is shown in Figure 6. Whether tumors were classified according to cTNM, pTNM, or bTNM stage, marked differences in outcome are seen with epithelioid histology being associated with the best outcome, and sarcomatoid, the worst. The 337 tumors reported as MPM not otherwise specified were associated with a survival virtually identical to that of tumors of biphasic histology (data not shown).

Survival was significantly different according to whether the surgical procedure was performed with curative

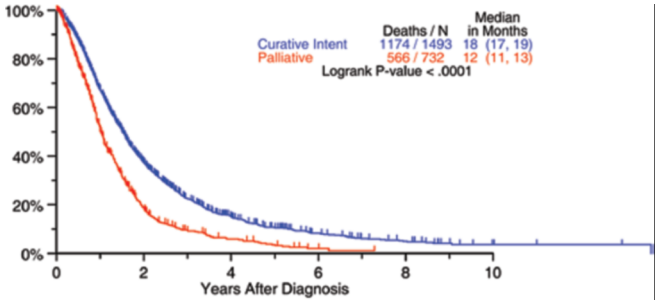

FIGURE 7. Survival in relation to the type of surgical procedure performed (curative versus palliative intent). The 95% confidence interval is shown in parentheses.

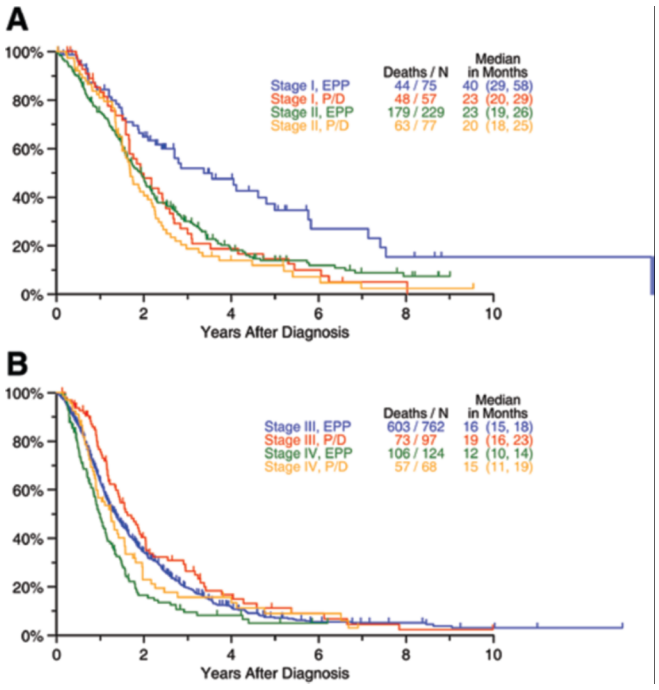

FIGURE 8. Survivals according to type of curative-intent procedure (EPP or P/D) and stage. ***A***, stage I–II and (***B***) stage III–IV. The 95% confidence interval is shown in parentheses. EPP, extrapleural pneumonectomy; P/D, pleurectomy/decortication.

versus palliative intent (median survival 18 versus 12 months, $p < 0.0001$; Fig. 7). Prognostic groups defined by the type of curative-intent procedure performed (EPP versus P/D) were examined in relationship to tumor stage (Fig. 8). Stage I tumors resected by EPP were associated with a median survival of 40 months whereas those managed by P/D had a median survival of 23 months. No differences in survival between EPP and P/D were identified in patients with higher-stage disease.

Among the patients undergoing curative-intent operations, 1162 received additional treatment, either chemotherapy or radiation or both. Relative to the 207 patients in this group who were managed with surgical resection alone (Fig. 9), the patients receiving multimodality treatment had a significantly better outcome with median survivals of 20 versus 11 months ($p < 0.0001$).

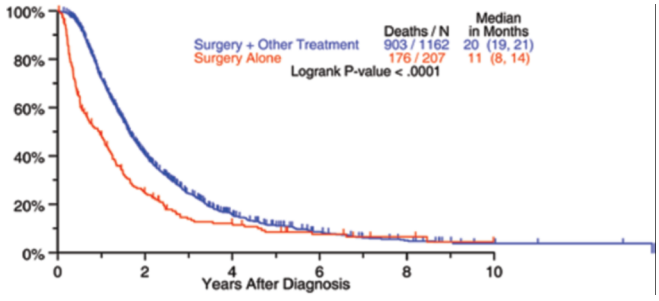

FIGURE 9. Survival for patients managed with curative-intent surgery only versus those managed with multimodality therapy. The 95% confidence interval is shown in parentheses.

Several multivariable analyses (Tables 3 and 4) were performed for patients undergoing any type of surgical procedure. Overall tumor stage ($p < 0.0001$), T category ($p < 0.0001$), N category ($p < 0.0001$), tumor histology ($p < 0.0001$), patient sex ($p = 0.0002$) and age ($p = 0.0025$), and type of operation (curative versus palliative, $p < 0.0001$) had a statistically significant impact on survival. Likewise, pairwise comparisons of adjacent stage groups and T and N categories yielded statistically significant differences in survival, with the exception of stages I versus II, T1 versus T2, and N1 versus N2.

DISCUSSION

During the past 20 years, improvements in surgical management, chemotherapy, and radiotherapy have led to an increasing use of multimodality therapy and to more clinical trials in MPM.[5–11] A clinically and pathologically accurate staging system is essential to selecting patients for treatment and to assessing the benefit of new therapies. The current MPM staging system and subsequent reports suggesting possible revisions are based on analyses of surgical series that were generally single institution, retrospective, and small in numbers.[12–18] This IASLC database, though retrospective, is the largest, multicenter, and international database in MPM to date.

TABLE 3. Cox Regression Model of Survival, Including Best Stage, Histology, Sex, and Age ($n = 2107$)

Variable	Hazard Ratio	*p*
II vs. I	1.16	0.1153
III vs. I	1.47	<.0001
III vs. II	1.27	0.0002
IV vs. I	1.86	<.0001
IV vs. III	1.26	0.0008
Other histology vs. epithelial	1.70	<.0001
Male vs. female	1.28	0.0002
Age, yrs		
50–45 vs. <50	1.23	0.0058
65+ vs. <50	1.31	0.0006
65+ vs. 50–64	1.07	0.2500
Palliative vs. curative surgery	1.71	<.0001

TABLE 4. Cox Regression Model of Survival, Including T and N Stage, Intent of Surgery, Histology, and Sex (n = 1972)

Any Surgical Procedure		
Variable	**Hazard Ratio**	***p***
T2 vs. T1	1.16	0.0907
T3 vs. T1	1.32	0.0011
T4 vs. T1	1.66	< 0.0001
N1 vs. N0	1.26	0.0071
N2 vs. N0	1.40	< 0.0001
Other histology vs. epithelial	1.70	< 0.0001
Male vs. female	1.25	0.001
Age, yrs		
50–45 vs. <50	1.16	0.0483
65+ vs. <50	1.24	0.008
Palliative vs. curative	1.77	< 0.0001
Additional Pairwise Comparisons		
Comparison		
T2 vs. T1	1.16	0.0907
T3 vs. T2	1.14	0.0319
T4 vs. T3	1.26	0.0035
N1 vs. N0	1.26	0.0071
N2 vs. N1	1.11	0.2771
Age 65+ vs. 50–64 yrs	1.06	0.2769

Our analyses not only indicate that the current staging system by and large appropriately distinguishes among T and N categories and overall stages but also highlight areas for potential revision. Differences in survival among T categories and overall stage classifications are most apparent among patients undergoing resection with curative intent. Unlike lung cancer in which the size and location of the primary tumor can be reproducibly measured, the extent of the tumor in MPM is not easily measured. The current T descriptors are qualitative and most applicable to pathological staging. Conceivably, in the future, volumetric tumor measurement on computed tomography could replace the current T descriptors.[19–24] However, this will require additional validation studies of this approach and widespread commercial availability of computed tomography software for automated volumetric measurements. For immediate purposes, revision of the descriptors for early-stage disease (T1–3) may be appropriate based on information regarding the clinically available anatomical extent of disease. For these initial analyses, few of the participating institutions were able to provide information about the precise anatomical extent of tumor leading to the assignment of T categories (e.g., scattered tumor nodules versus confluent pleural tumor, or presence or absence of chest wall invasion). This information will be necessary to recommend definitive revision of T categories. Our data also highlight the discrepancy between cTNM and pTNM staging, especially in early-stage disease and emphasize the need to develop standardized algorithms that provide the most accurate and cost-effective approaches to precise clinical staging.[25]

The application of lung cancer N categories to MPM in the original IMIG staging system was empiric because no data were available at the time to suggest alternatives. The grouping of both N1 and N2 disease into stage III disease was also empiric because all that was known at the time was that *any* lymph node involvement had an adverse impact on overall survival. Subsequent analyses of various surgical series suggested that the preferential pattern of lymphatic drainage in MPM is N2 lymph nodes including some mediastinal regions such as peridiaphragmatic and internal mammary lymph nodes, which are not usually involved in lung cancers.[16,26–28] These analyses have also suggested that the involvement of only N1 lymph nodes was associated with a better survival and that of multiple N2 lymph node stations, with a worse survival.[16] In univariate analysis, our data suggest a difference in survival for N1 versus N2 disease (Fig. 5) but these differences are not significant in multivariable analyses (Table 4). More detailed information about the extent of lymph node involvement will be needed from participating institutions to resolve this issue.

Stage groupings, especially for stages I and II disease, also need to be reassessed. Univariate analyses of this database (Figs. 2 and 3) suggest that the current stage groupings identify patient groups with distinctly different survivals. It would seem that the current staging system satisfies the requirement of TNM stage stratification based solely on anatomical definitions. Future analyses with more detailed information about T and N categories (as noted above) may alter stage groupings or lead to classification of stages I and II into *a* and *b* subcategories. It is also of some concern that multivariable analyses (Table 3) taking into account known significant prognostic factors do not show a significant difference between stages I and II. Future analyses with more detailed information about T and N categories (as noted above) should readdress this issue because it is important that stage groupings be applicable across histological subtypes and patient age and sex. Although the differences among stages II, III, and IV remain significant in these analyses, stages III and IV define broad categories of disease including locally advanced tumors (T3 and T4), regionally advanced disease (N1 and N2), and metastatic disease (M1). In the future, the addition of a larger group of patients with more advanced disease, staged clinically and managed nonsurgically may help determine whether stages III and IV should be classified into *a* and *b* subcategories.

The primary purpose of this database is to determine whether and how the current TNM staging system should be revised. Given retrospective data, heterogeneous data sources, and individualized treatment selection, evaluation of the effect of clinical interventions on survival can only be considered exploratory and hypothesis generating. Other studies, both retrospective and prospective, have suggested a beneficial effect of both curative-intent surgery and multimodality treatment on survival.[8,10,29–32] Our data (Table 3 and Fig. 9), absent details of adjuvant chemotherapy and radiotherapy, are consistent with previous reports in this regard. The role of EPP versus P/D remains highly controversial with impassioned views for and against the use of EPP.[33–44] A recent small, multicenter trial reported no survival benefit for patients undergoing EPP.[45] However, this trial and its analyses were severely criticized by

other investigators because it was not originally designed to assess the survival benefit of EPP, included a small number of patients, and reported an operative mortality substantially higher than that of any other contemporary series.[46] Thus the use of EPP versus P/D in MPM remains an open question. For the stage I patients in our data set, those treated with EPP survived longer than other patients did (Fig. 8). Why the EPP patients survived longer—because of superior intervention, better overall risk profile, or other considerations specific to the institution or region—cannot be determined without some understanding of how treatment was selected for these patients. Within the individual centers that contributed to this database, stage I disease was generally managed exclusively by EPP to the exclusion of P/D, or vice versa. As with lung cancer, different surgical procedures may be appropriate for different groups of patients having MPM. It is perhaps time to study this question prospectively with more restricted-stage and prognostic-factor eligibility than has been done in the past.

In summary, analyses of this database, the largest international one to date, suggest that the current MPM staging system does generally classify patients into groups with distinctly different outcomes but also highlights areas for potential revision. As IASLC and IMIG investigators continue to expand the database, more detailed information on T and N descriptors is needed; so is the addition of patients staged clinically and managed nonsurgically required to propose revisions. Analyses of prognostic factors are also an important aspect of this database and are the subject of a separate article.

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APPENDICES

Appendix A: IASLC International Staging Committee (at the time of conception of this article)

Peter Goldstraw, Past Chair, Royal Brompton Hospital and Imperial College, London, United Kingdom; Ramón Rami-Porta, Chair, Hospital Universitari Mutua Terrassa, Terrassa, Spain; Hisao Asamura, Chair Elect, National Cancer Center, Tokyo, Japan; David Ball, Peter MacCallum Cancer Institute, Melbourne, Australia; David Beer, University of Michigan, Ann Arbor, Michigan; Elisabeth Brambilla, Centre Hospitalier Universitaire Albert Michallon, Grenoble, France; Vanessa Bolejack, Cancer Research And Biostatistics, Seattle, Washington; Paul Bunn, Ex Office, University of Colorado Cancer Center, Aurora, Colorado; Kari Chansky, Cancer Research And Biostatistics, Seattle, Washington; John Crowley, Cancer Research And Biostatistics, Seattle, Washington; Frank Detterbeck, Yale University, New Haven, Connecticut; Wilfried Eberhardt, University of Essen, Essen, Germany; John Edwards, Northern General Hospital, Sheffield, United Kingdom; Françoise Galateau-Sallé, Centre Hospitalier Universitaire, Caen, France; David Gandara, Ex Office, University of California Davis Cancer Center, Sacramento, California; Dorothy Giroux, Cancer Research And Biostatistics, Seattle, Washington; Fergus Gleeson, Churchil Hospital, Oxford, United Kingdom; Patti Groome, Queen's Cancer Research Institute, Kingston, Ontario, Canada; James Huang, Memorial Sloan-Kettering Cancer Center, New York, New York; James Jett, Ex Office, National Jewish Health, Denver, Colorado; Catherine Kennedy, University of Sydney, Sydney, Australia; Jhingook Kim, Samsung Medical Center, Seoul, Korea; Haruhiko Kondo, Shizuoka Cancer Center, Shizuoka, Japan; Mark Krasnik, Gentofte Hospital, Copenhagen, Denmark; Diana Lowry, Cancer Research And Biostatistics, Seattle, Washington; Jan van Meerbeeck, University Hospital, Ghent, Belgium; Takashi Nakano, Hyogo College of Medicine, Hyogo, Japan; Andrew Nicholson, Royal Brompton Hospital, London, United Kingdom; Anna Nowak, University of Western Australia, Subiaco, Australia; Harvey Pass, Board Liaison, New York University, New York, New York; Michael Peake, Glenfield Hospital, Leicester, United Kingdom; Pieter Postmus, Free University Medical Center, Amsterdam, The Netherlands; Thomas Rice, Cleveland Clinic, Cleveland, Ohio; Kenneth Rosenzweig, Mount Sinai Hospital, New York, New York; Valerie Rusch, Memorial Sloan-Kettering Cancer Center, New York, New York; Nagahiro Saijo, National Cancer Center Hospital East, Chiba, Japan; Paul van Schil, Antwerp University Hospital, Edegem (Antwerp), Belgium; Jean-Paul Sculier, Institut Jules Bordet, Brussels, Belgium; Leslie Sobin, Armed Forces Institute of Pathology, Washington, DC; Charles Thomas, Oregon Health & Science University, Portland, Oregon; Charles F. Thomas Jr, Mayo Clinic, Rochester, Minnesota; William Travis,

Memorial Sloan-Kettering Cancer Center, New York, New York; Ming Tsao, The Princess Margaret Hospital, Toronto, Ontario, Canada; Masahiro Tsuboi, Board Liaison, Kanagawa Cancer Center, Yokohama, Japan; Andrew Turrisi, Sinai Grace Hospital, Detroit, Michigan; Eric Valliéres, Swedish Cancer Institute, Seattle, Washington; Johan Vansteenkiste, University Hospitals, Leuven, Belgium; Hirokazu Watanabe, National Cancer Center Hospital, Tokyo, Japan; Yi-Iong Wu, Guangdong Provincial Peoples Hospital, Guangzhou, People's Republic of China.

Appendix B: International Mesothelioma Interest Group (IMIG) Board Members

Steve Albelda, University of Pennsylvania, Philadelphia, Pennsylvania; Sam Armato, The University of Chicago Medical Center, Chicago, Illinois; Paul Baas, The Netherlands Cancer Institute, Amsterdam, The Netherlands; Courtney Broaddus, University of California San Francisco, San Francisco, California; Dean Fennell, Queen's University Belfast, Belfast, Northern Ireland, United Kingdom; Rabab Gaafar, Cairo University, Cairo, Egypt; Marie-Claude Jaurand, Institut National de la Santé et de la Recherche Médicale, Paris, France; Hedy Kindler, The University of Chicago Medical Center, Chicago, Illinois; Sakari Knuutila, University of Helsinki, Helsinki, Finland; Steven Mutsaers, University of Western Australia, Perth, Australia; Luciano Mutti, Vercelli Hospital, Vercelli, Italy; Takashi Nakano, Hyogo College of Medicine, Hyogo, Japan; Harvey Pass, New York University, New York, New York; Bruce Robinson, University of Western Australia, Perth, Australia; Jeremy Steele, St Bartholomew's Hospital, London, United Kingdom; Daniel Sterman, University of Pennsylvania, Philadelphia, Pennsylvania; Jim teWaterNaude, University of Cape Town, Cape Town, South Africa; Walter Weder, University Hospital Zurich, Zurich, Switzerland.

Appendix C: Advisory Board of the IASLC Mesothelioma Domain

Paul Baas, The Netherlands Cancer Institute, Amsterdam, The Netherlands; Jeremy Erasmus, MD Anderson Cancer Center, Houston, Texas; Seiki Hasegawa, Hyogo College of Medicine, Hyogo, Japan; Kouki Inai, Hiroshima University Postgraduate School, Hiroshima, Japan; Kemp Kernstine, City of Hope, Duarte, California; Hedy Kindler, The University of Chicago Medical Center, Chicago, Illinois; Lee Krug, Memorial Sloan-Kettering Cancer Center, New York, New York; Kristiaan Nackaerts, University Hospitals, Leuven, Belgium; David Rice, M.D. Anderson Cancer Center, Houston, Texas.

Appendix D: Participating Institutions

A. K. Cangir, Ankara University School of Medicine, Ankara, Turkey; L. Spaggiari and P. Solli, European Institute of Oncology (IEO), Milan, Italy; J. P. van Meerbeeck and B. Hasan, European Organisation for Research and Treatment of Cancer (EORTC), Brussels, Belgium; D. Waller and A. Nakas, Glenfield Hospital, Leicester, United Kingdom; T. Kishimoto, Japan Labour, Health, and Welfare Organization Hospitals (Rosai Hospitals), Japan; D. Rice, M.D. Anderson Cancer Center, Houston, Texas; R. Flores and V. Rusch, Memorial Sloan-Kettering Cancer Center, New York, New York; F. Galateau-Salle, MESONAT Registry, CHU, Caen, France; H. I. Pass, NYU Langone Medical Center, New York, New York; A. Olario and E. Ruffini, University of Torino, Ospedale San Giovanni Battista, Torino, Italy; H. Hoffmann and T. Muley, Thoraxklinik, University of Heidelberg, Heidelberg, Germany; M. de Perrot, Toronto General Hospital and Princess Margaret Hospital, Toronto, Canada; W. Weder, University Hospital, Zurich, Switzerland; F. Rea, University of Padova, Padova, Italy; B. McCaughan and C. Kennedy, University of Sydney (Strathfield Private Hospital Campus), Sydney, Australia.

