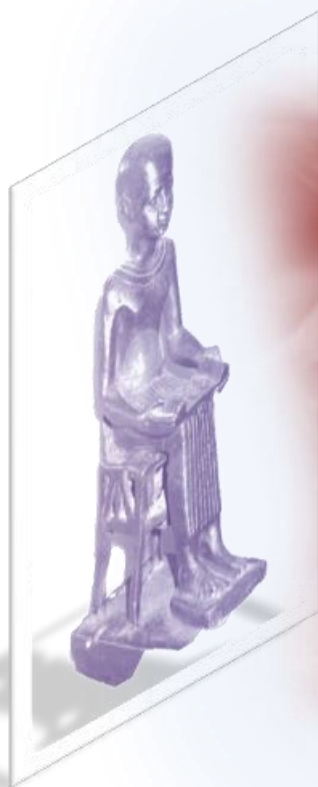


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Original Article

Transthoracic Ultrasonography for Evaluating Diaphragmatic Function in Patients with Non-expandable Lungs

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Abstract

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Background: Non-expandable lungs [NEL] are categorized into lung entrapment and trapped lungs, with distinct pathophysiologies. Patients with NEL are diagnosed by pleural manometry. Diaphragmatic dysfunction, often underdiagnosed due to non-specific presentation, can arise from various conditions. Diaphragmatic ultrasonography has evolved into an essential tool for assessing diaphragmatic function.

Aim of the study: The study aimed to evaluate diaphragmatic function/ mobility using pulmonary ultrasound in NELs.

Patients and methods: Eighty-four patients with pleural effusion underwent transthoracic ultrasound. The M mode was used to evaluate lung motion, calculate the ventilation pulse index, and assess diaphragmatic copula motion during tidal and maximal breathing, leading to the calculation of the diaphragmatic excursion index. The B mode examined pleural fluid and thickness. Patients were classified into NEL [N=39] and Expanded lung groups [N=45].

Results: Lung motion during respiration and heartbeats were significantly reduced in NELs, showing high diagnostic accuracy [76.2% and 73.8%]. Both parameters had greater negative predictive values, indicating better exclusion of NELs. Ultrasound effectively assessed ipsilateral copula motion with maximal breathing [Sensitivity: 69.2%, Specificity: 75.6%, PPV: 71.1%, NPV: 73.9%] and the diaphragmatic excursion index [Sensitivity: 46.2%, Specificity: 71.1%, PPV: 58.1%, NPV: 60.4%].

Conclusion: Transthoracic ultrasonography is a reliable, non-invasive tool that is more effective at excluding rather than diagnosing NELs. Diaphragmatic ultrasound offers advantages such as non-invasiveness, no radiation, widespread availability, accuracy, and repeatability at the bedside.

Keywords: Pleural Effusion; Non-expanded Lung; Diaphragmatic Ultrasound.



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INTRODUCTION

Patients with non-expandable lung [NEL] are often subjected to unnecessary interventions, such as thoracentesis, which can lead to complications like pneumothorax and significant discomfort, commonly presenting as chest pain [1]. Identifying chronic pathological processes and the possible progression to NEL early can prevent such adverse outcomes [2]. Contemporary diagnostic techniques, including pleural manometry and ultrasonography, play a crucial role in clinical practice to achieve this goal [3]. Particularly, NEL is prevalent in patients with malignant pleural effusion, where its presence might substantially influence therapy alternatives and patient prognosis [4]. Recognizing NEL is clinically significant as pleurodesis, a prevalent intervention for malignant pleural effusion, is contraindicated in the presence of NEL [5]. Ultrasonography, therefore, can be an effective tool to identify NEL before performing thoracentesis in these patients, potentially guiding better clinical decisions and improving patient care [6].

The diaphragm is the primary muscle engaged in respiration, functioning incessantly to facilitate the mechanics of breathing [7]. Diaphragmatic malfunction can arise from a variety of pathological conditions, yet it is frequently underdiagnosed in clinical practice due to its non-specific and often subtle presentation [8]. Despite the availability of multiple approaches for assessing diaphragmatic function, accurately diagnosing diaphragmatic dysfunction remains a challenge [9]. In recent years, diaphragmatic ultrasonography has emerged as a key diagnostic tool due to its numerous benefits. It represents a non-invasive method that does not subject patients to radiation, is broadly available, yields rapid findings, and offers precise evaluations [10]. Moreover, its ability to be used repeatedly at the bedside makes it an ideal method for continuous monitoring of diaphragmatic function [11].

This study aimed to evaluate diaphragmatic function/ mobility using pulmonary ultrasound in NELs.

PATIENTS AND METHODS

Study Design: This was a cross-sectional study.

Study Setting: Eighty-four patients diagnosed with pleural effusion using chest ultrasound [whether empyema or malignant effusion, as long as diagnosed with NEL] were recruited from inpatient and outpatient departments of Ain Shams hospitals.

Duration of the study: Twelve months

Inclusion Criteria: Patients eligible for the study were those above 18 years old with a validated diagnosis of moderate to massive pleural effusion by CT chest scan who agreed to participate in the study.

Exclusion Criteria: Patients having a minimal amount of pleural effusion, pregnant females, and those who declined to participate were excluded.

Data Collection: A comprehensive history was taken from all participants, including information on age, comorbidities, occupational exposure, smoking history [smoking index], duration of illness, dyspnea severity, chest pain, previous pleural fluid aspiration, and recurrence of the condition. A CT scan with

radiologic assessment was conducted to determine the side of pleural effusion, type [free or loculated], volume of the affected hemithorax, visceral and parietal pleural thickening, and any underlying lung pathology. Transthoracic ultrasonography was performed to assess diaphragmatic function [movement and excursion], pleural effusion characteristics [free or loculated], pleural effusion volume, and the presence of visceral and parietal pleural thickening, as well as any underlying collapsed lung.

Procedure: Transthoracic ultrasound examinations of the ipsilateral hemithorax were performed. Patients were assessed either in an upright sitting posture or a lateral decubitus position. All chest ultrasonographic scans were conducted by a well-trained pulmonologist.

Diaphragmatic ultrasound methodology:

For diaphragmatic excursion: Examination was done using a 3.5C [bandwidth 2–5MHz] convex phased array probe [with lower frequency and greater depth], in B mode. While patient lying supine, ultrasound probe was put at anterior axillary line, right subcostal and is directed medially, cephalic and dorsally using the liver as acoustic window for better visualization of the diaphragm [Figure 1]. The patient asked to take a deep inspiration followed by a deep expiration to measure diaphragmatic excursion during forced respiration which corresponds to diaphragmatic excursion during patients' exercise [Figure 2].

For diaphragmatic thickness An M12L linear array probe [bandwidth 5–13MHz] was put at right anterior axillary line at 7th or 8th intercostal space, obtaining an image showing liver and lung and a zone of apposition between them using B mode. Both pleural lining and peritoneal lining appeared clearly as two approximately parallel echogenic lines. The space between them resembling diaphragmatic thickness was measured during inspiration. Diaphragmatic thickness corresponds with muscle endurance.

Pleural manometry was performed during therapeutic pleural fluid drainage by inserting a catheter into the pleural effusion. The insertion site was used as the zero-reference point for pressure measurements on the water column. Intrapleural pressure was continuously monitored throughout the drainage process to observe pressure changes as fluid was removed from the pleural space. This monitoring helped assess the lung's ability to re-expand and distinguish between normal lung expansion, partial expansion due to lung entrapment, or failure to expand in cases of a trapped lung.

Ethical Considerations: All participants were adequately informed about the study protocol and signed informed consent.

RESULTS

Eighty-four patients with pleural effusion were recruited from both inpatient and outpatient departments of Ain Shams hospitals, comprising 68 males and 16 females [Table 1]. Depending on pulmonary ultrasound findings [Table 2], we categorized the patients into the NEL [39 patients, 46.4%] and Expanded Lung groups [45 patients, 53.6%].

The results showcased highly significant differences between both groups in terms of the type of pleural fluid, volume of the hemithorax, visceral and parietal pleura thickening, and underlying lung pathology [Table 3]. Pulmonary ultrasound assessments

showed significant differences between the groups concerning the excursion index and parietal pleural thickening [measured in mm]. Additionally, there were highly statistically significant differences regarding lung motion during respiration [mm], lung motion during heartbeats [mm], ipsilateral copula motion during tidal breathing [mm], and ipsilateral copula motion during maximal breathing [mm]. Differences were also observed in visceral pleura thickening, pleural effusion type, and intercostal space width [Table 4].

Herein, we deployed receiver-operating characteristic [ROC] curves to ascertain M-mode ultrasonography diagnostic performance in assessing lung motion with respiration and ipsilateral copula motion during maximal breathing for identifying NELs. The sensitivity and specificity for lung motion with respiration were 97.4% and 57.8%, respectively, while for ipsilateral copula motion during maximal breathing, they were 69.2% and 75.6%, respectively [Figures 3-4]. Furthermore, the excursion index of the diaphragm demonstrated diagnostic value for identifying NELs, with an overall accuracy of 59.5% [Figure 5].

Table [1]: Socio-demographic data and smoking among patients.

		Min.	Max.	Mean	SD
Age		22.00	79.00	60.01	15.95
Smoking		0.0	40.0	15.45	1378
		N		%	
Sex	Male	68		81.0%	
	Female	16		19.0%	

Table [2]: Nonexpanding lung.

		N	%
Nonexpanding lung	Yes	39	46.4%
	No	45	53.6%

Table [3]. Comparison between expanding and non-expanding lungs regarding CT chest

		Nonexpanding lung				X ^{2*}	P value
		Yes [N=39]		No [N=45]			
		N	%	N	%		
Type	Free	19	48.7%	45	100.0%	30.29	<0.001 HS
	Loculated	20	51.3%	0	0.0%		
Side	Right	22	56.4%	28	62.2%	0.29	0.59 NS
	Left	17	43.6%	17	37.8%		
Amount	Mild	11	28.2%	14	31.1%	0.19 FE	0.95 NS
	Moderate	24	61.5%	26	57.8%		
	Massive	4	10.3%	5	11.1%		
Volume of hemithorax	Normal	22	56.4%	40	88.9%	19.96 FE	<0.001 HS
	Increased	4	10.3%	5	11.1%		
	Reduced	13	33.3%	0	0.0%		
Visceral pl. thickening	No	26	66.7%	44	97.8%	14.56	<0.001 HS
	Yes	13	33.3%	1	2.2%		
Parietal pl. thickening	No	23	59.0%	42	93.3%	14.09	<0.001 HS
	Yes	16	41.0%	3	6.7%		
Underlying lung pathology	Collapsed	18	46.2%	43	95.6%	29.85 FE	<0.001 HS
	Consolidated	13	33.3%	2	4.4%		
	Lung nodule	8	20.5%	0	0.0%		

*Chi-square test [FE: Fisher Exact]

Table [4]: Comparison between expanding and non-expanding lungs regarding Transthoracic Ultrasonography.

		Nonexpanding lung				t*	P value
		Yes [N=39]		No [N=45]			
		Mean	SD	Mean	SD		
Lung motion with respiration [mm]		7.21	2.20	9.56	2.67	4.35	<0.001 HS
Lung motion with heartbeats [mm]		2.63	0.97	4.19	1.95	4.74	<0.001 HS
Ventilation pulse index		1.95	0.97	1.46	.77	2.62	0.01 HS
Ipsilateral copula Motion with tidal breathing [mm]		8.00	3.26	14.02	4.94	6.49	<0.001 HS
Ipsilateral copula Motion with maximal breathing [mm]		22.17	13.48	30.11	8.71	3.15	0.002 HS
Excursion index		1.96	1.76	1.28	.68	2.25	0.03 S
Parietal pl. thickening [mm]		1.88	1.20	1.23	1.24	2.44	0.02 S
Visceral pl. thickening [mm]		2.48	1.30	1.21	.87	5.16	<0.001 HS
		N	%	N	%	X ^{2**}	P value
PE Side	Right	22	56.4%	28	62.2%	0.29	0.59 NS
	Left	17	43.6%	17	37.8%		
PE Amount	Mild	11	28.2%	14	31.1%	0.19 FE	0.95 NS
	Moderate	24	61.5%	26	57.8%		
	Massive	4	10.3%	5	11.1%		
PE Type	Simple anechoic	6	15.4%	39	86.7%	45.55	<0.001 HS
	Complex non septated	16	41.0%	6	13.3%		
	Complex septated	17	43.6%	0	0.0%		
Ipsilateral copula Level at MCL	5 th space	2	5.1%	3	6.7%	5.70 FE	0.18 NS
	6 th space	20	51.3%	27	60.0%		
	7 th space	17	43.6%	11	24.4%		
	8 th space	0	0.0%	3	6.7%		
	9 th space	0	0.0%	1	2.2%		
		0	0.0%	1	2.2%		
ICS Width	Normal	33	84.6%	40	88.9%	11.20 FE	0.001 HS
	Wide	0	0.0%	5	11.1%		
	Narrow	6	15.4%	0	0.0%		

*Student t-test **Chi-square test [FE: Fisher Exact]



Figure [1]: Position of the patient and US probe during diaphragmatic examination



Figure [2]: Diaphragmatic excursion during forced respiration using B mode US

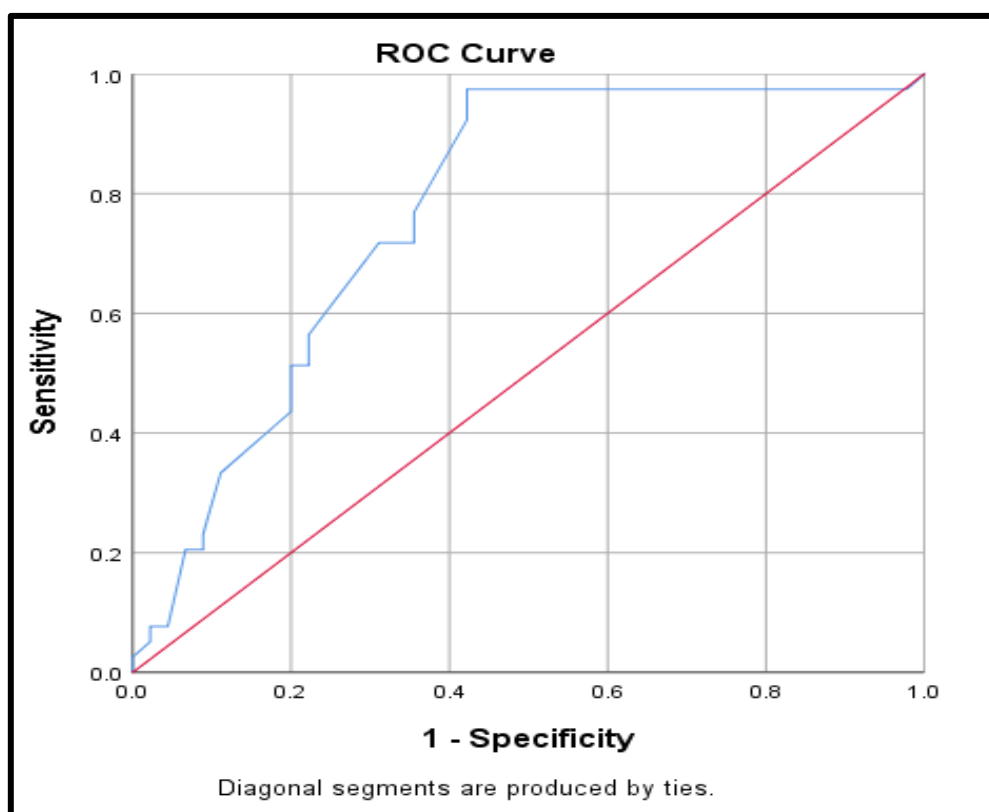


Figure 3. Validity of transthoracic ultrasonography for the diagnosis of non-expanding lung: Lung motion with respiration [mm].

Area	Std. Error	Asymptotic Sig.	Area Under the Curve	
			Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
0.771	0.052	<0.001 HS	0.668	0.873

Best cut off value ≤ 9.55 , Sensitivity = 97.4%, Specificity = 57.8%, Positive predictive value [PPV] = 66.7%, Negative predictive value [NPV] = 96.3%, Accuracy = 76.2 %

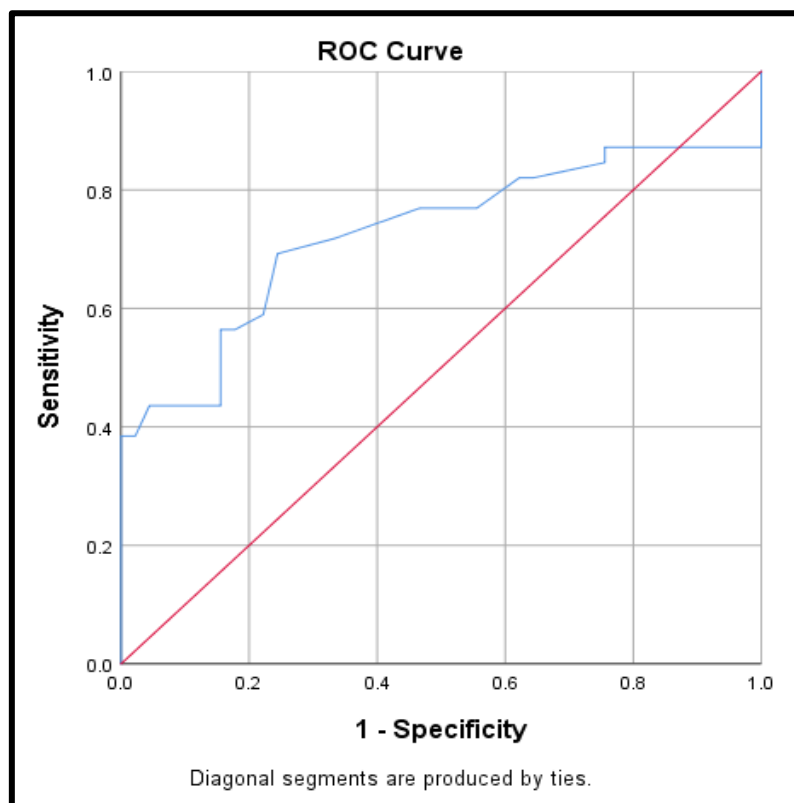


Figure 4. Validity of Ipsilateral copula Motion with maximal breathing [mm].

Area Under the Curve				
Area	Std. Error	Asymptotic Sig.	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
0.726	0.060	< 0.001 HS	0.608	0.843

Best cut off value ≤ 24.50 , Sensitivity = 69.2%, Specificity = 75.6%, PPV = 71.1%, NPV = 73.9%, Accuracy = 72.6%

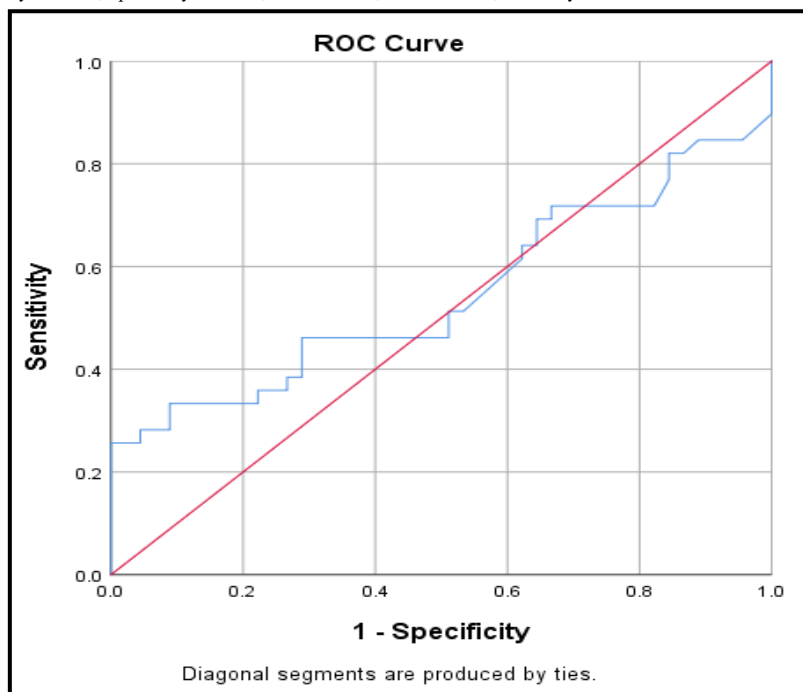


Figure [5]: Validity of diaphragmatic ultrasound regarding excursion index of diaphragm.

Area Under the Curve				
Area	Std. Error	Asymptotic Sig.	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
0.547	0.066	0.462 NS	0.417	0.677

Best cut off value ≥ 1.48 , Sensitivity = 46.2%, Specificity = 71.1%, PPV = 58.1%, NPV = 60.4%, Accuracy = 59.5%

DISCUSSION

The NEL denotes circumstances in which the lung is unable to expand within the thoracic cavity or the adjacent pleural space [13]. Basically, there exist three main aetiologies of NEL: [a] an endobronchial lesion obstructing the bronchial lumen, causing distal lobar collapse; [b] chronic atelectasis; and [c] visceral pleural limitation due to pleural disease, leading to trapped lung [14]. Initially recognized in 1967, a trapped lung is defined by the existence of a constricting visceral pleura that arises when a mature fibrous strip encircles the visceral pleura, consequently limiting lung expansion, frequently due to inflammatory processes [15].

Pleural inflammation is commonly caused by pneumonia and hemothorax, although other recognized causes include pneumothorax, thoracic surgery, uremia, and autoimmune disorders, including rheumatoid pleuritis [16].

In clinical practice, patients who have trapped lungs often exhibit chronic pleural effusion. Repeated thoracenteses conducted without subsequent lung re-expansion may result in negative consequences [17].

Upright and decubitus radiographs, together with chest computed tomography [CT], generally demonstrate pleural thickening and loculations [18].

Pleural fluid may demonstrate displacement with changes in posture, but it will not be freely flowing [19].

The paradoxical finding that the hemithorax with pleural effusion seems reduced in size compared to the opposite side suggests markedly increased negative pleural pressure on the affected side, hence reinforcing the diagnosis of trapped lung [5]. Post-thoracentesis radiographs may reveal air in the pleural space, reflecting the dimensions and contour of the previous effusion [20].

In this study, chest CT was employed and demonstrated high sensitivity for identifying NEL through markers such as visceral pleural thickening, parietal pleural thickening, and underlying lung pathology. The diaphragm serves as the primary muscle of respiration, contributing approximately 75% to lung volume increase during quiet respiration, with mean excursions of 1.5 cm on the right and 1.58 cm on the left. During forced breathing, diaphragmatic excursion reaches means of 5.6 cm and 6.6 cm, respectively, varying with gender and body composition. Ultrasound has emerged as the preferred modality for assessing diaphragmatic mobility, replacing fluoroscopy.

Unlike fluoroscopy, ultrasound avoids ionizing radiation and facilitates bedside evaluation of diaphragmatic function, allowing for direct quantification of diaphragmatic movement [21,22]. Given that diaphragmatic motion is essential for spontaneous respiration, monitoring diaphragm kinetics is critical [23].

The utilization of existing diagnostic instruments for this objective is frequently constrained by the hazards linked to ionizing radiation [e.g., fluoroscopy and CT] or by their intricacy, which requires a proficient operator [as demonstrated in trans-diaphragmatic pressure measurement, diaphragmatic electromyography, phrenic nerve stimulation, and magnetic resonance imaging] [24,25].

It is important to note that pleurodesis is contraindicated for malignant pleural effusion in the presence of NEL [26].

Ultrasound can assist in identifying NEL before thoracentesis in individuals with malignant pleural effusion [27]. Moreover, diaphragmatic dysfunction can result from multiple medical diseases and is frequently underdiagnosed in clinical contexts due to its non-specific manifestation [8,28].

This study elucidated highly significant differences between both groups regarding pleural fluid type, hemithorax volume, visceral and parietal pleura thickening, and underlying lung pathology.

Our pulmonary ultrasound assessment revealed significant differences between both groups concerning the excursion index and parietal pleural thickening [measured in mm]. Furthermore, highly significant differences were noted regarding lung motion with respiration [mm], lung motion with heartbeats [mm], ipsilateral copula motion during tidal breathing [mm], and ipsilateral copula motion during maximal breathing [mm]. Additionally, significant differences were observed in visceral pleura thickening, pleural effusion type, and the width of intercostal spaces. While a lot of studies have focused on various aspects of the topic or subject area, none of them deal with this particular research idea.

Conclusions:

Diaphragmatic movement is vital for spontaneous respiration, rendering the observation of diaphragm kinetics indispensable. The application of existing diagnostic tools for this purpose is frequently constrained by the risks linked to ionizing radiation from CT and fluoroscopy, in addition to the intricacies of other methods necessitating proficient operators, such as trans-diaphragmatic pressure measurement, phrenic nerve stimulation, diaphragmatic electromyography, and magnetic resonance imaging. Diaphragmatic dysfunction may result from NEL and is frequently underdiagnosed in clinical practice due to its non-specific presentation. Ultrasonography offers a valuable approach to detecting NEL before thoracentesis in patients with malignant pleural effusion, potentially preventing the failure of pleurodesis procedures.

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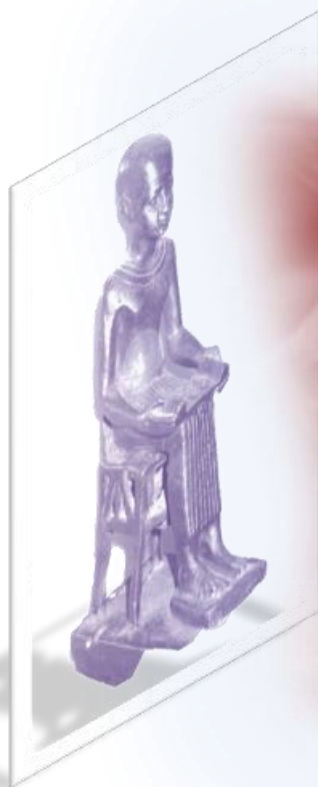
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