

Peer Review File

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Reviewer A

Structure:

- the article reflects the standard layout of a scientific article.

Materials and methods:

- Patient selection is on point, and the author specifically excluded the most common causes of selection bias.

Results:

- Data shows a clear statistical difference between the two groups regarding air leaks and operation time. The use of propensity score matching is on point, considering the retrospective nature of the study and the low population.

Relevance:

- This study is relevant, as air leak is a relatively common finding in lung resections, the use of felt could directly reduce hospital stay and rate of post-op complications, and it's a welcome addition to the surgeon's arsenal.

Strong points and weaknesses:

- The study confronts felt vs non felt stapling devices in a concised, precise, and well thought manner. Population, despite scarce, is matched using propensity score and reaches statistical significance.
- Confounding factors such as the use of both felt and non-felt staplers was correctly addressed as an exclusion factor.
- As stated by the author, low population count directly impeded to assess the role of pleural adhesions, which is a common factor in air leaks and blood loss.

References:

- References are on point.

Language clarity:

- Language is clear and understandable.

Recommendation of acceptance:

I recommend acceptance of this article without further revision.

Reply:

We appreciate Reviewer A's positive feedback.

Reviewer B

The authors present a retrospective study of patients that underwent pulmonary resections in their hospital between 2013 and 2021, attempting to assess the impact of the introduction of staplers with polyglycolic acid felt (PGA) in 2015 on pulmonary air leakage. The propensity scoring methodology based on the systematic review by Attaar and colleagues appears adequate for these purposes, correcting for patient characteristics that may influence the incidence of pulmonary air leakage.

The main issue with retrospective study methodology, concerns the question of causality, which should be scrutinized in the discussion. In this regard, I have several questions that I ask the authors to comment on:

- What other variables may influence the operating time in the PGA felt group?

Reply:

We thank Reviewer B for his/her important remarks.

We believed that the surgeon's experience and the learning curve may influence the operating time.

We have added this as a limitation in the Discussion section (Page 10, line 191).

- Is it possible that learning curve effects may have played a role due (e.g. between 2013 and 2015 for the non-PGA felt group and 2015 and 2021 for the PGA felt group)?

Reply:

Several surgeons performed the surgery between 2013 and 2021, so we are unable to present data showing the learning curve.

- What was done in the cases where intra-operative air leak was observed (e.g. do you have data to support higher use of other lung sealing products in these cases, increasing operating time)?

Reply:

If the intraoperative air leak was observed, additional sutures were usually performed. If the air leak was still persistent, we added fibrin glue application or thrombostatic sealant application. Although there were no positive data on the time of additional procedures due to intraoperative air leaks, it was clear that there was a prolongation of operative time due to additional procedures.

I also have several questions regarding the methodology:

- How was intra-operative air leak measured retrospectively? Was this based on operation reports? Were there any changes in how air leak was assessed intraoperatively in the study period? Was any attempt made to quantify the severity of the air leaks?

Reply:

We checked the intra-operative air leak using the operation reports and videos. There were no changes in how air leak was assessed intraoperatively in the study period. We did not make any attempt to quantify the severity of the air leaks.

We have added text on Page, line in the Methods section (Page 5, line 90).

- Do you have any data regarding the incidence of post-operative air leaks (i.e. drainage duration, time until drain removal)?

Reply:

We have added the incidence of prolonged air leak and drainage duration in the Methods, Results and Discussion section (Page 5, line 81-85) (Page 6, line 95-96) (Page 7, line 115-118) (Page 8, line 142-144) (Page 8, line 152) (Page 10, line 184-185) and table 3.

- Do you have any data regarding post-operative complications between the groups?

Reply:

We have added the incidence of post-operative complications between the groups in the Methods (Page 6, line 96) (Page 7, line 116) and table 3.

I am looking forward to your response and further considerations. Thank you for your efforts.

Reviewer C

I am honored to have an opportunity to review this article describing whether a stapling device with PGA felt reduce intraoperative air leak. The reviewer congratulates the authors on their hard work. The manuscript is well written, but some concerns should be addressed.

1. COPD has been investigated, but what about IP complications?

Reply:

We thank Reviewer C for his/her important remarks.

Meta-analysis of preoperative and intraoperative risk factors for prolonged air leaks by Attar et al. reported that interstitial pneumonia is not included as a risk factor for postoperative air leakage. Therefore, it was omitted from our study.

2. Was COPD defined solely by pulmonary function test results? I believe it is the strength of emphysema in the lung parenchyma that affects air leakage from the staple line during the surgery.

Reply:

Although the degree of emphysema may affect air leakage from the staple line, COPD was defined solely by

pulmonary function in this study. This is because previous studies in postoperative air leaks have also defined COPD by lung function and reported an association between them.

3. Since this is a retrospective study, it is unclear what stapler with PGA felt was used in which cases and for what reason. If the authors did not use it in all cases, there must be a reason why the authors used it.

Reply:

Staples with PGA sheets have been used since 2015 to reduce air leakage from staple lines. However, there are no specific criteria for using PGA sheets, and it is largely up to the surgeon's intraoperative judgment. Therefore, this study was designed to address this clinical question.

4. I think it is more important whether there is no air leak postoperatively than whether there is no air leak during the intraoperative sealing test. Even if there was no leak during the intraoperative sealing test, how many cases were there of postoperative leakage from the chest drain or delayed pulmonary fistula? We also need information on the duration of postoperative drainage, frequency of drain reinsertion, and length of postoperative hospital stay.

Reply:

We have added the incidence of prolonged air leak, drainage duration, and length of postoperative hospital stay in the Methods, Results and Discussion section (Page 5, line 81-85) (Page 6, line 95-96) (Page 7, line 115-118) (Page 8, line 142-144) (Page 8, line 152) (Page 10, line 184-185) and table 3.

5. I don't think Table 4 makes much sense; 70% are lobectomies or segmentectomies, which would naturally affect air leaks. I think there are many other factors that can affect it, such as detailed surgical procedure and fused fissure. I think this is out of line with the main point of this paper.

Reply:

We have excluded multivariate analyses of intraoperative air leak in conventional stapler group. We have removed Table 4.

Reviewer D

It is one of the most important things to reduce postoperative air-leak after pulmonary resections in thoracic surgeons because it can cause additional morbidities as the author insisted. Therefore, this retrospective study focusing on the usefulness of the stapler with bioabsorbable polyglycolic acid felt to avoid postoperative air-leak is very interesting.

However, this study has a serious problem.

The primary endpoint was set on the occurrence of intraoperative air-leak, which seemed serious mistake. If the sealing test was not appropriately performed, the occurrence of intraoperative air-leak was not detected, followed by the detection of the air-leak via drainage bottle, which frequently happened. I recommend that postoperative drainage time is better for the primary endpoint in this study.

Moreover, if the author changes the primary endpoint, wedge resection should be excluded from this study because postoperative air-leak after wedge resection is easy to be ceased compared to anatomical lung resections due to the large remaining lung volume.

Reply:

Thank you for your comment. We respectfully disagree that the primary endpoint was set on postoperative drainage time for the usefulness of the stapler with bioabsorbable polyglycolic acid felt because postoperative drainage time is reduced through a variety of factors, including additional intraoperative procedures such as fibrin glue application, thrombostatic sealant application, and low-pressure coagulation. Furthermore, the cause of postoperative air leaks cannot be identified without reoperation at the air leak point, and it is not known if the air leak is related to the staple line. As you have pointed out, it is important to discuss postoperative air leaks.

We have added that the secondary endpoint was the prolonged air leaks in the Methods, Results and Discussion section (Page 5, line 81-85) (Page 6, line 95-96) (Page 7, line 115-118) (Page 8, line 142-144) (Page 8, line 152) (Page 10, line 184-185) and table 3.

Minor problems were as below.

1. "Taco-seal" in line 59 should be changed to "thrombostatic sealant".

Reply:

We have changed from "Taco-seal" to "thrombostatic sealant" (Page 6, line 103).

2. Why was bilobectomy excluded?

Reply:

Bilobectomy was excluded from this study because of its large resection area and the high potential for intraoperative pulmonary fistula.

3. Please describe how to evaluate the occurrence of intraoperative air leak precisely.

Reply:

We checked the intra-operative air leak by using the operation reports and videos.

We have added text on Page, line in the Methods section (Page 5, line 90).

Reviewer E

Congratulations on your work.

I read with interest the paper from Makino et al. named: 'Can a stapling device with bioabsorbable polyglycolic acid felt reduce intraoperative leak.'

This is a retrospective observational single-center study on the potential advantages of using reinforced staplers for lung resections.

To begin with some general remarks regarding the paper as a whole.

- The text contains many grammatical and syntax errors, which somewhat influence the meaning. An English-speaking person should review the text before re-submission.

- Many lengthy sentences make it difficult to even follow the text at some points.

- Throughout the whole paper, there is much repetition. The most representative example is the reference of the 2 study groups (PGA felt group and the non-PGA felt group). I would suggest referring to the 'non-PGA felt group' as a conventional stapler or even a conventional group.

- Last but not least, the authors jump to a bold conclusion on line 47 (based on one single retrospective study), supporting the hypothesis that postoperative complications are risk factors for lung cancer recurrence.

Reply:

We thank Reviewer E for your valuable comment.

We have revised the entire manuscript by an English-speaking person.

We have changed from the non-PGA felt group to the conventional stapler group throughout the manuscript.

More specifically

- Throughout the whole text, I would suggest correcting the word 'staples' with staplers

Reply:

We have changed the word 'staples' to 'staplers' throughout the manuscript.

- In line 31, it is stated that 70.7% of patients in the non-PGA group underwent wedge-resection. This percentage seems false, and this mistake is repeated throughout the text.

Reply:

We have changed from 70.7% to 29.3% (Page 2, line 32) (Page 8, line 134).

- Line 45: In case of an air leak postoperatively, the thoracic drain would be left in place, and no 'placement of a thoracic drain' is necessary. Please rephrase,

Reply:

We have changed from placement of a thoracic drain to "a thoracic drain is left in place" (Page 4, line 47).

Line 51: 'Automatic sutures are used in lung resection': Do you mean motorized staplers by that, or what exactly? Please clarify.

Reply:

We have revised the term from "automatic sutures" to "the conventional staplers" (Page 4, line 53).

Lines 51-51: The percentage of air leakage you refer to is postoperatively and not intraoperative. Please correct accordingly. This point is also a significant factor that undermines the study. The intraoperative leakage could potentially be of minor importance, and there is no information regarding the amount of leakage (neither in ml/min nor in percentage of the Tidalvolumes intraoperatively)

Reply:

We have changed from intraoperative air leakage to postoperative air leakage (Page 4, line 47).

Line 59: Please correct 'Taco-Seal' with Tachosil

Reply:

We have revised the term from “Taco-seal” to “thrombostatic sealant” (Page 4, line 61).

Line 72: Total pleural adhesion: Please describe and define what you mean exactly.

Reply:

Definition of total pleural adhesion is extensive adhesion of all lung lobes to the surrounding area (Page 5, line 83).

Line 73: ‘lung resection’ I assume you mean the type or extent of lung resection (wedge, Segment, lobe). Please specify.

Reply:

We have revised the term from ‘lung resection’ to ‘lung resection (wedge resection, segmentectomy or lobectomy)’ (Page 5, line 80-81).

Line 88-90: Please rephrase

Reply:

We have revised from ‘When staples with PGA felt were used, a lubricant was needed, and the lungs were separated’ to ‘When the staplers with PGA felt were used, the PGA felt was lubricated’ (Page 6, line 99).

Line 99: I suggest changing the word sutures with cartridges.

Reply:

We have changed from “automatic sutures” to “sutures with cartridges” (Page 7, line 110).

Results Section

Line 124: n=214; in line 116, the number of patients was 211. Which of the two numbers is correct? Please check

Reply:

We changed it from 214 to 211 (Page 7, line 129).

Line 123: propensity-score matched patients were 144, however, the pairs were 67. Please check the numbers.

Reply:

We have changed the number from 144 to 134 (Page 7, line 130).

Line 155: ‘Large lung incisions’: Do you mean the surgical incision or the length of the stapler line? Please specify.

Reply:

We have revised from ‘large lung incisions’ to ‘major lung resection’ (Page 9, line 162).

Line 169: ‘exfoliated edge’: please rephrase.

Reply:

We have revised the term from “exfoliated edge” to “the staple line with PGA felt” (Page 10, line 176).

The Criteria based on the decision to utilize the conventional or PGA-felt stapler are not cleared and were probably surgeon preference dependent. Furthermore, we have no information on postoperative leakage (were there no patients with postoperative leakage?), duration of thoracic drainage, or length of stay. Was there any difference between the two groups?

Reply:

We have added the incidence of prolonged air leak, drainage duration and length of postoperative hospital stay in the Methods, Results and Discussion section (Page 5, line 81-85) (Page 6, line 95-96) (Page 7, line 115-118) (Page 8, line 142-144) (Page 8, line 152) (Page 10, line 184-185) and table 3.

Reviewer F

From 2013 to 2021, 211 patients diagnosed with lung cancer or pulmonary metastasis underwent lung resection using only PGA felt (n = 88) or non-PGA felt (n = 123) staples in order to compare the 2 techniques. In a propensity matched analysis of 67 pairs, the occurrence of intraoperative air leaks was significantly lower in the PGA felt than in the non-PGA felt group (16.4% vs. 56.7%, $p < .001$). The operation time was significantly shorter and intraoperative bleeding was significantly lower in the PGA felt group than in the non-PGA felt group ($p = .001$ and $p = .016$, respectively).

Please add more data regarding the cost efficacy of the PGA felt, and comparison with other reinforcements.

Reply:

We thank Reviewer F for his/her valuable remarks regarding the cost efficacy of the PGA felt.

We believe it is essential to perform a similar procedure (e.g. lobectomy) within a shorter timeframe to demonstrate cost-effectiveness. Therefore, this study cannot present accurate data and warrants future discussion. However, use of the PGA felt stapler was associated with decreased intraoperative air leak rates and a shorter chest tube duration in this study. The difference between a stapler with PGA sheet and a conventional stapler is \$148, making it likely to be cost effective when considering the expenses associated with additional procedures for intraoperative air leaks.