

## Peer Review File

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### Reviewer A

Comment 1: line 162-167: what is the difference between the 2 approaches? it's not very clear.

Reply 1: As you noted, the distinction between the two techniques was challenging to comprehend and lacked adequate explanation. In response, we have thoroughly revised the entire narrative delineating the surgical approach, incorporating comprehensive descriptions. The references have been partially changed. The revisions span from Line 205 to 240.

Comment 2: I would suggest to change the title "revascularization" with "vascular resection and reconstruction"

Reply 2: I've altered the title to "Vascular Resection and Reconstruction," as per your suggestion. The change is Line 269.

### Reviewer B

Comment 1: a focus on TET staging, reported the new TNM and the clear definition of locally advanced is necessary.

Reply 1: In this review, an exhaustive examination of the literature concerning locally advanced TETs from the year 2000 onward was undertaken. To achieve a consistent disease classification, the Masaoka classification was employed. Moreover, the specification of the staging for locally advanced TETs was further elucidated in the Methods section. The revisions span from Line 71 to 77.

Comment 2: surgical approach description (lines 156-169) should be completely reviewed.

Reply 2: As noted, the surgical approach has been fully revised and added. The revisions span from Line 205 to 240.

Comment 3: I would analyze the impact of minimally invasive surgery more in details in patients with advanced TET.

Reply 3: Presently, there is a notable scarcity of reports on minimally invasive surgery for locally advanced TETs; however, this area holds substantial promise for future developments. The existing limited literature from the past has been incorporated, highlighting the potential for future advancements. The revisions span from Line 250 to 254.

Comment 4: In the section of phrenic nerve reconstruction, I would add also the possibility of phrenic nerve preservation (references: 1. Aprile V, et al. Nerve-Sparing Surgery in Advanced Stage Thymomas. Ann Thorac Surg. 2019 Mar;107(3):878-884.; 2. Yano M, et al. Preservation of phrenic nerve involved by stage III thymoma. Ann Thorac Surg. 2010 May;89(5):1612-9.)

Reply 4: Thank you for your significant insight. The preservation of the phrenic nerve is equally crucial in cases of locally advanced TETs. I have incorporated a mention of the potential loss of pulmonary function resulting from phrenic nerve transection and emphasized the importance of preserving the phrenic nerve. The revisions span from Line 335 to 337 and Line 378 to 383.

Comment 5: The role of surgery in case of recurrence should be analyzed.

Reply 5: The role of surgical treatment at recurrence for locally advanced TETs is a very important item and very interesting. However, we have omitted it because it would require a new chapter and is outside the scope of this issue of perioperative management. If it is necessary for readers, we would like to add a chapter and describe it. In that case, I would appreciate it if you could point it out again in the revision.

### **Reviewer C**

Comment 1: Please check the authors name cited in the text (i.e. Lucchi and not Lucci).

Reply 1: As pointed out, there was a spelling error, which has been corrected for reference 35. Line 559 was corrected.

Comment 2: At page 9, row 185, surgeons' psychology is not a proper term. Since radicality should be the goal of such demolitive and challenging surgery a wide exposure allows a safer surgery, especially after induction therapy.

Reply 2: Thank you for your valuable comments. I have changed the phrase "surgeon's mind" to emphasize the radicality and safety of the surgery, which is certainly not appropriate. The revisions span from Line 259 to 262 and Line 265.

Comment 3: Discussion of the phrenic nerve involvement could be improved by reading the following article (PMID: 30336118.)

Reply 3: Thank you for your significant insight. The preservation of the phrenic nerve is equally crucial in cases of locally advanced TETs. I have incorporated a mention of the potential loss of pulmonary function resulting from phrenic nerve transection and emphasized the importance of preserving the phrenic nerve. The revisions span from Line 335 to 337 and Line 378 to 383.

Comment 4: The review is really interesting especially in the surgical management of advanced TET but there is no discussion on the pre-operative management (pre-operative work-up, anesthesiologist evaluation or the role of Myasthenia Gravis).

Reply 4: As pointed out, we believe that preoperative management of TETs is also important. Since there have been very few reports on the preoperative management of TETs in the past, we have created a new paragraph and added it, although it is a brief description. The revisions span from Line 79 to 101.

Comment 5: Several authors experienced ECMO and ECC (extracorporeal circulation), authors could cite this innovative approach.

Reply 5: Surgical treatment of TETs using cardiopulmonary bypass is a valuable option in certain cases, and we have incorporated this information based on prior reports. The revisions span from Line 177 to 182.

Comment 6: Discussion on the role of the different structures involved by advanced TET should be improved (PMID: 34252198 - PMID: 37104878).

Reply 6: Thank you for your valuable remarks. I have incorporated additional considerations based on the references you provided, with a specific focus on the number of invaded structures as a potential prognostic factor and the acceptability of microscopic incomplete resection in thymoma. The revisions span from Line 111 to 114 and Line 183 to 188.

Comment 7: Any discussion on the surgery of stage Iva TET has been proposed, this should be reported in the Material and Method.

Reply 7: As you pointed out, we have revised a "Methods" chapter to address stage IVa TETs as well. The revisions span from Line 71 to 77.

#### **Reviewer D**

Comment 1: In Abstract, the number of referenced articles with their patients' number should be included to indicated the quality of this review.

Reply1: As you pointed out, we have included the number of references and the total number of patients analyzed in the Abstract. The revisions span from Line 28 to 29.

Comment 2: L.31, "transverse nerve" is probably transferred, wrongly. "phrenic nerve" would be correct.

Reply 2: Thank you for pointing this out, phrenic nerve is correct and I have corrected it. The revision is Line 33.

Comment 3: L.65, How do authors evaluate the "reliability" to enroll into this review? The criteria should be described in more detail.

Reply 3: We have added our criteria for selecting references. The revisions span from Line 66 to 68.

Comment 4: L.102, Cyclophosphamide is not included in CAMP regimen. Prednisolone should be changed to methylprednisolone.

Reply 4: CAMP regimens include the cisplatin, doxorubicin, and methylprednisolone regimen reported by Yokoi et al. (1) and the cyclophosphamide, cisplatin, doxorubicin, and prednisolone regimen reported by Kim et al. (2) We have included both regimens in response to this suggestion. The revisions span from Line 137 to 138.

1) Yokoi K, Matsuguma H, Nakahara R, et al. Multidisciplinary treatment for advanced invasive thymoma with cisplatin, doxorubicin, and methylprednisolone. J Thorac Oncol. 2007;2(1):73-8.

2) Kim ES, Putnam JB, Komaki R, et al. Phase II study of a multidisciplinary approach with induction chemotherapy, followed by surgical resection, radiation therapy, and consolidation chemotherapy for unresectable malignant thymomas: final report. Lung Cancer. 2004;44(3):369-79.

Comment 5: In the paragraph for phrenic nerve reconstruction, authors comment about bilateral phrenic nerve resection during surgery for invasive TETs with the successful course. However, this procedure should be avoided as much as possible, because postoperative respiratory failure is sure to be complicated. The description should be carefully not to mislead the journal readers.

Reply 5: As you mentioned, in locally advanced TETs, preserving the phrenic nerve, even if it has been invaded, is an important consideration for functional prognosis. I have added a note emphasizing the importance of preserving the phrenic nerve. The revisions span from Line 378 to 383.

Comment 6: L.372, Acknowledgement for English editing company is not necessary. Delete it.

Reply 6: As noted, we have deleted the acknowledgement for English editing company.