Surgical management of non-small-cell lung cancer with ipsilateral mediastinal node metastasis (N2 disease)

Between 1979 and 1989, 876 patients with non-small-cell lung carcinoma were referred to our unit for surgical treatment. One hundred forty-six patients were judged not suitable for surgical treatment on clinical, radiologic, or bronchoscopic findings. Cervical mediastinoscopy or anterior mediastinotomy (or both) showed that 151 patients had mediastinal involvement by invasion or metastases into the ipsilateral (N2 disease) or contralateral (N3 disease) superior mediastinal lymph nodes and were therefore deemed inoperable. Except for one patient who had involvement of a single nodal station at mediastinoscopy, all other patients ($n = 578$) undergoing thoracotomy were thought, on the basis of computed tomographic scan or mediastinal exploration (or both) not to have N2 disease. Despite our efforts to avoid surgery on patients with N2 disease, at thoracotomy routine mediastinal node dissection disclosed that 149 patients had unsuspected N2 disease. Resection was possible in 130 (87.3 %) by pneumonectomy ($n = 72$), bilobectomy ($n = 7$), lobectomy ($n = 49$), or lesser resection ($n = 2$). In three patients the resection was incomplete (2.3 %), but in 127 a complete resection was performed (85 %). Histologic examination in these 149 patients showed that 72 tumors were squamous cell carcinoma, 54 adenocarcinoma, 14 large-cell carcinoma, and 9 of mixed type. Eight patients died in the hospital after thoracotomy. Adjuvant therapy was not used after complete resection. Complete follow-up was obtained in 134 patients and the mean follow-up period was 27.25 months (1 to 116 months). The actuarial 5-year survival for those having complete resection was 20.1 %. There was a statistically significant difference favoring long-term survival in those patients with squamous cell carcinoma ($p < 0.01$) and those in whom only one nodal station was involved ($p < 0.05$). Neither the extent of resection nor the involvement of any specific nodal station influenced long-term survival. Despite rigorous preoperative investigations, routine mediastinal node dissection demonstrated mediastinal node metastasis for the first time at thoracotomy in 26 % of our patients. We believe resection is justified in these patients, who have already necessarily incurred the morbidity and mortality of thoracotomy, so long as complete resection is possible. (J THORAC CARDIOVASC SURG 1994;107:19-28)

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Pulmonary resection remains the most effective treatment for carcinoma of the lung and is associated with excellent long-term survival. However, despite many publications in the past decade,¹⁻³ considerable controversy still exists regarding the surgical management of non-small-cell lung cancer (NSCLC) when associated with ipsilateral mediastinal node metastases (N2 disease).

Conflicting reports of long-term survival associated with the surgical treatment of N2 disease (Table I) may

Table 1. Published data on postoperative survival of patients with N2 disease

Authors	No. of cases of N2 disease	Total operations	No. of resections	Complete	Five-year survival (%)
Pearson et al. ¹ (1982)	DNP	141	124	76	9%*, 24%†
Mountain et al. ¹³ (1987)	DNP	DNP	DNP	92	25%
Martini and Flehinger ¹⁴ (1987)	706	404	DNP	151	30%‡
Naruke et al. ¹⁵ (1988)	DNP	DNP	426	242	5.9%§, 19.2%‡
Watanabe et al. ¹⁶ (1991)	325	236	153	84	17% (overall) 24%‡

DNP, Data not provided.

*Results of mediastinoscopy positive for N2 disease.

†Results of mediastinoscopy negative for N2 disease.

‡Complete resection only.

§Palliative resection.

be due to differences in the selection criteria used in different studies, resulting in the inclusion or exclusion of subsets of N2 disease that may have varying prognoses. Some studies have excluded from analysis patients with N2 disease who did not survive operation, those who had had a thoracotomy but did not undergo resection, and patients who did not undergo complete resection, the so-called "diminishing denominator."⁴ Perhaps because of this confusion, surgeons differ widely in their attitudes to the surgical treatment of N2 disease, the selection criteria applied to identify the presence of N2 disease before thoracotomy, and the role in this assessment, of mediastinoscopy.^{5,6}

It has been our policy to exclude from thoracotomy patients in whom N2 disease was identified by pretreatment investigations, which include mediastinoscopy supplemented by left anterior mediastinotomy in appropriate cases. Mediastinoscopy in our early series was routine, but lately we have used computed tomographic (CT) scanning of the chest to apply mediastinoscopy selectively.⁷ As intrathoracic staging has become more intensive, we have come to realize that despite our efforts to avoid surgery in patients with N2 disease, as many as 25% of our patients will have "unsuspected N2" disease at thoracotomy.^{6,9} Encouraged by the results of surgical treatment in this situation reported from Toronto,¹ we have continued with resection in the great majority of these patients. This retrospective review seeks to assess the effectiveness of surgery in these circumstances and to identify prognostic factors.

Patients and methods

Between 1979 and 1989, 876 patients with NSCLC were referred for surgical treatment to our unit. All these patients underwent pretreatment staging investigations according to the protocol described in a previous publication.¹⁰ After a history and physical examination, each patient underwent routine blood tests including hemoglobin, serum calcium, and alkaline phos-

phatase estimations. Patients with weight loss, bone pain, unexplained anemia, raised alkaline phosphatase levels, or a combination of these signs and symptoms underwent isotope bone scan. Bronchoscopic examination was routine. Before the introduction of CT scanning in 1982, all patients underwent mediastinal exploration, which included cervical mediastinoscopy, supplemented by left anterior mediastinotomy for tumors of the left upper lobe and those that have reached the left main bronchus. After an overlap period during which CT scanning was assessed, we now use mediastinal exploration selectively in those patients in whom the CT scan of the mediastinum suggests invasion or lymphadenopathy. Our use of CT scanning has steadily increased and for several years has included the routine study of brain, chest, and abdomen. Routine mediastinal nodal dissection was performed throughout this period, although in the early years it was not the extensive dissection which has been routine over the past 6 years. All nodes are excised, even those of normal size and consistency. Lymph nodes from each nodal station are separately labeled according to the chart developed by Naruke, Suemasu, and Ishikawa¹¹ and sent for histologic examination.

Follow-up of the patients who left the hospital was obtained from hospital records and by written questionnaires to the general practitioners, to the regional health authorities, or to the patient's relatives. Adjuvant therapy was not used after complete resection.

Statistical analysis was performed according to the guidelines published by the American Joint Committee on Cancer.¹² Actuarial survival rates were calculated by means of life tables with 95% confidence intervals. Comparison of survival proportions in two patient groups was performed by Z test and χ^2 test.

Results

One hundred forty-six patients were considered to have inoperable disease according to clinical, radiologic, or bronchoscopic criteria. In a further 151 patients mediastinal exploration disclosed invasion or nodal involvement, and except in one patient these were deemed inoperable. This patient had a thoracotomy as did 578 patients who were still thought to have N0 or N1 disease (66.1%). At thoracotomy, intraoperative staging by routine mediastinal node dissection revealed mediastinal node involve-

Table II. Resection and hospital mortality data of patients undergoing thoracotomy

	Thoracotomy	Resected	Complete	Mortality*
Overall	579	548 (95%)	545 (94%)	23 (3.9%)
N0/N1	430 (76%)	418 (97%)	418 (100%)	15 (3.5%)
		$p < 0.001$	$p < 0.001$	$p < 0.001$
N2	149 (26%)	130 (87%)	127 (85%)	8 (5.4%)

*In-hospital death.

ment in 148 patients. Of the 579 patients who were subjected to thoracotomy, 548 underwent resection (94.6% resectability). In 31 patients (5.35%) no resection was undertaken because of either tumor extension into the mediastinum or extensive N2 disease. The hospital mortality for the whole group was 3.9% (23/579).

Among the 430 patients whose status remained N0 or N1 at thoracotomy, the resection rate was 97% (418/430). Complete resection, defined as the removal of all macroscopic tumor and lymph nodes, with clear resection margins, was possible in all these cases. In-hospital mortality in this group was 3.5%. In those patients with unexpected N2 disease the resectability rate was 87% (130/149), and 85% of them underwent complete resection. The in-hospital mortality in this group was 5.4% (Table II).

Histologic examination in the 149 patients with N2 disease who underwent thoracotomy showed squamous cell carcinoma in 72 (48.3%), adenocarcinoma in 54 (36.2%), large-cell carcinoma in 14 (9.4%), and mixed features in 9 (6.4%). Among the 130 who underwent resection, pneumonectomy was performed in 72 (55.3%), lobectomy in 49 (37.7%), bilobectomy in 7 (5.4%), and wedge excision in 2 (1.5%) patients.

Histologic types among the patients who underwent resection were squamous cell carcinoma in 58, adenocarcinoma in 53, and mixed cell types in 19. In 98 patients only a single nodal station was involved, in 21 patients two nodal stations, were involved and in 11 patients more than two nodal stations were involved. Subcarinal nodes (lymph node station 7) were involved in 59 patients, either alone or with other nodal stations. The number of lymph nodal stations involved ranges between one and four with a mean of 1.35 lymph nodal stations per patient. The distribution of the involved lymph nodes in these patients with "unexpected N2 disease" is shown in Table III. The T stage of the patients who underwent resection was T1 N2 in 15 patients, T2 N2 in 82, and T3 N2 in 33.

Among the 141 patients who left the hospital, complete follow-up was obtained in 134; 118 had had resection and 16 did not. Of the 118 patients who underwent resection and for whom follow-up is available, 87 died of recurrent

Table III. Involved lymph nodes with unexpected N2 disease

Lymph node station	Negative results	
	Mediastinoscopy	CT scan
1	1	0
2		
Left	2	2
Right	2	10
3	2	5
4		
Left	14	10
Right	12	17
5	20	12
6	1	4
7	36	38
8	2	3
9	4	4
Total	96	105

carcinoma, 8 died of unrelated causes, and 23 were still alive at the time of follow-up. The overall actuarial 5-year survival of all patients undergoing thoracotomy for N2 disease was 17.8% (149). However, the actuarial 5-year survival of the 130 patients who underwent resection, including postoperative deaths, was 20.1% (Fig. 1). This figure includes patients who were lost to follow-up.

A number of variables have been studied to assess their influence on survival after resection for N2 disease. Squamous cell histology fared significantly better than adenocarcinoma (29.5% versus 4.4%, $p < 0.01$) (Fig. 2). The other cell types are too small to be compared. Involvement of a single node station carried a significantly better survival than involvement of multiple nodal stations for up to 3 years after resection ($p < 0.05$) (Fig. 3). Thereafter the survival curves converged. The extent of resection (Fig. 4), T staging (Fig. 5), and involvement of any specific nodal station (Fig. 6) had no significant effect on survival.

Most patients who did not undergo resection at thoracotomy received radiotherapy. Follow-up information could be obtained in 16 of these 19 patients. Their survivals ranged from 2 to 44 months with a mean of 18.7 months. A third of these patients survived beyond 2 years but none was alive at 5 years.

Among the 148 patients in whom N2 disease was discovered at thoracotomy, 62 had undergone preoperative mediastinal exploration, with results that were falsely negative. The other 86 patients were thought to have had a normal mediastinum on chest CT scan and proceeded directly to thoracotomy. However, the survival of patients undergoing resection for N2 disease after false-negative mediastinoscopy was no different from the survival of

Fig. 1. Actuarial survival curves of patients with N2 disease undergoing thoracotomy and resection. Overall survival includes patients who did ($n = 130$) and patients who did not have resection ($n = 19$) and includes perioperative deaths ($n = 8$).

Fig. 2. Actuarial survival after resection for N2 disease related to histologic types.

those undergoing resection after a false-negative CT scan of the mediastinum (Fig. 7).

Discussion

The results of surgical treatment for NSCLC depend on the stage of the disease at the time of surgery and most critically on the extent of nodal involvement. Although surgical resection offers long-term survival in 50% to 75% of patients with N0 and N1 disease,¹³ N2 disease detected before the operation is associated with poor results. The 5-year survival after surgical treatment of selected subsets of N2 disease reported in the literature vary between 15% and 33%.^{1,14,15} The results of surgery in these circumstances will vary depending on the subgroups studied,

reflecting the selection criteria used in preoperative assessment, and will also be affected by exclusions during analysis.

Pearson and associates¹ reported on 141 patients with involvement of the superior mediastinal nodes undergoing thoracotomy. Seventy-nine patients in one group had "mediastinoscopy positive," but otherwise favorable, N2 disease with a 5-year survival that was 9% overall and 15% for those having complete resection. Another group of 62 patients who were "mediastinoscopy negative" and were found to have unsuspected N2 disease at thoracotomy had a 5-year survival of 24% overall and 41% for those having complete resection. Coughlin and colleagues⁵ reported their experience with 36 patients under-

Fig. 3. Survival of patients with N2 disease who have a single nodal station involved compared with those with multiple nodal station involvement.

Fig. 4. Actuarial survival curves of patients with N2 disease who underwent either pneumonectomy ($n = 72$) or lesser resections (bilobectomy = 7, lobectomy = 49, local excision = 2).

going thoracotomy for “mediastinoscopy positive” N2 disease. Twenty-eight patients underwent resection with a projected 5-year survival of 18%. These two units routinely used mediastinal exploration as part of their preoperative assessment and did not offer thoracotomy to the great majority of patients in whom N2 disease was detected before the operation.

In contrast, Martini and Flehinger¹⁴ reported on 706

patients with N2 disease, of whom 404 underwent thoracotomy without prior mediastinoscopy. Of these, 179 patients were thought to have N2 disease before thoracotomy and complete resection was performed in only 32 (18%) patients. The other 224 patients were thought to have N0 or N1 disease before thoracotomy and were found to have “unsuspected N2 disease” at thoracotomy; of these, 119 underwent complete resection (53.1%). The

Fig. 5. Actuarial survival related to T stage of the tumor. There was no significant survival difference among the three groups (T1 = 15, T2 = 82, T3 = 33) at 3 years.

Fig. 6. Survival related to involvement of lymph node station 7 (LN 7). Lymph node 7 was involved either alone ($n = 38$) or with other nodes ($n = 21$) in 59 patients.

overall survival of the 151 patients who underwent complete resection was 30.1%. While calculating survival, however, this study did not take into account the patients having incomplete resection or no resection. Similarly, Naruke and associates¹⁵ published data on 480 patients with N2 disease who underwent thoracotomy without prior mediastinoscopy. Although the resection rate was 88.7%, complete resection was performed in only 242 patients (50.4%). The 5-year survival of patients who underwent curative resection in this group was 19.2%

with an overall survival of 14%. Watanabe and coworkers¹⁶ more recently reported on 203 patients who underwent thoracotomy with N2 disease (cN2) suspected on the basis of a chest CT scan. Of these, 194 underwent resection, but only 115 of these were confirmed to have N2 disease (pN2), of whom 53 (46%) had had curative resection. Furthermore, unexpected N2 disease was found at thoracotomy in another 47 patients, of whom 31 underwent curative resection (65.9%). The overall 5-year survival after resection for these differing subgroups of

Fig. 7. Actuarial survival curves of patients with N2 disease who underwent thoracotomy after either false-negative mediastinoscopy or false-negative CT scan of the chest.

patients with N2 disease was 17% and that of the patients undergoing curative resection was 24%. On the basis of these data, these authors suggest an aggressive approach toward the surgical management of N2 disease.

We believe surgical treatment has a limited but definite role in the management of N2 disease. We have attempted to identify a subgroup of patients with N2 disease who would benefit from resection while avoiding unnecessary thoracotomy in patients who are unlikely to undergo complete resection. We believe the preoperative evaluation of the mediastinum for lymph node metastases is crucial, inasmuch as it affects not just the possibility of resection, but also the desirability of undertaking resection.¹⁷ In experienced hands, mediastinal exploration by mediastinoscopy and left anterior mediastinotomy carries minimal morbidity and no mortality, while having a sensitivity of 91% and a specificity of 100%.¹⁸ Chest CT scanning could be relied on for mediastinal assessment, but this is less sensitive (69.6%)¹⁹ and less specific (70% to 80%). The major contribution of CT scanning for us has been its ability to select patients, before thoracotomy, who require surgical exploration of the mediastinum. Our attitude to resection in NSCLC is aggressive. If the superior mediastinal nodes are normal, we will explore the patients, disregarding other suggestions of unresectability. This attitude, in addition to our careful intrathoracic staging protocol, probably explains the high number of patients (26%) in whom "unexpected" N2 disease was discovered at thoracotomy. Our overall resection rate in patients undergoing thoracotomy is 94%. Resection was possible in 87.5% of patients found to have unsuspected N2 disease, with complete resection in 85%. This is a much higher rate of resection than in those published studies that did not use mediastinoscopy. We believe this

is a reflection of the judicious use of preoperative mediastinal exploration in patients with abnormalities of the mediastinum on CT scanning. Among patients who underwent resection, pneumonectomy was required in 55.3% with an overall in-hospital mortality of 5.1%. These figures are significantly higher than those of patients who underwent resection for N0 and N1 disease (Table II).

The histologic type after resection had a significant influence on long-term survival in our series. Squamous cell carcinoma was noted in 58 patients undergoing resection for N2 disease, and the 5-year survival in this group was 29.5%. Adenocarcinoma, on the other hand, was found in 53 patients undergoing resection for N2 disease, with 5-year survival of 4.4%. The difference in survival was significant ($p < 0.01$). This observation is consistent with other reports by Shields²⁰ (1975), Naruke¹⁵ (1988), Mountain²¹ (1985), and Pearson²² (1986). However, Martini² (1983), Watanabe,¹⁶ (1991), and their associates did not find any difference in survival in these two major histologic groups.

Martini and Flehinger¹⁴ found that patients with involvement of a single nodal station did significantly better than patients with multinodal station involvement ($p = 0.005$). In our series a single nodal station was involved in 98 patients and in the rest two or more nodal stations were involved. Survival was significantly better in the former up to 3 years after the operation ($p < 0.05$). Naruke, Suemasu, and Ishikawa¹¹ reported the survival of patients with subcarinal node (nodal station 7) involvement to be 9.1%, as opposed to a 29% 5-year survival for patients with N2 disease, without involvement of nodal station 7, who underwent resection. Among the patients in this series, 58 patients who underwent resection had involvement of nodal station 7, either alone or with other

nodal stations, but we failed to demonstrate that this had any adverse influence on survival.

The extent of pulmonary resection did not influence long-term survival in this study. Pneumonectomy was performed in 72 patients with N2 disease. Six died after the operation, and the 5-year actuarial survival was 21.1%. Lesser resections were carried out in 58 patients, with two postoperative deaths and a 5-year actuarial survival of 21%. As in the study by Pearson and colleagues,¹ we did not find that the extent of resection influenced survival. Tumor stage did not influence the survival in our study, whereas Martini and Flehinger¹⁴ found that patients with T1 N2 tumors had a better long-term survival ($p = 0.003$).

Despite several publications by leading authors in the field of lung cancer, the management of N2 disease still remains a challenge and many of the problems associated with it are still unresolved. Shields,⁴ in his commentary, brought home the dismal prognosis associated with the whole spectrum of N2 disease and highlighted the controversies. On the other hand, this current study, among others, has shown encouraging long-term survival in a selected subgroup of patients with N2 disease undergoing complete resection. We believe that it remains important to attempt to identify the presence of N2 disease before the operation, because these patients have reduced prospects for resection and little chance of long-term survival. In this respect, mediastinal exploration by cervical mediastinoscopy, supplemented by left anterior mediastinotomy for tumors of the left upper lobe and those that have reached the left main bronchus, remains the gold standard. Whereas some authors have attempted to use mediastinoscopy to select a tiny subset of patients with N2 disease in whom resection may still be of value, we have found this a difficult group to identify. CT scanning allows the selective application of mediastinal exploration. The discovery of "unexpected N2 disease" at thoracotomy by routine nodal dissection carries serious implications. Although complete resection may still be possible in 85% of these cases, the surgeon must weigh the increased perioperative mortality against the severely reduced prospects for long-term survival. In making this judgment, the surgeon must consider certain important factors: the age and fitness of the patient, the cell type, and the number of involved nodal stations. Although the extent of resection does not influence the chances of long-term survival in patients with resected N2 tumors, it still has an impact on perioperative mortality. The T stage may alter the extent of resection and hence the decision as to whether to proceed with resection, but it does not affect long-term survival. The position of

involved nodes has not been found to be significant in this study. With these provisos, complete resection in a subset of patients with "unexpected N2 disease" may be associated with reasonable long-term survival.

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Discussion

Dr. Nael Martini (*New York, N.Y.*). Clearly the patients referred to the surgical unit of Mr. Goldstraw were preselected, because 66% had surgical exploration, despite the extremely conservative attitude in Mr. Goldstraw's unit regarding treatment of nodal metastases.

We have always been proponents of surgical treatment in patients with N2 disease whenever possible. We have shown that, without the benefit of mediastinoscopy, a 5-year survival of 30% can be attained with complete resection. Those with positive results of mediastinoscopy are currently benefiting from our combined preoperative chemotherapy and surgery with encouraging long-term survivals. In these patients the 3-year survival after complete resection is 47% and the 5-year survival is 26%, with a median survival of 27 months. Those with negative results of mediastinoscopy are generally considered to be the best group to treat. I am puzzled why so many patients in this series, after rigorous preoperative investigation and negative mediastinoscopic results, were found to have N2 disease and why survival after complete resection in this most favorable subset of patients with N2 disease is as low as 20%. I would have anticipated the survival to be twice that number.

I have two questions for the authors. First, do you do a lymph node dissection routinely at the time of thoracotomy when the mediastinal lymph nodes are not enlarged or not palpable? Second, do you examine frozen sections of nodes sampled at the time of the operation? I agree with the authors' conclusions that some patients with N2 disease benefit from resection, but the numbers offered this treatment are far too few.

Dr. Mannam. Thank you for those comments, Dr. Martini. I think the 30% 5-year survival you mentioned is from the article you published in *Surgical Clinics of North America*. I believe you analyzed only the patients who had complete resection when considering survival. It was also not clear from that

study how many patients had incomplete resections and what their survival was. Regarding adjuvant chemotherapy, I am aware of the article you published in the *Annals of Thoracic Surgery* regarding 41 patients who had adjuvant chemotherapy, although in that paper you have given only 3-year survival statistics.

Regarding mediastinoscopy, most of our patients had involvement of lymph nodal station 7, and patients in whom results of mediastinoscopy were negative had inferior mediastinal nodes involved that could not be reached with a mediastinoscope. I do not think our overall results are inferior to any of the published studies. However, we are undertaking fewer thoracotomies to achieve the same results. Finally, we do do routine mediastinal node dissection and we excise all the nodes even if they are small and unpalpable. We do do frozen section biopsies when indicated. Our approach to N2 disease is not conservative. We exclude from thoracotomy only those with proven involvement of the superior mediastinal nodes within the reach of the mediastinoscope. All other patients are offered thoracotomy. The prevalence of "unexpected" N2 disease reflects this policy, but we have shown that we can safely perform resection in the vast majority and achieve reasonable survival figures.

Dr. Thomas R. J. Todd (*Ottawa, Ontario, Canada*). I too was puzzled by the high rate of N2 disease at thoracotomy, given a cervical mediastinoscopy. In the series initially reported from Toronto General Hospital, the prevalence of diseased nodes at thoracotomy was about 7%. Therefore I am wondering what nodal station was involved. You said that you used the Naruke map, so I presume that you gave a numerical designation to each nodal station that you sampled. Was there a preponderance of one nodal station? In the Toronto General Hospital series we found that most of those diseased nodes at thoracotomy were indeed in the posterior subcarinal location, which is inaccessible to cervical mediastinoscopy.

My second question concerns the difference in survival between involvement of a single nodal station and involvement of more than one nodal station. You indicated that survival was better with disease of a single nodal station. Intuitively, I would agree with you, but I did not find your graph to be convincing. Are the bars on your graph standard deviations or standard error bars?

Dr. Mannam. Thank you Dr. Todd. Of the total number of patients, 149, only 62 had mediastinoscopy. As part of the preoperative staging protocol, we use mediastinal exploration selectively in those patients with an abnormal mediastinum on the CT scan. Eighty-seven of our patients did not have mediastinoscopy before thoracotomy because the CT scan did not show any lymph node enlargement or invasion of the mediastinum. In the majority of patients who had undergone mediastinoscopy and at thoracotomy were found to have lymph node involvement, nodal station 7 was the one most frequently diseased.

In Fig. 3 we used standard error bars. In that illustration, up to 3 years, patients with involvement of a single nodal station had statistically better survival. After that the curves actually merged.

Dr. Harvey I. Pass (*Bethesda, Md.*). You have shown that you can do this operation safely in higher stage disease, but what do you do about patients in whom you find diseased mediastinal nodes? Also, what is the standard of practice at your institution with regard to postresectional adjuvant therapy at this time? Do

any of these patients with diseased nodes (all of them in your series) receive any adjuvant therapy, and did you see any difference in long-term survival with respect to histologic type as a result of that adjuvant treatment?

Dr. Mannam. Thank you Dr. Pass. We do not believe that patients in whom N2 disease could be detected before the operation do well in the long term with resection. Also, because of higher in-hospital mortality and less chance of complete resection, it is not worthwhile to subject this particular group to thoracotomy. They all received palliative radiotherapy with a mean survival of 18.7 months, and one third survived beyond 2 years, suggesting that survival in this category of N2 disease may not be as dismal as often thought.

None of the patients treated by resection underwent any kind of postoperative adjuvant therapy. There are not randomized trials in the literature to suggest a survival benefit with such treatment, although there may be a longer disease-free interval.

Dr. Thomas W. Shields (*Chicago, Ill.*). Regardless of whose series it is, when one selects patients, the prevalence of nodal disease discovered at thoracotomy will be between 17% and 25%. Unfortunately, the problem is that we are all talking about different things. First of all, the CT scan is very inaccurate for subcarinal nodes, it is relatively inaccurate for aortopulmonary window nodes, and it gives no information regarding the pulmonary ligament nodes or the paraesophageal nodes. In patients who have lower lobe lesions, significant numbers of those CT scans are going to be falsely negative.

Second, we talk about an extensive mediastinal exploration. With standard mediastinoscopy, only an exploration of the superior mediastinum is done. There is no exposure of the posterior subcarinal region, the paraesophageal region, or the pulmonary ligaments. Thus the mediastinal node status is not being evaluated appropriately in all patients.

In addition, one must be concerned about the mix of the patients. In Mr. Goldstraw's group, 58% of the patients underwent a pneumonectomy—a very high proportion compared with current practice in the United States. Obviously there were more central tumors, whereas the majority of Dr. Martini's patients in his N2 series had peripheral tumors. Thus completely different studies are being compared.

Among the patients that the authors excluded, by either preoperative studies or incomplete resections, they salvaged 10% of the patients with known N2 disease that were initially considered for resection. If you include the other third of the patients that were excluded for clinical reasons (probably a lot of those had mediastinal node disease), the salvage is even less. Thus, in patients with mediastinal node involvement, no more than 5% to 8% will be salvaged by aggressive surgery.

Ideally, Dr. Martini's most recent study will lead the way in neoadjuvant therapy and this will be the goal we have been searching for. However, let's conduct an appropriate randomized trial and see if it really works.