Peer Review File
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Reviewer A

Comment: Not including a pathologist and not mentioning the Department of Pathology is a major flaw in line of the extensive but imprecise pathological information: lines 97-98.

Reply 1: We thank the reviewer for this comment. The present study has a long duration over 37 years and many pathologists have been involved in the present study. Therefore, a certain or particular pathologist was difficult to be added in the present study. We described the information about Department of Pathology in the manuscript. Please see Page 7, line 99.

Comment 2: Abstract
Methods: Authors must state which staging system* is used and what the authors define as „early tumor stage". This is particularly relevant if the use the (outdated) *classical Masaoka stage.
Reply 2: We thank the reviewer for this comment. As the reviewer pointed out, the manuscript is lacking about staging system. We added it in the Materials. Please see Page 7, line 100-102. Regrettably, there was no enough space to describe in the abstract.

Comment 3: Results: Line 31: should read „…at earlier tumor stages…"
Reply 3: We thank the reviewer for this comment. We revised the manuscript. Please see Page 2, line 31.

Comment: 4: **Materials**
It is not clear whether the treatment strategies chosen followed any Japanese or international guidelines
Reply 4: We thank the reviewer for this comment. Our treatment strategies are basically based on the guideline of the Japan lung Cancer Society. The strategies based on our experience are also included in the earlier period cases because of the rarity of TC.

Comment 5: Lines 69 - 72: As to inoperability: Were there any restrictions in terms of age or health status of the patients?

Reply 5: We thank the reviewer for this comment. There is no restriction of the surgical treatment in terms of age. Regarding the health status, the patients of ECOG Performance Status (PS) 0-2 have surgical indication in general at our institution.

Comment 6: Lines 72-75: Please give rationale when radiotherapy, chemotherapy or chemoradiotherapy were used
Reply 6: We thank the reviewer for this comment. For the patients with distant metastasis, chemotherapy is selected. Regarding the inoperable patients with locally advanced TC, chemoradiotherapy is selected. Among the locally advanced TC patients, radiotherapy is selected when chemoradiotherapy was considered to be intolerable. We revised the manuscript. Please see Page 6, line 76-79.

Comment 7: Lines 76-79 the chemotherapy regimens used should be adequately referenced (and deviations from standards should be highlighted)
Reply 7: We thank the reviewer for this comment. We added the references in the manuscript.

Comment 8: Lines 83 Unclear: What is "relatively small-sized"? Was there any size (in cm) threshold?
Reply 8: We thank the reviewer for this comment. In our institution, small-sized for TETs means 3 cm or less as the previous report has shown (Yano M, et al. Surg Today. 2014; 44: 1817-22.). We revised the manuscript. Please see Page 6, line 90.

Comment 9: Line 84: „… in the most..." is unclear: „…in the most cases except for those with invasion of great vessels nowadays". It should be stated clearly since when you use MIS in Masaokoa-Koga (and TNM)? Stage I-III tumors (irrespective of size?) except if there is invasion of at least one great vessel. It should also be defined whether invasion of the brachiocephalic vein is an indication for open surgery.
Reply 9: We thank the reviewer for this comment. We revised the sentence. Please see Page 6-7, line 89-93.

Comment 10: Authors should state, when inoperable patients were considered operable after neoadjuvant approaches.
Reply 10: We thank the reviewer for this comment. We added the sentence. Please see Page 6, line 88-89.

Comment 11: Were there any patients with paraneoplastic symptoms/syndromes?
Reply 11: We thank the reviewer for this comment. None of all the 71 patients had paraneoplastic syndromes in the present study.

Comment 12: Authors should state, whether and since when they perform lymphadenectomy (at least for N1 nodes) in the context of MIS.
Reply 12: We thank the reviewer for this comment. We added the sentence. Please see Page 7, line 93-95.

Comment 13: Results
Lines 96-99 Were the cases reviewed by a pathologist or were the diagnoses taken from historic files. It would be interesting to learn, what the diagnoses were in the other 12 „types of carcinoma".
Reply 13: We thank the reviewer for this comment. In the present study, we referred to the database which is consist of the information of medical records. Regarding the other types of carcinomas, small cell carcinoma, large cell neuroendocrine carcinoma, basaloid carcinoma, sarcomatoid carcinoma, and mucoepidermoid carcinoma were diagnosed in the present study.

Comment 14: Line 111 To be able to appreciate the strikingly different R0 recetion ratest, the authors should give the means and medians of "tumor size" in both the earlier and later groups (and whether early vs. later tumor sizes were significantly different)
Reply 14: We thank the reviewer for this comment. We added the means and medians of "tumor size" in Table 2.

Comment 15: Discussion
Authors should discuss their indication of MIS in the light of the recent paper by Roden et al. In JTO 2022, PMID: 35227908
Reply 15: We thank the reviewer for this comment. We revised the discussion about the indication of MIS and the reference. Please see Page 12, line 189-192.

Comment 16: Were there any conversions of minimal-invasive towards open surgery? Is robotic surgery now the standard for MIS (since when?) or are robotic and VATS still used nowadays?
Reply 16: We thank the reviewer for this comment. In the patients of the present study, there was no conversion from MIS to open surgery. Regarding robotic surgery, it has

been performed since September 2018 at our institution and 90% of MIS were underwent by robotic surgery recently.

Comment 17: Ref. 1 is outdated in terms of the WHO classification 2021 (a new one is available)
Reply 17: We thank the reviewer for this comment. We revised the Reference 1. Please see Page 16, line 247-249.

Reviewer B

Comment 1: The "Materials" section should be supplemented with information:
- How was the prognosis assessed - in the results the authors mention a 5-year survival time. If so, how was this parameter assessed in patients treated in 2017 and later?
- What methods were the tumors detected by? This is only described in the results. Were resectable tumors biopsied prior to surgery to establish a diagnosis?
Reply 1: We thank the reviewer for this comment. We added the sentences in the material paragraph. Please see Page 5, line 67-70 and Page 7, line 101-102.

Comment 2: Line 93-94: Summing up the cases in all stages gives 51. I would suggest mentioning the remaining 20 cases of unknown stage so that the sum is correct. Otherwise, the reader may feel confused.
Reply 2: We thank the reviewer for this comment. We added the sentence in the manuscript. Please see Page 8, line 112.

Comment 3: How do the authors explain the greater number of complete resections in the later group compared to the earlier group? It would be worth adding a short comment.
Reply 3: We thank the reviewer for this comment. As the reviewer pointed out, it is worth mentioning about the reason of the greater number of complete resections in the later group. We considered that early detection by CT screening led to the greater number of complete resections. We added the sentence in the manuscript. Please see Page 11, line171-173.

Comment 4: For what reasons did the authors perform subtotal thymectomy in 9 cases? What were the indications? It would be worth commenting on.

Reply 4: We thank the reviewer for this comment. We added the explanation about the indication for limited thymectomy at our institution in the Materials. Please see Page 7, line95-98.

Comment 5: Table 4: row „Subjective symptom (n=)" - probably instead of „N0" there should be „no".
Reply 5: We thank the reviewer for this comment. We revised the word in Table 5.

Comment 6: The manuscript requires a slight linguistic correction.
Reply 6: We thank the reviewer for this comment. We had the manuscript re-corrected by the native check.

Reviewer C

Comment 1: This is an underpowered, study of three groups of patients with Thymic carcinoma treated with surgery between 1983 and 2009 (n=24), 2009 to 2020 (n=21), and those having no surgery (n=26).
There is no specific information about the chemotherapy and medical treatment: neoadjuvant, adjuvant, and in the palliative setting. The groups are heterogeneous in histology, surgical approach, staging methods, and tumor stage which makes any conclusion besides the time period when treatment was performed hard to justify.
The authors stated that incomplete resection to be acceptable in thymic carcinoma seems rather provocative.
Overall there is one valid finding: Tumor stage is of prognostic significance for survival in TC.
Altogether, this is a modest piece of work of no great value to the workers in the field. Although the raised question is of practical importance the weak design and the lack of essential information may not allow publication in my opinion.
Reply 1: We thank the reviewer for these comments. As the reviewer pointed out, there is no novel finding about the chemotherapy and medical treatment in the present study. However, regarding the prognosis of thymic carcinoma (TC), there have been few reports concerning the changes in the prognosis over time. Therefore, whether or not the treatment or prognosis has improved over the years remains unclear. The present study is a single center retrospective analysis; however, we think that it included relatively large number for TC and showed the tendency of a certain kind about the changes in the prognosis of TC. In the point of surgical treatment, small-sized thymic epithelial tumors

(TETs) have been treated more frequently than before due to the spread of CT and the application of minimally invasive surgery for TET has also spread recently. Moreover, regarding small-sized anterior mediastinal tumors, surgical treatment, including limited thymectomy, is selected without a preoperative diagnosis in most cases. Therefore, limited thymectomy for small-sized TC is often considered to be performed in clinical practice. So, we revealed the results of the MIS and limited thymectomy for small sized TC in the present study.

Reviewer D

Major comment 1: Even though the authors divided the patients in 2 groups based on the time of introducing minimally invasive surgery (MIA) in their institute, they mentioned that the improvement of prognosis may result from the change of imaging methods. It is not clear if CT imaging has been available since 2009 in their institute/their county. They should compare "modality of identification" between the periods in all 71 patients, not only in surgical treated cases.
Reply 1: We thank the reviewer for this comment. As the reviewer pointed out, it is necessary to analyze the comparison of "modality of identification" between the periods in all 71 patients, not only in surgical treated cases. We added the analysis and the table in the manuscript. Please see Table3 and Page 9, line 129-134.

Major comment 2: While the authors say that the surgical indication did not change throughout this study, the clinical stage was significantly higher in the latter group of non-surgical treatment. On the other hand, the prognosis of non-surgical treatment has not changed between the periods. This may be because the management of side-effect of chemotherapy has been improved.
Reply 2: We thank the reviewer for this comment. As the reviewer pointed out, improvement of the management for side-effect of chemotherapy may influenced these results above, which we think as well.

Minor comment: In Table 3 (the box of "Early period" and "Treatment") and p.7, line95-96, total number of cases does not reach 12.
Reply: We thank the reviewer's pointing out. We revised the table.

Reviewer E

Minor comment 1: How many surgeons were involved in the study? In other thoracic procedures, literature has shown that surgeons' volumes, for example esophagectomy, have been associated with improved survival. Is it possible that due to increased usage of CT scan in recent periods, recent surgeons have increased thymectomy volume, thus leading to better outcomes?

Reply 1: We thank the reviewer for this comment. The study period is too long and more than 10 surgeons were included. As the reviewer pointed out, today's general thoracic surgery in Japan, including thymectomy, has been performed twice as many as 20 years ago. So, recent surgeons have increased thymectomy volume as the reviewer mentioned above. On the other hand, perioperative mortality of thymectomy is much lower than that of pulmonary resection in our field. Therefore, regarding thymectomy, influence of experience value on the outcome may be limited.

Minor comment 2: The discussion section should also touch on length time bias, due to increased usage of CT scans. Length time bias is often discussed in the context of the benefits of cancer screening, and it can lead to the perception that screening leads to better outcomes when in reality it has no effect.

Reply 2: We thank the reviewer for this comment. As the reviewer pointed out, it is necessary to mention about length-time bias in the manuscript. We added the sentence in the limitation paragraph. Please see Page 13 line 210-212.

Minor comment 3: This retrospective study includes patients from 1983-2020, which is a relatively long time period. Granted, thymic carcinoma is a relatively rare tumor. However, I think the authors should briefly mention the relatively long time period for patient inclusion may introduce potential bias in the limitation paragraph.

Reply 3: We thank the reviewer for this comment. We added the sentence in the limitation paragraph. Please see Page 13 line 213-215.

Major comment 1: With the introduction of MIS, I wonder if the authors can touch on perioperative outcomes, specifically length of stay, operative time, perioperative complications, etc.

Reply 1: We thank the reviewer for this comment. We added the sentence in the introduction paragraph and references. Please see Page 4, line 52-54 and Page 18, 284-287.

Major comment 2: In the method section, the author mentioned that survival analysis was performed using Kaplan-Meier and univariable log-rank test. I wonder whether it is possible to can control for some of the more commonly employed covariates when performing survival analysis, such as stage and surgical approach. If the authors believe that a multivariate survival analysis is not appropriate for the study, please briefly discuss in the discussion.

Reply 2: We thank the reviewer for this comment. Thymic carcinoma is a rare disease, and the number of cases is limited, and the observation period of this study is too long. So, there are restrictions such as not knowing the detailed treatment for each case, and the number of factors to be compared has limited. We described limitations of this study at Discussion.

Major comment 3: The manuscript contains several syntax and grammatical mistakes. Though not critical, these mistakes should be corrected prior to acceptance.

Reply 3: We thank the reviewer for this comment. We had the manuscript re-corrected by the native check and revised.