

# Early detection of mediastinal spread of pulmonary carcinoma by mediastinoscopy

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To the great disappointment of all concerned, too many operations performed for pulmonary carcinoma still prove to be exploratory thoracotomies or non-curative resections, in spite of careful preoperative investigations.

A follow-up study of 168 patients operated upon for pulmonary carcinoma clearly shows that such non-curative procedures yield very disappointing results.

To reduce this number of unnecessary and often harmful operations mediastinoscopy was introduced as an aid in detecting mediastinal spread of the tumour. It was thought that such knowledge would make preoperative assessment more accurate and so make easier the decision whether to operate.

A comparison was made between two groups of patients—those who had and those who had no preoperative mediastinoscopy—to find out whether there was any difference in the post-operative results.

The first group of patients consisted of all those operated on for pulmonary carcinoma between 1958 and 1962 in the Department of Thoracic Surgery, University of Groningen. None of the patients in this group had had a preoperative mediastinoscopy. The second group consisted of patients operated on between 1966 and 1969 when preoperative mediastinoscopy was routinely performed. The results of the follow-up study are presented in Tables I and II.

It was found that 15.5% of all operations performed had to be regarded as exploratory thoracotomies. In these cases, the survival time never exceeded one year. Although our percentage of exploratory thoracotomies (15.5%) is significantly less than the 37% reported in Maassen's (1967) collective review, and although our mortality of two patients (7.8%) is below that

TABLE I  
BRONCHIAL CARCINOMA: FOLLOW-UP RESULTS 1958-62

Operative Procedure	No. of Patients	Primary Mortality
Exploratory Thoracotomy	26 (15.5%)	2
Resections		
Lobectomy	66	6
Pneumonectomy	76	15
Total	168	23 (13.7%)

TABLE II

SURVIVAL TIME AFTER PNEUMONECTOMY IN 76 PATIENTS

	No. of Patients	
	Primary mortality	Survival
Non-curative Pneumonectomy	12	46
Survival	34	
0-1 yr	13	
1-2 yr	4	
2-3 yr	2	
3-4 yr	1	
4-5 yr	1	
> 5 yr	0	
Curative pneumonectomy	3	30
Survival	27	
0-1 yr	27	
1-2 yr	23	
> 5 yr	18	

which Reynders (1963) gives in his thesis, it need not be pointed out that an exploratory thoracotomy is of no therapeutic value to the patient and should be avoided if possible. From a retrospective study of the pathological material it was possible to divide the patients treated by pneumonectomy during the period considered into two groups (Table II). The first group comprised 46 cases in which pathological anatomical examination of the resected specimen disclosed growth of the primary tumour or of lymph node metastases as far as (and therefore probably beyond) the resected edge. We have listed resections of this type as 'non-curative'. The second group, however, consisted of 30 patients whose tumour had produced no metastases or only as far as the nearest lymph nodes immediately

adjacent to the tumour as revealed by examination of the resected specimen. These resections were listed as 'curative'. Although we realize that our 'curativity' concept is inexact and has only relative value (since in particular haematogenous dissemination is not accounted for), the very marked difference in five-year survival time between the two groups (0% and 66%) demonstrates its validity as a prognostic parameter in actual practice.

In the group of 'non-curative' resections, only 13 patients were still alive one year after operation; 21 patients (61.7%) died within the first year. Within two years the deaths totalled 30 (88.2%). Only four patients of the entire group survived the operation longer than two years (Table II).

The causes of death for both groups are listed in Table III. Of the patients who had a 'non-curative' resection performed, 17 (50%) died from a local recurrence, while 12 (35.3%) died from the consequences of haematogenous metastases. Thus only a few patients survive two to four years after a 'non-curative' resection.

In view of these findings we regard dissemination to the carinal node, or into the paratracheal lymph nodes, as very unfavourable signs, and must regard this condition as incurable.

In an effort to reduce the number of exploratory thoracotomies and increase the number of curative resections, mediastinoscopy according to Carlens (1959) was introduced to the Groningen University Surgical Clinic in 1963, in collaboration with the Department of Lung Diseases (of the Medical Clinic). This intervention makes it possible to explore the paratracheal lymph nodes, carinal nodes, and the peribronchial dissemination of a primary bronchial tumour. Lymphogenous dissemination of a bronchial carcinoma up to or beyond the expected site of resection can be detected in time. In principle, mediastino-

scopy was performed in all patients suffering from or suspected of pulmonary carcinoma.

A comparison of the total number of thoracotomies performed after the introduction of mediastinoscopy (164, as shown in Table VI), with the number of thoracotomies performed for pulmonary carcinoma since its introduction (133+23+3=159, as shown in Table V), reveals that mediastinoscopy was omitted in only five cases. This group comprised patients with peripheral opacities, in whom mediastinoscopy was considered unlikely to produce positive findings. The fact that this assumption is unjustified became apparent in a patient in whom hilar node metastases were found although the opacity had been very peripheral.

If the mediastinoscopic findings agree with those obtained at pathological anatomical examination of the resected specimen, then the value of mediastinoscopy should become apparent through (a) a reduction in the number of exploratory thoracotomies, and (b) an increase in the number of resections deemed 'curative' in accordance with the above-mentioned criteria.

In this context we confined ourselves to the pneumonectomies because in these interventions there is a direct relation between the areas of lymphogenic spread on direct vision judged preoperatively by the mediastinoscopist and that assessed postoperatively by the pathologist.

In order to establish whether the purpose we had in mind was in fact achieved, we analysed the results obtained during the period 1 January 1966 to 22 April 1969. A total of 300 mediastinoscopies were performed, 268 in men and 32 in women. The mediastinoscopies were carried out by 10 different persons, including trainees, alternating as frequently as possible. The intervention produced complications in 11 patients (3.6%). One patient died six hours after the intervention from a pulmonary embolism. A haemorrhage was caused in five instances, but the blood loss exceeded 100 ml. in only one case (about 1 litre). In all cases pressure was the only measure required to control the haemorrhage. Two patients developed a unilateral pneumothorax which was controlled by a single suction drainage procedure. One patient showed an unmistakable subcutaneous emphysema, which disappeared spontaneously after three days. Transient recurrent nerve paresis was observed in one case, and mild wound infection in one. In no case was mediastinitis seen.

Table IV compares our number of complications with the figures given by van der Schaar

TABLE III

CAUSES OF LATE MORTALITY AFTER PNEUMONECTOMY IN 76 PATIENTS

Non-curative Pneumonectomy	Curative Pneumonectomy
46	30
-12 primary mortality	-3 primary mortality
34 →5-yr survival 0 (0%)	27 →5-yr survival 18 (66%)
↓	↓
34 deaths	9 deaths
↓	↓
Local recurrence 17	Local recurrence 5
Haematogenous spread 12	Haematogenous spread 3
Unknown, no definite recurrence 1	No follow-up 1
Unknown, probably cardiorespiratory 4	

TABLE IV  
COMPLICATIONS AFTER MEDIASTINOSCOPY

	Reynders (1963)	Bergh <i>et al.</i> (1964)	Akovbiantz and Aeberhard (1964)	van der Schaar van Zanten (1965)	Pearson (1968)	Personal Observations (1969)
No. of mediastinoscopies	164	300	128	145	239	300
No. of complications	13 (7.9%)	12 (4.0%)	3 (2.3%)	4 (2.7%)	7 (2.9%)	11 (3.6%)
Haemorrhage	2	3	1	1	2	5
Pneumothorax	1	2	1	1	2	2
Subcutaneous emphysema	2	—	—	—	—	1
Recurrent paresis	3	3	—	1	3	1
Oesophageal perforation	1	—	—	—	—	—
Wound infection	2	—	1	—	—	1
Postoperative pyrexia	—	2	—	—	—	—
Metastasis in mediastinoscopy wound	2	—	—	1	—	—
Death	—	2	—	—	—	1

and van Zanten (1965), Akovbiantz and Aeberhard (1964), Reynders (1963), Pearson (1968) and Bergh, Rydberg, and Schersten (1964); the comparison discloses a fair degree of agreement with their figures.

The 300 cases of mediastinoscopy were divided into two groups: a group of 230 patients in whom microscopical examination of the biopsy material disclosed normal lymph node tissue, and another group of 70 patients whose specimens contained pathological tissue (Table V). In the latter group, carcinoma was found in 53, Besnier-Boeck's disease in 14, and Hodgkin's disease in three cases; anthracosis and other non-specific or common inflammations were recorded as negative findings.

In 34 cases in which carcinoma metastases were demonstrated in the biopsy specimen, primary surgical treatment was rejected; in three patients whose specimens contained carcinoma metastases, a pneumonectomy was nevertheless

performed. In one case we were forced to do this because the patient was suffering from severe obstructive pneumonia which failed to respond to conservative therapy; in the other two cases a pneumonectomy was performed because interpretation of frozen sections and celloidin sections of the specimen offered difficulties.

In the context of our problem, the first group of 230 patients whose specimens contained no pathological tissue is, of course, of greater importance. In 62 cases mediastinoscopy was performed solely for diagnostic reasons; this group must therefore be excluded. In 168 cases a thoracotomy was performed but 12 of these cases must be excluded because they involved no malignant condition. In the remaining group of 156 patients, 133 resections were performed. In 23 cases, although the mediastinoscopy had demonstrated no dissemination, resection was impossible due to local tumour spread—local invasion of the aorta, thoracic wall, and mediastinum in nine, and glandular metastases in 12 cases. However, the localization of these metastases was such (behind the aorta, on the pulmonary artery, or in the pulmonary ligament) that they could not be observed at mediastinoscopy. In only two cases did thoracotomy disclose metastases which must have been overlooked at mediastinoscopy.

TABLE V  
HISTOLOGICAL FINDINGS IN 300 MEDIASTINOSCOPIES  
1966-69

	No. of Operations	
<i>Negative findings</i>		
Thoracotomy		168
Operable carcinoma	133	
Inoperable carcinoma	23	
Other findings	12	
No operation		62
TOTAL		230
<i>Positive findings</i>		
Bronchial carcinoma		53
No operation	34	
Other therapy (irradiation with/without subsequent operation)	16	
Pneumonectomy	3	
Besnier-Boeck's disease		14
Hodgkin's disease		3
TOTAL		70

TABLE VI  
OPERATIONS PERFORMED FOR BRONCHIAL CARCINOMA

	Total No. of Operations	Lobectomy	Pneumonectomy	Exploratory Thoracotomy
1958-62: without mediastinoscopy	168	66 (39.3%)	76 (45.2%)	26 (15.5%)
1966-69: with pre-operative mediastinoscopy	164	80 (48.8%)	61 (37.2%)	23 (14.0%)

TABLE VII  
PNEUMONECTOMIES PERFORMED FOR BRONCHIAL CARCINOMA

	Total	Curative	Non-curative
1958-62: before introduction of mediastinoscopy	76	30 (39.5%)	46 (60.5%)
1966-69: after introduction of mediastinoscopy	61	41 (67.2%)	20 (32.8%)

Table VI shows the total number of operations performed for carcinoma of the lung (164), that is the sum of the number of operations performed after mediastinoscopy (133+23+3) and those performed without preceding mediastinoscopy (5).

A comparison of the number of exploratory thoracotomies performed before (1958-62) and after (1966-69) the introduction of mediastinoscopy shows the former to be 26 (15.5% of the total number of surgical patients), while the latter was 23 (14.0%). This means that there was nothing even remotely like a significant decrease.

In an effort to prove the second statement, we compared the number of 'curative' and 'non-curative' pneumonectomies during each of the two periods. Table VII shows that during the period 1958-62 more 'non-curative' than 'curative' resections were performed (46 and 30, respectively). After the introduction of mediastinoscopy this ratio changed quite radically (20 and 41, respectively) (Table VII).

#### DISCUSSION

The data presented in Tables VI and VII afford unequivocal answers to the two questions studied. While it is true that Table VI shows only a slight diminution of the number of exploratory thoracotomies, it should be borne in mind that the percentage attained during the period 1958-62 was already to be regarded as very small. The fact that a number of exploratory thoracotomies did occur after negative mediastinoscopy is explained by the fact that mediastinoscopy chiefly assesses lymphogenous dissemination. The local dissemination to aorta, pulmonary artery, pericardium, left atrium, mediastinum, and diaphragm—which usually causes inoperability—generally proves to be beyond the scope of mediastinoscopy. This explains the inconsiderable decrease in the number of exploratory thoracotomies.

The answer to the second question is to be derived from Table VII, which shows an increase in the rate of curative pneumonectomies from

39.5% to 67%. It should be borne in mind that in three cases a pneumonectomy was performed although the mediastinoscopic findings had been positive. In future, therefore, the ratio between 'curative' and 'non-curative' resections is certainly likely to change in favour of the former. The improvement recorded might also be attributed to the fact that pneumonectomy was preferred to lobectomy in the second series. This might have reduced the number of non-curative lobectomies and increased the number of curative pneumonectomies. However, there is no indication of this in the ratio between the number of pneumonectomies and of lobectomies performed (Table VI).

On the contrary, relatively more lobectomies than pneumonectomies were performed during the second than during the first period. It might also be suggested that the surgical indications may not have been sufficiently stringent during the first period, and that the improvement seen during the second period must be attributed to a more exact determination of indications. The fact that even during the first period the rate of exploratory thoracotomies was as low as 15.5% is an argument against this suggestion.

The increase in the number of curative resections has therefore been achieved mainly by timely detection of apparently incurable cases with the aid of mediastinoscopy. Many of the 53 patients in whom mediastinoscopy discloses metastases beyond the expected site of resection would have been accepted for operation during the period 1958-62 and the small diminution in the number of exploratory thoracotomies indicates that non-curative pneumonectomies would probably have been performed in these cases.

Not only our personal experience (Table II) but also the data reported by Palva, Viikari, and Inberg (1969), whose five-year survival rate after curative resection was as high as 40%, warrant the expectation that an increased number of curative resections will improve the five-year survival rate. We have no information about haematogenous dissemination, although improved diagnostic techniques and mass x-ray examination in the past few years may have increased the number of fast-growing tumours treated by surgery at an earlier stage. Saxén and Hakama (1964), however, have reported that even with repeated mass x-ray screenings the number of slow-growing tumours detected will always exceed the number of fast-growing tumours. The manner in which these facts influence the five-year survival is as yet unknown.

Table V shows that resection was not feasible in 23 cases in spite of negative mediastinoscopic findings. This clearly demonstrates that mediastinoscopic findings do not always agree with the findings at thoracotomy or with those obtained in resected specimens at operation. In a number of cases the cause of the discrepancy is quite evident—infiltration or metastatic growth outside the field covered by the mediastinoscope.

Nevertheless, the number of non-curative resections (20 patients; Table VII) remains large. The non-curative resections in three patients with positive mediastinoscopic findings have been explained. In the remaining 17 cases non-curative resections were performed after negative mediastinoscopic findings. Technical imperfections in mediastinoscopic procedure must have been a contributing factor. Not only can metastases be overlooked, but exploration must be extended not as far as but beyond the expected site of resection. Of course this is not always technically feasible.

In conclusion, it can reasonably be claimed that the number of curative resections increased as a result of mediastinoscopy and because of this an increase in the five-year survival time is expected. This expectation alone warrants the use of a diagnostic aid which entails little risk. However, a high level of technical skill is required; it must be borne in mind that mediastinoscopy must be performed carefully and, if possible, beyond the expected site of resection. We find that mediastinoscopy chiefly assesses lymphogenous metastasization, and that local infiltration of the pericardium, aorta, or other organs is beyond its scope; therefore, we can expect a future decrease in non-curative resections but not in exploratory thoracotomies. The increase in the number of curative resections constitutes a substantial gain for the patient; on the other hand, the implications are that an even smaller proportion of the total number of patients with carcinoma of the lung will be found suitable for curative surgical therapy.

#### CONCLUSIONS

A follow-up study of 168 cases of pulmonary carcinoma treated surgically before the introduc-

tion of mediastinoscopy shows that 15.5% of the total number of operations must be regarded as exploratory thoracotomies. None of these patients survived longer than one year. A pneumonectomy was performed in 76 cases. The five-year survival in curative resections was 66%, that in non-curative resections was 0%; the criteria we used for curative and non-curative have thus assumed prognostic value. When used to separate patients submitted to mediastinoscopy into two groups, the value of mediastinoscopy should become apparent from the increase in the number of curative resections.

Our investigation shows that 46 non-curative versus 30 curative resections were performed before mediastinoscopy was introduced. After its introduction this ratio changed favourably to 20 non-curative versus 41 curative resections. As mediastinoscopy entails little risk, as demonstrated by the small number of complications, this intervention is a welcome asset in the selection of patients for thoracotomy. Because mediastinoscopy assesses mainly lymphogenous dissemination and local tumour spread is usually beyond its scope, the number of exploratory thoracotomies has diminished less than was expected.

The technical procedure of mediastinoscopy should take into account the necessity of extending examination beyond the eventual site of bronchial division at pneumonectomy.

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