Peer Review File

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First round of peer review

<mark>Reviewer A</mark>

Comment 1:

The authors say in lines 21-22 of page 4 that they "present three cases of pulmonary cavity as a late complication after Covid-19, who were successfully treated by minimally invasive surgical methods." But then they describe 2 of the 3 patients receiving thoracotomy. Even if it is a mini-thoracotomy, most surgeons would not consider that to be minimally invasive surgery. The authors should change that line.

Reply 1: All authors thank you for your in-depth review and constructive comments.

Changes in the text: In this article, we present three cases of pulmonary cavity as a late complication after Covid-19, who were successfully treated by surgical treatment. (Page 4, lines 21-22)

Comment 2: The authors claim that the patient in Case 1 was septic from a "destroyed left lower lobe." But they also say that the patient had negative PCR tests for COVID-19 at the time. Did they feel that the patient was actively septic from COVID-19 infection despite a negative PCR test? Do they feel that there was a superimposed bacterial infection causing sepsis? Was the patient condition not sepsis but an inflammatory response to parenchymal damage? The authors should clarify this point.

Reply 2: We definitively agreed that the patient was septic as a result of superimposed bacterial infection due the extended parenchymal damage. There was not a positive COVID-Infection at this time.

Changes in the text: As a result of the lobe destruction and an added bacterial superinfection the patient developed sepsis. Alveolar lavage and blood samples were positive for S. Aureus. We performed a limited thoracotomy for lobectomy on an emergency status. (Page 6, lines 2-5)

Comment 3: Related to comment 2, did the authors do cultures on the resected lungs? Did they check for active COVID-19 infection on the specimens?

Reply 3: The bacteriological result of patient one and two was positive for S. Aureus. In none of the three cases was a test for active covid infection performed on the specimen.

Changes in the text: Bacteriological result of the specimen revealed also S. aureus. (Page 6, lines 6-7). The bacteriological result was positive for S. aureus. (Page 7, line 1).

Comment 4: The management strategy that the authors have described is similar to what most surgeons would use in any case of cavitary destruction of the lung secondary to infection. How do the authors feel that their management is different in COVID-19 infection?

Reply 4: We agree with the reviewer, that we did not use a novel surgical method in the present report. However, according to the recently published articles, due to the increased perioperative risks after covid infection, it is suggested to perform a surgical operation first 6 weeks after covid symptoms. In this study, we will highlight that after discussing and accurate selection of the patient in an interdisciplinary team (even in patient with an active covid infection until 2 weeks before), remarkable postoperative outcomes could be achieved.

Changes in the text: We made changes in the text (Page 9, lines 17-23) and (Page 10, lines 2-4)

<mark>Reviewer B</mark>

Comment 1: The figures do not correspond to the text. Figure 1 (Page 5, line 19) was supposed to describe left lower lobe destruction and pleural effusion, but the actual figure on page 15 is a sagittal image that doesn't seem to show much effusion. Similarly, figure 2 was said to show lobar consolidation with pleural empyema (Page 6, lines 12-14), the actual image on page 16 showed mostly lobar consolidation, and the pleural empyema is very small and quite difficult to see. Figure 3 is said to show extensive lung consolidation (page 7, lines 9-10), but the actual image on page 17 showed a lung cavity instead of consolidation. Figure 4 did not add any value to the article and should be removed.

Reply 1: All authors thank you for your in-depth review and constructive comments.

Changes in the text: We made the changes to the images

Comment 2: The indications of proceeding with surgery should be clearly identified. In particular, the reasoning to proceed with surgery instead of persisting with medical treatment should be highlighted.

Reply 2: After the diagnosis of pulmonary cavity in reported patients, board-spectrum Antibiotics like Piperacilin/Tazobactam (Penicillins and beta-lactamase inhibitors) were first administrated. However, general condition, as well as laboratory results of the patients have worsened significantly over the time. The performed CT controls showed also degenerated pulmonary condition, thus a surgical therapy was indicated.

Changes in the text: In our report we mention three cases in which the indication for surgery was due to sepsis in two of them and in one hemoptysis. The prolonged use of antibiotics would not have improved the general condition of the patients. (Page 9, lines 7-10)

Comment 3: Based on the literature review that the authors have done, the discussion should include recommendations of the indications for conservative management and for surgical treatment.

Reply 3: According to the literature review and our experiences, in patients with a diagnosis of pulmonary cavity after Covid infection (without any sign of sepsis), a board-spectrum antibiotical therapy with Penicillins and beta-lactamase inhibitors like Piperacilin/Tazobactam should be administrated as a first-line therapy. In Patients without sign of destroyed lung and well-limited cavities, a CT-guided drainage could be also performed as a co-therapy. A routine bronchoscopy is very useful to rule out any defect with the intrabronchial tract.

The patients with persistent symptoms (Fever, Hemoptysis, etc.), impaired general condition, or any sign of sepsis should undergo a CT control to rule out other infection focuses/impaired lung. These patients should be thereafter discussed in an interdisciplinary team and evaluated for a possible

surgical therapy.

Changes in the text: We made the changes to the text (Page 9, lines 17-23), (Page 10, lines 1-4)

Reviewer C

Comment 1: Keyword. Consider changing "Uniport" to "late complications". I don't think the surgical approach is important in this article. Also, I think the term "Long COVID" is not yet common, it would be better to use the term "late complication" in addition to the term "long COVID". **Reply 1:** All authors thank you for your in-depth review and constructive comments.

Changes in the text: We made the changes suggested in the section on "Keyword" and also on the title. According to the context we made the changes suggested in the (Page 2, line 14), (Page 3, line 4), (Page 9, line 8).

Comment 2: Case 1 and Case 2. Add the degree of inflammation before surgery (e.g., heat type, WBC, CRP.). Also add the results of bacterial culture.

Reply 2: Thank you for your comment. We made the changes to the text

Changes in the text: WBC 19,7/nl and CRP level of 269 mg/l. (Page 5-6, line 22-1)

WBC 22/nl and CRP level of 180 mg/l. (Page 6, line 15-16). The bacteriological result was positive for S. aureus. (Page 7, line 1).

Comment 3: Case 3. Is the source of bleeding from a parenchymal pulmonary vessel or from a bronchial artery? Please describe the presumed findings. Are there any differences from usual surgery with regard to the surgical findings (Figure 4)? I think some explanation is necessary, such as that there were no special concerns about the avulsion, or that the adhesions were advanced.

Reply 3: According to another reviewer's suggestion, we decided to remove image 4, as it lacked a clinical relationship. Presumably the bleeding was caused by erosion of the parenchyma. Bronchoscopy prior to surgery showed no active arterial or venous bleeding

Changes in the text: we remove figure 4

Comment 4:

Please match the figures in the article. Figure $1 \rightarrow$ Figure 1A Unklar \rightarrow Unclear

Reply 4: Thank you for your comment. We made the changes to the text **Changes in the text:** Thank you for your comment. We made the changes to the text