Effectiveness of core-needle US-guided biopsy as a primary tool for diagnosis of thyroid nodules

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Background
In many nodular thyroid cases, fine-needle biopsy (FNB) under the guidance of ultrasound (US) has been a primary diagnostic test as it is a safe, minimally invasive method with a low cost. However, it may have "nondiagnostic" aspirates because of the sampling difficulties. On the other hand, a bigger tissue sample is obtained by core-needle biopsy (CNB), which can promote more precise diagnostic results with a reduction of the need for repeated aspiration.
Methods
In a case-series study, adult patients with suspicious thyroid nodules were assigned to a preoperative diagnosis by both US-guided FNB and CNB with correlation to the final postoperative pathology diagnosis.
Results
CNB had more accuracy in thyroid malignancy diagnosis (95.8%) than FNB (75%). Nondiagnostic results could be lessened by CNB more than FNB with calculated sensitivities of 70% and 90% and specificities of 80% and 100% for FNB and CNB, respectively. No significant complications resulted while acquiring the samples for both modalities.
Conclusion
US-guided CNB was more specific than FNB in the diagnosis of thyroid malignancy. A combination of FNB/CNB would be more precise than performing CNB only or FNB in nodular thyroid disease.

Keywords:
core-needle biopsy, fine-needle biopsy, thyroid malignancy, thyroid nodules, total thyroidectomy

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Introduction

Recently, there have been rising trends in the diagnosis of nodular thyroid disease, which could be from the increased age in the population and the increased performance of imaging for the head, neck, and chest [1]. Out of the vast amount of thyroid nodules discovered, up to 16% could be ultimately diagnosed as malignant [2].

The nodule may be discovered by the patients as a palpable nodule or incidentally discovered in an imaging study. The focus of clinical evaluations is to differentiate thyroid cancers from benign lesions [3]. Therefore, triaging nodular thyroid patients needs a precise tool in diagnosis [2].

The majority of thyroid nodule cases are euthyroid; it must be remembered that many patients do not come with obvious typical features of thyroid malignancy like hoarseness of voice or hard fixed lymph nodes. Medullary thyroid carcinoma is only represented by one in 250 nodules, and serum calcitonin monitoring is reserved for patients at high risk [3].

Ultrasound (US) is the chosen imaging study for thyroid nodules. It may detect nodules that are tiny for palpation, the involvement of several nodules, and neck lymphadenopathy; it has precise nodule diameter measurements. In addition, it enables the classification of nodules by sonographic appearance that indicates malignancy [3].

Currently, fine-needle aspiration biopsy (FNB) with the guidance of US is considered as the key diagnostic procedure for simple, accurate, and cost-effective determination of surgical cases without an unnecessary procedure. However, FNB is not diagnostic and had indeterminate cytology results. Most thyroid surgeries after the presence of abnormal cytology are due to benign lesions [4–6].

As an alternative diagnostic approach to the US–FNB, core-needle biopsy (CNB) of the thyroid nodules has been suggested, particularly to resolve the limits of inconclusive cytological diagnosis. CNB provides a larger tissue sample, which facilitates a more precise

histological diagnosis, especially in cases of "inadequate for diagnosis," "atypia," or follicular lesion with unclear significance after insufficient repeated FNB results [6].

Patients and methods

Study design and setting

The study was planned as a case-series study, which was performed in the Department of General Surgery in Kafrelsheikh and Alexandria University hospitals during the year of 2017. The ethics committee of Kafrelsheikh and Alexandria Universities granted ethical approval to the study that also abided by the tenets of the Declaration of Helsinki and met the CONSORT guidelines.

Selection criteria

We included patients with thyroid nodules with a diameter larger than 1 cm and suspicious US criteria with TIRADS category 3 or higher. Patients with a history of hemodynamic instability or inadequate coagulation profile were excluded.

Assessment and procedures

All patients underwent careful history taking, complete physical examination, and routine laboratory investigations prior to biopsy taking. US of the thyroid gland, including information of biopsied nodule (location, size, echogenicity, composition, presence of calcifications, and flow pattern), with Doppler analysis, had been done for evaluation and characterization as per the TIRADS classification [7] for the categorization of the risks of sonographic malignancy.

Patients had undergone both US–FNB and core biopsies with TRUCUT 18-G needle biopsies. On the slide that was labeled before the treatment, the aspirated cytology dispersed, then 95% ethyl alcohol was used to correct it. The sample was moved to the pathology department after that. The tissue biopsy samples were directly placed for further processing in a 10% formaldehyde solution. The location of the puncture was pressed, and the soft tissue of the neck was examined to rule out any potential complications. An expert cytopathologist who has had considerable experience in thyroid independently studied pathology samples. The categorical system of the Bethesda reporting system was used to perform the comparison of the diagnostic performance of both FNB and CNB. Each category of them has an insinuated cancer risk. This risk is up to 3% in the benign category and up to 100% in the malignant category. The categories are linked to evidence-based clinical management guidelines: category 1: nondiagnostic or unsatisfactory, category 2: benign, category 3: atypia of undetermined significance or follicular lesion of undetermined significance, category 4: follicular neoplasm or suspicious for a follicular neoplasma, category 5: suspicious for malignancy, and category 6: malignant [8].

Statistical analysis

We used Statistical Package for the Social Sciences (SPSS version 20.0, IBM Corp. Chicago, Illinois, USA) software. Numbers and percentages represented the qualitative data, while quantitative data were represented by mean (SD). We used the χ^2 test and Student t-test for differences for significance. The χ^2 test for difference and association of qualitative variables, and the Student t-test for differences between quantitative independent groups. Significant results had P value at <0.05.

Results

Characteristics of the patients

A total of 158 patients who had nodules larger than 1 cm in diameter and suspicious US criteria with TIRADS category 3 or higher were enrolled in the study. We excluded 10 patients who did not meet the study criteria, while 148 patients were included in the study. Among these patients, there were 34 men and 114 women. The age ranged from 23 to 62 years, with a median age of 39 years. Thirty-nine patients had solitary thyroid nodules; the rest had multiple nodules with a suspicious one. The suspicious nodules ranged in size from 1.2 to 4.3 cm (mean 3.2 (1.4) cm).

Assessment

By US, no nodules in our study were categorized as TIRADS category 1 or category 2. Fifty-two nodules were in category 3 (35.1%), and their biopsies were benign with no malignant diagnosis for this category. For category 4A, 15 (10.2%) nodules were benign, and 7 nodules (4.7%) were malignant in core biopsies. In 4B category, 6 nodules were benign (4.1%), and 8 nodules were malignant (5.4%) in core biopsies, while 60 nodules (40.5%), which were in grade 5, were proved to be malignant by both core and operative pathology report (Table 1).

Using the categorical system of the Bethesda reporting system, a comparative analysis of both FNB and CNB diagnostic efficiency was carried out to facilitate the comparison as in (Table 2). The CNB proved 68 nodules (46% of total nodules) to be definitely malignant (Bethesda VI), while FNB could only assign 38 nodules (26.7% of the total studied nodules) to this category. The CNB proved 74 nodules (50% of total nodules) to be benign (Bethesda II). Although FNB assigned 64 nodules (43.2% of the total studied nodules) to this category where it was proven later that

only 57 (77.3%) nodules were benign, 14 (22.7%) of those 64 nodules had a malignant diagnosis.

For categories Bethesda III (atypia of undetermined significance or a follicular lesion of undetermined significance) and IV (follicular neoplasm or suspicious for follicular neoplasm) with an uncertain diagnosis, CNB had six cases in those categories that were subsequently proven malignant papillary carcinoma by postoperative biopsy, while FNB had seven cases that were proven later to be three malignant nodules and four nodules had benign nature.

According to the histopathological classification of the lesions in our study, the most frequent diagnosis was that of benign colloid lesions (68 nodules), followed by papillary carcinoma (52 nodules) and then follicular carcinoma (16 nodules); also, six cases of lymphoma and another six pseudonodules of Hashimoto thyroiditis were diagnosed. There were 37 cases of FNB and 6 cases of core-tissue biopsy with no conclusive diagnosis (Table 3).

In our study, the cytology reports of the FNB were able to detect 77.9% of the benign colloid lesions, 100% of the papillary carcinoma nodules, and could assign six nodules with follicular carcinoma as a suspicious follicular lesion.

Although the CNB was able to detect 100% of the colloid benign nodules, 88.4% of the nodules with papillary carcinoma, and 16 nodules (100%) with follicular carcinoma, and detected accurately six cases of lymphoma of the thyroid gland and also diagnosed six pseudonodules to be an atrophic fibrotic stage of Hashimoto thyroiditis, while the FNB could not detect any of the two later pathologies.

Of the 148 nodules biopsied, 95 (64.5%) underwent surgery, and the surgical specimens were obtained for final diagnosis with pathological examination. For the remaining 53 benign thyroid nodules, both by FNB and core biopsy, follow-up every three months had been applied for two years.

The diagnostic accuracy for FNB was 75%, while that for CNB was calculated at 95.8%. Although the FNB sensitivity and specificity for malignant lesions were about 70.8% and 79.2%, those of the CNB were 91.6% and 100%, respectively.

Discussion

Although FNB is considered to be a more cost-effective procedure than the others in thyroid biopsy [1], many cytological preparations are inconclusive in diagnosis. There is a present interest in CNB as a better procedure for the assessment of thyroid nodules. Regrettably, it was limited in patients with inconclusive FNB examination [1,2].

It is widely agreed that recognition of risk indicators in a thyroid nodule by the US, increases the chance of malignancy [1,2]. Furthermore, FNB must be repeated in these cases, regardless of a benign cytological result [9]. In our study, the goal was to explore the diagnostic

Table 1 Descriptive analysis of the studied patients regarding the TIRADS classification (*n*=148)

TIRADS category	Benign	Malignant	Total
3	52 (35.1%)	0	52 (35.1%)
4A	15 (10.2%)	7 (4.7%)	22 (14.9)
4B	6 (4.1%)	8 (5.4%)	14 (9.5%)
5	0	60 (40.5%)	60 (40.5%)

Table 3 FNA and CNB in comparison with histopathological diagnosis of the studied group (*n*=148)

Postoperative Proved histological pathology	FNAC No. (%)	CNB No. (%)
Papillary carcinoma (*n*=52)	52 (100)	46 (88.4)
Follicular carcinoma (*n*=16)	6 (37)	16 (100)
Colloid benign nodules (*n*=68)	53 (77.9)	68 (100)
Hashimoto thyroiditis with pseudonodule (*n*=6)	0	6 (100)
Lymphoma (*n*=6)	0	6 (100)

CNB, core-needle biopsy; FNB, fine-needle biopsy.

Table 2 Comparison of FNA and CNB diagnosis of thyroid nodules in correlation with the Bethesda system

Diagnosis	FNB (*n*=148)	Diagnosis		CNB (*n*=148)	Diagnosis	
		Benign	Malignant		Benign	Malignant
Bethesda I (No—diagnostic)	7 (4.7%)	7 (100%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Bethesda II (benign)	64 (44.3%)	50 (78%)	14 (22%)	74 (50%)	74 (100%)	0 (0%)
Bethesda III (AUS or FLUS)	7 (4.7%)	7 (100%)	0 (0%)	6 (4%)	0 (0%)	6 (100%)
Bethesda IV (FN or SFN)	16 (9.8%)	7 (44%)	9 (56%)	0 (0%)	0 (0%)	0 (0%)
Bethesda V (suspicious)	16 (9.8%)	0 (0%)	16 (100%)	0 (0%)	0 (0%)	0 (0%)
Bethesda VI (malignancy)	38 (26.7%)	0 (0%)	38 (100%)	68 (46%)	0 (0%)	68 (100%)

AUS/FLUS, atypia of undetermined significance or a follicular lesion of undetermined significance; CNB, core-needle biopsy; FN/SFN, follicular neoplasm or suspicious for follicular neoplasm; FNB, fine-needle biopsy.

efficacy of CNB as opposed to FNB in sonographically suspect nodules.

The results showed that CNB had a more significant accuracy (95.8%) compared with that of FNB, which had about 75% diagnostic accuracy. CNB is suggested to be able to decrease nondiagnostic results compared with FNB as our study showed calculated sensitivity for malignant nodules of 91.6% compared with 70.8% of FNB and calculated specificity of CNB for malignant nodules of 100% compared with 79.2% of FNB.

Studies in recent literature have shown results that come very close to the results of our study, with the study by Choi *et al.* [9] showing a diagnostic performance of CNB of 98.4% compared with 60.0% of that of repeated FNB. This was also illustrated by Trimboli *et al* [10], who believed that even as an initial diagnostic phase, CNB could be applicable where, according to their report, CNB (97%) outpaced FNB (78%) substantially in terms of diagnostic precision.

When secondary thyroid lymphoma is suggested, CNB is preferable to FNB in several studies, as recommended by Buxey and Serpell [11]; this is consistent with our experience during the current study as we had a single case of secondary thyroid lymphoma that was diagnosed by CNB and had an inconclusive result by FNB.

Despite the fact that there were extremely low false-negative results of CNB with only one false-negative case in our study (5%), this may suggest that FNB/CNB combination may have more effect than the performance of CNB alone, especially in small nodules, that is supported by a previous publication about the high diagnostic accuracy of this combination in malignancy than CNB alone [12].

We suggested that the addition of CNB to FNB may have an effect in reducing the incidence of inconclusive diagnosis with more sensitivity and accuracy in diagnosis than FNB alone. It could lead to a significant decrease in repeated FNB procedures and surgeries (diagnostic and delayed therapeutics). These results agree with many previous studies that focused on the advantage of CNB over FNB, specifically in nodules that have previous nondiagnostic examinations on FNB [13,14].

Ideally, CNB should precede FNB, which was the case in most cases of our study, because an intact tissue component is needed by CNB, while FNB needs a cellular component that can be acquired after the performance of CNB. Because of the repeated to-and-fro motion of the needle, FNB can damage tissue integrity. In addition, the strong spring motion of the CNB needle in a hard calcification may enable certain thyroid nodules with macrocalcifications to collect an appropriate cellular portion in a subsequent FNB procedure. Even so, the nodule that displays prominent vascularity by Doppler US with a higher chance of hemorrhage, CNB, must be followed by FNB [15].

Accordingly, in the present study, we can explain the great sensitivity and correctness of CNB in the diagnosis of thyroid malignancy by the large-caliber CNB needle of 18G. This may increase the advantage of CNB, which is providing larger tissue samples, and increase the ability to an assessment of the histology and relationship with the remaining tissues on pathology. Samir *et al.* [13] stated that, however, their study had shown a significant rate of diagnosis of follicular neoplasm by CNB; there was a difficulty in separation of a cellular hyperplastic nodule from a follicular neoplasm by CNB as well as FNB. Assessment of the complementary role of US-guided CNB in follicular neoplasm diagnosis requires more investigations. In minimally invasive follicular carcinoma, capsular invasion is qualified if there is a full-thickness interruption of the capsule; the tumor expands in a mushroom-like fashion adjacent to the narrow violated segment of the capsule. Capsular rupture is distinguished from capsular invasion by the presence of a fissure-like quality containing foci of recent or old hemorrhage with florid stromal reparative changes [16]. In our experience, there are cheaters for capsular invasion; the capsule is typically thickened and irregular, needs penetration through the capsule (full thickness), and may have a reactive pseudocapsule around the invasion edge; this helps in the exclusion of CNB-site rupture.

Zhang *et al.* [17] stated that although experienced teams had safely performed CNB, some authors are concerned about the safety of the procedure. Some technical aspects of CNB may be recommended to decrease the incidence of complications; good local anesthesia and immediate compression may help to prevent hemorrhage; CNB may have some technical difficulties in certain circumstances, such as small nodules of the gland's posterior margin. CNB had some drawbacks, such as the discomfort of the patients, the requirement for local anesthesia, and the experience in thyroid intervention.

The study was limited by two factors. First, benign diagnosed nodules by FNB and CNB did not have

surgery. So, few nodules read as benign by both FNB and CNB were not proven by surgery and surgical pathology, but were dependent on the follow-up US, which may not be sufficient to exclude slowly-growing thyroid cancer.

Second, the large caliber of the CNB needle used of 18G, although providing sufficient tissue sampling, cannot be used in nodules smaller than one cm in diameter, because the shortest core length of the needle is 1 cm.

In conclusion, in the workup of thyroid nodules, CNB was more accurate for the diagnosis of thyroid malignancy than FNB, and we can suggest that a mixture of FNB/CNB would be more accurate than CNB or FNB alone in thyroid nodules when it is accessible. CNB could have a complementary role in the management of thyroid nodules, especially those categorized as TIRADS 3 or higher on US or when classified as Bethesda III or higher by FNB, and best surgical decision.

Conclusion

CNB was significantly more accurate with a calculated diagnostic accuracy of about 95.8% for the diagnosis of thyroid pathology than FNB, which had about 75% accuracy, according to our study. For suspicious thyroid nodules, according to the data obtained from our work, we suggest that CNB with FNB may reduce the incidence of inconclusive results and produce a more precise diagnosis than FNB alone.

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Conflicts of interest

There are no conflicts of interest.

References

1 Yassa L, Cibas ES, Benson CB, Frates MC, Doubilet PM, Gawande AA, *et al.* Long-term assessment of a multidisciplinary approach to thyroid nodule diagnostic evaluation. Cancer 2007; 111:508–516.

2 Cooper DS. American Thyroid Association (ATA) guidelines taskforce on thyroid nodules and differentiated thyroid cancer. Revised American Thyroid Association management guidelines for patients with thyroid nodules and differentiated thyroid cancer. Thyroid 2009; 19:1167–1214.

3 Bomeli SR, LeBeau SO, Ferris RL. Evaluation of a thyroid nodule. Otolaryngol Clin North Am 2010; 43:229–238.

4 Kiran T, Guler B, Aysan E, Arici DS. Correlation between simultaneous ultrasound-guided fine needle aspiration and core needle biopsy results in thyroid nodules of 44 cases. Diagn Pathol 2017; 2:2024–2476.

5 Yang J, Schnadig V, Logrono R, Wasserman PG. Fine-needle aspiration of thyroid nodules: a study of 4703 patients with histologic and clinical correlations. Cancer 2007; 111:306–315.

6 Nayar R, Ivanovic M. The indeterminate thyroid fine-needle aspiration: experience from an academic center using terminology similar to that proposed in the 2007 National Cancer Institute Thyroid Fine Needle Aspiration State of the Science Conference. Cancer 2009; 117:195–202.

7 Russ G, Bigorgne C, Royer B, Rouxel A, Bienvenu-Perrard M. [The Thyroid Imaging Reporting and Data System (TIRADS) for ultrasound of the thyroid]. J Radiol 2011; 92:701–713.

8 Cibas ES, Ali SZ. The 2017 Bethesda system for reporting thyroid cytopathology. Thyroid 2017; 27:1341–1346.

9 Choi SH, Baek JH, Lee JH, Choi YJ, Hong MJ, Song DE, *et al.* Thyroid nodules with initially non-diagnostic, fine-needle aspiration results: comparison of core-needle biopsy and repeated fine-needle aspiration. Eur Radiol 2014; 24:2819–2826.

10 Trimboli P, Nasrollah N, Guidobaldi L, Taccogna S, Modica DDC, Amendola S, *et al.* The use of core needle biopsy as first-line in diagnosis of thyroid nodules reduces false negative and inconclusive data reported by fine-needle aspiration. World J Surg Oncol 2014; 12:1–6.

11 Buxey K, Serpell J. Importance of core biopsy in the diagnosis of thyroid lymphoma. ANZ J Surg 2012; 82:90.

12 Sung JY, Na DG, Kim KS, Yoo H, Lee H, Kim J, *et al.* Diagnostic accuracy of fine-needle aspiration versus core-needle biopsy for the diagnosis of thyroid malignancy in a clinical cohort. Eur Radiol 2012; 22:1564–1572.

13 Samir AE, Vij A, Seale MK, Desai G, Halpern E, Faquin WC, *et al.* Ultrasound-guided percutaneous thyroid nodule core biopsy: clinical utility in patients with prior nondiagnostic fine-needle aspirate. Thyroid 2012; 22:461–467.

14 Yeon JS, Baek JH, Lim HK, Ha EJ, Kim JK, Song DE, *et al.* Thyroid nodules with initially nondiagnostic cytologic results: the role of core-needle biopsy. Radiology 2013; 268:274–280.

15 Yi KS, Kim J, Na DG, Seo H, Min HS, Won J-K, *et al.* Usefulness of core needle biopsy for thyroid nodules with macrocalcifications: comparison with fine-needle aspiration. Thyroid 2015; 25:657–664.

16 Rosai J. Handling of thyroid follicular patterned lesions. Endocr Pathol 2005; 16:279–283.

17 Zhang S, Ivanovic M, NemcekJr AA, DeFrias DVS, Lucas E, Nayar R. Thin core needle biopsy crush preparations in conjunction with fine-needle aspiration for the evaluation of thyroid nodules: a complementary approach. Cancer 2008; 114:512–518.