TRANSLATIONAL CANCER RESEARCH

Peer Review File

Article information: http://dx.doi.org/10.21037/tcr-19-2870

Reviewer A:

Comment 1. How long was the follow up period in this study? The patients were collected from January 2013 to December 2014 and why there wasn't more recent cases included in this research?
Reply 1. The follow up period is one year in our study (Page 7, line 143). This should be indicated in the part of method. We have deeply revised the patients' inclusion criteria and exclusion criteria including the period of follow-up (Page 7, line 137-153), and the figure 1 has been revised.
The period of patients' collection is incorrect in the original manuscript due to our carelessness. Actually, the patients were collected from January 2016 to December 2017, which has been revised in the manuscript (Page 6, line 131).

Comment 2. Does the data of the size of malignant thyroid nodules in Table 2 follow a normal distribution? For data not following normal distribution, results should be expressed as median and range.
Reply2. Thanks for your suggestion. We found the data of the size of malignant and benign nodules were skewed distribution by re-analysis. So, the nodules' size have been revised as the form of median and range (Table 2).

Comment 3. The description of Table 3 in the method part is hard to follow while reading. The result of Table 3 should be described from the top to bottom in the method part.
Reply 3. We have re-organized the part of results relating to Table 3 (Page 12, line 243-249).

Comment 4. Interpretation of the results should be added into the third paragraph of discussion part rather than just simply listing the outcome of this research.
Reply 4. Thank you for your suggestion. We added the interpretation of the results into the part of discussion (Page 13-14, line 285-301).

Comment 5. The length of abscissa and vertical axis should not be longer than 100.
Reply 5. This suggestion maybe right. However, the ROC curve that generated by MedCalc software (version 15.2.2) is the style like Figure 3. So the Figure 3 has not been revised.

Comment 6. As the author mentioned in Line 213, several sonographic features of a thyroid nodule are associated with an increased likelihood of malignancy. Analysis of

the relation between sonographic features and the likelihood of malignant nodules should be included.
Reply 6. In this study, we compared the differences in sonographic features between benign and malignancy, the results showed that solid, no spongiform, markedly hypoechoic, taller-than-wide morphology, lobulated/irregular margin, extra-thyroidal extension, micro-calcification, no halo, hypervascular or penetrating vessel and lymphadenopathy had higher percentages of malignancy, which could clarify this features were associated with the likelihood of malignant nodules on a side-note(Page 13, line 277-284).

Comment 7. The reason why there was no evaluation of the nodules with a size<10 mm should be present in the limitation part.
Reply 7. The nodules with a size >10 mm for FNA is recommended by most guidelines, including ATA guideline and TIRADS which were used in our study. So, there were no nodules with a size<10 mm evaluated in this study (Page 18, line 387-390)

Comment 8. Subgroup analysis of patients who went through pathological diagnosis by surgery should be include in this study to excavate the connection between sonographic features and the likelihood of malignant nodules.
Reply8. In this study, the thyroid nodules including TI-RADS 1, 2, 3, 4 and 5 were evaluated. However, the thyroid nodules with pathological results only TI-RADS 3, 4 and 5. Ensuring the integrity of nodule classification, we think that completely access the thyroid nodules of TI-RADS 1, 2, 3, 4 and 5 maybe feasibility. This maybe a limitation for our study. And this has been discussed in the part of limitations (Page 18, line 390-394).

Reviewer B:

Comment 1. The patients were collected from January 2013 to December 2014. Why were the patients not selected from a more recent time frame?
Reply 1. The period of patients' collection is incorrect in the manuscript due to our carelessness. Actually, the patients were collected from January 2016 to December 2017, which has been revised in the manuscript (Page 6, line 131).

Comment 2. In K-TIRADS, ACR-TIRADS, and EU-TIRADS, which is the general diagnostic form nowadays in China?
Reply 2. TIRDAS, a good assessing method for thyroid nodules, is widely used in China. However, different hospitals adopt different TIRADS (K-TIRADS, ACR-TIRADS, or EU-TIRADS) in China, which result in non-uniform for the thyroid nodule assessment. Based on this reality, we performed this study. Our study revealed that the K-TIRADS (AUC=0.827) maybe more workable in China. But, in

order to improve the efficiency of TIRADS, the TIRADS that is suitable for Chinese should be further studied for the researchers of China.

Comment 3. Figure 2 is not clear enough. Please provide clearer figures.
Reply 3. OK. Figure 2 has been replaced by a clearer one.

Comment 4. What progress has been made in the thyroid cancer diagnosis? Relevant content should be included in the introduction.
Reply 4. Thank you for your suggestion. We have added the relevant contents of thyroid cancer diagnosis progression into the part of introduction (Page4-5, line 77-99)

Comment 5. What are your suggestions for developing the diagnostic criteria for thyroid cancer in China? Relevant content should be included in the discussion.
Reply 5. Though large population in China, there is no uniform TIRADS that is used by all hospitals. Different hospitals adopt different TIRADS, such as K-TIRADS, ACR-TIRADS, and EU-TIRADS. In order to improve the diagnosing level of thyroid ultrasound, we performed this study. The results of our study revealed that K-TIRADS, ACR-TIRADS, and EU-TIRADS had values for thyroid nodules diagnosing. However, they cannot simultaneously achieve high sensitivity and high specificity. So, we think that more suitable for population of China should be established in the future. We have added this expectation in the part of conclusion (Page18, line396-403).