

Endocrine Surgeon-Performed US Guided Thyroid FNAC is Accurate and Efficient

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Abstract

Background Ultrasound guided fine needle aspiration cytology (US-FNAC) is a key diagnostic technique used to assess thyroid nodules. This procedure has been the domain of radiologists, but it is increasingly performed by endocrine surgeons. In the present study we aimed to assess the accuracy and clinical efficiency of US-FNAC performed by endocrine surgeons.

Patients and Methods This study was a retrospective review of consecutive patients in a 3-year period who underwent US-FNAC performed by endocrine surgeons and radiologists. Medical records, cytology results, and surgical pathology results were collected and analyzed.

Results A total of 576 US-FNAC were performed on 402 patients during the study period. The endocrine surgeons and radiologists performed 299 and 277 US-FNAC, respectively. The FNAC inadequacy rate was 5.3 % for the endocrine surgeons and 9.3 % for the radiologists ($p = 0.05$). For thyroid cancer, the sensitivity, specificity, and false negatives of the US-FNAC for the endocrine surgeons was 87 %, 98 %, and 3 %, respectively while that for the radiologists was 88 %, 95 %, and 3.5 %, respectively. Patients with thyroid cancer had a shorter time to surgery in the endocrine surgeons' group (mean 15.3 days) compared to the radiologists' group (mean: 53.3 days; $p = 0.01$).

Conclusions US-FNAC performed by an experienced endocrine surgeon is accurate and allows efficient surgical management for patients with thyroid cancer.

Introduction

Thyroid nodules are common and have become a significant clinical problem with the widespread use of diagnostic ultrasound. Accurately and efficiently distinguishing between clinically insignificant nodules and those requiring intervention is important [1]. Some 95 % of thyroid cancers present as solitary nodules, yet fewer than 15 % of thyroid nodules are malignant [2]. Ultrasound guided FNAC is a technique employed to help address the likelihood of thyroid cancer in patients with nodular thyroid disease [3]. Fine needle aspiration cytology is a safe and effective method of differentiating benign from suspicious or malignant nodules [4], with the sensitivity and specificity of thyroid FNAC being around 85 % and 90% in experienced hands [5]. Ultrasound guided FNAC is therefore able to help determine which patients with thyroid nodules require surgery, and to determine the extent of surgery. Traditionally, thyroid US-FNAC has been the domain of the radiologist, as ultrasound and US-FNAC is a core competency acquired during radiology training. Endocrine surgeons have begun to undertake US and US-FNAC training, and to perform the procedure as part of a surgical consultation [6]. As patients with thyroid nodules are often referred for a surgical opinion, this development may streamline patient care. Potential advantages include convenience for patients and direct feedback for surgeons. Before US performed by endocrine surgeons becomes accepted as standard, it is important to assess its accuracy and efficiency. We therefore conducted a retrospective comparison of the adequacy of US-FNAC samples obtained by surgeons and those obtained in the department of radiology at an academic hospital. We also assessed the time between biopsy and surgery for patients with thyroid cancer.

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Patients and methods

The present study was based on a retrospective review of US-FNAC results of all patients referred to the Radiology Department of The Royal Melbourne Hospital and the practices of two experienced endocrine surgeons from 1 July 2007 through 30 June 2010. Patient details, including age, gender, symptoms, investigations, and the type of surgery were extracted from the medical records. Thyroid nodule variables including US and FNAC reports were extracted from Department of Radiology reports or surgeons' files, and surgical pathology results were obtained from Department of Pathology databases. Patient follow-up was calculated from the time of biopsy. Two endocrine surgeons and three specialist radiologists performed the US-FNAC.

Imaging technique

The endocrine surgeons completed a thyroid US and FNAC course and had each performed more than 200 US-FNAC in the preceding 3 years, while the radiologists were board certified radiologists trained in performing US-FNAC. The

endocrine surgeons used a Sonosite M-Turbo ultrasound system (USA) and a Terason 2000+ Ultrasound system (USA), while the radiologists used Aplio XG Toshiba (Japan) and iU22 xMatrix Philips Ultrasound system (USA). A high-frequency linear 7.5–12 MHz transducer was used to examine the thyroid gland. Nodules were examined for their consistency (solid, cystic, or mixed), margins, echogenicity (hypoechoic, hyperechoic, isoechoic, and anechoic), and the presence of micro-calcifications. Internal vascularity was assessed by biphasic Doppler mode US (Fig. 1).

US-FNAC technique

Fine needle aspiration cytology was performed under US guidance with 23- or 25-gauge needles with no aspiration, unless cystic contents needed aspiration. A syringe was used to expel the needle content onto a glass slide, and both air-dried and wet fixed slides were prepared. Experienced cytology technicians attended US-FNAC procedures to prepare the slides and assess sample adequacy by holding the prepared glass slide in front of a light source and assessing visually for cellular material. Samples were taken

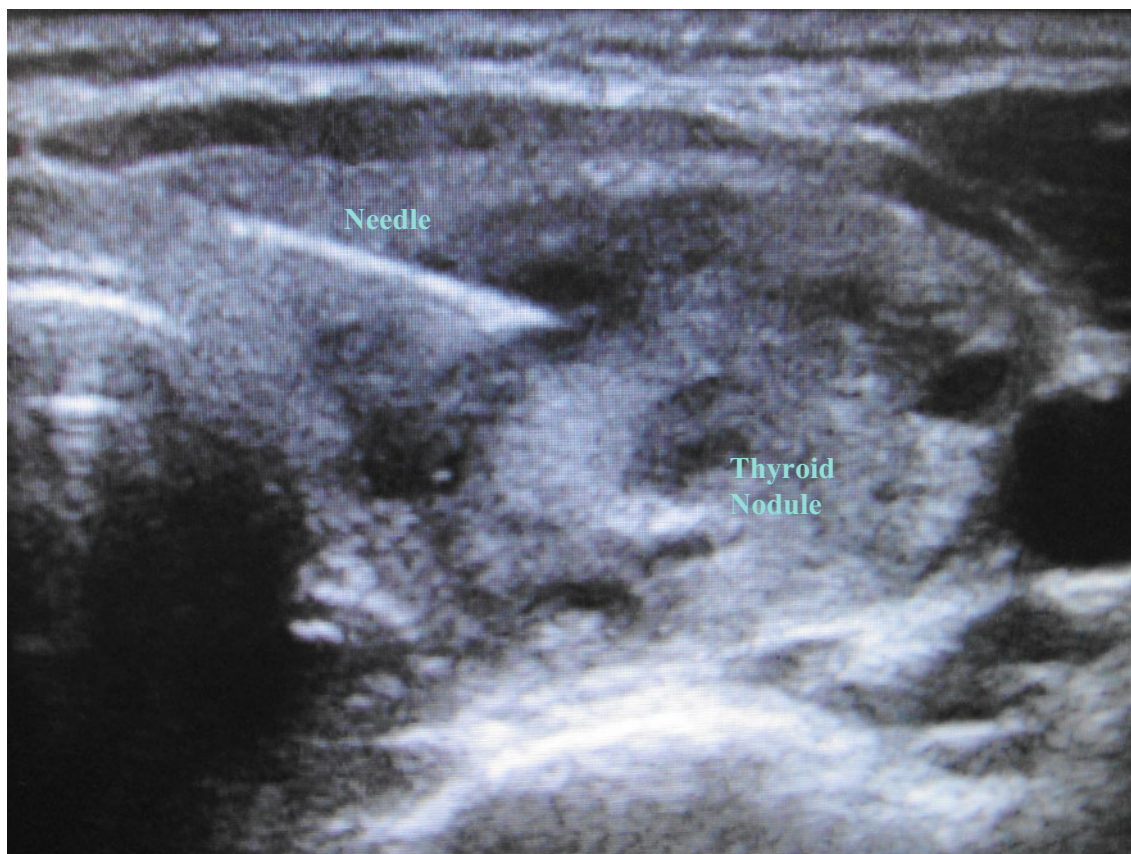


Fig. 1 Ultrasound image of a mixed echogenicity thyroid nodule undergoing biopsy with a 25 gauge needle

with one to three passes until the cytology technician was satisfied that there was an adequate sample.

Cytology reporting

Two cytologists analyzed and reported the slides. The Bethesda scale for rating thyroid cytology was adopted in the department in 2009 [7]. Samples reported before 2009 without applying the Bethesda criteria were reviewed and re-classified by one of the two cytopathologists, who was blinded to the outcome. Samples were rated as inadequate if there was cyst fluid only, a virtually acellular specimen, an inadequate number of follicular cells, or other features, such as obscuring blood and clotting artifact [7]. Patients whose FNAC was reported as Bethesda grade II with no clinical or radiological indications for thyroidectomy had clinical follow-up or repeat US, with FNAC in cases of nodule growth. Patients with Bethesda grade III FNAC returned for clinical follow-up or surgical resection, at the discretion of the treating surgeon. Patients with suspicious or malignant cytology (Bethesda grades IV, V, and VI) were advised to undergo surgery. Histologic results were compared with FNA findings.

Statistical analysis

Statistical evaluations were performed with PASW 18 2009 (IBM SPSS, Armonk, NY). Univariate analysis was performed with Fisher's exact test for categorical variables and Wilcoxon's test for continuous variables. A p value <0.05 was considered statistically significant. Sensitivity (suspicious or malignant FNAC/histological proven cancers + false negative biopsies) and specificity (number of benign biopsies/number of benign biopsies + the false positive biopsies) of the FNAC cytology were calculated after correlating with histopathologic results. False negative FNAC cytology was defined as a benign FNAC found on histology to be thyroid cancer. Time to surgery between the groups was compared with the Mann-Whitney U -test and Kaplan-Meier's survival curve.

Results

A total of 576 US-FNAC studies were performed on 402 patients. Median age of these patients was 51 years (range: 19–91 years). There were 342 female patients and 60 male patients. The endocrine surgeons performed 299 US-FNAC on 199 patients and the radiologists performed 277 US-FNAC on 203 patients. The age and gender distribution between two groups was similar (Table 1). A total of 134 US-FNAC were repeated within the study period (76 FNAC by the radiologists and 58 FNAC by the endocrine

Table 1 Patients' characteristics and indications for surgery, according to whether fine needle aspiration cytology (FNAC) was performed by endocrine surgeons or radiologists

	Endocrine surgeons	Radiologists	p value
Number of patients	199	203	
Age, years (range)	50 (21–87)	61 (19–91)	0.06
Gender			
F	172 (86.4 %)	170 (83.7%)	0.49
M	27	33	
Size of biopsied nodule, mm (range)	17.9 (5–90)	20 (5–60)	0.33
FNAC	299	277	
FNAC repeated	76	58	
FNAC on another nodule	24	16	
Underwent thyroid surgery	63 (31 %)	28 (13.7 %)	0.001
Indications for surgery			
Pressure symptoms or hyperthyroidism	27	13	0.001
Suspicious signs on US	13	2	0.001
Increase in nodule size	9	5	0.23
Suspicious or malignant FNAC	14	8	0.001

surgeons). Of these, 40 US-FNAC were performed on a different nodule in the thyroid gland of the same patient (24 and 16 FNAC for the endocrine surgeons and the radiologists, respectively).

Characteristics of the thyroid nodules

The median size of the biopsied thyroid nodules was 18 mm for the endocrine surgeons and 20 mm for the radiologists ($p = ns$). The overall incidence of suspicious and malignant nodules (Bethesda grades V and VI) was 3.9 % (4.6 % for the endocrine surgeons and 3.2 % for the radiologists; $p = 0.254$). The sensitivity, the specificity, and the false negative cytology of US-FNAC for thyroid cancer for the endocrine surgeons was 87 %, 98 %, and 3.1 %, respectively, whereas that for the radiologist was 88 %, 95 %, and 3.5 %, respectively (Table 2).

The rate of insufficient FNAC

Forty-one (7.1 %) US-FNA samples were reported as containing insufficient cellular material to give a cytologic diagnosis (Bethesda I). The median nodule size of the inadequate US-FNAC was 13 mm (range: 5–53 mm), compared with median size of 19 mm in the entire sample. Smaller nodules were associated with an increased incidence of inadequate sample on univariate ($p = 0.001$) and multivariate ($p = 0.015$) analysis. 15/299 (5.3 %) (

Table 2 Bethesda classification rating of ultrasound guided FNAC according to operator

	Endocrine surgeons	Radiologists	Total	<i>p</i> Value
Bethesda classification system for thyroid cytology				
I	15	26	41	0.05
II	222	210	432	0.33
III	34	31	65	0.53
IV	14	1	15	0.003
V	1	1	2	0.75
VI	13	8	21	0.34
Total	299	277	576	

13 nodules classified as Bethesda VI were true positive for cancers in the endocrine surgeons' group and 8 in the radiologists' group. Both Bethesda V nodules were false positive. Two nodules with a cytological Bethesda stage II diagnosis in the endocrine surgeons' group and one nodule in the radiologists' group were false negative for cancer

US-FNAC samples obtained by the endocrine surgeons were inadequate, compared to 26/199 (9.3 %) US-FNAC samples obtained by the radiologists (*p* = 0.05). Neither the echogenicity (*p* = 0.5) nor the texture (*p* = 0.27) of the nodules was associated with sample inadequacy.

Surgery

Ninety-one patients (22.6 %) had thyroid surgery for various indications (Table 1): 63 patients (31%) in the endocrine surgeons' group and 28 patients (13.7%) in the radiologists' group. More patients whose FNA was performed by a surgeon went on to require surgery (*p* = 0.001). Patients younger than 45 years old had more follicular adenomas and thyroid cancer than patients older than 45 years. In the older patients, the indication for surgery was more commonly multinodular goiter with

Table 3 Histopathology for operative cases

Final pathology	Surgeons' patients	Radiologists' patients	Total
Benign (MNG, colloid nodule, hyperplastic nodule)	25	17	42
Thyroiditis	5	1	6
Follicular adenoma (including Hurthle cell adenoma)	18	2	20
Follicular cancer (including Hurthle cell cancer)	2	0	2
Papillary cancer	12	7	19
Medullary cancer	1	0	1
Metastatic adenocarcinoma	0	1	1
Total	63	28	91

MNG Multi-nodular goiter

compressive symptoms. Table 3 shows the histopathologic results of the resection specimens.

False negative FNAC

There were three patients with benign FNAC (Bethesda stage II) who were found to have cancer at surgery: two in the endocrine surgeons' group and one in the radiologists' group. In these patients, the indication for surgery was a high index of suspicion by the treating clinician based on nodule growth or suspicious US findings. There may be other false negatives that did not lead to operation, and so are not yet apparent.

Time to surgery for patients with highly suspected or known thyroid cancer

Twenty-three (5.4%) patients were diagnosed with thyroid cancer on histologic specimens (Table 3). Fifteen patients in the endocrine surgeons' group had thyroid cancer related surgery (13 patients had FNAC classified as Bethesda stage VI, and two patients had Bethesda stage II cytology but suspicious US findings of micro-calcifications and abnormal internal vascularity). Eight patients in the radiologists' group had a cancer diagnosis after thyroid surgery,

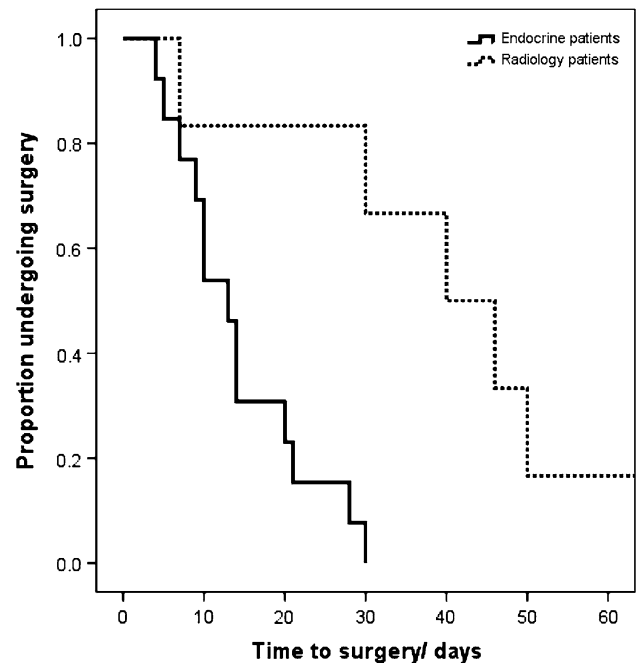


Fig. 2 Kaplan-Meier curve demonstrating time to surgery calculated from the time of ultrasound guided fine needle aspiration cytology (US-FNAC) to surgery for patients found to have Bethesda stage V and VI cytology and thyroid cancer following surgery. Patients who had US-FNAC performed by an endocrine surgeon had shorter time to surgery (*p* = 0.014)

7 patients with Bethesda VI cytology and one patient classified with Bethesda stage II, but with pressure symptoms, who was found to have papillary carcinoma. (One patient with papillary cancer on FNA was deemed unfit for surgery.) The mean time to surgery, calculated from the date of US-FNAC was 15.3 days for the endocrine surgeons' group and 53.3 days for the radiologists' group. The difference between the two groups was significant, with $p = 0.014$ (Fig. 2). The wait for an appointment with either of the two participating endocrine surgeons is 2–3 weeks, and the wait for a thyroid US-FNA in the Department of Radiology is 4–6 weeks.

Discussion

Fine needle aspiration cytology is the investigation of choice for thyroid nodules [8]. Ultrasound guided FNAC is preferable to freehand FNAC, as it reduces the sample inadequacy rate and the need for repeat biopsy [9–13]. The inadequacy rate of US-FNAC reported in the literature is 6–10 % [14, 15]. The sensitivity, specificity, and the false negatives of US-FNAC in this series were consistent with those published in the literature [16–19]. The overall rate of inadequate US-FNAC in this series is 7.1% which is comparable to previously published results [14, 15]. While both groups of practitioners had acceptably low inadequate sample rates, the endocrine surgeons had a 5 % rate of inadequate samples, compared with 9 % for the radiologists ($p = 0.05$). This study therefore supports the use of US-FNAC by endocrine surgeons with appropriate training. This practice can provide adequate and accurate samples with the benefit of fewer visits by the patient and streamlined care.

Some previous studies show that thyroid cysts are associated with a higher rate of inadequate samples. The FNAC performed in this series did not demonstrate this association. The presence of on-site cytology assessment has been shown to increase the adequacy of FNAC samples [20]. The presence of a cytology technician during each procedure may have reduced the incidence of inadequate FNAC sampling for thyroid cysts in this series, and it may be that the universal use of ultrasound guidance enabled sampling of the solid components [21]. However, in this series smaller nodules were associated with a higher inadequate sample rate on a multivariate analysis.

Patients referred to the endocrine surgeons and those referred to the radiology service differed (the former patients were more symptomatic and were more likely to undergo surgery). A likely explanation is that patients considered by the referring doctor more likely to require surgery are preferentially referred to a surgeon for evaluation. Our study supports this explanation, as patients referred to an endocrine surgeon had more thyroid cancer,

more suspicious nodules and more symptomatic goiters than the patients referred to radiology for FNA. Similarly these results do not mean that patients referred to endocrine surgeons will always have surgery, as 69 % of such patients did not undergo thyroid surgery. In addition, two patients in the endocrine surgeons' group with false negative FNAC results underwent surgery because the surgeon was concerned about the US appearance. While the FNAC findings of these two patients were recorded as false negatives, the US findings showed the nodules to be true positives that were acted on by the surgeon. This observation raises the question of whether an experienced endocrine surgeon may be more likely to act on suspicious US findings.

Patients appreciate rapid investigation and management of medical problems. Time to operation for multinodular goiter and benign thyroid nodules is variable and dependent on symptoms [1–22]. While thyroid cancer typically has a favorable prognosis, most patients feel a psychological urgency to proceed with surgery once a cancer diagnosis is made. Therefore, if there is a clinical suspicion of thyroid cancer, it may reduce patient anxiety to refer a patient directly to an endocrine surgeon capable of point-of-care ultrasound and biopsy. Patients with thyroid cancer underwent surgery a mean of 35 days sooner when a biopsy was performed by an endocrine surgeon than by a radiologist. When adding the waiting time to get a biopsy appointment with an endocrine surgeon (2–3 weeks) or a radiologist (4–6 weeks,) the difference becomes even greater.

Thyroid ultrasound in a department of radiology remains a cornerstone of thyroid nodule evaluation. Radiologists are an important part of any Multidisciplinary Thyroid Cancer Team and need to maintain their diagnostic and biopsy skills. We do not propose that all thyroid ultrasound and biopsy be performed by endocrine surgeons. However, our findings demonstrate that US-FNAC performed by an experienced thyroid surgeon more frequently produces quality samples for cytologic analysis than those performed by radiologists, while streamlining patient care and reducing time to surgery in patients found to have thyroid cancer. We recommend that patients with asymptomatic nodules without suspicious features are appropriately evaluated in a radiology department, whereas patients with suspicious thyroid nodules or clinical symptoms warranting surgery may benefit from direct referral to a thyroid surgeon who performs US-FNAC.

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