

Peer Review File

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Reviewer A

I would like to congratulate the authors with their manuscript entitled “Video-assisted thoracic surgery is feasible and safe for acute necrotizing mediastinitis: a retrospective cohort study”. It covers a large retrospective cohort series regarding a very rare but extremely relevant subject. The manuscript is providing a nice overview of this topic. The authors advocate a minimal invasive approach which is an important message to the readership.

I have the following comments:

General:

- Please involve a native English speaker, which will substantially improve the quality of your paper.

Reply: We regret there were problems with the English. The paper has been carefully revised and improved the grammar and readability.

- You quite often use the term “meanwhile”, mostly not in the correct context.

Reply: We are sorry for using the wrong conjunction. We have modified our text as advised. Thank you for your comments.

Change in the text:

Line 40 (Abstract-Methods-1st paragraph-3rd and 4th sentence);

Line 99 (Method-Patients-2nd paragraph-3rd sentence);

Line 123 (Method-Clinical procedures-2nd paragraph-4th and 5th sentence);

Line 150 (Method-Statistical Analysis-1st paragraph-2nd and 3rd sentence);

Line 174 (Results-2nd paragraph-3rd and 4th sentence);

Line 235 (Discussion-6th paragraph-2nd and 3rd sentence);

Introduction:

- Line 56: below the level of the fourth thoracic vertebra

Reply: We have modified our text as advised. Thank you for your comments.

Change in the text: Line 74 (Introduction-1st paragraph-6th sentence)

- Line 58: “numerous diseases are advocated using VATS” should be: numerous diseases are nowadays treated with use of VATS”

Reply: We apologize for not describing clearly here. We have modified our text as advised. Thank you for your correction.

Change in the text: Line 78-79 (Introduction-1st paragraph-9th sentence)

Methods:

- Line 72-73: why are these patients excluded? Where they treated via an alternative surgical approach, or where they non-operatively treated? Please elaborate.

Reply: These patients were excluded for not receiving treatment of VATS or thoracotomy. They have been treated with cervical approach. We are sorry for not mentioning this. We have made another description. Thank you for your comments.

Change in the text: Line 97-98 (Method-Patients-2nd paragraph-3rd sentence)

- Line 83-84: do you mean a thoracotomy in the 4th intercostal space? Or did you choose between either 4th and 5th? Please rephrase.

Reply: We are sorry that the description is not clear. In clinical practice, we choose the fourth or the fifth intercostal space as the approach of thoracotomy. The choice of the fourth or the fifth intercostal space depends on the location of lesion. We have changed the description. Thank you for your comments.

Change in the text: Line 117-118 (Method-Clinical procedures-2nd paragraph-4th sentence)

- Line 85: .. were selected for trocar placement

Reply: We are sorry for not mentioning this information in detail. The VATS approach included, an 1-cm incision for the thoracoscope in the seventh intercostal space on the midaxillary line, a 3-cm utility incision on the anterior axillary line in the third or fourth intercostal space, and a 2-cm assistant incision in the ninth intercostal space (between the posterior axillary line and scapular line). Thank you for your comments.

Change in the text: Line 118-121 (Method-Clinical procedures-2nd paragraph-5th sentence)

- Line 87: what do you mean by debridement of complete excision? Please rephrase

Reply: We are sorry that misunderstanding description. We want to express a complete excision of necrotic and infected tissue, which are similar to the preceding sentence “excision of infected tissues and pleura”. We have modified the text. Thank you for your comments.

Change in the text: Line 125-126 (Method-Clinical procedures-2nd paragraph-6th sentence)

- Line 89: please explain abbreviations the first time you use them (Fr = French)

Reply: We are sorry for no explanation of this abbreviation. We have added a reference to this abbreviation. Thank you for your comments.

Change in the text: Line 127 (Method-Clinical procedures-2nd paragraph-7th sentence)

- Line 90: the abscess content was collected and sent for bacterial and fungal cultures

Reply: We have changed the formulation. Thank you for your comments.

Change in the text: Line 129-130 (Method-Clinical procedures-2nd paragraph-8th sentence)

- Line 95: gender = sex

Reply: We have modified the text as advised. Thank you for your comments.

Change in the text: Line 137 (Method-Data collection-1st paragraph-1st sentence)

- Line 107-108: please provide a reference for SPSS

Reply: We have added the reference for SPSS in the text. Thank you for your comments. (SPSS: Statistical Product and Service Solutions)

Change in the text: Line 154-155 (Method-Statistical Analyses-1st paragraph-5th sentence)

- How did you decide to perform either an open or minimally invasive approach? Was this dependent on patient characteristics, or surgeon's preference? Was there a treatment protocol? Please elaborate.

Reply: We thank the reviewer for raising this question. The surgery of ANM is an emergency operation. Most of the surgeries are performed by surgeons on duty. The decision between thoracotomy and VATS is based on the individual preferences of these surgeons. As we know, there is currently no established treatment protocol that dictates the selection between an open

and minimally invasive approach. We have added this information in the methods section and discussion section.

Change in the text:

Line 113-114 (Method- Clinical procedures-1st paragraph-4th sentence)

Line 265-266 (Discussion-8th paragraph-4th sentence)

Results:

- Line 118-119: "Patients treated in our hospital were all sent sputum specimen and abscess secretion was obtained in surgery for bacterial and fungal cultures" belongs to the Methods section

Reply: We have deleted the sentence in the wrong section. Thank you for your comments.

Change in the text: Line 169-170 (Results-2nd paragraph-1st sentence)

- Line 128-131: Methods

Reply: We have modified this formulation of this paragraph in a proper way. Thank you for your comments

Change in the text: Line 179-189 (Results-3rd paragraph)

Discussion:

- Please start the Discussion section with the summary of the main results of your study.

Reply: We have started the discussion section with the following paragraph. "In this study, a total of 64 patients with ANM were enrolled, with 48 in the VATS group and 16 in the OPEN group. The most common origin of infection was the neck. The results showed that thoracotomy was more frequently chosen for patients with esophageal perforation. The postoperative outcomes of the two groups were compared and it was found that these outcomes were similar between the two groups. In general, the outcomes of both groups were comparable, which were consistent with previous report (Tanaka Y, Maniwa Y, Sugio K, et al. The efficacy of thoracoscopic surgery for descending necrotizing mediastinitis. *Interdisciplinary cardiovascular and thoracic surgery* 2023;36)". Thank you for your comments.

Change in the text: Line 192-196 (Discussion-1st paragraph)

- Line 144-145: please rephrase; if possible, add a reference to this paragraph

Reply: Thank you for your comments. We have rephrased the text and added a reference to this paragraph (Scaglione M, Pezzullo MG, Pinto A, et al. Usefulness of multidetector row computed tomography in the assessment of the pathways of spreading of neck infections to the mediastinum. *Semin Ultrasound CT MR* 2009;30:221-30).

Change in the text: Line 211-213 (Discussion-3rd paragraph-8th sentence)

- Please expand your limitations section (retrospective character, relatively low number of participants given the rare character of this entity, different forms of bias, loss to follow up, et cetera).

Reply: We have modified the limitation section as advised. "Several limitations existed in this study. First, the retrospective design of the study set a limit to the convincement of our conclusion. ANM is a rare and lethal disease, so it was difficult for us to conduct a prospective study. Furthermore, the choice of the surgical procedure was influenced by the

personal preferences of the surgeons, and with the advancements in VATS, it has become the more commonly chosen approach. As a result, the sample size of patients who underwent thoracotomy was relatively small, which may introduce statistical bias. Additionally, our study lacked long-term follow-up data”. Thank you for your comments.

Change in the text: Line 263-272 (Discussion-8th paragraph)

- Was there a trend over time in selection of surgical approaches? In other words, were thoracotomy patients included in the earlier days of your cohort and VATS patients more recently?

Reply: We have found a trend in selection of surgical approaches. It seems that in earlier time surgeons were more likely to choose thoracotomy from 2012-2015. Since 2016, VATS were more commonly chosen by thoracic surgeons, which can lead to statistics bias. We have added this in the discussion section. Thank you for your comments.

Years	Total	VATS	Thoracotomy
2012-2015	10	3 (30%)	7 (70%)
2016-2018	23	18 (78.3%)	5 (21.7%)
2019-2021	31	27 (87.1%)	4 (12.9%)

Change in the text: Line 265-266 (Discussion-8th paragraph)

Conclusion:

- Please consider: “Acute necrotizing mediastinitis is a rare but lethal condition. Aggressive treatment, including open or minimally invasive cervical and thoracic procedures is often necessary. In this retrospective cohort study, VATS has comparable outcomes compared to thoracotomy. Therefore, VATS should at least be considered as part of the armamentarium of treatment modalities, offering these critically ill patients the advantages of a minimal invasive approach.”

Reply: We are so grateful for your advice. We made changes in the conclusion section.

Change in the text: Line 275-281 (Conclusion-1st paragraph)

Table 1:

- Gender = sex

Reply: We have modified the text in Table 1. Thank you for your comments.

Change in the text: Line 374 (Table 1)

Reviewer B

I read this paper, and I would like to agree with acceptance for publication in this journal. However, you should rework it, below.

You should delete “in” at Page 4, Line 68, because you mistook to write “All the data of patients was provided in in anonymous and informed consent was waived.”

Reply: We are sorry for using “in” twice. We have modified our text as advised. Thank you for your comments.

Change in the text: Line 93 (Methods-1st paragraph-2nd sentence)

Reviewer C

The authors describe the relevance of VATS in the surgical treatment of ANM. However, the VATS approach is currently practiced in many centers and is not considered a new finding. We believe that the reasons for choosing open thoracotomy at your institution should be clarified.

Reply: We apologize for not describing clearly here. ANM is a lethal disease and aggressive surgical drainage is recommended in almost all series. Thoracotomy is the most commonly used surgery for mediastinal abscess drainage in the previous literature. VATS is a novel treatment and some researchers argued VATS may not as effective as thoracotomy, citing the latter's advantage of providing a wider surgical field and operating space. This study aims to explore and compare the outcomes of these two surgical methods. Thank you for your comments.

Reviewer D

In this retrospective single-institutional study, the authors compared the clinical characteristics and surgical outcomes of acute necrotizing mediastinitis (ANM) between VATS and thoracotomy. I have some comments.

1. About the choice of VATS and thoracotomy, the thoracotomy group includes more patients with esophageal perforation than the VATS group. Is VATS selected as the first choice for ANM in most case except for those with esophageal perforation in your institution? Or has VATS been chosen more frequently over time?

Reply: We are sorry that the description is not clear. The surgery of ANM is an emergency operation. Most of the surgeries are performed by surgeons on duty. The decision between thoracotomy and VATS is based on the individual preferences of these surgeons. The result revealed thoracotomy was more commonly chosen for patients with esophageal perforation. The reason may be that thoracic surgeons need wide operating space for repairing the esophagus and ensuring hemostasis. We have added this in the results and discussion section.

Change in the text:

Line 166-177 (Results-1st paragraph-7th sentence)

Line 193-194 (Discussion-1st paragraph-3rd sentence)

Line 235-237 (Discussion-6th paragraph-4th sentence)

Also, we have found a trend in selection of surgical approaches. It seems that in earlier time surgeons were more likely to choose thoracotomy from 2012-2015. Since 2016, VATS were more commonly chosen by thoracic surgeons, which can lead to statistics bias. We have added this in the discussion section. Thank you for your comments.

Years	Total	VATS	Thoracotomy
2012-2015	10	3 (30%)	7 (70%)
2016-2018	23	18 (78.3%)	5 (21.7%)
2019-2021	31	27 (87.1%)	4 (12.9%)

Change in the text: Line 265-266 (Discussion-8th paragraph)

2. This study includes a smaller number of patients undergoing bilateral surgical drainage and those undergoing repeated surgical drainage. The severity of ANM remains unclear. This study might include less severe cases.

Reply: In our clinical practice, most patients can be debrided and drained thoroughly by one side approach. After the surgery, we place silicone tubes for postoperative drainage. For most patients, these tubes can effectively drain the abscess in the cavity. With adjusted antibiotics according to the bacterial susceptibility testing after the surgery, most patients did not need reoperation. Therefore, the number of patients undergoing bilateral surgery and reoperation is small. Thank you for your comments.

3. Recently, a paper comparing the clinical outcomes of mediastinal drainage for descending necrotizing mediastinitis between VATS and thoracotomy was reported (Tanaka Y, et al. The efficacy of thoracoscopic surgery for descending necrotizing mediastinitis. *Interdisciplinary CardioVascular and Thoracic Surgery* 2023;36:ivad053). This paper should be cited in the presenting manuscript.

Reply: We have modified the text in the introduction section and discussion section as advised. Thank you for your comments.

Change in the text:

Line 79-80 (Introduction-1st paragraph-10th sentence)

Line 195-196 (Discussion-1st paragraph-5th sentence)

4. The definition of mortality remains unclear. It should be modified such as 90-day mortality and hospital mortality. Please reconsider.

Reply: We are sorry for not describing clearly here. The definition of mortality in our study meant hospital mortality. We modified in the text. Thank you for your comments

Change in the text: Line 144-145 (Methods-Data collection-4th sentence)

5. There are some typos found in this manuscript. Moreover, some references are duplicated. The revised manuscript should be checked again by English proofreading.

Reply: We regret there were these problems. We have modified the text and reference as advised. The paper has been carefully revised to improve the grammar and readability.

Change in the text: Line 305-372 (Reference)

Reviewer E

The authors reviewed their single institutional experience of acute necrotizing mediastinitis (ANM) regarding surgical management. Thank you for this review opportunity.

My concerns are about some points

1) What is the novelty of this study?

Reply: Acute necrotizing mediastinitis is a lethal disease. Thoracotomy is the most commonly used surgery for mediastinal abscess drainage. VATS is a novel treatment and is becoming a mainstream in thoracic surgery. However, whether VATS in treating ANM is as effective as thoracotomy is controversial. Our study revealed that the outcomes were comparable between the VATS and open surgery for the treatment of ANM. This outcome can provide these

critically ill patients with a minimal invasive treatment. Thank you for your comments.

2) Retrospective analysis cannot produce any statistical result, so any conclusion can be drawn.

Reply: There is no statistical difference in treatment outcomes of our study. But these results illustrated the comparable postoperative outcomes between the VATS and thoracotomy. Therefore, VATS can be an appropriate option for patients with ANM. When treating patients with critical infection, surgeons can have different options. Thank you for your comments.

3) No discussion has been given about the choice among the two technique (open vs VATS).

Reply: We are sorry for not describing clearly here. The surgery of ANM is an emergency operation. Most of the surgeries are performed by surgeons on duty. The decision between thoracotomy and VATS is based on the individual preferences of these surgeons. We have added this information in the discussion and limitations section. Thank you for your comments.

Change in the text:

Line 113-114 (Method- Clinical procedures-1st paragraph-4th sentence)

Line 265-266 (Discussion-8th paragraph-4th sentence)

4) Have you identified any risk factors of post-operative complications and outcome in your series?

Reply: In this retrospective study, we did not find any risk factors associated with post-operative complications and outcomes. In clinical practice, we noticed that patients with septic shock may have more postoperative complications and poor outcomes. However, the number of patients with septic shock was limited in both groups. In the future we will enroll a larger sample size of patients with ANM, both those treated with surgery and those without, in order to investigate the risk factors for complications and outcomes in this patient population. Thank you for your comments.