

Peer Review File

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**Reviewer A**

The original article entitled “Surgical treatment of multifocal, intermediate risk, DTC: single reference centre experience.” enrolled 92 patients with intermediate risk DTC and evaluated the preferable surgical management for patients with unilateral or bilateral multifocal intermediate-risk DTC.

Comments 1: This research topic is interesting and can provide readers a decision-making guidance to manage these kind of patients.

Reply 1: Thank you for your sentence.

Change in the text: none.

Comments 2. There are obvious language problems in this article, which seriously affects the reader's understanding of the content (even the topic is meaningful). It is strongly recommended that the article should be edited by a professional English editor.

Reply: We apologize for our error. The text has been currently edited by a professional English editor.

Change in the text: See the text.

Comments 3. Many sentences are inappropriate in linguistic context. For example:

- Line 6 “...countries, like Italy, with a high income”

Reply: We apologize because probably the language is not appropriate. We found different incidences among counties in the world (see table 7 -Ferlay J, Soerjomataram I, Dikshit R, Eser S, Mathers C, Rebelo M, Parkin DM, Forman D, Bray F. Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. Int J Cancer. 2015 Mar 1;136(5):E359-86. doi: 10.1002/ijc.29210. Epub 2014 Oct 9. PMID: 25220842.)

Change in the text: especially in high income countries, like Italy.

- Line 36 “When it is possible, HT is favourite due to perioperative morbidity reduction; when TT is chosen, recurrence risk and persistence of the disease could be reduced.” - It conflicts with the ATA guideline mentioned in the previous paragraph

Reply: ATA guidelines do not consider multifocality as a risk factor, so the choice of most correct surgical procedure depends by other factors. According to patients, in some Italian Centre is preferred a more aggressive surgical treatment. According to our centre not all patients should undergo total thyroidectomy. (Dobrinja et al, 2021

Hemithyroidectomy versus total thyroidectomy in the intermediate-risk differentiated thyroid cancer: the Italian Societies of Endocrine Surgeons and Surgical Oncology Multicentric Study. *Updates in Surgery*, 73, 1909-1921.

Change in the text: none.

- Line 38 “The purpose of the study was to determine the most correct surgical management for patients with unilateral multifocal intermediate-risk DTC thyroid cancer” -correct is an inappropriate description, may be replace by preferable or other word)

Reply: The scope of this study should be to define what is the right surgical procedure for these patients. We don't want to declare our favourite surgical procedure.

Change in the text: none.

- Line 50 “92 patients (75 women and 17 men) were selected between January of 2016 and June of 2021. “ - “select” is inappropriate, enrolled may be better, or the author should mention how selection process; also, the 92 patients with intermediate risk were selected from how many DTCs should be mentioned in method section).

Reply: We apologize for the lack of clarity. We have made some changes.

Change in the text: 883 patients with thyroid disease were selected between January of 2016 and June of 2021. Of these 92 patients (75 women and 17 men) were enrolled according to inclusion criteria. Only patient with a diagnosis of intermediate risk DTC were recruited. We considered intermediate risk definition declared in ATA guidelines [9].

- There are many similar problems in this article, which require extensive revision by the authors.

Comment 4. There is no clear explanation on the first use of abbreviations in this article (e.g. DTC, HT, TT...), and some abbreviations are inappropriate (e.g. Totalization procedure (T)).

Reply: We apologize for the lack of clarity. We have made some changes.

Change in the text:

- Line 31- However, hemithyroidectomy (HT) should be performed for cancer <1cm with healthy contralateral lobe, meanwhile for cancer with diameter between 1-4cm, it could be indicated HT or Total Thyroidectomy (TT).
- Line 42- (Totalization –T)-
- Line 58 Totalization (T) is the surgical removal of remaining lobe after HT and it was performed in some cases.

Comment 5. As the result “we found a strong correlation in term of age, FNAC, cancer node involvement, angioinvasion and extrathyroidal extension”, however, these statements cannot directly verify the conclusion. For example:

- “Both Hemithyroidectomy and Total Thyroidectomy are correct procedures for the treatment of mDTC.”

- “Hemithyroidectomy could be sufficient in older patient without extrathyroidal extension, angioinvasion and N0. In other condition Total Thyroidectomy must be applied.”

Reply: According to our study TT and HT are suitable procedures per patients with multifocal DTC. Please explain in detail your perplexity.

Change in the text: none

6. Table should be remade, correct the typos, increase the description of abbreviations.

Reply: We apologize for the lack of clarity. We have made some changes in the layout and the text.

Changes: see file tablemod

7. I hope the authors can increase the readability of the article and consider the way of presentation from the standpoint of the readers.

Reply: Thanks for your help.

Change in the text: none

## Reviewer B

Curto et al examine 92 thyroid cancer pts (PTC and FTC) classified as ATA-intermediate risk in a retrospective study. They substratified based on multifocal vs unifocal disease and looked for correlations in predictive factors on determining whether to recommend hemi vs total thyroidectomy. They concluded that hemithyroidectomy was sufficient in older patients without extrathyroidal extension, angioinvasion, and N0 stage.

The paper looks at an interesting question given the ambiguity of treatment approaches in intermediate risk patients. The aim of this ambiguity in the ATA guidelines was to give clinicians latitude on how aggressive they wished treatment to be. However, it is helpful to ascertain the consequences of allowing hemithyroidectomy in this class of patient.

Comment 1. The limitations of this paper given the indolence of these cancers is the low number and the limited follow-up period.

Reply: Among the limitations we underlined problems related to small cohort. Further studies are needed to enhance these data.

Change in the text: none

Comment 2. The authors found an association between young age and multifocal

cancers – but this has not necessarily been confirmed in other, larger reports.

Reply: We found many conflicting data.

Change in the text: none

Comment 3. It is also difficult to know the true extent of multifocality when not all cases underwent total thyroidectomy. I would clarify this limitation in the discussion.

Reply: It is not correct. 5 patients of the mDTC group underwent hemithyroidectomy, 4 of these underwent totalization for reasons explained in the manuscript. The missing data, therefore, concern only one patient who refused surgery.

Change in the text: none

Comment 4. The authors only complete univariable analysis, when a multivariate analysis to collectively consider all covariates would be more useful. Would clarify this in the discussion.

Reply: the authors decided not to perform a multivariate analysis. The study should be expanded and therefore it was decided to wait for stronger data.

Change in the text: none

Comment 5. There are numerous grammatical errors in the manuscript.

Reply: We apologize for our error. The text has been currently edited by a professional English editor.

## Reviewer C

Comment 1: In this study the authors examined their experience with multifocal DTC and surgical extent. They conclude that multifocality is not an indication for completion/totalization given the risks of bilateral surgery. However, only 4 patients underwent totalization/completion, and 2 had cancer in the contralateral lobe. These findings do not seem to fit with one another and would require additional patients with follow up data.

As the authors discuss, there are a number of studies that previously have examined this subject with larger patient populations. Additionally, there is not information on follow up in this analysis. I am not convinced that there is enough added new information to warrant publication of this manuscript in this journal, and would also suggest revision for language/grammar if resubmission is considered.

Reply: The number of patients with intermediate-risk multifocal carcinomas is very low. Therefore, multicenter studies would be needed to have more robust data. The study we carried out refers to a single regional reference center for thyroid disease. The scope of our study would completely change by expanding the sample to other centers. Anyway we will expand the sample in the future but this is not the purpose of

this study.

Change in the text: Language corrections