OPEN PEER REVIEW

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As a new feature for progressing towards transparency, we decided to open a new window for all of our editors as well as authors titled "**Open Peer Review**". We hope by this new facility, our reviewers will be more motivated and authors will be more satisfied with the review process. We believe that publishing our peer review reports could make a transparent and clear environment for all our efforts within a journal, but not all reviewers tend to publish their comments.

What is "Open Peer Review" process?

An "Open Peer Review" process is making the details of all review process (including reviewers, associate editors, and EICs comments) as "Public" as it is agreed by EIC, Authors, and reviewers.

Advantages of "Open Peer Review" process

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You can find out more at:
https://sites.kowsarpub.com/kowsar/knowledgebase/category/tree.html#opr.html

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Peer Review Report for "Longer Time to Reach Excellent Response to Treatment in Familial Versus Sporadic Non-medullary Thyroid Cancer (NMTC): A Matched Case-Control Study"

Author(s): Susan Shafiei, Mehrdokht Sadrolodabaei, Atena Aghaei, Narjess Ayati, Samira Zare Namdar, Donya Hemati, Seyed Rasoul Zakavi

Review Timeline:

Submit Date: 20 Oct 2020
Revised Date: 30 Mar 2021
Accepted Date: 13 Apr 2021

Revision (0)

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

REFEREE: Reviewer | **Revision** (0) 11 Nov 2020

Dear AE,
Comments for the authors:
1. Abstract: The number of patients in the methods and results sections is different and should be corrected.
2. Abstract, line 16: Please add time to achieve excellent response between 2 groups, before p-value.
3. Page 3, last para: How many patients had sporadic NMTC? In addition explain that after matching, how you selected the control group.
4. Page 4, first para: Here and in abstract, you wrote that 66 familial NMTC were available, while in results you have 81 patients with familial NMTC. These numbers are confusing, please clarify.
5. Please define which patients have received RAI therapy? Since the study has employed patients for 21 years, what were the indications for RAI therapy before and after 2010? Did were equal numbers in each of 2 groups received RAI in these 2 separate times?
6. Page 4, before Results: You should have a subtitle of “Definitions”. Define items such as”

complete, incomplete and successful response, etc…
7. Please add “Statistical analyses”, before “Results” and describe tests used for any special observation or comparisons, regressions, etc …
8. Results, page 4 last paragraphs: You should place a comparison between 2 groups before “the effect of the number of involved members”. In addition, use the word “influence” instead of “effect” in this title and throughout the text of the manuscript.
9. Discussion: Your findings differ from other reports; please explain many reasons for such differences, i.e. in aims, methodology, patients populations, analyses, etc …
10. Page 7: Prepare a table comparing all studies published in the literature and your findings. Compare important characteristics in regard to metrology, findings, and limitations.
11. Add two separate paragraphs regarding “Limitations” and “Conclusion”, at the end of the Discussion.
12. Please use only the family name of authors throughout the manuscript and add et al. (omit first names).
13. For abbreviations, write the full word and then abb. in parenthesis; such as thyroglobulin (tg).
14. Please combine tables 1 and 2 in one table.
15. Add newer references.
Thanks.

Hengameh Abdi: Reviewer | **Revision (0)** 14 Dec 2020

Dear AE,
The manuscript entitled “Longer Time of Excellent Response to Treatment in Familial versus Sporadic Non-Medullary Thyroid Cancer (NMTC), a Matched Case-Control Study” was reviewed.
My comments for the authors are as follows:
- The title of the manuscript is inappropriate. “Longer time of excellent response” is confusing! I think authors want to say “Longer time to reach an excellent response…”
- Abstract, “Results” section: The authors wrote about the “incidence” of 2.75% for familial NMTC. Is this percent an incidence rate?!
It should be clarified that the presented data are related to 66 patients (with their controls) and not all 81 individuals; this issue should also be noted in the main text.
- Methods: The ATA criteria for different response groups should be mentioned at least once in the main text or table footnote.
There is no data regarding laboratory measurements and their characteristics such as coefficients of variations, reference ranges and etc. Were all laboratory analyses done in one center? Were all kits used for measurements the same across the study period i.e. 21 years?!
Data regarding the site(s) and operator(s) of thyroid ultrasonography should be mentioned.
How did the authors define “cancer death”?
The manuscript needs a “Statistical analysis” section.
- Results
Number of the included patients in each table should be mentioned.
How many microcarcinomas were included in your cohort?
- Discussion:

I suggest starting the “Discussion” section with a summary of the study findings.
It is not necessary to write the authors’ names completely; for example, Antonio E Pinto et al……Pinto, et al is enough.
What is the “DFS” or “OS”??
There is no section describing the study limitations. I suggest making a separate paragraph to write about both the study strengths which have been mentioned in the 4th paragraph of the discussion section and limitations.
- Please search the literature again for the relevant studies.
- The whole manuscript should be read carefully and typos should be corrected.
Thanks.

Atieh Amouzegar: Associate Editor | **Revision** (0) 28 Dec 2020

Dear EIC,
Based on the reviewers' comments for the manuscript entitled" ", some major points should be considered before the final decision that is related to results and discussion.
Best regards

REFEREE: EIC | **Revision** (0) 29 Dec 2020

Dear Author,
Based on the reviewers comments the manuscript needs revision.
Thanks.

OPEN PEER REVIEW

Revision (1)

Reply to Reviewers

Ideally, the reviewing process can significantly improve the submitted manuscripts by allowing the authors to take into account the advice of reviewers. Author(s) must reply to all reviewers' comments in a separate Word file, point by point. A "**Reply to Reviewers**" document is submitted along with revised manuscript during submission of revised files, summarizing the changes that the authors made in response to the reviewers' comments. The responses to reviewers' comments specifies how the authors addressed each comment the reviewers made.

You can read the authors' responses to the reviewers' comments in the next page.

Point to point response:

Dear Editor in Chief;

Thank you and the respected reviewers for the invaluable comments that made our manuscript better and more attractive. We re-analyzed the data and revised the manuscript according to the reviewer's suggestions and comments. Below you can find the comments of the respected reviewers and our point by point responses and description of taken actions.

All revisions are highlighted in the main manuscript with yellow color.

Reviewer 1:

1. *The title of the manuscript is inappropriate. "Longer time of excellent response" is confusing! I think authors want to say "Longer time to reach an excellent response…"*
   Answer: Thank you so much for your comment. We changed the title according to your suggestion.
2. *Abstract, "Results" section: The authors wrote about the "incidence" of 2.75% for familial NMTC. Is this percent an incidence rate?!*
   It should be clarified that the presented data are related to 66 patients (with their controls) and not all 81 individuals; this issue should also be noted in the main text.
   Answer: Yes. 2.75% is the incidence rate of familial thyroid cancer in our database. We rephrased the sentence to make it clearer. We had mentioned in the abstract "methods section" that we are comparing 66 cases with 66 matched controls. Furthermore, we added it in the results section to clarify it again. However due to 250 words limit in the abstract we are forced to revise two sentences. All revised sentences are highlighted in yellow.
3 *Methods: A) The ATA criteria for different response groups should be mentioned at least once in the main text or table footnote.*
   Answer: The abstract of ATA response criteria is now added to the main text. It is too extensive to be added in the footnote.
   B) There is no data regarding laboratory measurements and their characteristics such as coefficients of variations, reference ranges and etc. Were all laboratory analyses done in one center? Were all kits used for measurements the same across the study period i.e. 21 years?!
   Answer: Being well aware of the importance of Tg measurement by a single laboratory, one type of kit and even a single technologist, nearly all of laboratory tests were done in the main reference laboratory. We added the name of the kits and coefficient of variations of each assay to the text.
   C) Data regarding the site(s) and operator(s) of thyroid ultrasonography should be mentioned.
   Answer: All US examinations were performed in 4 US centers by 4 radiologist which are expert in thyroid and cervical US. *The US device characteristics are added in the text.*

D) How did the authors define "cancer death"?

Answer: Cancer death was defined as death directly related to the thyroid cancer, which was explained in details in the text. Also, we added the reason for cancer death in each deceased patient.

E) The manuscript needs a "Statistical analysis" section.

Answer: We added statistical analysis before the results.

1. *Results*

A) Number of the included patients in each table should be mentioned.

Answer: We thank you for your comments. We added the number of patients in each table.

B) How many microcarcinomas were included in your cohort?

Answer: We added the number of patients with microcarcinoma to the results. Overall 11 patients had microcarcinoma, 4 of them was in control group.

2. *A) I suggest to start the "Discussion" section with a summary of the study findings.*

Answer: Thank you so much for your comments. We relocated the summary of our results to the first paragraph of the discussion.

B) It is not necessary to write the authors' names completely; for example, Antonio E Pinto et al……Pinto, et al is enough.

Answer: Names were changed as suggested.

C) What is the "DFS" or "OS"??

Answer: We expanded the abbreviations: DFS: disease free survival, OS: overall survival.

D) There is no section describing the study limitations. I suggest to make a separate paragraph to write about both the study strengths which have been mentioned in the 4th paragraph of the discussion section and limitations.

Answer: We added a paragraph describing the strength and limitations of our study which is now the last paragraph of the discussion.

E)- Please search the literature again for the relevant studies.

Answer: We reviewed recent literature again and added some new information to our article.

F) The whole manuscript should be read carefully and typos should be corrected.

Answer: Reviewed and corrected.

Reviewer 2:

1. *Abstract: Number of patients in methods and results sections is different and should be corrected.*

Answer: It is corrected. We had 81 patients in our cohort, but only 66 patients met the inclusion criteria to enter the study.

2. *Abstract, line 16: Please add time to achieve excellent response between 2 groups, before p value.*
   Answer: We added the numbers, but to avoid surpassing the 250 word limit of the abstract, we forced to delete few words in the abstract.
3. *Page 3, last para: How many patients had sporadic NMTC? In addition explain that after matching, how you selected the control group.*
   Answer: Out of 2944 patients with NMTC, 81 patients had familial and 2863 had sporadic NMTC. From 81 patients with familial NMTC, TNM staging was available in 78 cases and 66 patients had follow up data of at least 1 year after initial diagnosis. We defined a minimum follow up of 1 year as an inclusion criteria for both patients and controls. For each patient with FNMTC, we searched our databank based on age and sex and TNM stage, and year of diagnosis. If we could not find any control on the same year of diagnosis as the patient, we searched for a match in the previous year. This was repeated until we can find a match for every patient. If we found more than one control for any of the patients who met all of the criteria, we used the one which is nearest to the patients in terms of time of surgery.
4. *Page 4, first para: Here and in abstract you wrote that 66 familial NMTC were available, while in results you have 81 patients with familial NMTC. These numbers are confusing, please clarify.*
   Answer: Thank you for your comments. We clarified it in the manuscript. Out of 81 FNMTC, 66 patients had followed up for at least 1 year and were compared in terms of response to therapy.
5. *Please define which patients have received RAI therapy? Since the study has employed patients during 21 years, what were the indications for RAI therapy before and after 2010? Did where equal numbers in each of 2 groups received RAI in these 2 separate times?*
   Answer: We treated patients with radioiodine based on ATA guideline without considering familial predisposition. Actually all patients with tumor size of more than 1.5 cm were considered for RIT, however low dose of I-131 (i.e: 1110MBq) was more commonly used after 2010. Based on our protocol, three patients in case group and 7 patients in the control group did not receive radioiodine.
6. *Page 4, before Results: You should have a subtitle of "Definitions". Define items such as" complete, incomplete and successful response, etc…*
   Answer: The abstract of ATA response criteria is added to the main text.
7. *Please add "Statistical analyses", before "Results" and describe tests used for any special observation or comparisons, regressions etc*
   Answer: Thank you for your comments. We added a section of statistical analysis before the results.
8. *Results, page 4 last paragraphs: You should place comparison between 2 groups before "the effect of number of involved members". In addition, use word "influence" instead of "effect" in this title and throughout the text of the manuscript.*
   Answer: It is done
9. *Discussion: Your findings differ from other reports; please explain many reasons for such differences, i.e. in aims, methodology, patients populations, analyses etc …*

Answer: We compared our study with others and explained the reasons behind any difference. We added a paragraph in the discussion.

10. *Page 7: Prepare a table comparing all studies published in the literature and your findings. Compare important characteristics in regard to metabology, findings and limitations.*
    Answer: We added a table with all studies included with their important findings.
11. *Add two separate paragraphs regarding "Limitations" and "Conclusion", in the end of Discussion.*
    Answer: A paragraph is added at the end of the discussion.
12. *Please use only family name of authors throughout the manuscript and add et al. (omit first names).*
    Answer: It is done
13. *For abbreviations, write full word and then abb. in parenthesis; such as: thyroglobulin (tg).*
    Answer: It is done
14. *Please combine tables 1 and 2 in one table.*
    Answer: We think that merging two tables will not fully represent our data and will force us to omit some important data. The number of patients and some other values are different in these two tables.

15. *Add newer references.*

Answer*: N*ew references were added.

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Revision (1)

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

REFEREE: Reviewer | **Revision** (1) — 7 Apr 2021

Dear AE,
The authors have revised their manuscript according to reviewers comments and the article is now acceptable for publication in the IJEM.
Thanks.

Hengameh Abdi: Reviewer | **Revision** (1) — 12 Apr 2021

Dear AE,
The revised manuscript is acceptable for publication.
Thanks.

REFEREE: Associate Editor | **Revision** (1) — 12 Apr 2021

Dear EIC,
The authors have responded to the reviewers' comments satisfactorily. The manuscript is now acceptable for publication in the IJEM.
Thanks.

REFEREE: EIC | **Revision** (1) — 13 Apr 2021

Dear Author,
The manuscript is suitable for publication in the IJEM.
Thanks.