Peer Review File

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Reviewer A: The extent of thyroidectomy for papillary thyroid carcinoma limited to the one lobe has been a matter of debate because of its inherent uncertainty about the effectiveness. The authors conducted a literature review to produce a reasonable critical synthesis on the relationships between the extent of surgery and clinical outcomes. The evidence is expected to play an essential role in the shared-decision making. In this regard, the authors should systematically perform the literature review. Relevant studies should be sought systematically and appraised critically.

Comment 1: A sample size of a study is a significant concern in appraising the evidence. But it should not be the first consideration. Even a study with a small sample size < 300 may still be valid internally and externally.
Reply 1: *All the studies with few cases (<300) didn't show any significative difference. For thesereason we decided to consider only the large studies that in point of fact were the great majority. We hope to have better explained this point of view. We could discuss these works but we 'd lenghten the paper with no real advantages.*

Comment 2: Japanese endocrine surgeons have their clinical practice guidelines published in 2020, which is missed in this review.
Reply 2: *We are grateful to the reviewer for the precious suggestion. We have enclosed these guidelines now (line 128-132) and we have analyzed two more papers cited in them (line 216-223) .*

Comment 3: The authors should provide relevant evidence for the critical issues. For example, they concluded that "patients should be warned that lobectomy of a size between 2 and 4 cm can be associated with an increased risk of local recurrence and a probable reduced overall survival." What the magnitude of the association? How big is the risk? The relative risk or odds ratios would be the most appropriate numbers as evidence.
Reply 3: *Sincerely our purpose was to write a narrative review and not a meta- anlysis. However we have specified when Odds ratio was > of 1 in the table 2.*

Comment 4: The authors also should clarify that how biases in the appraised literature affected the evidence.
Reply 4: *Sincerely we don't understand exactly the request however we have try to be clearer.*

Reviewer B
Comment 1: This is an interesting manuscript of the review of mainly ATA guidelines and the recent thrust on lobectomy up to 4 cm. The authors have analyzed the data and made relevant comments regarding the extent of thyroidectomy and the size of the primary tumor. Even though the information is well analyzed, I don't think they have discussed much about the NCDB data and SEER data as to extent of thyroidectomy and no outcome difference. In the Abstract section, the authors have concluded "patients should be warned that lobectomy for

tumors of a size between 2 and 4 cm can be associated with an increased risk of local recurrence and with a probable reduced overall survival." This conclusion is more hypothetical and no patient would ever agree for lobectomy between 2 to 4 cm if we tell them that there is increased risk of local recurrence and reduced overall survival. This conclusion needs to be revisited and it would be more important that the authors conclude individualizing the treatment in this group of patients and lobectomy is still an attractive option. There is no discussion in the paper regarding quality of life after lobectomy and total thyroidectomy, which is a major basis of decision making. The role of radioactive iodine needs to be explained in view of our current de-escalation of treatment. Line 148 in the manuscript the authors' spelling is incorrect. It should be HAIGH. Lines 254-256 need to be revisited in view of the above comments.
Reply 1*: We have revisited and re-edited, as suggested by the Reviewer, especially we have discussed the better quality of life after lobectomy and revisited the conclusion: "patients should be warned that lobectomy for tumors of a size between 2 and 4 cm can be associated with an increased risk of local recurrence and with a probable reduced overall survival" (line 281-282, 298-303) . We have done this in the discussion and also in the abstract inserting in the discussion a mention about better quality of life in lobectomy.*
We don't understand exacly "I don't think they have discussed much about the NCDB data and SEER data as to extent of thyroidectomy and no outcome difference"

Reviewer C
Comment 1: In the manuscript, "TOTAL THYROIDECTOMY VS. LOBECTOMY IN DIFFERENTIATED THYROID CANCER: IS THERE A REASONABLE SIZE CUT-OFF FOR DECISION? -A NARRATIVE REVIEW," the authors cursorily review guidelines for differentiated thyroid cancer and studies comparing LT to TT. The manuscript suggests a <2cm cutoff for thyroid cancer, but there are several issues in the way the authors make this recommendation. First, the authors provide a biased review of prior studies – for example, studies favoring TT for size 1-4 cm are not critically evaluated, but studies indicating TT and LT are equivalent are more thoroughly critiqued. Second, the authors suggest a 2 cm cutoff for LT, but then indicate that a 4cm is acceptable in low risk differentiated thyroid cancer. This implies that LT is acceptable in high risk differentiated thyroid cancer, which contradicts most current guidelines.
Reply 1*: We meant that LT can be enough for post-surgical low-risk cancer we hope we have better stated the apparent contradiction as stated by the reviewer.*

Major concerns
Comment 2: The manuscript should be reviewed for grammar and syntax, ideally by an English language manuscript editing service.
Reply 2*: We have revised the manuscript by a skilled mother tongue. This is the mother tongue who usually review all our papers and we hope now is good*.

Comment 3: The Abstract does not include any key points from the manuscript, but rather states the number or articles that were identified and used in the review.

Reply 3: *We have written the abstact according to the "information for Authors" stating key point in "Objective" or maybe we don't understand well the concern*

Comment 4: Using the keywords of "total thyroidectomy vs. lobectomy in differentiated thyroid cancer" seems very narrow in scope and would likely exclude relevant articles. Lobectomy is often referred to as hemithyroidectomy (and this identifies different articles on Pubmed), and differentiated thyroid cancer may be referred to as PTC or FTC.
Reply 4*: We are grateful to the reviewer for this precious suggestion and we could find further intersting papers (line 235-251). We have better specified when necessary, PC and FC throughout the whole manuscript.*

Comment 5: The authors say in the methods that they exclude small studies, but a study of 128 patients is included. Furthermore, excluding "small" studies that may have 200 patients but including expert opinion seems counterintuitive and likely places too much weight on opinion over evidence.
Reply 5*: Sorry if we didn't explain well. We excluded small studies because the were also retrospective and without enough power, while the study of 128 case was prospective and showed a significativity in the results.. We have better specified now.*

Comment 6: Review of the paper by Adam et al, does not indicate that this paper did not include recurrence free survival.
Reply 6*: We have modified our text as advised (line 143)*

Comment 7: All scores should be explained (MACIS, AMES, AGES).
Reply 7*: We think it could be too long to explain these complex scores but we have inserted a reference. We hope it can be good.*

Comment 8: It is unclear why papers from 1980s and 1990s that do not provide information regarding size are included.
Reply 8*: We don't exactly understand the comment. We included all the papers we could find in the stated fonts of researches*.

Comment 9: Critical details of the papers cited are not include in the review. For example, although Bilimoria et al., demonstrated that TT was associated with improved overall survival compared to TL, no mention of the fact that this study did not control for comorbidities, multifocality, extrathyroidal extension, and completeness of resection
Reply 9: *For some papers we didn't want to be too long. Regarding paper of Bilimoria we have added now these important informations as suggested (line 199-200)*

Comment 10: The paragraph on expert opinion provides no valuable information.
Reply 10: *In pont of fact "expert opinion" are very different and really don't provide so valuable information. We have bettere explained the reasons and we think that this can have an some interest the same. We can delete if it's required but we think that it can be important to realize that "expert opinion" can be so different.*

Comment 11: The Conclusion paragraph is confusing because the authors initially suggest a cutoff of <2cm for LT, but then recommend <4cm based on pathology. Most current guideline referenced by the authors recommend LT for differentiated thyroid cancer only for low risk pathology, so it is unclear why a cutoff of 2 cm would be appropriate for higher risk differentiated thyroid cancer.
Reply 11: *We don't understand well. Just we wanted to mean that in the pre-surgical risk evaluation is not always so easy to understand the risk and for this reason "pricipled" Intervention should be TT for cancer > 2.0 cm. We have revised this paragraph hoping it's clear now.*

Comment 12: *Table 2 would benefit from including hazard or odds ratios instead of "BETTER."*
***Reply 12**: We have done this when > of 1*

<u>Minor concerns</u>
Comment 13: Abbreviations in the abstract are not described.
***Reply 13**: We have described the abbreviatios*

Comment 14: In line 65 "consensus" should be "consensus statement.
***Reply 14**: We have modified our text as advised*

Comment 15: Contractions should be avoided.
***Reply 15**: We don't undertand contraction of what*

Comment 16: References should be provided in line 107.

Comment 17: In line 108, which guideline does "this last guideline" refer to?
***Reply 17**: We have revised the whole manuscript we hope now is clear*.

Comment 18: In line the meaning of "revised downward" is unclear.
***Reply 18**: We have revised the whole manuscript we hope now is clear.*

Comment 19: Abbreviation for CP is not described.
***Reply 19**: We have done this (line 57)*

Comment 20: "TT e LT" is not English.
***Reply 20**: We have used these acronyms which can be found in same other papers. We can change if requested.*

Comment 21: In line 154, "The Author himself," is inappropriate for a manuscript with multiple authors.
***Reply 21**: It has been corrected*

Comment 22: Abbreviation for PC is not described.

Reply 22*: We have done this (line 57)*

Comment 23: Abbreviation for MACIS and definition is not provided.
Reply 23: *We have provided a reference for MACIS; AGES and AMES*

Comment 24: In line 174, "Memorial Sloan Kattering Cancer Center," is spelled incorrectly.
Reply 24*: We have corrected (line 186)*

Reviewer D: The authors have attempted to undertake a narrative review of lobectomy vs total thyroidectomy for differentiated thyroid cancer under 4cm. They have analysed numerous guidelines and some recent original papers examining the topic.

Comment 1: The narrative review is written more as English prose than a scientific paper. The paper requires signifcant editing by a native English speaker.
The analysis of the data is superficial and the discussion technique relates to reporting on guidelines and repeating data from papers addressing the topic. I fail to see how this paper adds anything substantial to the already voluminous noise on this issue in the literature.
Reply 1*: We have re-edited the paper by a native English speaker but manteining the style of a narrative review. Regarding" how this paper adds anything substantial to the already voluminous noise on this issue in the literature" sincerely we think that this paper, after the further revision as requested, is the paper that analyze most completely all work in the literature. To date we think no review is so complete.*