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Clinical and Thoracoscopic Predictors of Malignant Pleural Effusion

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ORIGINAL ARTICLE

Clinical and Thoracoscopic Predictors of Malignant Pleural Effusion

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Abstract

Introduction: **The management of malignant pleural effusion (MPE) is still a therapeutic challenge to both the pulmonologist and oncologist with the primary goal being directed towards the improvement of life quality and symptom reduction. The presence of cancerous cells in the fluid or tissue biopsy is typically required to distinguish between MPE and benign pleural effusions (BPE). The value of the clinical, thoracoscopic features to early predicts MPE cases has not yet been established.**

Aim: **This study aimed to assess the clinical and thoracoscopic predictors of MPE to permit rapid management of these patients.**

Patients and methods: **Forty patients who were 18 years of age or older and had an undiagnosed pleural effusion who were scheduled for thoracoscopy at the Chest Department of El-Hussein University Hospital from January 2022 to January 2023 participated in this study.**

Results: **The thoracoscopic findings revealed that the MPE group had a statistically significant increase in the visceral and partial pleural nodules, hyperemia, and thickening compared with the BPE group. Additionally, compared with the BPE group, the MPE group displayed a statistically significant increase in costal pleural nodule, hyperemia, and thickness. The MPE group significantly outperformed the BPE group in terms of hyperemia and confined lungs.**

Conclusion: **The correlation between the clinical, laboratory, radiological, and thoracoscopic criteria of MPE may permit better indication of thoracoscopy in the study of pleural effusion with better and rapid management of these cases.**

Keywords: Malignant pleural effusion, Pleurodesis, Thoracoscope

1. Introduction

One of the main factors contributing to pulmonary morbidity and death is pleural effusion.[1] Malignant pleural effusion (MPE), the second most common cause of exudative pleural effusions, can affect up to 15 % of all cancer patients.[2–4] MPE typically implies a more advanced stage of cancer, with a survival outlook of 3–12 months after diagnosis.[4,5] Therefore, it is essential to make therapeutic options for patients with MPE early on using an accurate and noninvasive method of diagnosis.[5,6] The primary benefit of thoracoscopic biopsy is the ability to perform pleurodesis and evaluate a specimen of the most aberrant pleural surface simultaneously.[7–9] Pleurodesis is typically not performed during a thoracoscopy and should be delayed until histological confirmation.[7–12] This prolonged the care of the chest tube, raised the risk of complications, and extended the length of hospitalization. Since several patients declined thoracoscopic care out of concern for the danger of infection transmission, the length of hospitalization itself has been a problem since the beginning of the COVID epidemic.[13] To permit rapid management of the patients with MPE, our study evaluated the clinical and thoracoscopic predictors of MPE.

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2. Patients and methods

Forty patients aged 18 years or older participated in this study from January 2022 to January 2023. They had an undiagnosed exudative lymphocytic pleural effusion and were scheduled for a medical thoracoscopy at the Chest Department of El-Hussein University Hospital. Patients with a contraindication for medical thoracoscopy were excluded from the study, as those who could not maintain lateral decubitus for at least 30–45 min, patients with an unstable hemodynamic or cardiovascular state, patients with severe uncorrected hypoxemia despite the provision of supplemental oxygen, and patients with coagulation abnormalities. Prothrombin concentration and platelet count should both be at least 60 % and 60 000/mm, respectively.

All of the study participants had undergone written informed permission. The included patients were subjected to revision of the clinical, laboratory and radiological findings. Then, all patients were subjected to medical thoracoscopy with identification and documentation of the pleural macroscopic findings and biopsies for histopathological examination. Finally, the correlation of the clinical, radiographic, thoracoscopic, and histological results in patients with MPE to identify the predictors of MPE.

2.1. Statistical analysis

Data was gathered, coded, and entered into a spreadsheet using Microsoft Excel 2016 for Windows, of Microsoft Corporation, in the United States. The IBM SPSS Statistics for Windows, Version 26.0 (IBM Corp., Armonk, New York, USA), statistical package for social sciences, was used to analyze the data. To confirm the distribution's normality, the Kolmogorov–Smirnov test was used. Data that was continuous was expressed as mean, SD, median, and interquartile range, whereas data that was categorical was expressed as numbers and percentages. The statistical significance thresholds of 0.05 and 0.01 are regarded as low and high, respectively.

3. Results

Figures 1 to 3, Tables 1–4.

Discussion

Regarding the study's presenting symptoms, our findings are consistent with those of Herrera Lara et al.,[13] who found that dyspnea is the most common symptom 70.4 % and commonly occurs in MPE patients 87.1 %. Therefore, of the clinical data and history findings in our study; only advanced age, dyspnea and chest pain can be considered to be suggestive of malignancy. However, in clinical practice, they are nonspecific to malignancy.

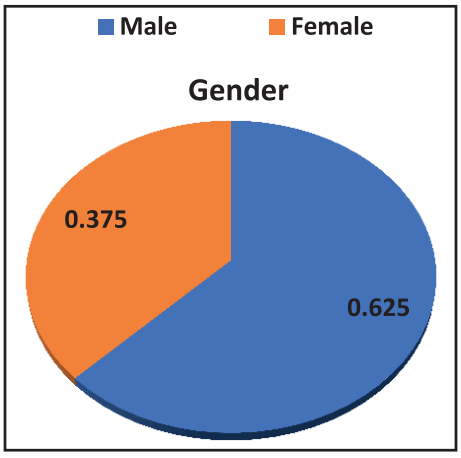

Fig. 1. Sex distribution of studied patients.

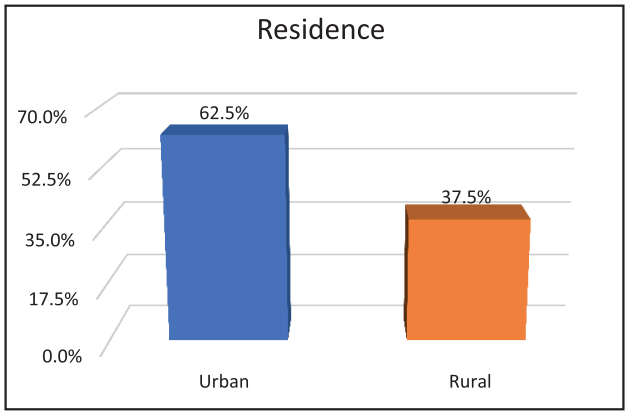

Fig. 2. Residence distribution of studied patients.

The MPE group showed a statistically significant increase in the pleural fluid total leucocytes count mean 381.73 ± 99.34, lymphocytic count mean 85.47 ± 5.08, LDH mean 447.63 ± 47.05 and total protein mean 4.65 ± 0.74 compared with the benign group. The MPE group showed a statistically significant decrease in the pleural fluid ADA mean 13.29 ± 4.23 compared with the benign group mean 26 ± 18.24. Total protein and lactate dehydrogenase (LDH) were significantly different between the MPE and BPE groups in the study by Ellayeh and colleagues mean total protein 39 g/l and SD 8 in the benign group and 45 g/l and SD 8 in the malignant group; unpaired *t* test, mean difference of 6.3, 95 % confidence interval for the difference 3 to 10, $P = 0.001$. The mean LDH in the benign group was 346 IU/l and SD 310 while in the malignant group, it

Fig. 3. Distribution of studied patients regarding pathology results.

Table 1. Comparison between the two groups regarding different clinical variables.

	MPE ($N = 30$)		BPE ($N = 10$)		Test value	P value
	Mean	SD	Mean	SD		
Age	58.50	10.23	50.60	6.88	−2.253	0.024
BMI	29.73	4.43	30.30	3.68	−0.299	0.765
	n (%)		*n* (%)			
Sex						
Male	18 (60)		7 (70)		0.32	0.57
Female	12 (40)		3 (30)			
Smoking						
No	12 (40)		2 (20)		1.31	0.250
Yes	18 (60)		8 (80)			
Residence area of known exposure						
Yes	15 (50)		4 (40)		0.301	0.58
Occupation work of known exposure						
Yes	7 (23.3)		1 (10)		0.83	0.36
Family history of malignancy						
Yes	8 (73.3)		1 (10)		1.19	0.27
Family history of MPE						
Yes	4 (13.3)		1 (10)		0.076	0.78
Past history of malignancy						
Yes	8 (73.3)		1 (10)		1.19	0.27
Cough						
Yes	17 (56.7)		8 (80)		1.74	0.187
Dyspnea						
Yes	30 (100)		7 (70)		9.73	0.002
Chest pain						
Yes	20 (66.7)		3 (30)		4.13	0.042

BPE, benign pleural effusion; MPE, malignant pleural effusion.

was 673 IU/l and SD 1054 ($P = 0.04$).[12] In the study done Herrera Lara and colleagues, although the serohematic aspect predominates in MPE and the amber-like aspect in benign cases, they observed no changes in the pleural fluid's macroscopic aspect. The malignant group's pleural fluid glucose levels were lower than those of the benign group. There was no statistically significant difference between the mean pleural LDH in MPE and BPE, which was 346 ± 108−6270 and 214 ± 90−10 225, respectively.[13]

The radiographic findings in our study demonstrated that only the MPE group's pleural thickening had increased statistically when compared with the BPE group. According to Herrera Lara and colleagues study from 2017, the radiological characteristics of the patients were lung nodules in up to 60 % of MPE patients and lung mass in up to 86.7 % of patients. Only one patient had an unknown histology, whereas the other cases − all of the lung masses and 59.1 % of the lung nodules − had malignant histology and 36.4 % were benign. Pleural thickening outnumbers BPE groups in patients with MPE ($P = 0.031$).[13] Two-thirds of the hemithorax is taken up by effusions, of which more than half are cancerous. Malignant cases are more likely to have mediastinal adenopathies ($P = 0.009$), although both groups' rates of pulmonary atelectasis are roughly identical.[13] However, computed tomography (CT) imaging was able to distinguish between malignant and benign causes of pleura in the study conducted by Grosu et al.[14] Additionally, Kim et al.'s[15] study from 2011 found that the sensitivity and specificity of CT imaging for the diagnosis of MPE were 83.3 and 88.8 %, respectively.

Thoracoscopic findings showed that there was no statistically significant difference in the quantity of effusion between the MPE and BPE groups. The majority of patients in the malignant group in Ellayeh et al.'s[12] study from 2022 had big effusions 62 %, compared with the majority of patients in the benign group 47 %, who had intermediate effusions.

Also, in our thoracoscopic findings; the MPE group considerably outperformed the BPE group in terms of hyperemia and trapped lung. Minimal adhesions were seen in 42.5 % and extensive adhesions in 22.5 % of cases. In the study done by Ellayeh et al.,[12] absent adhesions were seen in 31.4 % of BPE cases and 46.7 % of MPE cases, less than three adhesions were seen in 47.1 % of BPE cases and 35.6 % of MPE cases and adhesions were extensive in 21.6 % of BPE cases and 17.8 % of MPE cases. Absent adhesions and light adhesions were seen in MPE in 14 % of cases in the Bielsa et al.[16] study. The different classification systems for adhesions and the high proportion of mesothelioma cases in our analysis may be the cause of the discrepancy across studies reporting moderate to severe adhesions.

Table 2. Comparison between the two groups regarding laboratory findings.

	MPE ($N = 30$)		BPE ($N = 10$)		Test value	P value
	Mean	SD	Mean	SD		
Blood						
WBCs	9.08	2.88	10.24	3.15	−1.116	0.264
Neutrophil	79.10	6.62	68.55	7.80	−3.274	0.001
Lymphocyte	20.70	6.28	15.90	5.67	−2.000	0.046
Platelet	302.23	82.74	282.70	23.26	−1.484	0.138
ESR	59.37	32.33	76.10	24.94	−1.675	0.094
CRP	30.30	12.20	11.13	5.85	−3.711	0.0002
Total protein (g/dl)	7.36	0.76	7.43	1.15	−0.896	0.370
Pleural fluid						
TLC cells/cmm	381.73	99.34	290.10	38.36	−1.156	0.009
Neutrophils%	14.53	5.08	13.50	3.37	−0.383	0.702
Lymphocytes%	85.47	5.08	80.90	5.11	−0.228	0.028
LDH (IU/l)	447.63	47.05	350.40	94.77	−1.437	0.001
Total protein (g/dl)	4.65	0.74	3.76	0.73	−3.005	0.003
ADA (IU/l)	13.29	4.23	26.00	18.24	−2.853	0.004

BPE, benign pleural effusion; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; LDH, lactate dehydrogenase; MPE, malignant pleural effusion; TLC, total leukocyte count; WBC, white blood cell.

Table 3. Comparison between the two groups regarding the radiological findings.

	MPE ($N = 30$)	BPE ($N = 10$)	Test value	P value
	n (%)	n (%)		
Right side of pleural effusion				
Yes	20 (66.7)	7 (70)	0.89	0.35
Left side of pleural effusion				
Yes	10 (43.3)	3 (30)	0.56	0.46
Pleural thickening				
Yes	18 (60)	1 (10)	7.51	0.006
Thickening >1 cm				
Yes	8 (26.7)	1 (10)	1.19	0.27
Mediastinal pleural thickening				
Yes	4 (13.3)	0	0.076	0.78
Circumferential thickening				
Yes	3 (10)	0	0	1
Pleural nodularity				
Yes	4 (13.3)	0	0.76	0.78
Mediastinal lymphatic enlargement				
Yes	2 (6.7)	1 (10)	0.12	0.73
Pulmonary consolidation/infiltration				
Yes	8 (26.7)	2 (20)	1.48	0.22
Pulmonary mass or nodules				
Yes	3 (10)	0	0	1
Collapsed lung				
Yes	7 (23.3)	0	0.83	0.36

BPE, benign pleural effusion; MPE, malignant pleural effusion.

According to our study, our study showed that visceral pleural nodules, pleural lymphatic enlargement, and hyperemia were seen in half patients and pleural thickening in 60%of cases. Costal pleural nodules were seen in 77.5 % of cases, hyperemia was seen in 67.5 % of cases, and pleural thickening in 70 % of cases. A diaphragmatic pleural nodule was seen in 30 % of cases, hyperemia was seen in 27.5 % of cases, and pleural thickening in 40 % of cases. The visceral pleural nodules, pleural lymphangitis, hyperemia, and pleural thickening were statistically significantly higher in the MPE group compared to the BPE group. Also, the MPE group had statistically increased costal, hyperemia, and pleural thickening.

In both the benign and malignant groups, the costal pleura was the surface that was most affected by nodules, inflammation, and/or lymphangitis, which was similar to a prior study in which parietal pleural involvement was observed in 97 % of cases while visceral invasion was found in 58.9 %.[17] Costal pleural involvement may be explained by the fact that there are numerous pathways for tumor spread to the parietal pleura, including direct implantation, the bloodstream, and lymphatics, as these pathways suggest that parietal pleural spread occurs before the other pleural surfaces.[18] Our investigation found nodules in both groups, which is contrary to past studies that claimed nodules were pathognomonic of malignant disease.[19]

Porfyridis et al.,[20] reported that visual assessment during thoracoscopy had a high sensitivity of 100 % but low specificity of 46 %, so it may lead to false positives. Ferrer et al.,[21] showed that the combination of CT chest suggestive of malignancy, 30 days symptomatic period, blood-tinged pleural effusion, and absent fever are the variables that are associated with high prediction of malignancy detection on thoracoscopy.

Our results show that no patients with one or no criteria had MPE. However, the correlation between the clinical, laboratory, radiological and thoracoscopic criteria of MPE may permit a better indication of thoracoscopy in the study of pleural effusion with better and rapid management of these cases. Our study might affect clinical practice. We have discussed the potential differential patterns of

Table 4. Comparison between the two groups in the thoracoscopic findings.

Description	MPE group ($N = 30$)	BPE group ($N = 10$)	Mann–Whitney U test	
	Mean ± SD	Mean ± SD	t value	P value
Amount of effusion (l)	2.94 ± 1.41	2 ± 0.89	0.344	0.731
	n (%)	n (%)	χ^2 test	
			t value	P value
Visceral pleural				
Nodules	18 (60.0)	2 (20.0)	4.80	0.028
Hyperemia	18 (60.0)	2 (20.0)	4.80	0.028
Pleural thickening	21 (70.0)	3 (30.0)	5.0	0.025
Costal pleural				
Nodules	25 (83.3)	6 (60.0)	3.32	0.126
Hyperemia	25 (83.3)	2 (20.0)	13.71	<0.001
Pleural thickening	26 (86.7)	2 (20.0)	15.87	<0.001
Diaphragmatic pleural				
Nodules	16 (53.3)	3 (30.0)	1.637	0.201
Hyperemia	9 (30.0)	2 (20.0)	0.376	0.540
Pleural thickening	14 (46.7)	2 (20.0)	2.22	0.136
Hyperemia				
Yes	28 (93.3)	3 (30.0)	17.25	<0.001
Trapped lung				
Yes	10 (33.3)	0	4.44	0.035
Adhesions				
Minimal	13 (43.3)	4 (40.0)	0.034	0.853
Extensive	6 (20.0)	3 (30.0)	0.430	0.512

BPE, benign pleural effusion; MPE, malignant pleural effusion.
Comparison between groups done by Pearson's χ^2 test and Mann–Whitney U test.
P value less than or equal to 0.05 is considered statistically significant, P value less than or equal to 0.01 is considered high statistically significant.

clinical, laboratory, radiological, and thoracoscopic findings of malignant and BPEs and their significance if collectively correlated to early diagnosis of the MPE cases to perform immediate pleurodesis at the thoracoscopy without needing to wait for the results of the biopsy. Our research has made it possible to pinpoint the primary anomalies that characterize benign and malignant diseases, which may be useful for targeting biopsies. To develop criteria from this correlation, further research must be done over a longer duration and with a bigger patient population. Another drawback is that the lesion's size and nodules sizes could not be reliably accurately evaluated from a macroscopic perspective. Additionally, this study have a larger percentage of mesothelioma patients than previous comparable studies; we attribute this to the location of the patients who were included in the study. As a result, including additional patients with a wider range of residences may improve the results.

Conclusion

The correlation between the clinical, laboratory, radiological, and thoracoscopic criteria of MPE may permit better indication of thoracoscopy in the study of pleural effusion with better and rapid management of these cases.

Conflicts of interest

Nothing to declare.

References

1. Krishna R, Antoine MH, Rudrappa M. Pleural effusion. StatPearls Treasure, Island (FL): 2884(6)2-52.
2. Skok K, Hladnik G, Grm A, et al. Malignant pleural effusion and its current management: a review. *Medicina (Kaunas)*. 2019 Aug 15;55(8):490.
3. Arora RD, Boster J. Malignant pleural effusion. In: *StatPearls*. 2023 Feb 26. Treasure Island (FL): 34662-055.
4. Wu A, Liang Z, Yuan S, et al. Development and validation of a scoring system for early diagnosis of malignant pleural effusion based on a nomogram. *Front Oncol*. 2021 Dec 7;11: 775079.
5. Psallidas I, Kanellakis NI, Gerry S, et al. Development and validation of response markers to predict survival and pleurodesis success in patients with malignant pleural effusion (PROMISE): a multicohort analysis. *Lancet Oncol*. 2018 Jul; 19(7):930–939.
6. Jany B, Welte T. Pleural effusion in adults-etiology, diagnosis, and treatment. *Dtsch Arztebl Int*. 2019 May 24;116(21):377–386.
7. Ali M, Surani S. Pleurodesis. 2022 Jul 25. In: *StatPearls*. Treasure Island (FL): StatPearls Publishing; 2023 Jan. PMID: 32809520.
8. Feller-Kopman D, Light R. Pleural disease. *N Engl J Med*. 2018 May 3;378(18):1754.
9. Akl Y, Kaddah S, Abdelhafeez A, et al. Epidemiology of mesothelioma in Egypt. A ten-year (1998–2007) multicentre study. *Arch Med Sci*. 2010 Dec;6(6):926–931.
10. Beer TW, Shepherd P, Pullinger NC. Immunostaining is related to prognosis in malignant mesothelioma. *Histopathology*. 2001 Jun;38(6):535–541.
11. Vogelzang NJ, Rusthoven JJ, Symanowski J, et al. Phase III study of pemetrexed in combination with cisplatin versus

cisplatin alone in patients with malignant pleural mesothelioma. *J Clin Oncol*. 2003 Jul 15;21(14):2636–2644. Corrected and republished in: J Clin Oncol. 2023 Apr 20;41(12): 2125–2133.
12. Ellayeh M, Bedawi E, Banka R, et al. Objective thoracoscopic criteria in differentiation between benign and malignant pleural effusions. *Respiration*. 2022;101(1):46–56.
13. Herrera Lara S, Fernández-Fabrellas E, Juan Samper G, et al. Predicting malignant and paramalignant pleural effusions by combining clinical, radiological and pleural fluid analytical parameters. *Lung*. 2017 Oct;195(5):653–660.
14. Grosu HB, Kern R, Maldonado F, et al. Predicting malignant pleural effusion during diagnostic pleuroscopy with biopsy: a prospective multicentre study. *Respirology*. 2022 May;27(5): 350–356.
15. Kim BS, Kim IJ, Kim SJ, et al. Predictive value of F-18 FDG PET/CT for malignant pleural effusion in non-small cell lung cancer patients. *Onkologie*. 2011;34(6):298–303.
16. Bielsa S, Martín-Juan J, Porcel JM, et al. Diagnostic and prognostic implications of pleural adhesions in malignant effusions. *J Thorac Oncol*. 2008 Nov;3(11):1251–1256.
17. Wu YB, Xu LL, Wang XJ, et al. Diagnostic value of medical thoracoscopy in malignant pleural effusion. *BMC Pulm Med*. 2017 Aug 4;17(1):109.
18. Greillier L, Astoul P. Mesothelioma and asbestos-related pleural diseases. *Respiration*. 2008;76(1):1–15.
19. Boutin C, Cargnino P, Viallat JR. Thoracoscopy in the early diagnosis of malignant pleural effusions. *Endoscopy*. 1980 Jul; 12(4):155–160.
20. Porfyridis I, Georgiadis G, Michael M, et al. Rapid on-site evaluation with the Hemacolor rapid staining method of medical thoracoscopy biopsy specimens for the management of pleural disease. *Respirology*. 2016, 27-080382.
21. Ferrer J, Roldán J, Teixidor J, et al. Predictors of pleural malignancy in patients with pleural effusion undergoing thoracoscopy. *Chest*. 2005 Mar;127(3):1017–1022.