

## Peer Review File

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### Review comments

#### Reviewer A

I sincerely appreciate the opportunity to review the manuscript " UNIPORTAL VATS IVOR LEWIS ESOPHAGECTOMY" submitted by Aslan S and Batirel H.

As the authors describe in this manuscript, minimally invasive surgery is rapidly replacing open chest and abdominal surgery, and its effectiveness has been reported in various papers. In general, the development of resolution and light intensity of thoroscopes and laparoscopes, advances in uniportal VATS instruments, and navigation using thoracic CT and 3D image analysis tools have made it possible to safely perform highly difficult, fully endoscopic procedures.

The paper is well-written and close to acceptance, but some issues need to be clarified. Please read the following comments carefully, improve the paper, and respond to them.

**Comment 1:** Uniportal VATS esophagectomy may be misinterpreted as if everything is done in one wound, including intraperitoneal surgery. Wouldn't the more accurate title be Uniportal VATS combined with three-port laparoscopic surgery for Ivor Lewis esophagectomy?

**Reply 1:** It is important to highlight the Uniportal Video-Assisted Thoracic Surgery (VATS) section in the title, as it is planned to publish at a special series named advanced Uniportal VATS. However, we also give information about our abdominal part technique in Ivor Lewis procedure. In addition, in an article describing the minimally invasive esophagectomy technique, we don't think that it is possible to perform 2-field surgery from a single 4 cm incision with today's data.

**Comment 2:** Minimally invasive surgery has two aspects. One is the point that the authors emphasize, namely, smaller and fewer surgical wounds. On the other hand, if the operation time

and blood loss increase, it can no longer be called minimally invasive surgery. We would appreciate your comments on this point with the authors' data.

**Reply 2:** In our recently published article we also included the comparison of the uniportal technique with other techniques in the literature (1). Similarly, in this article, we add our data with certain headings in the **Table 1**.

**Ref (1)** Sezer Aslan, MD, Gamze Gul Tiryaki, MD, Jeyhun Pashayev, MD, Cagatay Cetinkaya, MD, Ali Fuad Durusoy, MD, Nezih Onur Ermerak, MD, Hasan Batirel, MD, PhD, Uniportal VATS (Video-assisted Thoracoscopic Surgery) Esophagectomy Outcomes in Forty Consecutive Patients, *Interdisciplinary CardioVascular and Thoracic Surgery*, 2023;, ivad034, <https://doi.org/10.1093/icvts/ivad034>

**Changes 2:** Table 1 was added to page 13, lines 287-292 and uploaded as a separate file. Recently published paper was added at discussion part on page 10, lines 216,219

**Comment 3:** Uniportal VATS from a 4 cm wound is often severely limited by the thoracic wall, such as the width of the intercostal space, the obliquity of the ribs, and the size of the thoracic cavity. In particular, we are concerned that the automatic stapler may not be oriented as desired, and that the operation may proceed with excessive force on the anastomosis due to the progressive pressure on the tissue. Please give me your opinion.

**Comment 4:** I have seen a previous uniportal VATS paper by the authors, which mentions the possibility of using the 5th intercostal space for the chest port. Currently, it seems that you are fixing it at the 6th intercostal space. Please explain this point.

**Reply 3-4:** We consider that the 4 cm incision in the thoracic part is enough to complete the surgery. We did not have conversion or extension of incision in our patients because of incision size. When we first defined the Uniportal VATS esophagectomy technique, we used 5<sup>th</sup> intercostal space routinely. However, we realized that 6<sup>th</sup> intercostal space was more suitable to provide flexibility in movements in the thorax and to place the stapler at a more suitable angle, especially during anastomosis and we changed our incision preference (1). We used the 2<sup>nd</sup> port in two patients during anastomosis because we thought the angle was not ensured for lateral wall formation (2).

**Ref (1)** Batirel H. Uniportal VATS Approach in Esophageal Cancer - How to Do It Update. *Front Surg.* 2022 Mar 25;9:844796. doi: 10.3389/fsurg.2022.844796. PMID: 35402499; PMCID: PMC8990028.

**Ref (2)** Sezer Aslan, MD, Gamze Gul Tiryaki, MD, Jeyhun Pashayev, MD, Cagatay Cetinkaya, MD, Ali Fuad Durusoy, MD, Nezh Onur Ermerak, MD, Hasan Batirel, MD, PhD, Uniportal VATS (Video-assisted Thoracoscopic Surgery) Esophagectomy Outcomes in Forty Consecutive Patients, *Interdisciplinary CardioVascular and Thoracic Surgery*, 2023;, ivad034, <https://doi.org/10.1093/icvts/ivad034>

**Comment 5:** I would appreciate your opinion on the timing and decision to move to a conversion surgery, such as a multi-portal VATS or open chest surgery.

**Reply 5:** According to our recently published data, 77.5% of the patients were completed uniportally and no conversion to thoracotomy. We needed an extra port due to pleural adhesions, difficulty in visualization of large tumor and inappropriate angle of stapler.

### **Reviewer B**

Thank you for the opportunity to review the manuscript. The authors report on uniportal VATS Ivor Lewis Esophagectomy technique. The advantages on MIE are well reported and documented in the literature, thus the manuscript does not add any novelty to the literature.

My concerns are

**Comment 1:** The number of ports does not matter as we quite often add one or more trocar to accomplish the task. Doing the abdominal part with 3 trocars is commendable but what kind of patients are they operating on (very low BMI, benign disease only?) Male patients with central obesity are often difficult as the omentum is thick and adhered to the distal transverse colon which requires at least 5 abdominal trocars whether it is done laparoscopic or robotic.

**Comment 2:** Same applies to the thoracic part as the curvature of the spine and size of the lung vs thoracic domain dictates the number of trocars used.

**Reply 1,2:** We agree with your views on the extra port. If there is a situation that puts the patient and oncological principles at risk, extra port and even open surgery may be considered. But, if

comparable literature outcomes can be reached with least invasive techniques, it is acceptable and valuable. We think that the assumption of low BMI or benign patients were operated is not correct. We have a heterogeneous patient population. In 40 patients who were operated for esophageal cancer, conversion to quadriport was in 2 patients and open was in one patient during abdominal part. We reported the median duration of abdominal surgery as 70 (57.5-85 IQR) mins and the mean total number of lymph nodes as  $24 \pm 9.5$ . We think technique has comparable results. In addition, 77.5% of patients completed uniportally during thoracic part and there was no conversion to open surgery (1).

**Ref (1)** Sezer Aslan, MD, Gamze Gul Tiryaki, MD, Jeyhun Pashayev, MD, Cagatay Cetinkaya, MD, Ali Fuad Durusoy, MD, Nezhir Onur Ermerak, MD, Hasan Batirel, MD, PhD, Uniportal VATS (Video-assisted Thoracoscopic Surgery) Esophagectomy Outcomes in Forty Consecutive Patients, *Interdisciplinary CardioVascular and Thoracic Surgery*, 2023;, ivad034, <https://doi.org/10.1093/icvts/ivad034>

**Comment 3:** The manuscript needs clinical data for validation, and to compare it to open/MIE.

**Reply 3:** As with all techniques, uniportal VATS esophagectomy technique will follow the path of case reports, technical papers, initial results and comparison studies, respectively. Our last article presents uniportal VATS esophagectomy patients with current literature data. Of course, randomized controlled trials are needed for the technique to gain general acceptance.

### **Reviewer C**

I appreciate the possibility of reviewing this interesting paper. It has been well presented and logically ordered, but there are some concerns that should be addressed:

**Comment 1:** Uniportal VATS esophagectomy mainly refers to Uniportal VATS approach for thoracic stage of the procedure. Abdominal stage is probably beyond the aim of this special issue and this paper. If the author's describe this stage, they should focus on SIMIO (single-incision minimally invasive oesophagectomy) as described by several authors. If not, the title should include 3-port laparoscopic abdominal stage. Criteria for a 3-port laparoscopy vs a 5-port should then be addressed.

**Reply 1:** In the invitation letter we received from the editors, we saw that the technical paper for Uniportal VATS Ivor Lewis Esophagectomy was requested. In the Ivor Lewis technical article, we thought that we should also give information about the abdominal part. Also uniportal VATS Ivor Lewis Esophagectomy is better define thoracic part with uniportal thoracoscopy than single-incision esophagectomy. If it is thought that only the information about the thoracic part would be more appropriate in the article, we can make the necessary arrangements.

**Comment 2:** Some Figure including anatomical landmarks whithin the chest during Uniportal VATS approach would be interesting for reader's orientation.

**Reply 2:** Descriptive markings were made on the figures.

**Changes 2:** Changes were made on the figures 3-4-5. Description of the figures were added to page12 and lines 270-273, lines 277-278, lines 284-286

**Comment 3:** Esophagectomy can be performed either with intrathoracic anastomosis (Ivor-Lewis) or neck anastomosis (McKeown), and both can be performed via Uniportal VATS. Authors should describe both techniques with specific technical aspects, not only Ivor-Lewis technique as described but also for McKeown's technique, with description of pitfalls and caveats, and some technical tips as described in Ivor-Lewis.

**Reply 3:** We prepared the article for uniportal VATS Ivor Lewis esophagectomy technique upon request. For this reason, when we consider that there is no difference in the surgical technique other than anastomosis, we did not feel the need to emphasize for Mckeown. If it is requested to mention both techniques in the article, we can make changes.

**Comment 4:** Side-to-side anastomosis is well described, but authors have not mentioned neither described End-to-end anastomosis using a transoral EEA stapler which is one of the frequently used techniques for Ivor-Lewis. Please also consider including this variation.

**Reply 4:** The most feared issue during uniportal VATS intrathoracic anastomosis is tension. Stapler shaft at circular stapler more straight than fully curved linear endoscopic stapler. Although we mostly performed the anastomosis at high thoracic level, we needed an extra port in 2 patients because of the stapler anger was not suitable even in the fully curved position. Therefore, we don't use the circular stapler in the uniportal technique. Usually 28 mm circular

stapler is recommended for intrathoracic anastomosis and the size is large for intercostal space. Significant trauma to rib periosteum occurs during insertion of circular stapler and we do not have the same problem with endoscopic linear stapler.

**Comment 5:** Figure 5 is essential for understanding the technique, but some anatomical landmarks could be added, 5B seems to be taken far for detail appreciation, and 5D does not show clearly the purpose of lateral wall stapling

**Reply 5:** Figure 5B changed. Landmarks pointed on the Figure 5D. With the approval of the editors, we can prepare and present a short video for anastomosis.

**Changes 5:** Changes were made on the figure 5. Descriptions of the figure were added to page 12 and lines 284-286.

**Comment 6:** There are some methods for addressing the adequate vascularization of the end of esophageal and gastric conduit, as ICG near infrared visualization. Could the authors describe this and other methods, and share data about their own experience with ICG or their preferred method for assessing vascularization of conduits?

**Reply 6:** We don't use ICG in our cases. After the right gastroepiploic arcade is well preserved, tissue color and oozing during anastomosis provide information about tissue perfusion.

**Comment 7:** Authors show some evidence regarding open vs MIE, Uniportal vs Multiportal MIE, and RAMIE vs MIE. This comparative evidence may be more clearly shown by using some Tables with data. Please consider including comparative data in Tables.

**Reply 7: Table 1** is prepared.

**Changes 7:** Table 1 was added to page 13, lines 287-292 and uploaded as a separate file.

**Comment 8:** Robotic-assisted MIE is mentioned during the discussion, but is beyond the purpose of a Uniportal VATS paper. I think that it can be avoided within this paper, and focus on different variations of Uniportal VATS techniques.

**Reply 8:** The robotic era will inevitably take place in most surgical techniques. We think that comparing uniportal VATS with open, multiportal techniques as well as comparing it with RAMIE data which is having similar results will make uniportal technique stronger.

**Comment 9:** Manual anastomosis can also be performed through uniportal VATS. Do the authors think it's valuable or really challenging? Does it provide any benefit over stapling anastomosis?

**Reply 9:** Manual anastomosis can be done technically, but we do not think that it is superior to stapler techniques. Esophageal and gastric conduits are exposed to minimal trauma in stapler anastomosis technique and time consuming, it takes median 12 mins (11-16 IQR) (1).

**Ref(1):** Sezer Aslan, MD, Gamze Gul Tiryaki, MD, Jeyhun Pashayev, MD, Cagatay Cetinkaya, MD, Ali Fuad Durusoy, MD, Nezih Onur Ermerak, MD, Hasan Batirel, MD, PhD, Uniportal VATS (Video-assisted Thoracoscopic Surgery) Esophagectomy Outcomes in Forty Consecutive Patients, *Interdisciplinary CardioVascular and Thoracic Surgery*, 2023;, ivad034, <https://doi.org/10.1093/icvts/ivad034>

**Comment 10:** Authors have not mentioned the possibility of oversewing the stapling line manually, what do they think about it? Do they perform it routinely? Has it shown to improve the rates of anastomotic leak?

**Reply 10:** We do not routinely oversee the stapler lines and anastomosis. Most part of the anastomosis remains embedded in the posterior mediastinal fatty tissue and provides some support. Current ERAS recommendations on oversewing are also lacking (1).

**Ref (1):** Low DE, Allum W, De Manzoni G, et al. Guidelines for Perioperative Care in Esophagectomy: Enhanced Recovery After Surgery (ERAS®) Society Recommendations. *World J Surg* 2019 Feb;43(2):299-330.

### **Further Review comments**

#### **Reviewer A**

I have now reviewed the above article for Video-Assisted Thoracic Surgery.

With respect to the author's response to my remarks, the paper has been appropriately revised. Regarding the paper's title, I understand that it was given this title because it is a special issue of “Uniportal VATS”.

I hope that this article and the other articles in this special issue will be well received by our readers.

**Reply:** Thanks to the reviewer for contributions and good wishes.

### **Reviewer C**

After careful review of author's response to Reviewers and Editor's comments, I think they have answered with humbleness and common sense.

**Reply:** Thanks to the reviewer for contributions and good wishes.

Regarding my comments, I'd like to suggest the authors:

**Comment 1:** I think the author's responses to Reviewer C comments 4, 6, 9 and 10 could be added to the manuscript text, because they clarify some of the concerns that readers could have.

**Reply 1:** These are valuable suggestions. We made a detailed explanation in the paper about our choice of anastomosis from the previous revision. However, this is a technical paper of uniportal VATS esophagectomy and those topics (ICG use, manual anastomosis, oversewing) are beyond scope of this article.

**Changes 1: Changes were made under the heading of Discussion, page:13 lines:282-288**

Stapler shaft of circular stapler is not mobile and is straighter than fully curved linear endoscopic stapler. We frequently performed the anastomosis at high thoracic level. We needed an extra port in 2 patients because stapler angle was not suitable even in the fully curved position. 28 mm

circular stapler is used for a typical esophagogastric anastomosis and passage of the stapler through the intercostal space is very traumatic. Placement of pursestring suture is technically demanding and time-consuming in multi-portal VATS. Therefore, we don't think use the circular stapler is feasible in the uniportal technique.

**Comment 2:** Regarding Comment 5, please include the short video illustrating the anastomosis technique

**Reply 2:** We prepared and shared the video.

**Changes 2: Changes were made at page:8, line:180 and page:18 line:360**

**Comment 3:** Regarding comment 7, Table 1 is really interesting, but it compares author's series with other Uniportal and multiportal series. If they can add a Table 2 comparing their series to open or robotic series, that would be great.

**Reply 3:** In the first revision, we were warned by reviewer that it was beyond the main purpose of the article to mention RAMIE. We responded that we had given information about RAMIE and it could strengthen our technique. However, we also think that going into more detailed information is beyond the main purpose of the article.

**Changes 3: -**