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Ultrasound-Guided Percutaneous Thyroid Nodule Core Biopsy: Clinical Utility in Patients with Prior Nondiagnostic Fine-Needle Aspirate

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Background: Five percent to 20% of thyroid nodule fine-needle aspiration (FNA) samples are nondiagnostic. The objective of this study was to determine whether a combination of FNA and core biopsy (CFNACB) would yield a higher proportion of diagnostic readings compared with FNA alone in patients with a history of one or more prior nondiagnostic FNA readings.
Methods: We conducted a retrospective study of 90 core biopsies (CBs) performed in 82 subjects (55 women and 27 men) between 2006 and 2008 in an outpatient clinic.
Results: CFNACB yielded a diagnostic reading in 87%. The diagnostic reading yield of the CB component of CFNACB was significantly superior to the concurrent FNA component, with CB yielding a diagnosis in 77% of cases and FNA yielding a diagnosis in 47% ($p < 0.0001$). The combination of CB and FNA had a higher diagnostic reading yield than either alone. In 69 nodules that had only one prior nondiagnostic FNA, CB was diagnostic in 74%, FNA was diagnostic in 52%, CFNACB was diagnostic in 87%, and CB performed significantly better than FNA ($p = 0.0135$). In 21 nodules with two or more prior nondiagnostic FNAs, CFNACB and CB were diagnostic in 86%, FNA was diagnostic in 29%, and CB was significantly better than FNA ($p = 0.0005$). Clinical, ultrasound, or histopathologic follow-up was available for 81% (73/90) of the CFNACB procedures. No subject with a benign CFNACB reading was diagnosed with thyroid malignancy in the follow-up period (range 4–37 months, mean 18 months), although one subject had minimal increase in nodule size and was awaiting repeat sonography at study conclusion.
Conclusion: Thyroid nodule CFNACB is safe and clinically useful in selected patients when a prior FNA reading is nondiagnostic. CFNACB is superior to either CB or FNA alone. CFNACB should be strongly considered as an alternative to surgery in individuals with two prior nondiagnostic FNAs.

Introduction

Nodular thyroid disease is common. Palpable thyroid nodules are present in 4%–7% of North American adults (1–3). Nonpalpable thyroid nodules are even more common, found in up to 65% of subjects in sonographic and autopsy studies (2). Five percent to 15% of isolated thyroid nodules or nodular thyroids will ultimately harbor a thyroid malignancy (4–7). Consequently, the accurate diagnosis of nodular thyroid disease is a common and important clinical problem.

Fine-needle aspiration (FNA) is widely utilized for the detection of malignancy in thyroid nodules and has been extensively validated for this purpose (8–10).

Sonographically guided FNA biopsy of neck masses has high sensitivity (8–10). The low cost, ease of the procedure, ready availability, and safety make FNA the method of choice for nodule sampling (11,12). However, FNA of thyroid nodules is nondiagnostic in 5%–20% of patients, even with the use of ultrasound (US) guidance (13). A nondiagnostic thyroid nodule FNA does not assure a benign nodule (14,15). Therefore, uncertainty about the presence of thyroid malignancy remains a common clinical problem after nondiagnostic FNA.

Although core needle biopsies are widely used in other anatomic regions, relatively few series of US-guided core needle biopsy (CB) of thyroid nodules have been reported (16–21). Current American Thyroid Association (ATA) thyroid

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nodule management guidelines and the Society of Radiologists in Ultrasound Consensus Statement do not discuss the role of thyroid nodule core biopsy (CB) in the evaluation of thyroid nodules (8,12). In fact, several practice guidelines suggest that surgical excision may be appropriate after several nondiagnostic FNAs (8,22). The recent American Association of Clinical Endocrinologists (AACE), Associazione Medici Endocrinologi (AME), and European Thyroid Association (ETA) thyroid nodule guidelines mention the potential use of CNB but do not specifically recommend its use after nondiagnostic biopsies (9). We therefore thought it relevant to review our experience to determine the diagnostic utility of combined FNA and CB (CFNACB) in patients with prior nondiagnostic thyroid nodule FNA.

Materials and Methods

Medical record review

Three authors (M.K.S., W.C.F., and A.E.S.) retrospectively identified all patients who underwent CFNACB of a thyroid nodule at the Massachusetts General Hospital (MGH) between January 1, 2006, and December 31, 2008, by searching the interventional radiology divisional database, and manually reviewing all thyroid-related cytology and histopathology reports during this 3-year period. During this time period 5542 thyroid FNAs were performed; 762 of these were nondiagnostic. Our analysis is restricted to those patients with nondiagnostic FNAs who subsequently had a CFNACB. Permission was obtained from our Institutional Review Board (IRB) for retrospective review of medical records of these patients; the IRB waived the requirement to obtain informed consent. Confidentiality of the research subjects was maintained in accordance with the requirements of the Health Insurance Portability and Accountability Act.

The following parameters were obtained from each medical record: (i) nodule size, (ii) patient age and sex, (iii) number and result of prior FNA procedures, (iv) result of CFNACB, (v) subsequent management, and (vi) outcome. FNA and CB needle size and the number of passes were recorded when available. The Electronic Longitudinal Medical Record (LMR) was reviewed for mention of any biopsy-related complication. Two board-certified radiologists, one with 10 years of experience in thyroid US (A.E.S.), and the other with 6 years of experience (M.K.S.) reviewed each patient's imaging to determine nodule size by consensus. Inclusion criteria included the following: (i) a prior nondiagnostic thyroid nodule FNA performed and interpreted at our institution and (ii) subsequent CFNACB of the same nodule performed and interpreted at our institution. Each pathology and cytology report was assigned to an ordinal diagnostic category. The LMR was reviewed for postbiopsy follow-up information. All cytology or pathology reports that remained equivocal were reviewed by A.E.S. and W.C.F., a board-certified cytopathologist with 12 years of experience, to reach consensus prior to assigning a diagnostic category. Reviewers were blinded to surgical pathology results when classifying biopsy results.

CFNACB procedure

All CFNACB procedures were performed by a staff interventional radiologist with an interventional radiology fellow or radiology resident using real-time US guidance. Tyco Healthcare Monoject needles (25 gauge, 5 cm in length) (Sherwood Medical, St. Louis, MO) were used for all FNA procedures, and Temno Evolution cutting CB needles (20 gauge, 6 cm in length) (Cardinal Healthcare, Dublin, OH) with a 10 or 20 mm adjustable needle throw were used for all CBs. After obtaining informed consent, each patient was placed in the supine position with a pillow under the shoulders to slightly extend the neck. Initial US examination was performed to identify the thyroid nodule of interest. Images of the thyroid nodule were then obtained. After the administration of subcutaneous and perithyroidal local anesthesia (5–10 cc of 1% lidocaine), four to six freehand US-guided FNAs were performed. Two to four CBs were subsequently obtained under US guidance. When performing thyroid CBs, our goal is to obtain a visually estimated total core length of at least 20 mm; however, total CB length is not routinely documented. A postprocedure sonogram was performed to assess for hematoma. The patient was discharged at the conclusion of the procedure.

Specimen preparation

FNA specimens were collected and smears were prepared by the radiologist. Our departmental protocol is to smear two aspirates on glass slides, which are then immediately fixed in 95% ethanol. Two to four additional, US-guided aspirates were performed and placed in their entirety into a CytoLyt (Cytyc Corp., Marlborough, MA) liquid preservative solution. The specimens were stained in the cytology laboratory using the modified Papanicolaou procedure and submitted for cytologic assessment.

While in the US suite, the CB samples were placed in normal saline and transported to the cytology laboratory on the same day. Upon arrival in the cytology laboratory, the CB samples were immediately decanted into formalin and after being embedded into paraffin blocks using standard protocols, cut into 5 μm sections and stained with hematoxylin and eosin prior to histopathologic assessment.

Specimen interpretation

A board-certified attending staff cytopathologist reviewed all FNA specimens. Specimens were considered nondiagnostic if insufficient cellular material (fewer than six groups of cells containing >10 cells each) was present and no evidence of cellular atypia was found. A board-certified attending staff pathologist reviewed all CB samples. Cytology and histopathology results were available to the pathologist and cytopathologist, respectively, at the time of their interpretations.

Results interpretation

Each FNA and CB result was recorded, and then classified into one of seven categories according to the Bethesda classification scheme (Table 1). Each result was then classified as either diagnostic or nondiagnostic, based on the cytopathology report and clinical notes.

Diagnostic accuracy of CFNACB

The diagnostic accuracy of CFNACB was determined by a review of surgical pathology in cases that underwent

Table 1. Classification of Results of Combined Fine-Needle Aspiration and Core Biopsy

FNA result	*CB result*	*Result coded as per Bethesda system*	*Usual management*
Nondiagnostic	Unsuccessful procedure Nondiagnostic; no thyroid tissue present Nondiagnostic; scant thyroid present	Nondiagnostic	Repeat FNA with US guidance
Benign nodule Suspicious for benign nodule Macrofollicular lesion Suspicious for macrofollicular lesion Mixed, predominantly macrofollicular lesion Suspicious for mixed, predominantly macrofollicular lesion Subacute/granulomatous/ DeQuervain's thyroiditis Chronic/lymphocytic/Hashimoto's thyroiditis Suspicious for Hashimoto's thyroiditis	Macrofollicular lesion Mixed, predominantly macrofollicular Subacute/granulomatous/ DeQuervain's thyroiditis Chronic/lymphocytic/Hashimoto's thyroiditis Suspicious for Hashimoto's thyroiditis Riedel's thyroiditis Graves' disease Normal thyroid Benign scar/fibrosis Benign	Benign	Follow-up
Nuclear atypia	Nuclear atypia	Atypia (atypia of undetermined significance)	Repeat FNA
Mixed micro/macrofollicular lesion Suspicious for mixed micro/ macrofollicular lesion	Mixed micro/macrofollicular lesion	FLUS	Repeat FNA
Microfollicular lesion Mixed, predominantly microfollicular lesion	Microfollicular lesion Mixed, predominantly microfollicular lesion	FN or Susp FN	Excision
Suspicious for papillary carcinoma Suspicious for carcinoma	Suspicious for papillary carcinoma Suspicious for Hurthle cell carcinoma	Suspicious for malignancy	Excision
Poorly differentiated carcinoma Papillary carcinoma	Papillary carcinoma Invasive carcinoma	Malignant	Excision

CB, core biopsy; FLUS, follicular lesion of undetermined significance; FNA, fine-needle aspiration; Susp FN, suspicious for follicular neoplasm; US, ultrasound.

thyroidectomy and by change in nodule size by US or clinical assessment in patients who did not have surgery.

Statistical analysis

McNemar's test was used to assess whether an observed difference in yield between CB and FNA was statistically significant. A p-value of <0.05 was considered to indicate a statistically significant difference.

Results

Demographics and indications for CFNACB

Between January 1, 2006, and December 31, 2008, 5542 thyroid FNAs were performed at the MGH. Seven hundred and sixty-two FNAs were nondiagnostic. Of these 762 nondiagnostic FNAs, 90 CFNACB procedures were performed in 82 patients (55 women, 27 men, age range 29–82 years, mean age 60 years). Nodules ranged in maximal dimension from 0.6 to 4.4 cm with a mean of 2 cm. Three nodules (3.3%) were less than 1 cm in maximal dimension. Endocrinologists and endocrine surgeons referred the majority of these patients for CFNACB.

The indication for CFNACB was a prior nondiagnostic FNA in all 90 nodules. There was one prior FNA in 77% of nodules (69/90), two prior FNAs in 20% of nodules (18/90), and three prior FNAs in 3% of nodules (3/90). Thirteen additional thyroid nodule CFNACBs were excluded from the study as the prior FNA was performed and interpreted outside our institution.

Complication rate of CFNACB

The LMR and interventional radiology databases were reviewed for any documented complications. Procedure reports and follow-up visit notes were available for all patients. There were no reported complications.

Diagnostic yield of CFNACB

Overall, the combined procedure (CFNACB) yielded a diagnostic result in 87% of nodules (78/90). Both FNA and

Table 2. Diagnostic Yield of Core Biopsy and Fine-Needle Aspiration Components of Combined Fine-Needle Aspiration and Core Biopsy in Patients with Prior Nondiagnostic Fine-Needle Aspiration

		Core component diagnostic	*Core component nondiagnostic*	*Total*
One prior nondiagnostic FNA	FNA component diagnostic	27	9	36
	FNA component nondiagnostic	24	9	33
	Total	51	18	69
Two prior nondiagnostic FNAs	FNA component diagnostic	6	0	6
	FNA component nondiagnostic	12	3	15
	Total	18	3	21
Overall results	FNA component diagnostic	33	9	42
	FNA component nondiagnostic	36	12	48
	Total	69	21	90

CB were diagnostic in 37% of nodules (33/90). In 40% of nodules (36/90), CB was diagnostic when FNA was not. In 10% of nodules (9/90), FNA was diagnostic when CB was not (Table 2).

For the entire subject group, CB was diagnostic in 77% of nodules, whereas repeat FNA was diagnostic in only 47% ($p < 0.001$).

The diagnostic yield of CFNACB was further analyzed with respect to prior FNA procedures.

Relative yield of CB versus FNA following one prior nondiagnostic FNA

Sixty-nine nodules had only one prior nondiagnostic biopsy. Of these 69 nodules, CFNACB was diagnostic in 87% (60/69), CB was diagnostic in 74% (51/69), and repeat FNA was diagnostic in 52% (36/69) (Table 2). In this subgroup, the diagnostic performance of CB was significantly superior to that of concurrent FNA ($p = 0.0135$).

Relative yield of CB versus FNA following two or more prior nondiagnostic FNA procedures

Twenty-one nodules had at least two prior nondiagnostic FNAs. Of these 21 nodules, CFNACB was diagnostic in 86% (18/21), CB was diagnostic in 86% (18/21), and FNA was diagnostic in 29% (6/21). Of those with two prior nondiagnostic biopsies, there were no instances where the FNA was diagnostic and the CB was not. In this subgroup, the diagnostic performance of CB was significantly superior to concurrent FNA ($p = 0.0005$). Three nodules had previously had three nondiagnostic FNAs. The CB was diagnostic in all three cases whereas none of the FNAs were diagnostic.

Discordant cytology and pathology findings for the FNA and CB components of CFNACB were uncommon, occurring in 8 of 90 nodules (9%). There are currently no data to guide management in this situation. Therefore our approach is to err on the side of caution by accepting the most (rather than the least) concerning diagnosis. In some of these cases patients declined surgery. The outcome of these eight cases is tabulated in Table 3.

Table 3. Follow-Up of Nodules with Discordant Combined Fine-Needle Aspiration and Core Biopsy Results

FNA diagnosis	*Concurrent CB diagnosis*	*Outcome*
Atypia (FLUS)	Benign	Lost to follow-up
Benign	Susp FN	Stable US 28 months
Benign	Atypia (FLUS)	Stable US 8 months
Benign	Susp FN	Stable on US at 17 months
Benign	Atypia (FLUS)	Stable US 12 months
Benign	Susp FN	Surgery—papillary cancer
Benign	Susp FN	Surgery—adenoma
Benign	Susp FN	Stable US 33 months

Diagnostic accuracy of CFNACB

CFNACB yielded a benign diagnosis in 40% of nodules (36/90). Of these 36 nodules, follow-up data were available in 22 (61%). Seventeen (47%) were followed with US (mean follow-up 18 months, range 4–37 months). Sixteen of 17 nodules (94%) were stable or decreased in size; one nodule (6%) had a minimal increase in size after 12 months and is awaiting a repeat US. Of the three nodules followed with clinical examination, all were stable. One patient with Reidel's thyroiditis was treated with glucocorticoids and one patient with Graves' disease was treated with radioactive iodine. Follow-up data were not available for 14 patients (39%).

CFNACB yielded an atypical diagnosis (atypia of undetermined significance or follicular lesion of undetermined significance) in 10% of nodules (9/90). Follow-up data were available for all of these nodules. Five of these nodules underwent surgery and all were benign follicular adenomas (Table 4). Four nodules were followed with serial USs and were stable (mean follow-up 16.5 months, range 2.8–28.9 months).

CFNACB yielded a diagnosis of follicular neoplasm or suspicious for a follicular neoplasm in 31% of nodules (28/90). Follow-up data were available in 26 of these 28 nodules (93%). Twenty-two were removed surgically and four were followed with sonography. Of these, 2 of 22 (9%) were malignant, 18 of 22 (82%) were benign follicular adenomas, and 2 of 22 (9%) were nodular Hashimoto's thyroiditis. Four of 26 nodules (15%) were stable on serial US examination (mean follow-up 21 months, range 10–39 months). Two subjects were lost to follow-up.

Table 4. Thyroidectomy Surgical Pathology Diagnosis of Nodules That Underwent Combined Fine-Needle Aspiration and Core Biopsy

CFNACB pathology (n)	*Surgical pathology* (n)
Malignant (4)	Papillary carcinoma (4)
Malignant (1)	Squamous cell carcinoma (1)
Susp FN (22)	Papillary carcinoma (1) Follicular carcinoma (1) Follicular adenoma (18) Multinodular goiter (2)
FLUS (5)	Follicular adenoma (5)
Nondiagnostic core and FNA (5)	Follicular adenoma/ Hashimoto's (5)

CFNACB yielded a suspicious for malignancy or malignant diagnosis in 5.5% of nodules (5/90). Follow-up was available in all cases and all were malignant at surgery.

CFNACB yielded a nondiagnostic result in 13.3% of nodules (12/90). Follow-up data were available for 11 of these 12 subjects (92%). Five of these patients had surgery and all had benign pathology (four follicular adenomas, and one Hashimoto's thyroiditis. Five nodules were stable on serial US (mean follow-up 18.5 months, range 5–26 months). One was stable on follow-up physical examination and one was lost to follow-up.

Discussion

The primary goal when evaluating thyroid nodules is to detect a thyroid malignancy, which occurs in 5%–15% of thyroid nodules and nodular thyroid glands (23). Since current imaging studies are unable to reliably exclude malignancy in the majority of thyroid nodules, FNA is usually recommended for nodules that exceed 10–15 mm in size or that demonstrate sonographic characteristics that increase the probability of malignancy (8,9).

US-guided FNA is safe, sensitive, and cost effective, and has become the diagnostic procedure of choice in thyroid nodule evaluation (8,9,24).

FNA biopsy samples are nondiagnostic in 5%–20% of biopsies, even when sonographic guidance is used (13). Unfortunately, it is difficult to predict which patients will have a nondiagnostic FNA. Patient age, sex, thyroid function, gland size, and nodule multiplicity do not reliably predict a nondiagnostic FNA (25). The only factor that consistently predicts a nondiagnostic FNA is a >50% cystic component of the nodule (13). Furthermore, a nondiagnostic thyroid nodule FNA does not reduce the likelihood of malignancy (14,15). Consequently, a nondiagnostic FNA remains a significant problem in the clinical management of patients with thyroid nodules.

Sonographically guided thyroid nodule CB has been shown to be accurate, safe, and well tolerated (15,17,19,26–28). There are several theoretical reasons why sonographically guided CB might be useful when thyroid nodule FNA is nondiagnostic: CB can provide more tissue than a nondiagnostic FNA and cellular architecture is retained, facilitating accurate histologic diagnosis (26,29,30). Several retrospective CB series have demonstrated a reduced rate of unsatisfactory and suboptimal thyroid biopsy results using this technique (20,31,32). On the other hand, other series have not demonstrated any additional benefit when comparing a CB to an FNA in the primary assessment of thyroid nodules (14). We are not advocating the use of CBs as the initial diagnostic procedure for thyroid nodules.

Recent ATA thyroid nodule guidelines and the Society of Radiologists consensus statement on thyroid nodules and the National Cancer Institute (NCI) State of the Art conference do not discuss the utility of thyroid CB (8,12). The ATA guidelines note: "Partially cystic nodules that repeatedly yield nondiagnostic aspirates need close observation or surgical excision. Surgery should be more strongly considered if the cytologically nondiagnostic nodule is solid. Recommendation rating: B" (8). Baloch *et al.* summarized the NCI State of the Art conference position on this point by noting: "If repeat smears are 'nondiagnostic,' surgery ought to be considered" (10). The recent AACE/AME/ETA guidelines do note: "CNB, performed under US guidance with a 20- to 21-gauge cutting needle by experienced operators, may offer additional information to FNA biopsy in selected cases of thyroid or neck masses with repeated inadequate FNA biopsy cytology"(9). These guidelines do not provide a specific recommendation for the use of core needle biopsies.

Our study addresses the utility of CFNACB in evaluating thyroid nodules after one or more prior nondiagnostic FNAs.

Overall, 77% of our thyroid nodule CBs yielded diagnostic material (69/90 nodules). Screaton *et al.* reported a 95% diagnostic rate and Renshaw *et al.* reported an 82% diagnostic rate for CBs in a mixture of patients, with and without prior nondiagnostic FNAs (21,32). In contrast, all of our patients had at least one prior nondiagnostic FNA.

The FNA component of CFNACB was diagnostic in 47% of patients (42/90). This is lower than the 62% diagnostic rate on repeat FNA reported by Chow *et al.* (14), the 63% diagnostic rate reported by Alexander *et al.* (13), and the 75% diagnostic rate on repeat FNA reported by Baloch *et al.* (33). Patients studied by Chow *et al.* (14) and Baloch *et al.* (33) had a mixture of US-guided and palpation-guided FNAs as their initial technique whereas the patients of Alexander *et al.* (13) and our patients had an US-guided FNA as the initial procedure. The inclusion of subjects who underwent prior palpation-guided FNA in the Chow and Baloch series conflates the known superior yield conferred by US guidance with the additional yield expected from a second FNA procedure (24).

Alexander *et al.* reported that the likelihood of obtaining a diagnostic sample on initial and repeat FNA is inversely proportional to the cystic change in the nodule (13). Table 5 analyzes the rate of diagnostic repeat FNA based on the cystic component of the nodule and compares these results to those of Alexander *et al.* (13). The trend of a higher diagnostic rate in nodules with a greater solid component is also seen in our series. In our cohort only three nodules were predominantly cystic and FNA yielded a diagnostic result in two of them resulting in a 67% diagnostic rate, a finding of questionable statistical significance given the small number of predominantly cystic nodules.

It is important to note that most patients with initial nondiagnostic FNA at the MGH were not referred for CFNACB. We are unable to quantitate the specific reasons why some patients were referred for CFNACB while others underwent repeat FNA, as this was not routinely documented in the medical record, but it is tempting to speculate that patients with technically more difficult nodules to biopsy were referred for CFNACB.

In our series, CB was superior to FNA in obtaining diagnostic material in individuals with only one prior nondiagnostic FNA

Table 5. Rate of Diagnostic Repeat Fine-Needle Aspiration Among Different Categories of Nodules with Initial Nondiagnostic Specimens

Samir et al. *(This study)*		*Alexander* et al. *(13)*	
Cystic vs. solid	*Repeat diagnostic FNA (%)*	*Cystic vs. solid*	*Repeat diagnostic FNA (%)*
Solid $n=50$	48	Solid $n=54$	76
Predominantly solid (<25% cystic) $n=28$	36	<25% cystic $n=21$	85
Mixed (25%–75% cystic) $n=8$	38	25%–50% cystic $n=17$	60
		50%–75% cystic $n=26$	54
Predominantly cystic (>75% cystic) $n=3$	67	>75% cystic $n=71$	48
Total $n=89$	43	Total $n=189$	62

(74% vs. 52%, $p=0.0135$) and CFNACB (87%) was superior to either CB or FNA alone ($p<0.004$). This finding is consistent with several CFNACB series that have been reported (26,27,31), although at least one large retrospective series did not demonstrate an increased diagnostic yield with CFNACB compared with FNA (14). It is possible that this is due to differences in subject population. In our series, an incremental benefit of CFNACB over CB alone was only found in those subjects who had a single prior nondiagnostic FNA.

For the 21 patients who had two or more prior nondiagnostic FNAs, the difference is even more striking. The CB yielded diagnostic material in 86% of biopsies whereas only 29% of FNAs were diagnostic ($p=0.0005$). In these subjects with two or three prior nondiagnostic FNA procedures, FNA did not add incremental diagnostic value to the CB. A reduction in yield of repeat FNA after multiple prior nondiagnostic FNAs was also seen in the series of Alexander *et al.*, where 10 patients underwent a third FNA after two nondiagnostic FNAs, and only 30% were diagnostic.

CFNACB of the thyroid gland is a safe technique with a very low rate of complications (19,31). In a systematic review of clinical complications following thyroid FNA, the authors reported that the rate of major complications ranged from 0.036%–1% (34). In our series there were no complications from CFNACB (0%; 95% confidence interval 0%, 4.02%). This is concordant with the low rate of complications reported in other CB series. For example, in a series of 209 CBs, Screaton *et al.* reported no major complications, and four self-limited minor complications—three small postbiopsy hematomas and one episode of hemoptysis (21). In a series of 377 CBs, Renshaw and Pinnar reported a single postbiopsy hematoma that was described as "large," but which did not require hospitalization (32). Although the complication rate of CFNACB is low, the procedure results in the acquisition and interpretation of additional specimens and is therefore more expensive, more time consuming, and requires additional expertise. There is no evidence that CFNACB is superior to FNA for the initial diagnosis of thyroid nodules. Therefore, FNA continues to be the preferred initial biopsy technique for thyroid nodules.

Our study has several potential limitations. Although we reviewed the results of a cohort of patients who were referred for CFNACB after a nondiagnostic FNA, we have not studied all patients with an initial nondiagnostic FNA. Many of our referring physicians choose to repeat a single nondiagnostic FNA, and only refer cases considered to be more difficult for CFNACB. It is possible that an unrecognized selection bias influenced the outcome of CFNACB in our cohort. However, this selection bias appears to have made little difference to the overall diagnostic yield of CFNACB, which was similar in subjects with one or two prior nondiagnostic FNAs. Another limitation is that our study is retrospective and the post-procedural follow-up is incomplete. However, this should not impact the diagnostic rate of CFNACB. Finally, the interpreting cytologists and histopathologists were not blinded to each other's assessments: it is possible that this has biased the diagnostic rate of FNA or CB. However, it is likely that this potential bias would decrease the apparent additional benefit of the CB component compared with FNA alone.

To our knowledge, this is the first study to systematically assess the diagnostic yield of CFNACB after prior nondiagnostic FNA for thyroid nodules. Our study provides strong evidence for the high diagnostic yield and safety of CFNACB after prior nondiagnostic FNA. Our results suggest that CFNACB has the potential to reduce the number of repeat biopsies and unnecessary thyroidectomies in patients with one or more nondiagnostic prior FNA procedures. Based on these data, we strongly recommend CB or CFNACB as an alternative to surgical excision for nodules with two prior nondiagnostic FNAs. The role of CFNACB as an alternative to repeat FNA after a single nondiagnostic FNA requires additional study with prospective randomized trials.

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Disclosure Statement

The authors have nothing to disclose.

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