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Comparison of Core Needle Biopsy and Repeat Fine-Needle Aspiration in Avoiding Diagnostic Surgery for Thyroid Nodules Initially Diagnosed as Atypia/Follicular Lesion of Undetermined Significance

Leehi Joo[1], Dong Gyu Na[2, 3], Ji-hoon Kim[4], Hyobin Seo[3]

[1]Department of Radiology, Korea University Guro Hospital, Seoul, Korea; [2]Department of Radiology, GangNeung Asan Hospital, University of Ulsan College of Medicine, Gangneung Korea; [3]Department of Radiology, Human Medical Imaging and Intervention Center, Seoul, Korea; [4]Department of Radiology, Seoul National University College of Medicine, Seoul, Korea

Objective: To compare core needle biopsy (CNB) and repeat fine-needle aspiration (rFNA) to reduce the rate of diagnostic surgery and prevent unnecessary surgery in nodules initially diagnosed as atypia/follicular lesions of undetermined significance (AUS/FLUS).

Materials and Methods: This study included 231 consecutive patients (150 female and 81 male; mean age ± standard deviation, 51.9 ± 11.7 years) with 235 thyroid nodules (≥ 1 cm) initially diagnosed as AUS/FLUS, who later underwent both rFNA and CNB. The nodules that required diagnostic surgery after the biopsy were defined using three different scenarios according to the rFNA and CNB results: criterion 1, surgery for low-risk indeterminate (categories I and III); criterion 2, surgery for high-risk indeterminate (categories IV and V); and criterion 3, surgery for all indeterminate nodules (categories I, III, IV, and V). We compared the expected rates of diagnostic surgery between CNB and rFNA in all 235 nodules using the three surgical criteria. In addition, the expected rates of unnecessary surgery (i.e., surgery for benign pathology) were compared in a subgroup of 182 nodules with available final diagnoses.

Results: CNB showed significantly lower rates of nondiagnostic, AUS/FLUS, and suspicious for malignancy diagnoses ($p \leq 0.016$) and higher rates of follicular neoplasm or suspicious for a follicular neoplasm ($p < 0.001$) and malignant diagnoses ($p = 0.031$). CNB showed a significantly lower expected rate of diagnostic surgery than rFNA for criterion 1 (29.8% vs. 48.1%, $p < 0.001$) and criterion 3 (46.4% vs. 55.3%, $p = 0.029$), and a significantly higher rate for criterion 2 (16.6% vs. 7.2%, $p = 0.001$). CNB showed a significantly lower expected rate of unnecessary surgery than rFNA for criterion 1 (18.7% vs. 29.7%, $p = 0.024$).

Conclusion: CNB was superior to rFNA in reducing the rates of potential diagnostic surgery and unnecessary surgery for nodules initially diagnosed as AUS/FLUS in a scenario where nodules with low-risk indeterminate results (categories I and III) would undergo surgery.

Keywords: *Thyroid nodule; Biopsy; Fine-needle aspiration; Surgery; Ultrasonography*

INTRODUCTION

Ultrasonography (US)-guided fine-needle aspiration (FNA) is the standard primary procedure for pathologic examination of thyroid nodules [1]. However, FNA has limitations due to a high rate of inconclusive results, including nondiagnostic results (12.9%) and atypia/follicular lesions of undetermined significance (AUS/FLUS)

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Corresponding author: Dong Gyu Na, MD, PhD, Department of Radiology, GangNeung Asan Hospital, University of Ulsan College of Medicine, 38 Bangdong-gil, Sacheon-myeon, Gangneung 25440, Korea.
• E-mail: nndgna@gmail.com

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(9.6%) [2]. The rate of AUS/FLUS diagnosed by FNA varies from 3.0% to 20.5% in different institutions [3-10], and the interobserver agreement regarding the diagnosis of AUS/FLUS among cytopathologists is low [11]. The nodules diagnosed as AUS/FLUS are associated with varying risks of malignancy from 6% to 30% [12]. The clinical management of these nodules is controversial, and unnecessary diagnostic surgery may be inevitable in some cases.

The recommendations for the management of AUS/FLUS nodules differ somewhat between the various clinical guidelines, and include surveillance, repeat FNA (rFNA), molecular tests, and diagnostic surgery [12-16]. All guidelines recommend rFNA as a management method for AUS/FLUS nodules; however, the role of rFNA in cases initially diagnosed as AUS/FLUS might be controversial. Although rFNA might decrease the rate of diagnostic surgery in cases diagnosed as benign (25.1%–61.6%) [9,17-24], there are concerns about the considerably high rate of repeatedly inconclusive results, such as nondiagnostic (1.0%–45.5%) and AUS/FLUS (19.8%–44.3%) [9,17-25], which might lead to diagnostic surgery for these nodules.

US-guided core needle biopsy (CNB) is gaining wider acceptance as an alternative to FNA for thyroid nodules. In previous studies comparing rFNA and CNB for nodules initially diagnosed as AUS/FLUS, CNB consistently showed a lower rate of inconclusive results and better diagnostic performance [18,22,25-28]. Based on these results, CNB might be superior to rFNA in reducing the rate of diagnostic surgery. However, its role in reducing the potential rate of diagnostic surgery and unnecessary surgery has not been adequately investigated, and a recent study [29] reported that CNB for AUS/FLUS nodules did not reduce the rate of diagnostic surgery compared to rFNA. Therefore, the purpose of our study was to compare CNB and rFNA in reducing the rate of potential diagnostic surgery and preventing unnecessary surgery in nodules initially diagnosed as AUS/FLUS.

MATERIALS AND METHODS

This retrospective study included consecutive patient data from two institutions. The Institutional Review Board of each institution approved the study, and the requirement for informed consent for this study was waived (IRB No. 2010-028-1162; Seoul National University Hospital, IRB No. HI2020-01; Human Medical Imaging and Intervention Center).

Study Population

Between January 2010 and December 2014, a total of 798 thyroid nodules (10.4%) were initially diagnosed as AUS/FLUS out of consecutive FNA procedures performed for 7657 thyroid nodules in two institutions. Of the 798 thyroid nodules, 297 nodules less than 1 cm and 266 nodules with no follow-up biopsy or with either rFNA or CNB results alone were excluded. Finally, 231 patients (150 female and 81 male; mean age ± standard deviation, 51.9 ± 11.7 years; range, 19–78 years) with 235 nodules were enrolled for this study (Fig. 1). The inclusion criteria were as follows: 1) nodules equal to or larger than 10 mm and 2) nodules for which both rFNA and CNB were performed after the initial diagnosis of AUS/FLUS by a previous FNA. Simultaneous rFNA and CNB were performed for 208 (88.5%) nodules, and rFNA or CNB was performed at specific time intervals (median, 12 months; interquartile range [IQR], 6–24 months) for 27 (11.5%) nodules. Second or more rFNAs and CNBs were performed on 29 nodules and 26 nodules, respectively.

The final diagnoses were obtained for 182 nodules, of which 29 (15.9%) were diagnosed as malignant and 153 as benign (84.1%). All malignant nodules were histopathologically confirmed after surgical resection. The final diagnosis of a benign nodule was based on surgery, at least two benign results on CNB or rFNA, or one benign result on rFNA or CNB. Among nodules with one benign result on rFNA or CNB, nodules with discordant results (suspicious for neoplasm or malignancy) on follow-up FNA or CNB or with increased size on US follow-up were excluded from the final diagnosis of benign nodules. Of the 235 nodules, the final diagnosis confirmed by surgical or biopsy results could not be obtained for 53 nodules (49 nodules, including AUS/FLUS [n = 27], follicular neoplasm or suspicious for follicular neoplasm [FN/SFN] [n = 20], suspicious for malignancy [n = 2], three nodules with one benign result and increase in size at follow-up, and one nodule with one benign result and suspicious for malignancy at follow-up FNA) (Fig. 1).

US-Guided FNA and CNB Techniques

All procedures were performed by two radiologists with 15 and 3 years of experience in FNA and 3 and 1 years in CNB using high-resolution color Doppler US with a 5–12 MHz linear transducer (iU22, Philips Healthcare; AplioXG, Toshiba). US-guided FNA using a freehand method was performed using capillary and aspiration

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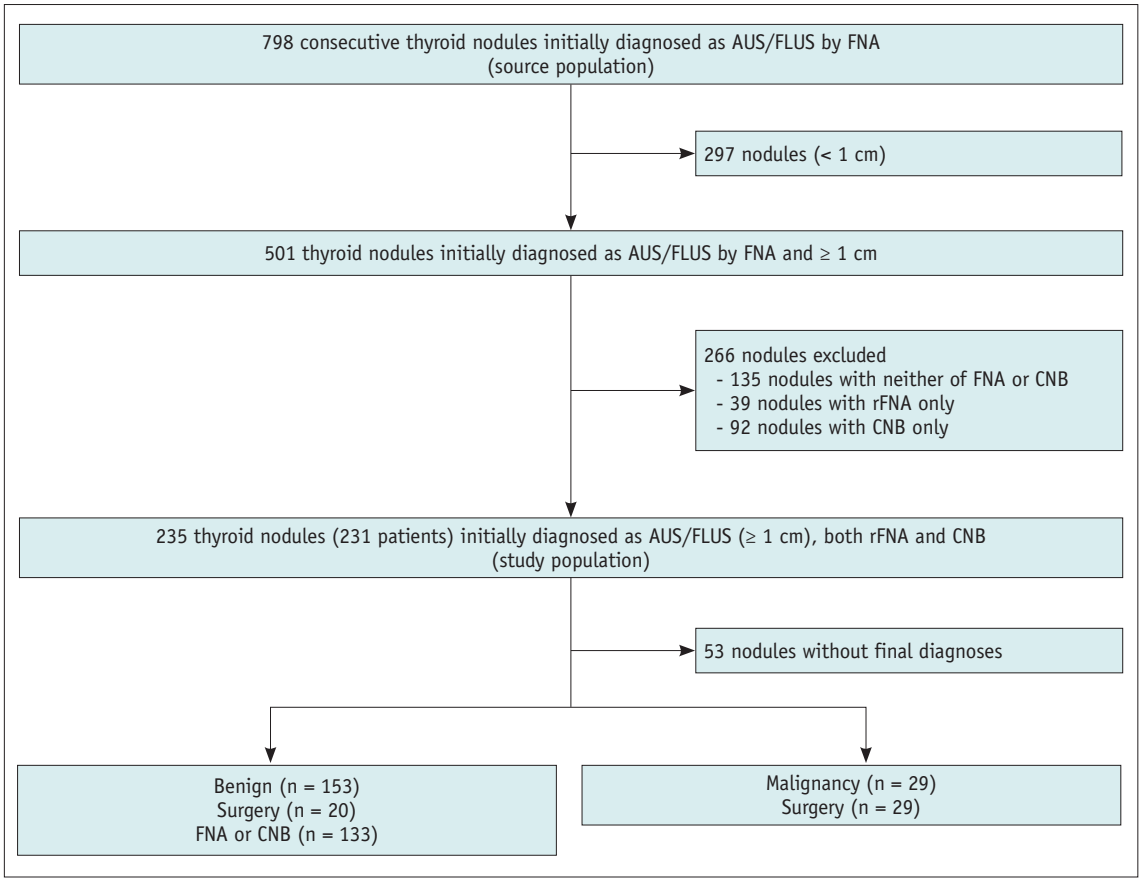

Fig. 1. Flow diagram of patient enrollment. AUS/FLUS = atypia/follicular lesion of undetermined significance, CNB = core needle biopsy, FNA = fine-needle aspiration, rFNA = repeat FNA

techniques with 23-or 25-gauge needles, and at least two samples were obtained from each nodule. Direct smear or SurePath™ liquid-based cytology was used to establish a cytopathologic diagnosis of the FNA sample. US-guided CNB procedures were performed using a disposable 18-gauge, single- or double-action spring-activated needle (approximately 1 or 2 cm excursion; TSK Acecut or Stericut; Create Medic) as described previously [18]. For all CNB procedures, 1% lidocaine was administered as local anesthesia. The notch of the CNB needle was positioned to harvest a small portion of the normal parenchyma (about 2–3 mm in length) at the nodule margin of a suspected follicular lesion, and strict vessel mapping along the approach route was performed using color Doppler US during the procedure to avoid vascular injury. The number of CNB samples was one or two in most cases, and two samples were routinely obtained from nodules with large sizes and heterogeneous components to avoid sampling errors. A modified technique of introducing a pre-fired stylet needle into the neck was allowed for the CNB procedure using a double-action CNB needle. When simultaneous FNA and CNB were performed, CNB was performed after FNA in most cases. The biopsy site was immediately compressed after withdrawal of the biopsy needle, and the patients were under observation with manual self-compression of the biopsy site for 20–30 minutes after the procedure.

Cytology and Histology Diagnoses

The cytology results from rFNA were interpreted according to the six categories of the Bethesda System for Reporting Thyroid Cytopathology (TBSRTC): nondiagnostic (I), benign (II), AUS/FLUS (III), FN/SFN (IV), suspicious for malignancy (V), and malignant (VI) [12]. The standardization of CNB diagnostic criteria for thyroid nodules had not been established at the time of the study, and the histological results of CNB were classified into six categories based on the Bethesda System by pathologists [18]. No molecular or immunohistochemical study results were used for CNB diagnosis.

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Data Analysis

Diagnostic surgery was defined as surgery for nodules diagnosed as AUS/FLUS by a previous FNA in which definite benign or malignant diagnosis was not obtained by rFNA or CNB. The nodules that underwent diagnostic surgery according to the rFNA and CNB results were determined using three different scenarios: criterion 1, surgery for low-risk indeterminate (categories I and III); criterion 2, surgery for high-risk indeterminate (categories IV and V); and criterion 3, surgery for all indeterminate nodules (categories I, III, IV, and V). We compared the expected rates of diagnostic surgery for the three criteria based on the rFNA and CNB results. We also compared the expected rate of unnecessary surgery for nodules with the final diagnoses. Unnecessary surgery was defined as surgery for nodules diagnosed as benign by diagnostic surgery.

Statistical Analysis

Continuous variables are presented as median (IQR) or mean ± standard deviation, according to the nonparametric or parametric distribution, respectively. Categorical variables are presented as frequencies and percentages. McNemar's test was used to compare the diagnostic results of rFNA and CNB according to the categories based on TBSRTC. McNemar's test was also used to compare the rates of potential diagnostic surgery and unnecessary surgery for benign nodules according to criteria 1 to 3 between the rFNA and CNB outcomes. Statistical analysis was performed using the SPSS software package (version 24.0 for Windows; IBM Corp.), and a p value < 0.05 was considered statistically significant.

RESULTS

Demographic Data

The size (maximal diameter) of the thyroid nodules ranged from 10 to 67 mm (median, 14 mm [IQR 11–19 mm]). The final diagnoses of the 29 malignant nodules were as follows: 16 conventional papillary thyroid carcinomas (55.2%), 7 follicular variants of papillary thyroid carcinoma (24.1%), 5 minimally invasive follicular carcinomas (17.2%), and 1 widely invasive follicular carcinoma (3.4%). The final diagnoses of 153 benign nodules were based on the following procedures: surgery (n = 20), at least two benign results on rFNA or CNB (n = 80), and one benign rFNA or CNB result (n = 53). In the 53 nodules with one benign rFNA or CNB result, the nodule size decreased (n = 14) or was stable (n = 31) on US follow-up > 12 months later (median, 36 months [IQR 22–48 months]), while follow-up US was not available for 8 nodules. The final diagnoses of surgically proven benign nodules were nodular hyperplasia (n = 11; 55%), follicular adenoma (n = 8; 40%), and Hurthle-cell adenoma (n = 1; 5%). The final diagnoses of 49 nodules were made by surgery in 48 patients, and the two follicular adenomas in one patient were diagnosed by histopathologic correlation of the surgical specimen.

There were no major complications, such as serious hemorrhage, in any of the patients, and none required hospital admission or intervention. Six patients (2.6%) developed perithyroidal hemorrhage (n = 2), intrathyroidal hemorrhage (n = 3), or both perithyroidal and intrathyroidal hemorrhage (n = 1) after CNB. The hematoma and parenchymal edema resolved after compression for approximately 1 hour.

Comparison of Repeat FNA and CNB Diagnosis in Nodules Diagnosed as AUS/FLUS

Table 1 shows the comparison of diagnostic results between rFNA and CNB in nodules initially diagnosed as AUS/FLUS. CNB showed significantly fewer nondiagnostic results than rFNA (0.4% and 7.2%, p < 0.001). The rates of diagnosis of AUS/FLUS and suspicious for malignancy on CNB were significantly lower than those on rFNA (p = 0.009 and 0.016, respectively). CNB showed significantly higher rates of FN/SFN and malignant diagnoses than rFNA (p < 0.001 and p = 0.031, respectively), while there was no significant difference in the rate of benign diagnoses between rFNA and CNB (p = 0.115) (Table 1).

Table 1. Comparison of the Results of rFNA and CNB in Nodules Initially Diagnosed as AUS/FLUS in All Study Nodules

Biopsy Results (Category)*	rFNA (n = 235)	CNB (n = 235)	*P*
Nondiagnostic (I)	17 (7.2)	1 (0.4)	< 0.001
Benign (II)	100 (42.6)	115 (48.9)	0.115
AUS/FLUS (III)	96 (40.9)	69 (29.4)	0.009
FN/SFN (IV)	8 (3.4)	37 (15.7)	< 0.001
Suspicious for malignancy (V)	9 (3.8)	2 (0.9)	0.016
Malignant (VI)	5 (2.1)	11(4.7)	0.031

Data are number of nodules with percentage in parentheses.
*Diagnoses according to the 6 categories of The Bethesda System for Reporting Thyroid Cytopathology. AUS/FLUS = atypia/follicular lesions of undetermined significance, CNB = compare core needle biopsy, FN/SFN = follicular neoplasm or suspicious for follicular neoplasm, rFNA = repeat fine-needle aspiration

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Comparison of the Rates of Potential Diagnostic Surgery between Repeat FNA and CNB

The expected rate of potential diagnostic surgery according to the three criteria showed significant differences between rFNA and CNB (Table 2). Based on criterion 1, the rate of diagnostic surgery was significantly lower based on the CNB results than with the rFNA results (29.8% and 48.1%, respectively, $p < 0.001$). Based on criterion 2, the rate of diagnostic surgery was significantly higher based on CNB results than that based on the rFNA results (16.6% and 7.2%, respectively, $p = 0.001$). For all the nodules with indeterminate results (criterion 3), the rate of diagnostic surgery was significantly lower based on the CNB results than that based on the rFNA results (46.4% and 55.3%, respectively, $p = 0.029$).

Final Diagnosis of Repeat FNA and CNB for Nodules Initially Diagnosed as AUS/FLUS

The rFNA and CNB results in 182 nodules and the final diagnoses are listed in Table 3. Table 3 demonstrates the difference in the percentage of malignant tumors diagnosed by rFNA or CNB. The majority (58.6%) of malignant tumors were found in nodules diagnosed as AUS/FLUS (34.5%) and suspicious for malignancy on rFNA (24.1%). A majority (72.4%) of the malignant tumors were found in nodules diagnosed as FN/SFN (34.5%) and malignant (37.9%) on CNB, which was significantly higher than the rate of malignant tumors (27.5%) found in nodules diagnosed as FN/SFN (10.3%) and malignant (17.2%) on rFNA ($p < 0.001$). The malignancy rate of low-risk indeterminate nodules (criterion 1) was significantly lower than that of high-risk indeterminate nodules (criterion 2) with rFNA (18.2% and 83.3%, $p < 0.001$) and with the CNB (15.0% and 57.9%, $p = 0.001$).

Comparison of the Rate of Potential Unnecessary Surgery for Benign Nodules between Repeat FNA and CNB

A significant difference in the expected rate of potential unnecessary surgery for benign nodules between rFNA and CNB was observed only for criterion 1 (low-risk indeterminate results) (Table 4). The rate of unnecessary surgery was significantly lower based on the CNB diagnosis compared

Table 2. Comparison of the Expected Rates of Diagnostic Surgery Based on the Results of rFNA and CNB in All Study Nodules

Criteria for Diagnostic Surgery	Expected Surgery Rate			*P*
	rFNA (n = 235)	CNB (n = 235)	Difference between rFNA and CNB	
Criterion 1 (categories I and III)	113 (48.1)	70 (29.8)	43 (18.3)	< 0.001
Criterion 2 (categories IV and V)	17 (7.2)	39 (16.6)	22 (9.4)	0.001
Criterion 3 (categories I, III, IV, and V)	130 (55.3)	109 (46.4)	21 (8.9)	0.029

Data are number of nodules with percentage in parentheses. Criterion 1, low-risk indeterminate results; Criterion 2, high-risk indeterminate results; and Criterion 3, all indeterminate results. Category I, nondiagnostic; Category III, atypia/follicular lesions of undetermined significance; Category IV, follicular neoplasm or suspicious for follicular neoplasm; Category V, suspicious for malignancy. CNB = core needle biopsy, rFNA = repeat fine-needle aspiration

Table 3. Results of rFNA and CNB in Nodules Initially Diagnosed as AUS/FLUS in Nodules for Which the Final Diagnoses Were Available

Biopsy Results (Category)*	rFNA			CNB		
	Total (n = 182)	Benign (n = 153)	Malignancy (n = 29)	Total (n = 182)	Benign (n = 153)	Malignancy (n = 29)
Nondiagnostic (I)	12 (6.6)	10 (6.5)	2 (6.9)	1 (0.5)	0	1 (3.4)
Benign (II)	99 (54.4)	97 (63.4)	2 (6.9)	112 (61.5)	111 (72.5)	1 (3.4)
AUS/FLUS (III)	54 (29.7)	44 (28.8)	10 (34.5)	39 (21.4)	34 (22.2)	5 (17.2)
FN/SFN (IV)	5 (2.7)	2 (1.3)	3 (10.3)	18 (9.9)	8 (5.2)	10 (34.5)
Suspicious for malignancy (V)	7 (3.8)	0	7 (24.1)	1 (0.5)	0	1 (3.4)
Malignant (VI)	5 (2.7)	0	5 (17.2)	11 (6.0)	0	11 (37.9)

Data are number of nodules with percentage in parentheses. Category I, nondiagnostic; Category II, benign; Category III, atypia/follicular lesions of undetermined significance; Category IV, follicular neoplasm or suspicious for follicular neoplasm; Category V, suspicious for malignancy; Category VI, malignant. *Diagnoses according to the 6 categories of the Bethesda System for Reporting Thyroid Cytopathology. AUS/FLUS = atypia/follicular lesion of undetermined significance, CNB = core needle biopsy, FN/SFN = follicular neoplasm or suspicious for follicular neoplasm, rFNA = repeat fine-needle aspiration

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Table 4. Comparison of the Expected Rates of Unnecessary Diagnostic Surgery Based on the Results of rFNA and CNB in Nodules for Which the Final Diagnoses Were Available

Criteria for Surgery	Expected Surgery Rate			*P*
	rFNA (n = 182)	CNB (n = 182)	Difference between rFNA and CNB	
Criterion 1 (categories I and III)	54 (29.7)	34 (18.7)	20 (11.0)	0.024
Criterion 2 (categories IV and V)	2 (1.1)	8 (4.4)	6 (3.3)	0.109
Criterion 3 (categories I, III, IV, and V)	56 (30.8)	42 (23.1)	14 (7.7)	0.130

Data are number of nodules with percentage in parentheses. Criterion 1, low-risk indeterminate results (I and III); Criterion 2, high-risk indeterminate results (IV and V); and Criterion 3, all indeterminate results (I, III, IV, and V). Category I, nondiagnostic; Category III, atypia/follicular lesions of undetermined significance; Category IV, follicular neoplasm or suspicious for follicular neoplasm; Category V, suspicious for malignancy. CNB = core needle biopsy, rFNA = repeat fine-needle aspiration

to the rFNA-based diagnosis by 11.0% (18.7% vs. 29.7%, $p = 0.024$) for criterion 1; however, there was no significant difference in the rate of unnecessary surgery between the diagnoses made by rFNA or CNB for criteria 2 and 3.

DISCUSSION

Our study demonstrated significantly lower rates of Bethesda categories I, III, and V, and higher rates of categories IV and VI with CNB than with rFNA among nodules previously diagnosed as AUS/FLUS. Our results demonstrated that CNB significantly reduced the rates of potential diagnostic surgery for nodules with low-risk (criterion 1) and all indeterminate results (criterion 3), and the rate of potential unnecessary surgery for nodules with low-risk indeterminate results (criterion 1) compared to rFNA.

Previous studies [18,22,26,28] have consistently demonstrated that CNB showed lower rates of inconclusive results (categories I and III) than rFNA for nodules initially diagnosed as AUS/FLUS (rFNA 34.9%–63.0% and CNB 1.0%–40.9%), and that CNB could considerably reduce the rate of inconclusive results (categories I and III) compared to rFNA (reduction rate, 19.7%–33.9%) in these nodules. These results suggest that CNB might effectively reduce the rate of potential diagnostic surgery for nodules with repeated inconclusive results (categories I and III). This is in line with our results, which showed that CNB was superior to rFNA in reducing the expected rate of potential diagnostic surgery. However, a recently published study by Yoon et al. [29] reported that CNB did not reduce the rate of diagnostic surgery for nodules initially diagnosed as AUS/FLUS. Results from the study were in line with those of previous studies showing that CNB resulted in significantly lower rates of inconclusive results (categories I and III) than rFNA. However, the criteria for inconclusive results (categories I and III) were excluded from the criteria for potential diagnostic surgery in their study. Categories I and III are necessary to evaluate the rate of diagnostic surgery. The different results of our study may also be related to differences in the study population. We compared the results of rFNA and CNB in the same nodules, unlike those in previous studies [29], which compared the results of rFNA and CNB in different, unmatched study populations that might have had differences in the nodule characteristics and disease spectrum.

Our results showed that CNB could reduce the expected rate of potential unnecessary surgery for criterion I (low-risk indeterminate results, categories I and III) by 11.0%, compared to rFNA. Although CNB showed a higher rate of diagnostic surgery for criterion 2 (high-risk indeterminate results, categories IV and V) than rFNA, there was no significant difference in the rate of unnecessary diagnostic surgery for criterion 2 between CNB and rFNA, and the majority of unnecessary diagnostic surgeries were seen for nodules with low-risk indeterminate results. The management of nodules with high-risk indeterminate results (categories IV and VI) is different from that for nodules with low-risk indeterminate results, as surgery might be necessary for most of the nodules with high-risk indeterminate results.

Variable rates of repeated AUS/FLUS results (0%–35.7%) have been reported in studies from different institutions [18,22,28,29], when CNB was performed for nodules initially diagnosed as AUS/FLUS. The wide range can be explained by several factors, including the various preferences and experience of pathologists in CNB-based diagnosis, absence of widely accepted and established pathologic criteria for CNB, and possible differences in the experience of the operators. This indicates the need

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for standardized pathologic criteria for CNB to reduce interobserver variability and increase diagnostic accuracy. Meanwhile, the use of CNB for diagnosing thyroid nodules might also vary between institutions with different patterns of clinical practice depending on the physician and individual experience level of the operators. For further evaluation of the appropriate clinical role of CNB, standardized guidelines for pathological diagnosis and procedural techniques should be established that can guide clinicians to use CNB [30,31]. The low rate of complications (2.6%) of CNB in our study was similar to the reported complication rates (0% to 4.1%) of CNB [30,32,33], and was also comparable to the reported complication rate (0.3%–6.4%) of FNA in other studies [34].

Recently, molecular tests have been implemented in clinical practice as a rule-out test for indeterminate nodules diagnosed as AUS/FLUS or FN/SFN. Molecular tests have the advantage of being non-invasive compared to rFNA or CNB, and recently introduced new molecular tests showed high sensitivities and high negative predictive values for malignancy in indeterminate nodules [35,36]. Nodules showing repeated indeterminate results by rFNA and CNB could be appropriate candidates for molecular testing if initially diagnosed as AUS/FLUS; however, the role of molecular tests and repeat biopsies in the management algorithm of AUS/FLUS nodules need to be further clarified.

Our study had several limitations. First, this was a retrospective study, and there might have been a selection bias due to the exclusion of patients who did not undergo both rFNA and CNB. However, the potential selection bias in the study population and possible differences in the operator factors between the rFNA and CNB groups would have been minimized because simultaneous FNA and CNB were performed in most of the nodules. Second, the reference standard for benign diagnosis was based on one benign biopsy result in 53 nodules to reduce selection bias, which might inevitably produce false-negative results in rare cases. However, this may not have had a significant effect on the results because the malignancy risk is very low in AUS/FLUS nodules with one benign result on rFNA [37]. Third, we did not consider the US features of the nodules along with cytopathological categories. Fourth, considering the time gap between the present and the study period, the results of this study might be different from the results of applying the currently used CNB diagnostic guidelines because there have been advances in CNB procedural techniques and histopathologic CNB diagnosis. The histopathologic diagnostic criteria of CNB have been updated, and immunohistochemical studies are more widely used for CNB diagnosis, which may have improved the diagnostic accuracy of CNB [31].

In conclusion, CNB was superior to rFNA in reducing the rates of potential diagnostic surgery and unnecessary surgery for nodules initially diagnosed as AUS/FLUS in a scenario where low-risk indeterminate results for thyroid nodules (categories I and III) would undergo surgery.

Availability of Data and Material

The datasets generated or analyzed during the study are available from the corresponding author on reasonable request.

Conflicts of Interest

Dong Gyu Na and Ji-hoon Kim who is on the editorial board of the *Korean Journal of Radiology* was not involved in the editorial evaluation or decision to publish this article. All remaining authors have declared no conflicts of interest.

Author Contributions

Conceptualization: Dong Gyu Na. Data curation: Dong Gyu Na, Ji-hoon Kim, Hyobin Seo. Formal analysis: Dong Gyu Na, Leehi Joo. Funding acquisition: Dong Gyu Na. Investigation: Dong Gyu Na, Leehi Joo. Methodology: Dong Gyu Na, Leehi Joo. Project administration: Dong Gyu Na. Resources: Dong Gyu Na. Supervision: Dong Gyu Na. Validation: all authors. Writing—original draft: Leehi Joo. Writing—review & editing: Dong Gyu Na, Ji-hoon Kim, Hyobin Seo.

ORCID iDs

Leehi Joo
https://orcid.org/0000-0002-5527-0476
Dong Gyu Na
https://orcid.org/0000-0001-6422-1652
Ji-hoon Kim
https://orcid.org/0000-0002-6349-6950
Hyobin Seo
https://orcid.org/0000-0002-9759-1876

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