Peer Review File

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Reviewer A

While the report is well-written, I do not believe that it adds significantly to the literature that is already available on the relationship between nodule size and malignancy risk for Bethesda III-V thyroid nodules. There are a plethora of studies which have investigated this exact question, many of which have sample sizes significantly larger than the current study. There are also multiple published meta-analyses which combine data from all of these studies to investigate the relationship between nodule size and malignancy risk. While I commend the authors for their treatment of thyroid malignancies, I do not think that the results of this retrospective review of 113 patients add significantly to what is already known about this topic.

Reply: Thank you for your thoughtful analysis of the current state of the literature. However, the relationship between nodule size and risk of malignancy in indeterminate thyroid nodules (ITNs) remains a topic of debate, with discordant results and conflicting conclusions. In addition, the extent to which nodule size may be used as the sole criteria for surgical intervention is controversial. Thus, our study aimed to investigate the impact of nodule size as a predictor of malignancy in ITNs. We believe that our study makes a significant contribution to the literature because there are currently no established criteria that can effectively differentiate between malignant and benign ITNs. Furthermore, the number of studies on this specific problem related to ITNs is limited. We also believe that the inclusion of a cohort of patients from our local community is notable as thyroid malignancies are becoming increasingly common here. Thus, these findings may align with or oppose other published data. This will encourage further research in the field, thereby leading to improvements in patient outcomes and treatment strategies. Nonetheless, we agree with you regarding the limitations in our sample size and retrospective study design, and these have been noted in our discussion section.

Reviewer B

I have though some remarks which should from my point of view be addressed prior to a possible publication in Gland Surgery.

Comment 1: In the highlight box, the last line looks truncated.
Reply 1: We apologize for the inconvenience of this error. This occurred when converting the Word file to PDF.
Changes in the text: In the last line of the "Highlight box," the omitted words "indeterminate thyroid nodules" have been highlighted in yellow.

Comment 2: In line 68, you cite over 60,000 thyroidectomies … each year "without relating the data to a source, so we do not learn in which country these procedures are performed.
Reply 2: We are sorry for this misunderstanding. These data are from the USA and were reported in 2016.

Changes in the text: We chose to remove this ambiguous section to enhance the coherence and clarity of the text. (see Page 5, line 68).

Comment 3: Line 158 describes the group of 100 patients < 55 years with percentages of 84,6 % and 90,5 % for nodules larger and smaller than 4 cm, respectively. This cannot be true. Please, correct these figures.
Reply 3: We appreciate your careful review of our data and apologize for this error.
Changes in the text: We have modified the corresponding text as follows: "In the group of patients aged < 55 years, a total of 33 patients (33%) presented with nodules measuring ≥ 4 cm, whereas 67 (67%) had nodules < 4 cm in size." (see Page 9, lines 153-154).

Comment 4: In lines 196 to 205 you discuss the invasive diagnostic features of FNA. Please, insert a short comment on the role of needle biopsy. This method can alternatively be performed and is currently under extensive international discussion.
Reply 4: We appreciate this suggestion which strengthens our discussion.
Changes in the text: We have modified the text as follows: "FNA is a useful method to assess TNs. It demonstrates high accuracy rates in detecting most benign and malignant nodules, especially when used in conjunction with US, leading to decreased sampling errors in large nodules (1,2). Notably, core-needle biopsy is an alternative method that is currently under extensive debate. Nevertheless, the optimal management strategy for nodules that are ≥ 4 cm remains unclear (2)." (see Pages 10-11, lines 192-195).

Comment 5: The morbidity of TL vs. TT reported in line 243 has to be referenced. I am sure you have either your own data published or you can cite a reference.
Reply 5: We agree that this data requires a reference and apologize for the omission.
Changes in the text: The reference has been added. (see Page 13, line 242).

Comment 6: The scope of therapeutic approaches is nowadays no longer limited to surgery and surveillance. The recently introduced thermoablative modalities represent minimal-invasive treatment options to patients with benign symptomatic TN. Indications for surgery in large TN are occasionally not only justified by ROM, but also because of symptomatic disease, which is not unusual in large TN. Again, here is a field where an ongoing international debate arises whether results of local ablative treatments can compete with those obtained by conventional surgery. This field should be at least shortly mentioned in the discussion.
Reply 6: We appreciate this instructive suggestion and agree that discussion regarding this field is warranted.
Changes in the text: We added the following data: "Currently, therapeutic approaches have expanded beyond surgery and surveillance. Radiofrequency ablation, a newly proposed minimally invasive technique, is currently a subject of ongoing international debate. It is performed under US guidance and considered a viable option for individuals with benign or low-risk TNs. Moreover, the technique is believed to decrease the nodule volume from 60% to 100% (24). Nonetheless, further research is required to elucidate the risks and advantages of this procedure compared with more conventional surgeries. (see Page 14, lines 259-264).

Reviewer C

I would personally reject the paper due to small sample size and findings that are contradict I've what was published by many other groups.

Reply: The relationship between nodule size and risk of malignancy in indeterminate thyroid nodules (ITNs) remains a topic of debate, with discordant results and conflicting conclusions. In addition, the extent to which nodule size may be used as the sole criteria for surgical intervention is controversial. Thus, our study aimed to investigate the impact of nodule size as a predictor of malignancy in ITNs. We believe that our study makes a significant contribution to the literature because there are currently no established criteria that can effectively differentiate between malignant and benign ITNs. Furthermore, the number of studies on this specific problem related to ITNs is limited. We also believe that the inclusion of a cohort of patients from our local community is notable as thyroid malignancies are becoming increasingly common here. Thus, these findings may align with or oppose other published data. This will encourage further research in the field, thereby leading to improvements in patient outcomes and treatment strategies. Nonetheless, we agree with you regarding the limitations in our sample size and retrospective study design, and these have been noted in our discussion section.