

## Peer Review File

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### Reviewer A

*Comment 1:* Congratulations on a Large series of sleeve lobectomy done over a 13 year period.

*Comment 2:* Main take home message of this manuscript is, it not only describes clinical risk factors for bronchial complications but also a novel objective method of assessing anastomosis healing by bronchoscopy grading and using this grading for prognosis and subsequent clinical management.

*Reply 1 and 2:* We thank you for the review of our manuscript and the constructive criticism. The anastomosis classification was published back in 2012 (1). The present work represents also a validation of this classification based on a large number of cases. See also reply to comment 3.

*Changes in the text:* See changes in the text regarding comment 3.

*Comment 3:* In view of this suggest changing the manuscript title to Clinical and bronchoscopic factors for bronchial healing after sleeve resections for lung cancer.

*Reply 3:* We agree that bronchoscopic classification plays a leading role in this study. We therefore agree to change the title and propose the following: “Clinical and bronchoscopic aspects of bronchial healing after sleeve resections for lung cancer: a multivariate analysis of 541 cases.”

*Changes in the text:* The title was changed (see page 1, lines 1-2).

*Comment 4:* Was all surgeries done open or some open versus minimally invasive. was check bronchoscopy done at end of surgery as a baseline. and is there is any correlation between intra-op bronchoscopy and bronchoscopy at 7 days.

*Reply 4:* We agree that the proportion of thoracoscopic sleeve resection is an important information for the readers. Until 2019 we performed 11 sleeve resections in our hospital per VATS in patients with lung cancer. A higher proportion was performed in carcinoid tumors and were therefore excluded from analysis. We have added the numbers and included them in the statistical analysis. Intraoperative bronchoscopy to check the anastomosis was not performed as a standard procedure so that a comparison with bronchoscopy on day 7 is not possible. We clarify this in the

methods section.

*Changes in the text:* In table 1 we added the number of thoracoscopic sleeve resections. In page 6, lines 131-132 we state that intraoperative bronchoscopies were no standard procedure.

*Comment 5:* what is the long term strictures rates in patients in all grades of patients especially those treated conservatively and those undergoing revision surgery.

*Reply 5:* We would also have been very interested in this data. Unfortunately, the documentation of the aftercare was very incomplete, so that no usable data was available in this regard.

*Changes in the text:* None.

*Comment 6:* What is the local cancer recurrence rate.

*Reply 6:* Our tumor registry does not distinguish between local recurrence and distant recurrence, so unfortunately, we are not able to present these data.

*Changes in the text:* None.

*Comment 7:* How do you decide at time of revision salvage surgery whether to do completion pneumonectomy vs primary repair . If primary repair do you revise the whole anastomosis or only the dehiscence part.

*Reply 7:* The decision whether to perform a pneumonectomy or a revision of the anastomosis depends on many factors and is always an individual decision. This decision depends primarily on the extent of bronchial necrosis and whether lung tissue is involved. In general, we try to avoid a secondary pneumonectomy. Because of these uncertainties, no general recommendation can be made in these cases. To give an overview of the individual procedures and decisions, we have added a table with all cases with anastomotic insufficiency. This lists the original surgical procedure, the procedure after the insufficiency was identified, and the further clinical course for each case.

*Changes in the text:* Table 4 was added to the manuscript. We describe the different procedure for the treatment anastomotic insufficiency in page 6 lines 138-139. We have added a paragraph (pages 11-12, lines 319-329) to the discussion where we discuss possible treatments for insufficiency.

*Comment 8:* Your recommendation about the grading should be more clear to the readers. If I am not mistaken, you recommend surgery for all grade 5 and conservative management for grade 3/4 and failing which then salvage surgery.

*Reply 8:* Neither the original paper on classification by Ludwig et al. nor our paper makes a general recommendation for surgery for grade 5 anastomoses. This is always an individual decision. It has been our experience that anastomoses with low dehiscence can be successfully treated with antibiotics. In fact, in our study, 60% of patients who had insufficiency (grade 5) were treated conservatively.

*Changes in the text:* See changes in the text regarding comment 7.

## Reviewer B

*Comment 1:* This is a single-center analysis in 541 sleeve resections. First of all, my main concern with this study is novelty and the way to show the results. I agree with the general idea that identifying the predictors in these patients is important for surgeons and pulmonologists to manage the patients appropriately, but what is the novelty in this study? From my view point, the predictors shown in this study are already well-known so that's why many surgeons are covering the anastomosis site by pericardial fat tissue or others in such patients.

*Reply 1:* We would like to thank you for the review of our manuscript. There are only a few studies on risk factors for impaired anastomotic healing. To our knowledge systematic investigations were carried out only for preoperative irradiation, where a negative influence on anastomotic healing could be demonstrated (1-3). Other risk factors have not been sufficiently investigated. Various factors have been accused of influencing anastomotic healing, but this has never been scientifically proven. In our opinion, the novelty of this study therefore lies in the fact that we were able to prove or disprove suspected risk factors. On the other hand, we were able to validate an existing classification for the assessment of anastomosis. We know which patients we can safely send home (grade 1 and 2) and which need further attention (grade 3-5).

*Changes in the text:* We now present this in more detail in the introduction and discussion (page 4 lines 78-80 and page 9 lines 237-241).

*Comment 2:* Also, you're showing the survival-curve by stratifying the patients as "critical anastomosis = grade 3 or higher" and "grade 1-2" but I believe before showing this figure, you need to show the result of multivariate analysis to identify the risk factors for survival. I'm afraid that some of the analysis or result in your manuscript are out of your original purpose. So please address this issue by adding the

purpose or removing the survival curve.

One more thing would be if you want to show the survival curve by dividing the patients, I believe there could be many confounding factors including age, smoking history, induction therapy, nutritional status, and pathological status etc. So I believe it's not fair to show the survival curve in the way you're describing in the figure. This is another reason that the result of multivariable analysis for survival needs to be shown in the manuscript. Also, it would be more interesting that the authors can show the data of propensity score matching and survival curve. Since the number of the patient in the manuscript is outstanding as a single-center analysis, it should be more reasonable to have that data.

*Reply 2:* We understand your objection, only we think that focusing too much on survival would miss the point of the study. A multivariate analysis to analyze independent risk factors for survival after sleeve resection or a propensity score matching would be topics for a separate study. Because we focused on risk factors for poor anastomotic healing in this study and the degree of anastomosis is ultimately the result of these factors, we believe it is legitimate to compare survival of patients with critical and noncritical anastomosis.

*Changes in the text:* We have now added a paragraph on survival in the discussion section (page 12, lines 352-357), where we also address the limitations of this presentation.

*Comment 3:* My other comments are listed below. I hope you will consider these comments or revise the manuscript to make it even better.

1) Line 46: please remove one of "on".

*Reply 3:* Thank you for the note. We have deleted the duplicate word.

*Changes in the text:* The double "on" was removed in page 2, line 49.

*Comment 4:* 2) Please show your rationale to divide the patients using "grade 3 or higher" and "grade 1-2". Not only your reference #1

*Reply 4:* One of the 2 goals of this work was to verify the anastomosis classification of Ludwig et al. published in 2012. The division into noncritical and critical anastomoses was made in this work. For this reason, we had to adhere to this classification. Therefore, we do not have another rationale.

*Changes in the text:* In the introduction and discussion, we now go into more detail about Dr. Ludwig's classification (page 4, lines 78-81 and page 8, lines 233-241).

*Comment 5:* 3) How many “standard” lobectomy or lung cancer surgery were done in the study period? I’m curious about the percentage of sleeve resection in your institute.

*Reply 5:* We agree that this is an interesting information for the readers. We have added the corresponding numbers in the methods section.

*Changes in the text:* We added the numbers in pages 4-5, lines 88 to 101.

*Comment 6:* 4) Line 165-167: Dr. Ludwig is one of the co-author, correct? If so, please replace it to us or something.

*Reply 6:* This is correct, Dr. Ludwig is one of our co-authors. We have changed the sentence to “in our institution”.

*Changes in the text:* The sentence was modified in page 8, lines 223-224.

*Comment 7:* 5) Line 197- 198: It is stated that, in your institution, wrapping of the anastomosis is performed as a standard procedure after neoadjuvant radiation therapy. It is also stated that covering of the anastomosis in non-pretreated patients was performed at the surgeon’s preferences. Then how many patients were performed covering of the anastomosis in each group? Using what types of tissue? (Pericardial fat tissue? Intercostal muscle? Diaphragm? Pedicle or non-pedicle?) I believe this kind of information would be great interest of the readers as you discussed in line 199-202.

*Reply 7:* We would also have been very interested in the proportion of covered anastomoses. Unfortunately, we don’t have data for all patients that were not pre-treated. When we wrote “covering of the anastomosis in non-pretreated patients was performed at the surgeon’s preferences”, we meant the standards and procedures in our clinic.

*Changes in the text:* We describe which flaps are used as standard in our clinic on pages 5-6, lines 117-126. In addition, we have added a paragraph in the discussion where we address the issue of coverage (pages 12-13, lines 330-350).

*Comment 8:* 6) Would it be possible to make one table how the author managed the patients with anastomosis grade  $\geq 3$ ? In methods, it is stated that systemic antibiotic treatment and further bronchoscopy were performed but no additional interventional or surgical approach?

*Reply 8:* The clinical course in patients with grade  $\geq 3$  cannot be traced with certainty in all patients. We have added a table in which we list all patients who

suffered anastomotic insufficiency (grade 5). Here, the initial surgery, the degree of anastomosis at day 7 and the further clinical course are stated.

*Changes in the text:* Table 4 was added to the manuscript. The results are discussed on pages 11-12, lines 319-329.

*Comment 9:* 7) As I commented above, please show the novelty of this study clearly in the discussion part. Current version is a bit difficult to figure out the new findings.

*Reply 9:* See reply to comment 1.

*Changes in the text:* See Changes in the text referring to comment 1.

*Comment 10:* 8) Line 260: available at ?? Please specify.

*Reply 10:* The data sharing statement file was submitted together with the manuscript. The three dots will be replaced by a link to this file if the manuscript is accepted.

*Changes in the text:* none.

### Reviewer C

*Comment 1:* Congratulations on a very difficult and large study. The study was very informative. I do have a comment.

Were all the cases done by open thoracotomy? There is no mention of thoracoscopic surgery (VATS). If a considerable portion was done by VATS, were there any differences in operative times, morbidity, survival, etc.?

*Reply 1:* We would like to thank you for the review of our manuscript. We have added the number of thoracoscopic sleeve resections to the manuscript and included them in the statistical analysis. See also reply 4 to reviewer A.

*Changes in the text:* In table 1 we added the number of thoracoscopic sleeve resections.

### Reviewer D

*Comment 1:* They retrospectively investigated the complications of bronchial anastomosis. I think the analysis by 5 classification of them is interesting.

Preoperative the presence or absence of diabetes or steroid administration should be stated. In addition, I think the results of the multivariate analysis should be examined.

*Reply 1:* We would like to thank you for the review of our manuscript. This information would also have been of interest to us. Unfortunately, the perioperative data collection did not include pre-existing diseases and medications taken. We addressed this issue this in the limitations section.

Changes in the text: We have discussed the lack of this data on page 13, lines 358-363.

*Comment 2:* Don't authors have sleeve segmentectomy cases at their institute? If so, they should also investigate sleeve segmentectomy cases. I think their manuscript will be an even more informative.

*Reply 2:* After exclusion of carcinoids, only one sleeve segmentectomy remained in the data set. In order to focus on a homogenous group, we decided to exclude this case.

*Changes in the text:* In line x we address the exclusion of the segmentectomy.

Comment 3: Minor:

I think that "on on" on page 3, line 46 is a mistake.

*Reply 3:* Thank you for the note. We have deleted the double "on".

*Changes in the text:* We have deleted the double "on" in line x.

## **Reviewer E**

Using a retrospective cohort of sleeve lobectomy patients, the authors studied negative predictive factors of anastomotic healing. Overall, this is an interesting paper, however there are some comments I'd like to make:

*Comment 1:* Who performed the bronchoscopy postoperatively? Was it the same surgeon who performed the sleeve lobectomy? If it was the same operating surgeon, this might introduce some level of bias that should be discussed.

*Reply 1:* We would like to thank you for the review of our manuscript. The bronchoscopy was performed by a member of the surgical team, usually by the surgeon that performed the operation. Of course, we cannot exclude the possibility that the surgeon who performed the operation may assess the anastomosis with some subjectivity. However, in our experience, this is hardly the case. The anastomosis classification was developed to make the results of the bronchoscopy comparable. This should also leave less room for subjective nuances in the assessment of anastomosis.

*Changes in the text:* We added the information that the bronchoscopy was performed by the operation surgeon or a member of the surgical team to the methods section on page 6 lines 131-132.

*Comment 2:* What variables were included in the univariable analysis? This can be



included as a supplementary table. Please also report your cut-off for inclusion in the multivariable analysis.

*Reply 2:* The variables that were included in the multivariate analysis were reported in the methods section (lines xxx). All variables showing statistical significance ( $p < 0.05$ ) were included in a logistic regression analysis. The classifying cut-off value was set 0.5.

*Changes in the text:* This information was added on page 6, lines 145-147.

*Comment 3:* Did the authors have any data on timing between completion of chemo/radiation and surgery? This could be a significant variable to include.

*Reply:* The influence of timing between radiation and surgery and anastomotic healing was published by our research group in 2020 (4). For the current data set, we lack this information.

*Changes in the text:* None.

*Comment 4:* Do the authors have data on other comorbidities, such as heart disease, which might negatively impact postoperative healing?

*Reply 4:* The perioperative data collection did not include pre-existing diseases and medications taken. We addressed this issue in the limitations section. See also reply 1 to reviewer D.

*Changes in the text:* We have discussed the lack of this data on page 13, lines 358-363.

*Comment 5:* What is your hypothesis for elevated pre-operative CRP in some of these patients?

*Reply 5:* Elevated CRP is often observed in lung cancer patients as a sign of inflammation and increased tumor burden. This was already explained in the discussion section on pages 10-11, lines 281-303.

*Changes in the text:* none.

*Comment 6:* Surgeon experience can influence outcomes, especially when performing such a complex operation. Do the authors have data on the surgeon experience at the time of the operation (i.e., years in practice at the time of the operation)?

*Reply 6:* We agree that the surgeons experience would be very informative in would probably have been a risk factor for impaired anastomotic healing. Unfortunately, we do not have this data. We already addressed this issue in the limitation section of our



manuscript (page 13, lines 358-363).

*Changes in the text:* None.

*Comment 7:* Please provide data on how these sleeves were performed - open vs. VATS? This variable should be included in your statistical analysis.

*Reply 7:* We have added the number of thoracoscopic sleeve resections to the manuscript and included them in the statistical analysis. See also reply 4 to reviewer A.

*Changes in the text:* In table 1 we added the number of thoracoscopic sleeve resections.

### **Reviewer F**

The authors report analyses on anastomotic healing after bronchial sleeve resection for lung cancer using their original bronchoscopic assessment.

This is a single-institutional retrospective study. Even so, its sample size is not small. Therefore, it could be published in JTD.

I generally agree with the results and logical discussions of the study. However, there are some revisions required that would be helpful to understand the study appropriately.

*Comment 1:* The bronchoscopic assessment of anastomotic healing reported firstly by Ludwig, et al. is simple, but is subjective only from bronchoscopic findings on POD7. I guess there could be a discrepancy between examiners. How were anastomoses classified in the study? Please comment.

*Reply 1:* We would like to thank you for the revision of our manuscript. In the original classification day 7 was chosen for parthophysiological reasons. As early as 7 days after resection, neoangiogenesis promotes revascularization and healing of the anastomosis. However, we do not know whether an earlier bronchoscopy (e.g., on day 5) would have produced the same results. Reviewer comments indicated that our comments on Ludwig's classification were too brief and imprecise. We have now gone into more detail on aspects of the classification in the discussion section. We agree that there could be discrepancies between the examiners concerning the classification of anastomoses. But the anastomosis classification was developed to make the results of the bronchoscopy comparable. This should also leave less room for subjective nuances in the assessment of anastomosis.

*Changes in the text:* More details addressing the objectives and limitations of the classification was added to the discussion section (page 9, lines 237-241).

*Comment 2:* As the authors described, I agree the assessment on POD7 of anastomotic healing can be an effective tool to predict the postoperative course or further anastomotic healing. On the other hand, I'm skeptical to consider the effectiveness of further treatment for anastomotic problems. Because the best treatment for the anastomotic failure is unclear in the study, also in the real world. For example, no treatment may lead successful course in some patients.

Please comment.

*Reply 2:* We agree that the best treatment for anastomotic insufficiency is not clear. The decision for a therapy depends on many factors and is always an individual decision. Due to these uncertainties, no general recommendation can be made. It has been our experience that anastomoses with low dehiscence can be successfully treated with antibiotics. In fact, 60% of patients with insufficiency (grade 5) were treated conservatively in our study.

*Changes in the text:* We added table 4 where the treatment and the clinical course of every patient with anastomotic insufficiency is stated. We discuss this table on pages 11-12, lines 319-329.

*Comment 3:* There are no discussions about the results of long-term survival.

I would like request to include some discussions or comments about that.

*Reply 3:* We added the discussion of the long-term-results to the discussion section.

*Changes in the text:* The discussion was added on page 13 in lines 352-357.

*Comment 4:* Additionally, I have a simple question regarding the radiotherapy.

Are all of patients with preoperative radiotherapy received more than 60 Gy irradiation?

*Reply:* That is correct. In our hospital, patients are irradiated with a total dose of 60-66 Gy as standard.

*Changes in text:* None.

## Reviewer G

The authors should be congratulated for this work with reports on bronchoscopic and clinical outcomes from a large number of bronchial sleeve resection over a 14 year period. Carcinoid tumours have been wisely excluded as they occur in a different

patient population. Bronchoscopic appearances at post operative day 7 have been meticulously graded 1-5 as per Ludwig et al.'s previous work. The outcome data from those with anastomosis grade 3+ will be interesting to the thoracic community. The multivariate analysis mostly confirms previously recognised risk factors.

Some comments:

*Comment 1:* Risk factors of diabetes, preoperative steroids and peripheral vascular disease would be useful to include in analysis

*Reply 1:* We would like to thank you for the review of our manuscript. Unfortunately, the perioperative data collection did not include pre-existing diseases and medications taken. We addressed this issue this in the limitations section.

*Changes in the text:* We have discussed the lack of this data on page 13 in lines 358-363.

*Comment 2:* coverage of anastomosis in those not treated with preoperative radiation should be included- does this seem to impact on anastomotic healing

*Reply 2:* We would also have been very interested in the proportion of covered anastomoses. Unfortunately, we don't have data for all patients that were not pre-treated.

*Changes in the text:* We have added a paragraph in the discussion where we address the issue of coverage (page 12-13, lines 332-351).

*Comment 3:* Aside from starting antibiotics in those with poor healing, I don't think the authors have fully explored how routine bronchoscopy day 7 impacted on the patients' outcome. The authors could consider exploring calculations on Numbers Needed to Treat to pick up one case of anastomosis insufficiency. Line 108 states 'further bronchoscopies were performed to control bronchial healing.' As bronchoscopy is not a treatment, this would be more accurate if the word 'monitor' replaced 'control.'

*Reply 3:* Only 4 anastomotic insufficiencies were detected on bronchoscopy on postoperative day 7. In this light, nearly 135 bronchoscopies had to be performed to identify insufficiency. The purpose of bronchoscopy and anastomosis evaluation was not primarily to identify insufficiencies. Rather, we wanted to know which patients we could discharge and which we needed to continue to monitor. 16 Anastomotic insufficiencies developed after postoperative day 7. In all but one case, bronchoscopy at POD 7 had revealed a critical anastomosis. Without bronchoscopy, we might have

sent these patients home. Of course, we cannot prove with our figures whether the administration of antibiotics and further bronchoscopic checks can actually prevent anastomotic insufficiency. This therapeutic regime is based on the experience that insufficiencies and an inflammatory state often occur together. Whether the inflammation leads to the insufficiency or the insufficiency leads to the inflammation is not clear here. Overall, we think that the purpose of bronchoscopy on postoperative day 7 and the consequences we draw from this in clinical practice were not presented clearly enough in the original manuscript. We have now gone into more detail on aspects of the classification in the discussion section.

*Changes in the text:* More details addressing the objectives and limitations of the classification was added to the discussion section (page 8, lines 237-241). We replaced “control” (page 6, line 137) with “monitor”.

*Comment 4:* Leading on from the usefulness of routine bronchoscopy, for those of us who don't routinely perform early bronchoscopy, it would be interesting to see how factors such as day 6 or 7 CRP/WCC/air leak impacted on the prevalence of poor healing. Could this be an indication for bronchoscopy?

*Reply 4:* A (suddenly) elevated fistula and elevated infection parameters always make us immediately think of the anastomosis and often a previous bronchoscopy is performed in addition to a CT scan. From our experience, we can confirm that increased inflammatory parameters and fistula volume can correlate with the degree of healing of the anastomosis. Since we do not have data on inflammatory parameters and fistula rates at day 7, we cannot prove this.

*Changes in the text:* See changes in text referring comment 3.

## Reviewer H

Dear Authors,

It is my pleasure to participate in the review of your manuscript. In my opinion, these analysis regarding complex surgical techniques are more than necessary to assess our performance and how effective we are in a try to avoid pneumonectomies. However I do have some comments/suggestions for your consideration.

Major comments:

*Comment 1:* Abstract:

- The conclusion about the lack of coverage is not supported in M&M or in Results section. Please, remove from conclusions or give some data in the above mentioned

sections.

*Reply 2:* We would like to thank you for your thorough review of our manuscript and your constructive criticism. We agree that this sentence is misleading and have removed it.

*Changes in the text:* We removed the sentence.

*Comment 2:* Manuscript:

- The objective of the manuscript should be reviewed: to assess the performance of a specific technique regarding its capability of diagnosis (or the predictive power of diagnosis), the statistical analysis (methods) has to be carried out accordingly. The second part of the "aims" is perfectly stated.

I would suggest to rephrase. It seems that authors pursued to described the incidence of anastomosis problems in their bronchial sleeve resection serie.

*Reply 2:* We pursued 2 goals with our work. First, we wanted to test a classification that we have been using for a long time but that has not yet been validated for its predictive probability regarding anastomotic insufficiency. Second, we wanted to identify independent risk factors for impaired healing. We have now tried to present this more clearly in the introduction. We have also gone into more detail about the classification of Ludwig et al in the discussion.

*Changes in the text:* page 3, lines 78-81 and page 9, lines 233-236.

*Comment 3:* - Following the rationale of the previous statement, these results may lead to a change in their surveillance protocol . Would it be of help to indentify critical anastomosis earlier if the bronchoscopy is performed at day 4 + day 7 after surgery? Maybe more patients could received antibiotics as conservative treatment starting as early as possible.

It could be added to the discussion section, if authors consider so.

*Reply 3:* In the original classification day 7 was chosen for parthophysiological reasons. As early as 7 days after resection, neoangiogenesis promotes revascularization and healing of the anastomosis. However, we do not know whether an earlier bronchoscopy would have produced the same results. The fact that we perform a bronchoscopy routeniley on the 7th postoperative day does not exclude earlier bronchoscopies. If there is a suspicion of a healing disorder of the anastomosis, for example due to increased inflammation values, the condition of the patient or an increased fistula, we perform a bronchoscopy sooner.

*Changes in the text:* We addressed this question in the discussion section (page 9,

lines 237-241). On page 6, lines 133-134 we now state that bronchoscopies before day 7 were performed wenn clinically necessary.

*Comment 4:* - One of the main controversies in the Discussion section is the paragraph about the coverage of the anastomosis. It is clear that covering the anastomosis, specially after neoadjuvant chemo-radiation, might play a role in the healing process. The authors stated that they covered all anastomosis in which the patient received preop radiation. However, the covarage apparently did not prevent the event of insufficiency of the anastomosis. If fact, from my point of view, their results might be interpreted as that the covarege of the anastomosis has no impact in the outcome. Looks like that it does not matter if you cover or not the anastomosis.

*Reply 4:* This a good point. The insufficiency rate in the patients that received neoadjuvant radiation was 6.8%. In fact, we don't know if covering the anastomosis doesn't work or if the insufficiency rate would have been higher if we didn't cover. This cannot be said from our data and requires further studies. We addressed this question and the controversy over the coverage of the anastomosis in the discussion section.

Changes in the text: We addressed this question on pages 12-13, lines 337-351.

*Comment 5:* How many of the grade 3 or higher anastomosis were covered with any kind of flap?

I think this needs to be clarified.

*Reply 5:* We would also have been very interested in the proportion of covered anastomoses in non-pretreated patients. Unfortunately, we don't have data for all patients that were not pre-treated.

*Changes in the text:* none.

*Comment 6:* - In my opinion, the Conclusion section should be changed in accordance with the suggestions made.

*Reply 6:* We agree that the conclusions were too brief and perhaps too vague. We have tried to reproduce them more clearly now and relate them more to our findings, but without dragging out this section too much.

Changes in text: The conclusion .

Strong points:

- Univariate and multivariate analysis do not show anything new in terms of risk

factors. On the other hand, I think reinforce the idea that surgeons have to be vigilant when a bronchial sleeve resection is carried out.

- The discussion section is the best part of the manuscript (apart from the coverage, commented above). Very well conducted and very well explained.

Minor comments:

*Comment 7:* Abstract: review double “on”, line 46.

*Reply 7:* Thank you for the note. We deleted the double “on”

*Changes in the text:* the double “on” on page 2 in line 49 was deleted.

1. Ludwig C, Stoelben E. A new classification of bronchial anastomosis after sleeve lobectomy. J Thorac Cardiovasc Surg. 2012;144(4):808-12.
2. Koryllos A, Lopez-Pastorini A, Zalepugas D, Ludwig C, Hammer-Helmig M, Stoelben E. Bronchus Anastomosis Healing Depending on Type of Neoadjuvant Therapy. Ann Thorac Surg. 2020;109(3):879-86.
3. Yamamoto R, Tada H, Kishi A, Tojo T. Effects of preoperative chemotherapy and radiation therapy on human bronchial blood flow. J Thorac Cardiovasc Surg. 2000;119(5):939-45.
4. Koryllos A, Lopez-Pastorini A, Zalepugas D, Galetin T, Ludwig C, Hammer-Hellmig M, et al. Optimal timing of surgery for bronchial sleeve resection after neoadjuvant chemoradiotherapy. J Surg Oncol. 2020;122(2):328-35.