



# Response to: Letter to the Editor Regarding “Validation of CT-Based Risk Stratification System for Lymph Node Metastasis in Patients With Thyroid Cancer”

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We would like to thank Drs. Lim and Sim for their thoughtful letter [1] expressing interest in our recent publication, “Validation of CT-Based Risk Stratification System for Lymph Node Metastasis in Patients with Thyroid Cancer” [2]. We appreciate the opportunity to address your questions, particularly regarding the optimization of the biopsy criteria for lymph nodes (LNs) in thyroid cancer.

Regarding fine-needle aspiration (FNA) for suspicious or indeterminate LNs, our clinical practice aligns with our findings. We perform FNA on all LNs classified as suspicious or indeterminate in the preoperative setting, regardless of their size, if they affect the surgical extent. The presence of lateral neck LN metastasis in thyroid cancer significantly

affects both the surgical extent and patient prognosis. Moreover, with the increasing implementation of active surveillance, the significance of detecting lateral neck LN metastases has been increasingly emphasized. While we acknowledge the biopsy criteria recommended by the Korean Society of Thyroid Radiology [3], our priority is to detect metastatic LNs to determine the appropriate surgical extent or select candidates for active surveillance, even in LNs smaller than those defined by the conventional criteria. However, regarding LNs with calcification on computed tomography (CT), we acknowledge that benign conditions can lead to calcification, as highlighted in your letter. Although our study demonstrated a 100% malignancy risk for LN with calcification, it is essential to recognize the inherent limitations of overestimating the malignancy risk of LNs in retrospective studies. In clinical practice, we consider additional factors such as patient history, distribution of LNs with calcifications, and T staging of thyroid cancer to guide the decision for FNA of LN with calcification on CT.

Regarding indeterminate LNs, as Dr. Lim mentioned, several studies highlight an inverse relationship between malignancy risk and LN size [4-6]. This is likely due to the small size of metastatic foci in indeterminate LNs, which makes it challenging to detect suspicious features on imaging. If the LN size increases due to the presence of tumor cells, suspicious features become more discernible on imaging. Therefore, when a large LN lacks suspicious features on imaging, the enlargement is more likely to be related to reactive changes than to metastasis. The inverse relationship between the malignancy risk and size of indeterminate LNs suggests the need to reassess the biopsy size criteria for indeterminate LNs.

Previous studies have noted that ultrasound-detected indeterminate LNs can be reclassified as benign or suspicious on CT in 25.4% of cases [7]. Thus, when ultrasound indicates an indeterminate LN, performing a CT scan could assist in the classification into a conclusive category. In addition, recent studies have suggested that primary tumor characteristics such as multiplicity, extrathyroidal extension, and nonparallel orientation may serve as risk factors for metastasis in indeterminate LNs. Nevertheless, determining whether to proceed with biopsy of indeterminate LNs poses a complex challenge. Given the low malignancy risk associated with indeterminate LNs,

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performing biopsies of all indeterminate LNs may lead to a high rate of unnecessary biopsies. However, there is a risk of overlooking LN metastases when selectively biopsying indeterminate LNs. Therefore, meticulous risk-benefit evaluation is critical in determining the necessity of biopsies for indeterminate LNs, prompting the need for further studies in this area.

### Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

### Author Contributions

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