Letters to the Editor

The role of mediastinoscopic biopsy in preoperative assessment of lung cancer

To the Editor:

In their report in the December 1992 issue of the JOURNAL (1992;104:1688-95), Funatsu and colleagues give details of a series that must be unique in contemporary literature. They appear to have undertaken mediastinoscopy in 619 patients, proceeded to thoracotomy in all of them, and went onto resection in more than 90% of cases, irrespective of finding N2 or N3 disease. I wonder whether this was indeed the case and whether there were additional cases where the findings at mediastinoscopy deterred even these workers from proceeding with the operation. In the 117 cases in which the results of mediastinoscopy were truly positive, only 13 patients could undergo curative resection and in the whole group only 6% were alive at 5 years. This marginal benefit must have been further offset by perioperative mortality, but we are not given the number of postoperative deaths. Because complete resection is the minimum qualifying criterion for cure in lung cancer, I wonder what benefit could have been expected for the 26 patients whose mediastinoscopic results were positive and who underwent exploratory thoracotomy and also for the 78 patients in that group who underwent noncurative resection. I conclude that a positive result of mediastinoscopy remains a contraindication to thoracotomy and resection for the vast majority of patients.

I thank the authors for the interesting data they provide on patterns of nodal spread and the accuracy of mediastinoscopy in assessing tumors in various locations, but I wonder if they still undertake mediastinoscopy. If they do? what use do they make of this information?

I concur with their findings as to the value of resection when N2 disease is found for the first time at thoracotomy without being found at mediastinoscopy (false negative). In our series of 149 cases of "unexpected N2," we have found complete resection feasible in 86% of these patients and at 5 years almost 20% are still alive.

My belief in the value of mediastinoscopy has been reinforced by the data of Funatsu and colleagues. It is a highly selective evaluation of the mediastinum. Patients with gross and often extensive N2 disease all have a positive result of mediastinoscopy, and in all but exceptional circumstances these patients should be considered to have inoperable disease. Patients with less extensive N2 disease, will not have it found by mediastinoscopy. The surgeon will then proceed with thoracotomy and the N2 disease will only be discovered at this stage. This latter group may still benefit from complete resection, which is feasible in the vast majority of our cases.

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Reply to the Editor:

We appreciated Dr. Goldstraw's letter to the Editor referring to our article, "The Role of Mediastinoscopic Biopsy in Preoperative Assessment of Lung Cancer" 1992;104:1688-95). It seems we have had different opinions on mediastinoscopy, but his comments may be based on a misunderstanding of our paper. We would like to add some data to make our position clear.

First, as we stated many times in the paper, the purpose of mediastinoscopy is to assess N factors in lung cancer before surgery and not to decide whether an operation should be done. We have never refrained from operating merely because the patients had positive results of mediastinoscopy. T factors, M factors, performance status, and pulmonary functions have always been considered. Thirty-eight patients with lung cancer underwent mediastinoscopy alone without open chest surgery, and they accounted for 6% of all patients who underwent mediastinoscopy. Of these patients, some had mediastinoscopically positive results or had small-cell carcinoma. In addition, some whose results were true negative mediastinoscopically were too old to tolerate an operation or may have refused to undergo an operation.

Second, we found that some patients who underwent complete resection survived for a long time, despite the fact that they had mediastinoscopically positive results.^{1,2} In the article, we did not discuss the specific criteria for patient selection for surgery because our experience with patients who had positive results of mediastinoscopy and yet benefited from surgery was limited. However, we suggested this possibility because we believe strongly that it is time to reconsider the possible use of surgery in patients whose mediastinoscopic results are positive.

Dr. Goldstraw said in his letter, "My belief in the value of mediastinoscopy has been reinforced In all but exceptional circumstances these patients should be considered to have inoperable disease." This statement seems to be based on a misinterpretation of our patient series. We believe that the feasibility of surgery differs between patients at T1 N2 M0, with only one positive mediastinal lymph node at mediastinoscopy, and those at T3 N2 M0, with multiple mediastinal lymph node involvement. Prognosis of patients with adenocarcinoma or squamous cell carcinoma with mediastinoscopic evidence of N2 was analyzed by their T factors. As shown in Fig. 1, the 5-year survival was 18% for T1 N2 M0 and 28% for T2 N2 M0; no patients with T3 or T4 disease survived for 3 years (the detailed data will be reported elsewhere). Table I shows the results of analysis by T factors in 24 patients with squamous cell carcinoma and 76 with adenocarcinoma out of 117 patients who had mediastinoscopically positive results.

In our article, curative operation ($n = 13$) was defined as resection of primary tumors plus complete mediastinal dissection including all positive lymph nodes with postoperative histologic evidence of disappearance of all cancer lesions. The following two groups of patients underwent noncurative operation

Fig. 1. Survivals are shown for N2 cases with positive mediastinoscopic results according to T factor.

Table I. Results of positive mediastinoscopic findings according to T factor

T factor	Cases	Adeno	Squamous	N2	N3	Curative operation	Noncurative operation		Exploratory operation (nonresectable)
							A	B	
T1	14	11	3	11	3	4	7	3	0
						29%	50%	21%	0%
T2	37	28	9	24	13	6	22	9	0
						16%	60%	24%	0%
T3	28	23	5	19	9	3	9	9	7
						11%	32%	32%	25%
T4	21	14	7	14	7	0	4	5	12
							19%	24%	57%
Total cases	100	76	24	68	32	13	42	26	19
						(55)*			

Adeno, Adenocarcinoma; Squamous, squamous cell carcinoma; Curative operation, resection of the primary tumor and all accessible mediastinal lymph nodes with no gross tumor left behind and all margins of resections microscopically clear of tumor; Noncurative operation—A, resection of the primary tumor and the involved mediastinal lymph nodes with no gross tumor left behind, all margins of resections microscopically clear of tumor, without the dissection of all accessible mediastinal lymph nodes; Noncurative operation—B, palliative resections that left gross or microscopically identifiable tumor behind at its completion.

*Cases with a complete resection of all gross tumor as well as all involved mediastinal lymph nodes.

($n = 68$). In group A ($n = 42$), complete resection of primary tumors and involved lymph nodes was performed, but there was no definite evidence that the cancer lesions had disappeared completely because mediastinal dissection was not sufficient or was not performed. In group B ($n = 26$), there was macroscopic or histologic evidence of remaining cancer lesions despite complete resection of the primary tumors and all involved lymph nodes. This means that 55 patients, 13 with curative resection and 42 with noncurative resection of group A, underwent complete resection of lesions plus involved lymph nodes. We understand that the purpose of the operation was achieved in 55% of patients who had mediastinoscopically positive results. Dr. Goldstraw queried our data on 5-year survival. However, his doubts are not well-founded. We calculated the 5-year survival by the Kaplan-Meier method, including surgical deaths within 1 month after operation and also deaths from other causes.

Dr. Goldstraw mentioned "unexpected N2," which may be defined differently from our "false negative cases." We classi-

fied a case as false negative when intraoperative or postoperative biopsy showed metastasis in the lymph nodes in a patient who had mediastinoscopically negative results, because the operator had overlooked involved lymph nodes that could be sampled or had obtained biopsy specimens of only part of the swollen lymph nodes. The prognosis of patients of this group did not differ significantly from that of those whose results were mediastinoscopically positive (J THORAC CARDIOVASC SURG 1992;104:1691). In contrast, Dr. Goldstraw's "unexpected N2" may refer to metastasis to lymph nodes 5, 6, 8, and 9, which cannot be reached by a mediastinoscope. If so, such cases would be included in our data as mediastinoscopically true negative cases. There were 50 of these patients, and their 5-year survival was 26%, which is virtually the same as the results presented by Dr. Pearson³ and Dr. Goldstraw.

To avoid any misunderstanding, let us repeat: It should not be taken for granted that surgery is not feasible for any patient with positive results of mediastinoscopy. We need to review the

data objectively and analyze them to find patients who might benefit from surgery. For this reason, we believe strongly that we should retain our view on mediastinoscopy, which enables us to assess N factors accurately before the operation.

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Extragonadal malignant germ cell tumor of the lung

To the Editor:

Although malignant extragonadal germ cell tumors of the lung are extremely rare, their recognition is of clinical importance because of their curability. We report here the case history of a patient with an advanced undifferentiated pulmonary tumor, the germ cell origin of which was not initially recognized because of its unusual location. The possibility of curative treatment was therefore not considered at first.

A 25-year-old male patient with pain in the right upper part of the chest, chronic cough, and hemoptysis was admitted after a diagnosis of inoperable undifferentiated lung cancer had been made and chemotherapy with doxorubicin (Adriamycin), cyclophosphamide, and vincristine had achieved only a short, minor response. Chest radiograph and computed tomographic scan are shown in Fig. 1. Thoracotomy and partial resection of

the middle lobe were performed. Histologic examination (Fig. 2) with immunostaining and elevated embryonal serum tumor markers alphafetoprotein and β -human chorionic gonadotropin established the diagnosis of malignant germ cell tumor. Clinical and radiologic staging procedures showed the thoracic mass to be the only tumor manifestation. Three courses of cisplatin, etoposide, and bleomycin were administered, resulting in tumor-marker normalization, shrinkage, and cystic transformation of the pulmonary mass. Right-sided pneumectomy showed the residual tumor to be completely surrounded by lung tissue and to consist of seminoma and embryonal carcinoma. Intrathoracic lymph nodes, as well as chest wall tissue, were free of tumor. The patient has been without evidence of disease for 32 months. Thorough clinical and sonographic follow-up have so far failed to show tumor or scarring in either testis.

According to Einhorn,¹ any extragonadal mass occurring in a patient without a detectable or subsequent appearance of a tumor in either testis and in whom the absence of metastatic disease in the lower aortic and iliac nodes has been demonstrated should be considered a primary extragonadal tumor if it meets the histologic criteria for such malignancies. Pathogenesis of extragonadal germ cell disease has been discussed extensively² and is generally explained as the result of a neoplastic transformation of primordial germ cells displaced at various points along their normal pathway of migration to the urogenital ridge. Most of these tumors arise from midline structures (e.g., from the mediastinum and the retroperitoneum). Extragonadal germ cell tumors of the lung are among the rarest tumors encountered in pathology. Mediastinal and extrapulmonary origins must be excluded before a diagnosis of germ cell tumor of the lung can be confirmed. A review of the literature revealed 12 published cases of malignant germ cell-derived tumors. Eleven of these 12 cases involved teratomas with malignant transformation; only one case of germ cell cancer without components of somatic differentiation was reported. In contrast to this finding, undifferentiated germ cell cancers such as seminoma or embryonal carcinoma are frequently found in mediastinal germ cell-derived tumors. The explanation for this difference may have a histogenetic background, but it may also be true that extragonadal undifferentiated germ cell cancers of the lung were not recognized as such before serum tumor markers

Fig. 1. Thoracic radiograph (A) and computed tomographic scan (B).