

## Application of autologous blood patch in patients with non-expanded lungs and persistent air leak

*Akciğerleri ekspanse olmayan ve uzamış hava kaçağı olan hastalarda otolog kan yaması uygulaması*

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### ABSTRACT

**Background:** This study aims to evaluate the effectiveness of pleurodesis procedure by ensuring the expansion of the lung and occluding lung parenchyma leaks with an autologous blood patch.

**Methods:** A total of 24 patients (17 males, 7 females; mean age 59.9±12.2 years; range, 30 to 86 years) who underwent autologous blood patch pleurodesis in our clinic between November 2015 and November 2019 were retrospectively analyzed. The patients were not eligible to undergo chemical pleurodesis due to a non-expandable lung or poor general condition. Demographic and clinical characteristics of the patients and postoperative data were evaluated.

**Results:** The air leak stopped within 48 h after autologous blood patch pleurodesis in seven patients. The air leak significantly decreased in 13 patients, while it remained unchanged in four patients. A Heimlich valve was placed in the patients in whom the air leak stopped or significantly decreased. The follow-up chest X-rays showed that the respective lungs of these patients became completely expandable.

**Conclusion:** Our study results suggest that the autologous blood patch procedure is a favorable option for the patients who are unable to benefit much from the conventional chemical pleurodesis methods due to contraindications to surgery or the presence of non-expandable lungs.

**Keywords:** Blood patch, pleurodesis, prolonged air leak.

### ÖZ

**Amaç:** Bu çalışmada, akciğerin ekspanse olması ve akciğer parankim kaçaklarının otolog kan yaması ile tıkanması sağlanarak, plörodez işleminin etkinliği araştırıldı.

**Çalışma planı:** Kasım 2015 - Kasım 2019 tarihleri arasında kliniğimizde otolog kan yama plörodezisi uygulanan toplam 24 hasta (17 erkek, 7 kadın; ort. yaş 59.9±12.2 yıl; dağılım, 30-86 yıl) retrospektif olarak incelendi. Hastalar akciğerin ekspanse olamaması veya kötü genel durum nedeniyle kimyasal plörodez için uygun değildi. Hastaların demografik ve klinik özellikleri ve ameliyat sonrası verileri değerlendirildi.

**Bulgular:** Hastaların yedisinde otolog kan yama plörodezisinden sonraki 48 saat içinde hava kaçağı kesildi. Hava kaçağı 13 hastada anlamlı düzeyde azalır iken, dört hastada herhangi bir değişiklik görülmedi. Hava kaçağı kesilen veya anlamlı düzeyde azalan hastalarda Heimlich valfi takıldı. Takip akciğer grafisinde, bu hastaların akciğerlerinin tamamen ekspanse olduğu görüldü.

**Sonuç:** Çalışma sonuçlarımız, cerrahi kontraendikasyonlar veya ekspanse olmayan akciğerlerin varlığı nedeniyle, konvansiyonel kimyasal plörodez yöntemlerinden çok fayda sağlayamayan hastalarda, otolog kan yaması işleminin uygun bir seçenek olduğunu göstermektedir.

**Anahtar sözcükler:** Kan yaması, plörodez, uzamış hava kaçağı.

Received: November 18, 2019 Accepted: February 18, 2020 Published online: July 28, 2020

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### Cite this article as:

Apilioğulları B, Dumanlı A, Ceran S. Application of autologous blood patch in patients with non-expanded lungs and persistent air leak. Turk Gogus Kalp Dama 2020;28(3):521-526

Air leak persisting longer than five to seven days in pneumothorax patients having a chest tube is defined as prolonged air leak (PAL).<sup>[1,2]</sup> The PAL is an adverse event which may potentially occur after surgical procedures or spontaneous pneumothorax. It may prolong the time to hospital discharge with an increased risk for impossibility to remove the chest tube, and it may cause pain, limitation of movements, and infection.<sup>[2]</sup> Methods such as surgical treatment and pleurodesis are the commonly performed procedures to overcome this condition. However, the potential for surgery is usually ruled out in elderly patients with secondary spontaneous pneumothorax; patients with comorbidities and impaired cardiopulmonary functions, and in severely cachectic patients. Then, chemical pleurodesis is commonly performed. To achieve success with chemical pleurodesis, the lung must have started expanding and the pleural layers should be spaced close enough to allow adhesion.<sup>[3]</sup> A wide space between the pleural layers causes failures in most patients having a non-expandable lung with significant packs of air.

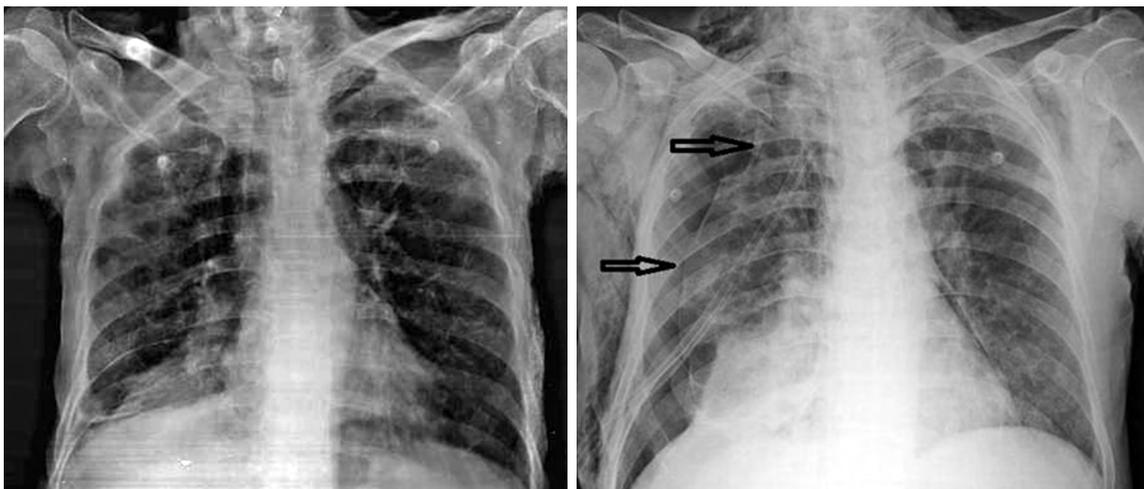
Moreover, the side effects of chemicals used in the chemical pleurodesis procedure require care to be exercised. The blood clot in the autologous blood patch procedure obstructs the spaces in the lung parenchyma where the air leak occurs, stopping the air leak, although the lung is non-expandable. In the literature, side effects and complications of the autologous blood patch procedure are significantly less compared to chemical pleurodesis. In this study, we aimed to evaluate the effectiveness of pleurodesis procedure by ensuring the expansion of the lung and occluding lung parenchyma leaks with an autologous blood patch.

## PATIENTS AND METHODS

A total of 24 patients (17 males, 7 females; mean age  $59.9 \pm 12.2$  years; range, 30 to 86 years) who underwent autologous blood patch pleurodesis due to pneumothorax and PAL in our clinic between November 2015 and November 2019 were retrospectively analyzed. Data were obtained from hospital charts and radiological images. The patients were ineligible for conventional pleurodesis methods. In addition, the patients who underwent conventional pleurodesis but were unable to benefit from such procedures were also included. Data including demographic and clinical characteristics of the patients and operative and postoperative data were recorded. A written informed consent was obtained from each patient. The study protocol was approved by the Ethics Committee of the Necmettin Erbakan University, Meram Faculty of Medicine. The study was conducted in accordance with the principles of the Declaration of Helsinki.

### Operative technique

A chest tube was placed, and underwater seal drainage was applied to all patients undergoing autologous pleurodesis. All our patients had PAL lasting more than seven days. The amount of air leak did not cause respiratory distress, but prevented expansion in the lungs. Considering the health status of patients, a second operation was considered very risky. Classical pleurodesis agents were not used, since lung expansion was not achieved. Instead, we used the autologous pleurodesis method with a low complication rate, compared to other agents (Figure 1). We attempted to enable patients to tolerate this method more comfortably.



**Figure 1.** Chest X-ray images showing autologous blood patch technique in patients with a non-expandable lung and persistent air leak and achieving successful results.

Since the air leak was persistent, the chest tube was not clamped in any of the patients to prevent tension pneumothorax. Instead, the chest tube was placed at a position above the chest level (Figure 2) so that the backflow of the blood from the drain was prevented. The patient was brought to the Trendelenburg position. At the bedside, the venous blood of the patient was taken at a volume of 1 to 2 mL/kg (50 to 70 mL) and the collected blood was administered to the patient via the chest tube. After the bed was brought to the horizontal position, it was ensured that the patient stayed in bed for 4 h with the chest tube remained above the chest level. After 4 h, the bottle of the chest drain was placed to the original position below the chest level. A Heimlich valve drain was placed in the patients in whom the air leak stopped or significantly decreased.

The procedure was repeated after two days in four of our patients whose air leakage was not stopped. The same procedure was applied. However, success was unable to be achieved and unfortunately three died. We did not repeat the procedure in patients with lung leakage, but not expansive lungs. The patients were followed up with daily posteroanterior chest radiographs.

### Statistical analysis

Statistical analysis was performed using PASW for Windows version 17.0 software (SPSS Inc., Chicago, IL, USA). Descriptive data were presented in mean  $\pm$



**Figure 2.** The chest tube was placed at a position above the chest level.

standard deviation, median (min-max) or number and frequency.

## RESULTS

The pathology occurred in the right hemithorax in 15 patients and in the left hemithorax in nine patients. No lung expansion was achieved in four patients and three patients died during the follow-up period. Lung expansion was achieved in 17 patients during the follow-up period (Table 1).

**Table 1. Patient data and procedural data of the study are presented as number of patients**

	n	Mean
Affected side		
Right hemithorax	15	
Left hemithorax	9	
Total	24	
Age (year)		59.9
The smallest	30	
The biggest	86	
Primary lung cancer		
Lung cancer	11	
Metastatic lung cancer	4	
Breast cancer metastasis	1	
Nasopharyngeal cancer metastasis	1	
Cervical cancer	1	
Carcinoma metastasis	1	
Iatrogenic pneumothorax (malignant pleural effusion drainage)	4	
Bullous lung	6	
Chronic disease	3	
Familial Mediterranean fever	1	
Pneumonia	1	
Bronchiectasis	1	
Operation		
Lobectomy	6	
Right upper lobectomy	3	
Left lower lobectomy	3	
Wedge resection		
Left upper lobe	1	
Metastasectomy	4	
Bullectomy	4	
Expanded lung	17	
Unexpanded lung	4	
Death	3	

Fifteen of 24 patients had malignant diseases. Eleven patients had primary lung cancer, one patient had carcinoma metastasis, one patient had breast cancer metastasis, one patient had cervical cancer metastasis, and one patient had nasopharyngeal cancer. In addition, one patient had spontaneous pneumothorax, one had familial Mediterranean fever, five had a bullous lung, one had bronchiectasis, and one had chronic inflammation (Table 1).

Right upper lobectomy was performed in three patients, left lower lobectomy in three patients, left upper wedge resection in one patient, metastasectomy in one patient, and a video-assisted thoracoscopic surgery in one patient. In 15 patients who underwent surgery, complete lung expansion was unable to be achieved and air leak persisted postoperatively. Biopsies were performed in four patients. Pneumothorax and persistent air leak developed in four patients during the pleural effusion drainage.

The air leak stopped within 48 h after autologous blood patch pleurodesis in seven patients. The air leak significantly decreased in 13 patients, while it remained unchanged in four patients. A Heimlich valve was placed in the patients in whom the air leak stopped or significantly decreased. The follow-up chest X-rays showed that the respective lungs of these patients became completely expandable.

## DISCUSSION

The persistence of an air leak longer than seven days is considered PAL in a patient with a chest tube placed for the treatment of pneumothorax.<sup>[4]</sup> It directly affects the patient's health adversely. A chest tube, unable to be removed for a long time, sets the ground for infections, limits the movements of the patient, and causes untoward consequences including pain and prolonged length of hospital stay.<sup>[2]</sup> In daily practice, chest surgeons use many methods to overcome this problem.

The most common methods are surgery and pleurodesis. However; several patient conditions exclude surgery from being an option. These conditions include impaired cardiopulmonary functions, severe cachexia, and inability to tolerate anesthesia particularly in patients with secondary pneumothorax. Pleurodesis appears to be an effective method in such cases.<sup>[5,6]</sup>

Pleurodesis is described as the procedure performed to prevent pneumothorax or collections of pleural effusion by applying several methods to induce adhesion between the layers of the parietal or visceral pleura.<sup>[7]</sup> The variety of methods include

chemical, immunological or mechanical pleurodesis to be utilized for the abovementioned purposes. The main goal is to create adhesions between the layers of pleura by inducing non-bacterial inflammation and pleural fibrosis.

Chemical pleurodesis is the most commonly used form of pleurodesis. The first agent introduced for use in pleurodesis is the silver nitrate, which was started to be used in the early 20<sup>th</sup> century owing to its caustic effects leading to pleurodesis in the pleural space.<sup>[8,9]</sup> However, it is not preferred to be used currently, as it is associated with severe pain and excessive effusion. On the other hand, several studies have shown evidence that these side effects can be alleviated with dose reductions and that it may be as effective as the talc powder.<sup>[6]</sup> These studies have also demonstrated that low-dose silver nitrate causes fewer systemic inflammations, despite a high-grade pleural inflammation.<sup>[10,11]</sup>

Currently, the most preferred pleurodesis agent is the talc powder. It was first used in 1935.<sup>[12]</sup> It is preferred owing to high availability, high success rates of pleurodesis, and low side effects. In European countries, the procedure is performed in accordance with the recommendations in the British Thoracic Society (BTS) guidelines.<sup>[13]</sup> The inflammation induced by the procedure causes adhesion of the pleural layers. Although it is associated with fewer side effects, it may cause serious complications such as acute respiratory distress syndrome (ARDS).<sup>[5]</sup> At least 32 cases of ARDS have been reported after talc pleurodesis performed for the treatment of spontaneous pneumothorax in the literature.<sup>[14,15]</sup> Mostly occurring within 48 hours, this untoward condition is related to the particle size and dose of talc powder. It is reported that the likelihood of this complication can be reduced by reducing the dose.<sup>[11]</sup> In the literature, it has been suggested that the amount of talc powder to be used should not be more than 5 mg due to the high likelihood of developing ARDS with doses higher than 10 g.<sup>[5,16,17]</sup> However, there are other case reports in the literature, reporting the emergence of ARDS with the use of only 2 g of talc powder.<sup>[16]</sup> Therefore, close monitoring and examination of the patients are essential after talc pleurodesis.

Tetracycline derivatives and bleomycin are the other agents commonly used for chemical pleurodesis. Tetracycline is known to be an effective and safe agent, but parenteral forms of this medicine are not available commercially. The lack of sterility of the commercially available oral form is a critical issue.<sup>[9,10]</sup> Furthermore, studies with alternative agents such as quinacrine and

iopovidone are being carried out in addition to the agents currently used for pleurodesis.<sup>[10]</sup>

In 1987, Robinson<sup>[18]</sup> was the first to report that autologous blood could be used for pleurodesis. He treated 25 patients with the autologous blood patch method for the treatment of PAL.<sup>[18]</sup> A consensus has been reached in general that this method is more cost-effective, less painful, and simpler compared to other pleurodesis methods.<sup>[19]</sup> Also, it is reported to be at least as effective as other methods of pleurodesis.<sup>[1,20]</sup>

The main effect of chemical pleurodesis agents is to induce inflammation and ultimately fibrosis following their administration to the pleural space. The ultimate objective is to create adhesion between the layers of pleura. The most important criterion for this to occur is that the lung should be expandable, and the pleural layers should be spaced closely. Therefore, pleurodesis would not be successful, if the area of pneumothorax is large enough to prevent the adherence of pleural leaves in the patient with PAL.<sup>[17]</sup>

In autologous blood pleurodesis, the pulmonary defect causing the air leak is directly closed by the clot formation after administering the patient's blood to himself or herself. In this way, the air leak either stops or decreases, helping the lung to expand again. Then, the fibrogenic activity of the blood generates pleurodesis by inducing pleural irritation and inflammation.<sup>[21,22]</sup> Blood is irritant outside its usual environment. In the literature, pleurodesis has been shown to occur via the induced pleural irritation and inflammation following the administration of the blood to the pleural area.<sup>[21]</sup> Compared to other pleurodesis methods, its major advantages include the lack of significant pain and having no need for the use of analgesics and sedatives.<sup>[5,14]</sup> In the literature, fever and empyema are reported as major complications. Cagirici *et al.*<sup>[23]</sup> reported occurring empyema in three (9%) of the cases in their study. Empyema did not occur in any of our patients. In 1992, Dumire *et al.*<sup>[24]</sup> reported the successful use of autologous blood patch in PAL after lung resection. Chambers *et al.*<sup>[20]</sup> reported that the autologous blood patch technique was effective in 92.7% of PAL developing after lung resection.

The main limitations of the present study include its retrospective design and small and heterogeneous sample size.

In conclusion, our study results suggest that autologous blood patch technique can be used as an option for the treatment of patients with non-expandable

lungs and persistent air leak. The pulmonary defect that causes the air leak is closed by clot formation in the administered autologous blood taken from the patient. Since the agent used for the pleurodesis procedure is the patient's blood itself, adverse effects are significantly fewer compared to the other pleurodesis agents, facilitating the use of autologous blood patch method even in patients with poor general conditions. In our patients, this method seems to be beneficial, at least allowing the patients to be discharged from the hospital uneventfully.

#### **Declaration of conflicting interests**

The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

#### **Funding**

The authors received no financial support for the research and/or authorship of this article.

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