

Peer Review File

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Reviewer A

The study's subject are interesting, but I kindly give my opinion that some major revisions are needed. I express my comments about the manuscript below this paragraph.

1. Authors said that there was no statistic significance of clinicopathological characteristics among three groups, but there is no mention of p-value about the comparison of three groups in Table 1 of Figure 1. It is necessary to mention p-value if data analysis was conducted.

Since our study mainly focused on the differences between single FTC and synchronous FTC&PTC patients, which did not involved any single PTC patients at all, there were only two groups in our cohort and all the statistical analysis were performed between these two groups.

2. Single PTC group showed the largest tumor diameters and single FTC group showed the smallest one.

-> These sentences would be an error and need to be corrected.

These sentences have been corrected.

3. The difference between the number of synchronous group and the other two groups is too large. The synchronous groups is only 42 patients, so it is less statistically reliable. In this case, the additional analysis including the propensive score matching would be needed to reduce the difference in the characteristics of each group.

Due to the relatively low incidence of PTC and FTC patients, only 42 PTC and FTC patients have been collected in our center.

4. In the 42 cases of synchronous PTC and FTC, 6 patients went FNA preoperatively and 4 patients were diagnosed as PTC. In the 36 patients without preoperative FNA, 10 cases were considered as benign nodules through ultrasonic manifestation (TI-RADS level 3 or lower), 17 were suspicious for single malignant nodule (TI-RADS level 4a or higher), and 8 patients were suspicious for multiple malignant nodules.

-> Additional explanation is needed for this part. If only 6 of the 42 people in the group performed preoperative FNAB, why did the remaining 36 people have the surgery? In normal cases, surgery is performed when malignancy is confirmed or suspected through FNAB. Surgery is not performed simply because of suspected malignancy on ultrasound. In addition, the reason for the surgery of a patient who was considered benign on ultrasound needs to be further explained.

The accuracy and specificity of FNA are not absolute, especially for patients with follicular tumors, and there is currently no particularly effective preoperative identification of benign and malignant malignancy. Therefore, not all patients in our hospital must undergo FNA diagnosis after surgery, especially for follicular tumors.

5. Authors said that the synchronous group need to receive more complete treatment than FTC groups, but there is too little evidence. In the result, the authors only mentioned the DFS (disease free survival) for the evidence of the synchronous group's aggressiveness even though the univariate analysis didn't show any significance. More evidence would be needed to argue that the synchronous group is mor aggressive than FTC group.

It has been reformulated.

6. There is no analysis about the treatment modality of PTC & FTC patients. The comparison of treatment modality between synchronous groups & PTC, FTC groups would be essential for the author's logic. Without this, the DFS comparison between groups would be less meaningful because there is no evidence that no bias is existed about the treatment modality between groups. More information & analysis about the treatment modality is needed.

At present, the treatment of single papillary thyroid cancer or papillary carcinoma combined with follicular carcinoma still includes gland resection, TSH suppression, and radioactive iodine therapy. Therefore, the treatment is almost the same.

Reviewer B

1. A **highlight box** is needed to highly summarize the key findings/recommendations, innovation, and potential implications of the study. Please provide a highlight box for your manuscript.

- No reference should be cited in the highlight box. The box should be concise with **no more than 250 words**.
- Here is the template:

Key findings

- Report here about key findings of the study.

What is known and what is new?

- Report here about what is known.
- Report here about what does this manuscript adds.

What is the implication, and what should change now?

- Report here about implications and actions needed.

We've modified it

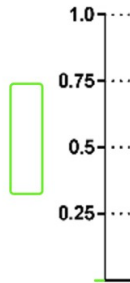
2. Please recheck the full name of "qPCR" in the text.

Sanger sequencing, real-time polymerase reaction (qPCR).

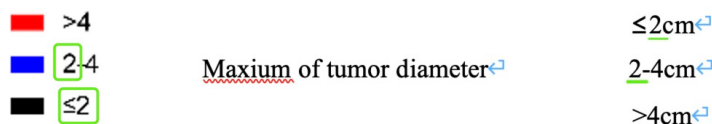
We've modified it

3. Figures and Tables

- **All abbreviations** in figures/tables and legends should be explained. “PTC” “FTC” “ETE” “LNM” “AJCC” in Figure 1, and “PTC” “FTC” “AJCC” in Table 1 for example. Please check all abbreviations and provide the full names in the corresponding figure legend.
- Please add unit for **Age/Tumor size** in Figure 1.
- Please add description for the y-axes in Figure 1 and supplement the scale bar 0.0.



- Please check which group was 2 included in Figure 1 and Table 1.



- Please indicate the meaning of “*” “**” “***” “ns” in Figure 1 legend.
- Please indicate the meaning of “***” “ns” in Figure 2 legend.
- Please indicate the meaning of +, - in Figure 1 legend.
- Please provide Figure 3 in higher resolution.
- Each figure must be saved and submitted as a separate file. The preferred format for figures is **JPG/TIFF** format

- Please add unit for **Age** in Table 1 and Table 5.

- Table 1: there is a spelling error.

right lobe/0.3cm can not be assessed
 bilateral focus/1cm can not be assessed

- Please indicate the meaning of +, - in Table 1-3, 5 footnote.
- Please add a table head for the first and second column of Table 4.

Table 4 NGS results of synchronous patients				
			PTC	FTC
	BRAF	BRAF Val600Glu	17	0
		BRAF Lys601Glu	0	2

- For the references cited in Table 5, please regular round brackets with a space before. For example, “Patient 1 (9)”.

patient	age/gender	maximum of size)	maximum of size)
patient 1[9]	31/female	left lobe/1.3cm	left lobe/5cm
patient 2[9]	61/male	right lobe/6cm	right lobe/0.3cm

- Please recheck the data in Table 1.

Regional lymph node	+↵	9(3.7%)↵	16(35.7%)↵
metastasis↵	-↵	235(96.3%)↵	26(64.3%)↵

- Please recheck the highlight content in the following sentences, since they are inconsistent with those in Table 1.
 - “The median ages of the synchronous group, single PTC group, and single FTC group were 47, 46, and 44, respectively”
 - “Among the 15 patients with regional lymph node metastasis in the synchronous group, 10 patients were revealed to be PTC metastasis whereas 5 patients were undefined (not listed in table). There was no statistical significance among the 3 groups.”
- It is suggested to recheck the data in the following sentence.
 - “Targeted NGS detected 77 mutation and 1 fusion genes in 32 out of 35 patients (Fig. 3 and Table 4)”
- Only 2 patients are list with MTC in Table 5.
 - “More rarely, 3 patients had a simultaneous medullary thyroid carcinoma (MTC), and 1 patient had a simultaneous anaplastic thyroid carcinoma (ATC) and died 2 months after surgery due to widespread distant metastasis.”
- In all tables, please uppercase the first letter of each column.

We've modified it