

Peer Review File

Article information: <https://dx.doi.org/10.21037/jtd-23-1201>

Reviewer A

Evaluation of the QoL and sharing-decision making is of crucial importance when two comparable from the oncological point of view treatment methods are considered.

SBRT and surgery for stage IA NSCLC were not compared in the completed randomized trial thus though surgery is still a treatment of choice for suitable for lobectomy patients; a discussion with a patient about possibilities of treatment should also include data on the QoL after treatment. From this point of view, a choice of the subject of the study is interesting and well justified in the manuscript.

The results that shortly after surgery QoL is worsening but improves afterwards was predictable; however, such a result demonstrated on the large group of patients is valuable and may be of value in the discussion with a patient who is afraid before surgical treatment.

The interpretation of the results obtained in the small group of patients receiving SBRT, should be changed, because may lead to the wrong conclusions that SBRT in comparison with surgery leads to the worsening of QoL.

First of all, the unfavorable characteristics of the SBRT group in comparison with surgery group should be emphasized. They had significantly higher co-morbidity index, thus their baseline QoL (PCS) was worse. SBRT does not cure underlying medical conditions, thus no one may expect the improvement of PCS after treatment. Serious medical conditions prevented surgical treatment, thus it is not surprising that patients deteriorated throughout one year after treatment. This should be underlined.

Response: We acknowledge that compared to surgical group, the sample size in SBRT group is smaller and SBRT patients tends to be older and with more comorbidities, we have reworded and toned down the interpretation of our SBRT results. We have also emphasized the unfavorable baseline characteristics of SBRT patients and that the sustained poorer physical health outcomes of SBRT patients were very likely not due to the treatment but overall poorer baseline health and other factors (Discussion Page 16, line 13-17).

FACT-LCS did not significantly changed after one year post -SBRT (from 22.53 to 21.27) and the symptoms from stage IA NSCLC are little probable; the symptoms evaluated by this scale may be identical than symptoms related to the deterioration of the concomitant respiratory and cardiac problems.

Response: This is a good point and is now included in the Discussion section (page 16, lines 8-10)

Additionally, patients who had a cancer progression during a period of the evaluation should be excluded from the analysis or at least (if not evaluated) this should be acknowledged.

Response: Patients with cancer progression, additional treatment(s) or metachronous primaries were not included in our analysis, we have modified the Methods section to clarify this point (page 6, line 18-20).

Discussion, page 9; lines 271-274: References and interpretation of the results are inappropriate: ref. 19: this was not about SBRT but about protracted SBRT schedules; I think that in the stage IA NSCLC patients, as in this study, SBRT was given in 1-3 fractions (by the way; providing SBRT schemes would be of value); and ref. 20; we have not data that the volume of irradiated tissue was related to the radiation toxicity (= QoL). In the Stage IA, all tumors were small.

Response: Ref 19 and 20 has been further examined and removed to avoid misunderstandings.

Discussion, page 10; lines 285-288: too speculative; as above, we have not data that this treatment was long, SBRT is rather shorter than surgery; usually this is completed within one week.

Response: We have also modified the discussion in the text accordingly (page 17, lines 5-8).

In total, Abstract and Discussion should be reworded, too avoid a feeling that SBRT was less effective than surgery for preservation of the QoL. There were different characteristics of patients referred for these two treatment methods.

Response: Abstract and discussion have been modified.

Reviewer B

Zhang and colleagues describe QoL outcomes in stage IA NSCLC patients treated with surgery or SBRT and use sophisticated statistical methods to determine inflection curves for postoperative QoL changes. The authors determined that physical QoL at 12 months postoperatively was better for patients undergoing surgery but worse for those treated with SBRT. The manuscript was interesting and mostly well-written. However, there are repeated instances of typos or formatting inconsistencies that should be addressed. My minor comments, divided by section:

Abstract:

1. Define QoL acronyms if possible (likely limited by word count)

Response: Definition of QoL acronym has been added to the Background section of Abstract (Page3, line3)

Introduction:

1. The introduction reads well but is a bit lengthy. Consider shortening by 20% or so.

Response: Introduction has been shortened considerably

2. Line 80: Surgery should not be capitalized

Response: It's changed to "surgery".

Methods:

1. Why was 80% of the data used as the span for the LOWESS curve?

Response: The span of 80% was chosen to achieve a balance between capturing broader trends and minimizing overfitting due to local variability. It allowed us to capture general trends effectively while avoiding noise and the risk of overinterpretation of minor fluctuations. It's based on preliminary analyses with various spans, and we found 80% to be the most balanced, avoiding overly smoothed or fluctuating curves.

2. Did the Authors consider performing a propensity score-matched analysis? If it is possible to match SBRT and surgery patients, this may allow for a more robust comparison of the groups. If the groups are too different to match, consider stating this.

Response: We did perform a propensity score-matched analysis, and it yielded results consistent with our presented adjusted findings. We chose to present the adjusted results in the manuscript as it allowed for the inclusion of a larger number of patients, providing a broader and more inclusive perspective. We stated our approach and the rationale behind choosing to present the adjusted results over the propensity score-matched analysis in the discussion section of the revised manuscript. A brief summary of results from the propensity score analysis has been incorporated into the results section and discussed in the limitation.

Results:

1. Line 172: fix typo "vs.55%"

Response: fixed

2. Consistency with "p=x.xx", first paragraph of the section has inconsistent formatting.

Response: fixed

3. Line 182: Consider moving MICE explanation to Methods.

Response: The explanation of MICE imputation has been added to the Methods section (page 9, line 4-6).

4. Lines 184-186: It seems like a bit of a stretch to say they both decreased with SBRT decrease was -.10 with a p value=.92. Please state that one is a slight trend (essentially zero change), while the other is statistically significant.

Response: It has been rephrased to indicate that the change for SBRT was minimal (page 11, line 15).

5. Lines 196-198: This sentence essentially repeats what is said previously and could probably be removed
Response: The sentence has been removed.
6. Lines 207-209: in similar fashion to above, this summary sentence is not needed. Consider removing or moving to Discussion section.
Response: The summary sentence has been removed.
7. Line 211: fix typo “.Within”
Response: typo fixed.
8. Line 212: Surgical shouldn’t be capitalized
Response: typo fixed.
9. Lines 211-213: In similar fashion to comment 3, stating that both are decreases, when one is statistically significant and the other has a p value=.8, feels like a bit of a stretch
Response: The sentence has been rephrased (page 12, line 20).
10. Line 214, 217, 221, 227, 234, 236: Surgical is not a proper noun and should not be capitalized
Response: typo fixed.
11. Lines 219-220: Being unfamiliar with the specific questions of the FACT-LCS, this sentence is slightly confusing. Consider including the survey as a supplementary figure, adding an additional figure to demonstrate this subanalysis, or removing the sentence.
Response: Questions of the FACT-LCS was introduced in the Method section (FACT-LCS) (page 8, line 16-18). And additional figure (Figure 3) has been added to demonstrate this subanalysis.
12. Lines 232-233: this seems to include an interpretation of the data, which should be reserved for the Discussion section.
Response: The sentence has been removed.
13. Lines 237-239: this is again a summary of the paragraph and isn’t required
Response: summary sentence was removed.
14. You mention differences depending on Race, but I wonder what differences, if any, are dependent on gender (M vs. F)? Or other predictors of QoL change (positive or negative)?
Response: No significant associations were found between QoL outcomes and gender, smoking status, and nodule size of patients. It has been added to the end of the

paragraph (page 14, line 13-15).

15. Consider breaking Results into subsections.

Response: The Results section has been divided into subsections.

Discussion:

1. Consider starting the discussion with a restatement of the overall goals of the study.

Response: A restatement of the overall goal has been added in the beginning of the Discussion section (page 15, line 2-3).

2. Lines 269-271: This essentially rephrases the prior sentence without adding any information. Consider removing or revising.

Response: The sentence has been rephrased (page 16, line 7-10).

3. Lines: 274: Fix typo. Also, “papers” is fairly casual. Consider changing.

Response: Typo fixed and “papers” were rephrased.

4. Line 280: Consider including more contextualization of these data with similar studies

Response: Discussion of other similar studies has been added (page 16, line 20-23).

5. Lines 202-293: Fix typo in this sentence

Response: typo fixed.

6. Line 299: I appreciate the acknowledgment of the non-randomized nature of this study. However, I would consider emphasizing this a bit more at the beginning of the Discussion, and that because of this, you cannot directly compare the groups

Response: While randomized controlled trials are the gold standard, multiple studies have demonstrated that observational studies are particularly suitable for investigating real-world outcomes and can provide valuable insights, especially when RCTs are not feasible due to ethical or logistical reasons, and that previous RCTs designed to study the comparison of surgery and SBRT were closed prematurely due to failed accrual. Furthermore, as pointed out by the reviewer, we have acknowledged the non-randomized nature of our study and employed rigorous statistical methods, such as propensity score matching and mixed effect models to control for potential confounders in an effort to minimize biases and make the groups more comparable. Finally, we have been transparent about the limitations of our study design and have discussed potential biases and confounding factors in the manuscript.

Given these considerations, we believe it would be more appropriate to mention the non-randomized nature of this study in the limitation section rather than at the beginning of the discussion. Highlighting it prominently at the start might unduly

overshadow the strengths and contributions of our research.

Table 1.

1. Add p-value for Sex, Education, Histology

Response: p-value added

2. Consider mentioning or defining Comorbidity Ordinal Score in Methods or Results

Response: Comorbidity Ordinal Score was defined in Method section (page 7, line 12-13)