Measurement of pleural pressure during therapeutic thoracentesis (pleural manometry) as a safe and objective method in the assessment of pleural effusion effect on symptom expression

Merjenje tlakov plevralnega prostora med razbremenilno punkcijo (plevralna manometrija) kot varna in objektivna metoda pri ocenjevanju vpliva plevralnega izliva na izražanje simptomov

Anita Meglič,1 Katja Adamič,2 Vladimir Dimitrić,2 Vesna Nikolić,2 Aleš Rozman,2 Mateja Marc Malovrh2

Abstract

Background: Patients with pleural effusion often require therapeutic thoracentesis (TT), which results in more or less pronounced dyspnea relief. Due to safety concerns, it is recommended to remove up to a maximum of 1500 mL effusion in one session.

Methods: 96 patients in whom TT was indicated were included in the study. VAS dyspnea score before, immediately after, two hours after TT, and in 73 patients additionally 24 hours after TT was collected. The amount of fluid removed was measured. During TT, water manometer was used to measure pleural pressures, from which pleural space elastance was calculated. Based on their elastance curves characteristics, the patients were divided into different groups.

Results: We found a correlation between initial pleural pressure/volume of effusion removed and dyspnea relief after TT. TT was most often terminated due to the onset of symptoms, in 16 patients it was terminated due to pleural pressure measurement. 74 patients were classified in the group with a normal elastance curve, in 22 patients we detected unexpandable lungs. Although more than 1500 mL of effusion was removed in 32 (33%) patients, there were no important complications during TT.

1 Faculty of Medicine, University of Ljubljana, Ljubljana, Slovenia
2 Interventional Pulmonology Department, University Clinic of Respiratory and Allergic Diseases Golnik, Golnik, Slovenia

Correspondence / Korespondenca: Anita Meglič, e: anitameglic@gmail.com

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Ključne besede: dispneja; vizualna analogna lestvica; elastančne krivulje; nezmožnost razpenjanja pljuč

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1 Introduction

Pleural effusion is the presence of an increased amount of free fluid in the pleural space, which frequently causes shortness of breath (1). Not every pleural effusion causes breathing difficulties, so evaluating which symptoms a pleural effusion causes, if any, is important (2). The mechanisms by which a pleural effusion causes shortness of breath (dyspnoea) are complex and not wholly explained. The displacement and change in the shape of the diaphragm, mechanoreceptors that detect changes in lung volume and susceptibility to irritation caused by excess pleural fluid probably all likely contribute (1,3).

A large pleural effusion is managed by ultrasound (US) guided therapeutic thoracentesis (TT) with which as much fluid as possible is removed for symptomatic relief, obtaining material for further diagnostic analysis and sometimes also to facilitate other necessary invasive tests (4,5). To prevent possible TT complications (chest pain, pneumothorax, re-expansion pulmonary oedema (RPO)), removal of only 1,500 mL of pleural effusion in one session is recommended (7,8). One study showed that removing more than 1,500 mL of fluid resulted in 3.8 times more complications and five times as many cases of pneumothorax than removing smaller amounts of effusion (7). Pleural manometry is a technique used for measuring pleural pressures during TT (9). A simple water manometer or variants of more sophisticated electronic manometers are used (10). The measurements themselves are not time consuming, so TT duration is not significantly extended due to manometry (11). There is currently no consensus on the routine use of pleural manometry during TT (6). During TT, pleural pressure varies from patient to patient depending on the volume of fluid removed (9). Based on this finding, three different elastance curves were developed to help with diagnosing unexpandable lung (9,12). In lungs capable of normal expansion, the removal of pleural fluid causes the initially positive pleural pressure to gradually drop with a calculated pressure drop of less than 14.5 cm H₂O per 1 litre of removed fluid (elastance < 14,5 cm H₂O/L) to normal pleural pressures (from –3 to –5 cm H₂O): we observe a normal elastance curve. In lungs incapable of expansion due to sequelae of previous active inflammatory or malignant disease (the causes for this are different, e.g. atelectasis, thickened visceral pleura, etc.), the elastance curve can initially follow the normal curve and breaks from it at the point where lung expansion cannot follow the removal of pleural fluid. With further removal of fluid, the pleural pressure falls (normally in the negative pressure range): we observe a biphasic elastance curve. In trapped lung, the initial part of the normal elastance curve is missing and pleural pressure drops faster from the onset: we observe a monophasic curve with high elastance (12,13).
The aim of the study was to determine the possible association between initial pleural pressure with the degree of dyspnoea before TT and dyspnoea relief after TT and to see if the dynamics of changing pleural pressure can help with the decision to stop with TT. We further sought to determine whether larger amounts of pleural fluid than otherwise recommended could be safely removed at one time.

2 Methods

The study was conducted at Interventional Pulmonology Department at the University Clinic Golnik and was approved by the National Medical Ethics Committee (approval ns. 206/03/13 and 0120-83/2020/9).

The study included patients who required TT and who were admitted to the Interventional Pulmonology Department during the 18-months study period. Inclusion criteria were a pleural effusion, visible on chest radiography, which required TT, age over 18 years and a signed consent form. Exclusion criteria were an inability to sit during TT, not wishing to take part in the study or an inability to give an adequate estimate of the degree of dyspnoea on a visual analogue scale (VAS). Age, prior TT or other pleural space interventions, underlying disease, pleural effusion cause and size did not affect the inclusion of patients in the study.

All TT with manometry was performed by pulmonologists employed at the Interventional Pulmonology Department according to the standardized TT procedure of the University Clinic Golnik. Before TT, the appropriate site for thoracentesis needle insertion in the lower part of the pleural effusion was determined by ultrasound examination of the hemithorax. A water manometer, normally intended for measuring central venous pressures, was used to measure pleural pressures.

Following insertion in the pleural space, the thoracentesis catheter was connected to a tube with two outlets, allowing for selective closing or opening of both distribution outlets. One outlet was connected via sterile tubing to an infusion system filled with normal saline, connected to a manometer, and the other with a 2,000 mL collecting bag placed in a container on the floor where the pleural fluid drained. The pleural fluid was drained with the help of the hydrostatic pressure difference between the pleural space and the lower collecting bag. The pleural pressure was first measured after removing 20 mL of effusion, followed by measurements after every 100 mL of removed fluid, and finally at the end of TT before the removal of the thoracentesis catheter. We measured the end-expiratory pleural pressure. Prior to TT start, the height of the diaphragm dome was determined and marked in the posterior axillary line with ultrasound, which was considered the reference point for all further measurements. The height of the diaphragm dome was checked with US during TT (for every 200 mL of fluid removed) and at the end. We considered the difference between the dome height marks before and after TT as a diaphragm elevation. Prior to TT, we also instructed patients to report any symptoms that would appear during TT. We ended the procedure when:

- the fluid stopped draining;
- the pleural space pressure fell to –20 cm H₂O or pressure fell for more than 4 cm H₂O between two measurements in a patient with an already negative pleural space pressure;
- symptoms such as persistent chest pain or unrelenting cough appeared;
- for other reasons, as decided by the pulmonologist.

VAS is a 100 mm long horizontal line, marked with «without any breathing difficulties» at one end and «severe breathing difficulties» at the other and is also equipped with appropriate pictures. The patient marks a point on the line that they believe represents their current condition. The VAS value is the distance between the start of the line and the marked spot (14). All included patients were asked to evaluate their level of dyspnoea before, immediately after and two hours after TT. In 73 patients, VAS values were additionally obtained 24 hours after TT (in 23 patients we could not obtain this score as they had already left the hospital on the day of the procedure, and for some, we forgot to record the data). Afterwards, we calculated the VAS changes immediately and two and 24 hours after VAS, depending on the initial VAS value before TT.

Dyspnoea relief greater than 20 mm on VAS was labelled as clinically significant. The 20 mm limit was chosen based on the results of the study by Mishra et al, which found that patients perceived dyspnoea relief of 19 mm and more as clinically significant (15).

The pleural space elastance was calculated by dividing the change in pleural pressure in cm H₂O by the volume of fluid removed in litres. For biphasic curves, the elastances of the first and second parts of the curve were calculated separately. According to the dynamics of changes in pleural pressures during TT, patients were divided into two groups. The first group with a normal elastance curve included patients in whom the pleural pressures changed throughout TT in proportion to the volume of the fluid removed. In these patients, the elastance curve was monophasic and the pleural space...
elastance less than 14.5 H₂O/L at all times. The second group included patients in whom an accelerated decline in pleural pressures (elastance> 14.5 cm H₂O/L in at least two consecutive measurements in the negative range) could be detected during TT with manometry at the beginning or in the second part of TT.

Before and after TT, chest radiography was performed in the posteroanterior and lateral projections. The size of the pleural effusion was determined based on pulmonary opacification.

From the BIRPIS system we obtained data on the general demographic characteristics of the patient (age, sex), assessment of performance status according to the World Health Organization (WHO), the cause of pleural disease (carcinosis, malignant mesothelioma, infection, cardiovascular disease, unspecified effusion), possible pleural effusion treatment before TT and during the one-month period after TT.

GraphPad Prism, version 8.4.3 (GraphPad Software, San Diego, USA) was used for statistical data processing. The Shapiro-Wilk test was used to test the normality of data distribution. To test statistically significant differences between the two groups, we used the t-test for independent samples when the data were normally distributed. In case the data were not normally distributed, we used the Mann-Whitney test. The Spearman correlation coefficient was used to test the intensity of the correlation of the two variables. Data with a calculated value of p <0.05 were considered statistically significant.

3 Results

3.1 Patient characteristics

The study included 96 patients, of whom 68 (70.8%) were men and 28 (29.2%) were women. The mean patient age was 71 ± 1 year. Most of the patients had a good performance status score, 71 (74%) were classified in the first or second functional class, and 25 (26%) in the third class according to the assessment of performance status according to the World Health Organization (WHO).

Depending on the pleural effusion size on the pre-TT chest radiograph, 43 (44.8%) patients had an effusion that was smaller than half of the hemithorax and 53 (55.2%) patients had an effusion that was larger than half of the hemithorax, of whom 12 (12.5%) had an effusion that opacified the entire hemithorax.

The causes of pleural effusion in included patients are shown in Table 1.

### Table 1: Pleural effusion causes in patients, included in the study.

<table>
<thead>
<tr>
<th>Cause</th>
<th>Number of patients</th>
<th>Proportion of patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pleural carcinomatosis</td>
<td>60</td>
<td>62.5</td>
</tr>
<tr>
<td>Pleural mesothelioma</td>
<td>10</td>
<td>10.4</td>
</tr>
<tr>
<td>Infection</td>
<td>11</td>
<td>11.5</td>
</tr>
<tr>
<td>Cardiovascular diseases</td>
<td>4</td>
<td>4.1</td>
</tr>
<tr>
<td>Unspecified</td>
<td>11</td>
<td>11.5</td>
</tr>
</tbody>
</table>

3.2 Amount of fluid removed, pleural pressures and VAS values during therapeutic thoracentesis

The median value of the amount of effusion removed during TT was 1,250 mL (800–1,700 mL interquartile range). More than 1,500 mL of fluid was removed in 32 (33%) patients. The median value of the initial pleural pressure was 5 cm H₂O (interquartile range 2–9.8 cm H₂O). Negative pleural pressure at TT onset was measured in 10 patients, two of whom were below −5 cm H₂O. The median value of the final pleural pressure was −4 cm H₂O (interquartile range −6–0 cm H₂O).

![Figure 1: Time-dependent visual analogue scale values displayed by median, interquartile range, and range.](image-url)
The median value of diaphragm lift during TT was 2 cm (interquartile range 1–4 cm).

VAS values before, immediately after, two hours after and 24 hours after TT are shown in Figure 1. Clinically significant dyspnoea relief (change in VAS > 20 mm) was observed immediately after TT in 40 (41.6%) patients and in 56 (58.3%) patients two hours after TT. Of the 73 patients in whom a VAS score 24 hours after TT was collected, clinically significant dyspnoea relief immediately after TT was reported by 31 (42.4%) patients, two hours after TT by 41 (56.2%) patients and in 46 (63%) patients 24 hours after TT. Clinically significant dyspnoea worsening was observed in three (3.1%) patients immediately after TT.

Fluid volume removed was statistically significantly associated with dyspnoea relief immediately after TT (\( \rho = -0.22; p = 0.028 \)), dyspnoea relief two hours after TT (\( \rho = -0.21; p = 0.04 \)) and dyspnoea relief 24 hours after TT (\( \rho = -0.27; p = 0.019 \)).

Initial pleural pressure was associated with pre-TT VAS (\( \rho = 0.20; p = 0.049 \)), dyspnoea relief two hours after TT (\( \rho = -0.22; p = 0.028 \)) and dyspnoea relief 24 hours after TT (\( \rho = -0.32; p = 0.006 \)), but not with dyspnoea relief immediately after TT (\( \rho = -0.15; p = 0.14 \)). We also found an association between initial pleural pressure and final pleural pressure (\( \rho = 0.67; p < 0.001 \)), diaphragm elevation (\( \rho = 0.44; p < 0.001 \)) and fluid volume removed (Figure 2).

3.3 Reasons for discontinuing therapeutic thoracentesis

Reasons for TT discontinuation and parameter values in patients with different causes of TT discontinuation are shown in Table 2.

Of the 34 patients in whom TT was discontinued due to symptoms, four reported chest pain and 30 reported an unrelenting cough. Patients in whom TT was discontinued due to a fall in pleural pressure or low pleural pressure, statistically significantly less fluid was removed and lower final pressures were recorded than in patients in whom TT was discontinued due to cessation of fluid drainage (\( p < 0.001 \)), physician decision (\( p < 0.001 \)) or onset of symptoms (\( p < 0.001 \)). Patients in whom TT was discontinued due to a fall in pleural pressure or low pleural pressure had statistically significantly smaller changes in VAS changes immediately after TT compared to patients in whom TT was discontinued due to physician decision (\( p = 0.035 \)); the same was true two hours after TT (\( p = 0.016 \)). The same trend was observed in comparison with other groups, but did not achieve statistical significance.

3.4 Pleural space elastance

According to the dynamics of pleural pressure changes, 74 (77.1%) patients were classified in the group with
a normal elastance curve, and 22 (22.9%) patients in the group with unexpandable lung. Examples of patients with individual elastance curves are presented in Figure 3.

A group of six patients with unexpandable lung reported symptoms during TT; five developed a cough and one experienced chest pain.

In 10 patients, pressures followed the biphasic elastance curve. The cause of the pleural effusion was pleural malignancy in eight patients, infection in one (parapneumonic effusion in the fibrinopurulent phase) and active fibroproductive pleuritis in one. In all the pleural effusion persisted on the chest radiograph after TT. Two hours after TT, clinically significant dyspnoea relief was reported by five patients with a biphasic elastance curve.

In 12 patients, pleural pressures during TT followed the monophasic curve with high elastance. In these patients, the predominant cause of the pleural effusion was infection (parapneumonic effusion sequelae in six patients), followed by pleural malignancy (five patients) and unspecified chronic pleuritis in one patient. After TT, two patients reported clinically significant dyspnoea relief, even though only 120 mL and 200 mL of pleural fluid was removed; in other patients, TT had no effect on symptoms. After TT, all 12 patients still had a pleural effusion on chest radiography. No patient in this group required additional TT during the one-month follow-up period after TT.

### 3.5 Complications and safety

After TT, we found pneumothorax on chest radiography in two patients; of these, the pneumothorax was only minimal in one patient, a 74-year-old patient in whom 150 mL of effusion was removed with TT due to trapped lung. Pneumothorax also developed in an 81-year-old patient in whom 2,300 mL of effusion was removed. During TT, pleural pressure fell from +10 cm H₂O to −5 cm H₂O. Both patients were without problems after TT and also in the following days. Despite the resulting pneumothorax, both reported an improvement in VAS scores. Apart from observation, no further action was required.
4 Discussion

The study, which sought to evaluate the usefulness of measuring pleural space pressures during TT, included 96 patients who were hospitalized at the Interventional Pulmonology Department at the University Clinic Golnik during the study and required TT due to pleural effusion.

An important part of our study was determining the possible association between initial pleural pressure, volume of fluid removed and the degree of dyspnoea before TT and dyspnoea relief after TT. The expected correlation between the initial pleural space pressure and the volume of fluid removed was confirmed. Higher initial pleural pressure was also weakly associated with greater diaphragm lift during TT.

Dyspnoea severity after TT was clinically significantly reduced in 42% of patients immediately after TT. The proportion of patients with clinically relevant dyspnoea relief increased to 58% after two hours and to 63% after 24 hours. The temporal dynamics of symptoms suggest that the actual effect of TT on dyspnoea relief is more correctly assessed at least two hours after TT and not immediately afterwards, when patients still have problems with lung expansion and frequent cough or other symptoms. A study by Boshuizen et al found that most patients felt the greatest relief two days after TT, but unfortunately, we did not perform the VAS assessment in later days in our study (14).

The degree of dyspnoea relief was influenced by the amount of fluid removed, but the association was otherwise weak. In other studies, too, little or no association was found between the amount of fluid removed and dyspnoea relief after TT (14,16). Therefore, the volume of removed pleural effusion alone is not a good prognostic factor for dyspnoea relief after TT.

We did not find studies on the effect of pleural pressure on the degree of dyspnoea. In our study, we found an association between initial pleural pressure and the degree of dyspnoea before TT and the degree of dyspnoea relief two and 24 hours after TT; the connection was otherwise weak. We can conclude that the association between initial pleural pressure and the degree of dyspnoea relief after TT is too weak to predictably determine which patients will benefit symptomatically from TT only by assessing initial pleural pressure. By monitoring and recording the dynamics of pleural pressures during the entire course of TT, we obtained important data on the pleural space events during the procedure, particularly the inability to expand the lungs. If negative pleural pressures are detected at any point during TT while the effusion is still present and high elastance is detected after further drainage, it is a certain sign that the lungs are incapable of further expansion and the patient would not benefit from additional fluid removal. There are the previously described cases of two groups of patients in whom pleural pressures during TT follow a biphasic elastance curve in the steep part, or the monophasic curve with high elastance, characteristic of trapped lung. Patients with trapped lung normally have less symptoms due to pleural effusions. Efficient treatment is surgical with decortication, rather than TT (13). In all patients in whom we suspected unexpandable lung from pleural space pressures during TT, chest
radiography after TT still showed a pleural effusion (additionally, we found pneumothorax in two patients), which confirmed our suspicions. In patients whose pleural pressures followed a monophasic curve with high elastance, the suspicion of trapped lung during manometry was additionally confirmed by the subsequent course, in which their symptoms did not progress during the one-month follow-up after TT and they did not need additional effusion removal.

Metastatic malignancy was the cause of the pleural effusion in more than 70% of patients, which explains the higher proportion of large effusions (more than half of the hemithorax) and the significant proportion of incompletely expanded lungs after TT (13,17). In patients with malignancy, the presence of central tumours or extensive visceral pleura involvement which can prevent complete lung expansion is possible, so complete removal of the effusion is not possible or reasonable. In our study, opacification of more than half of the hemithorax on chest radiography was found in 53 patients and more than 1,500 mL of fluid was removed in 31 (32%) patients, which is three times more than in the Lentz group, in which more than 1,500 mL was removed in only 7 (11%) patients. At the same time, we can observe than in 37 (38%) patients included in our study, pleural effusion was not detected or was only minimal on chest radiography after TT, which is a lower proportion than in the Lentz group, in which and US-visible residual effusion was reported in only 40% of patients (18).

Although the median volume of the effusion removed during TT was 1,250 mL and we removed more than 1,500 mL of effusion in one third of the patients, no significant complications were detected. We found two (2.1%) instances of otherwise asymptomatic pneumothorax ex vacuo with chest radiography after TT among 96 patients. In both cases an inability to expand the lung was found; in one case, the pressure changes followed the monophasic curve with high elastance and the biphasic curve in the second. The lower proportion of pneumothorax in our study compared to the study by Lentz et al, in which pneumothorax was detected in 5% of patients, and the study by Villena et al, in which pneumothorax was detected in 14.8% of patients, can be attributed to a more conservative approach and TT discontinuation with less negative pressures in cases where we detected a rise in elastance, which we believe is the correct approach (18,19). RPO, a rarely described complication of TT, was not detected in any patient.

In 35% of patients, the onset of symptoms was the cause of TT discontinuation. Similar results were published by Lentz et al, who discontinued TT in 37% due to the onset symptoms, and by Feller-Kopman et al, who discontinued TT in 17% due to the onset of symptoms, but in their studies, contrary to our results, chest pain was the most common symptom (18,20). Interestingly, in both our and the aforementioned studies, chest pain was not associated with either large volumes of fluid removed or low final pleural pressures. Other, still unexplained factors obviously contribute to the discomfort, so chest pain cannot be prevented with pleural manometry. In our patients, the most common TT-associated symptoms were a cough, which is not the consequence of the fall in pleural pressure, but rather the consequence of lung expansion and resolution of atelectasis, which occur due to the removal of excess fluid (20).

The study’s shortcoming is that we chose a change in the degree of dyspnoea, which was assessed by VAS, to evaluate the effect of TT. Dyspnoea is an important symptom, which affects the patient’s quality of life, but it is difficult to objectively evaluate; we use subjective tools, which are by their nature not very reliable. Using more objective methods, such as measuring the patient’s performance with a 6-minute walk test, oxygenation at rest and during exertion and sleep abnormalities with polysomnography to evaluate the effect of TT on the patient’s quality of life would mean an upgrade to our study.

In 15 patients, TT was discontinued due to physician decision, which is probably the reason for the incorrect classification of some patients in the group with a normal elastance curve. We hypothesize that should TT continue, the transformation of the elastance curve into a biphasic one would manifest in some of these patients, as most had pressures in the negative range with the effusion still present.

5 Conclusion

Based on the findings of our study, we can predict the volume of fluid removed and change in the degree of dyspnoea after TT from the initial pleural pressure, although the association is weak. The main advantage of pleural manometry is its ability to detect patients whose lungs cannot expand during the procedure itself, thus allowing it to be discontinued in time, reducing the possibility of complications. With TT, more 1,500 mL of fluid can be safely removed with simultaneous pleural pressure measurements.

Conflict of interest
None declared.
References


