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Reviewer A

Thank you for asking me to review this manuscript. I have some remarks:

1. The authors report about tumors <3 cm located in the lung periphery. What was the CT ratio of the tumors?

Comment: CTR was from 0 – 0.5

Changes in text: Page 5, line 124

2. Experience has shown that peripheral tumors >1 cm can be palpated or are located so centrally that direct anatomical resection is indicated. This should be discussed.

Comment: We agree. We emphasize using iVATS for small, peripherally located tumors (outer 1/3), not for centrally located tumors (inner 2/3).

Changes in text: Page 5, line 125

3. If tumors are more central and a wedge resection is performed first, the staple sutures often interfere to perform an anatomical segmental resection with visualization of the vein, artery and bronchus. For this reason, a primary segmental resection is performed in our clinic in these cases. What is the experience of the authors? Please discuss.

Comment: We use iVATS for outer 1/3 (or peripheral) lesions. We do not use it for more centrally located tumors. Generally, wedges and segmentectomies are performed for lesions < 2cm, and lobectomies for lesions > 2cm. Also, in general, a staple line or parenchyma does not preclude subsequent segment.

Changes in the text: Page 5, line 125

4. If the tumor is not palpable, how is a safe distance to the resection margin ensured? If you cut through the tumor, there is a risk of tumor cell distribution. What was the R0 resection rate?

Comment: We use ring forceps to estimate the distance. The distance across the ring from the tip to the crosspoint of the instrument is known and is a convenient intracorporeal measuring device. Also, the staplers have metric marks on the staple loads. Finally, the placement of the fiducial includes an exact measure of distance from skin to target and pleura to target. Combined, these make it straightforward to obtain proper depth for R0 resection. Our R0 resection rate was 100%.

Changes in the text: Page 11, line 249; page 13, line 295

5. How many secondary segmentectomies and lobectomies were performed?

Comment: Two procedures were converted to lobectomies. One demonstrated micropapillary pattern and another had an aggressive pattern on frozen pathology. There were no secondary segmentectomies.

Changes in the text: Page 12, line 284

6. What is the cost of the device and the resulting cost per patient?

Comment: The average hospital cost was \$89,000.

Changes in the text: Page 13, line 295

7. Since an T-bar was inserted into each of the tumors, it can be assumed that the tumors were all preoperatively punctate. Was surgery then always necessary?

Comment: Our goal is to remove the nodule. There is a growing body of evidence suggesting that these small, non-palpable, even ground glass nodules can harbor malignancy. Our own experience demonstrates that of the 37 patients who had partially solid nodules on imaging, 29 of them (78%) were found to be invasive cancers on pathology.

Changes in the text: Page 6, line 146

Reviewer B

The paper is well written and is very clear in describing the pros and cons of each technique and method for localizing pulmonary nodules. So I have no particular questions or criticisms. However, it reports data from the literature that is already widely known and does not add anything new to the existing scientific literature on the topic. Furthermore, as highlighted by you, this paper is not a systematic review of the literature but a

modest review of what is in the known literature. Given your great experience in this field, I would advise you to proceed with a systematic review.

Comment: This is a great suggestion, and we will focus on this for our next review. The purpose of this particular review was to highlight our experiences and supplement it with additional literature. We acknowledge that this is not a comprehensive review.

Changes in the text: none

Reviewer C

Thank you for submitting a manuscript of Review concerning iVATS of single center experience and review of various institutes.

I read it with much interest.

This article well compacted the small history of iVATS until today and is also educational.

Comment: Thank you for the above comments!

The main stem of the contents is composed of your institute's data described in references #9 and #19, written by the current co-authors, not by you.

Comment: I am currently working at the institution where my co-authors implemented iVATS. Some have since moved to another institution; however, the information provided in the manuscript reflects practices that initially began at our institution.

Changes in the text: none

This manuscript is titled " A Single Center Experience and Review ", and the previous reference published in 2020.

Comment: This was an invited review specifically charged with more detail surrounding technique. We wanted to supplement our institutional experience with additional literature that has been published regarding this topic. That is what we meant by "Review" in the title.

Changes in the text: none

If you have any more data in your institute ever since, additions are hoped.

Reviewer D

I would like to congratulate the Authors for this comprehensive review of iVATS. In the present study they share their experience and discuss other groups findings regarding indications, benefits, technique and outcomes of iVATS. I consider their paper as another milestone in the spreading of this breaking new surgical technique.

Comment: Thank you so much!

I would suggest the following minor revisions:

- page 4, line 96: why screening detected nodules only? I would consider for iVATS every patient with a non-palpable pulmonary nodule requiring a diagnostic wedge resection.

Comment: We agree. iVATS should be considered for patients with small, non-palpable nodules. By 'screening detected,' we meant that these nodules are often detected in the first place BECAUSE patients are either eligible for lung cancer screening according to the USPSTF guidelines or they were scanned for another reason and the lesion was discovered.

Changes in the text: none

- page 5, line 147: why left lateral decubitus? Is "left" a misprint?

Comment: We will correct this to say "lateral decubitus"

Changes in the text: Page 8, line 178

- page 9, line 252: can the authors briefly describe how collaborators were trained? How is the learning curve?

Comment: When comparing our data from real-world experience to the phase I and II clinical trials, we found no differences in radiation exposure and time for placement of T-bars, induction to incision time, incision to closure times, and R0 resection rates. This indicates successful translation of the iVATS procedure into the clinical setting. The specific learning curve for iVATS is further described by Hsieh and colleagues. The authors divided 30 consecutive patients who underwent resection via iVATS for solitary pulmonary nodules into two groups of 15 patients each (early group I and late group II). Between the early group and late group, the authors discovered a reduction of approximately 50% in localization time (49 vs. 24 minutes) and radiation exposure (224 mGy vs. 70.7). There was also an inverse association between procedural time and surgical experience.

Changes in text: Page 13, line 295