

Peer Review File

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Reviewer A

Comment 1: I congratulate the authors for this very well-written manuscript. It is an excellent topic with immediate clinical implications.

Reply 1: Thank you for reviewing our manuscript.

Reviewer B

Comment 1: The study focusing on the cutoff value of FNA-Tg is interesting. However, I think the design of the study could be improved.

FNA cytology is the most important diagnostic method for lymph node metastasis in papillary thyroid cancer. When malignancy is suspected by imaging findings such as US, but cytology is not positive, FNA-Tg can be a complementary diagnostic method.

Therefore, it does not make much sense to look at the relevance of the results of cytology in setting the cutoff for FNA-Tg. It is better to set the cutoff so that FNA-Tg can be used to diagnose when the cytology is negative. A comparison of FNA-Tg in normal and metastatic lymph nodes could also be considered. It is also advisable to design the study taking into account the novelty and differences from previous reports (refs. 24, 25).

Reply 1: I agree with your opinion, which the cutoff of FNA-Tg can be used to diagnose when the cytology is negative. In table 5, we tried to evaluate the optimal cutoff value of FNA-Tg. We confirmed that the proportion of patients with negative cytology results was significantly higher in the FNA-Tg<20ng/mL. In the case of negative cytology, FNA-Tg values were also low. In this study, we tried to find new method to increase the diagnosis rate of LN metastasis. Not only FNA-Tg but also Tg ratio will increase the diagnosis rate. The concept of a comparison of FNA-Tg in normal and metastatic LNs is a very good idea. We will perform further study.

Reviewer C

The manuscript indicated that measurement of FNA-Tg level and Tg ratio were useful before thyroid surgery to detect lymph node metastasis. This study was well established, and the result of this study is useful for clinical practice in thyroid cancer treatment.

Comment 1: I have one question. Did the term of tumor size mean target lymph node size? Since this study described lymph node metastasis, I thought so. However, the tumor size often means the size of primary thyroid tumor. The term should be changed to avoid confusion.

Reply 1: I inserted "Tumor size means the size of primary thyroid cancer" as a footnote in all Tables.

Comment 2: There might be some mistake of words of inequality. For example, in line 4 of page 9, the sentence described "Seventy patients (41.4%) were >45". However, authors should use " \geq " in this sentence. Similarly, in line 13 of page 13, the sentence described "level >20 ng/mL".

Please check carefully these words of inequality.

Reply 2: I corrected several mistakes. Thank you for checking the mistakes.

Reviewer D

The authors performed a retrospective review of 169 patients who underwent modified radical neck dissection (mRND) for PTC. They included 149 newly diagnosed PTC patients that underwent TT with mRND and 20 patients' that underwent mRND for recurrent PTC. The authors examined how serum Tg levels, serum TgAb levels, FNA-Tg, and FNA-Tg level to Serum Tg level ratio (FNA-Tg/S-Tg ratio) correlated to FNA cytology. They found serum Tg and TgAb did not differ between FNA positive and negative results, but that FNA-Tg was higher in the FNA positive group. They found a FNA-Tg levels >20 and FNA-Tg/S-Tg ratio > 3 to be associated with the highest sensitivity and accuracy.

Comment 1: Discussion, page 13, line 3-6: This was not included in the Methods section. Can intraoperative decision making be further outlined in the Methods section to clarify?

Reply 1: In method section, page 6, line 6-9, this content is included.

Comment 2: What was the false negative and false positive rate of FNA-cytology?

Reply 2: False negative; 0.25. In this study, since we included all cancer patients, we cannot calculate the false positive.

Comment 3: How did FNA compare to the frozen section mentioned in Discussion, page 13, lines 3-6?

Reply 3: We performed needle localization on suspicious LNs before the frozen section.

Comment 4: Why was frozen section used to make the decision for whether or not to proceed with mRND?

Reply 4: Although FNA was negative results, LN metastasis on preoperative US was very suspicious.

Comment 5: How did FNA cytology results compare to surgical pathology?

Reply 5: We performed needle localization on suspicious LNs before the frozen section. So we could accurately compare FNA cytology and surgical pathology.

Comment 6: Why was surgical pathology not considered the standard for ROC curve analysis.

Reply 6: 169 patients were included in this study. All patients were diagnosed as lateral LN metastasis on surgical pathology. ROC curve analysis is a method to judge the usefulness of the test and cutoff value. Since, surgical pathology were all positive, we could not use the ROC curve analysis in this study.