

## Peer Review File

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### To Reviewer1

**Comment 1:** The number of patients who underwent lobectomy with GGO-dominant cT1a-bN0 NSCLC during the study period should be described in the manuscript and in Figure 1. How many patients underwent lobectomy despite having GGO-dominant cT1a-bN0 NSCLC? Because this study is a retrospective analysis, selection bias between lobectomy and segmentectomy should be considered.

**Reply 1:** Thank you for your valuable comments and inquiries regarding our manuscript. We appreciate your attention to the details of our study population and the types of surgical interventions analyzed.

Regarding your question about the inclusion of patients with GGO-dominant cT1a-bN0 NSCLC who underwent lobectomy, our study primarily focused on the outcomes of different types of segmental and subsegmental resections. As such, patients who underwent lobectomy were indeed rare in our dataset and were not the primary focus of our analysis. This decision was based on the initial study design, which aimed to explore intra-group differences among various lesser invasive surgical approaches, rather than comparing these to the more extensive lobectomy.

Importantly, it should be noted that the few lobectomy cases in our study involved tumors located deep within the lung parenchyma, specifically in the inner region as determined by our depth ratio measurement method. In contrast, all cases included in our analysis were situated in the middle or outer regions. This distinction in tumor location further influenced our surgical approach and focus on segmental and subsegmental resections.

We acknowledge that this may limit the generalizability of our findings to all surgical options for GGO-dominant cT1a-bN0 NSCLC. We believe, however, that our focused analysis provides valuable insights into the specific segmental and subsegmental approaches, which are increasingly relevant in clinical practice for managing such cases.

Thank you again for your constructive critique, which will undoubtedly help strengthen our manuscript. We look forward to revising our study to better reflect the concerns you have raised.

**Changes in the text:** No.

**Comment 2:** Why did the authors divide the patients into four groups? The comparisons between these four groups seem complicated and unnecessary. The data, such as surgical margin and postoperative complications can be presented in all patients. Otherwise, how is the comparison between resections with/without subsegmentectomy?

**Reply 2:** Thank you for your insightful comments concerning the organization of our study groups. We appreciate the opportunity to clarify the rationale behind our methodology, which we believe is essential for the accurate interpretation and appreciation of our findings.

**1. Purpose and Novelty of Group Division:** The primary focus of existing studies on segmental and subsegmental resections has largely been technical descriptions, with less emphasis on the indications and clinical outcomes such as surgical margins and recurrence rates. Our study seeks to contribute to the existing literature by reporting these critical outcomes, leveraging our center's unique dataset and clinical experience. This initial analysis is part of an ongoing effort to better understand the implications of different surgical approaches, with the hope that future data will allow us to refine our analysis and expand upon these findings. We acknowledge the preliminary nature of this study and anticipate that subsequent research will further clarify and enhance our understanding of optimal surgical approaches.

**2. Comparative Analysis:** We specifically chose to present the data for the four surgical approaches separately to examine potential differences in efficacy and safety among them. This comparative framework is crucial as it enables a direct evaluation of each approach's impact on surgical outcomes, providing insights that are vital for surgical decision-making. By distinguishing between these groups, we can offer more targeted recommendations and understand which approaches might be preferable under certain clinical conditions.

**3. Surgical Margin and Resection Choices:** The choice between resections with/without subsegmentectomy in our center is influenced by a balance between maintaining adequate surgical margins and preserving as much lung tissue as possible. This study compares these different resection approaches regarding how much lung tissue is preserved and explores the initial criteria for choosing one approach over another. We recognize the complexity of these decisions and the preliminary nature of our findings. We hope that our results will be useful in informing future guidelines, although further research will undoubtedly be necessary to refine these recommendations.

**Changes in the text:** Line 189, 204, 227.

**Comment 3:** Readers of the journal should be interested in long-term postoperative outcomes, especially local control and surgical margin recurrence. Follow-up periods should be presented in the manuscript.

**Reply 3:** Thank you for your constructive feedback regarding the presentation of our follow-up protocol. We have revised the Methods section to clearly articulate the follow-up schedule and assessments used to monitor long-term postoperative outcomes, such as local control and surgical margin recurrence.

We appreciate your guidance in helping us improve the clarity and detail of our manuscript.

**Changes in the text:** Line 164-170.

**Comment 4:** The authors describe that the distance from the lesion to the intersegmental boundaries is defined by the segmental veins. In my opinion, although the actual intersegmental boundaries are uneven surfaces, a 3D-CTBA can provide some segmental veins. How did you ensure the surgical margin  $\geq 2$ cm from the intersegmental boundaries based on segmental veins using a 3D-CTBA and/or CT? I mean, if the surgical margin is decided based on segmental veins only, the distance from the actual intersegmental boundaries may be shorter than 2 cm in some part.

**Reply 4:** Thank you for your insightful observations regarding our description of the intersegmental boundaries and the role of segmental veins. We acknowledge that our previous wording may have been overly simplistic and could potentially lead to misunderstandings.

As you rightly pointed out, the actual intersegmental boundaries are uneven, and the segmental veins, while serving as guides on the intersegmental planes, are not definitive borders themselves. Recognizing this, we have revised our manuscript to clarify that achieving a distance of at least 2cm from the lesion to the segmental veins is intended as a minimal standard to ensure, as far as possible, that the distance from the lesion to the actual intersegmental boundaries is also at least 2cm. This is indeed a baseline measure rather than a comprehensive guarantee.

Furthermore, in our center, the 3D-CTBA software is utilized to generate a simulated surgical margin sphere of at least 2cm around the lesion. For example, in the case of an S<sup>6</sup> resection, if

the simulated surgical margin sphere involves  $V^6c$ , we would consider a combined resection of  $S^{10a}$ . Similarly, involvement of  $V^6b$  would prompt consideration of a combined resection of  $S^9a$ . This preoperative planning approach has been applied in all 173 cases handled, ensuring that the surgical margins are at least equal to the maximum diameter of the lesion.

We hope that these amendments and explanations address your concerns and provide a clearer picture of our methodologies and their rationale. We are grateful for the opportunity to enhance the precision and clarity of our study with your guidance.

**Changes in the text:** Line 142-146.

### To Reviewer2

**Comment 1:** In the introduction I suggest inserting the reference of another recent randomized controlled trial about the oncological role of segmentectomy.

**Reply 1:** Thank you very much for your valuable suggestion regarding the inclusion of additional references in the introduction. In response, we have added a reference to the study titled “Survival outcomes in a prospective randomized multicenter Phase III trial comparing patients undergoing anatomical segmentectomy versus standard lobectomy for non-small cell lung cancer up to 2 cm”.

**Changes in the text:** Line 96.

**Comment 2:** Regarding margins, I think that an  $MTR > 1$  is sufficient in nodule with GGO component  $> 50\%$ .

**Reply 2:** Thank you for your valuable suggestion regarding the adequacy of a margin-to-tumor ratio (MTR) greater than 1 for nodules with a ground-glass opacity (GGO) component exceeding 50%. We appreciate your insight into this aspect of surgical planning for lung nodules.

In our study, we implemented preoperative planning using 3D-CTBA to ensure a distance of at least 2cm from the lesion to the segmental veins is intended as a minimal standard to ensure, as far as possible, that the distance from the lesion to the actual irregular intersegmental boundaries is also at least 2cm. This approach was consistently applied across all 173 cases we handled.

The postoperative results confirmed that the surgical margins achieved were at least equal to the maximum diameter of the lesion in every case. Furthermore, our follow-up outcomes did not reveal any instances of recurrence, aligning with your perspective that an MTR>1 is generally sufficient for nodules with significant GGO components.

We believe this strategy has been effective in ensuring optimal surgical outcomes and supports the safety and efficacy of our surgical margins approach.

Thank you once again for your constructive comments, which have provided an opportunity for further discussion and validation of our methodology.

**Changes in the text:** No.

**Comment 3:** Please specify the aim and the groups on which the authors made the comparison in the paragraph methods for a well readable paragraph.

**Reply 3:** Thank you for your insightful feedback regarding the clarity of the aims and group comparisons within our methodology section. We acknowledge that our initial manuscript primarily focused on reporting results without sufficiently articulating the intent of the comparisons among groups, which may have impacted the readability of the text.

In response to your comment, we have revised the results section to include a clear statement of the aim at the beginning of each part. We have also integrated concise conclusions within these sections to enhance the flow and logical progression of the narrative, thereby aligning more closely with your standards.

We appreciate the opportunity to refine our manuscript and believe these amendments will greatly improve its readability and coherence.

**Changes in the text:** Line 189-201, 204, 211, 214, 227-231, 237-240.

**Comment 4:** Please do not use the word correlation without a statistical correlation analysis.

**Reply 4:** Thank you for your insightful comments. I appreciate your emphasis on the precision of terminology used in statistical analysis. Specifically, we replaced ‘show significant correlation’ with ‘are significantly associated’ to more accurately reflect the observed relationships without implying a statistical correlation analysis. This change ensures the terminological accuracy throughout our study.

**Changes in the text:** Line 194.

**Comment 5:** I suggest inserting the number of dissected lymph node and the number of dissected lymph nodal station for every technique.

**Reply 5:** Thank you for your valuable suggestion regarding the inclusion of the number of dissected lymph nodes and the number of dissected lymph nodal stations for each technique. Your suggestion is indeed very helpful and would undoubtedly contribute to improving the comprehensiveness of our study.

We sincerely apologize that, due to the retrospective nature of our study, we do not have access to this specific data. We deeply regret this limitation. Your suggestion is invaluable, and we will make it a priority to incorporate this aspect in our future explorations.

Thank you again for your thoughtful recommendation and understanding, which will guide our further research endeavors.

**Changes in the text:** No.

**Comment 6:** I noticed that the authors reported the recurrence rate and it was 0 for every group. The authors need to clarify the duration and the methods of the follow-up.

**Reply 6:** Thank you for your valuable comments concerning the follow-up duration and methods reported in our study. We appreciate your attention to these details and have clarified these aspects in the Methods section of our manuscript.

To ensure comprehensive assessment, we conducted regular follow-up visits up to five years post-surgery and included a final telephone follow-up in June 2024, just before manuscript preparation. This approach allowed us to confirm the absence of recurrence, with follow-up periods ranging from 3.5 to nearly 9 years, depending on the initial treatment date between August 2015 and November 2020.

We hope this additional information addresses your concerns and provides a clearer understanding of our follow-up process.

**Changes in the text:** Line 164-170.

**Comment 7:** The results of the paper are quite weak in my opinion and the major finding is that with an adequate pre-operative imaging study, the results of single segmentectomy or

subsegmentectomy are very good in patients with pure GGO that could be managed with observation or a simple (less technically demanding) wedge.

**Reply 7:** We understand and appreciate your criticism. As you rightly pointed out, wedge resection is often sufficient for managing these cases. That said, more precise anatomical segmentectomy or subsegmentectomy could potentially offer advantages, particularly in addressing deeper lesions.

The primary focus of existing studies on segmental and subsegmental resections has largely been on technical descriptions, with less emphasis on the indications and clinical outcomes such as surgical margins and recurrence rates. Our study seeks to contribute to the existing literature by reporting these critical outcomes, leveraging our center's unique dataset and clinical experience.

This initial analysis is part of an ongoing effort to better understand the implications of different surgical approaches. We hope that future data will allow us to refine our analysis and expand upon these findings. We acknowledge the preliminary nature of this study and anticipate that subsequent research will further clarify and enhance our understanding of optimal surgical approaches, potentially including wedge resection and lobectomy cases for more in-depth study.

**Changes in the text:** No.

### **To Reviewer3**

Thank you for your thoughtful and constructive feedback. Your insights have deepened our understanding of key aspects of our research. We sincerely appreciate the time and effort you have invested in reviewing our work.

#### **Regarding Our Response Format:**

We acknowledge that your comments largely expressed support for our research methodology and did not request specific textual changes. Accordingly, our response consists primarily of expressing our gratitude and noting that no substantive text modifications have been made in response to your review. We aim to communicate our respect and consideration for your feedback clearly.

We hope this dialogue will help the editors and reviewers better understand our research and appreciate the opportunity to refine our work through your review process.

Thank you once again for your invaluable feedback.

