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Use of chest ultrasonography to compare two methods of pleurodesis (autologous blood versus doxycycline)

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Abstract

Introduction: It has been proven that pleurodesis with sclerosing agents is an efficient palliative technique for MPE. Ultrasound is a simple, affordable, and accurate way to determine whether pleurodesis is effective by utilizing the pleural sliding sign. That depicts the movement of the parietal pleura in relation to the visceral pleura.

Aim of the study: To compare two pleurodesis techniques, autologous blood versus doxycycline, using chest ultrasonography.

Subjects and methods: Thirty patients with malignant pleural effusion were included in that study. Fifteen patients underwent pleurodesis by ABP, where the other fifteen had doxycycline through a chest tube. All patients underwent thorough clinical assessment, full medical history review, chest computed tomography, thoracentesis, pleural biopsy, doxycycline or autologous venous blood pleurodesis, and chest ultrasounds (US). All investigations were performed before and after the procedure.

Results: In the current study, 14 (93.3%) out of 15 patients in the autologous venous blood group had successful pleurodesis, while 13 (86.7%) out of 15 patients in the doxycycline group had successful pleurodesis. US score before pleurodesis in successful cases was 6.89 ± 1.05 , while in failed was 7.67 ± 0.58 . The mean US score after pleurodesis in successful cases was 2.37 ± 1.47 , while in failed cases was 5.67 ± 0.58 , with a significant statistical difference between the two groups ($P < 0.05$).

Conclusion: For the easy and precise detection of successful pleurodesis and follow-up, use ultrasound.

Keywords: Pleurodesis; MPE; autologous blood; doxycycline; chest ultrasound.

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1. Introduction

Pleurodesis is the application of substance into the pleura to cause adherence to parietal and visceral pleura and obliteration of the potential space between them. This is mostly indicated for MPE or recurrent pneumothorax [1].

Unless the patient has a trapped lung or a short life expectancy pleurodesis is a better option for recurrent malignant pleural effusion, than thoracentesis [2, 3]. By using chest ultrasound, it is possible to find

pleural fluid, as little as 50 ml and confirm

2. Subjects and methods

2.1. Subjects

The current prospective randomized comparative study was performed in the chest department, faculty of medicine, Fayoum University, between January 2019 and September 2020. The study recruited 30 patients with malignant pleural effusion. Half of patients were subjected to ABP pleurodesis, and the rest were subjected to doxycycline pleurodesis through a chest tube.

2.2. Methods:

All participants were subjected to the following investigations:

Reporting of the full medical history

With focusing on the previous malignancy issues (primary site, history of chemo or radiotherapy), radiological examinations, and pleural fluid aspiration for chemical and cytological analysis.

Chest US

US machine Philips HD11XE US machine (Philips, Amsterdam, Netherlands) was used to assess the pleural fluid at all anatomical areas before and after pleurodesis.

Before pleurodesis

The convex transducers were utilized during the examination to scan the whole chest. Perpendicular to the intercostal space, the transducer was positioned. The front chest wall was separated into upper and lower portions and defined from the sternum to the anterior axillary line (approximately

that the pleural surfaces are adherent [4, 5].

from the clavicle to the second-third intercostal spaces and from the third space to the diaphragm). The anterior-to-posterior axillary line served as the boundary between the upper and lower sections of the lateral zone [6]. An echo-free area between the parietal and visceral pleura was the US hallmark of pleural fluid. Chest US focused on the detection of pleural effusion to categorize the various sonographic patterns and predicts whether they were exudates or transudates [7]. The following categories were used to categorize pleural effusions based on their appearance:

- Anechoic pattern (echo-free spaces).
- Complex non-septated pattern.
- Complex septated pattern.
- Homogenously echogenic pattern.

US was used to distinguish between encysted and free effusion. It was used to look for pleural thickening or malignancies and for tumor invasion into the pleura and chest wall, as well. After that, biopsies were taken by different modalities included medical thoracoscopy, sonar guided biopsy, EUBS, and bronchoscopy. Afterward, pleurodesis was performed either by autologous venous blood (1ml/kg maximum 100 mg) or doxycycline (1mg/kg maximum 600 mg). In all cases, a second chest X-ray was taken during the following 24 hours, and the chest tube was removed once the patient's lungs had totally re-expanded and the drainage level had dropped to 150 ml.

After pleurodesis

There were eight distinct sections on the chest wall:

Back: suprascapular, interscapular, and intrascapular.

Anteriorly: supra-mammary, mammary, and inframammary.

Laterally: upper and lower axillary areas.

The investigator identified the breath-related movement of the pleura, or so-called sliding sign, at each stage of the examination [8]. Each area received a score based on the presence of the lung sliding sign (1) or absence (0). If the patient's score was less than the cutoff value of 5, then pleurodesis was successful. The pleural thickness brought on by the pleurodesis's union of the parietal and visceral pleura.

Thirty days following the procedure, the effectiveness of Pleurodesis was evaluated [9] by:

1. Complete response: no pleural effusion was found.
2. Parietal response: after pleurodesis, minimal pleural fluid was observed

3. Results

In the study, pleurodesis was done by autologous venous blood in fifteen cases and by doxycycline in fifteen cases. The mean age of the autologous venous blood (AVB) group was (61.60 ± 14.08) , and the mean age of the doxycycline (D) group was (60.87 ± 12.52) .

Regarding the demographic characteristics of the study population, it was shown that six males and nine females

without the need to repeat thoracentesis or drainage.

3. No response: after pleurodesis, a large amount of effusion was observed or there was a need for repeated thoracentesis or pleurodesis.

Complete and parietal responses were determined by how well the pleurodesis performed when assessed by radiography and chest ultrasound at 48 hours, 15 days, and 30 days after the procedure.

2.3. Statistical methods

The statistical package for the social sciences (SPSS) version 26 was used to enter coded data (IBM Corp., Armonk, NY, USA). Quantitative data were summarized using mean, standard deviation, median, minimum, and maximum; categorical data were summarized using frequency (count) and relative frequency (%). The non-parametric Mann-Whitney test was used to compare numerical variables [10].

receive AVB for pleurodesis. Nine of them were housewives, four farmers, one worker, and one employee. Three from Tamia, three from Senores, three from Etsa, two from Fayoum, two from Yousef El Sadik, and two from Abshway. regarding the medical history, four smokers, six with a history of breeding birds and biomass exposure, two with a history of breeding birds only, and

three with no special habitus of medical importance.

In the D group, there were four males and eleven females. Nine were housewives, three farmers, one seller, and two employees. Four from senores, one from Etsa, six from Fayoum, three from Yousef El Sadik, and one from Abshway. Four with a history of smoking, six with a history of breeding birds and biomass exposure, three with a history of breeding birds only, and two with no special habitus of medical importance.

There was no difference in statistically significant between the two groups regarding sex, resident, occupation and special habitus. The most common site

as primary site of malignant pleural effusion was the lung in 12 cases followed by the breast in nine, pleura in four, and others were the colon, renal oncocytoma, and myeloma.

In the chest US findings in the AVB group, free fluid was found in 33.3%, nodules on the parietal pleura in 40%, nodules on the diaphragmatic pleura in 20%, and nodules on the parietal pleura with hypercellular fluid in 6.7%. In the D group, free fluid was found in 33.3%, nodules on parietal pleura in 20%, nodules in diaphragmatic pleura in 6.7%, nodules on parietal pleura with bulky lung in 6.7%, bulky lung in 26.7% and nodules on visceral and parietal pleura in 6.7% (Table 1).

Table 1: Description of the chest us findings of the study population.

Chest US (n=30)	AVB group (n=15)	D group (n=15)	P-value
Bulky lung	0 (0.0%)	4 (26.7%)	0.128
Free fluid	5 (33.3%)	5 (33.3%)	
Nodules on diaphragmatic pleura	3 (20.0%)	1 (6.7%)	
Nodules on parietal pleura	6 (40.0%)	3 (20.0%)	
Nodules on parietal pleura and bulky lung	0 (0.0%)	1 (6.7%)	
Nodules on parietal pleura with hypercellular fluid	1 (6.7%)	0 (0.0%)	
Nodules on visceral and parietal pleura	0 (0.0%)	1 (6.7%)	

Comparing US scores before and after pleurodesis, the mean US scores before pleurodesis in successful cases were 6.89±1.05, while in failed were 7.67±0.58. The mean US score after pleurodesis in successful cases was 2.37±1.47, while in the

failed cases was 5.67±0.58, which was statistically significant ($P=0.001$). The current study showed that 14 (93.3%) and 13 (86.7%) patients had successful pleurodesis in the AVB and D groups, respectively (Table 2).

The main score in the AVB group before pleurodesis was 6.93 ± 0.96 , while the D group was 7 ± 1.13 . After pleurodesis, the

score in the AVB group was 2.53 ± 1.6 , while in the D group was 2.87 ± 1.88 (Figures 1, 2).

Table 2: Description of the chest us findings of the study population.

Chest US score	Succeded	Failed	P-value
Before	6.89 ± 1.05 7 (5-8)	7.67 ± 0.58 8 (7-8)	0.253
After	2.37 ± 1.47 2(0-5)	5.67 ± 0.58 6 (5-6)	0.001*

*Significant at $P < 0.05$.

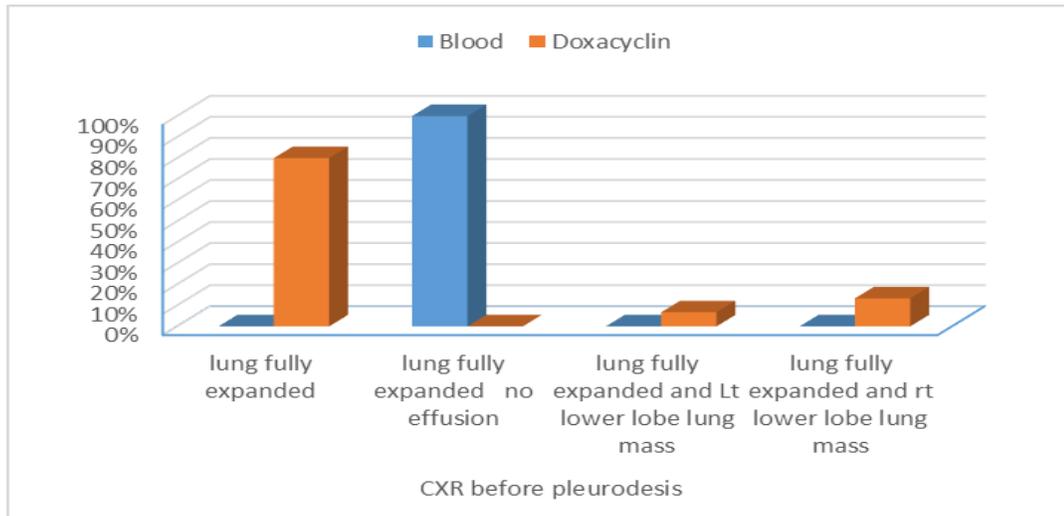


Figure 1: Comparison of AVB and D groups according to CXR findings before (24 h) and 30 days after pleurodesis.

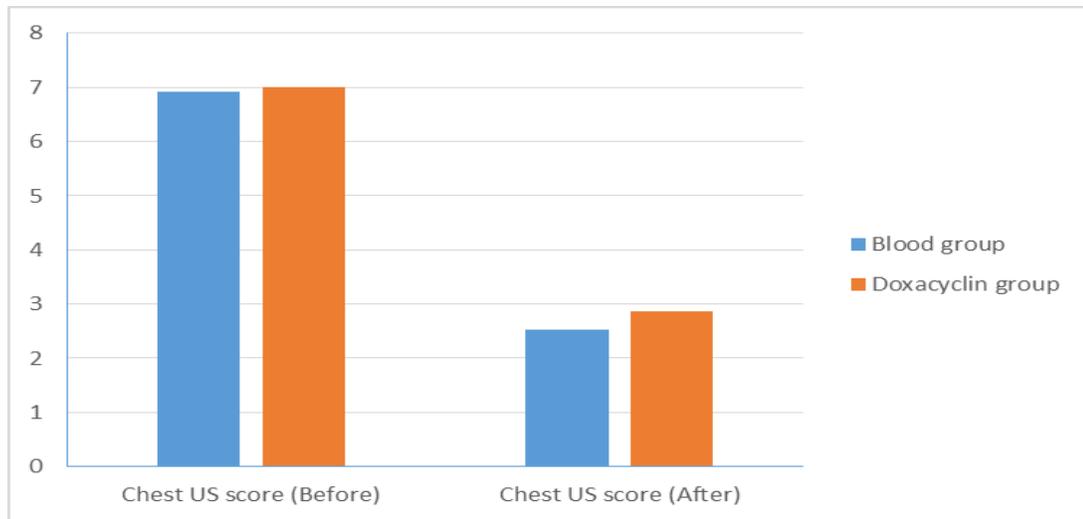


Figure 2: Lung sliding scores of autologous venous bloods versus doxycycline pleurodesis.

4. Discussion

Pleurodesis with sclerosing agents has been established as an effective palliative treatment option for MPE management [11]. The sliding sign is a TUS sign caused by the gliding of the pleural membranes; pleurodesis is expected to abolish this sign [12]. In the present study, we aimed to use chest US to compare two methods of pleurodesis (autologous venous blood versus doxycycline).

In the current study, the mean ages of the AVB and D groups were 61.60 ± 14.08 and 60.87 ± 12.52 years, respectively. The study included 10 (33.3 %) males and 20 (66.6%) females who underwent pleurodesis.

That was consistent with Saleh et al., 2020, who reviewed 104 patients of malignant pleural effusion, who were treated palliatively in their cardiothoracic surgery department at Mansoura University Hospital in 2020, and their mean ages were $57.55 \pm$

9.02 years [13]. El-Kolaly *et al.*, 2016, found that 28 (62.22%) of the 45 patients with recurrent malignant pleural effusion were female, compared to 17 out of 45 patients (37.78%) who were male [14].

The current results of the chest US before pleurodesis showed free fluid in 33.3%, nodules on parietal pleura in 30%, nodules on diaphragmatic pleura in 13.3%, nodules on parietal pleura with hypercellular fluid in 3.3%, nodules on parietal pleura with bulky lung in 3.3%, bulky lung in 13.3%, and nodules on visceral and parietal pleura in 3.3% of patients.

Results in 32 patients who had been referred for pleurodesis and assessed by chest US by Abozaid *et al.*, 2018 were identical to ours. Pleural nodules or masses were present on the costal pleura in 12.5% of patients, the diaphragmatic pleura in 15.6%, and both costal and diaphragmatic pleura in 6.3% of patients [15]. In the study

by El-Hadidy *et al.*, 2017, 28/30 (93.4%) patients had multiple small nodules across their pleura on chest ultrasound, while one patient had a mass with small nodules and another with nodules-free pleura [16].

The primary site of a tumor in our study was; lung 12 (40 %), breast 9 (30 %), pleura 4 (13.3%), colon 3 (10%), renal oncocyoma 1 (3.3%), and multiple myeloma in 1 (3.3%). While Abozaid *et al.*, 2018, found that there were 18.8% of patients with lung cancer, 15.6% with breast cancer, 15.6% with colon cancer, 9.4% with HCC, 6.3% with prostate cancer, 3.1% with uterine cancer, 3.1% with ovarian cancer, 6.3% with bladder cancer, 3.1% with osteosarcoma, 3.1% with lymphoma, and 3.1% with leukemia [15]. According to the study by Ong *et al.*, 2000, there were 19 pleurodesis patients' comorbidities with lung cancer, ten with breast cancer, and nine with other malignancies [17].

The current study demonstrated complete response to pleurodesis in the AVB group in 13 (86.7%), parietal response in 1 (6.7%), and no response in 1 (6.7%) while in the D group in complete response in 12 (80%), parietal response in 2 (13.3%), and no response in 2 (13.3%).

In contrast, Keeratichananont *et al.*, 2015, demonstrated that the pleurodesis efficacy of the AVB group showed a complete response rate of 41.7%, a parietal response rate of 41.7%, and a nonresponse rate of 16.6%. Tetracycline displayed a 37.5% total response rate, a 50% parietal response rate, and a 12.5% nonresponse rate. A complete response was seen in the blood group in 22 (39.2%), a parietal response in

24 (42.8%), and no response in 10 (18%) patients.

According to this study, 13 patients (86.7%) who were in the D group and 14 patients (93.3%) in the AVB group had effective pleurodesis at 30 days. Keeratichananont *et al.*, 2018, compared pleurodesis with talc, where 82% of cases in the ABP group had effective pleurodesis at 30 days (82.0% versus 87.0%). Also, they showed 48 individuals had a one-month overall success rate of pleurodesis of 87.5% in the tetracycline group and 83.4% in the AVB group [18].

Lung sliding scores before pleurodesis were 5 in 10%, 6 in 23.3%, 7 in 26.6%, and 8 in 40% of the studied cases. Lung sliding scores after pleurodesis were 0 in 13.3%, 1 in 10%, 2 in 23.3%, 3 in 23.3%, 4 in 13.3%, 5 in 10%, and 6 in 6.6% of patients.

That was similar to Abozaid *et al.*, 2018, who showed the lung sliding scores before pleurodesis were 6 in 6.3 %, 7 in 12.5 %, and 8 in 81.3 % of patients [15]. The lung sliding score after pleurodesis were 0 in 3.1 %, 1 in 12.5 %, 2 in 18.8 %, 3 in 12.5 %, 4 in 12.5 %, 5 in 12.5 %, 6 in 18.8 %, and 7 in 9.4% of cases. The main US sliding score after successful pleurodesis was (2.37 ± 1.47) while in failed pleurodesis was (5.67 ± 0.58) [15].

After pleurodesis, the US lung sliding score was performed to determine whether or not the pleurodesis was successful. A score of fewer than 5 indicates successful pleurodesis. Two patients in the AVB group had lung sliding scores of 5, one

of whom underwent successful pleurodesis while the other failed. Two patients in the D group had lung sliding scores of more than 5, and both had failed pleurodesis.

Abizaid *et al.*, 2018, agreed with our finding as in their study after pleurodesis, US was performed to determine whether or not the procedure was successful using the lung sliding score. If the score was less than 5, the pleurodesis was successful [15].

That was similar to Awad *et al.*, 2018, who conducted their study on 30 patients using chest US to assess successful pleurodesis in malignant pleural effusion [19].

El Hadidy *et al.*, 2017, showed eight patients underwent pleurodesis with doxycycline; of these, five (62.5%) showed

Conclusions

The current study suggests Chest US for the easy and precise detection of successful pleurodesis and follow-up.

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the absence of the sliding sign in follow-up chest ultrasound after 30 days, while three (37.5%) showed persistence of the sliding sign and an increase in the amount of effusion [16]. The intercostal chest tube also induced pleurodesis in eight patients; in the follow-up ultra-sound, seven (87.5%) patients showed an absent sliding sign, and one patient had a positive sliding sign with an increase in the amount of effusion (12.5%) failed pleurodesis which consistent with our study.

That also matches the pilot study by Corcoran *et al.*, 2018, where 18 volunteers were chosen, and at 24 hours after talc instillation, pleurodesis failure participants had a lower pleural adherence score than successful participants (difference of 6.27; 95% CI, 3.94-8.59) [20].

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