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# Intraoperative bronchial stump air leak control by Progel® application after pulmonary lobectomy

Mohsen Ibrahim<sup>a,\*</sup>, Fioralba Pindozi<sup>b,†</sup>, Cecilia Menna<sup>c</sup> and Erino A. Rendina<sup>a</sup>

<sup>a</sup> Division of Thoracic Surgery, Sant'Andrea Hospital, 'Sapienza' University of Rome, Rome, Italy

<sup>b</sup> Division of General Surgery, Sant'Andrea Hospital, 'Sapienza' University of Rome, Rome, Italy

<sup>c</sup> Division of Thoracic Surgery, G. Mazzini Hospital of Teramo, University of L'Aquila, L'Aquila, Italy

\* Corresponding author. Division of Thoracic Surgery, Sant'Andrea Hospital, 'Sapienza' University of Rome, Via di Grottarossa 1035, 00189 Rome, Italy.  
e-mail: mohsen.ibrahim@uniroma1.it (M. Ibrahim).

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## Abstract

Diffuse tracheobronchial calcification is a physiological condition associated with advanced age, especially in women. A calcified bronchus can be fractured during major lung resections (lobectomy, bilobectomy, and pneumonectomy), exposing patients to intraoperative air leakage and broncho-pleural fistula (BPF) occurrence. We retrospectively evaluated the use of Progel® application on the suture line of bronchial stump after pulmonary lobectomy analysing the intraoperative air leak and BPF occurrence. Between January 2014 and December 2014, Progel® was applied in 11 patients who presented intraoperative bronchial fractures after suture resection by mechanical staplers and air leak from bronchial stump, in order to treat air leakage. Patients were 7 men and 4 women, aged between 56 and 81 years (mean age  $71.2 \pm 12.1$  years). Surgical procedures included 6 upper lobectomies (4 right, 2 left), 1 bilobectomy and 4 lower lobectomies (3 right, 1 left). Mean hospital stay was  $4.5 \pm 2.6$  days (2–8 days). None of the patients had postoperative air leakage. No Progel® application-related complications occurred. No other major complications occurred. No mortality occurred. Progel® proved to be useful in treating intraoperative air leakage during major lung resections, particularly those occurring as a result of fracture of the bronchus from a mechanical stapler.

**Keywords:** Lung cancer surgery • Surgery complications

## INTRODUCTION

Diffuse tracheobronchial calcification is a physiological condition associated with advanced age [1].

Tracheobronchial cartilage calcification is a relatively common finding on chest X-ray in the elderly population. It is typically associated with other conditions: chondrodysplasia punctata, adreno-genital syndrome, dystrophic dysplasia, history of warfarin therapy [1, 2]. Calcification of the tracheobronchial tree has been reported in 37% of patients over 75 years. Computed tomography scan demonstrated tracheobronchial calcification in 26% of patients aged between 40 and 59 years; this percentage rises up to 65% for men and 40.5% for women over 60 years. Another chest X-ray series of 200 patients aged between 90 and 102 years found tracheobronchial calcification in 55% of cases [3]. This condition usually does not have any clinical relevance and is rarely diagnosed because of its benign clinical course but a thick, calcified bronchus is often fragile and can be fractured during major lung resections (lobectomy, bilobectomy, and pneumonectomy), exposing patients to intraoperative or postoperative air leakage and broncho-pleural fistula (BPF) occurrence.

<sup>†</sup>The first two authors equally contributed to this work.

Various materials have been developed in order to support or replace sutures and staplers. Progel® is a polymeric hydrogel sealant, a combination of polyethylene glycol-based cross-linker, functionalized with succinate groups (PEG-(SS)2), with human serum albumin-USO added at the moment of usage. Once mixed, this sealant polymerizes to form a clear, flexible, cross-linked hydrogel matrix. This matrix at first contact with lung tissue strongly adheres to the tissue and follows its movements of expansion.

We retrospectively evaluated the use of Progel® on the suture line of bronchial stump after pulmonary lobectomy analysing the intraoperative air leak control and BPF occurrence.

## MATERIALS AND METHODS

Between January 2014 and December 2014, at our institution, Progel® was applied in 11 patients presenting intraoperative bronchial fractures after suture resection by mechanical staplers and consequent air leak occurrence from bronchial stump, in order to treat air leakage. Informed consent was obtained from all patients. Patients were 7 men and 4 women, aged between 56 and 81 years (mean age 71 years). Eight patients had history of chronic obstructive pulmonary disease (COPD); 9 patients had smoking

habit. All the surgical procedures were performed via muscle-sparing thoracotomy. Patients' characteristics are given in Table 1.

Progel® was applied on the staple lines in a discrete quantity at first (one-third of the provided vial of 4 ml). One minute later, it was re-applied in greater quantity (the last two-thirds of provided vial), to incorporate the nearest 2 cm of tissue.

Intraoperative air leakage was assessed by saline submersion test under airway pressure up to 25 cm H<sub>2</sub>O. To determine air leakage, Macchiarini scale was used (0 = absent, no bubbles; 1 = mild, countable bubbles; 2 = moderate, stream of bubbles; 3 = severe, coalesced bubbles) [4]. Patients with grade 1 or 2 air leaks received reinforcement of bronchial stump with Progel®. Patients with grade 3 air leaks underwent further suturing followed by a supplementary submersion test: if the new air leak score downgrades to 1 or 2, Progel® was applied. Suturing the bronchial stump could further damage the adjacent fragile bronchial tissue and cause ischaemia, increasing the risk to develop the dehiscence. Once Progel® was applied, another submersion test was performed.

Postoperative air leakage and volume of drained pleural fluid were assessed every 24 h up to drain removal. Chest tube permanence, postoperative complications and hospital stay were assessed.

The aim of the study is to show the efficacy of the Progel® in treating intraoperative air leakage during major lung resections, particularly due to fracture of the bronchus from mechanical stapler.

## RESULTS

Surgical procedures included 6 upper lobectomies (4 right, 2 left), 1 bilobectomy and 4 lower lobectomies (3 right, 1 left). Histological findings were 5 adenocarcinomas, 3 squamous cell carcinomas, 2 benign conditions, 1 bronchial carcinoid.

The intensity of air leakage after the first water submersion test was grade 1 in 7 patients, grade 2 in 3 patients, whereas only 1 patient had grade 3 air leakage. This last patient, after further suturing of the suture line, downgraded to grade 1 air leakage;

successively Progel® was applied. All patients had grade 0 air leakage after Progel® application.

Results are given in Table 2. One patient presented atrial fibrillation treated with specific therapy and daily cardiologist assessment resolved in 3 days, one patient presented atelectasis of the right side after a right upper lobectomy detected at the postoperative day 1 routine X-ray chest. Secretion retention was removed from the right lower lobar bronchus by flexible bronchoscopy. None of these complications was considered to be related to Progel® use. No perioperative mortality occurred. Drainage tube permanence was 4.1 ± 1.8 days (2–7 days). Mean hospital stay was 4.5 ± 2.6 days (2–8 days). No postoperative air leak and consequent BPF occurred.

All the patients underwent clinical examination at 1 week after surgical procedure and chest X-ray with clinical examination at 1 month after surgical procedure, without reporting any postoperative complication.

## DISCUSSION

Intraoperative bronchial stump air leakage during lung surgery remains one of the major complications that thoracic surgeons have to face with in their daily practice because of the risk of BPF [5]. While minor air leakage can be treated easily, persisting air leakage (on or after postoperative day 5) often contributes to increase morbidity (longer drainage, greater postoperative pain, increased risk of infections and/or thromboembolism), length of hospitalization and costs [6]. Air leakage from bronchial stump put the patient at high risk to develop empyema and BPF with a dramatic mortality rate. Since air leakage and BPF can be life-threatening conditions leading to high morbidity and mortality, prevention is the first measure thoracic surgeons have to adopt. Preoperative conditions like anaemia, COPD, diabetes, infections and malnutrition must be first addressed and treated prior to surgery. During surgery, excessive bronchial devascularization, excessive use of electrocautery, ligation of bronchial arteries could lead to BPF [7]. Intraoperative repair of air leak from suture lines on the bronchus is considered essential for the prevention of postoperative development of BPF [8]. In addition to suturing the bronchial stump, other several intraoperative techniques have been developed to reduce intraoperative air leakage from the bronchial stump [9]. Bronchial stump can be reinforced and covered with vascularized tissues, such as omentum, pleura,

**Table 1:** Clinical characteristics of patients

Variable	Patients (n = 11)
Sex	
Male (n/%)	7/64
Female (n/%)	4/36
Mean age/SD/range (years)	71.2/12.1/56–81
Smoking (n/%)	9/82
Active	7/78
Former	2/22
COPD (n/%) <sup>a</sup>	8/73
Stage I	5/63
Stage II	3/37
Surgery (n/%)	
Upper lobectomy (4 right, 2 left)	6/55
Bilobectomy (middle/lower lobe)	1/9
Lower lobectomy (3 right, 1 left)	4/36

SD: standard deviation; COPD: chronic obstructive pulmonary disease; FEV1: forced expiratory volume in 1 s.

<sup>a</sup>According to GOLD COPD Guidelines 2011.

**Table 2:** Results

Variable	Patients (n = 11)
Hospital stay (mean/SD/range, years)	4.5/2.6/2–8
Duration of drainage tube (mean/SD/range, days)	4.1/1.8/2–7
Intraoperative bronchial stump air leak <sup>a</sup> (n/%)	0/0
Postoperative air leak (n/%)	0/0
Postoperative complications (n/%)	
Atrial fibrillation	1/9.1
Atelectasis	1/9.1
Mortality (n/%)	0/NA

NA: not applicable; SD: standard deviation.

<sup>a</sup>After Progel application.

pericardium, intercostal muscle [8]. In fact, pedicled vascular flaps guarantee early neoangiogenesis and stimulate microcirculation. In addition to traditional surgical techniques, buttressing the staple line and using sealing agents, such as fibrin sealants, synthetic hydrogels and collagen fleece-bound sealants, are the newest techniques to close the leaks. A Cochrane database showed that surgical sealants are able to reduce postoperative air leaks [9]. Lung surgical sealants are especially useful intraoperatively in patients at highest risk of prolonged air leakage: patients with COPD, emphysema, forced expiratory volume in 1 s less than 35% of predicted value, and those with intraoperative large air leaks [9].

Progel® is a polymeric hydrogel sealant, which is easy to apply, rapid acting, highly adherent, flexible, tear-resistant, biodegradable, safe and effective.

A pivotal randomized controlled, multicentre clinical trial demonstrated that Progel® is safe and efficient in the management of intraoperative pulmonary air leaks [10]. It has been proven to be superior to standard intraoperative air leak closure methods in reducing intraoperative and postoperative pulmonary air leaks and length of hospitalization [10]. No difference in morbidity, mortality, duration of chest tube drainage and immune responses has been noticed when two groups of patients were compared [10]. Moreover, the cost of Progel® is 380€. Since January 2014, we have decided to apply Progel® when a bronchial fracture and consequent air leak from bronchial stump occurred in patients with calcified bronchus stump undergoing pulmonary lobectomy through mechanical stapler. After Progel® was applied, the intensity of air leakage was Grade 0 in all patients. All the patients underwent clinical examination at 1 week after surgical procedure and chest X-ray with clinical examination at 1 month after surgical procedure, without reporting any complication. Since this is a retrospective study, it lacks data regarding a control group without the use of Progel® to repair intraoperative air leak. However, in cases of the absence of intraoperative and postoperative air leakage, application of Progel® on the bronchial stump can be considered to be encouraging. The present study clearly showed that Progel® can be useful in treating intraoperative air leakage from the bronchial stump line suture during major lung resections. In conclusion, our new method to repair intraoperative air leaks from the bronchial stump might be helpful for thoracic surgeons

as an alternative, less invasive and faster procedure to deal with intraoperative air leak from bronchial stump.

Larger cooperative prospective randomized studies need to be conducted in order to establish more powerful conclusions regarding the use of Progel® for intraoperative air leakage.

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**Conflict of interest:** none declared.

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