

Peer review file

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Reviewer A

Comment 1: Could you please explain the positioning of the team members? Does the first operator stand anteriorly or posteriorly to the patients?

Reply 1: The position of the operating surgeon is always posterior, whereas the position of the first assistant is anterior to the patient.

Changes in text: Lines 116-117 added the text “The operating surgeon positions himself posterior to the patient, whereas the first assistant is subsequently anterior to the patient.”

Comment 2: Could you please specify how do you visualize the left phrenic nerve using a right sided approach?

Reply 2a: That is an excellent point that the reviewer mentions. As mentioned on lines 119-120 of the manuscript, we find that a “5mm thirty-degree angled thoracoscope provides optimal visualization from phrenic nerve to phrenic nerve.”

Changes in text: We could certainly expand upon the degree with which we find the thirty-degree angled thoracoscope ideal if necessary for publication in your fine journal, but as we feel most surgeons are familiar with this scope, we would opt on the sake of brevity.

Regarding the results, could you please specify if you had any phrenic nerve injury/diaphragmatic palsy?

Reply 2b: Another excellent point; we fortunately have not experienced any phrenic nerve injury or diaphragmatic palsy in our cohort of early-stage thymoma.

Changes in text: We added the following on lines 169-170: “There were no recorded phrenic nerve injuries in the entire cohort.” As well as line 351 in Table 3: “Phrenic nerve injury and diaphragmatic palsy: 0 (0.0).”

You had a median length of stay of just 1 day! Could you please give us information regarding the post-operative management of patients?

Reply 2c: Thank you. Every patient receives multi-level intercostal nerve-blocks as well as standard multi-modality post-operative pain management w/narcotic PCA and

NSAIDs.

Changes in text: We added the following on lines 124-126: “All patients receive multi-level intercostal nerve block, as well as multi-modality post-operative pain control with non-steroidal anti-inflammatory (patient’s creatinine clearance and bleeding are taking under consideration) and narcotic-based, patient-controlled analgesia pump.”

Reviewer B

[Comment 1: Currently the TNM system is also used for thymoma. It would be more up-dated to mention in your study.](#)

Reply 1: As all 17 of our cases were either Masoaka stage I or IIa, we did not see any tumors that progressed beyond microscopic transcapsular invasion e.g. there was not any macroscopic invasion into surrounding fatty tissue. Further, there was no tumor with direct invasion of the pericardium (either partial or full-thickness). Further, since there was no metastasis to lymph nodes, local or distant structures, all tumors were stage I.

Changes in text: This was a valid point that the reviewer brings up. As such, we added the following to line 351 table 3:

| | |
|--------------------|------------|
| TNM tumor stage | |
| Stage I | 17 (100.0) |
| Stage II | 0 (0.0) |
| Stage III (A or B) | 0 (0.0) |
| Stage IV (A or B) | 0 (0.0) |

[Comment 2: Line 81. spelling mistake. Year/date.](#)

Reply 2: We were unable to find a spelling error in lines 79-83: “Single-incision, or uniportal, VATS thymectomy has been reported (14-17), however, to date, no data exists

regarding intermediate-term oncologic outcomes. Consequently, we retrospectively evaluated the overall survival (OS) and recurrence-free survival (RFS) in all patients undergoing single-incision VATS thymectomy for early-stage thymoma at our institution.”

Changes in text: As we were unable to find any spelling errors, we were unable to make any corrections.

Comment 3: You mentioned that the upper limit of the thymoma is 6 cm in your practice, but in line 100 and Figure 2, you have shown a 9 cm thymoma. Is it a typo?

Reply 3: Thank you to the reviewer for bringing this error to our attention. It was indeed an error, it should have read 9cm.

Changes in text: We have made the correction on line 235 and 351 (Table 3) from 6.0cm to 9.0cm.

Comment 4: In Figure 2, the marker shows that the large of the thymomas are less than 5 cm, but you mentioned 9 cm! Can you explain the difference?

Reply 4: Thank you to the reviewer for bringing this error to our attention. It was indeed an error upon submission, as we had several images carefully considered for publication in your journal and the wrong image was submitted.

Changes in text: We will certainly resubmit the appropriate image, with the 9cm thymoma amongst them.

Comment 5: How can you remove a 9 cm (or 6cm) thymoma via a sub3 cm skin incision? Do you cut apart the tumour?

Reply 5: As the thymomas are rarely uniform in size, while 9cm is certainly the largest measured diameter, it is not a 9x9x9cm mass. As such, once placed in an endoscopic retrieval bag, the 9cm tumor is only limited by its thickest diameter. Further, the intercostal muscle may be extended for help of tumor removal, while the skin stays <3.0cm. Additionally, the skin's elastic property provides ample space to remove such large tumors.

Changes in text: As mentioned on lines 105 – 106, we utilized an endoscopic retrieval bag for all tumors. However, we added on line 106 “(which helps to facilitate the removal of large tumors once).“

Comment 6: In your figure both tumour is left sided. Don't you use a left side approach if the tumour is big?

Reply 6: We do. We have found that the 5mm thirty-degree angled thoracoscope, that we mention on lines 119-120 of the manuscript, affords us optimal visualization.

Changes in text: An excellent question by the reviewer. We do employ a left-sided approach, utilizing the abovementioned thoracoscope.

Comment 7: What is your protocol about the lymph node management during the resection?

Reply 7: We remove all suspicious lymph nodes based on preoperative imaging. Furthermore, we routinely perform en-bloc resection of the thymus and perithymic, prevascular, and supradaphragmatic lymph nodes. In addition, right paratracheal and para-aortic lymph nodes are dissected when operating for advanced thymomas and/or thymic carcinomas.

Changes in text: We added “We remove all suspicious lymph nodes based on preoperative imaging. Further, we perform en-bloc resection of the thymus, perithymic, prevascular, and supradaphragmatic lymph nodes. In addition, right para-tracheal and para-aortic lymph nodes are dissected when operating for advanced thymomas and/or thymic carcinomas.” To lines 109 – 112 on the revised marked copy.

Reviewer C

The Authors must be congratulated for their manuscript that is clearly and well written, for the superb minimally invasive surgical technique (single port, less than 3cm incision) and for the outcomes (no conversions, 1day median hospital stay, 100% radicality of surgery). Thank you very much for your review, as well as your kind words.

In my opinion, there are nevertheless some limitations:

Comment 1: This is a relatively small series of cases collected retrospectively (17cases in almost 5 years is 2-3 cases per year) despite the long median follow-up.

Reply 1: Yes, we agree that it is a relatively small case sample size, as mentioned on lines 241-242 in our manuscript.

Changes in text: While a relatively small sample size, it still remains the only report

providing intermediate-term oncologic data for uniportal VATS thymectomy.

Comment 2: There is a plethora of papers in the literature reporting on the results of minimally invasive surgery for early stage thymoma and this include also robotic, multiportal, uniportal, subxiphoid, single side or bilateral and awake non intubated surgery. Please find below a list with some relevant papers among the multitude of various surgical techniques.

Reply 2: While we agree there have been reports in literature discussing short- and intermediate-term oncologic outcomes for VATS thymectomy, there are not any report such for the uniportal VATS thymectomy.

While the 7 papers provided are exemplary depictions of surgical technique, none of them mentioned short or intermediate-term oncologic data.

Article 1 Descriptive paper discussing different minimally invasive approaches towards thymectomy, however does not mention any results with regards to early or intermediate-term oncologic data of their own.

Articles 2, 3, 6, 7 All excellent technical papers with regards to the subxiphoid approach, however none of them not mention any results with regards to early or intermediate-term oncologic data of their own.

Article 4 Another superb technical paper with regards to the multiport “microthymectomy” approach, however does not mention any results with regards to early or intermediate-term oncologic data of their own.

Article 5 A very interesting technical paper with regards to the subxiphoid approach towards rib resection, however not only does this not mention a thymectomy, but does not mention any results with regards to early or intermediate-term oncologic data of their own.

Changes in text: While all excellent papers, they do not change the fact that there are no reports discussing the intermediate-term oncologic outcomes for uniportal VATS thymectomy.

Comment 3:

Minor comment: to me is difficult to understand how a tumour of 9cm of diameter can be retrieved through a <3cm incision.

Reply 3: As the thymomas are rarely uniform in size, while 9cm is certainly the largest measured diameter, it is not a 9x9x9cm mass. As such, once placed in an endoscopic retrieval bag, the 9cm tumor is only limited by its thickest diameter. Further, the intercostal muscle may be extended for help of tumor removal, while the skin stays <3.0cm. Additionally, the skin's elastic property provides ample space to remove such large tumors.

Changes in text: As mentioned on lines 105 – 106, we utilized an endoscopic retrieval bag for all tumors. However, we added on line 106 “(which helps to facilitate the removal of large tumors once).“

In my opinion, this nice presentation unfortunately does not add any significant message to the current literature (VATS could be applied to early stage thymomas with good long- and short-terms outcomes is a well established concept). My suggestions for the Authors is to consider to record/edit a procedure and evaluate the submission as an “how to do it” communication of the surgical technique. I am definitely convinced that the final impact would be highly amplified.

Reply 3: An excellent idea. However, while we appreciate the reviewer's advice, and certainly have discussed the concept of a “how to do it” paper, we feel that the overall meaning of our current data would be overshadowed by the technicality of a “how to do it” paper.

Changes in text: As we do not feel that the overall message of our paper should change, at the moment, we do not want to change the paper to a “how to do it” paper. We do, however, concede that should our revisions not garner acceptance into your paper, we will strongly consider changing the context of the paper. Further, if accepted, we will consider a “how to do it” paper as well.

1. Minimally invasive techniques in thymic surgery: a worldwide perspective. Batirel HF. J Vis Surg. 2018 Jan 10;4:7. doi: 10.21037/jovs.2017.12.18. eCollection 2018. Review.
2. Subxiphoid Uniportal Video-Assisted Thoracoscopic Surgery Procedure. Suda T. Thorac Surg Clin. 2017 Nov;27(4):381-386. doi: 10.1016/j.thorsurg.2017.06.006. Epub 2017 Aug 10. Review. PMID: 28962710
3. Uniportal subxiphoid video-assisted thoracoscopic thymectomy. Suda T. J Vis Surg.

- 2016 Jul 22;2:123. doi: 10.21037/jovs.2016.07.03. eCollection 2016. Review.
4. Video-assisted thoracoscopic microthymectomy. Dunning J. Ann Cardiothorac Surg. 2015 Nov;4(6):550-5. doi: 10.3978/j.issn.2225-319X.2015.11.04. Review. PMID: 26693152
 5. Subxiphoid uniportal video-assisted thoracoscopic surgery: A cosmetically superior approach to submammary rib tumor resection. Luo M, Kong D. Thorac Cancer. 2019 Dec;10(12):2316-2318. doi: 10.1111/1759-7714.13218. PMID: 31668007
 6. Non-intubated subxiphoid uniportal video-assisted thoracoscopic thymectomy. Liu Z, Yang R, Sun Y. Interact Cardiovasc Thorac Surg. 2019 Nov 1;29(5):742-745. doi: 10.1093/icvts/ivz181. PMID: 31408154
 7. Nonintubated Uniportal Thoracoscopic Thymectomy with Laryngeal Mask. Liu Z, Yang R, Sun Y. J Thorac Cardiovasc Surg. 2019 Sep 15. doi: 10.1055/s-0039-1696950 PMID: 31522429

Reviewer D

[Comment 1: The authors reported their experience on the single port thymectomy using the lateral approach and the efficacy. The article is well written. However, the type of study, retrospective, and the small number of cases makes impossible to assume the conclusions. In addition, we have already experienced the superiority of the subxiphoid approach than the lateral approach in thymectomy.](#)

Reply 1: While we agree there have been reports in literature discussing short- and intermediate-term oncologic outcomes for VATS thymectomy, there are not any report such for the uniportal VATS thymectomy.

Further, while the 2 papers provided are exemplary depictions of surgical technique, none of them mentioned short or intermediate-term oncologic data.

Article 1 and 2 Both are excellent technical papers with regards to the subxiphoid approach, however none of them not mention any results with regards to early or intermediate-term oncologic data of their own.

Changes in text: While all excellent papers, they do not change the fact that there are no reports discussing the intermediate-term oncologic outcomes for uniportal VATS thymectomy.

1. Suda T. Single-port thymectomy using a subxiphoid approach-surgical technique. *Ann Cardiothorac Surg.* 2016 Jan;5(1):56-8.
2. Yano M, Moriyama S, Haneda H, Okuda K, Kawano O, Oda R, Suzuki A, Nakanishi R, Numanami H, Haniuda M. The Subxiphoid Approach Leads to Less Invasive Thoracoscopic Thymectomy Than the Lateral Approach. *World J Surg.* 2017 Mar;41(3):763-770.

Reviewer E

First of all, I would like to bring your attention to two small mistakes, which I think you have already noticed and corrected.

[Comment 1: In line 25 RFS is it Risk-Free or Recurrence-Free.](#)

Reply 1: We thank the reviewer for pointing this error out.

Changes in text: We have changed ‘risk’ to ‘recurrence,’ as it should have been. This is reflected on line 28 of the “Marked” manuscript.

[Comment 2: In line 81 a number is missing on 201?.](#)

Reply 2: Again, we thank the reviewer for pointing this error out.

Changes in text: We have changed ‘201’ to ‘2014,’ as it should have been. This is reflected on line 87 of the “Marked” manuscript.

[Comment 3: I would only like a comment on the technique used; What about carbon dioxide insufflation with bi- or tri- portal technique, do you have any experience?](#)

Reply 3: We do have experience with both two-port and three-port VATS, both with and without CO2 insufflation. As we found it capable of performing the same oncologically sound operation via a uniportal approach – with anecdotally better length of stay and post-operative pain control – we prefer our uniportal approach.

Changes in text: We have changed ‘201’ to ‘2014,’ as it should have been. This is reflected on line 87 of the “Marked” manuscript.

[Comment 4: Any experience with uniportal SILS permitting carbon dioxide usage? Do you think it could be useful for a better exposure of mediastinum?](#)

Reply 4: We do have experience with SILS with CO2 insufflation. However, we find

that we have better mobility and dexterity of VATS instruments without a port in place. Further, as we found it capable of performing the same oncologically sound operation via a uniportal approach without SILS port placement, we prefer our uniportal approach. Changes in text: While we appreciate the SILS technique, we do not believe it would help achieve better exposure, but equal exposure is certainly possible.

Reviewer F

This report was well written and interesting because it showed intermediate outcome after thymectomy by single incision was feasible, comparing with previous reports on thymectomy by 3 port VATS. However, minor revisions are needed to complete this report.

[Comment 1: At 81 line in page 4, please change "July 201" to "July 2014".](#)

Reply 1: We thank the reviewer for pointing this error out.

Changes in text: We have changed '201' to '2014,' as it should have been. This is reflected on line 87 of the "Marked" manuscript.

[Comment 2: I want to know your "thymectomy" in detail, in surgical approach and instruments. Where did you resect cranial margin of thymus? Left bronchial artery? As the same way, I want to know where the opposite side margin or caudal margin.](#)

Reply 2: Our surgical approach is depicted on lines 115 – 121 “All patients are placed in left lateral decubitus position and secured to the bed, such that they can be placed at a forty-five-degree angle with regards to the floor (our preference is to utilize a bean-bag positioner with silk tape placed across the hip). A single sub-three-centimeter incision is created in the fifth intercostal space between the mid- and anterior-axillary lines (Figure 3A). This incision affords enough space for simultaneous use of multiple instruments (Figure 3B). For larger specimens, the muscular portion of the incision may be extended, however the extent of the skin incision does not need to be enlarged.”

Our instruments are depicted on lines 124 – 127 “A 5mm thirty-degree angled thoracoscope provides optimal visualization from phrenic nerve to phrenic nerve. Dissection is carried out utilizing standard VATS instruments (curved and straight ringed forcep, curved lymph node grasper, curved blunt-tip metal suction, harmonic

scalpel and endo Kittner). No SILS port or wound-protectors were utilized.”

As far as our margins:

Cranial: thymic horns up into the low anterior neck

Lateral: from phrenic nerve to phrenic nerve

Caudal: diaphragm

Anterior: sternum

Bronchial artery: we are unsure how to answer this question, as we make not special approach towards the left bronchial artery.

Changes in text: We chose to maintain the text as such, which we feel answered the reviewers comments appropriately.