

Accuracy of Fine Needle Aspiration Cytology in Solitary or Dominant Nodular Goitre: A Single Centre Study

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ABSTRACT

Background: Thyroid swelling or goitre is a common condition, either asymptomatic or symptomatic. The diagnosis is usually established by ultrasound or fine needle aspiration cytology (FNAC) as a gold standard. The sensitivity of the test is inversely related to increasing size of the nodule. The objective of this study is to evaluate the accuracy of FNAC especially in cases of large goitre. **Material and methods:** This is a retrospective study on patients who underwent thyroidectomy between January 2000 to December 2007 for solitary or dominant nodular goitre. The analysis was made only on those patients with complete data on FNAC and histology. **Result:** There were 235 patients, but only 161 patients were analysed after excluding the suspicious and inadequate sample. The patients' mean age was 42.1 year old (21 to 60). The size of the thyroid nodule ranged from 2.1 to 5.0 cm (mean = 3.9 cm). The overall sensitivity was 67.4% and the overall accuracy was 86.3%. The accuracy of FNAC according to the sizes above and below the value were as follows; 2 cm (72.2% vs. 88.1%); 3 cm (88.0% vs. 87.4%) ; 4 cm (86.6% vs. 84.4%) ; 5 cm (87.3% vs. 78.8%). This was most obvious in the sensitivity of the FNA which also showed reducing trend as the nodules increased in size. **Conclusion:** FNAC is an essential diagnostic tool in the management of nodular goitre. Our study showed that the accuracy of FNAC decreased as the size of the nodule getting bigger. Cautious approach should be taken in the management of large goitre and decision should not be based only on the result of FNAC.

KEYWORDS: thyroid, goitre, cytology, biopsy, aspiration

INTRODUCTION

Fine needle aspiration cytology (FNAC) is an established procedure and frequently been used as the first line investigation for thyroid nodules or any lumps occurring anywhere in the body. The procedure is least invasive and has become the gold standard tool for the diagnosis of palpable lesions especially in the neck. Recently, a diagnostic ultrasound of the thyroid before biopsy has changed the management of thyroid diseases. Suspicious features on ultrasound will guide the operator to the area to be biopsied and this improved the accuracy of the biopsy.¹ Unfortunately, it becomes very useful only when a positive result is obtained. In the presence of a negative result or benign condition, the predictive value decreases

significantly.²⁻⁷ Study by Carillo et al showed that false negative of FNAC was clinically significant when the size of the thyroid nodule was more than 4 cm.² Looking at the risk of malignancy in large goitre, Brucanardi et.al found a 15% incidence of malignancy, hence recommended thyroid lobectomy for cysts greater than 4 cm in diameter and complex cysts with solid and cystic components.⁶

Therefore, the objective of this study is to evaluate the sensitivity of FNAC in detecting malignancy in nodular thyroid goitre in patient who had undergone surgery at the Universiti Kebangsaan Malaysia Medical Centre (UKMMC) from year January 2000 to December 2007.

METHODOLOGY

This is a retrospective study on all patients with solitary or dominant thyroid nodule who underwent thyroid surgery at the Surgical Department, UKMMC from January 2000 to December 2007. Data were collected from the hospital computer system and analysis was performed only on patients with complete histopathology report (HPE) and fine needle aspiration cytology (FNAC), either standard free hand or ultrasound-guided. The procedure was performed by trainees in pathology and read by cytopathologist. When there was more than one

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biopsy taken, only the latest FNAC was taken for analysis. Other parameters collected were gender, age and histological size (diameter) of largest nodule. Size of nodule taken was the size reported on gross specimen for histopathological examination.

RESULTS

There were 403 patients who had a form of thyroid surgery in UKM Medical Centre from year 2000 until 2007 for various indications. Eighty patients (19.9%) were diagnosed with thyroid cancer (Table 1). Only 235 (58.3%) patients had FNAC prior to the operation and available for analysis. Majority (86%) of the patients were female. Sixty five percents of the patient were between 41 to 50 years old. Malay ethnic patients formed the majority of the patients consisting of 151 patients (64.3%), followed by Chinese 67 patients (28.5%) and Indians 16 patients (6.8%). The mean size of the tumour was 3.9 cm with 85% of patients having a solitary or dominant thyroid nodule larger than 2 cm.

Two hundred and thirty five patients underwent FNA with 124 patients (52.8%) having benign result.

Table 1. General clinical characteristic distribution of study population

	Variables	Total (N=235)	%
Gender	Male	33	14.04
	Female	202	85.96
Age (years)	≤20	12	5.11
	21-30	41	17.45
	31-40	54	22.98
	41-50	65	27.66
	51-60	36	15.32
	61-70	23	9.79
	≥71	4	1.70
Ethnicity	Malay	151	64.26
	Chinese	67	28.51
	Indian	16	6.81
	Others	1	0.43
Size of largest or dominant nodule (cm)	≤ 1.0	4	1.70
	1.1-2.0	30	12.77
	2.1-3.0	66	28.09
	3.1-4.0	46	19.57
	4.1-5.0	46	19.57
	5.1-6.0	25	10.64
	6.1-7.0	7	2.98
7.1-8.0	7	2.98	
≥ 8.1	4	1.70	

Thirty seven patients (15.7%) were reported as malignant, 60 patients (25.5%) suspicious and 14 patients (6.0%) had inadequate sampling. Table 2

showed the distributions of FNAC compared to the histopathology examination (HPE) report.

Amongst the patient with benign FNAC (n=124), 11.3% (n=14) had malignant thyroid cancer on histology. Out of 37 patient who had malignant FNAC sampling, 21.6%(n=8) had benign disease on their final histology.

Table 2: Distribution of FNAC and Histopathology Examination(HPE) result

		HPE		Total
		Benign	Malignant	
FNAC	Benign	110	14	124 (52.8%)
	Inadequate	13	1	14 (6.0%)
	Suspicious	46	14	60 (25.5%)
	Malignant	8	29	37 (15.7%)
	Total	177	58	235

Table 3 shows the result of the analysis after the exclusion of suspicious and inadequate FNAC (n=161). In this group of patients, 23% had malignant FNAC with 77% had benign FNAC. With this finding, the sensitivity of the FNAC was 67.44% with specificity of 93.2%. False positive rate was 6.8%, false negative of 32.6% and the accuracy of 86.3%.

The analysis was further performed by grouping them according to the size of the nodule. The sensitivity, specificity, false-positive, false negative, accuracy, positive predictive value and negative predictive value were further calculated. Table 4 showed that the sensitivity of FNA reduced with increasing size of the thyroid nodule. Similarly, the negative predictive value also reduced dramatically with the increasing size of the thyroid nodule.

Table 3: FNAC compared to HPE and the predictive values (n=161)
(Suspicious and inadequate FNAC were excluded)

		HPE		Total
		Malignant (positive)	Benign (negative)	
FNAC	Malignant (positive)	29	8	37
	Benign (negative)	14	110	124
	Total	43	118	161

Sensitivity, 29/43 (67.44%); specificity, 110/118 (93.22%); false-positive, 8/118(6.78%); false-negative, 14/43 (32.56%); and accuracy 139/161 (86.34%).

Table 4: Sensitivity, Specificity and Predictive Value of FNAC at different nodule size

Size (cm)	FNAC benign (N=124)		FNAC Malignant (n=37)		Sensitivity	Specificity	Negative predictive value	Positive predictive value	Accuracy
	HPE benign n=110	HPE malignant n=14	HPE malignant n=29	HPE benign n=8					
< 2	7	2	6	3	0.75	0.70	0.78	0.67	0.72
≥ 2	103	12	23	5	0.66	0.72	0.90	0.82	0.82
< 3	31	3	11	5	0.78	0.86	0.91	0.69	0.88
≥ 3	79	11	18	3	0.62	0.96	0.88	0.86	0.87
< 4	56	4	15	7	0.79	0.89	0.93	0.68	0.87
≥ 4	54	10	14	1	0.58	0.98	0.84	0.93	0.86
< 5	84	7	19	8	0.73	0.91	0.92	0.70	0.87
≥ 5	26	7	10	0	0.59	1.00	0.78	1.0	0.84

DISCUSSION

Thyroid malignancy is not an uncommon condition but thyroid nodules are a common finding on the ultrasound of the neck. Clinical factors that point towards malignancy include older age (more than 50), hard nodule and size of the nodule more than 4 cm.^{2,8} Fine needle aspiration cytology is the most essential part of the diagnostic investigation for the thyroid nodule. The sensitivity and specificity of the test been reported to be as high as 95%²⁻⁹ but are affected by several factors including size of the thyroid nodule and operator learning curve in performing the procedure and interpreting the result.¹⁰

Carillo et al published an article in year 2000 looking the accuracy of FNAC of thyroid nodule in combination with clinical and radiological evaluation. There were 159 patients who had FNAC and underwent thyroid surgery for various reasons. The clinical parameters analysed were age of patient, lesion mobility, quality of borders, consistency of the nodule, type of growth and ultrasound echogenicity. The study concluded that the only associated false negative result was thyroid nodule size more than 4 cm.²

Stang and Carty published in 2008 and concluded that FNAC was the most accurate predictor of thyroid nodule malignancy with false negative rate between 1-11%, and varied widely due to diagnostic category.⁸ They also found that the significant cause of FNAC sampling error which leads to false positive was due to large thyroid nodule. Based on this study, they proposed that thyroid nodule bigger than 4cm should undergo lobectomy regardless of the FNAC result. In their series of patient with more than 4 cm nodules, their false negative rate of FNAC was 12.7% with cancer detection rate at 19.3%. They also found that that FNAC of follicular neoplasm category had histological malignancy of 33%.

In our study, there was a high false negative rate for thyroid nodule more than 4 cm (41.7%). For nodules bigger than 3 cm, the false negative rate of FNAC was still high at 37.9%. While for nodule less than 3 cm and 4 cm, the false negative rate were 21.4% and 21.1% respectively, which was nearly similar. Looking at the nodules bigger than 5cm, the false negative rate markedly increased to 46.7%, with drop in accuracy to only 83%. These result suggested that the larger thyroid nodules were associated with more false negative FNAC. This is consistent with other reports which suggested similar findings.

The problem with studies comparing FNAC to HPE report is that only a few benign thyroid nodules less than 3cm or 4cm had been operated.¹¹⁻¹⁵ Our data showed that the sensitivity tests for small thyroid nodules of size less than 3 cm and 2 cm were good at 78% and 75% respectively. But the result may not be accurate as many patients with small benign nodules were not operated to be included in the study. Data on free hand and ultrasound guided were analysed together as the sample size is small which might also affect the result as the accuracy of the two techniques might be different. What is evident from this study, the accuracy of FNA decreases with enlarging size of the nodule, which might be due to a large nodule harbouring small area of malignancy.

CONCLUSIONS AND RECOMMENDATION

The sensitivity of FNA decreases with increasing size of the nodule. Therefore, the current recommendation to remove nodule bigger than 4 cm is justified. But this should not prevent clinicians to proceed with FNAC for large thyroid as positive result will still be useful in the management of the patient. Targeted FNAC using ultrasound guidance on lesions with sonographic evidence of malignancy should be explored for better and precise cytology.

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