A Comparison Of Fine-Needle Aspiration Versus Non-Aspiration Cytology Of Thyroid Nodules

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Abstract

Background Fine needle aspiration (FNA) is considered the investigation of choice in cytological sampling of thyroid nodules. Non-aspiration fine needle cytology (NAC) has been described as an alternative method with technical and interpretive advantages. This study compares the sampling adequacy and diagnostic accuracy of NAC with FNA in predicting neoplasia and malignancy in thyroid nodules. Methods
Patients presenting to a single surgeon with a thyroid nodule had both NAC and FNA performed. Both NAC and FNA specimens of all those who had subsequent thyroid resection were retrospectively graded and correlated with the histological diagnosis to determine rates of adequacy and diagnostic accuracy. Results Both NAC and FNA plus surgical resection were performed on 65 thyroid nodules. NAC produced less inadequate specimens (26%) than FNA (37%). Combining both techniques reduced the inadequacy rate to 20%. In predicting malignancy, FNA and NAC were equally sensitive (89%) but FNA had higher specificity (66 v 54%) and accuracy (71 v 60%). In predicting neoplasia, FNA again had higher specificity (90 v 77%) and accuracy (85 v 79%) but sensitivity rates were similar (81 v 81%). Conclusion
NAC is a technically simple method of sampling thyroid nodules and appears to produce more adequate specimens. It has similar sensitivity to FNA in predicting neoplasia and therefore surgery. However, FNA appears to have better overall accuracy. In order to maximise yield it may be appropriate to use both sampling methods in the cytological investigation of thyroid nodules.

INTRODUCTION

Fine needle aspiration cytology is a well-established technique in the investigation of soft tissue swellings. It is considered the investigation of choice in assessing thyroid nodules and selecting patients for thyroid resection. Its advantages include minimal invasion and it has been reported to have high sensitivity, specificity and accuracy. Disadvantages, however, include inadequate specimens and cytological interpretation.

An alternative sampling method, non-aspiration fine needle cytology, was developed in France in the 1980s and described in the investigation of thyroid lesions by Santos in 1988[1,2]. Utilising just a needle and capillary pressure to suck cells into the needle lumen, it avoids aspiration and has been reported to overcome the problem of inadequate and bloody specimens obtained from the highly vascular thyroid gland.

The aim of this study was to compare the adequacy of non-aspiration fine needle cytology (NAC) with fine needle aspiration (FNA) and also diagnostic accuracy in predicting neoplasia and malignancy in thyroid nodules.

METHODS

PATIENT SELECTION

All patients with a dominant thyroid nodule attending a single surgeon in a district general hospital had both FNA and NAC performed. The details of all those who subsequently had thyroid resection and definitive histological diagnosis were retrieved and their cytological specimens reviewed.

SAMPLING TECHNIQUE

Sampling was performed either by the consultant surgeon or specialist registrar in the outpatient clinic. Ultrasonic guidance and immediate reporting were unavailable. NAC was performed first using a 23-gauge needle. The needle was passed through the nodule several times but without suction. The needle was then withdrawn and a 20ml syringe attached. The needle contents were then smeared onto slides half of which where air-dried, half alcohol-fixed.

In obtaining the FNA sample a 23 gauge needle was also used but with a 20ml syringe attached mounted on a syringe

holder. Whilst applying suction the needle was passed through the thyroid nodule several times. Negative pressure was released prior to the needle emerging from skin. The aspirate was then smeared onto slides which were prepared as described above.

CYTOLOGICAL INTERPRETATION

A single cytopathologist retrospectively examined both the FNA and NAC slides for each thyroid nodule. The patients' treatment had been completed and was not related to the findings in this study. The cytopathologist was blinded as to which sampling technique had been utilised, the original cytological findings and to the subsequent histological diagnosis. A standard grading system was used in the cytological interpretation of specimen (Table 1).

Figure 1

Table 1 Cytology Grading System

Grade	Cytological Features
C0	No thyroid follicular cells
C1	<6 groups of follicular cells
C2	Benign – >6 groups of follicular cells, no neoplastic features
C3	Equivocal – hyperplastic nodule v follicular neoplasm
C4	Atypia, suspicious of malignancy
C5	Malignant

C0 and C1 are cytologically inadequate. C2 suggests a benign non-neoplastic lesion. C3 is equivocal, suggestive of either a cellular colloid nodule or follicular neoplasm and excision is therefore advised as cytology cannot reliably distinguish between a follicular adenoma and carcinoma. C4 is suspicious of and C5 diagnostic of malignancy. In clinical practice a grading of C3-5 requires thyroid surgery.

STATISTICAL ANALYSIS

Data was collected using a standard spreadsheet. Having been cytologically graded the histological diagnosis for each thyroid nodule was obtained and utilised to compare the diagnostic accuracy of NAC and FNA. Inadequate samples (C0-1) were excluded from the analysis for prediction of malignancy and then prediction of neoplasia.

The sensitivity, specificity and accuracy of both NAC and FNA were then calculated. Sensitivity was defined as the ratio of true positives to the total number of patients with the disease. Specificity was defined as the ratio of true negatives to the total number of patients without the disease. Accuracy was defined as the ratio of true positives plus true negatives to the total number of patients.

RESULTS

PATIENTS

A total of 70 patients with a dominant thyroid nodule had both NAC and FNA performed and underwent subsequent thyroid resection – either lobectomy or total thyroidectomy. Complete data i.e. all NAC and FNA slides and histological diagnosis were obtained for 65 of these 70 patients. Of these, 58 were female (89%) and the age range was 25-78 years with a mean age of 49 years.

HISTOLOGY

The histological diagnoses from the 65 resected specimens were obtained (Table 2).

Figure 2

Table 2 Histological diagnoses

Histological Diagnosis	N(65)	%
Non-neoplastic	**32**	**49.2**
Multinodular goitre	24	36.9
Colloid nodule	3	4.6
Hashimoto's thyroiditis	4	6.2
Multinodular goitre + incidental papillary carcinoma	1	1.5
Neoplastic	**33**	**50.8**
Benign	***24***	***36.9***
Follicular adenoma	20	30.7
Follicular adenoma + incidental papillary carcinoma	2	3.1
Multinodular goitre + incidental Hurthle cell adenoma	1	1.5
Thyroiditis + incidental Hurthle cell adenoma	1	1.5
Malignant	***9***	***13.8***
Papillary carcinoma	5	7.7
Follicular carcinoma	3	4.6
Medullary carcinoma	1	1.5

For the 2 patients with an incidental Hurthle cell adenoma (not the dominant nodule), the histology was considered non-neoplastic for correlation with the cytology. Two patients had a follicular adenoma with an incidental papillary microcarcinoma. In these cases, for correlation with cytology, the histological diagnosis was considered neoplastic and benign whilst for the patient who had an incidental papillary carcinoma with a multinodular goitre, the histology was considered as non-neoplastic.

ADEQUACY

Samples graded C0 or C1 were considered inadequate. These samples had insufficient cellular material for cytological diagnosis. Of the 65 NAC samples obtained, 17 (26%) were inadequate compared with 24 (37%) of FNA samples. Combining both techniques, the inadequacy rate

was reduced to 20% (13/65). Table 3 summarises the histological diagnosis of the inadequate samples.

Figure 3

Table 3 Histological diagnosis of inadequate cytology specimens

Diagnosis	N
NAC	**17**
Multinodular goitre	9
Follicular adenoma	5
Colloid nodule	2
Hashimoto's thyroiditis	1
FNA	**24**
Multinodular Goitre	10
Follicular adenoma	8
Follicular adenoma with incidental papillary carcinoma	2
Colloid nodule	2
Hashimoto's thyroiditis	1
Multinodular goitre with incidental Hurthle cell adenoma	1

Of the inadequate NAC samples, 20.4% were neoplastic. 41.7% of the inadequate FNA samples were neoplastic on histology but there were 2 incidental malignancies amongst the 10 neoplasms.

DIAGNOSTIC ACCURACY

Table 4 demonstrates the correlation between the cytological and histological findings in the adequate specimens.

Figure 4

Table 4 Cytological and histological findings

	Histological Diagnosis			
C Grade	NAC (N=48)		FNA (N=41)	
	Non-Neoplastic	*Neoplastic*	*Non-Neoplastic*	*Neoplastic*
C2 Non-neoplastic	17	5	18	4
C3 Possible neoplasia	5	16	1	14
C4/5 Suspicious of Malignancy / Malignant	0	5	1	3

In the NAC specimens, 80% of malignancies were classified as neoplastic or malignant (C3-5); 76% of the follicular adenomas were neoplastic on NAC and 77% of non-neoplastic lesions were correctly classified as C2.

In the FNA specimens, 89% of malignancies were classified as neoplastic or malignant; 75% of follicular adenomas were classified neoplastic and 90% of non-neoplastic nodules were correctly classified as C2. One false positive was obtained with a non-neoplastic multinodular goitre classified as possibly malignant.

Table 5 summarises the statistical findings in comparing NAC and FNA in the prediction of malignancy and neoplasia.

Figure 5

Table 5 Prediction of malignancy and neoplasia

	Prediction of Malignancy		Prediction of Neoplasia	
	NAC (%)	FNA (%)	NAC (%)	FNA (%)
Sensitivity	88.9	88.9	80.8	81.0
Specificity	53.8	65.6	77.3	90.0
Accuracy	60.4	70.7	79.2	85.4
Negative Predictive Value	95.5	95.5	77.3	81.8
Positive Predictive Value	30.8	42.1	80.8	89.5
False Negative Rate	2.1	2.4	10.4	9.8

DISCUSSION

Fine needle aspiration cytology has been established as the gold standard in the investigation of thyroid swellings. It is a simple, safe, cost-effective technique with a low complication rate which facilitates diagnosis and surgical planning. It has been described as minimally invasive and reported to have a high sensitivity, specificity and overall accuracy[3]. However, it has well-recognised limitations which include inadequate specimens requiring repeated aspirations[4]. As the thyroid gland is highly vascular, samples can contain significant quantities of blood and inferior quality cellular material thus compromising cytological interpretation and diagnostic accuracy.

Santos and Leiman in 1988 first described the use of non-aspiration cytology in thyroid lesions[2]. Several terms have been used to describe the technique - cytopuncture, non-aspiration cytology, fine-needle non-aspiration, fine needle sampling and fine-needle capillary sampling[5]. Whilst sharing many of the advantages of FNA, it was reported that, in not applying suction, NAC was less traumatic, producing less bloody and higher quality smears. Other reported advantages include an enhanced appreciation of the lesion being sampled and less pain in comparison with FNA[6,7].

This study compared the adequacy of the two techniques based on the cytological scoring system listed in Table1. C0 or C1 samples contained insufficient or no cellular material and were thus deemed inadequate. In this study NAC had a lower inadequate rate compared with FNA (26% and 37% respectively). This may be explained by the absence of traumatic suction with less blood and more architecturally

intact cells.

Of the inadequate NAC and FNA samples, 100% had a benign histological diagnosis, though 2 incidental malignancies were identified in the resected specimen. . Although nodules which produce smears of low cellularity are unlikely to be malignant, repeat sampling or biopsy should be performed.

23.5% of nodules with inadequate NAC samples had an adequate FNA compared with 45.8% of inadequate FNA samples which had an adequate NAC. Of the total of 65 thyroid nodules sampled, 13 (20%) had inadequate samples with both cytological techniques. Therefore utilising both techniques produced an overall higher yield of adequate cellular material.

Published data report inadequate FNA sample rates of 9-31%[8]. Adequacy rates have been influenced by the number and experience of the aspirators and the criteria used to define a satisfactory sample.

Several studies have compared the adequacy of NAC with FNA utilising scoring systems with both qualitative and quantitative criteria to grade samples. Some have used descriptions of cellular architecture whilst the amount of cellular material obtained has been compared by others[9-13]. NAC has been reported to produce diagnostically superior yields and less 'unsuitable' specimens with FNA producing more cellular though overall inferior material. A recent meta-analysis, however, concluded that there was no difference in the quality of specimen obtained by either technique[5].

Both FNA and NAC are aspirator-dependent with lower inadequate rates obtained with single rather than multiple aspirators. Lower rates may also be obtained if the cytopathologist who subsequently examines the specimen obtains the cytology specimen. The use of ultrasound guidance also can also reduce inadequacy rates[13,14].

This study also compared the diagnostic accuracy of NAC with FNA. In predicting malignancy, sensitivities were equal (88.9%) though FNA had a higher specificity and accuracy compared with NAC. The false negative rates were similar. The interpretation of the equivocal category (C3) impacts on the calculation of sensitivity and specificity. In this study, C3 specimens were included in the prediction of malignancy thus increasing sensitivity, but the high false positive rates due to benign neoplasia decreased specificity and positive predictive values.

The prediction of neoplasia is of more use in clinical practice as thyroid neoplasia is an indication for surgery due to the inability of cytology to differentiate between follicular adenoma and follicular carcinoma. Here, the sensitivities of NAC and FNA were similar (80.8 and 81%, respectively) and comparable with studies of thyroid FNA (78.4-86%)[3,15,16]. FNA had a higher specificity (90 v 77.3%) and accuracy (85.4 v 79.2%). Just one other study was found which compared the diagnostic accuracy of NAC with FNA (88.9 and 75% respectively)[12]. However, it was unclear whether this was in prediction of malignancy or neoplasia.

CONCLUSION

Both FNA and NAC are recognised methods of obtaining cellular material in the investigation of thyroid nodules. NAC is technically easier to learn and perform and may produce more adequate and better quality samples. In predicting neoplasia and therefore the need for surgery, it has similar sensitivity to FNA. However, FNA appears to have overall better accuracy. In order to maximise yield it may be appropriate to use both sampling methods in patients undergoing cytological investigation of thyroid nodules, particularly if radiological guidance and immediate cytological examination are unavailable.

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