Peer Review File
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Reviewer A

Comment 1: My reflection is that this meta-analysis does not add any novelty on the topic. As discussed you included the JCOG study which is the major study on the topic. You only added small studies that were already included in the last meta-analysis of Winckelmans in EJCTS (2020).
Reply 1: Undoubtedly, there exists a multitude of research works, primarily retrospective studies, pertaining to the current topic. Notably, JCOG0802 stands as the largest study within this domain, and our meta-analysis encompasses its inclusion, conferring a distinct advantage previously unattained by earlier meta-analyses. Winckelmans et al.'s meta-analysis, on the other hand, incorporates literature of varying quality, with the authors duly acknowledging a pronounced risk of bias and confounding baseline factors across 22 articles. In their discussion section, the authors also raise the point of including nodules within the 0-3 cm range within the stage IA adenocarcinoma cohort, prompting the necessity for further comparisons between stage IA tumors measuring 2-3 cm in size and those below 2 cm. Therefore, to derive the utmost veracity in our conclusions, we executed a stringent screening process during the literature inclusion phase, culminating in the incorporation of a final selection of 10 articles, allowing for a comprehensive subgroup analysis based on tumor size within the stage IA adenocarcinoma category.

Comment 2: The discussion is just based on comment of the JCOG trial. I don't understand why you are discussing about recurrence and pulmonary functions, since the data were not analyzed in your meta-analysis... It should be re-written.
Reply 2: To enhance the rigour of our findings, we meticulously reevaluated the data sourced from the included literature, expanding the scope to encompass perioperative outcomes such as surgical blood loss, operative time, and the number of lymph node dissection. Furthermore, we undertook a thorough reconfiguration of the discussion section. Beyond appraising the outcomes of the JCOG0802 study, our revised discussion provides distinct elucidations concerning the combined dataset from the included studies.
Changes in the text: We added some data of perioperative outcomes such as surgical blood loss, operative time, and the number of lymph node dissection (see Page 7 and 8, line 181-194, Figure 5). We have modified our discussion as advised (see Page 9-11, line 234-302)

Reviewer B

Comment 1: This systematic review and meta-analysis establish a very interesting comparison between segmentectomy and lobectomy for tumors 2-3cm in size in contrast to those <2cm in size. If a $p<0.05$ was defined as statistically significant, then the sentence in line 173 may be changed to "the difference was almost statistically significant $p=0.06$ instead of slightly". The size cut off of 2cm has always seemed a bit arbitrary to me: should we offer a segmentectomy to a patient with a 1.9cm tumor and not to a 2.1cm even if both tumors were located in the same

exact place and had the same degree of differentiation? do other factors matter in deciding segmentectomy vs lobectomy such as you would be ok doing a segmentectomy in a 2.1cm part-solid nodule slowly growing in size over 5 years as opposed to one that double in size in 2 years? ok to do tri-segmentectomy for a 3 tumor located in the apex of the left lung as opposed to one in the lingula? Unfortunately, large databases do not have details to answer those questions, so we rely on size, and in the absence of details, safer to offer lobectomy to patients who have the pulmonary reserve to tolerate it, as long as no synchronous multifocal tumors found which would favor lung parenchyma preservation.

Reply 1: In our opinion, the tumor size cutoff of 2.0cm is indeed arbitrary. However, tumor size does affect the prognosis of tumors. In fact, this represents a trend that the smaller the tumor, the smaller the probability of recurrence and metastasis. For lung cancer, the decision between segmentectomy and lobectomy is essentially a contradiction between adequately removing the tumor tissue, preserving more lung tissue, and maintaining high survival and recurrence-free rates. Our study is just based on the conclusion of the study after summarizing the data of previous studies. In the real world, the choice of surgical procedure should not be based solely on the results of a single study or guidelines. It is necessary to find out the population who really benefit from the individualized treatment. With the deepening of the research on lung cancer, in addition to the differentiation of imaging, the pathological classification of lung cancer also includes adenocarcinoma in situ, minimally invasive adenocarcinoma, and invasive adenocarcinoma. Invasive adenocarcinoma was further subtyped. At present, the classification system of lung cancer is based on the multidisciplinary research of pathology, imaging, molecular biology and so on. Through preoperative CT imaging features to guide the selection of surgical methods, intraoperative frozen pathology to determine the invasiveness of lung cancer and identify high-risk subtypes, to guide surgical resection, not only some unnecessary lobectomy, but also some unsafe segmentectomy can be avoided, truly achieve individualized surgical treatment strategy selection.

Changes in the text: We have modified our text as advised (see Page 8, line 214-216)

Reviewer C

Comment 1: The article was well presented, it focused on a very actual and popular topic. The English language needs some revision.

Reply 1: I have received your feedback regarding the quality of the English writing in my article, and I fully recognize my shortcomings in English writing, which is an important issue that cannot be ignored for a researcher. In order to address this problem, I have decided to seek the assistance of a native English speaker to ensure that the language expression in the article is more accurate and fluent. Through collaboration with a native English speaker, I have thoroughly revised the article and made efforts to align it with the norms and requirements of academic writing. I have rechecked the grammar, vocabulary, and sentence structures, and made appropriate modifications to the expression to ensure that the article is more comprehensible and reads smoothly.

Comment 2: Although reading about segmentectomies is very interesting for any thoracic surgeon nowadays, the issue with more popular topics is relevance, in this case I consider this

article less relevant compared to other works that are circulating throughout the scientific community.

Reply 2: While I understand your perspective on the relevance of segmentectomies in the context of current scientific discussions, I respectfully disagree with the notion that this article holds less relevance compared to other works circulating in the scientific community. It is important to recognize that the significance of a topic can vary depending on the specific interests and needs of different individuals or research groups.

Segmentectomies, as a surgical procedure, have gained considerable attention and significance in recent years due to their potential benefits in the treatment of certain lung diseases, such as early-stage lung cancer. The approach offers the advantage of preserving lung function while effectively removing the affected segment, thus reducing the need for a full lobectomy. This technique has shown promising results in terms of postoperative outcomes and long-term survival rates.

While it is true that other topics may be more popular at the moment, such as emerging technologies or novel treatment approaches, it does not diminish the importance of segmentectomies in the field of thoracic surgery. Moreover, scientific relevance is not solely determined by popularity, but also by the potential impact on patient outcomes, advancements in surgical techniques, and contributions to the overall body of knowledge.

Therefore, I believe that exploring and understanding the intricacies of segmentectomies remains crucial for thoracic surgeons, as it enables them to provide the most appropriate and tailored treatments to their patients. This article, even if it may not be as currently popular as other works, can still offer valuable insights and contribute to the collective understanding of thoracic surgical techniques.

Comment 3: The size of revised articles is very small, only 10; this is without doubt because there are not yet many valid studies as well as long term studies about segments but in order to retrieve new scientific information there is the need to compare bigger number of studies and to focus on different topics besides proper indication.

Reply 3: We are very grateful to your valuable comments, for which we would like to express our heartfelt gratitude. Allow me to explain why only 10 literatures were finally included. First, we set strict inclusion and exclusion criteria, we screened the included articles, and the baseline data and characteristics of the patients were generally consistent between the two groups. Secondly, in some previous meta-analyses, the long-term survival indicators such as RFS, DFS, or OS reported in the original articles were of different lengths of follow-up. To reduce reporting bias, we screened only articles that reported 5-year survival outcome indicators. In addition, we included the JCOG0802 study, which is the largest known randomized controlled trial with a sample size. In order to retrieve new scientific information, we added three perioperative measures in the revised manuscript, and the outcome indicators with statistically significant differences were analyzed in the discussion.

Changes in the text: We added some data of perioperative outcomes such as surgical blood loss, operative time, and the number of lymph node dissection (see Page 7 and 8, line 181-194).

We have modified our discussion (see Page 9-11, line 234-302)

Comment 4: About the conclusions, the fact that segmentectomy are indicated in nodules < than 2 cm is now a relatively well known facts, this articles fails to add to the scientific knowledge and is so of minor scientific value.

Reply 4: Although segmentectomy are indicated in nodules < than 2 cm is now a relatively well-known fact. However, according to the results of our sensitivity analysis, lobectomy still has an OS advantage in stage IA lung cancer < 2 cm. Segmentectomy should be performed in carefully selected patients with stage IA< 2 cm. As the JCOG0802 study PI: Hisao Asamura emphasizes, JCOG0802 is only a scientific experiment, and the published conclusions are only a scientific conclusion based on its study design. In the meantime, he believes that lobectomy should remain the standard of care for small peripheral lung cancer, and JCOG0802 is not enough to change clinical guidelines. The reason is that segmentectomy has not been proven to preserve lung function, and the operation time is longer, the local recurrence rate and the postoperative air leakage rate are higher. The higher non-lung cancer mortality in the lobectomy group may have contributed to the better OS with segmentectomy.

Changes in the text: We added some data of perioperative outcomes such as surgical blood loss, operative time, and the mean number of lymph node harvested (see Page 7 and 8, line 181-194). And discussed the possible reasons for the difference of the mean number of lymph node harvested between the two groups (see Page 11, line 296-302)

Reviewer D

Comment 1: This systematic review is well conducted from a methodological point of view, with inclusion of only high-quality studies (2 randomized trials and 8 retrospective studies all with propensity score matching). The paper is well written with a clear message. Even the discussion is reasonable. What I am not convinced about is the usefulness of this paper because it essentially reaches the same conclusions as the many reviews published in the last 10 years. I think this deserves a comment.

Reply 1: We are very grateful to your valuable comments, for which we would like to express our heartfelt gratitude. Here is our answer to your question

In the past decade, original studies and meta-analyses on the comparison of segmentectomy and lobectomy have emerged, but a topic that can be discussed for 10 years is worth studying and has not yet been accurately answered. With the development of time, the answer to this question will become clearer. In 2022, the Japan Cancer Collaborative Group published its blockbuster study JCOG0802. Hisao Asamura prof believes that lobectomy should remain the standard of care for small peripheral lung cancer, and JCOG0802 is not enough to change clinical guidelines. The reason is that segmentectomy has not been proven to preserve lung function, and the operation time is longer, the local recurrence rate and the postoperative air leakage rate are higher. The higher non-lung cancer mortality in the lobectomy group may have contributed to the better OS with segmentectomy. The discussion of segmentectomy and lobectomy has not ceased. Therefore, in this context, we conducted a meta-analysis to identify the role of segmentectomy in stage IA lung cancer by including high-quality literatures published within the last 10 years. According to the results of our meta-analysis after sensitivity

analysis, lobectomy still has an OS advantage in stage IA lung cancer < 2 cm. Segmentectomy should be performed in carefully selected patients with stage IA< 2 cm. That's based on the latest researches, though it's consistent with many other previous studies. But it also tells us that the research on segmentectomy and lobectomy has to continue.