

## ORIGINAL ARTICLE

# THE IMPACT OF SYNOPTIC CYTOLOGY REPORTING ON FINE-NEEDLE ASPIRATION CYTOLOGY OF THYROID NODULES

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**Background:** Fine-needle aspiration cytology (FNAC) is integral to the diagnosis and management of patients with thyroid nodules. We introduced synoptic cytology reporting for thyroid nodules in 2004. The aim of this study was to examine the effect of synoptic cytology reporting in our institution.

**Methods:** A comparative study of two 2-year periods (1 August 2002 to 1 August 2004 and 2 August 2004 to 2 August 2006) before and after the introduction of synoptic reporting was conducted from a prospectively collected database of patients presented with thyroid nodules. The only change during these periods was the format of FNAC reporting. We used the same radiological practice and cytopathology service throughout the study period. All patients are still being followed up.

**Results:** There were a total of 660 patients. Of these, 376 were operated and 284 non-operated. The female to male ratio was 7:1. Comparing the two periods, the overall FNAC sensitivities were 60% versus 79.1%; specificities, 83.7% versus 79.4%; accuracy, 76% versus 79.3%; false-positive result, 16.3% versus 20.6% and false-negative result, 40% versus 20.9%. The non-diagnostic rates were 7.4% versus 3.15%. FNAC prompted surgery in 66.7% versus 100% in carcinoma and 56.4% versus 73.6% in adenoma. A benign FNAC prompted surgery in 15% versus 19.8% of cases. There was no thyroid cancer detected in the current follow up.

**Conclusions:** Synoptic cytology reporting has resulted in an overall improvement in all measures of the tests. It is a simple and effective tool to use. Synoptic cytology reporting is therefore recommended for all endocrine surgical units.

**Key words:** fine-needle aspiration cytology, nodule, sensitivity, synoptic reporting, thyroidectomy.

Abbreviations: FNAC, fine-needle aspiration cytology; LR, likelihood ratio; NPV, negative predictive value; PPV, positive predictive value; US, ultrasound.

## INTRODUCTION

Thyroid nodules are common. They are clinically detected in up to 50% of the elderly population, especially when ultrasound (US) is used.<sup>1,2</sup> The majority of thyroid nodules are benign. In Victoria, 305 cases of thyroid carcinoma were detected in 2004, an increase from previous reporting of thyroid cancer.<sup>3,4</sup> Thyroid cancer predominantly affects females, with a ratio of 3:1.<sup>5</sup> As such, it is important to be able to decide which nodules require surgical excision and which can be followed up conservatively. Fine-needle aspiration cytology (FNAC) is well established as a first-line test in the evaluation of patients with a thyroid nodule, in terms of cost effectiveness and accuracy.<sup>6,7–14</sup> However, the reporting of thyroid FNAC has been very confusing. This is in large because of the fact that no definitive cytological features separate malignant from benign follicular lesions.<sup>2,15</sup> Follicular lesions in particular are malignant in up to 20% of the cases.<sup>2,16</sup>

Various reporting formats of thyroid FNAC are described in published works. Different reporting formats are used by different institutions and cytopathologists. However, many FNAC reports

do not clearly identify inadequate, benign and malignant subgroups or comment on the important features of clinical significance that determine management.<sup>17</sup> Patient management would therefore benefit from a standardized approach of thyroid FNAC reporting.<sup>18</sup>

At Frankston Hospital, synoptic reporting of thyroid FNAC was introduced in August 2004 after careful collaboration between the Endocrine Surgical Unit and the cytopathologists. This study was carried out to examine the effect of synoptic cytology reporting on FNAC of thyroid nodules.

## PATIENTS AND METHODS

A comparative study of 2 years (1 August 2002 to 1 August 2004 and 2 August 2004 to 2 August 2006) before and after introduction of synoptic cytology reporting was conducted from a prospectively collected database of patients presented with thyroid nodules. We used the same radiological practice and cytopathology service throughout the study period. Both the radiologists and cytopathologists were aware of the data collection since the database's being set up in 1998. All data were analysed and calculated with Microsoft excel.

From the database, 410 diagnostic FNAC in 376 patients who had definitive thyroid histology after surgery were identified. These were from a series of 660 consecutive thyroid patients referred to an endocrine surgeon (J. W. S.) from 2002 to 2006. The comprehensive database was designed using FileMaker Pro

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(FileMaker, Santa Clara, CA, USA), and details from demographic were entered prospectively. The data recorded include patient details, clinical features and investigation including FNAC results, surgery and histology. The cytology results before 2 August 2004 were summarized in these five groups: 'malignant' (malignant, papillary carcinoma), 'suspicious for malignancy', 'inconclusive' (follicular cells, follicular neoplasm or Hurthle cell neoplasm), 'non-neoplastic' (included colloid mixed with follicular cells, cysts) and 'non-diagnostic'. These five groups were created to simplify the previous reporting format (which had multiple categories) for the ease of comparison with the second period. The FNAC results after 1 August 2004 were reported as shown in Figure 1. Each category is referred to by a numeric number. In the new reporting system, the 'inconclusive' group from previous period is termed 'indeterminate'. It is our standard practice to have two cytopathologists analyse the FNAC before a report was produced. The sensitivity, specificity, accuracy and positive and negative predictive values (PPV and NPV) of FNAC were calculated in diagnosing thyroid neoplasms. Statistical analysis was carried out using the  $\chi^2$ -squared test. A positive cytology result was one for which thyroidectomy was necessary ('malignant', 'suspicious for malignancy' or 'inconclusive' (follicular or Hurthle cell neoplasm)).<sup>2,6</sup> All FNAC were carried out under US guidance. A pathologist was present to ascertain adequacy of the sample, and if at the time thought not to be adequate, a second or more samples were taken.<sup>19-22</sup>

## RESULTS

Of 660 patients in the 4-year period, there were 376 operated on and 284 non-operative. There were 410 preoperative diagnostic FNAC and postoperative histology. The female to male ratio was 7:1. The average age was older in male versus female in both periods (60 vs 52 years and 57 vs 53 years).

Table 1 correlates cytology with histology in the patients between 1 August 2002 to 1 August 2004. There were 15 FNAC of 13 patients with invasive thyroid cancer, namely papillary ( $n = 4$ ), follicular ( $n = 7$ ) and medullary ( $n = 2$ ). Using FNAC

as a diagnostic test, the cytology prompted surgery in 10/15 (66.7%) aspirates. There were 55 FNAC of 49 patients with thyroid adenoma, namely follicular ( $n = 46$ ) and Hurthle cell ( $n = 3$ ). Cytology prompted surgery in only 32/55 (58.2%). There were 147 FNAC of 134 patients with non-neoplastic conditions of the thyroid gland; all had some form of nodular goitre (varying from a simple multinodular goitre to an adenomatous or hyperplastic nodule). Cytology prompted surgery in 22/147 (15%) by indicating a false-positive 'inconclusive' or 'suspicious for malignancy' results, but these were subsequently found to be non-neoplastic after histology. Table 2 correlates cytology with histology in the patients in the period 2 August 2002 to 2 August 2004. There were 14 FNAC of 14 patients with invasive thyroid cancer, namely papillary ( $n = 11$ ), follicular ( $n = 2$ ) and medullary ( $n = 1$ ). Cytology prompted surgery in 14/14 (100%). There were 53 FNAC of 38 patients with thyroid adenoma, namely follicular ( $n = 34$ ), Hurthle cell ( $n = 3$ ) and papillary ( $n = 1$ ). Cytology prompted surgery in only 39/53 (73.6%). There were 126 FNAC of 117 patients with non-neoplastic conditions of the thyroid gland. Cytology prompted surgery in 25/126 (19.8%).

The data were dichotomized (Table 3) assuming the clinical algorithm that a positive cytology is one that prompts thyroidectomy (malignant, suspicious for malignancy or indeterminate – follicular). Table 4 shows the overall value of FNAC diagnosing thyroid tumour of the two periods (2002–2004 vs 2004–2006). The sensitivities were 60 versus 79.1%; specificities, 83.7 versus 79.4%; PPV, 63.6 versus 67.1%; NPV, 81.5 versus 87.7% and accuracy, 76 versus 79.3%.

For each cytology result, the likelihood ratio (LR) has been calculated (Tables 4,5). A 'malignant' FNAC has an infinite LR+, indicating that the test is virtually conclusive that the patient has a thyroid neoplasm. There were no false-positive 'malignant' FNAC (specificity 100.0%) in either period. A 'suspicious for malignancy' and 'inconclusive/indeterminate' FNAC have LR+ of 3.15 versus 1.88 and 3.34 versus 2.98, respectively, for the two periods, indicating an increased pretest to post-test probability that the patient has a thyroid neoplasm. A 'non-neoplastic' FNAC has low LR+, 0.39 versus 0.26.

Category	Cytology	Implication
1. Non-diagnostic	Inadequate material	Repeat
2. Benign	Colloid or hyperplastic (adenomatous) nodule Thyroiditis	Observe
3. Indeterminate follicular lesion	(a) Favour colloid/hyperplastic nodule over follicular neoplasm	Decision based on correlation of cytology, clinical and radiological findings
	(b) Follicular lesion – NOS	Remove
	(c) Favour follicular neoplasm over hyperplastic nodule	Remove
	(d) Consistent with follicular neoplasm	Remove
4. Suspicious	Usually papillary carcinoma	Remove
5. Malignant	Carcinoma Lymphoma ? Metastasis	Remove

**Fig. 1.** Synoptic reporting format in Frankston Hospital for thyroid fine-needle aspiration cytology.

**Table 1.** Correlation between cytology and histology 2002–2004

Cytology	Histology (n)			Total
	Carcinoma	Adenoma	Non-neoplastic	
Malignant	4	0	0	4
Suspicious	1	2	2	5
Inconclusive	5	30	22	57
Non-neoplastic	4	17	114	135
Non-diagnostic	1	6	9	16
Total	15	55	147	217

**Table 2.** Correlation between cytology and histology 2004–2006

Cytology category	Histology (n)			Total
	Carcinoma	Adenoma	Non-neoplastic	
5	12	1	0	13
4	1	1	2	4
3	1	37	24	62
2	0	13	95	108
1	0	1	5	6
Total	14	53	126	193

**Table 3.** Overall performance of fine-needle aspiration cytology in diagnosing thyroid neoplasm

Cytology	Histology (n)		Total
	Neoplastic	Non-neoplastic	
2002–2004			
Neoplastic	42	24	66
Non-neoplastic	28	123	151
Subtotal	70	147	217
2004–2006			
Neoplastic	53	26	79
Non-neoplastic	14	100	114
Subtotal	67	126	193

**Table 4.** Overall fine-needle aspiration cytology performance

	2002–2004	95% CI	2004–2006	95% CI
Sensitivity (%)	60.0	49–71	79.1	69–89
Specificity (%)	83.7	78–90	79.4	72–86
PPV (%)	63.6	52–75	67.1	57–77
NPV (%)	81.5	75–88	87.7	82–94
Accuracy (%)	76.0		79.3	
False +ve (%)	16.3		20.6	
False –ve (%)	40.0		20.9	
LR+	3.68	2.34–5.55	3.83	2.66–5.52
LR–	0.48	0.36–0.64	0.26	0.16–0.42
Prevalence (%)	32.26	26–38	35.0	28–41

CI, confidence interval; LR, likelihood ratio; NPV, negative predictive value; PPV, positive predictive value.

Non-neoplastic histology was found in 22/57 versus 24/62 ‘inconclusive’ FNAC, and 21/135 versus 13/108 ‘non-neoplastic’ FNAC were found to be adenoma ( $n = 17$  vs 13) or carcinoma ( $n = 4$  vs 0) (Tables 1,2).

Therefore ‘non-neoplastic’ FNAC did little to alter the pretest probability of the presence of thyroid neoplasm. The LR– for all

**Table 5.** Positive and negative LR for each fine-needle aspiration cytology result

Cytology	Histology (n)		LR+	LR–
	Neoplastic	Non-neoplastic		
2002–2004				
Malignant	4	0	$\infty$	0.94
Suspicious	3	2	3.15	0.97
Inconclusive	35	22	3.34	0.59
Non-neoplastic	21	114	0.39	3.12
Non-diagnostic	7	9	1.63	0.96
2004–2006				
5	13	0	$\infty$	0.81
4	2	2	1.88	0.99
3	38	24	2.98	0.53
2	13	95	0.26	3.28
1	1	5	0.38	1.03

LR, likelihood ratios.

cytology results except ‘non-neoplastic’ are between 0.53 and 1.03, indicating little change from pretest probability of the absence of thyroid neoplasm. LR– of 3.12 versus 3.28 were found for ‘non-neoplastic’ cytology, which indicated that it would be hazardous to rule out a neoplastic thyroid nodule based on this test alone. In other words, FNAC has a significant number of false-negative results, and this was predominantly seen in those patients with histologically proven adenoma; 17/55 (31%) versus 13/53 (25%) FNAC were ‘non-neoplastic’ (Tables 1,2).

The non-diagnostic rates were 7.4 versus 3.1%. The total rate of surgery was reduced by 2.7% from 58.3 (197/338) to 55.6% (179/322). All the patients are still being actively followed up with no missed thyroid neoplasms.

## DISCUSSION

In this study, the overall performance in the second period (2004–2006) has improved in terms of sensitivity, accuracy and in particular the overall false-negative rate (40 vs 20.9%). The non-diagnostic rate has decreased from 7.4 to 3.1%. The rate of surgery was reduced by 2.7%. It has to be clear that the only change that was made during the two period studied was the introduction of synoptic cytology reporting in August 2004. We have been using a specific radiological practice to obtain the FNAC specimens and a specific team of cytopathologists to analyse the aspirates. It has been a standard practice of our unit to hold a regular endocrine meeting for reviewing the final histology and discuss management of patients. These practices were constant for the two periods. FNAC accuracy will improve not only with image guidance but also with more experienced operator.<sup>6</sup> Synoptic reporting encouraged the cytopathologist to reach a more conclusive and consistent diagnosis with more consistent terms.

An ideal diagnostic strategy for thyroid nodules should positively identify all thyroid carcinomas and avoid unnecessary surgery for benign diseases. FNAC of the thyroid is used principally as a triage procedure for this purpose.<sup>4</sup> Synoptic reporting of FNAC is intended to achieve a comprehensive diagnosis of thyroid lesions with confidence.

Our earlier FNAC reporting had no defined categories, and the results could be confusing for those unfamiliar with thyroid cytology. The cytological findings included ‘non-diagnostic – cystic/solid’, ‘benign cyst’, ‘colloid nodule’, ‘colloid and follicular cells’, ‘follicular cells’, ‘suspicious for cancer’ and clearly

malignant lesions, such as 'follicular neoplasm', 'lymphoma' and 'papillary carcinoma'. However, the synoptic cytology reporting divided the FNAC into five diagnostic groups: 'non-diagnostic', 'benign', 'indeterminate follicular lesion', 'suspicious' and 'malignant'. Each category comprises cytological findings accompanied with their implications, followed by a recommendation for management (See Fig. 1). The five-category synoptic reporting format enables the cytopathologist to clearly communicate complex and varied findings to the surgeon, providing the relevant information in more consistent categories. These reports thus can be used more effectively for audits and comparison of results between different laboratories. It also reduces the time spent by clerical staffs in chasing ambiguous reports.

In the presynoptic reporting format, 'Hürthle cell neoplasm' was a category by itself apart from follicular lesions. The diagnosis of Hürthle cell neoplasm and follicular neoplasm in general relies on somewhat different features, but the clinical implications for the two are similar.<sup>15</sup> Therefore, it is not deemed necessary to include a separate category for Hürthle cell neoplasm in the synoptic reporting format.

The 'follicular' or 'indeterminate' is the most difficult category to interpret with confidence.<sup>2,16</sup> Synoptic reporting further stratifies follicular lesions into four different risk categories. This caters to the inherent limitation of thyroid FNAC, which is its inability to separate malignant from benign follicular lesions, which depends on capsular and vascular invasion that can only be assessed on histology. Therefore, cytopathologists rely on other features, such as amount of colloid and architectural arrangement of follicular cells to assess the cancer risk of follicular lesions. The evaluation of these features lack reproducible criteria and tend to be subjective, arbitrary and subject to the individual cytopathologist's experience.<sup>7</sup> Further dividing follicular lesions into four risk categories makes the reporting more consistent.

Correlation with clinical findings helps decide further management plan for the 'indeterminate' and 'suspicious' findings. FNAC, a clinicocytological diagnosis, is part of the triple assessment (i.e. clinical examination, thyroid function test and FNAC) for thyroid nodules. Hence, correlation with clinical findings is mandatory for success. It is best handled in a multidisciplinary setting with experienced cytopathologists and dedicated surgeons. It has always been our unit's policy to have endocrine meetings on a fortnightly basis. The endocrine surgical unit, cytopathologists and the endocrinology team are present at these meetings. We review and discuss the cytological findings together with patients' symptoms and risk factors for thyroid carcinoma during the meetings. High-risk factors for cancer include age (>60 year), sex (male), large size (>4 cm), rapidity of growth, rock hard texture of the nodule, vocal cord paralysis, previous exposure to radiation, family history of medullary thyroid carcinoma and growth during adequate thyroxine suppression.<sup>4,6</sup> Management plan also takes the patients' request into consideration, such as cosmetic factors. If necessary, repeat aspirations will be carried out. Aspirates from multiple sites of the nodule(s) are more likely to provide representative cytological results than are several smears from a single aspirate.<sup>8</sup>

An important cause of non-diagnostic or inadequate specimen reports is a scanty or acellular sample as a result of sampling error or interpretation mistakes. Sampling error often occurs with cystic or vascular lesions. Examining cystic fluid, biopsy of the cyst wall or repeat biopsy will produce more satisfactory results.<sup>8,9</sup> Sampling error is also greater in larger (>4 cm) and smaller (<1 cm) nodules, where lesion is missed with sample containing normal

thyroid architecture.<sup>8</sup> This can be minimized with aspiration under image guidance.<sup>6,10</sup> In our institution, all FNAC are carried out under US guidance, with one designated radiologist as the aspirator, in the presence of a cytopathologist. With an on-site cytopathologist, the adequacy of samples can be determined correctly, hence allowing minimal numbers of attempts to ensure patient comfort. Also, an on-site cytopathologist can often provide a preliminary report of aspirates, and thus an immediate preliminary diagnosis can be provided. In the majority of cases, a final report is issued within 24 h of the receipt of aspirate specimen. Rapid reporting is one of the important assets of FNA. Timely communication relieves patient anxiety, obviates further unnecessary investigations, shortens or eliminates the hospital stay and ensures prompt therapeutic action.<sup>3</sup>

Interpretation mistakes can occur, which will result in false-positive and false-negative errors. False-negative errors are more significant because they imply missed malignant lesions. On average, only approximately 5% of patients with benign cytological findings underwent thyroid surgery.<sup>8,10</sup> A possible solution is to carry out histological examination on every patient undergoing FNAC. This, however, may not be accepted because of its invasiveness, potential procedural complications and a significant increase in health-care costs. Another way of evaluating missed malignancies is by putting patients with negative cytological results on follow-up plans. This involves checking on progress of nodules and patient's symptoms over a fixed number of years with comparison and correlation to further investigations. Other solutions include evaluation of discrepant cytological and histological findings, communication on ambiguous results with surgeons and cytopathologists and improving imaging guidance and tools for sampling as discussed.

## CONCLUSION

With the introduction of synoptic reporting since 2004 in our institution, there has been an overall improvement in all aspects. It is simple to understand with a respectable result without substantial changes in a surgeon's practice. It is therefore recommended for all endocrine units.

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