

Endobronchial Treatment for Bronchopleural Fistula After Lung Resection

Akciğer Rezeksiyonu Sonrası Görülen Bronkolplevral Fistüllerde Endobronşiyal Tedavi

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ABSTRACT

Objective: In this study, we aimed to show the place of endobronchial fistula repair in the treatment of bronchopleural fistula (BPF) which is still one of the most feared complications of pulmonary resection.

Method: Between February 2006 - April 2010, 22 patients developed BPF after lung resection. The study included retrospective evaluation of 15 patients with fistula size of 3-10 mm that underwent endobronchial repair. Demographic characteristics of the patients were analyzed. Also concomitant systemic diseases of the patients, steroid usage, malnutrition, adjuvant and neoadjuvant chemo/radiotherapy, pleuropulmonary infections, remaining residual carcinomatous tissue in the bronchial stump, postsurgical stage of the disease were accepted as risk factors for fistula formation.

Results: All of the cases participated in the study were male and the age range was 50-80 (median: 61.3) years. When the primary disease was evaluated, 14 patients (93.3%) were operated for malignancy and 1 patient (6.7%) was operated due to multidrug resistant tuberculosis. Right standard pneumonectomy was performed in 11 patients. In addition; one patient underwent right sleeve pneumonectomy, one patient right lower bilobectomy plus diaphragm resection and two patients left standard pneumonectomy. Success was achieved in 12 of the 15 patients who underwent bronchopleural fistula repair using N-butyl cyanoacrylate by endoscopic method. The success rate was 80%.

Conclusion: As a result, we think that application of tissue adhesives such as n-butyl cyanoacrylate by endoscopic method with the right technique that can be used as the first choice of treatment especially in BPF under 10 mm because of their low price and easy application.

Keywords: bronchopleural fistula; n-butyl cyanoacrylate glue; bronchoscopy; endobronchial treatment

ÖZ

Amaç: Bu çalışmamızda akciğer rezeksiyonu sonrası, hâlâ en korkulan komplikasyonlardan olan bronkoplevral fistül (BPF) tedavisinde endobronşiyal fistül onarımının yerini göstermeyi amaçladık.

Yöntem: Şubat 2006-Nisan 2010 tarihleri arasında, BPF gelişen 22 hasta içinden fistül büyüklüğü 3-10 mm olan ve endobronşiyal onarım yapılan 15 hasta, retrospektif olarak değerlendirildi. Hastaların demografik özelliklerine bakıldı. Ayrıca eşlik eden sistemik hastalıklar, steroid kullanımı, malnutrisyon, plöropulmoner enfeksiyon, adjuvant ve neoadjuvan kemoradyoterapi, bronşiyal güdükte rezidüel karsinomatöz doku kalması cerrahi sonrası evre, fistül oluşumunda risk faktörü olarak kabul edildi.

Bulgular: Çalışmaya katılan olguların hepsi erkekti ve yaş aralığı 50-80 (ortalama: 61,3) idi. Olgularda primer hastalık göz önüne alındığında, 14'ü (% 93,3) malignensi nedeniyle, 1'i (% 6,7) mdr tbc nedeniyle opere edildi. Olgularımızın 11'i sağ standart pnömonektomi, 1'i sağ sleeve pnömonektomi, 1'i sağ bilobektomi inferior ve diyafram rezeksiyonu, 2'si sol standart pnömonektomi uygulandı. Endoskopik yöntemle n-butil siyanoakrilat kullanılarak bronkoplevral fistül onarımı uygulanan 15 hastanın 12'sinde başarı sağlandı ve başarı oranını %80 olarak belirlendi.

Sonuç: Sonuç olarak endoskopik metodla doğru teknikte uygulanan n-butil siyanoakrilat gibi doku yapıştırıcılarının, ucuz olmaları ve kolay uygulanabilmeleri nedeniyle özellikle 10 mm altındaki BPF'de ilk tercih olarak kullanılabilir tedavi yöntemlerinden biri olduğunu düşünüyoruz.

Anahtar kelimeler: bronkoplevral fistül, n-butil siyanoakrilat, bronkoskopi, endobronşiyal tedavi

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INTRODUCTION

Bronchopleural fistula (BPF), which occurs after pulmonary resection, is still one of the most feared and difficult to treat complications. In the analysis of large series, BPF rates after pulmonary resection (pneumonectomy, lobectomy, segmentectomy) ranged from 1.3% to 4.5% ⁽¹⁾. Various local and systemic risk factors have been identified such as comorbidities (nutritional status, chronic obstructive pulmonary disease, diabetes mellitus etc.), application of different technical methods ⁽²⁾ (pneumonectomy, bilobectomy, inferior lobe resection, manual closure, mechanical ventilation), advanced disease and residual tumor remnants ⁽³⁾. Although these factors are well known, they are often unmanageable ⁽⁴⁾. The location and size of the fistula are two main determining factors to choose between endoscopic procedures and open surgical approach. If the patient is severely cachectic or patients life expectancy is limited, palliation can sometimes be achieved via surgically creating pleura-skin pathway to permanently or temporarily drain the pleural cavity ⁽⁵⁾. Various bronchoscopic approaches have been tried as an alternative to surgery. While success rates are very variable, the lack of a consensus currently indicates the lack of optimal treatment. On the contrary, existing interventions appear to be complementary and point to the need for individualization of treatment ⁽⁶⁾.

The aim of this study was to determine the efficacy and long-term results of using n-butyl cyanoacrylate tissue adhesive (LiquiBand Medlogix PLYMOUTH, UK) in the closure of fistulas less than 10 mm.

MATERIAL and METHODS

Between February 2006- April 2010, 527 pulmonary resections were performed in Süreyyapaşa Chest Diseases and Thoracic Surgery Training and Research Hospital. Twenty-two patients developed BPF after surgery. The study included retrospec-

tive evaluation of 15 patients with fistula size of 3-10 mm that underwent endobronchial repair surgery (Figure 1).

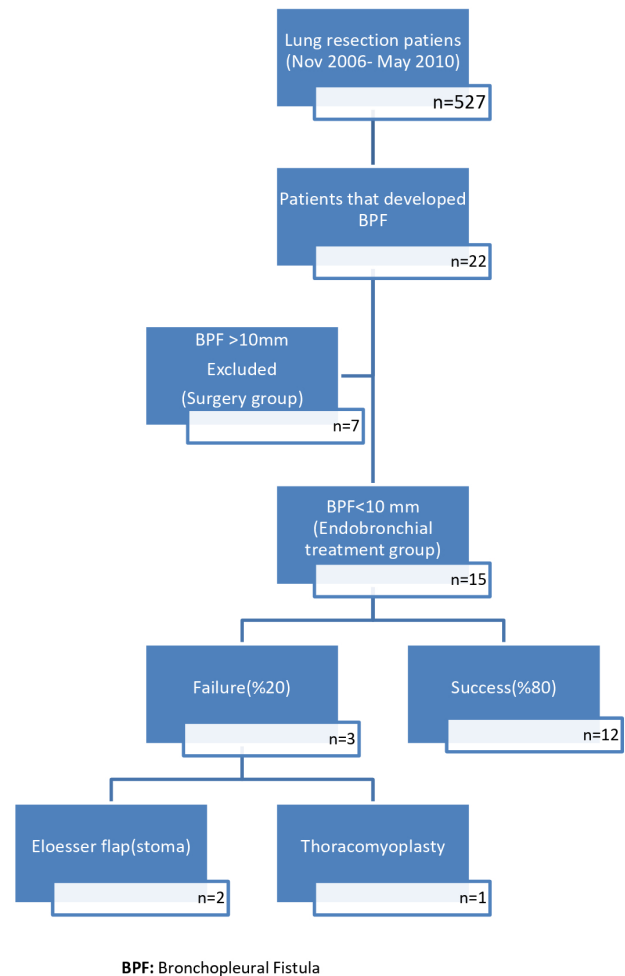


Figure 1. Participant flow chart.

Approval for the clinical trial was obtained from the Republic of Turkey University of Health Sciences İstanbul Süreyyapaşa Chest Diseases and Thoracic Surgery Research and Training Hospital scientific research committee (IRB Number: B10.4.İSM.4.34.59.27-133, Date: 22.01.2010).

Methods

Demographic characteristics of the patients such as age, and gender were analyzed. Also concomitant systemic diseases of the patients, steroid usage, malnutrition, adjuvant and neoadjuvant chemo/radiotherapy, pleuropulmonary

infections, remaining residual carcinomatous tissue in the bronchial stump, postsurgical stage of disease were accepted as risk factors for fistula formation. All this information was saved. Prior to the operation all patients underwent following tests such as: complete blood count, electrocardiogram, basic biochemical blood tests (sodium, potassium, chlorine, bicarbonate, BUN, magnesium, creatinine, glucose). All patients underwent physical examination, sequential PA/L (posteroanterior/lateral) chest radiography, bronchoscopy, endobronchial methylene blue injection and computerized thorax tomography (CT) for diagnosis. None of the cases underwent lung scintigraphy, sonogram or bronchography. In addition, bronchoscopy (biopsy, brushing, lavage, culture) and sputum examination were performed in all cases to screen for recurrence of multidrug-resistant tuberculosis and malignancy. All cases were classified as those having early (<1 month), intermediate (1-3 months), late (> 3 months) fistulas according to postoperative fistula drainage time. But for all cases, only the size of the fistula was taken into consideration for procedure decision. At the time of diagnosis, the tube thoracostomy was always performed. Eleven (73%) patients had pleuropulmonary infection which was the most common risk factor. For the treatment of infections of these patients, in addition to tube thoracostomy and antibiotherapy, we performed pleural cavity washing with 5% dacon. Post-pneumonectomy cavities were irrigated until the infection was resolved clinically and laboratory findings got better and drainage of the cases were reduced. All patients had preoperative nutrition support and optimal conditions were achieved.

Application of tissue adhesives (methyl-2 cyanoacrylate) during bronchoscopy for BPF repair described by Scappaticci et al (1994) was used in all patients (7). Patients with fistula up to 10 mm which was detected with FOB (fiberoptic bronchoscopy) underwent rigid bronchoscopy under general anesthesia. Firstly, oxygen saturation of

the patients was stabilized by entering the non-fistula side, and then the bronchoscope was directed to the fistula side. The fistulous area was dried with cotton, after the fistula was checked again with fiberoptic bronchoscope, about 2 cc of n-butyl cyanoacrylate was sprayed into the fistula orifice with the tip-cut Fogarty catheter. Immediately afterwards, 20 cc air was injected through the same Fogarty catheter. Then the remaining n-butyl cyanoacrylate was sprayed and the fistula mouth was dried. Again, the fiberoptic bronchoscope was used to check whether the fistula hole had been closed (Figure 2). To prevent the patient from coughing away the dried tissue adhesive (n-butyl cyanoacrylate), the patient was intubated and followed in intensive care unit without waking him/her up. After an average of 2 hours, the patient was extubated and awakened. While no complication was observed during the procedure, one patient had respiratory failure due to the escape of frozen cyanoacrylate into the intact lung in the postoperative period which was cleaned by emergency rigid bronchoscopy. The median follow-up period was 21 months (min.3, and max. 3 years).

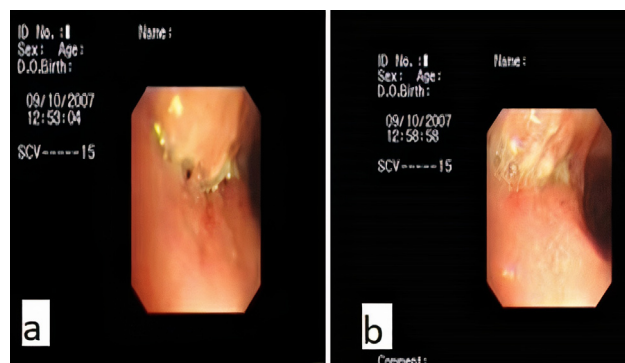


Figure 2. a. bronchoscopic view of fistula in the right main bronchus b. bronchoscopic view of fistula covered with N-butyl cyanoacrylate.

Statistical analysis

Clinical findings, pathologic diagnoses and sociodemographic features of the patients operated in our clinic were presented in numbers and percentages using descriptive statistical data.

RESULTS

Data for 15 patients were analyzed. All of the cases participated in the study were male and the age range was 50-80 (median: 61.3) years. Primary surgical indications were as follows: malignancy (n=14:93.3%), [including stage 1B (n=9), IIB (n=3), IIIB (n=1, IIIA (n=1) malignancies] multidrug-resistant tuberculosis (n=1: 6.7%). Right standard pneumonectomy was performed

in 11, right sleeve pneumonectomy in 1, right lower bilobectomy plus diaphragm resection in 1, and left standard pneumonectomy in 2 cases. For primary bronchial closure stapler was used in 10 (66.6%) 3-0 pds (polydioxanone) in 2 (13.3%) 3-0 prolene in 2 (13.3%) and 3-0 vicryl sutures in 1 case (6.6%). The cases included 15 patients with a fistula size of 3-10 mm. Diabetes mellitus (DM) was present in 7 cases and 5 patients received neoadjuvant therapy Table 1.

Table 1. Endobronchial BPF (bronchopleural fistula) treatment results with N-butyl cyanoacrylate.

Gender	Age/ year	Stage	Bronchial Closure	Etiology	Fistula size/mm	Fistula repair	Comorbidity
Male	55	Bronchial carcinoma (E-IB)	Primary 3-0 Pds	Left Pneumonectomy	3 mm	Exist	DM Pİ
Male	52	Bronchial carcinoma (E-IIIB)	Bronchial Stapler	Right Pneumonectomy	2 mm	Exist	CT Alb<2.5
Male	67	Bronchial carcinoma (E-IB)	Bronchial Stapler	Right Pneumonectomy	5 mm	Exist	Pİ
Male	53	Bronchial carcinoma (E-IIIB)	Bronchial Stapler	Right Pneumonectomy	3 mm	Exist	-
Male	66	Bronchial carcinoma (E-IB)	Primary 3-0 Vicryl	Right Pneumonectomy	8 mm	Exist	Pİ Alb<2.5
Male	75	Bronchial carcinoma (E-IB)	Bronchial Stapler	Right Pneumonectomy	7 mm	None	HT-SVO
Male	69	Bronchial carcinoma (E-IB)	Bronchial Stapler	Right Pneumonectomy	5 mm	Exist	HT-KOAH Pİ
Male	53	Bronchial carcinoma (E-IB)	Primary Prolen	Right Pneumonectomy	4 mm	Exist	DM-HT Pİ
Male	54	MDR-Tbc	Primary 3-0 Pds	Right Pneumonectomy	4 mm	None	Pİ Alb<2.5
Male	61	Bronchial carcinoma (E-IIIB)	Bronchial Stapler	Right Pneumonectomy	5 mm	Exist	DM Pİ
Male	59	Bronchial carcinoma (E-IB)	Bronchial Stapler	Right Sleeve Pneumonectomy	3 mm	Exist	HT, DM Pİ
Male	57	Bronchial carcinoma (E-IIIA)	Primary Prolen	Right Pneumonectomy	4 mm	Exist	Alb<2.5 CT-RT Pİ
Male	71	Bronchial carcinoma (E-IIIB)	Bronchial Stapler	Right Lower Bilobectomy + Diaphragm Resection	5 mm	None	HT, DM Pİ
Male	67	Bronchial carcinoma (E-IB)	Bronchial Stapler	Right Pneumonectomy	5 mm	Exist	-
Male	60	Bronş karsinomu (E-IB)	Bronchial Stapler	Right Pneumonectomy	4 mm	Exist	Alb<2.5 Pİ

HT: Hypertension DM:Diabetes mellitusPİ:Pleuropulmonary infections CT: ChemotherapyRT: Radiotherapy SVO: cerebrovascular case

Early fistulas (<1 month) were present in 8 (53%), and late fistulas (>1 month) in 7 patients (47%), the average drainage time of the early fistulas was 13.2 (8-27 days) days, and the average drainage time of the late fistulas was 88 (42-192) days. Re-thoracotomy and re-suturing was not performed in any early fistula cases with a fistula size between 2-5 mm.

Success was achieved in 12 of the 15 patients who underwent bronchopleural fistula repair using n-butyl cyanoacrylate by endoscopic method. The success rate was 80%. In 7 of the successfully managed patients this process had to be repeated 2 times, and in 2 patients this process had to be repeated 3 times. Twelve patients whose treatment was successful were followed up for an average of 21 months. A total of 4 patients were lost. Patients were accepted as late mortality (>30 days after the procedure). One case whose treatment was successful had distant metastasis detected during the follow-up period which caused the death of this patient. All of 3 patients with treatment failure were lost due to sepsis. When the culture results of 9 successful patients with pleuropulmonary infections were negative, modified Clagett method was applied and they were discharged after removal of their drains⁽⁸⁾. Drains of 3 patients without infection who had successful fistula closure were removed after an average of 4 (2-7) days before they were discharged. Mean hospitalization time of patients who had successful surgery was 21 days. In 3 patients three attempts were made per patient but procedure failed, so two of these patients underwent stoma surgery at a later stage. One patient whose endoscopic procedure failed underwent thoracomyoplasty. All of these 3 patients who were diagnosed with lung cancer, underwent right pneumonectomy (n=2) or left pneumonectomy (n=1). There was no mortality in the first postoperative month.

DISCUSSION

The most common cause of BPF is lung resec-

tion⁽⁹⁾. Once the diagnosis is made, a drain should be placed in the pleural cavity in order to evacuate empyema. The drain is also useful in preventing mediastinal shift and aspiration pneumonia. However, there are some difficulties in applying this maneuver for the following reasons: (I) Severe changes in anatomy due to elevated diaphragm and mediastinal shift after pneumonectomy. (II) Ideally tube needs to be placed in the bottom of the cavity to ensure effective drainage^(10,11). In addition to drain the cavity, the following measures should be taken for successful treatment: aggressive control of infection, obliteration of the residual cavity, and closure of the fistula with a vascularized tissue. Despite all advances in technology, the ongoing dilemma in choosing fistula treatment still increases mortality rates by up to 15%⁽⁴⁾. The choice of treatment depends on the patient's functional capacity, the size of the BPF, how long BPF has been present, and clinical characteristics of the disease. Aggressive surgical options such as thoracoplasty, omentopexy, open window drainage (stoma), intrathoracic muscle transposition, transsternal mediastinal approaches can be quite risky for this group of patients whose lungs have been already injured⁽¹²⁾. Some studies have shown that endoscopic procedures are useful and safe for these patients^(13,14). Endoscopic approaches may be the only curative alternative to open surgical repair, especially for patients who cannot be operated due to high surgical risk⁽¹⁵⁾. Different bronchoscopic techniques have been reported with various success rates depending on the size of BPF⁽¹⁶⁾. BPF size appears to be an important factor in predicting the outcome of the procedure. Endoscopic treatment is not suitable for BPFs larger than 8 mm. On the other hand endoscopic treatment in BPFs with a size of 1-3 mm is associated with the highest success rates⁽⁴⁾. As stated in some studies, bronchoscopic approaches had low success rates in fistulas larger than 5 mm⁽¹⁷⁾. Different endoscopic methods have been tried in patients with BPF, but these treatments were not compared with each other. In these methods, various mate-

rials were applied to the fistula area such as, gel foam and tetracycline ⁽¹⁸⁾, autologous blood patch ⁽¹⁹⁾, albumin glutaraldehyde tissue adhesive ⁽²⁰⁾, cryoprecipitate fibrin glue ⁽²¹⁾, n-butyl 2 cyanoacrylate ⁽⁷⁾. In the treatment of small size (<2-3 mm.) fistulas, submucosal 0.5-2ml polidocanol (hydroxypolyethoxydodecane) injection with 21 G needle under local anesthesia with the aid of fiberoptic bronchoscope is an alternative method ⁽²²⁾. N-butyl cyanoacrylate tissue adhesive (LiquiBand) has been used as a tissue adhesive for many years, with many advantages such as; proven effectiveness, easy application and low material price. In many areas cyanoacrylate has been used successfully including solid organs, vascular structures, abdominal wall surgical areas ⁽²³⁾. In addition, cyanoacrylate adhesives have been widely used in medicine for the closure of fistula or anastomotic leaks, including endoscopic control of gastric variceal bleedings ⁽²⁴⁾. In our study, the fact that most patients were not willing to undergo major surgery due to the high risk of the operation, it was used effectively for different methods. The high rate of failure in large fistulas has been recently eliminated with the use of the Amplatzer device as an effective and reliable method ^(16,24). The absence of an effective treatment for intermediate-sized fistulas has resulted in continued studies on this topic. In one of these methods, n-butyl cyanoacrylate tissue adhesive is injected into the fistula (3 mm <fistula <6 mm) with the aid of fiberoptic bronchoscope. The procedure mechanically occludes the fistula and causes a local inflammatory reaction that causes the proliferation of the bronchial mucosa. This mucosal proliferation process is responsible for the long-term closure of the fistula. The adhesive needs to be injected through a catheter to protect the bronchoscope duct. If the fistula is not completely closed, the procedure may be repeated at another adhesive dose at the same setting ⁽²⁵⁾. Chawla et al, reported success in 8 (88.8%) of 9 BPF cases using cyanoacrylate with the aid of fiberoptic bronchoscopy ⁽⁹⁾. Similarly, 80% success rate was achieved in our study.

Ueno et al. pointed out the importance of some factors for successful endoscopic cyanoacrylate treatment such as size, location, and depth of BPF, availability of adequate filling material and right application method ⁽²⁶⁾. Subacute and chronic forms of BPF are usually associated with infection which occurs more commonly in patients with multiple comorbidities, frail, and immunosuppressed patients. Subacute and chronic forms of BPF are usually associated with infections and they are more commonly seen in weakened and immunocompromised patients with multiple comorbidities. The subacute form is usually insidious and characterized with nausea vomiting, fever and weakness. However, chronic form causes infectious process and fibrosis on pleural surface ⁽²⁷⁾. In our study, coexistence of BPF with pleuropulmonary infection was observed in 11 cases (73%). We aimed to eliminate the infection in the pleural cavity by using preoperative irrigation and modified Clagett method in postoperative period, which we think is effective for the success of the procedure. Otherwise, BPF repair is difficult in cases with empyema. Endoscopic closure with glues, sclerosing agents or stents is considered impossible ⁽²⁷⁾.

Limitation: The limitation of our study was that we did not compare N-butyl cyanoacrylate with other endobronchial repair methods of BPF.

Conclusion

As a result, we think that application of tissue adhesives such as n-butyl cyanoacrylate by endoscope is a cheap and easily applicable method. If necessary, this method can be repeated successfully. Furthermore, if this method fails, this treatment will not lower success rates of further surgical treatments. We think that this method is one of the treatment methods that can be used as the first choice of treatment especially in BPFs smaller than 10 mm.

Conflict of Interest: The authors have no conflict of interest in this study.

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