# Peer Review File

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# Reviewer A:

# Major Comment 1:

Authors frequently said that there have been no reports of RATS thymectomy for thymic carcinoid. This would be apparently wrong. A case report shown as below already have demonstrated RATS thymectomy for advanced thymic neuroendocrine tumor. I wish authors should refer to this article.

Yanagiya M, Hiyama N, Matsumoto J. Dual-scopic robotic thymectomy for a large thymic malignant tumor. J Surg Case Rep. 2021; 2021(6): rjab280.

# **Reply:**

As suggested, we confirmed that this is not the first report of robot-assisted thymectomy for thymic tumor. We have now revised the manuscript as follows.

# **Changes in text:**

<Abstract; page 2, line 32-33>

There have been few reports of patients who received RATS thymectomy for thymic carcinoid.

# <Discussion; page 6, line 164-165>

To our knowledge, complete resection of thymic typical carcinoid using a robotic approach is rarely reported.

<Discussion; page 7, line 183-184>

We reported a rare case of thymic typical carcinoid that was able to be completely resected using RATS approach.

# **References:**

- 1. Dual-scopic robotic thymectomy for a large thymic malignant tumor. Yanagiya M, Hiyama N, Matsumoto J. J Surg Case Rep. 2021; 2021(6): rjab280.
- 2. Subxiphoid approach for robotic single-site-assisted thymectomy. Park SY, Han KN,

Hong JI, Kim HK, Kim DJ, Choi YH. Eur J Cardiothorac Surg. 2020 Aug 1; 58 (Suppl 1): i34-i38.

- 3. Single-institution experience on robot-assisted thoracoscopic operations for mediastinal diseases. Rea F, Schiavon M, Di Chiara F, Marulli G. Innovations (Phila). 2011 Sep; 6 (5): 316-22.
- 4. Application of robotic-assisted techniques to the surgical evaluation and treatment of the anterior mediastinum. Savitt MA, Gao G, Furnary AP, Swanson J, Gately HL, Handy JR. Ann Thorac Surg. 2005 Feb; 79 (2): 450-5; discussion 455.

### Minor comment 1:

In lines 79, authors said, "The patient was placed in the supine position." I doubt if this description was right. Following sentences suggested that the patient seemed to be in the lateral position and right lateral approach via RATS would be conducted. Please check the description again. And if authors can, they should show the patient's position as a figure.

### **Reply** :

We reviewed the operative record and confirmed that the surgery was performed in the supine position, with the arms positioned along the body as far back as possible to provide enough space for the robotic arms.

## Changes in text:

#### < Case Presentation; page 4, line 92-93>

The patient was placed in the supine position, with the arms positioned along the body as far back as possible to provide enough space for the robotic arms.

#### Minor comment 2:

Because this case report tried to focus on robotic surgery, the details of surgery needed to be described more. The description of surgical procedure was poor. I hope that they should state what kind of instruments or devices were used, and how to dissect tissues with what device. Lots of instruments and approaches are available in robotic surgery. Details of these things should be represented in the main text.

## **Reply:**

As suggested, the description of robotic surgery was revised to include more detail.

## Changes in text:

### <Case Presentation; page 4, line 100-102>

Carbon dioxide (CO2) with 10 mmHg of pressure was infused to include this pleural space further. Fenestrated bipolar forceps in the left arm and a permanent cautery spatula in the right arm were mainly used during the procedure.

## <Case Presentation; page 4, line 105- page 5 line 116>

The Thymus was isolated from the pericardium while moving superiorly from the lower pole of the thymus mainly using a cautery spatula; the thymic vein was dissected from the right innominate vein and cut using a VesselSealer. The thymus, including the tumor, was extirpated. The surrounding adipose tissue was also removed, including the mediastinal lymph nodes, as lymph node dissection.

#### Minor comment 3:

## Did authors conduct lymph node dissection in addition to thymectomy?

## **Reply:**

We removed the surrounding adipose tissue around the thymus, including the mediastinal lymph nodes, as a lymph node dissection. We have now mentioned this in description to the manuscript.

### **Changes in text:**

<**Case Presentation**; page 4, line 108- page 5 line 116>

The thymus including the tumor was extirpated. We removed the surrounding adipose tissue around the thymus to include the mediastinal lymph nodes as a lymph node dissection.

# Minor comment 4:

Regarding Figure 1, the maximum standard uptake of the tumor was 9.09. I assume that this uptake would be too high for indolent thymomas. Based on this abnormal uptake, thymic cancer, thymic carcinoid or thymoma B3 should be initially suspected. Did authors

have a plan to convert open thoracotomy or sternotomy if the tumor had invaded the neighboring organs?

## **Reply:**

As you mentioned, the maximum standard uptake of 9.09 was relatively high, and we also suspected a highly malignant tumor, such as thymoma B3.

We initially proposed thymectomy through a median sternotomy median sternotomy approach. However, the patient did not give his consent, so we performed RATS surgery as a less-invasive surgery. Depending on the intraoperative findings, we were prepared to convert to open thoracotomy.

For clinical stage I thymic tumors, patients who received RATS surgery tended to have longer progression-free survival (PFS) than those with VATS or open surgery. The present patient is still alive with no recurrence of the disease.

## Changes in text:

# <Case Presentation; Page 4, line 89-91>

We initially proposed thymectomy through a median sternotomy median sternotomy approach. However, the patient did not give his consent, so we performed RATS surgery as a less-invasive surgery.

# **References:**

- Li XK, Xu Y, Cong ZZ, et al. Comparison of the progression-free survival between robot-assisted thymectomy and video-assisted thymectomy for thymic epithelial tumors: a propensity score matching study. J Thorac Dis 2020; 12(8): 4033-43.
- 2. Marulli G, Maessen J, Melfi F, et al. Multi-institutional European experience of robotic thymectomy for thymoma. Ann Cardiothorac Surg. 2016; 5 (1) : 18-25.

### Minor comment 5:

Was the autosuture device a DaVinci's stapler?

### **Reply:**

We did not use autosuture devices specifically designed for the da Vinci stapler.

# Changes in text:

### <Case Presentation; page 4, line 103-105>

The tumor invaded the right upper lobe (Fig. 2A), and partial resection was performed

using autosuture devices (Endo-GIA purple 60mm×1 and purple 45mm×1) (Fig. 2B, 2C).

# <u>Reviewer B</u>:

# Comment 1:

This paper is a case report of a robot-assisted thymectomy performed on a thymic carcinoid.

Thymic carcinoids have been reported to cause lymph node metastasis. Robotic surgery with the lateral chest approach does not seem to be able to remove lymph nodes better than the median sternotomy approach.

# **Reply:**

In the present case, the patient requested minimally invasive surgery, so robotic surgery was performed. The surrounding adipose tissue was also removed, including the mediastinal lymph nodes, as lymph node dissection. For clinical stage I thymic tumors, patients who received RATS surgery tended to have longer progression-free survival (PFS) than those with VATS or open surgery. The patient is still alive with no recurrence of the disease.

## **Changes in text:**

<Case Presentation; page 4, line 108- page 5 line 116>

The thymus, including the tumor, was extirpated. The surrounding adipose tissue was also removed, including the mediastinal lymph nodes, as a lymph node dissection.

# **References:**

- Li XK, Xu Y, Cong ZZ, et al. Comparison of the progression-free survival between robot-assisted thymectomy and video-assisted thymectomy for thymic epithelial tumors: a propensity score matching study. J Thorac Dis 2020; 12(8): 4033-43.
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# Comment 2:

Did you search for Cushing's Syndrome or MEN type 1 complications?

## **Reply:**

The diagnostic criteria for Cushing's syndrome are as follows: the presence of specific symptoms, such as full moon face and striae cutis distensae; and elevated ACTH levels in the blood. In the present case, complication with Cushing's syndrome was ruled out because there were no specific symptoms, and the ACTH level was in the normal range. The diagnostic criteria for MEN type 1 are as follows: the presence of other endocrine disorders and 2. the presence of a family member with the disease. In the present case, there were no endocrine abnormalities and nor any family history of MEN type 1, so the

complication with MEN type 1 was also ruled out.

Due to the word limit, this information was not included in the manuscript.

# Comment:

Robot-assisted surgery for thymic carcinoid has already been reported.

1) Subxiphoid approach for robotic single-site-assisted thymectomy.

Park SY, Han KN, Hong JI, Kim HK, Kim DJ, Choi YH. Eur J Cardiothorac Surg. 2020 Aug 1; 58 (Suppl 1): i34-i38.

2) Single-institution experience on robot-assisted thoracoscopic operations for mediastinal diseases.

Rea F, Schiavon M, Di Chiara F, Marulli G. Innovations (Phila). 2011 Sep; 6 (5): 316-22.

*3) Application of robotic-assisted techniques to the surgical evaluation and treatment of the anterior mediastinum.* 

Savitt MA, Gao G, Furnary AP, Swanson J, Gately HL, Handy JR. Ann Thorac Surg. 2005 Feb; 79 (2): 450-5; discussion 455.

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- Subxiphoid approach for robotic single-site-assisted thymectomy. Park SY, Han KN, Hong JI, Kim HK, Kim DJ, Choi YH. Eur J Cardiothorac Surg. 2020 Aug 1; 58 (Suppl 1): i34-i38.
- Single-institution experience on robot-assisted thoracoscopic operations for mediastinal diseases. Rea F, Schiavon M, Di Chiara F, Marulli G. Innovations (Phila). 2011 Sep; 6 (5): 316-22.
- Application of robotic-assisted techniques to the surgical evaluation and treatment of the anterior mediastinum. Savitt MA, Gao G, Furnary AP, Swanson J, Gately HL, Handy JR. Ann Thorac Surg. 2005 Feb; 79 (2): 450-5; discussion 455.

### Reviewer C

First of all, I would like to congratulate you on your article. Your approach to resect thymic tumors by RATS and the way it is explained is excellent. I have only two comments:

# Comment 1:

I think that you should include the traditional tumor, nodes, metastasis (TNM, 8th edition) stage (lines 35, 77, 93). Both Masaoka-Koga and TNM staging systems have a prognostic significance and it has to be correctly reflected.

### Reply :

We modified all staging in the text to include both the Masaoka-Koga and TNM

classifications.

#### Changes in text:

<Abstract; page 2, line 30-32>

A histopathological examination revealed a typical thymic carcinoid of Masaoka-Koga stage III, pT3N0M0 StageIIIa(TNM, 8th edition).

<Case Presentation; page 3, line 87-89>

The tumor was suspected to be a Masaoka–Koga stage I, cT1N0M0 StageI(TNM, 8th edition) thymoma.

#### <Case Presentation; page 5, line 123-124>

Finally, the tumor was diagnosed as a typical thymic carcinoid of Masaoka–Koga stageIII, pT3N0M0 StageIIIa(TNM, 8th edition) classification.

## Comment 2:

If the clinical postoperative period was regular, why was the hospital stay 7 days?(lines 94 and 95). In our experience, mainly in VATS thymectomy, the postoperative recovery is faster (including cases with lung resection) and the mean hospital stay is 2 days.

#### **Reply:**

Since the patient lived alone and was anxious about his life after discharge, he was admitted to the hospital for a slightly longer stay.

#### Reviewer D

## Comment:

Interesting Case report but need more medical and surgical informations et references didn't support the authors' statements. Need more informations and ref citations as requested in the attached supplementary file.

## **Reply:**

We checked the points you mentioned and added more information. We have also reorganized the references and removed the obviously outdated ones.

### Changes in text:

#### <Introduction; page 3, line 58-61>

With the advantages of minimal invasiveness and rapid recovery, video-assisted thoracoscopic thymectomy has been adopted more often in recent years to treat thymic tumors. And now, the role of robot-assisted thoracoscopic thymectomy in the treatment of thymic tumors has been growing (2-4).

## <Case presentation; page 3, line 75- page 4, line 86>

Positron emission tomography CT showed strong F-18 fluorodeoxyglucose accumulation in the same area; the maximum standardized uptake value of the mass was 9.09 (Fig. 1C). There was no abnormal accumulation in mediastinal or hilar lymph nodes, or other organs.

#### < Case presentation; page 4, line 87-89>

The tumor was suspected to be a Masaoka–Koga stage I, cT1N0M0 StageI(TNM, 8th edition) thymoma, and RATS thymectomy was performed as follows.

#### <Case Presentation; page 4, line 103-105>

The tumor invaded the right upper lobe (Fig. 2A), and partial resection was performed using autosuture devices (Endo-GIA purple 60mm×1 and purple 45mm×1) (Fig. 2B, 2C).

### <Case Presentation; page 5, line 123-124>

Finally, the tumor was diagnosed as typical thymic carcinoid of Masaoka–Koga stageIII, pT3N0M0 StageIIIa(TNM, 8th edition).

### <Discussion; page 6, line 161-164>

In addition, despite the narrow space at the apex of the lung, the infiltration of the lung was easily controlled with flexible movement of the robot's arms, contributed to the absence of vascular accidents or the need for surgical conversion.

### <Discussion; page 6, line 165- page 7, line 181>

While RATS group shows similar length of hospital stay  $(4.48\pm2.376 \text{ and } 4.68\pm2.740, P=0.65)$  and frequency of complications compared with VATS, it is reported to have

significantly shorter surgical time (102.10 $\pm$ 14.13 and 106.22 $\pm$ 13.24, P=0.042). Moreover, the progression-free survival (PFS) in the RATS group tended to be longer than that in the VATS group for thymic malignancies (81.5% and 75.4%, P=0.095) (2).