Original Article

Medical thoracoscopy: Analysis on diagnostic yield through 30 years of experience

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Abstract:

BACKGROUND: Medical thoracoscopy (MT) or pleuroscopy is a procedure performed to diagnose and treat malignant and benign pleural diseases. Totally 2752 pleuroscopies executed in 1984–2013 in our center were considered in this study.

METHODS: A retrospective observational study was performed. Observational time was divided into six series of 5 years. We calculated MT diagnostic yield and analyzed trends of main diseases diagnosed along the time.

RESULTS: Along the 30 years population became progressively older. Number of pleuroscopies firstly increased, then stabilized and decreased in the last 5 years. The overall diagnostic yield of MT was 71%, increasing from 57% to 79%. The diagnostic yield was significantly higher in the presence of monolateral pleural effusion. Cancer represented more than half of diagnosis; tuberculosis was the most common nonneoplastic disease. The frequency of all cancers, mesothelioma, and lung cancer increased through the time; tuberculosis first decreased and then increased. All specimens resulted appropriate during the last 25 years.

CONCLUSION: MT has a great diagnostic yield that can be improved by practice, permitting to achieve a specific histological diagnosis in about 80% of patients. Our experience demonstrates that the accurate selection of the patients undergoing to MT is very important to reach these results.

Key words:

Chest ultrasound, diagnostic yield, lung cancer, medical thoracoscopy, pleural malignant mesothelioma

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Medical thoracoscopy (MT) or pleuroscopy is a diagnostic and therapeutic procedure idealized by Jacobeus, in 1910. At the beginning, pleuroscopy was applied mainly in the treatment of tuberculosis (obtaining lung collapse through the lysis of pleural adhesions),[1] but after the development of medical treatments for tuberculosis, this procedure began to be used with other indications. Nowadays, MT is performed to diagnose malignant and benignant pleural diseases, in addition to therapeutic intents achieved through pleurodesis or empyema treatment.[2-4] In English literature, data considering the MT's diagnostic effectiveness for the assessment of a certain histological diagnosis are inconstant, based on little groups of patients and often not referred directly to the percentage of specific histological results.[5-24] We started to perform MT in 1984 and since then more than 2800 MTs have been realized. In this study, we considered 2474 consecutive diagnostic MTs executed in 1984–2013. We studied MT's diagnostic yield in this large cohort of patients, analyzing also the changes occurred through the years.

Methods

We conducted a retrospective observational study regarding all consecutive MTs performed with diagnostic intent from 1984 to 2013. All data were extracted from our database. This analysis included traditional MTs normally performed using 7 mm Karl Storz Endoskope set (Tuttlingen, Germany) and 59 minithoracoscopies realized employing 3.3 mm telescope (Karl Storz Endoskope; Karl Storz; Tuttlingen, Germany) and one 3.0 mm biopsy forceps.[25] In 2000, we began to study all patients with chest ultrasonography before performing MT. This innovative approach let us not only to discard preparatory pneumothorax but also to perform MT in the absence of pleural effusion.[26] Since 2002, propofol sedation was

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implemented progressively in addition to local anesthesia with a resuscitator cooperation.

In this study, the 30 years observational time was divided into six series of 5 years: first period from 1984 to 1988, second period from 1989 to 1993, third period from 1994 to 1998, fourth period from 1999 to 2003, fifth period from 2004 to 2008, and sixth period from 2009 to 2013. We calculated the number of MTs and the mean age of patients in every period. The diagnostic effectiveness of MT was assessed considering data globally and in every period computing the percentage of MT resulted in a specific histological diagnosis and the percentage of inconclusive MT (histological diagnosis of unspecific pleural inflammation or inadequate material). The diagnostic effectiveness was related also to the different clinical indications for MT, computing the difference between monolateral, and bilateral disease (Fisher's exact test). In addition, frequencies of the different diseases diagnosed were calculated considering the six groups separately. Comparing values of each period to each other through Chi-square for trend test, we analyzed the variability of the patients' mean age, of the percentage of diagnostic MTs and the changeability of the frequencies of each disease. We produced line graphs displaying these data.

Results

During the 30 years analyzed, 2752 consecutive MTs were performed in our center. The mean age of the patients was 61.1 years (standard deviation ± 14.4), 1800 (65.4%) patients were males and 952 (34.6%) were females. Calculating mean age of the patients grouped in the six series of 5 years, it appeared that population undergoing to MT became progressively older reaching a statistically significant difference comparing the first and the third period. Then, mean age stabilized in the last 15 years [Figure 1].

During the early periods, the number of MTs performed progressively increased [Figure 2], in fact, more than a duplication was registered reaching the peak during the third period analyzed (from 146 to 640). Then, nearly stabilization through the subsequent 10 years was evident. Finally, it was registered a swing during the last quinquennium. The total number of MTs declined by almost a third.

A total of 2474 pleuroscopies were performed with diagnostic intent and the other 278 MTs were executed with therapeutic intents (almost entirely for empyema and pneumothorax). Table 1 shows the histological diagnostic results reached through the totality of the diagnostic MTs performed in our center from 1984 to 2013. The percentage values are represented in Table 2. The overall diagnostic yield of MT was 71.0%, increasing from 57.1% to 79.2%. During the six periods, the percentage of MTs that did not result in a specific histological diagnosis decreased almost constantly. These data included either thoracoscopies that did not provide adequate samples and thoracoscopies that led to the unspecified histological diagnosis of pleuritis (either cases of acute pleurisy secondary to viral infection or chronic pleurisy due to liver, heart, or systemic autoimmune diseases and cases of underdiagnosis of specific histological patterns). Anatomopathological samples resulted inadequate for histological analysis only during the first period. Indeed, virtually all specimens resulted appropriate during the next 25 years [Table 2]. The diagnosis of unspecified pleuritis constantly decreased after the second period, reducing below 20% and reaching a statistically significant difference from the fourth period [Figure 3].

Analyzing the indications for MT reported in the 1577 diagnostic pleuroscopies performed from 1998 to 2013, the diagnostic yield of MT resulted significantly lower if pleural effusion was bilateral than in the case of monolateral disease: it was, respectively, 46% and 77% ($P < 0.001$).

Considering the histological results, it appeared that more than a half of the MTs were diagnostic for cancer. Malignant pleural mesothelioma and lung cancer metastasis were the most frequent tumors detected (about 21% each one). Breast cancer secondarisms represented almost 14% of all cancers diagnosed. Among nonneoplastic diseases, tuberculosis was the most common (about 6%).

Analysis of the trend of each histological diagnosis revealed that all cancers, mesothelioma, lung cancer, and tuberculosis

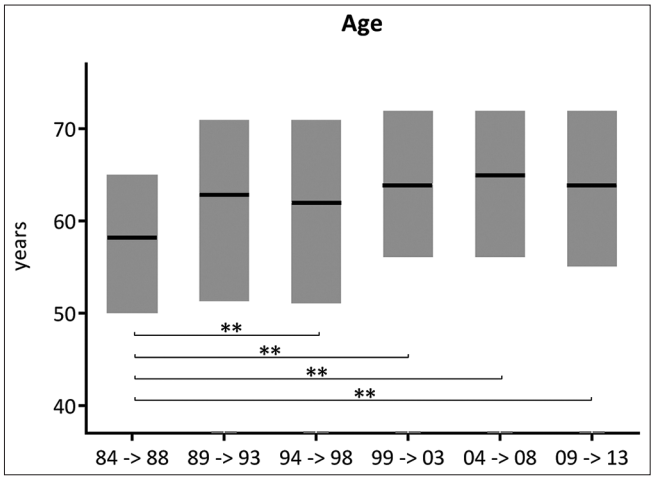

Figure 1: Mean age of patients divided into the six series of 5 years. Horizontal bars indicate the statistically significant difference between the mean (**$P < 0.001$)

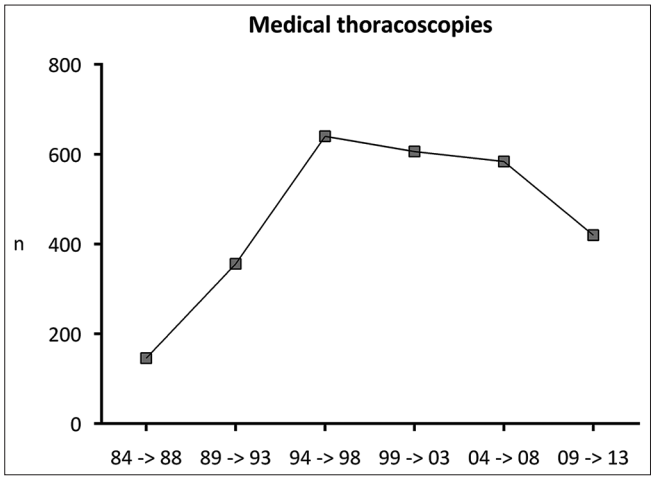

Figure 2: Number of medical thoracoscopies performed in our center until 2013, divided into the six series of 5 years

Table 1: Number of medical thoracoscopies performed divided by diseases and grouped by periods of 5 years

Histological diagnosis	84->88	89->93	94->98	99->03	04->08	09->13	Total
Specific	72	172	382	411	411	309	1757
Cancer	56	145	328	387	369	270	1555
Mesothelioma	21	26	111	142	116	108	524
Epithelioid	16	20	85	116	96	93	426
Biphasic	4	3	12	19	14	11	63
Sarcomatoid	0	0	3	7	6	4	20
Unspecified	1	3	11	0	0	0	15
Lung	7	53	82	119	143	100	504
Breast	9	20	47	65	50	27	218
Emathologic	2	5	10	8	10	10	45
Kidney	2	4	10	15	3	6	40
Gastro-intestinal	1	2	10	6	7	1	27
Others	2	9	28	24	40	18	121
Unspecified	12	26	30	8	0	0	76
Tuberculosis	14	13	38	15	34	35	149
Others	2	14	16	9	8	4	53
Inconclusive	54	116	184	151	131	81	717
Unspecified pleural inflammation	45	116	183	151	131	81	707
Inadequate material	9	0	1	0	0	0	10
Total	126	288	566	562	542	390	2474

Table 2: Percentage of diseases grouped by periods of 5 years

Histological diagnosis	84->88	89->93	94->98	99->03	04->08	09->13	Total
Specific	57.1	59.7	67.5	73.1	75.8	79.2	71.0
Cancer	44.4	50.3	58.0	68.9	68.1	69.2	62.9
Mesothelioma	16.7	9.0	19.6	25.3	21.4	27.7	21.2
Epithelioid	12.7	6.9	15.0	20.6	17.7	23.8	17.2
Biphasic	3.2	1.0	2.1	3.4	2.6	2.8	2.5
Sarcomatoid	0.0	0.0	0.5	1.2	1.1	1.0	0.8
Unspecified	0.8	1.0	1.9	0.0	0.0	0.0	0.6
Lung	5.6	18.4	14.5	21.2	26.4	25.6	20.4
Breast	7.1	6.9	8.3	11.6	9.2	6.9	8.8
Emathologic	1.6	1.7	1.8	1.4	1.8	2.6	1.8
Kidney	1.6	1.4	1.8	2.7	0.6	1.5	1.6
Gastro-intestinal	0.8	0.7	1.8	1.1	1.3	0.3	1.1
Others	1.6	3.1	4.9	4.3	7.4	4.6	4.9
Unspecified	9.5	9.0	5.3	1.4	0.0	0.0	3.1
Tuberculosis	11.1	4.5	6.7	2.7	6.3	9.0	6.0
Others	1.6	4.9	2.8	1.6	1.5	1.0	2.1
Inconclusive	42.9	40.3	32.5	26.9	24.2	20.8	29.0
Unspecified pleural inflammation	35.7	40.3	32.3	26.9	24.2	20.8	28.6
Inadequate material	7.1	0.0	0.2	0.0	0.0	0.0	0.4
Total	100.0	100.0	100.0	100.0	100.0	100.0	100.0

statistically changed during the period considered [Figure 4]. The frequency of all cancers [Figure 4a], at the beginning constant, increased from second to fourth period, remaining then at the same level until 2013. This trend resulted in an appreciable increment between the first and last period. This global increase was evident also studying mesothelioma, after a decreasing between the first and second period [Figure 4b]. Lung cancer secondarisms augmented comparing the first period to the others. The rise stopped only between the second and third period and between the fifth and sixth period [Figure 4c]. The trend of tuberculosis was biphasic [Figure 4d]. A decrease of its frequency was evident between the first and the fourth period while in the further periods, it increased progressively.

Discussion

We present an analysis based on data collected along 30 years and including more than 2470 MTs performed with diagnostic intent. During the early years, a considerable increase in the amount of MTs was observed and then they steadied and nowadays they are decreasing a little [Figure 1]. This trend should be the result of the advent of video-assisted

thoracoscopic surgery (VATS) in our hospital that was in 1995. Despite the spread of this relatively new technique,[27] we believe that MT is keeping its absolute usefulness in the study of pleural diseases. The implementation of chest ultrasonography during preoperative care allowed to expand the indications of MT even in patients without pleural effusion.[26,28] In our opinion, MT and VATS should be performed currently even in the same medical center because each one enjoys different clinical indications. Moreover, these procedures should be performed by different specialists. In this way, these two different techniques do not result in contrast, let alone alternative.

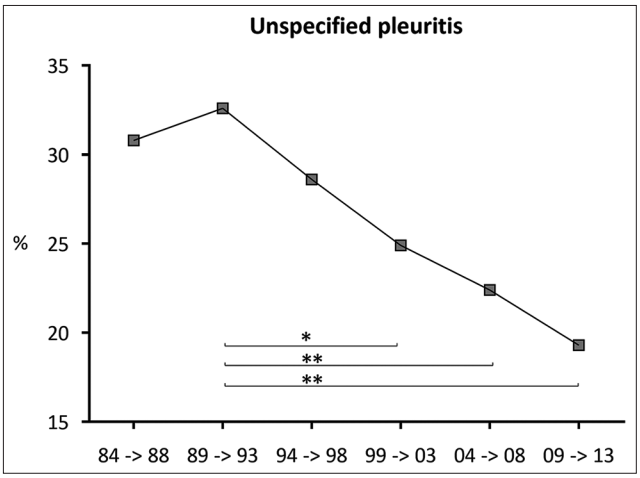

Figure 3: Graphs displaying the percentage frequency of unspecified pleuritis along the consecutive six series of 5 years. Horizontal bars indicate the statistically significant difference between the frequencies (*P < 0.05, **P < 0.001)

The main contribution of this study is to investigate the real direct diagnostic yield of MT, defined as the percentage of diagnoses that are reached only with the histological analysis of the specimen collected with MT. In literature, data regarding MT diagnostic yield are poor and inconstant. Indeed, they vary from 42% to 95% and they derive from heterogeneous studies including little groups of patients and often not centered on the percentage of specific diagnosis achieved only with MT.[5-24] Our analysis differs from the others because it includes a large cohort of patients (more than 2400) and considers every consecutive MT performed with diagnostic intent without any selection. Furthermore, the long period examined permits to analyze changes of MT diagnostic yield through the time. A follow-up time was not contemplated since the specificity of anatomopathological results obtained with MT has been already established.[6] This study established an overall diagnostic capability of 71.0% and a statistically significant improvement from the 57.1% to 79.2%. It demonstrated that practice improves continuously clinicians' and pathologists' skill. Indeed, the inadequate histological samples were present only during the first 5 years and none of them was registered during the following 25 years. In addition, the frequency of unspecific pleuritis diagnosis decreased progressively during the observational time from about 35% (1/3) to 20% (1/5), with a mean cumulative frequency of 28.6%. These unspecific histological diagnoses included either

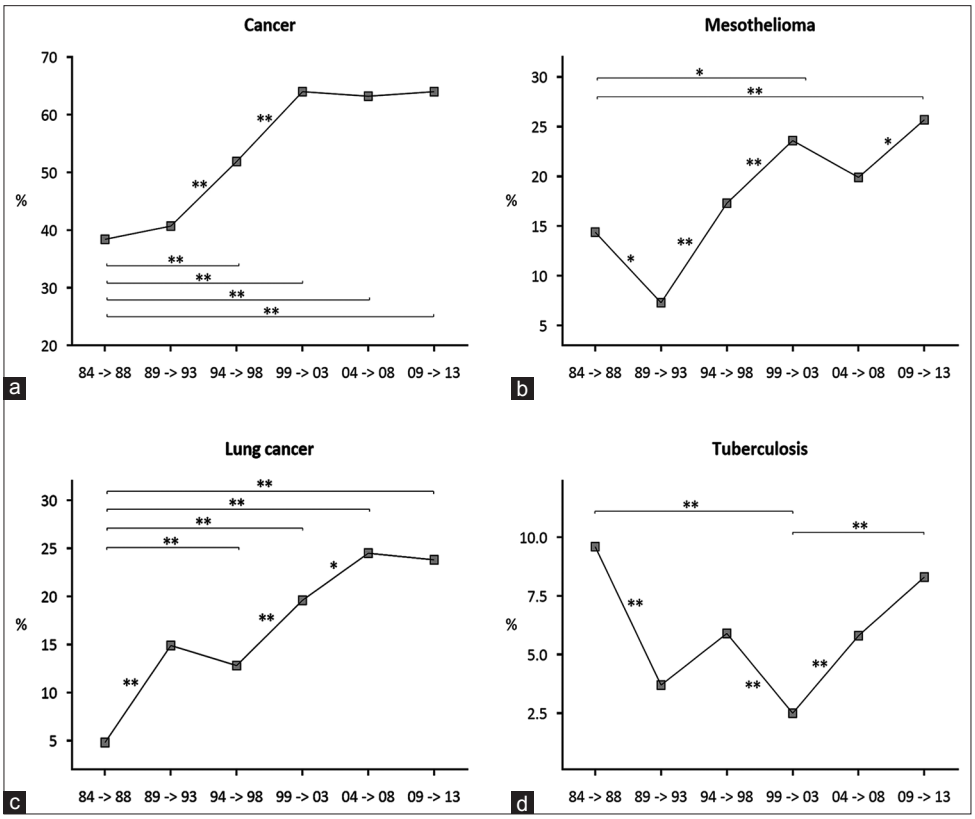

Figure 4: Graphs displaying the percentage frequency of overall cancer (a), mesothelioma (b), lung cancer pleural secondarisms (c), tuberculosis (d), along the consecutive 6 series of 5 years. Horizontal bars indicate the statistically significant difference between the frequencies (*P < 0.05, **P < 0.001)

benign diseases such as parapneumonic pleural effusions or viral pleuritis that are characterized not only by peculiar histological patterns but also by underdiagnosed diseases (false negative histological patterns). In our opinion, the increasing effectiveness in specimen collection and the improvements in anatomopathological examination permitted to decrease false negative results.

The analysis of clinical indications for MT, performed dividing the diseases into two groups (monolateral diseases and bilateral diseases), permitted to assess that MT in bilateral diseases provides a specific diagnosis in <50% of cases. In our opinion, this evidence assumes a very important clinical implication. In the presence of bilateral pleural effusions, the conclusive contribute of MT is lower than one out of two cases. We suggest an accurate clinical evaluation in these cases, in particular considering systemic diseases such as cardiogenic, kidney, liver, or rheumatic diseases and thinking to MT only in selected clinical conditions.

Our data confirm that the most frequent diagnosis resulted after MT is cancer. In the second half of the 30 years analyzed more than 60% of patients were affected by cancer, this rate stabilized after an initial enhancement. Pleural and lung cancers represented the most frequent diagnosed diseases. Pleural mesothelioma rate nearly doubled from the beginning. This trend is consensual to the increasing incidence rate registered in Italy and Europe during the years analyzed.[29] Interestingly, we specified the incidence of the different histologic subtypes. The epithelioid variant was confirmed to be the most common, comprising more than 80% of all mesotheliomas, biphasic subtype represented about 12%, and sarcomatoid variant resulted very rare. These frequencies remained constant during the 30 years analyzed. Moreover, during the second half of the period, our center was always able to identify the specific histologic subtypes of all malignant mesothelioma. This result could be due to a progressive skill acquisition by the clinical or anatomopathological staff or by both of them together.

Along the years MT became very useful for the diagnosis and the management of pleural involvement in lung cancer. MT performed for lung cancer increased from a light 5% to the current 24%. This trend could be partially explained by the increase along the time of adenocarcinoma that is generally more inclined to involve pleura in its metastatic spread. This is entirely our supposition because we have no data about lung cancer subtypes.

The MT contribution to the diagnosis of pleural involvement in tuberculosis is quite suspicious. In contrast to an almost stable Italian incidence of tuberculosis since 1975 with a little temporary increase in 1995 (observed also in our cohort during the third period), we registered a notable decrease until 1999–2003. Then the incidence increased to the original value. We can suppose that the new wave of immigrants from east Europe and Africa could be responsible of this unexpected increase. Indeed, MT is useful, especially for the late diagnosis of tuberculosis, when the pleura is involved in the pathological process. It is realistic that this delay in the diagnosis could occur properly in these subgroups of the population where the sanitary conditions are poor or suboptimal.

Interestingly, less than 2% of all diagnosed diseases did not belong to any groups previously described.

This fact indicates that MT can diagnose a limited number of diseases in which it is demonstrated to be highly specific and sensitive.

Conclusion

To the best of our knowledge, this is the first study that illustrates directly on a large cohort of patients the power of MT in the diagnosis of pleural diseases. We report data of more than 2470 consecutive MTs. No patient selection was performed and no follow-up time was considered. Our cancer frequency (63%) is similar to that one calculated using data presented in the literature.[10] It suggests that the sensitivity in detecting malignancy of our procedure is as high as previously reported.

In this study, the mean cumulative frequency of unspecific pleuritis amounts to 29% and assuming specificity almost complete as largely accepted,[30] we can affirm that our data demonstrate that MTs alone permit to reach a certain diagnosis in more than 70% of the cases analyzed. Interestingly the unspecific pleuritis rate decreases progressively during the observational time from about 43% reaching the frequency of 21%. Surely, this subgroup of patients includes false negative results but even several benign forms such as parapneumonic pleural effusions, or viral pleuritis. Unfortunately, more detailed data about this subgroup are not available because our database included only anatomopathological results excluding subsequent clinical interpretation. In our opinion, this reduction should be determined by more effective specimen collection and anatomopathological examination improvements resulting in a missing diagnosis decreasing (false negative results), rather than a contraction of the benign forms included. In addition to technical skills, we think that our team acquired along the years expertise in patient selection. We approached with MT a progressive lower percentage of bilateral pleural effusion. Moreover, the implementation with chest ultrasonography gave us several advantages in patients' selection and during preoperatory evaluation. For these reasons, we think that the percentage of false negative results included in unspecific pleural inflammation should reduce along the years although we cannot demonstrate this result.

In conclusion, we can affirm that MT has a great diagnostic yield that can be improved by practice, permitting to achieve a specific histological diagnosis in up to 80% of patients. It is adapted to diagnose diseases characterized by a peculiar histological pattern, otherwise, it helps to reach the right clinical diagnosis ruling out several specific diseases with high accuracy (e.g., excluding cancer).

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Nil.

Conflicts of interest

There are no conflicts of interest.

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