# Progel Use is Not Associated with Decreased Incidence of Postoperative Air Leak after Nonanatomic Lung Surgery

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## ABSTRACT

**Context:** Progel Pleural Air Leak Sealant (CR Bard, Warwick, RI) is a US Food and Drug Administration-approved hydrogel designed for application to surgical staple lines to prevent air leak after lung surgery. This product has demonstrated efficacy in reducing intraoperative air leaks compared with standard air leak closure methods. However, the impact on chest tube duration and length of hospital stay has not been reported.

**Objective:** To evaluate the effect on rates of postoperative air leak, chest tube duration, and hospital stay in surgical patients with and without use of Progel.

**Design:** Retrospective study of 176 patients aged 18 to 80 years who underwent video-assisted thoracoscopic wedge resections between 2014 and 2016. Eighty-four (48%) cases using Progel were included, as well as a representative sample of non-Progel cases (n = 92; 52%).

**Main Outcome Measure:** Presence of postoperative lung air leak.

**Results:** No difference existed between the Progel and non-Progel groups in the rate of postoperative air leak (20/84, 23.81% Progel; 16/92, 17.39% non-Progel; p = 0.33). The length of time patients had a chest tube was similar (23.5 vs 23 hours, p = 0.721), as was percentage of patients with a less than 2-day hospitalization (77.17% non-Progel vs 82.14% Progel, p = 0.414).

**Conclusion:** Our results suggest that Progel, used routinely in patients undergoing non-anatomic lung resection, does not have a significant impact on postoperative air leak, chest tube duration, or length of hospital stay. Further studies are warranted to evaluate the utility of Progel in reducing postoperative complications after thoracoscopic wedge resection in those treated for air leak or in the reduction of postoperative air leak in high-risk patients.

## INTRODUCTION

Postoperative parenchymal air leak is one of the most common complications of lung surgery and when prolonged may result in substantial morbidity and mortality. The incidence of air leak after nonanatomic lung resection is variably reported to be between 30% and 60%, and *prolonged air leak,* defined as persisting greater than 4 days after surgery, has an incidence of 5% to 10%.[1,2] Intraoperative air leaks are not typically clinically significant and resolve spontaneously within hours of surgery by apposition of the lung to the parietal pleura. However, persistent air leaks increase the length of hospital stay, duration of chest tube use, expense to hospitals and patients, and risk of other postoperative complications such as pneumonia and empyema.[3,4] Air leak after lung resection has been described as the most important factor in determining the length of postoperative hospital stay.[2]

Several intraoperative maneuvers, such as use of buttressed staples, oversewing staple lines, and use of sealants, are often employed. However, the utility of each method is poorly understood. Cochrane Database Review meta-analyses report that sealants reduce postoperative air leak and chest tube duration but have no effect on length of hospital stay.[5] However, these reports evaluate multiple studies simultaneously and do not distinguish type of sealant used, protocol followed, or type of surgical procedure performed.

Progel Pleural Air Leak Sealant (CR Bard, Warwick, RI, formerly by NeoMend Inc) is a US Food and Drug Administration-approved hydrogel designed for application to surgical staple lines to prevent air leak after lung surgery. In a single prospective, randomized clinical trial, this product has demonstrated efficacy in reducing intraoperative air leaks during open, anatomic and nonanatomic lung resections compared with standard air leak closure methods, as well as in decreasing length of hospital stay.[6] A second study, a retrospective chart review of patients undergoing open or minimally invasive, anatomic or nonanatomic lung resections reported decreased rates of postoperative air leak and chest tube duration. Again, Progel was used only on patients with visible intraoperative air leak.[7] The utility of Progel in video-assisted thoracoscopic surgery and nonanatomic resections has not been determined, to our knowledge.

We performed a retrospective analysis of patients who underwent video-assisted thoracoscopic wedge resections with and without the use of Progel to evaluate the effect on the rate of postoperative air leak, chest tube duration, and hospital stay.

## METHODS

We performed a retrospective study of patients aged 18 to 80 years who underwent video-assisted thoracoscopic wedge resections performed by board-certified thoracic surgeons from 2014 to 2016. Surgeries were performed at 1 of more than 10 hospitals within a single institution. We initially identified 491 qualifying wedge resections performed by 4 surgeons known to use Progel sealant. Eighty-four cases using Progel were identified by searching for the terms *Progel*, *sealant*, or *glue* in the operative report and then verified by close clinical review. A random sample of 92 Progel-unexposed patients were chosen from the remaining cases using a proportional sampling method stratified by surgeons (Figure 1). Progel was used at the discretion of the operating surgeon, whether or not a visible intraoperative air leak was present. Patients were excluded after careful clinical review if they had

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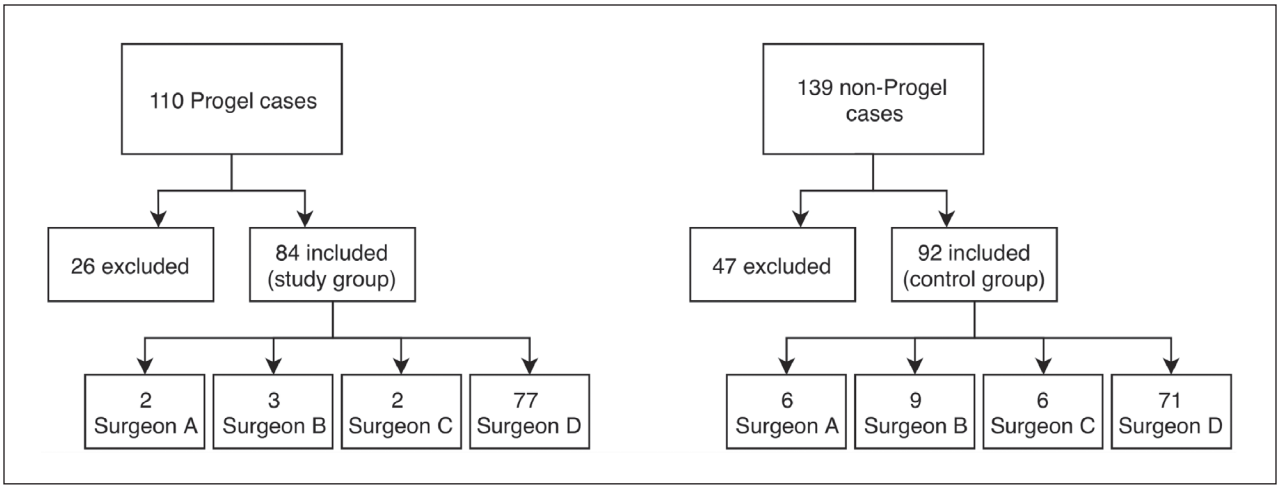


Figure 1. Patient selection for Progel and non-Progel groups.

other forms of staple line reinforcement, pleurodesis, open surgery, or postoperative positive pressure ventilation. The study was approved by the Kaiser Permanente Northern California institutional review board.

When used, Progel was applied to staple lines in an even coat, in the manner indicated by the manufacturer. All patients received chest tubes intraoperatively, which were placed to -20 mmHg suction. Each patient underwent an upright plain film of the chest within 90 minutes of completion of surgery to evaluate chest tube location and for presence of pneumothorax. Chest tube removal was performed when patients demonstrated no *air leak,* defined as air passing through the water seal chamber, and no clinically significant pneumothorax. Patient comorbidities were indexed, including type 2 diabetes mellitus and chronic obstructive pulmonary disease, as was a history of thoracic radiotherapy, exposure to chemotherapy, or ipsilateral thoracic surgery.

Patient characteristics by Progel exposure status were described and compared using $\chi^2$ or Fisher exact test for categorical variables and the Kruskal-Wallis test for continuous variables.

The primary endpoint was the presence of postoperative lung air leak identified at any time during hospitalization. Secondary endpoints included postoperative *pneumothorax* (defined as pneumothorax seen on chest radiography performed within 90 minutes of surgery completion), length of time with chest tube, discharge to home with chest tube, length of hospital stay, 30-day readmission, 30-day pneumothorax, and 30-day mortality. Patient outcomes by Progel exposure status were compared using the same bivariate statistics described in the previous paragraph.

## RESULTS

Clinical features of both Progel-exposed and unexposed groups are shown in Table 1. The median patient age was 66 years for the unexposed group and 65 years for the Progel-exposed group. Most patients in both groups underwent surgery for removal of a lung nodule. Both groups were evenly divided between men and women. Type 2 diabetes mellitus was the most common of the tracked comorbidities, affecting approximately one-fourth of both groups. After exclusions were made, 77.17% of Progel-unexposed surgeries and 91.67% of Progel-exposed surgeries were done by a single surgeon (Table 1). There were no further statistical or clinically relevant differences in demographics, diagnoses, history, or indication for surgery in comparing Progel-exposed and unexposed groups. Two patients in the Progel group (2.38%) had an intraoperative air leak, 1 of whom also had a postoperative air leak. No patients in the non-Progel group had a documented intraoperative air leak (p = 0.2264).

No statistically significant difference between patients who did or did not receive Progel was found in the primary endpoint or any secondary endpoint (Table 2). Patients in the control and study groups had similar rates of postoperative air leak (20/84, 23.81% in the Progel group; 16/92, 17.39% in the unexposed group; p = 0.33). Approximately half of these air leaks were clinically significant, defined as necessitating discharge to home with a chest tube in place (9.52% of Progel group vs 6.67% of unexposed group, p = 0.49). Thirty-four patients in each group had a pneumothorax visible on chest radiography performed in the upright position within 90 minutes of surgery completion (p = 0.632). Operative mortality was 1% in both unexposed and Progel-exposed groups and was secondary to ischemic stroke and colonic perforation in the setting of high-dose corticosteroid administration. This study was not powered to detect variation in outcomes stratified by comorbidities.

## DISCUSSION

Postoperative air leak after lung resection is a common complication, with a reported incidence as high as 60%.[1–3] Reduction of postoperative air leak is a significant target to reduce morbidity and cost associated with lung surgery.[3] There are several methods designed to reduce the incidence of air leak, including use of buttressed staples and sealants. Progel is a hydrogel sealant intended for intraoperative application to staple lines to reduce air leaks. It is applied with a blunt syringe, readily adheres to lung parenchyma, and stretches as the lung is reinflated, allowing maintenance of staple line coverage.

Studies evaluating its efficacy are limited, but the results suggest its use is associated with reduced intraoperative air leak for open anatomic lung resections, and with superiority to use of buttressed staples and staple line reinforcement with sutures. A single retrospective study of 121 consecutive patients who underwent any type of lung surgery and demonstrated an intraoperative air leak with or without use of Progel showed marked reduction in postoperative air leak, chest tube duration, and length of hospital stay.[7]

The use of Progel has not been studied specifically in patients undergoing nonanatomic lung resection or video-assisted thoracoscopic surgery. To our knowledge, no study has evaluated the prophylactic use of Progel in this patient population. We evaluated 176 patients undergoing video-assisted thoracoscopic wedge resection with or without the use of Progel, regardless of visible intraoperative air leak. No statistical or clinically meaningful difference was demonstrated in the rates of postoperative air leak, chest tube duration, or length of hospital stay between the 2 groups. Complication rates between the study and unexposed groups were similarly low. Routine use of Progel as a prophylactic agent to prevent postoperative air leak and to reduce hospitalization time is not supported by this study.

This study is limited by study size, which was not powered to detect variation in outcomes related to comorbidities. Although there was no statistically significant difference between participating surgeons, there was a trend toward significance (p = 0.078), despite sampling efforts employed to ensure a similar distribution by surgeon. Unequal case distribution between surgeons could introduce selection bias, and it limits generalizability of the outcomes.

There were 2 Progel-exposed patients for whom intraoperative air leak was noted, 1 of whom also had a postoperative air leak. The absence of intraoperative air leak in the non-Progel group may represent a source of selection bias. However, the number of patients with a postoperative air leak was exponentially higher than the small number of patients with an intraoperative air leak, which minimizes this effect and questions the association between the presence of intraoperative and postoperative air leaks. Equalization of postoperative outcomes despite the higher incidence of intraoperative air leak may be suggestive of a benefit to the use of Progel. Patients in the Progel and non-Progel groups had similar rates of postoperative air leak, few of which affected clinical management. It is possible that low rates of clinically significant postoperative air leak further limited the study power, although the proportions are very similar. Variability in the time from decision to remove a chest tube to the time of removal may also skew the mean chest tube duration. Furthermore, this patient group underwent thoracoscopic wedge resection for diagnosis of interstitial lung disease or for

**Table 1. Descriptive characteristics of the Progel[a] and non-Progel cohorts**

| Descriptor | Non-Progel (n = 92, 52.27%) | Progel (n = 84, 47.73%) | p value[b] |
|---|---|---|---|
| Age, y | | | |
| Median | 66.5 | 65.0 | 0.568 |
| Interquartile range | 60-71 | 55-71.5 | |
| Sex, no. (%) | | | |
| Women | 47 (51.09) | 41 (48.81) | 0.763 |
| Men | 45 (48.91) | 43 (51.19) | |
| Diagnoses and History, no. (%) | | | |
| History of radiation | 4 (4.44) | 4 (4.76) | > 0.99 |
| History of chemotherapy | 3 (3.33) | 5 (5.95) | 0.485 |
| History of thoracic surgery | 0 (0) | 3 (3.57) | 0.110 |
| History of DM type 2 | 25 (27.78) | 21 (25.00) | 0.678 |
| COPD | 12 (13.33) | 12 (14.29) | 0.856 |
| Indication for surgery, no. (%) | | | |
| Interstitial lung disease | 32 (34.78) | 25 (29.76) | 0.477 |
| Nodule | 60 (65.22) | 59 (70.24) | |
| Surgeon, no. (%) | | | |
| A | 6 (6.52) | 2 (2.38) | 0.078 |
| B | 9 (9.78) | 3 (3.57) | |
| C | 6 (6.52) | 2 (2.38) | |
| D | 71 (77.17) | 77 (91.67) | |

[a] Progel Pleural Air Leak Sealant (CR Bard Inc, Warwick, RI).
[b] Categorical p values calculated using $\chi^2$ or Fisher exact test; continuous p values calculated using Kruskal-Wallis test.
COPD = chronic obstructive pulmonary disease; DM = diabetes mellitus.

**Table 2. Postoperative and 30-day outcomes among Progel[a] and non-Progel cohorts**

| Outcome, no. (%) unless noted otherwise | Non-Progel, n = 92 (%) | Progel, n = 84 (%) | p value[b] |
|---|---|---|---|
| Intraoperative leak | 0 (0) | 2 (2.38) | 0.226 |
| Postoperative pneumothorax | 34 (36.96) | 34 (40.48) | 0.632 |
| 30-dy pneumothorax | 1 (1.12) | 0 (0) | > 0.99 |
| Postoperative leak | 16 (17.39) | 20 (23.81) | 0.326 |
| 30-d readmission | 8 (8.89) | 4 (4.76) | 0.283 |
| 30-d mortality | 1 (1.12) | 1 (1.19) | > 0.99 |
| Discharge with chest tube | 6 (6.67) | 8 (9.52) | 0.489 |
| Length of stay < 2 d | 71 (77.17) | 69 (82.14) | 0.414 |
| Chest tube duration, h | | | |
| Median | 23.5 | 23 | 0.721 |
| Interquartile range | 20-29 | 20-27 | |

[a] Progel Pleural Air Leak Sealant (CR Bard Inc, Warwick, RI).
[b] Categorical p values calculated using $\chi^2$ or Fisher exact test; continuous p values calculated using Kruskal-Wallis test.

nodule resection. The broad inclusion criteria could mask a statistically significant result among patients with certain pulmonary pathologic findings or comorbidities.

## CONCLUSION

Future studies should evaluate the utility of Progel to reduce postoperative air leak by surgery type, in open vs video-assisted thoracoscopic surgery, and in patients with elevated risk of postoperative air leak. Patients with comorbidities that increase the risk of air leak are at particular risk of prolonged postoperative air leak, including those with chronic obstructive pulmonary disease, with impaired wound healing, or those receiving positive pressure ventilation. Understanding the potential benefit of lung sealant in these patients would be of particular utility. Additionally, Progel should be evaluated against other established methods to reduce postoperative air leak, including buttressed staples and oversewing. Chest tube duration, length of stay, and cost should be secondary endpoints in follow-up studies. Additional studies with greater power are required to determine efficacy in reducing complications when Progel is used prophylactically. ❖

**Disclosure Statement**

*The author(s) have no conflicts of interest to disclose.*

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### Five Things

Five things are proper to the duty of a Chururgian: To take away that which is superfluous; to restore to their places such things as are displaced; to separate those things which are joined together; to join those things that are separated; and to supply the defects of nature.

— Ambroise Paré, 1510-1590, French barber surgeon