

Peer Review File

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Reviewer A

Comment 1: The authors use the subxiphoid approach, but there is no evaluation as to whether the pericardial fat tissue was actually sufficiently excised. It has been pointed out that the subxiphoid approach has a good cervical field of view, but the pericardium near the port is difficult to see. Is the pericardial fat tissue really removed in this study? It seems that some ingenuity is required to remove the pericardial fat tissue with the subxiphoid approach. How did you remove it?

Reply 1: The authors are thankful to the reviewer for this question. We always inserted ports in the both (left and right) thoracic cavities at the extended thymectomy. If the dissection line of the left and right pericardial fat tissue was difficult to check from the subxiphoid incision, a thoracoscope was moved to the lateral thoracic port to check not leaving pericardial fat tissue. At the end of the operation, it was confirmed by thoracoscope from the left and right ports that there was no residual pericardial fat tissue around the pericardium.

Changes in the text: We added the next sentences at Page 8, line140-142.

At the end of the operation, it was confirmed by thoracoscope from the left and right ports that there was no residual pericardial fat tissue around the pericardium.

Comment 2: Where is the boundary between the thymus lower lobe and pericardial fat tissue?

Reply 2: The authors are thankful to the reviewer for this question. The resected specimens were confirmed the boundary between the thymus lower lobe and pericardial fat tissue and separated by the change in the color tone. Although the boundary between the thymus lower lobe and pericardial fat tissue was unclear, the extent of resection was decided by an intraoperative inspection, so in this study, the boundary was determined by visual inspection of the resected specimen. Pathological examination revealed pericardial fat tissue at the side of thymus lower lobe in a few cases.

Comment 3: I think it is not uncommon for thymoma to form on the pericardium.

How would you explain it?

Reply 3: The authors are thankful to the reviewer for this comment. As the reviewer pointed out, we experience the cases of thymoma to form on the pericardium. Since most of them can be detected by preoperative imaging, including CT and MRI, we think it need to remove the surrounding pericardial fat tissue extensively in such cases.

Comment 4: Is it okay to remove the site without a Germinal center? Some patients with MG have thymic tissue without Germinal center (Case 7, 11, 17). Is it okay to consider that thymic tissue without Germinal center does not need to be resected?

Reply 4: The authors are thankful to the reviewer for this comment. All cases of MG without thymoma (Case 1-6) had germinal centers in the thymus. About the cases without germinal centers (Case 7,11,17), two cases were MG with thymoma and one case was thymoma with anti-acetylcholine receptor antibody positive, so extended thymectomy underwent.

Comment 5: If the Pericardial fat tissue has no thymic tissue or does not need to be excised, I think that a one-sided approach without excising the contralateral Pericardial fat tissue is also a good result. Do you have any thoughts on this?

Reply 5: The authors are thankful to the reviewer for this comment. We think that a one-side approach results in inadequate resection of the thymus and surrounding fat tissue around contralateral phrenic nerve, which is inferior to the subxiphoid approach and the bilateral thoracic approach.

Comment 6: The discussion is too long. The same thing is repeated in the material and method and in the discussion. Please rewrite it more concisely.

Reply 6: The authors are thankful to the reviewer for this comment. We have erased some sentences in the discussion and modified the discussion as advised.

Comment 7: The conclusion states that the subxiphoid approach may not require excision of the pericardial fat tissue, but isn't the same true for the lateral chest intercostal approach?

Reply 7: The authors are thankful to the reviewer for this comment. Since the field of

view and the surgical procedure by the lateral chest intercostal approach are different from the subxiphoid approach, we think it is necessary to consider the pathological germinal centers evaluation of the thymic tissue resected by the lateral chest intercostal approach.

Reviewer B

Comment 1: How did Authors evaluate the germinal centers? HE staining or immunohistological staining?

Reply 1: The authors are thankful to the reviewer for this question. We evaluated the germinal centers by HE staining.

Changes in the text: We changed the sentences at Page 7-8, line 124-127.

The pathologist (H.H.) evaluated the number of germinal centers in the all area of the resected thymus and pericardial fat tissue by hematoxylin and eosin staining and mainly investigated the presence or absence of germinal centers in the pericardial fat tissue.

Comment 2: Did Authors evaluate the thymus as whole tissue or partial tissue?

Reply 2: The authors are thankful to the reviewer for this question. We evaluated the thymus as whole tissue.

Changes in the text: We changed the sentences at Page 7-8, line 124-127.

The pathologist (H.H.) evaluated the number of germinal centers in the all area of the resected thymus and pericardial fat tissue by hematoxylin and eosin staining and mainly investigated the presence or absence of germinal centers in the pericardial fat tissue.

Comment 3: Can we evaluate germinal center number at each area?

I think the rate (the number of germinal center / the area (cm²) is suitable for this study. How did Authors think it?

Reply 3: The authors are thankful to the reviewer for this comment. We evaluated germinal centers at each area, and showed the distribution of germinal centers in each lesion in Table 1. In this study, we did not check the rate (the number o germinal center / the area (cm²) and it is impossible to evaluated it from now on. We would like to evaluate it at the next examination.

Comment 4: How did Authors evaluate the rate of remission of MG symptoms?

Reply 4: The authors are thankful to the reviewer for this question. We evaluated MGFA score before surgery and at the time of final outpatient visit. Because the median follow-up period was 32months (range, 3-75 months), it is not possible to evaluate accurately. We described at discussion (at Page 12, line 214-216) as limitation about this.

Changes in the text: We added the sentence at Page 9, line 156-157.

No obvious pericardial fat tissue could be confirmed on the images.

Comment 5: Did Authors evaluate the area of extended thymectomy using RATS or VATS?

Reply 5: The authors are thankful to the reviewer for this question. We evaluated the area of extended thymectomy before surgery. And follow-up CT was performed within 1 year after the operation in all patients.

Changes in the text: We added the sentence at Page 9, line 156-157.

No obvious pericardial fat tissue could be confirmed on the images.

Comment 6: Did Authors evaluate whole tissue of thymus?

Reply 6: The authors are thankful to the reviewer for this question. We evaluated the thymus as whole tissue.

Changes in the text: We changed the sentences at Page 7-8, line 124-127.

The pathologist (H.H.) evaluated the number of germinal centers in the all area of the resected thymus and pericardial fat tissue by hematoxylin and eosin staining and mainly investigated the presence or absence of germinal centers in the pericardial fat tissue.

Comment 7: Could the MG patients reduce the steroid amount?

Reply 7: The authors are thankful to the reviewer for this question. We described the steroid usage at Page 9 line 159-162.

Changes in the text: We changed the sentences at Page 9-10, line 162-164.

Remission after surgery was achieved in all patients with generalized MG; 5 of the 11 patients showed complete remission (no need for medication), while the dosage of

steroids or immunosuppressant agents could be reduced in the other 6 patients.