Peer Review File
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First Round Peer Review

Comment 1: I have questions, as number of patients transplanted in your center per year, incidence of complications, etc.. to bette precise your experience.
Reply: Thank you for the question, we are one of the highest volume transplant centers in the country, we performed 645 lung transplants during the time of the analysis which we added to the paper. We do not have overall incidence of airway complication available.
Changes in Text: p6 line 19

Comment 2: 50 patients, 380 stents: it's very much! patients may have nearly 8 stents in mean? you said that there are Removals for secretions; do you use nebulization to clear regularly the stents?
Reply: We encourage patients to regularly perform airway clearance maneuvers and prescribe inhaled mucolytics for those with frequent mucus plugging
Changes in Text: Page 5 line 4-6

Comment 3: Do you remove stents for granulation? do you practice removal of granulomas ?
Reply: We will remove stents for granulation tissue. The decision to remove the stents while treating granulation tissue is left to the discretion of the operator.
Changes in Text: p8 line 12-13

Comment 4: I think it's not the 1st study of safety of hybrid bronchial stents, a french study explain how they manage bronchial complications after transplantation, with rigid bronchoscopy coupled with silicone and hybrid stents, for long duration. And the rigid bronchoscopy help them to avoid systematic removal of stents, when secretions or granuloma... economy and ecology
Reply: You are correct that this is not the first study of safety of hybrid bronchial stents. We compared our study to Fortin's extensively in our discussion (p9 line 1-15). Our study has a larger cohort of patients and we used flexible, not rigid, bronchoscopy for all stent placement and removal.
Changes in Text: The study is already included in our text as detailed above.

Comment 5: For the moment, i have reservation about stent use, patients studied and management of others anastomotic complications.
Reply: We appreciate the reviewers concerns about stent use.
Changes in Text: Changes in the text are not indicated for the reviewer's concern.

Comment 6: Hypothesize - The authors state "we hypothesize that covered metallic stents placed by flexible bronchoscopy have an acceptable safety profile with a low risk of major morbidity and mortality." This is not a prospective research study with a question that they are seeking to answer that generates a hypothesis, but rather a retrospective data analysis of their patient experience. This sentence should be changed to reflect that fact and be in alignment with the abstract.
Reply: We appreciate the reviewer's comment that the rigor of this study could be strengthened by being done in a prospective approach. However, we feel that it is acceptable to still have a hypothesis for a retrospective study.
Changes in Text: We would like to maintain our hypothesis statement as it is currently stated as we feel that it is fair for a retrospective study to still have a hypothesis. If there is specific wording that you would like use to change, please let us know and we will kindly oblige.

Comment 7: "some form of tissue ablation. Data specific to these ablative interventions is not included in this analysis." While the focus of the manuscript is the safety of the airway stents, procedural related safety and potential post-procedural complications are driven by all modalities used during the procedure. Thus, the ablative therapies utilized still drive potential complications. Please provide a justification as to why this info was not included when it would be easily found during the chart reviews that were performed.
Reply: Thank you for this question, we agree that procedural safety is driven by all modalities used during the procedure. We had to rely on retrospective chart reviews as you noted, however we recognize that all procedural documentation cannot quantify the impact of tissue ablative procedures like electrocautery and APC. There was inconsistent documentation about the wattage used and the extent to which each intervention was utilized in each specific procedure. Additionally, procedural documentation cannot capture the cumulative impact of these interventions on each patient. For example, a patient with a new allograft receiving APC for the first time will have a different response to the intervention than a patient who has had chronic allograft dysfunction or multiple airway complications and required multiple interventions
Changes in Text: We do not feel the need to further justify our methodology and change the text.

Comment 8: Number of airway stents and procedure - As of now, one could estimate that each patient had ~7.5 airway stents placed (376 stents/50 patients), but there is no indication as to how many procedures were done to accomplish this end result. Also, this is unlikely to be the case as there are likely some patients that drove the bulk of the procedure. Please provide more details regarding the number of airway stents placed per patient, number of bronchoscopies performed total and the number of procedures each patient underwent, and how many stents were placed during each procedure.
Reply: We have added the median number of stents placed per patient which was 4 with an IQR of 8.75. We had great variability in the number of stents each patient required and the distribution was not normal. We do not have the total bronchoscopies each patient underwent available but we did note that there was 774 bronchoscopies that involved stents.
Changes in Text: We have added this data to table 2

Comment 9: Complications - as the authors mention in the limitations section, the grading/reporting of complications is quite subjective, both in terms of the initial procedure/operative note documentation and the chart review extrapolation. While grading the severity of the complications was not possible, some objective measures could be reported, including admission post procedure for outpatients, change in level of care for inpatients, development of pneumothorax, Grade 2 or higher bleeding, etc. Please provide this information to justify the conclusion of the paper, namely that hybrid metalic airway stents are stable in post-lung transplant airway disease.
Reply: Thank you for sharing your concern about our limitations in grading complications. We unfortunately do not have data to determine change in level of care for inpatients or admission to the hospital. There were no pneumothoraxes in our cohort. We did clarify our definition of major and minor complications. We defined minor complications as those that could be managed with repeat bronchoscopy and did not require further intervention. We defined major complications as those that required interventions beyond bronchoscopy or led to direct morbidity or mortality for the patient.
Changes in Text: p6 line 3-6

Comment 10: Grammer and Syntax - There are numerous run on sentences and errors in punctuation and capitalization that need correcting.
Reply: Thank you for these suggestions regarding grammar and syntax. We have attempted to correct these errors in the text.
Changes in Text: All grammar and syntax errors have been corrected in the text and changes are colored in red.

Comment 11: 1. It would be good if the authors could state at the beginning of the results the number of patients transplanted at their centre during the period studied to have a denominator.
Reply: Please see response to comment 1

Comment 12: The introduction is quite long, and the authors might consider shortening the introduction by including some of the literature review in their discussion.
Reply: We have shorted the introduction and highlighted the literature review in paragraph 2 of the discussion
Changes in Text: Discussion

Comment 13: The manuscript might benefit from the inclusion of some Kaplan Meier figures perhaps showing the time to stent complication / time to stent removal / time to first stent insertion.
Reply: We appreciate the author's suggestion and have an included a Kaplan Meier figure showing time to stent removal.
Changes in Text: Figure 3

Comment 14: I recognize the numbers in the dehiscence group are small, but was there any difference in the number of stents required for this group compared to those with stenosis? It would be worth mentioning this in the results.
Reply: The aim of our study is to evaluate the safety of hybrid bronchial stents. Given the large difference in number of patients who had stents placed for dehiscence vs bronchial stenosis we do not think that comparing the number of stents in each group will add to our primary aim.
Changes in Text: No changes indicated to the text at this time.

Comment 15: Were any stents removed and not reinserted because the indication for the stent had resolved? It would be worth stating this in the results.
Reply: Thank you for sharing your concern. This is a difficult question to answer as the stent journey is different for each patient. Some patients still had stents in place at the time of our end analysis. Other patients died with stents in place from other causes. Alternatively, some patients had ongoing bronchial stenosis and required further intervention but did so without stenting. As such given the heterogeneity in the patient cohort, we thought it would be difficult to add this data in a meaningful way.
Changes in Text: Not indicated at this time.

Comment 16: The results should include some detail on the timing post-transplant that the stents were inserted. It would also be helpful to include some detail on the proportion of time during the persons entire post-transplant period that a stent was in situ.
Reply: The majority of stents were placed within the first two years after transplant. We do not have exact data available on the proportion of time during the persons entire post-transplant period that a stent was in situ. Although we recognize that this data could be informative, we do not think that this would significantly add to the primary aim of this paper which is to evaluate the safety of hybrid metallic stents for patients with transplant airway disease
Changes in Text: No change indicated at this time.

Comment 17: In addition to stent days the authors should include the mean/median number of stents inserted per patient.
Reply: Thank you for your concern, we have added this to table 2.
Changes in Text: Table 2

Comment 18: Most patients appear to have required numerous stents. In general, were stents removed and immediately reinserted or were there gaps? I am struggling to get a clear picture in my mind of what the typical journey is for a patient in this cohort who has a stent inserted – it would seem that every 22.5 days the stent is removed and replaced; but this might not be the correct interpretation of the results. I think the authors could improve the messaging in the results to make this clearer. A figure to show this journey would be very helpful, I'm just not sure what form this would take.
Reply: Although we have an entire cohort of lung transplant patients, the frequency and severity of airway complications in our cohort was heterogenous. There is no typical journey for one patient but to clarify the variability in stent duration we have added a Kaplan-Meier curve showing time to stent removal
Changes in Text: Figure 3

Comment 19: Introduction: it should be shortened since many sentences are part of the discussion. Generally, it should address three questions: What, why, and how? After finishing the introduction, the reader should know what the paper is about, why it is worth reading, and how you'll build your arguments
Reply: Thank you for this suggestion. We have shortened the introduction and tried to better integrate the literature review into the discussion
Changes in Text: Introduction and Discussion

Comment 20: Materials and Methods: How the evaluation period was chosen? How many operators have placed the stents? In our opinion, the following data should be moved to the results paragraph "Most of these patients 1 (88%, n=44) were also treated with balloon dilation and some form of tissue ablation". What was the protocol for airway clearance?
Reply: The evaluation period was chosen based off when our institution began to utilize hybrid metallic stents. Two operators placed the stents. Regarding airway clearance please see our response to comment 2. We understand how you may think that the tissue ablation needs to be included in our results however we only included this information to offer clear context for our metholodology which does not specifically account for the impact of these interventions.
Changes in Text: None indicated

Comment 21: Results: Can the authors provide additional information about the case of stent related mortality from major hemorrhage after removal? What was the exact cause of the bleeding?
Reply: We have added information about the two major complications. For the patient with stent related mortality after removal, we believe the bleeding occurred from the pulmonary artery. This patient had had numerous procedures and required intervention for palliative reasons. His bronchus intermedius was likely thinned from repeat interventions and this led to bleeding after the stent was removed.
Changes in Text: p7 line 9-12

Comment 22: The median duration per stent was 22.5 days. It is a very short duration. How can the authors explain it? Mucus plugging and granulomas were the most frequent reasons why stents were removed. With such a short removal time, it is surprising that the authors did not wait for the effects of flexible or rigid bronchoscopy associated with electrocoagulation for example. From our point of view, a figure showing the anastomotic lesions, the different stents and their complications is missing.
Reply: We appreciate the concern about the short stent duration. We added an extensive section to our discussion discussing our stent duration compared to Fortin and Ma and offered a few explanations. Our cohort consisted of lung transplant patients who are immunosuppressed and have a more dynamic airway environment as they are immunosuppressed and more prone to developing mucus plugging. Additionally, we stented proximal and distal airway complications, whereas Fortin and Ma focused primarily on proximal airways. Finally we acknowledge in our limitations section that our stent duration was likely impacted by the practice patterns of our two operators. Finally, regarding the complications with each stent please take note of Figure 2 and table 3.
Changes in Text: p9 line 1-16

Comment 23: The authors concluded the procedure with hybrid stents for the stenosis in patients with lung transplantation is safe. However, the frequency of stent removal due to the stent-related complications seems to be unacceptably high. Are the complications which need to remove/re-insert stents under general anesthesia minor? The median duration per stent was as short as only 22.5 days. In other words, the patients had to undergo stent replacement under general anesthesia every three weeks. What are the definitions of minor and major complications? The authors should call for attention for the frequent complications.
Reply: We added definitions for major and minor complications to our methods section, please see our response to comment 9. We do not think that undergoing outpatient bronchoscopy under general anesthesia needs to be classified as a major complication as the vast majority of patients have improved symptoms and are able to go home shortly after the procedure. Please see our response to comment 22 regarding the concerns for our stent duration being a median of 22.5 days.
Changes in Text: p6 line 3-6, p9 line 1-16

Comment 24: Please describe the details of 2 patients with major complications related to hemorrhage.
Reply: Please see our response to comment 21
Changes in Text:

Comment 25: . Abstract: Please describe more details about the "minor" complications.
Reply: Thank you for sharing your concern. We note in the abstract that the most frequent reason stents were removed was secretions which is a minor complication. We also note that of the major complications, the only one that was specific to a stent subtype was stent fracture. We appreciate the reviewers concern and can certainly alter the abstract if we get a more specific suggestion about what details to include
Changes in Text: None indicated at this time.

Comment 26: How many patients underwent eternal stent removal due to the expansion of anastomotic regions?
Reply: We appreciate the reviewers but question but feel we cannot address it as we do not understand what "eternal stent removal" exactly refers to. We will certainly address the comment if we can get better clarification about the concern
Changes in Text: No changes indicated in the text at this time.

Comment 27: Please discuss the safety of hybrid stenting by comparing to the study on silicone stenting.
Reply: We discussed the safety of hybrid stenting and compared our work to the studies by Fortin and Ma which utilized silicone stents in the discussion (see page 9 line 5-12)
Changes in Text: see page 9 line 5-12

Comment 28: Table 2. Change "Right Mainstem Bronchus" to "RMSB."
Reply: Thank you for the suggestion, this change has been made
Changes in Text: See revised table 2.

Comment 29: Please revise the title in reflecting that this is a single-center experience.

Reply: Thank you for the suggestion, we have revised the title according to your recommendation
Changes in Text: See page 1 line 4-5

Comment 30: I would avoid using the word "popularity" regarding airway stenting as it implies favoring this as a first-line approach in these patients. Please remove "popularity" and replace with another appropriate term (pg 4, line 1-2).
Reply: We appreciate the reviewers comment and have changed the wording to make it clear that airway stenting is not a first-line approach.
Changes in Text: See page 4 line 1-2, we note that the use of stenting has increased over the past three decades and that it is a potential intervention when other interventions like dilation fail.

Comment 31: SEMS are FDA approved for bronchial strictures related to malignant disease which is why there was a black box warning for off-label use on its use for benign disease. Newer stents such as Bonastent are also only FDA approved for malignant disease. Please add and revise.
Reply: We discussed in our introduction that SEM are only FDA approved for malignant disease. A bonstent falls into this category of stent, we do not feel that we need to add additional clarification to this as we discussed the FDA warning in our introduction (see p4 line 14-20).
Changes in Text: No changes indicated at this time.

Comment 32: Detailed comparison with other experiences regarding airway stents for benign disease should be moved to the discussion section.
Reply: We have shortened the introduction and moved the detailed comparison with other experiences for benign disease to the second paragraph of the discussion section
Changes in Text: p9 line 1-16

Comment 33: Authors mention "acceptable safety profile". Please define this and provide literature support. This will need to be emphasized when they report their data.
Reply: There is no literature consensus for "acceptable safety profile". However, we have better defined major and minor complications. Ultimately the decision to view stents as having an acceptable safety profile is our perspective from our data that we have reviewed. There were only 2 major complications in 50 patients over 5 years with over 700 bronchoscopies performed. If the reviewer has issues with our wording, please let us know and we can consider an alternative phrasing.
Changes in Text: None indicated at this time.

Comment 34: As a general overview, please provide a description of your lung transplant practices including lung transplant criteria, listing process, number of transplants per year, use of ISHLT grading systems, and post-transplant surveillance practices. This will give the reader context.
Reply: We appreciate the reviewer's comment. However, we feel that some of these suggestions are not pertinent to the scope of this paper specifically the listing process and criteria for transplant. We are a high-volume lung transplant center. We use ISHLT grading systems to evaluate the anastomosis however documentation is often inconsistent, so we did not include this

data in our paper. We noted in our methods that post transplant surveillance for airway complications is done on a case by case basis. Regarding surveillance bronchoscopy for rejection, practices vary between individual providers at our institution
Changes in Text: No changes indicated

Comment 35: Please define "major stent related complication"
Reply: Please see our response to comment 9
Changes in Text:

Comment 36: Please state how many proceduralists were involved in stenting interventions and removal.
Reply: Two proceduralists were involved in stenting interventions and removal
Changes in Text: page 6 line 1

Comment 37: Median duration per stent was 22.5 days which seems short at first glance, especially when the data suggests they exchanged stents ~7.82 times within the average of 176 stent days. What is the surveillance practice post-stenting? Does the group have a post-stenting hygiene regimen (i.e. nebulizers, flutter valve, etc)? These practice differences may confound the generalizability of the results. All of this data will need to be included in this manuscript
Reply: Thank you for sharing your concerns about the frequency of our stent removal. As we noted in the methods section of the text, surveillance is done largely on an as needed basis with patient symptoms being the most significant reason for repeat interventions. We encourage all patients to perform airway clearance maneuvers and prescribe inhaled mucolytics to all patients with frequent mucus plugging. We have clarified this in our response to comment 2.
Changes in Text: See page 6 line 4-6

Comment 38: The authors report that the most frequent cause for stent replacement was secretions. In fact, they replaced 193 stents due to this which seems very frequent especially with a median stent duration of 22.5 days. Does the group prefer replacing stents rather than therapeutic suctioning? What is the groups criteria for replacing stents?
Reply: Our group effectively utilizes therapeutic suctioning and do not feel that replacing stents is necessarily always the better modality. However, our patients are treated on a case by case basis and some need frequent exchange for palliation of their symptoms. There is not a uniform criteria for replacing stents which is one of the defined limitations of this study as it is retrospective
Changes in Text: No changed indicated to the text at this time.

Comment 39: The authors report one mortality involving stent removal. How does the group perform stent removal (i.e. rigid or flexible)? Please explain in detail
Reply: All stents were placed and removed using flexible bronchoscopy, we clarified this in our methods.
Changes in Text: See page 6 line 1

Comment 40: Authors report fracture in 15 Bonastents. How is fracture defined? Is it based off bronchoscopic images with gross confirmation?

Reply: We relied on retrospective chart review and counted fractures that were noted in procedural documentation. We did not have definitive bronchoscopic images available in all of the notes to confirm the fracture.
Changes in Text: No changes indicated to text at this time.

Comment 41: The authors report that any amount of granulation tissue is a criterion for stent replacement. This is not typically routine practice amongst other IP physicians, including myself. Please provide a rationale.
Reply: We do not have a defined amount of granulation tissue as a criterion for stent replacement. The decision to treat granulation tissue and whether or not to replace the stent is left to the discretion of the provider. We have clarified this in the text
Changes in Text: See page 8 line 19-20

Comment 42: Please provide a detailed discussion on the comparison between your current study with Fortin et al and Ma et al. Readers should know what the criteria is for stent exchange between each study.
Reply: Please see our response to comment 22
Changes in Text: p9 line 1-16

Comment 43: Provide a paragraph describing each stent used and pros/cons of placing stents about complications. I think it's important to emphasize that stenting in this population should not be first-line.
Reply: Figure 1 contains detailed descriptions about each of the stents. As noted in our results we did not find a different significant difference between each of the stents with regard to complications except for the increased incidence of fracture in the bonastent group.
Changes in Text: No changed indicated.

Comment 44: Please discuss the limitations of a single-center experience in your limitation paragraph
Reply: We have included this in our limitation paragraph
Changes in Text: See p9 line 19-22

Comment 45: Table 2. please add stent length.
Reply: Thank you for your concern we have added median stent length for each type of stent in table 2. If you would like us to format it differently, please let us know
Changes in Text: Table 2

Comment 46: "Data Sharing Statement" is a statement made by authors to confirm their willingness of sharing raw data/patient information related to the article with others. We attached a template for your reference.

Reply: We do not wish to participate in data sharing without prior discussion with collaborators
Changes in Text: NA

Comment 47: The COI form is required for each author. Please collect and provide them from each author. The forms must be submitted to the editorial office along with the revision, and will be published along with the paper.
Reply: thank you for your concerns we will resubmit the COI form for each author along with the revision
Changes in Text: not indicated

Comment 48: Please confirm that all figures/tables/videos in your manuscripts are original and are not adapted from published ones. If a figure/table/video has been previously published or has appeared in copyrighted form elsewhere, acknowledge the original source and submit written permission from the copyright holder (usually the publisher) to reproduce the material. Permission is required, regardless of authorship or publisher except for documents in the public domain. According to our policy, most of the adapted work will still need written permission from the copyright owner.

Reply: All figures and tables are original and not adopted from previously published content.

Comment 49: Please indicate if any of the authors serves as a current Editorial Team member (such as Editors-in-Chief, Editorial Board Member, Section Editor) for this journal.

Reply: None of the authors serve as an editorial team member for this journal
Changes in Text: No changes indicated in the text.

Comment 50: Please follow the below "Submission Checklist for Authors" and revise your paper. Place "Y" if you confirm your manuscript has followed the requirement. Place "N/A" if not applicable. If the paper does not follow the following requirements, it will be seen as IMCOMPLETE and will be sent back to author for revision or be rejected.

Reply: We have followed the submission checklist for authors.
Changes in Text: No changes indicated in the text

Second Round Peer Review

Reviewer A

While the authors have answered some of the questions, concerns, and comments of all of the reviewers, numerous suggestions were not addressed, which significantly limits the manuscript as a whole. I would recommend reassessing these concerns to strengthen the manuscript.

RESPONSE:
Thank you for your comment. I have included the comments below from our original point by point response, which are likely felt to be insufficient. This represents 7 out of 50 comments (14%). We addressed the remainder of the comments, added an additional figure and modified our tables and our text significantly. We did not have the data available to answer these

questions. Please let us know specifically what else we can address within the limitations of the data and retrospective study design.

We can include the grade 2 or higher bleeding. I can only think of 1 KC having a bronchial blocker placed for bleeding after a stent exchange and she is already included as one of the major complications.

For change of level of care. This is a high-risk group of elderly transplant patients with multiple co-morbidities. Change in level of care even after routine bronchoscopy procedures is common and doesn't necessarily indicate adverse procedural complication and could reflect anesthesia. Our dataset does not contain this and we currently do not have the resources to perform repat data collection.

Grade	Findings at Bronchoscopy	Rationale
1	Suctioning of blood required for less than 1 minute	Minimal bleeding of no clinical consequence to the patient or the provider.
2	Suctioning more than 1 minute required or repeat wedging of the bronchoscope for persistent bleeding or instillation of cold saline, diluted vasoactive substances or thrombin	Requirement of one or more tools to control or prevent further bleeding.
3	Selective intubation with ETT or balloon/bronchial blocker for less than 20 minutes. Or premature interruption of the procedure.	Meaningful but short-term change in the clinical status of the patient involving more invasive procedures and causing interruption of the planned procedure.
4	Persistent selective intubation > 20 minutes or new admission to the ICU or PRBC transfusion or need for bronchial artery embolization or resuscitation.	Change in level of care and requiring advanced ventilatory support and/or transfusion of PRBC.

From original revision submission

Changes and new comments are marked in red text

Comment 9: Complications - as the authors mention in the limitations section, the grading/reporting of complications is quite subjective, both in terms of the initial procedure/operative note documentation and the chart review extrapolation. While grading the severity of the complications was not possible, some objective measures could be reported, including admission post procedure for outpatients, change in level of care for inpatients, development of pneumothorax, Grade 2 or higher bleeding, etc. Please provide this information to justify the conclusion of the paper, namely that hybrid metalic airway stents are stable in post-lung transplant airway disease.

Reply: Thank you for sharing your concern about our limitations in grading complications. We unfortunately do not have data to determine change in level of care for inpatients or admission to the hospital. There were no pneumothoraxes in our cohort. We did clarify our definition of major and minor complications. We defined minor complications as those that could be managed with repeat bronchoscopy and did not require further intervention. We defined major complications as

those that required interventions beyond bronchoscopy or led to direct morbidity or mortality for the patient.
Changes in Text: p6 line 3-6

Comment 14: I recognize the numbers in the dehiscence group are small, but was there any difference in the number of stents required for this group compared to those with stenosis? It would be worth mentioning this in the results.
Reply: The aim of our study is to evaluate the safety of hybrid bronchial stents. Given the large difference in number of patients who had stents placed for dehiscence vs bronchial stenosis we do not think that comparing the number of stents in each group will add to our primary aim.
Changes in Text: No changes indicated to the text at this time.

Comment 15: Were any stents removed and not reinserted because the indication for the stent had resolved? It would be worth stating this in the results.
Reply: Thank you for sharing your concern. This is a difficult question to answer as the stent journey is different for each patient. Some patients still had stents in place at the time of our end analysis. Other patients died with stents in place from other causes. Alternatively, some patients had ongoing bronchial stenosis and required further intervention but did so without stenting. As such given the heterogeneity in the patient cohort, we thought it would be difficult to add this data in a meaningful way.

Comment 16: The results should include some detail on the timing post-transplant that the stents were inserted. It would also be helpful to include some detail on the proportion of time during the persons entire post-transplant period that a stent was in situ.
Reply: The majority of stents were placed within the first two years after transplant. We do not have exact data available on the proportion of time during the persons entire post-transplant period that a stent was in situ. Although we recognize that this data could be informative, we do not think that this would significantly add to the primary aim of this paper which is to evaluate the safety of hybrid metallic stents for patients with transplant airway disease
Changes in Text: No change indicated at this time

Comment 26: How many patients underwent eternal stent removal due to the expansion of anastomotic regions?
Reply: We appreciate the reviewers but question but feel we cannot address it as we do not understand what “eternal stent removal” exactly refers to. We will certainly address the comment if we can get better clarification about the concern. However, if the meaning is how many stents were removed and not needed to be replaced we cannot answer that effectively as our data set is limited and the aim of the study was to comment on safety and not efficacy of a stent as intervention.
Changes in Text: No changes indicated in the text at this time.

Comment 33: Authors mention "acceptable safety profile". Please define this and provide literature support. This will need to be emphasized when they report their data.
Reply: There is no literature consensus for "acceptable safety profile". However, we have better defined major and minor complications. Ultimately the decision to view stents as having an acceptable safety profile is our perspective from our data that we have reviewed. There were only 2 major complications in 50 patients over 5 years with over 700 bronchoscopies performed. If the reviewer has issues with our wording, please let us know and we can consider an alternative phrasing. To better address this question, we expanded our literature search and found the paper "Safety and Efficacy of Trachebronchial Bonastent: A Single Center Case Series" by Holden V,K in Respiration 2020. This study concluded that tracheobronchial stents have an acceptable safety profile. In this study, 50 patietns who had 60 Bonastents were evaluated. 48% of stents were removed at a mean of 74 days and the overall complication rate was 54% at a mean follow up of 111 days. We have a similar complication rate so this could validate our decision to use "acceptable safety profile". However this was a patient population that had primarily malignant disease (90%) so that definition may not apply to our study.

Changes in Text: None indicated at this time. Please let us know if you would like us to include the paper mentioned above

Comment 34: As a general overview, please provide a description of your lung transplant practices including lung transplant criteria, listing process, number of transplants per year, use of ISHLT grading systems, and post-transplant surveillance practices. This will give the reader context.
Reply: We appreciate the reviewer's comment. However, we feel that some of these suggestions are not pertinent to the scope of this paper. However for context, Temple lung transplant program is a high-volume center performing more than 100 transplants per year. The lung transplant population would be considered high risk due to prevalence of the following: age >70, severe coronary artery disease requiring coronary artery bypass grafting at time of lung transplant, ECLS and re-transplantation. We conform to standard ISHLT/UNOS listing practices. Surveillance for rejection and lung transplant airways disease is as follows; all patients undergo bronchoscopy in the operating room at the time of surgery and then again prior to extubation in the ICU. An elective bronchoscopy is performed at 2-4 weeks to allow documentation of airway anatomy and grading of anastomotic complications. We have adopted the ISHLT grading system since its publication in 2018. Additional bronchoscopies in the immediate post operative period are dictated clinically. Surveillance biopsies are performed at 3-month intervals in the first year and if otherwise clinically indicated.

Changes in Text: No changes indicated, please let us know if you would like to include this in the text.

Reviewer B

I appreciate the authors efforts in addressing our comments in a timely manner. The authors conclude that their data shows that hybrid metallic stents are a safe intervention for patients with transplant airway complications. I would argue the opposite. Although the intrinsic safety is

notable, this has been well cited in the literature. The one aspect I find difficult to overcome with regards to safety, is the high frequency of stent deployment. They report one exchange per patient on average of 22.5 days which total 8 new stents placed in less than a 6-month period per patient.

We appreciate the concerns about the high frequency of placement. Our dataset does not have a normal distribution and we reported a median stent duration of 22.5 days with an IQR of 29. The median stent exchanges per patient was 4 with an IQR of 8.75, again reflecting a non-normal distribution. We had multiple stents in our analysis that remained in place for over a year including one that was in still in place at end analysis at 898 days. A lot of the stent exchanges were driven by some patients in our cohort that required weekly exchanges to maintain a reasonable quality of life and stay out of the hospital. We believe another reason for frequent replacement is diminishing returns after the initial intervention. When stents are placed we aim to keep them in place for at least 3 months. Unfortunately, when extensive secretions, infective colonization or granulation tissue occurs, some patients will need more frequent replacements or holidays to avoid further complications.

In my opinion, this practice is at one far end of the spectrum of the management of complex airway disease.

This is a valid point and we agree that our practice is just one end of the spectrum. Contributing factors include the high-risk population, on average older and as a result high utiolization of single lung transplant. Single lung transplant recipients tolerate airway complications poorly due to their reliance on the graft. So even moderate mucostasis of a stent can create significant symptoms warranting intervention. this is a single center experience in a population with a majority of single lung transplants (54%) and a high risk population (older average age than the majority of centers). Despite this, we avoided significant complications.

The authors have failed to provide concrete rationale on their decision making regarding the degree of granulation tissue, mucostasis, and migration that necessitated stent exchange.

We acknowledge this is an issue of the retrospective study design. To provide this information without inserting significant bias due to retrospective interpretation would require a prospective study.