The pattern of lymph node involvement influences outcome after extrapleural pneumonectomy for malignant mesothelioma

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Objective: We sought to examine the distribution and prognostic implications of nodal metastasis in patients undergoing extrapleural pneumonectomy for malignant mesothelioma in a specialist center.

Methods: We have examined the lymphadenectomy specimens from 92 consecutive cases of malignant mesothelioma undergoing extrapleural pneumonectomy from September 1999 through February 2005 inclusive. Nodal stations (Naruke) were assigned to all nodes, and patients were staged according to the current International Union Against Cancer system. The status and number of nodes in each station were recorded, and results were correlated with the results of preoperative mediastinoscopic findings (n = 30) and survival.

Results: The nodal distribution was 48 N0, 9 N1, and 35 N2. Single and multistation nodal involvement was present in 20 and 24 cases, respectively. Among the patients undergoing mediastinoscopy, N2 disease after extrapleural pneumonectomy occurred in 10 (33%). Skip N2 metastasis was present in 10 (42%) cases. Positive N2 nodes inaccessible by mediastinoscopy were present in 17 (49%) cases. N2 metastasis was associated with reduced survival ($P = .02$), but there was no difference between N1 and N2 cases ($P = .4$). The number of positive nodes correlated with survival ($P = .001$), although the number of involved stations and their anatomic location did not. There was no difference in survival between skip N2 cases and either other N2 or N1 cases.

Conclusions: The classical anatomic location is not as important as the scatter of nodal involvement. Every effort should be made to obtain biopsy specimens from as many stations as possible before undertaking extrapleural pneumonectomy for malignant mesothelioma.

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Read at the Eighty-fifth Annual Meeting of The American Association of Thoracic Surgery, San Francisco, Calif, April 10–13, 2005.

Received for publication April 13, 2005; revisions received Nov 22, 2005; accepted for publication Nov 30, 2005.

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J Thorac Cardiovasc Surg 2006;131:981-7

0022-5223/$32.00

doi:10.1016/j.jtcvs.2005.11.044

A number of different staging systems has been used over the years for malignant mesothelioma (MM).[1] The most widely used in current practice is the TNM staging system proposed by the International Mesothelioma Interest Group in 1995 and subsequently adopted by the International Union Against Cancer (UICC). With regard to nodal metastasis, the same distinction between ipsilateral parenchymal-hilar (N1) and mediastinal (N2) nodes is made as for non–small cell lung cancer (NSCLC).[2] Extrapleural nodal metastasis has been identified as a poor

Abbreviations and Acronyms
EPP = extrapleural pneumonectomy
MM = malignant mesothelioma
NSCLC = non–small cell lung cancer
UICC = International Union Against Cancer

prognostic factor in many published series. Sugarbaker and colleagues[3] noted that metastasis to extrapleural lymph nodes confers a poor prognosis, being an independent prognostic factor that they incorporated into the Brigham staging system.

MM arises first in the parietal pleura before nodules on the visceral surface appear.[4] This is reflected in the UICC TNM staging system, within which T1a designates multiple isolated tumor nodules over the parietal pleural surface, with the visceral surface remaining macroscopically normal.[1] However, the lymph drainage from the parietal pleura does not flow to bronchopulmonary or hilar nodes but might pass through those lying alongside the internal thoracic artery or diaphragm.

There are few data regarding the pattern of nodal spread of MM. Skip metastases, cases in which N2 nodes are involved but N1 nodes are not, have not been characterized in MM as they have in NSCLC, where they might confer a better prognosis than other N2 categories.[5] The implications of lymph node drainage to nonmediastinal N2 nodes (internal thoracic artery and diaphragmatic) is unclear. The aim of this study was to validate the current nodal staging system for MM and to examine the clinical implications of any variance from this classification for staging before extrapleural pneumonectomy (EPP).

Patients and Methods

Since August 1999, patients with early-stage MM have been assessed at our institution with a view to EPP. The 92 consecutive patients entered into this study up to and including February 2005 had MM proved at either video-assisted thoracoscopy or open pleural biopsy. The histopathologic diagnosis was confirmed with the use of immunohistochemical techniques. All patients underwent contrast-enhanced computed tomographic scans. Contrast-enhanced magnetic resonance imaging scans were performed in patients in whom there was doubt regarding local invasion potentially precluding respectability.[6] Finally, we have used video-assisted mediastinoscopy for biopsy of lymph nodes in stations 2/4L, 2/4R, and 7, regardless of their size on the computed tomographic scan, after our finding that nodal size did not correlate with malignant involvement.[7] Patients' tumors were judged to be resectable if the tumor did not show extrathoracic extension or invade mediastinal organs or across the diaphragm (clinical T1-3 N0-1). We have not performed staging laparoscopy in this series.

Assessment of operability involved the calculation of the predicted postoperative forced expiratory volume in 1 second and postoperative carbon monoxide transfer factor. Differential quantitative radionuclide ventilation-perfusion scanning was used in borderline cases. Transthoracic echocardiography was performed in all cases. Operability criteria included a postoperative forced expiratory volume in 1 second and postoperative carbon monoxide transfer factor of greater than 50% of predicted value and a mean pulmonary artery pressure estimated at less than 35 mm Hg with good ventricular function.

Left EPP was performed through a posterolateral thoracotomy, in the majority through the seventh intercostal space alone. Initially, right EPP was performed through a right posterolateral thoracotomy, although latterly a median sternotomy has been the incision of choice. En bloc excision of the lung, pleura, hemipericardium, and hemidiaphragm, followed by reconstruction of the pericardium and diaphragm, was performed according to standard techniques.[8]

Systematic lymph node dissection was performed according to the technique described by Graham and associates[9] for NSCLC. After fixation of the main specimen and separately sent lymph nodes in formalin, samples were selected by a pathologist and embedded in paraffin. Hematoxylin and eosin–stained tissue sections were analyzed by means of light microscopy to determine lymph node involvement. In certain cases in which the possibility of nodal disease was suggested by the presence of atypical cells, immunohistochemisty was used to clarify the origin of the cells, and lymph node stations were derived according to the Naruke map.[2] The total number of nodes and the number involved were noted for each station.

EPP was offered intentionally as part of a multimodality treatment program, including either chemotherapy, radical radiotherapy, or both.

Video-assisted mediastinoscopy was performed in 30 patients, including 2 patients who also underwent a positron emission tomographic scan. Positron emission tomography alone was used as mediastinal staging in a further 3 patients. EPP was carried out in 92 patients (median age, 57 years; age range, 38-70 years; 82 male patients). Right EPP was performed in 46 patients, and this was by means of median sternotomy in 23 patients.

Statistical analysis was carried out with the software package SPSS for Windows, version 11 (SPSS Inc). Differences between groups in survival from the date of diagnosis were estimated according to Kaplan-Meier methods by using the log-rank test. The date of diagnostic biopsy was used rather than the date of surgical intervention to remove bias from patients who underwent neoadjuvant chemotherapy. Patients dying in the immediate postoperative period from causes not related to tumor progression were censored in the survival analyses. Differences in distribution of variables between groups were examined with the χ^2 test.

Results

Data are expressed as medians (ranges).

The operation time was 3.75 hours (range, 1.5-6.3 hours), and postoperative stay was 13 days (range, 5-184 days). There were 7 (7.6%) in-hospital deaths. Final pathologic stage was I, II, III, and IV in 6, 8, 54, and 24 patients, respectively. There were 48 node-negative patients, 9 N1 (5 stage III and 4 stage IV) and 35 N2 (20 stage III and 15 stage IV). The final histologic subtype was nonepithelioid in 21 cases.

TABLE 1. Anatomic distribution of the nodes sampled at extrapleural pneumonectomy

Station	Skip metastases	Positive N2 nodes in false-negative mediastinoscopy cases	Positive N2 nodes inaccessible to mediastinoscopy
No. of patients	14	10	17
No. of nodes	18	16	1
2/4L	2	1	
2/4R	5	2	
5		1	1
6			1
7	4	6	
8	2	1	7
9	1	1	1
Internal thoracic artery	2	2	2
Pericardial	2		3
Diaphragmatic		2	3

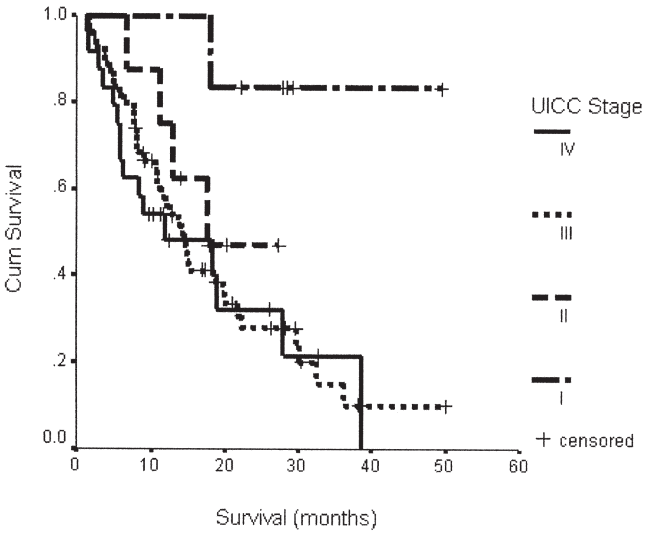

Figure 1. Kaplan-Meier plot of UICC Stage, which did not satisfy survival accurately ($P = .11$).

Nodal Stage

The number of nodes reported by the pathologist was 14 (range, 1-48). The median number of positive nodes was 3 (range, 1-15) from 2 (range, 1-5) stations. Skip metastases, in which N2 nodes were positive but N1 nodes were negative, occurred in 14 (40%) of the 35 patients with N2 nodes. The distribution of the 17 nodal stations positive in these 14 patients is shown in Table 1. Positive N1 nodes were found in a total of 30 patients (9 staged N1 and 21 staged N2). After mediastinoscopy, false-negative N2 disease was found in 10 (33%) patients. The negative predictive value for video-assisted mediastinoscopy was 97% for stations 2/4L, 94% for stations 2/4R, and 79% for station 7. Among the 35 patients with N2 nodes at lymph node dissection, positive nodes inaccessible to mediastinoscopy were found in 17 (49%) patients (Table 1). In 8 patients (23% N2 positive), these were the only positive N2 nodes found.

Nonsurgical Treatment Modalities

The patients referred originated from 28 oncology centers. Since September 2002, our referring oncologists have administered neoadjuvant chemotherapy to 20 patients. All patients in whom neoadjuvant chemotherapy was completed underwent EPP. Only 10 received adjuvant chemotherapy, and to date, 14 have received chemotherapy at the time of symptomatic disease progression. Radical trimodality therapy, including hemithorax irradiation, has been successfully completed in 6 cases.

Survival

Overall median survival for the whole cohort of patients (including the postoperative deaths) was 14.9 months. One- and 2-year survival rates were 59% and 34%, respectively. Among those surviving surgical intervention, UICC TNM stage did not predict survival (stage I and II median survival not reached; stage III, 15.1 months; stage IV, 18.8 months; $P = .11$, Figure 1). Nodal status, expressed as N0 versus N1 versus N2, was associated with a significant survival difference between groups ($P = .02$), as was combining the N0 and N1 groups (N0 and N1, 27.9 months; N2, 14 months; $P = .02$, Figure 2). Survival in the skip N2 metastasis group did not differ from that in the N1 group or the other N2 group ($P = .3$ and $P = .6$, respectively).

Significant differences in survival were apparent between those with 0 to 3 positive nodes (79 patients) compared with those with greater than or equal to 4 positive nodes (13 patients, $P = .001$) and also those with a higher than median proportion of positive nodes in either N1 ($P = .04$, Figure 3) or N2 ($P = .04$) stations. Among the patients with N2-positive disease, there was no significant survival difference between those positive in stations 2, 4, and 7 and those only positive in other stations ($P = .9$).

Other Prognostic Factors and Multivariate Analyses

Other factors in this series that predicted good prognosis in univariate analysis with the log-rank test were a hemoglobin value at diagnosis of greater than 14 g/dL (n = 49, $P = .009$) and receipt of either neoadjuvant or adjuvant chemotherapy (n = 30, $P = .008$). Sex, histologic subtype, performance status, and T stage were not significant prognostic factors. Comparing the above nodal categories together in a Cox proportional hazards model, the only significant factor in the multivariate model was the number of positive nodes (0-3 vs ≥4, hazard ratio, 3.6; 95% confidence interval,

TABLE 2. Significant prognostic variables identified in a forward, stepwise, multivariate Cox proportional hazards model

Variable	*P* value	Hazard ratio	95% Confidence interval
No neoadjuvant or adjuvant chemotherapy	.001	3.4	1.6-7.0
Hemoglobin <14 g/dL	.001	3.1	1.6-5.9
≥4 positive lymph nodes	.009	3.0	1.3-6.9

1.6-8.1; $P = .002$). The number of positive nodes was an independent prognostic factor together with the hemoglobin value at diagnosis and the receipt of neoadjuvant or adjuvant chemotherapy (Table 2).

Discussion

The purpose of this study was to examine whether the existing UICC staging system for MM, first proposed by the International Mesothelioma Interest Group in 1995,[1] is appropriate, taking into consideration what is known about the lymphatic drainage of the pleura. MM is believed to arise on the costal and diaphragmatic parietal pleura,[4] which is reflected in T1a tumors being limited to the ipsilateral parietal pleura without involvement of the visceral pleura. The lymph drainage of the costal parietal pleura flows initially through intercostal lymphatic channels, anteriorly to internal thoracic artery nodes or posteriorly to internal intercostal lymph nodes. Drainage can also be directly into axillary or cervical lymph nodes. Diaphragmatic lymph can flow into mediastinal, internal thoracic, or abdominal nodes.[10] Visceral pleural lymph nodes might drain through intersegmental or interlobular septae to intraparenchymal nodes or to hilar nodes directly through surface channels, hence to mediastinal lymph nodes: this is equivalent to the lymph drainage of the lung parenchyma itself. Hence lymph drainage of parietal and visceral pleura can be considered to have 2 separate distributions, albeit with a proportion of the parietal pleural drainage joining that of the visceral pleura in the mediastinal lymph nodes.

Six different staging systems have, over the years, addressed the point of nodal staging in different ways. Three have assigned stage with and 3 have assigned stage without TNM criteria. With regard to nodal status, the systems devised by Butchart and associates,[11] Mattson,[12] and Sugarbaker and colleagues[13] all placed extrathoracic lymph nodes in stage III. The first TNM staging system[14] placed N1 (hilar) nodes in stage II and mediastinal (N2) nodes in stage III. The initial UICC system[15] did not mention ipsilateral N2 internal thoracic artery nodes. Currently, the UICC identifies ipsilateral internal thoracic artery nodes as N2, whereas diaphragmatic nodes are not specifically considered.

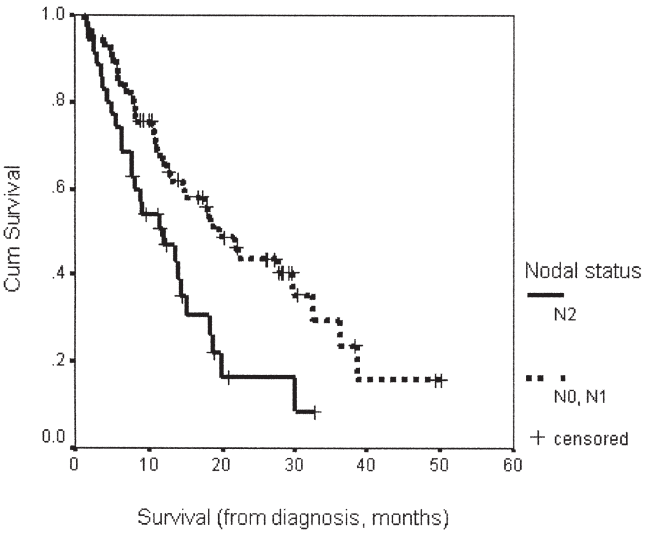

Figure 2. Kaplan-Meier plot demonstrating the correlation between positive N2 status and poor survival ($P = .02$).

In the light of the pattern of lymphatic drainage of the parietal pleura, the concept of identifying all extrapleural nodes as N2 might need to be revised. Unfortunately, there were few patients with N1 disease alone or with isolated positive extrapleural nodes in our study, as well as in others published since 1996.[16] This denied us the statistical power to test accurately the hypothesis that, for example, internal thoracic artery, diaphragmatic, and pericardial nodes deserve categorization as N1 nodes rather than N2 nodes. This was raised in the article by Rusch[1] presenting the IMIG staging system in 1995. We noted that these nodal stations represented the site of skip metastases in 4 of the 14 cases.

Limitations of studies such as this include the uniformity of systemic lymph node dissection. It is possible that despite our best efforts, bias existed in the extent of surgical lymph node sampling throughout the course of the study. Similarly, there is possible bias in the uniformity of pathologic analysis (ie, the number of nodes retrieved from the resected specimen and embedded in paraffin or the number of section levels through each tissue block). These 2 points are suggested by a trend toward an increased number of nodes noted in the pathology report with increasing case load, although the trend was weak.

The question remains as to whether routine cervical mediastinoscopy is justified in the selection of patients for EPP. We believe that the exclusion of patients with mediastinoscopy-positive N2 disease is justified on the basis of their relatively short postoperative survival. Thus every effort should be made to obtain biopsy specimens from as many of the 7 lymph node stations accessible by means of mediastinoscopy as possible. However, it is accepted that a

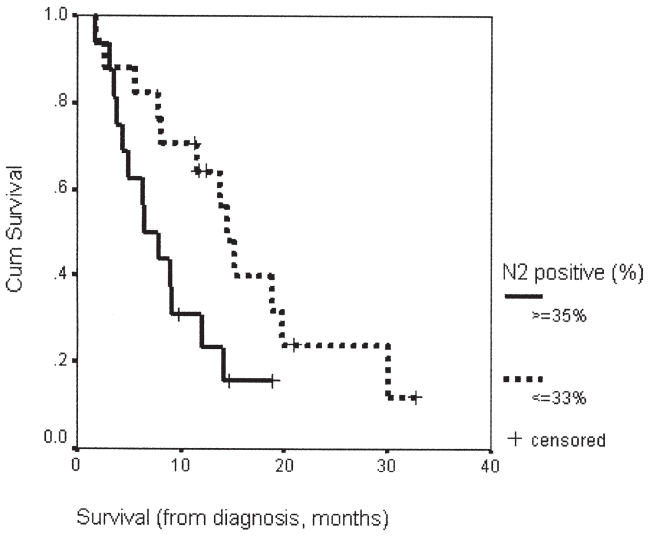

Figure 3. Kaplan-Meier plot to show the negative impact on survival of a proportion of positive N2 nodes greater than the median ($P = .04$).

high proportion of patients with N2 disease will not be revealed by means of conventional mediastinoscopy (biopsy specimens from stations 1-4 and 7) because of the false-negative rate of the investigation and the wide anatomic distribution of N2 stations. However, we found that stations 2, 4, or 7 were involved in 27 (77%) of the 35 N2-positive cases, although the negative predictive value for station 7, in particular, was not high. There are no data regarding extended mediastinoscopy[17] in MM, which might not be possible in many cases because of pleural thickening.

With a number of groups, including our unit, using mediastinal staging to exclude patients with N2 disease from radical surgery protocols,[7,18-20] it might be more difficult in the future to obtain the data required for prospective studies and the sufficient number of patients with N2 disease to clarify the prognostic hypotheses raised by this study.

Skip metastases are a common feature of MM after radical surgical intervention. We were unable to demonstrate differences in survival between skip N2 and the other nodal categories. Larger studies are required to examine whether skip metastases and the first-level nodes draining the parietal pleura confer a different prognosis to mediastinal N2 nodes.

Rusch[1] considered the number of nodes involved and found, as in this study, a significant survival difference between those with 0 to 3 and those with greater than or equal to 4 positive nodes. We were not able to stratify survival by the absolute number of involved nodes in those patients with malignant lymphadenopathy ($P = .11$). However, the proportion of nodes analyzed does seem to be a better indicator of prognosis, both with respect to N1 and N2 nodes separately and combined. To determine whether cephalad nodes in the mediastinal chain (stations 2, 4, and 7) bore a worse prognosis, those with these stations positive were compared with those with the involved nodes confined elsewhere. The latter group represent those with the only positive nodes in locations not accessible to mediastinoscopy. There was no survival difference.

In conclusion, because we have not seen the differential prognosis between the N1 and N2 stages, we believe that revision of the UICC staging system needs to be considered. One cannot transfer the anatomic conclusions of NSCLC to MM because of intrinsic differences in the lymphatic drainage patterns. Furthermore, although mediastinoscopy cannot assess all N2 stations, it is a useful tool for EPP selection and should be performed routinely.

GTS

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Discussion

Dr Raja M. Flores *(New York, New York)*. The incidence of mesothelioma in Europe is increasing, with a projected 250,000 new cases expected over the next 30 years. Therefore it is only fitting that we collaborate with our European colleagues to try and improve treatment. Edwards and his group from the United Kingdom present data on 92 patients undergoing EPP. This study is a useful addition to the literature because it provides confirmatory data concerning the effect of lymph node involvement on survival. Significant positive findings in this study include the following: positive N2 nodes portend a worse prognosis than negative N2 nodes, patients with 4 or more positive nodes do worse than patients with less than 4 nodes, and patients with a greater proportion of positive nodes also do worse. These findings are in accord with the 183 patients from Sugarbaker in Boston and the data on 231 patients from Rusch from our own institution in New York. In contrast, another large European study by Aziz from Scotland on 111 surgically resected patients did not demonstrate a statistically significant difference in survival when patients were stratified on the basis of nodal status. An important negative finding of this study is that there is no difference in survival among patients with positive N2 nodes accessible by means of mediastinoscopy (ie, level 4 and level 7) when compared with N2 nodes inaccessible to mediastinoscopy (ie, levels 8, 9, and internal thoracic artery). However, the numbers are small. Inconclusive areas of this study include the influence of N1 nodes, which were only present in 9 cases, and the influence of N2 skip nodes, which were present in only 14 cases.

I disagree with the presenter's conclusion that all patients with positive N2 nodes should be denied surgical resection at this point in time. No single prognostic factor should be taken by itself. The extent of primary tumor, histology, the role of newer and more effective chemotherapeutic regimens (eg, gemcitabine and pemetrexed), and the role of high-dose hemithoracic radiation must be considered before denying surgical intervention to appropriate patients.

The numbers are much too small and not without some contradiction to draw any firm conclusions. Rather than deny these patients surgical intervention, patients with positive nodes, as well as all patients with mesothelioma, should be treated in a clinical trial setting.

The most significant predictor of survival is histology. As a matter of fact, that is probably the only thing that everyone in this room would agree on. Although you excluded patients with sarcomatoid disease from the beginning on the basis of open lung biopsy, Bueno and the group from Boston reported on 302 patients. Forty-four percent of patients initially thought to have epithelioid disease on the basis of histology were found to not have epithelioid disease on the basis of histology at surgical resection. Therefore it is unlikely that all 92 patients who were initially given diagnoses of epithelioid disease actually have epithelioid disease at final resection. I did not see a stratification of survival by final histologic subtype, nor did I see a multivariate analysis performed including histology and nodal status. Was such an analysis performed? If not, the addition of these data would greatly strengthen the content of this already important contribution.

Dr Edwards. I agree that we do need to perform a multivariate analysis, and that will be done. There were 17 of the 92 patients who had mixed or biphasic histology. I do not have the data on me to confirm how many of those were previously identified as having epithelioid disease on the basis of biopsy, but those data can be obtained.

Dr Flores. My second question is with regard to multimodality treatment. It appears as if the majority of your patients underwent surgical intervention alone. Later in the study, 20 patients underwent induction therapy, and 6 underwent adjuvant therapy. Why did you change your treatment? Also, did any patients receive postoperative radiation? If so, was this routine, and what was the dosage given?

Dr Edwards. The intention was to offer surgical intervention as part of the multimodality program, and this is a multi-institutional study, although operations were performed by a single surgeon in a single center. Oncologic treatment was administered in 28 centers around the country, over which we had no jurisdiction. Six patients had trimodal therapy, and 9 had further radical radiotherapy in a dose of between 20 and 54 Gy.

Dr Flores. My next question is a difficult one regarding the role of mediastinoscopy. Of the 30 patients who underwent mediastinoscopy, 10 had false-negative results in the level 4 and level 7 areas. In addition, 8 patients had positive lymph nodes inaccessible to mediastinoscopy, which adds up to a total of 18. Therefore 18 of 35 patients with positive N2 nodes would be identified by means of mediastinoscopy. The chances of identifying those patients are just as good as if flipping a coin. Therefore taking this into account, how should patients with positive N2 nodes be managed by means of mediastinoscopy or not, and how does this change your management?

Dr Edwards. I agree that although mediastinoscopy cannot assess all N2 stations that we found—and I draw your attention to those 8 of the 35 patients who had N2 disease purely in stations other than 2, 4, and 7—we do believe that it is a useful exclusion tool for EPP on the basis of our survival data. We do not believe that we should offer EPP in those who we know have N2 disease on the basis of a median survival of 12 months. It does not justify the mortality and morbidity.

Dr Flores. And then one quarter of your 92 patients had EPP performed through a median sternotomy. The picture shows a significant amount of diaphragm remaining. What are the advantages to sternotomy in performing this procedure, and in cases in

which complete diaphragmatic resection is necessary, have you had difficulty in reconstruction and placing the patch at a low enough level to facilitate postoperative radiotherapy?

Dr Edwards. As presented at the Society of Thoracic Surgeons meeting in Tampa earlier by my colleague, Dr Martin-Ucar, we now use this incision routinely for right EPP because of benefits in operative time, postoperative pain, and hospital stay. The picture I showed you was a patient in whom the tumor could be mobilized without resecting the entire diaphragmatic muscle, and I agree that it has been difficult to reconstruct, but we have been able to reconstruct at the original level in all patients.

Dr Flores. This is much needed confirmatory data in the literature.

Dr Edwards. Which is out with this talk.

Dr W. Roy Smythe *(Temple, Tex)*. I enjoyed your presentation.

Knowing what we know about the difficulty in discerning the extramediastinal lymph nodes preoperatively by means of positron emission tomographic scanning, because often the pleural tumor is adjacent to the mediastinal nodes, it is difficult to tell what is a tumor and what is a node. Especially with a bulky tumor, you can often not discern a positive internal thoracic, a paraesophageal, or an inferior pulmonary ligament node from the tumor itself.

Dr Edwards. Absolutely.

Dr Smythe. Therefore I want you to explain to me how we are to evaluate those nodal stations preoperatively and exclude those patients who exhibit evidence of nodal involvement.

Dr Edwards. We do not have any experience with positron emission tomography in this series, and I think it will remain very difficult to evaluate those nodes that you mentioned.

Dr David J. Sugarbaker *(Boston, Mass)*. I have a couple of questions.

Back in 1994, initial series showed that positive nodes of any kind had a statistical reduction in overall survival with EPP followed by chemotherapy and radiation. That was then updated, and what fell out was that the N1 nodes and N0 nodes, similar to what I think you were alluding to, although I am hoping you can help me out, were similar, but we used the term *extrapleural nodes* as being ones that had a real negative effect on long-term survival.

Now on the one hand you used the term *N2 disease*, and on the other hand you used the term *extrapleural disease*. There is a significant amount of literature regarding the fact that extrapleural disease in nodes has a negative prognostic overall effect on survival. Therefore are you calling it N2? Are you calling it extrapleural? What is your terminology, because I am really losing you.

Dr Edwards. The definition of N2 is that used by the UICC system. That is effectively what we have used.

Dr Sugarbaker. But you also used the term *extrapleural nodes*.

Dr Edwards. Well, I use *extrapleural*, and I do use that interchangeably. By extrapleural I do mean N2 nodes because the N2 nodes are extrapleural by definition.

Dr Raphael Bueno *(Boston, Mass)*. I thought you said that your results did not correlate in terms of survival with the UICC staging. Maybe I am wrong, but I thought I heard that. Did you try any other staging systems?

Dr Edwards. We have not in this study. I have done previously, but not with these numbers, no.

Dr Sugarbaker. Specifically, have you tried the Brigham staging system?

Dr Edwards. I just might do that.

Dr Sugarbaker. Because it is not unusual to see those lines like spaghetti with the staging system that you used. I will just throw that out there.

Dr Joseph S. Friedberg *(Philadelphia, Pa)*. I am also interested in the median sternotomy approach. For a tumor that likes to seed incisions, it seems like the marrow of the exposed sternum might be a problem. Have you seen any recurrences in that area?

Dr Edwards. We have not seen recurrence in the 23 patients.

Dr Friedberg. Do you include that in your postoperative radiation field?

Dr Edwards. Well, as I say, our uptake of adjuvant therapy has been low. I am not sure whether any of those patients have received adjuvant therapy. I do not think so.

Dr Sugarbaker. How about your subcarinal dissection through a sternotomy, have you found that at all difficult?

Dr Edwards. We have managed to clear out down the contralateral bronchus each time.