

**Research Article**

# Efficacy of talc pleurodesis for malignant and paramalignant pleural effusion: a retrospective analysis of 61 cases



Talk plörodezinin malign ve paramalign plevral efüzyonda etkinliği: 61 olgunun retrospektif analizi

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**ABSTRACT**

**Introduction:** Malignant-paramalignant effusions are common after malignancies. Treatment of malignant-paramalignant pleural effusion is directed towards palliation of symptoms and improvement in quality of life. Chemical pleurodesis has been widely used to control malignant and para-malignant pleural effusion. The present study aims to reveal the effects of chemical pleurodesis on malignant and paramalignant pleural effusions commonly coexisting with malignant diseases.

**Methods:** 61 patients were retrospectively examined between October 2017 and December 2019. Drainage with 8F intrapleural catheter and chemical pleurodesis (sterile talc powder) were employed in 61 patients with malignant and/or paramalignant effusion. The patient group consisted of patients treated at the thoracic surgery service or consulted from other services. The patients demographics and data on their operated side (left/right), recurrence rate, length of postoperative hospital stay, and complications were extracted from their files.

**Results:** The sample consisted of 48 male (78.6%) and 13 female (21.3%) patients. The patients were between 22 and 82 years and the average age was  $60.0 \pm 13.2$  years. 33 patients (54.0%) were operated on the right side, while 7 (11.4%) and 21 (34.4%) were operated bilaterally or on the left side, respectively. The most common cause of malignant and paramalignant pleural effusion was found to be lung cancer, accounting for 38 (62.2%) of the patients. Postoperative recurrence was observed in 15 (24.5%) patients. The Mann-Whitney U test was used for skewed variables, and the Chi-Square test (or Fisher's exact test) was used for categorical variables. No significant difference was observed in terms of surgery side ( $p=0.676$ ), gender ( $p=0.156$ ) and malignant disease ( $p=0.979$ ). The average length of hospital stay was 5.3 days.

**Conclusions:** The primary principle is to control the symptoms by removing the intrapleural effusion in the cases of malignant and paramalignant effusions. When recurrence rates were evaluated, intrapleural catheter drainage and chemical pleurodesis are an effective and safe method in selected patients.

**Keywords:** Catheter; pleurodesis; pleural effusion

**ÖZ**

**Giriş:** Malign ve paramalign efüzyonlar malignitelerden sonra yaygındır. Malign-paramalign plevral efüzyon tedavisi semptomların hafifletilmesine ve yaşam kalitesinin iyileştirilmesine yöneliktir. Kimyasal plörodez, malign ve paramalign plevral efüzyonu kontrol etmek için yaygın olarak kullanılmaktadır. Bu çalışmada malign hastalıklarla yaygın olarak birliktelik gösteren malign-paramalign plevral efüzyonlarda kimyasal plörodezinin etkisini saptamayı amaçladık.

**Yöntem:** 2017 Ekim ve 2019 Aralık yılları arasında 61 hasta retrospektif olarak değerlendirilmiştir. 61 hastaya tarafımızdan malign ve/veya paramalign efüzyon nedeniyle 8F intraplevral kateter ile drenaj ve kimyasal plörodezis (steril talk pudrası) uygulandı. Hastalar göğüs cerrahisi servisinde tedavi edilen veya diğer servislerden konsültasyon yapılan hastalardan oluşmaktaydı. Hastaların demografik verileri, operasyon tarafı (sol/sağ), rekürrens oranı, postoperatif hastanede kalış süresi ve komplikasyonları dosyalardan değerlendirildi.

**Bulgular:** Kırksekiz hasta (%78,6) erkek iken, 13 (%21,3) hasta kadındı. Yaş ortalaması  $60,0 \pm 13,2$  olup yaş aralığı 22-82 yaş idi. 33 (%54,0) hasta sağ tarafından opere edilirken 7 (%11,4) hasta bilateral, 21 (%34,4) hasta sol tarafından opere edildi. En sık malign-paramalign plevral efüzyon nedeni 38 (%62,2) hasta ile akciğer kanseri idi. Postoperatif rekürrens 15 (%24,5) hastada izlendi. Niceliksel değişkenler için Mann-Whitney U testi ve kategorik değişkenler için Chi-Square testi (veya Fisher'in exact test) kullanıldı. Cerrahi taraf ( $p = 0,676$ ), cinsiyet ( $p = 0,156$ ) ve malign hastalık ( $p = 0,979$ ) açısından anlamlı fark gözlenmedi. Hastaneden ortalama yatış süresi 5,3 gündü.

**Sonuç:** Malign-paramalign efüzyonlarda intraplevral efüzyonun boşaltılarak semptomların kontrol altına alınması ana prensiptir. Rekürrens oranları değerlendirildiğinde, intraplevral kateter ile drenaj ve kimyasal plörodezis, seçilmiş hastalarda etkili ve güvenli bir yöntemdir.

**Anahtar kelimeler:** Kateter; plörodez; plevral efüzyon

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## Introduction

Malignant pleural effusion is a condition that occurs between parietal and visceral pleurae and has a global incidence of 0.06% [1]. Malignant or paramalignant pleural effusion may recur during the course of many malignant diseases or after the treatment of the primary disease. Malignant pleural effusions (MPE) are diagnosed during cytologic examination of the pleural fluid or by the identification of cancer cells in the pleural biopsy. The fluid in paramalignant effusions is generally associated with secondary causes, such as lymphatic invasion, bronchial obstruction, or pulmonary embolism, and malignant cells are not detected in cytologic evaluation [2]. The incidence of MPE and the associated medical charges are expected to increase owing to the globally growing prevalence of cancer and advanced systemic therapies [3]. Carcinoma in any organ is capable of leading to pleural metastasis and is expected to potentially cause pleural metastasis and effusion in the presence of neighboring lung cancers and involvement thereof in the circulatory system. As a matter of fact, in all the case series studies, the most common cause of MPE is reported as lung cancer [4], followed by breast cancer (BC), gynecological cancers, lymphoma and malignant mesothelioma [5].

The patient's clinical history, physical examination, chest radiography, and thoracentesis analysis can allow for the detection of the cause of pleural effusion [6]. As the amount of pleural effusion starts to increase, the symptoms start to appear. Among the most prevalent symptoms are pleuritic pain, non-productive cough, and dyspnea [7]. In the treatment of malignant pleural effusion, the methods to obliterate the pleural space should be employed after the pleural fluid is drained. Pleuroctomy or pleural abrasion, chemical pleurodesis, thoracoscopy, and thoracotomy are the methods to prevent MPE from recurring [4]. Chemical pleurodesis is the most commonly used method of pleurodesis. Many agents are used for chemical pleurodesis. There are bleomycin, Corynebacterium parvum extract, interferons, silver nitrate, tetracycline/doxycycline, iodopovidone, quinacrine, interleukin-2, and several chemotherapeutic agents [8]. In a new meta-analysis, talc was found to produce pleurodesis successfully than tetracycline/doxycycline, C.parvum extract, bleomycin and mitosatron did,yet it was not a significantly better agent than the others [9]. Accordingly, this study is intended to retrospectively evaluate chemical (sterile talc) pleurodesis by investigating the related etiology, patients' response to treatment, postoperative complications, and length of hospital stay in relation to the patients with malignant and paramalignant pleural effusion, in whom we employed intrapleural catheter.

## Methods

The study was conducted over 61 patients at Çanakkale Onsekiz Mart University (ÇOMU) between October 2017 and December 2019. Sixty-one patients who were followed up in the thoracic surgery service or consulted from other services were included in the study.

Pleurodesis was performed when the daily drainage in the patients treated with intrapleural catheter reduced to 100-150 ml and in the occurrence of radiological re-expansion. The sterile talc powder [sterile talc powder (NovatechSA, La Ciotat, France) of 4 gr, which was diluted with 100cc physiological saline solution by 9.0%, was administered together with 3 mg/kg (maximum 250 mg) local anesthetic with 2.0% prilocaine hydrochloride. Subsequently, the tube was clamped for 1-2 h. Meanwhile, the patient was rotated every 30 min. The administration of the tube was completed in 24-72 h [10]. In the cases where therapeutic pleural aspiration is performed, a recurrence of 98.0-100.0% is observed [10]. In this study, the cases in which patients attended the researcher's hospital with massive pleural effusions within the postoperative 30 days and did not die in the meantime were construed as recurrences.

61 patients diagnosed with malignant and paramalignant pleural effusion and treated with chemical (talc powder) pleurodesis were included in the present study. 27 patients not diagnosed with malign-paramalign effusion and two patients with unobtainable data were excluded from the sstudy. Figure 1.

## Ethical approval

The ethical approval was obtained from the local ethics board of the School of Medicine at Çanakkale Onsekiz Mart University (IRB Number: 2019-21, Date: 02.01.2020).

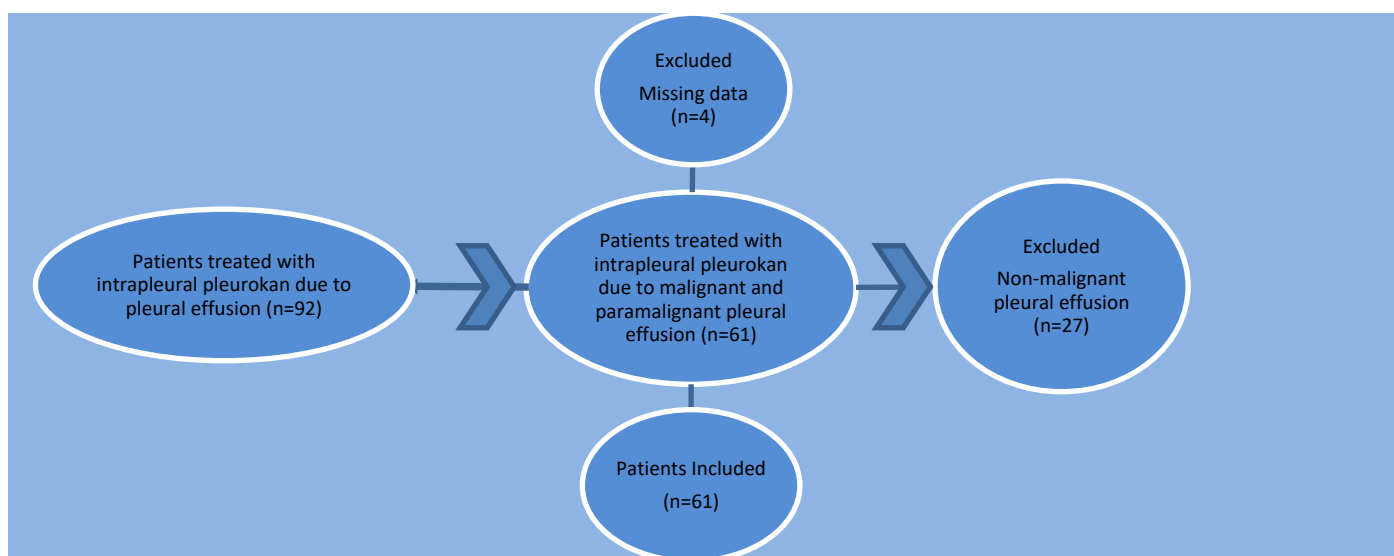


Figure 1. Participant Flow Chart

The patients' demographics and data on their operated side (left/right), recurrence rate, length of postoperative hospital stay, and complications were extracted from their files. All the patients' posteroanterior (PA) chest radiography, computed tomography (BT), electrocardiography, complete blood counts, and basic biochemical tests (sodium, potassium, chloride, bicarbonate, blood urea nitrogen (BUN), magnesium, creatinine, and glucose) were evaluated preoperatively. Eight French intrapleural catheter were used in the patients under local anesthesia and they were evaluated based on postoperative PA chest radiography. Upon the establishment of favorable conditions, the tube catheter thoracostomy was discontinued in the patients treated with chemical pleurodesis after the repeated checking of the PA chest radiography. All the collected data were checked twice by the researcher. If needed, some of the patients were called to clarify certain data. After all the data were imported in a computer, error check and error elimination were performed.

### Statistical analysis

Data were evaluated by using licensed IBM SPSS20.0. The descriptive data such as clinical findings, pathologic diagnoses, and sociodemographic facts of the patients operated in the author's clinic were presented as numbers and percentages. The Kolmogorov-Smirnov test was performed to test if the numerical variables were normally distributed. The independent samples t-test was used to compare data meeting parametric assumptions. The Mann-Whitney U test was used for skewed variables, and the Chi-Square test (or Fisher's exact test) was used for categorical variables. A linear regression analysis was performed to check for variables independently. A p-value of <0.05 was considered statistically significant.

### Results

61 patients were analyzed. The sample consisted of 48 male (78.6%) and 13 female (21.3%) patients. The patients were between 22 and 82 years and the average age was  $60.00 \pm 13.22$  years. While 33 patients (54.0%) were operated on the right side, whereas 7 (11.4%) were operated bilaterally and 21 (34.4%) on the left side, respectively (Table 1).

The most common cause of malignant and paramalignant pleural effusion was lung cancer, accounting for 38 (62.2%) of the patients, which was followed by seven patients (11.4%) with breast cancer and six (9.8%) with gastric cancer (Table 2).

**Table 1.** Demographic data and outcome of the study

Age (mean±SD)	60.0 ± 13.2
Duration of hospitalization (mean±SD) <sup>§</sup>	5.3 ± 3.9
<b>Sex</b>	
Male n (%)	48 (78.6)
Female n (%)	13 (21.3)
<b>Side of the lesion</b>	
Right n (%)	33 (54.0)
Left n (%)	21 (34.4)
Bilateral n (%)	7 (11.4)
<b>Postoperative complication</b>	
Absent n (%)	0
Present n (%)	2 (3.2)
<b>Type of postoperative complication</b>	
None n (%)	59 (96.7)
Acute pain n (%)	2 (3.2)

**Table 2.** Underlying malignancy associated with effusion

	n	%
Lung cancer	38	62.2
Breast cancer	7	11.4
Gastric cancer	6	9.8
Lymphoma	4	6.5
Pancreatic cancer	3	4.9
Renal cell cancer	2	3.2
Endometrial cancer	1	1.6

Postoperative recurrence was observed in 15 patients. Because eight patients died within the first follow-up 30 days, they were excluded from the calculation of the recurrence rate. When recurrence rate was evaluated, no significant difference was observed in terms of surgery side ( $p=0.676$ ), gender ( $p=0.156$ ) and malignant disease ( $p=0.979$ ) (Table 3).

The chemical pleurodesis in the remaining 38 patients was considered to be successfully executed and the success rate was calculated to be 71.6%. In the follow-up evaluation, partial adhesion was observed in seven patients; no reoperation was considered. Two patients were observed to suffer from postoperative pain for a short while although the intrapleural operation was accompanied by the administration of local anesthesia. Yet it was controlled with medical therapy. No mortality was observed. The average length of hospital stay was 5.3 days.

**Table 3.** The rate of postoperative recurrence

	Recurrence n (%)	No recurrence n (%)	Total n (%)	P value
<b>Sex</b>				0.156
Male	10 (18.8)	32 (60.3)	42 (79.2)	
Female	5 (9.4)	6 (11.3)	11 (20.7)	
<b>Side of lesion</b>				0.676
Right	8 (15)	18 (33.9)	26 (49.0)	
Left	6 (11.3)	14 (26.4)	20 (37.7)	
Bilateral	1 (2.1)	6 (11.3)	7 (13.2)	
<b>Etiology</b>				0.979
Lung cancer	10 (18.8)	23 (43.3)	33 (62.2)	
Breast cancer	2 (3.7)	4 (7.5)	6 (11.3)	
Gastric cancer	0	6 (11.3)	6 (11.3)	
Lymphoma	1 (1.8)	3 (5.6)	4 (7.5)	
Pancreatic cancer	2 (3.7)	0	2 (3.7)	
Renal cell ca	0	2 (3.7)	2 (3.7)	

## Discussion

Malignant pleural effusions (MPE) are very common and associated with severe symptoms and they cause high hospital charges [11]. The most prevalent symptom thereof is dyspnea [10]. The most frequent complaints of this research's patients were dyspnea and chest pain. Life expectancy is very low and while mortality in the first postoperative month is 54.0%, it is 84.0% in the first six months [2]. Malignant pleural effusion is very common in patients with metastasis and observed in 15.0% of the ones suffering from cancer [12]. Majority of the patients herein were diagnosed with lung cancer. In patients with relatively better health status and in the cases where patients with dyspnea benefited from therapeutic thoracentesis, chemical pleurodesis is accepted as the treatment of first choice [13]. Chemical pleurodesis refers to the administration of sclerosing agents to the pleural space to produce adhesion between the visceral and parietal pleurae. The ideal sclerosing agent for pleurodesis remains as a controversial issue [14]. A total of 1,168 patients with MPE were analyzed for efficacy. The success rate was reported as 64.0% in patients undergoing chemical pleurodesis [15]. Compared to all chemical pleurodesis agents, talc has been shown as the most effective agent and its effectiveness is 90.0% [9, 16]. Pleurodesis with talc is a specific form of chemical pleurodesis, and pleurodesis in the presence of malignant pleural effusion is among the most effective sclerosing agents available [17]. Depending on the origin of the formulation, varying amounts of calcium, aluminum, iron, and lead can exist in talc powder. Talc may also contain a couple of mineral contaminants (e.g. magnesite, dolomite, kaolinite, calcite, chlorite, serpentine, and quartz). No asbestos exists in the medical talc formulation [18]. Safety concerns over talc pleurodesis arise from acute respiratory distress syndrome (ARDS), which is induced by minuscule talc particles introduced to systemic circulation and believed to originate from extrapleural inflammation [19]. The most common side effects following talc pleurodesis are fever (10.0-17.0%), pain, and gastrointestinal symptoms [16,20, 21]. The present study observed no serious postoperative side effects and although two patients had postoperative pain, it was controlled with medical therapy.

The success rate concerning talc pleurodesis is reported as 81.0-100.0% [22]. In a study on 611 patients, the long-term success rate of talc pleurodesis performed with VATS is reported as 69.0% [23]. A study, conducted on 482 patients, has yielded a success rate of 71.0-78.0% achieved by talc pleurodesis which was performed by using poudrage or slurry [24]. Yıldırım et al explained the recurrence rate as 18.0% in their pleurodesis study with talc powder [25]. In the current study, eight patients died within the first postoperative month. The chemical pleurodesis in 38 patients was considered to be successfully executed and the success rate was calculated to be 71.0%. In our study, we could not find a statistically significant relationship between recurrence and operation side, gender and malignant disease ( $p>0.05$ ).

As indicated in the related literature, performing the procedure in the form of suspension may prevent uniform distribution and cause fluid accumulations in some regions of the pleural space [26]. This results in incomplete pleurodesis and caused loculations. The relatively lower success rate hereof can be accounted for in view of this phenomenon. MPE method is closely associated with tumor type, pulmonary re-expansion, performance status, symptoms, and life expectancy [27].

## Limitations

This is a retrospective study. The results concerning the talc pleurodesis agent could not be explicitly revealed since it could not be compared with other pleurodesis agents in malignant and paramalignant effusions.

## Conclusion

Consequently, malignant and paramalignant pleural effusion is a common symptom in advanced lung cancer and other cancers. Therapy is not intended for the primary disease but to increase patient's quality of life by controlling the symptoms. It is well-known that new developments are still needed for the treatment of malignant and paramalignant pleural effusions. Drainage with 8F intrapleural catheter and chemical pleurodesis are effective at controlling the symptoms and the method should be decided upon according to the patient.

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