Endocr Pathol (2009) 20:204–208
DOI 10.1007/s12022-009-9092-0

Adequacy and Diagnostic Accuracy of Aspiration vs. Capillary Fine Needle Thyroid Biopsies

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Published online: 15 September 2009

Abstract Thyroid nodules can be biopsied by fine needle aspiration (FNA) or fine needle capillary (FNC) biopsies. However, there is controversy on whether one technique is superior to another. In a randomized cytopathologist-blinded cross-sectional study, 260 patients (238 females, age 43.2±12.6) with nodular (82.7%) and diffuse goiter (17.3%) underwent 520 FNAs and 520 FNCs (not guided by ultrasound). Smears were scored for sample adequacy, and diagnosed as malignant, benign, suspicious, or non-diagnostic. Diagnostic accuracy was calculated based on the histological findings of 58 patients submitted to surgery. Intra-technique diagnostic accuracy and sample adequacy was seen in all samples. FNA and FNC provided similar cytological diagnosis, respectively (benign: 75.8% vs. 74.2%, p=0.600; malignant: 3.8% vs. 3.8%, p=0.871; suspicious: 10.4% vs. 10.8%, p=0.913; and nondiagnostic: 10.0% vs. 11.2%, p=0.598). Adequacy scores were similar by FNA (7.94±2.84) and FNC (7.96±2.81, p=0.909). The same proportion of adequate or superior samples was seen in both techniques (91.6%). Sensitivity was equal to 85.7% for FNA and 100% for FNC. Similarly, specificity was 100% for both techniques. FNA and FNC provide the similar sample adequacy and diagnostic accuracy. The choice of technique should be based on the operator's personal preferences and experience.

Keywords aspiration · biopsy · capillary · fine needle · goiter · nodule · thyroid

Introduction

In the management of thyroid nodules, fine needle biopsy is required in the vast majority of cases. Aspiration biopsy was the first method described in the literature [1] and employed in the clinical setting. However, that technique may be frequently complicated by the aspiration of significant quantities of fresh blood, which compromises cellular concentration, preservation, and interpretation [2].

Fine needle capillary (FNC) biopsy is an alternative to fine needle aspiration (FNA) biopsy. That technique is supported by the capillary tension created by a narrow needle, which makes the tissue sample spontaneously ascend to the needle, eliminating the need for active aspiration [2]. This makes the procedure simpler, faster, less expensive, and less traumatic [3, 4]. In addition, the adequacy of the biopsies may increase, since the aspiration of fresh blood is considerably decreased. Combined, these factors can alter accuracy.

In our study, we aimed to evaluate the adequacy of specimens obtained through FNA and FNC. In addition, we aimed to determine the diagnostic accuracy of both techniques.

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Patients and Methods

Patients

This is a randomized cytopathologist-blinded cross-sectional study. Two hundred sixty patients with thyroid diseases requiring cytological diagnosis (238 females, 22 males, age 43.2±12.6) were consecutively selected from the thyroid outpatient clinic of the Hospital de Clínicas da Universidade Federal do Paraná, Curitiba, Brazil. By palpation, 82.7% (n=215) had nodular goiter and 17.3% (n=45) had diffuse goiter. One hundred seventy-two patients were submitted to 2D thyroid ultrasound (US) with a 7.5-MHz transducer (Sonoline, Siemens Corp, New York, NY), and 205 patients underwent ^{131}I scintigraphies (scintillation chamber, Helix), obtained 24 hours after the administration of 100 μCi of ^{131}I. Thyroid function was evaluated by measuring TSH (Abbott Diagnostics, Abbott Park, IL, reference values 0.49–4.67 mU/L, sensitivity 0.006 mU/L, CV≥20%) and free T4 (micro-particle enzyme immunoassay, AxSYM Free T4, Abbott Diagnostics, reference values 0.71–1.85 ng/dl, sensitivity 0.40 ng/dl, CV≥10%). Patients with purely cystic nodules, as well as patients with overt hyperthyroidism, were not included in the study.

Methods

Each participant was submitted to two fine needle aspiration biopsies (FNA) and to two fine needle capillary biopsies of the same nodule (the dominant, in case of multinodular goiter) or area of diffuse goiter. Patients were randomized in groups A (n=118) and B (n=142). Patients in group A were first submitted to FNA, followed by FNC on the same day. Similarly, patients in group B were first submitted to FNC, followed by FNA on the same day.

Each patient had only one nodule (the dominant, in case of multinodular goiter) or one area of diffuse goiter biopsied. Patients with diffuse goiter were submitted to FNA in order to provide cytological data for the diagnosis of diseases such as amyloidosis and lymphocytic thyroiditis. Nodules with increased uptake were biopsied in case of suspicious ultrasound findings, family history of thyroid cancer, and/or previous exposure to radiation to the neck. A total of 520 samples were obtained through FNA, and 520 samples were obtained through FNC.

The biopsies were undertaken with 23-gauge needles with an outer diameter of 0.6 mm. The FNAs were performed with 10-ml syringes attached to a syringe holder, according to the standard technique described elsewhere. The FNCs were obtained by inserting the needle, held between the thumb and forefinger, into the thyroid parenchyma and moving the needle rapidly in and out, until a sample of thyroid tissue ascended spontaneously to the needle by capillarity. All biopsies were performed without anesthesia, under clean conditions, without the guidance of US, and by the same trained investigator. The samples obtained through the biopsies were expressed by a syringe filled with air onto glass slides, and four to six smears were prepared for each biopsy. The slides were air-dried and dyed following the May–Grünwald–Giemsa technique (not on-site).

A different trained investigator analyzed all smears. That investigator was blinded for the technique used for the biopsies. The adequacy of each smear was determined by the scoring system developed by Mair et al. [5]. In that system, the adequacy of the smear is determined by the scoring of five criteria (background of blood or clot, amount of cellular material, degree of cellular degeneration, degree of cellular trauma, and retention of appropriate architecture). Smears with scores between 0 and 2 are categorized as "insufficient for diagnosis", smears with scores between 3 and 6 are categorized as "adequate for diagnosis", and smears with scores between 6 and 10 are categorized as "superior for diagnosis". Each biopsy was also diagnosed as benign, malignant, suspicious (samples with the diagnosis of follicular lesion, Hürtle cell neoplasia, or abundant atypic cells), or nondiagnostic (less than two smears with more than six groups of cells, with more than ten preserved cells).

In case of malignant or suspicious results, or in the presence of local compressive symptoms or cosmetic complaints, patients were referred for surgery. Frozen biopsy was randomly performed in 33 out of the 58 patients submitted to surgery.

Statistical analysis was performed using the SPSS software, Version 10.0 (SPSS Inc., Chicago, IL, USA). The scores obtained by FNA or FNC were compared by the Student paired t test. Sensitivity, specificity, positive predictive value, negative predictive value, accuracy, false positives, and false negatives of each modality of biopsy were also calculated, by using the results obtained through histopathological results from patients submitted to surgery. Two-sided tests were used with $p<0.05$ considered significant.

Table 1 Cytological results of each biopsy

	FNA	FNC	p value
Benign	394 (75.8%)	386 (74.2%)	0.600
Malign	20 (3.8%)	20 (3.8%)	0.871
Suspicious	54 (10.4%)	56 (10.8%)	0.913
Nondiagnostic	52 (10.0%)	58 (11.2%)	0.598

Values shown in absolute numbers (percentages)

Table 2 Mean adequacy scores of the samples obtained by FNA and by FNC

	Mean score		*p* value
	FNA	FNC	
Background of blood or clot	1.39±0.71	1.39±0.72	1.000
Amount of cellular material	1.54±0.68	1.51±0.69	0.480
Degree of cellular degeneration	1.71±0.58	1.72±0.58	0.781
Degree of cellular trauma	1.70±0.61	1.74±0.55	0.267
Retention of appropriate architecture	1.63±0.67	1.58±0.69	0.236
Total score	7.94±2.84	7.96±2.81	0.909

The Ethical Committee of the Hospital de Clínicas of the Universidade Federal do Paraná approved the study and all patients signed an informed consent form.

Results

Among the 172 participants submitted to US, 16 (9.3%) had diffuse goiter and 156 (90.7%) had nodular goiter. Among those patients with nodular goiter, 62.8% had a single nodule and 37.2% had multiple nodules. Considering only the dominant nodules, 64.8% were solid and 35.2% were mixed (cystic-solid).

Among the 205 patients submitted to scintigraphy, 5.4% had nodules with increased uptake, 19% had nodules with normal uptake, and 75.6% had nodules with decreased uptake.

Two biopsies were obtained by each technique, totaling four biopsies per patient. Those two biopsies were concordant between themselves in all cases, regarding sample adequacy and final diagnosis. Aspiration and capillary biopsies conferred similar cytological diagnosis (Table 1).

Among the mixed nodules, nondiagnostic material was obtained in 10.8% of the FNAs, and in 13.0% of the FNCs. Eleven patients had nondiagnostic results, both by FNA and FNC. The diagnosis of malignancy was made by both techniques in the same 10 patients.

The adequacy scores of the samples were similar in the aspiration (7.94±2.84) and the capillary techniques (7.96± 2.81, p=0.909). When the five criteria for sample adequacy were analyzed separately, no differences among both techniques were observed (Table 2).

When the first and the second criteria of the scoring system were combined and analyzed separately, no statistical difference could be seen in both techniques. The mean score obtained by FNA was 2.92±1.32. By FNC, the mean score was 2.90±1.32 (p=0.807).

The combination of the mean scores of the two first criteria were positively correlated with the combination of the mean scores of the third, fourth, and fifth criteria, equally in both techniques (r=0.78, p<0.001)

Both techniques provided samples of superior adequacy (score between 7 and 10) for most of the patients (78.8% and 79.6%, for FNA and FNC, respectively). Conversely, adequate samples (score between 3 and 6) were observed in 13.1% of the aspiration biopsies and in 12.3% of the capillary biopsies. The same proportion of samples insufficient for diagnosis (score between 0 and 2) was obtained by both techniques (8.1%). Therefore, the proportion of adequate or superior samples was the same in both techniques (91.6%).

The mean scores were also similar among both techniques, when analyzed according to the final diagnosis (Table 3).

Histopathological diagnosis was available for 58 patients, who were submitted to surgery due to malignant or suspicious findings in the biopsy, or due to the presence of local compressive symptoms or cosmetic complaints. Among those patients, 33 were submitted to frozen biopsy as well. Table 4 correlates the cytological findings with the surgical results, for FNA and FNC. The sensitivity, specificity, positive predictive value, negative predictive value, accuracy, false positives, and false negatives of FNA, FNC, and frozen biopsy obtained before surgery were calculated by two approaches: by excluding all suspicious

Table 3 Mean adequacy scores of the samples obtained by FNA and by FNC, according to the final diagnosis

	FNA	FNC	*p* value
Lymphocytic thyroiditis	8.43±1.77	8.78±1.79	0.404
Hürtle cell neoplasia	7.96±2.81	8.21±2.41	0.724
Papillary and anaplasic carcinoma	9.30±1.89	9.80±0.63	0.438
Colloid goiter	8.69±1.96	8.69±1.70	1.000

Table 4 Comparison between the cytological findings obtained by FNA and FNC, with the histological results obtained after surgery in 58 patients

Cytological diagnosis	Surgical diagnosis			
	FNA		FNC	
	Negative	Positive	Negative	Positive
Benign	28	1	31	0
Malignant	0	6	0	6
Suspicious	10	8	8	7
Nondiagnostic	4	1	3	3

Values shown in absolute numbers

cytologies from the analysis, and by considering them all as malignants. That approach was chosen due to the loss to follow-up of nine patients with suspicious cytology. In addition, four patients with the cytological diagnosis of malignancy were lost to follow-up. None of those patients were submitted to surgery. Table 5 illustrates those findings, comparing FNA, FNC, and frozen biopsy.

Discussion

In our study, we observed that FNA and FNC provided adequate samples in similar proportions. Furthermore, FNA and FNC had comparable rates of sensitivity, specificity, predictive values, accuracy, false negatives, and false positives.

The adequacy of the thyroid samples obtained through FNA or FNC has been evaluated by previous studies [2–10]. Those studies have shown that FNC provides samples at least as adequate as FNA, with the advantage of being a simpler, faster, and cheaper technique. In addition, FNC provides better perception of the consistency of the tumor and control of the hand [11].

For a reliable cytological diagnosis of a thyroid nodule, the adequacy of the sample is essential, which can be evaluated by the scoring system developed by Mair et al. [5]. When comparing the scores of the samples obtained through FNA and FNC, not only the total scores were similar, but also the individual ones. These results were in discordance with a study showing that FNC provides more cellular samples [8].

In the scoring system, the first and the second criteria are determined exclusively by the biopsy technique, as opposed to the remaining criteria, which also depend on the sample preparation. The separate analysis of first two criteria also showed that FNA and FNC provided samples of similar adequacy, which reinforces the hypothesis that both techniques provide adequate samples.

Mixed nodules are more likely to present nondiagnostic results. Our results suggest that the rate of nondiagnostic biopsies is similar between FNA and FNC.

The biopsies were performed with 23-gauge syringes, following the approach adopted at the Karolinska University Hospital [12]. Although narrower syringes are less traumatic, they can be inadequate for cystic lesions. We chose that caliber because it can be used both for solid and cystic lesions. That decision did not increase our rate of nondiagnostic samples (10.0% to 11.2%), which is in concordance with the literature [13].

Both techniques, FNA and FNC, had similar sensitivity, specificity, positive predictive value, negative predictive value, and accuracy, in concordance with a recent study that evaluated US-guided biopsies [9]. Sensitivity was slightly lower by FNA, despite the fact that both techniques provided samples with similar adequacy. One case of false negative was observed by FNA, evidenced after that patient was submitted to surgery for cosmetic reasons. In addition, FNA and FNC had more favorable results when compared to frozen biopsy. As already shown in the literature, frozen biopsy had very low sensitivity.

Our study has some limitations. The biopsies were not guided by US, which, in theory, may lead to discordant results intra- and inter-technique. However, we have not observed any discordant results intra-technique, and all malignant results were concordant. In addition, a previous study has shown that US-guided FNA and FNC sampling result in comparable diagnostic cytologic adequacy rates [10]. Moreover, we do not think that the heterogeneity of our sample, with some patients without thyroid nodules, is

Table 5 FNA, FNC, and frozen biopsy diagnostic characteristics, based on histological findings of 58 patients

Percentages calculated excluding all suspicious cytologies from the analysis (outside parenthesis), and by considering them all as malignants (inside parenthesis)

	FNA	FNC	Frozen biopsy
Sensitivity	85.7% (93.3%)	100% (100%)	33.3% (50%)
Specificity	100% (73.7%)	100% (79.5%)	100% (88%)
Positive predictive value	100% (58.3%)	100% (61.9%)	100% (57.1%)
Negative predictive value	96.5% (96.6%)	100% (100%)	84.6% (84.6%)
Accuracy	97.1% (79.3%)	100% (84.6%)	85.7% (78.8%)
False negative	14.3% (6.7%)	0% (0%)	66.7% (50.0%)
False positive	0% (26.3%)	0% (0%)	0% (12.0%)

a limitation of our study. In fact, our results suggest that FNA and FNC are equally effective in a broad variety of thyroid diseases. Another weakness of our study is the fact that the analyses of the smears were performed by a single cytopathologist. If the analyses were done by two equally skilled pathologists, our study would be further strengthened.

In conclusion, FNA and FNC equally provide adequate samples for the diagnosis of thyroid diseases. In addition, the diagnostic accuracy of both techniques is similar. Taken these findings into account, both techniques can be used in the clinical setting, and the choice of the technique can be made based on personal preferences.

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