Clinical Value of Cervical Mediastinoscopy in the Staging of Bronchial Carcinoma

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Abstract

Whether mediastinoscopy is indicated in the preoperative staging of bronchogenic carcinoma is still a controversial issue. It may be performed routinely (to exclude locally inoperable patients from surgery), selectively, or it may be regarde as superfluous (in centers which prefer an extended lymphoadenectomy at the time of thoracotomy). We regard mediastinoscopy as indicated for the following purposes: 1) staging of NSCLC and SCLC; 2) diagnostic (mediastinal masses or lung tumors without previous histology); 3) restaging after primary chemotherapy; 4) assessment of prognosis in patients with borderline operability. The indication for 224 mediastinoscopies performed at our institution in the period from September 1991 through March 1999 was mainly for staging (59.2%) or diagnostic (30.6%). Eight (5.4%) patients underwent mediastinoscopy for the assessment of operability, and 7 (4.8%) after primary chemotherapy for the restaging of loco-regionally advanced lung cancer. Sensivity and specificity rates were 87% and 100%, respectively, with an accuracy of 93% for the mediastinoscopy performed for the staging of lung cancer at all stages. If we consider the N2 tumors (42 cases) alone, the sensivity was 76.7% and the specificity 100%, with an accuracy of 83.3%. Overall positive and negative predictive value resulted 100% and 87%, respectively, according to the data reported in literature. Our data confirm the role of mediastinoscopy as the gold standard for regional staging of lung cancer.

Key words: Mediastinoscopy, staging of bronchogenic carcinoma, diagnosis of bronchogenic carcinoma.

Riassunto

Le indicazioni alla mediastinoscopia nella stadiazione preoperatoria del cancro del polmone sono ancora oggi oggetto di controversie. La procedura può essere impiegata routinariamente (per escludere dal trattamento chirurgico i pazienti con malattia localmente non operabile), selettivamente, oppure essere considerata superflua (nei centri nei quali si predilige eseguire un'estesa linfoadenectomia mediastinica al momento della toracotomia). Gli Autori riservano la mediastinoscopia ai casi che presentano le seguenti indicazioni: 1) stadiazione del NSCLC o del SCLC; 2) diagnosi/tipizzazione (lesioni mediastiniche di n.d.d. o neoplasie polmonari non tipizzate con altre metodiche); 3) ristadiazione dopo chemioterapia primaria; 4) definizione della prognosi di pazienti con operabilità «al limite». L'indicazione alle 224 mediastinoscopie eseguite presso la

Indications

Whether mediastinoscopy is indicated in the preoperative staging of bronchial carcinoma is still a controversial issue. It may be performed routinely (to exclude locally inoperable patients from surgery)[8, 9, 10] or it may be regarded as superfluous (in centers where an aggressive approach to the management of such tumors with an extended lymphadenectomy is preferred)[18]. According to Tsang and Watson[11], 44% of British surgeons in 1990 performed neither mediastinoscopy nor CT preoperatively. The third alternative is a selective mediastinoscopy, when the computed tomography (CT) indicates a mediastinal lymph node involvement associated with tumor.

We regard mediastinoscopy as indicated for the following purposes:

1) staging
2) diagnostic
3) restaging
4) assessment of operability.

1) The mediastinoscopy indication for staging is based on suspect CT-scans for lymph node involvement or generally for lymph nodes measuring more than 1 cm in diameter at CT.

2) Mediastinoscopy for diagnostic purposes is performed in patients with a strong clinical suspicion of carcinoma, but without a histological diagnosis, and in the presence of lymphadenopathy or a mediastinal mass at CT.

3) For small-cell carcinomas, restaging mediastinoscopy is performed in order to define the degree of remission. In future, it will be indicated more and more for the assessment of the response to induction chemotherapy in non small cell carcinoma.

nostra istituzione nel periodo settembre 1991- marzo 1999 è rappresentata prevalentemente dalla stadiazione (59.2%) o dalla diagnosi istologica (30.6%). Otto (5.4%) pazienti sono stati sottoposti alla procedura per definirne l'operabilità e 7 (4.8%) per la ristadiazione dopo chemioterapia primaria di un carcinoma polmonare in stadio loco-regionale avanzato. La sensibilità e la specificità sono risultate rispettivamente dell'87% e del 100% con un accuratezza del 93% per le mediastinoscopie di stadiazione del carcinoma polmonare. Considerando separatamente le neoplasie in stadio N2 (42 casi), la sensibilità si è attestata al 76.7% e la specificità al 100%, con un accuratezza dell'83.3%. Il valore predittivo positivo e negativo sono risultati del 100% e dell'87%, rispettivamente, in linea con i dati presentati in letteratura. I nostri risultati confermano la mediastinoscopia come gold standard nella stadiazione regionale del cancro del polmone.
Parole chiave: Mediastinoscopia, staging del carcinoma bronchiogeno, diagnosi del carcinoma bronchiogeno.

4) In rare cases of patients with borderline functional and local operability and with suspected lymph node involvement, mediastinoscopy is performed in order to assess the prognosis on the basis of mediastinal N-involvement and the expectation of a risky operation for the patient.

In those centers where mediastinoscopy is not performed routinely or where the surgeon does not proceed directly to the thoracotomy for mediastinal N-staging, an indicator is needed in order to establish the selective indication for mediastinoscopy. This indicator is provided by CT. The accuracy of the latter in defining pathological lymph nodes is, however, limited (Tab. I).

Lymph nodes measuring more than 1 cm in diameter are generally considered suspect; the sensitivity and specificity of CT for lymph nodes 1 cm, however, range from maximum values of 68% and 81%, respectively, to minimum values of 47% and 32%. These parameters improve appreciably when the cut-off value chosen for the lymph node diameter is 2 cm[1, 10]. This morphometric datum, however, is not particularly useful for clinical purposes, since lymph nodes of this size are very likely to be positive and also because it eliminates lymph nodes between 1 and 2 cm, which constitute the majority of our findings. This is more evident if we consider the observations reported by De Leyn *et al.*[8] who found positive lymph nodes at mediastinoscopy in 20% of patients with CT scans assessed as negative and who therefore advocate that mediastinoscopy should be performed routinely.

Without going so far as to share the recommendation of these authors, who largely found N2 involvement – which does not necessarily rule out resective therapy – we believe it is advisable to perform mediastinoscopy in selected cases, precisely because of its good sensitivity and specificity (Tab. II).

Clinical value

The clinical objective of mediastinoscopy is to avoid surgery in those patients who, as a result of the extensive spread of the tumor (N3), would not, on the basis of our current knowledge, obtain any therapeutic benefit from

Tab. I – ACCURACY OF COMPUTED TOMOGRAPHY IN THE STAGING OF BRONCHOGENIC CARCINOMA

Ref.	*Author*	*Year*	*#*	*Diameter*	*Sensitivity*	*Specificity*	*Accuracy*	*PPV*	*NPV*
4	Rhoads, A.C.	1986	75	> 1 cm	57%	69%	64%		
1	Ferguson, M.K.	1986	61	> 2 cm	95%	83%	88%		
12	Van Schil, PE	1989		> 1 cm	68%	57%	61%		
10	Mori, K	1992	133	> 1 cm	57%	81%			
				> 2 cm		100%			
7	Meffert, R.	1997	182	–	47%	32%			
9	Gdeedo, A.	1997	74	> 1 cm	48%	53%	51%	49%	61%
5	Disdier, C.	1998	33	–	93%	54%		68%	87.5%

Tab. II – ACCURACY OF MEDIASTINOSCOPY

Ref.	*Author*	*Year*	*#*	*Sensitivity*	*Specificity*	*Accuracy*
12	Van Schill, PE	1989	85	91%	100%	
10	Mori, K.	1992	33	70%	100%	
13	Cassina, P.	1993	197	75%	100%	
7	Meffert, R.	1997	182	74%	100%	
6	Porte, H.	1998	127	92%	100%	94%
	Personal series	1998	147	87%	100%	93%

an operation. In addition, the procedure provides useful information regarding the prognosis of the tumor.
In N2 tumors, the surgical approach is fairly controversial. Many surgeons also automatically exclude N2 tumors as candidates for primary surgery, especially if there are additional risks.
T3 tumors are known to have distinctly variable prognoses, depending on whether they are associated with N1 or N2 lymph node status, so much so, indeed, that sleeve resection is inadvisable in the presence of N2-disease, precisely because of the very poor prognosis. Therefore it is so important to define the regional extent of the tumor by mediastinoscopy and possibly spare the patient a particularly risky operation.
In N2 cases, when an aggressive approach is followed, a knowledge of the stations involved will prompt the surgeon to be even more diligent in performing as radical a lymphadenectomy as possible.
As a result of several studies,[15, 16] in N2 cases detected at mediastinoscopy, induction chemotherapy appears to be an effective therapeutic option, with encouraging results in terms of survival. In the light of this, mediastinoscopy can be expected to play an important role in the planning of lung cancer treatment in the future.
The mediastinoscopy procedure makes it possible to appreciably reduce the number of exploratory thoracotomies performed, thus eliminating the operative risk and enhancing the quality of the patient's life.
Mediastinoscopy enables surgeons to distinguish preoperatively between lymph node metastases and extracapsular growth, which is associated with a poorer prognosis.
After deciding against surgical resection, the therapeutic alternatives consist in chemo- and/or radiotherapy, the indication for which is based on the loco-regional staging established by mediastinoscopy, which is more accurate than the CT scans (Tab. I, II and III).
Of particular clinical importance is the restaging of small-cell carcinomas after primary chemotherapy.
Lastly, when bronchoscopy or needle-biopsies are not able to provide the histological diagnosis, the clinical contribution of mediastinoscopy could be of decisive importance.
We shall now discuss the clinical importance of mediastinoscopy on the basis of the data obtained in our patient series.

Tab. III – ACCURACY OF CT ALONE vs. CT PLUS MEDIASTINOSCOPY IN N2-DISEASE

	Sensitivity	*Specificity*	*Accuracy*	
CT alone	54%	73%	67.5%	**
CT + MEDIA	67%	89%	82.5%	

** $p = 0.03$
(10) MORI, K et al. Jpn J Clin Oncol 1992 Feb;22 (1):35-40

Tab. IV – INDICATIONS FOR MEDIASTINOSCOPY IN 147 LUNG CANCER PATIENTS

	#	%
Diagnostic	45	30.6
Staging: small cell	7	4.8
Staging: NSCLC	80	54.4
Operability	8	5.4
Restaging	7	4.8
Total	147	100.0

Indications

The indications for mediastinoscopy are given in Tab. IV. The intention was mainly for staging (59.2%) or diagnostic (30.6%). Mediastinoscopy was performed in 8 patients at high surgical risk with tumors extending to the mediastinum. In 7 cases the result was negative, while in one the mediastinoscopy was not technically feasible. Six patients were therefore submitted to surgery and operation was withheld in one case owing to cardiorespiratory inoperability.

Diagnostic indication

Of 224 mediastinoscopies performed over the period from September 1991 to March 1998, 123 were diagnostic, 45 of which for suspected lung cancer (Tab. V).
In 35/45 cases (78%) the cancer suspicion was confirmed, in 8/45 cases (18%) mediastinoscopy yielded negative results, and in 2 cases (4%) the procedure was not technically feasible owing to adhesions and struma. When mediastinoscopy is diagnostic, the staging is also obtained, which will obviously be N2 or N3. In one case a T4 tumor was diagnosed.
Clearly, diagnostic mediastinoscopy is indicated only in case of radiologically visible mediastinal lymph nodes, which can be reliably biopsied. In this context, must be mentioned the findings reported by De Leyn *et al.*[8], who found N2 lymph node involvement in as many as 14.5% of patients with negative CT scans.
The clinical value of mediastinoscopy is on a par with the diagnostic validity of the procedure, i.e. with its sensitivity and specificity rates. In our experience these rates were 87% and 100%, respectively, with an accuracy of 93% for mediastinoscopy performed for the staging of lung cancer at all stages. If we consider the N2 tumors (42 cases) alone, the sensitivity was 76.7% and the specificity 100%, with an accuracy of 83.3%. This means that mediastinoscopy enables us to define the regional stage of bronchial carcinoma with a probability of 76.7%, while

Tab. V – DIAGNOSTIC VALUE OF MEDIASTINOSCOPY

Mediastinoscopy: procedures 1991-1998	:	*224*	
Diagnostic mediastinoscopy	:	*123 (55%)*	
For Lung Cancer 45 (37%)		*For Other Disease* 78 (63%)	
Small Cell	9	Sarcoidosis	43
Adenocarcinoma	9	Lymphadenopathy, NOS (Benign)	14
Squamous Cell	7	Lymphoma	8
Undifferentiated	8	Benign Disease	3
Large Cell	2	Malignant Disease (Miscellanea)	3
Negative	8	Carcinoid	1
Technically Not Feasible	2	Negative	6
⇓ *Mediastinal Staging*			
T4	1		
N2	16		
N3	18		
NX	8		
Technically not feasible	2		

there is no risk of false-positive findings. The sensitivity and specificity values for the total number of mediastinoscopies performed in our center are even better with a positive predictive value of 100% and a negative predictive value of 87%; these are not only the percentages emerging from our own data but also those reported in the literature (Tab. II) and it is this accuracy that makes mediastinoscopy the gold standard for regional staging of lung cancer.

NSCLC staging

Out of 147 mediastinoscopies performed for histologically confirmed lung cancer (102 cases) or for a suspected lung cancer (45 cases), 46 positive mediastinoscopies (31.3%) were recorded with ipsilateral lymph node involvement in 21 cases (14.3%), N3 findings in another 21 cases (14.3%), extracapsular involvement in 3 patients (2.0%) and confirmation of a suspected T4 (tracheal infiltration) stage in one case (0.7%) (Tab. VI).

Tab. VI – MEDIASTINOSCOPY: STAGING OF MEDIASTINAL NODES

Mediastinoscopy for Lung Cancer : 147 cases			
Negative	90	(61.2%)	
Positive	46	(31.3%)	
	N2	*2*	
	N3	*2*	
	extracapsular	*3*	
	ipsilateral	*2*	
	contralateral	*1*	
	T4	*1*	
Nodes not found		3	(2.0%)
Technically not Feasible		8	(5.5%)

Table VII gives the anatomic distribution and histotypes of the mediastinal lymph node metastases. It should be noted that the carina, either alone or along with other stations, was involved in only 10.9% of positive cases.

Twenty-two patients with involvement of N3 stations were excluded from surgery on the basis of the current oncological guidelines. Moreover, if we consider that 19 patients with lymph node stage N2 were not operated on, we have a total of 41 patients (28%) who, thanks to mediastinoscopy, were spared having to undergo a useless operation. Four patients (3 with N2, 1 with N3) underwent surgery with a radical intent which seemed feasible on the basis of the site of the lymph nodes and the possibility of reaching them for the purposes of radical resection.

In those cases where surgery was performed with preoperative N2 at mediastinoscopy, which are rare in our experience, we regard the indication to mediastinoscopy as being particularly important, because the surgeon is there obliged to perform a systematic mediastinal lymphadenectomy.

The data available are too limited to allow any assessment of the preferential sites of the various histotypes and their tendency to metastasize.

Eighteen patients (13%) presented involvement of more than one lymph node station at mediastinoscopy (Tab. VIII); one third were diagnosed as N2 and the others as N3.

In view of the poorer prognosis for multinodal sites, which are to be considered as a systemic disease, there will be a greater propensity in such cases to chemo- or chemoradiotherapy. A precise staging by mediastinoscopy

Tab. VII – ANATOMIC SITES OF LYMPH NODE METASTASES (diagnosis by mediastinoscopy)

Station		#	%
N2	Upper paratracheal	9	19.5
N2	Lower paratracheal	7	15.3
N2	Carinal	3	6.5
N2	Upper + lower paratracheal	4	8.7
N2	Upper paratracheal + carinal	1	2.2
N3	Upper paratracheal	5	10.9
N3	Lower paratracheal	5	10.9
N3	Upper + lower paratracheal	2	4.3
N3	Upper paratracheal + N2 upper paratracheal	3	6.5
N3	Lower paratracheal + N2 upper paratracheal	3	6.5
N3	Lower paratracheal + carinal	1	2.2
N3 + N2	More than 2 stations	3	6.5
Total		46	100.0

DISTRIBUTION ACCORDING TO "N" STAGE AND HISTOLOGY

Histology	*Total*	*N2*	*N3*
Adenocarcinoma	16	9	7
Large cell	2	1	1
Squamous cell	12	5	7
Small cell	7	2	5
Undifferentiated	7	5	2

provides important prognostic indications in such cases with expected therapeutic consequences.

At thoracotomy we found an N2 stage in 10 cases after negative mediastinoscopy; 7 of these were false-negatives, which lowered the sensitivity of the procedure to 87% (Tab. II). The other 12 N2 cases not detected at mediastinoscopy were located in stations which were inaccessible to the procedure.

N0 staging represents a typical indication for primary surgery (Tab. IX).

From the clinical point of view, however, we should point out that out of 90 patients with N0, the surgery was non-radical in 5 cases and in another 12 cases exploratory thoracotomy was the only procedure due to unexpected local inoperability or to intraoperative complications (Tab. IX).

This is explained by the fact that mediastinoscopically N0 staged patients with extended central tumors represent a clear indication for a thoracotomy with radical intent, in spite of the central location of tumor. The thoracotomy findings or the presence of intraoperative complications, however, subsequently prevented the resection being performed.

A total of 20 patients with N0 stage tumors did not undergo surgery. The reasons for withholding surgical therapy are given in Tab. IX.

While mediastinoscopy and evidence of lymph node metastases make it possible to spare patients with a poor

Tab. VIII – RESULTS OF 353 BIOPSIES BY MEDIASTINOSCOPY

	Mediastinal stations	*Patients*
Biopsies (total)	353	137
Positive	70	47
	More than one positive station	*18*
Negative	283	90

Number of biopsied stations (mean) per procedure: 2.58

prognosis a stressful, debilitating operation, it is by no means always certain that mediastinoscopic N0 findings will be synonymous with operability or local radicality.
At this point, we need to mention the issue of false-negative mediastinoscopic findings. In our experience, the incidence of such findings was 5% (7 cases). It is important to point out, however, that 4 N2 findings at thoracotomy were located in the lymph node station 5, which is not accessible to standard cervical mediastinoscopy. But this procedure, too, has its limits, and its range of exploration is confined to the upper paratracheal, lower paratracheal, and carinal lymph nodes with the additional possibility of reaching the supraclavicular lymph nodes via the mediastinoscopy incision[17].

Restaging

Of particular clinical importance is the restaging of small-cell carcinoma after primary chemotherapy, especially when surgery is planned. In our series we had very few cases because our pneumologists are more oriented towards CT remission findings and therefore they do not necessarily request the mediastinoscopy. Thus sparing the patient additional operative stress and a delay in surgery, considering that the mediastinoscopy will always be accompanied by a complete mediastinal lymphadenectomy. Moreover, of 8 patients operated on after induction chemotherapy, only 2 presented N2 tumors: one of them lived for 5 years, and we have no information about the other. Staged N3 small-cell tumors, that is to define "extended disease", are not in any case an indication for surgery.
In our opinion, there will be considerable scope in future for mediastinoscopic restaging, with a view to surgical intervention, after induction therapy for small-cell carcinoma.

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Tab. IX – SURGICAL OPERATIONS IN 90 "N0" PATIENTS (AFTER MEDIASTINOSCOPY)

Treatment		#
Radical surgery		53
Non-radical surgery		5
Exploratory toracotomy		12*
No surgery		20
CAUSES OF NO SURGICAL TREAMENT		
Inoperability (severe comorbidity)	10	
Treatment refused	3	
Small cell lung cancer	2	
Locally advanced disease (T4)	2	
Distant metastases (M1)	2	
Death	1	

ESPLORATORY SURGERY AFTER NEGATIVE MEDIASTINOSCOPY

* *Causes of non-radical surgery*	#	*Notes*
Intraoperative non-resectability (T4)	7	
Non-operability due to comorbidity	3	Indication: histologic diagnosis
Tumor of unknown origin (lung, thymus, other)	1	Indication: histologic diagnosis
Intraoperative death due to myocardial infarction	1	

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