



Factors to Consider When Interpreting the Diagnostic Performance of Fine-Needle Aspiration and Core-Needle Biopsy in a Specific Study Population

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Dear Editor,

We read with great interest the article by Shin, et al.¹ comparing the diagnostic performance of fine-needle aspiration (FNA) and core needle biopsy (CNB). This head-to-head comparison in a specific patient population revealed that CNB is not superior to FNA for diagnosing thyroid nodules, which is inconsistent with the result reported by a previous study involving similar head-to-head comparisons in the general patient population.^{2,3}

Several factors should be considered when interpreting the results reported by Shin, et al.¹ First, the study population included a specific group of referred patients who underwent both FNA and CNB at other clinics and underwent surgery (the gold standard for diagnosing thyroid nodules in the study) at the authors' institution. The disease spectrum in the specific study population may not be representative of patients in general clinical practice, as the prevalence of malignant tumors was very high (87.2%), compared to the real-world prevalence of malignant tumors in patients undergoing biopsy for thyroid nodules in clinical practice (approximately 10-20%). When interpreting the diagnostic accuracy of a test in a study population and evaluating the applicability of the study results, disease prevalence in the study population should be considered.⁴ The positive and negative predictive values of a test directly depend on disease prevalence, and therefore, they are not applicable in situations with markedly different disease

prevalences. Although the sensitivity and specificity of a test are commonly believed to not vary with disease prevalence, they may do so due to differences in the patient spectrum and other potential mechanisms.⁴ In a previous study, the specificity of a test tended to be lower with higher disease prevalence, although its sensitivity was less affected by disease prevalence.⁴ When surgery is used as the gold standard for diagnosing thyroid nodules, many true negative benign nodules without surgical diagnosis are inevitably excluded from the study population, and the specificity is lowered due to partial verification bias.⁵ In the study by Shin, et al.,¹ the malignancy rate of benign CNB results was extraordinarily high [CNB, 87.5% (7/8); FNA, 33.3% (6/18)], which is markedly different from the true malignancy rate (<3%) in nodules with benign FNA⁶ and CNB⁷ results in the general patient population. Therefore, the estimated specificities in this specific study population may not be generalizable to real-world clinical practice.

Second, the pathologic classification of CNB diagnostic results into six diagnostic categories highly depends on the experience of a pathologist in reading CNB samples according to the pathological diagnostic criteria for CNB. In the study by Shin, et al.,¹ the CNB pathologic reports were categorized into six categories based on the Bethesda System by a radiologist, and therefore, it is uncertain whether CNB diagnostic results, except the definitively benign or malignant results, were accurately categorized according to the pathological diagnostic criteria of CNB.

Third, apart from the limitation of the specific study population, there is a concern that the result interpretation was biased. Previous studies involving similar head-to-head comparisons have consistently shown that compared to FNA, CNB has a higher sensitivity and similar specificity for diagnosing thyroid malignancy in the general patient population with first-line or second-line CNB.^{3,8,9} In the study by Shin, et al.,¹ CNB showed a significantly higher sensitivity with criteria 3 (criteria for therapeutic and diagnostic surgery) and criteria 5

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(criteria for therapeutic surgery) and a marginally higher sensitivity with criteria 4 for malignancy than FNA in the entire study population. Further, CNB showed a higher sensitivity than FNA with criteria 5 in the subgroup patients with nodules ≥ 1 cm. This conflicts with the conclusion of the study by Shin et al., which suggests that CNB is not superior to FNA for diagnosing thyroid nodules. Therefore, these factors should be considered in the interpretation of the study results.

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