Endocrine surgeon-performed US guided thyroid FNAC is accurate and efficient.

Dhafir Al-azawi, G. Bruce Mann, Rodney T Judson, Julie A. Miller

Department of Surgery, University of Melbourne

Endocrine Surgery Unit, Royal Melbourne Hospital

Abbreviations: R= Radiologists, ES= Endocrine Surgeons, US FNAC= Ultrasound Guided Fine Needle Aspiration Cytology.

Key wards: Thyroid nodules, US-FNAC, Thyroid cancer

Abstract:

***Background and Aim*:** US guided FNAC (US-FNAC) is a key diagnostic technique used to assess thyroid nodules. This procedure has been the domain of radiologists (R), but is increasingly performed by endocrine surgeons (ES). We aimed to assess the accuracy and clinical efficiency of ES performed US-FNAC.

***Patients and methods*:** Retrospective review of consecutive patients in a 3-year period who underwent US-FNAC performed by ES and R. Medical records, cytology results, and surgical pathology results were collected and analysed.

Results: 576 US-FNAC were performed on 402 patients during the study period. The ES and R performed 299 and 277 US-FNAC respectively. The FNAC inadequacy rate was 5.3% for ES and 9.3% for R, 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 radiologist was 88%, 95% and 3.5% respectively. Patients with thyroid cancer had a shorter time to surgery in the ES group (mean 15.3 days) compared to the radiologists group (mean 53.3 days) p=0.01

***Conclusion**:* US-FNAC performed by experienced ES is accurate and allows efficient surgical management for patients with thyroid cancer.

Introduction

Thyroid nodules are common and have become a bigger clinical problem with the widespread use of diagnostic ultrasound. Accurately and efficiently distinguishing between clinically insignificant nodules and those requiring intervention is important (1). 95% of thyroid cancer presents as solitary nodules yet fewer than 15% of thyroid nodules are malignant (2). US-FNAC is a technique employed to help address the likelihood of thyroid cancer in patients with nodular thyroid disease (3). FNAC 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). US-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 ES-performed US is 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.

Patients and Methods

A retrospective review of US-FNAC results of all patients referred to Radiology Department of The Royal Melbourne Hospital and the practices of two experienced endocrine surgeons from July 1 2007 through June 30 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. Patients' follow up was calculated from the time of biopsy. Two endocrine surgeons and three specialist radiologists performed the US-FNAC.

Imaging technique

The ES 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 ES used Sonosite M-Turbo ultrasound system (USA) and 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 using biphasic Doppler mode US. Figure 1

US-FNAC technique

FNAC was performed under US guidance using 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 air dried and wet fixed slides were both 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 with one to three passes until the cytology technician was satisfied of an adequate sample.

Cytology reporting

Two cytologists analysed and reported the slides. The Bethesda scale for rating thyroid cytology was adopted in the department in 2009 [7]. Samples reported before 2009 without using 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 artefact (7). Patients whose FNAC was reported as Bethesda grade II and no clinical or radiological indications for thyroidectomy had clinical follow up or repeat US, with FNAC in cases of nodule growth. Patients with Bethesda III underwent clinical follow up or surgical resection at the discretion of the treating surgeon. Patients with suspicious or malignant cytology (Bethesda IV, V and VI) were advised to undergo surgery. Histologic results were compared with FNA findings.

Statistical Analysis

Statistical evaluations were performed using PASW 18 2009 (IBM SPSS. NY, USA). Univariate analysis was performed using Fisher's exact test for categorical variables and Wilcoxon's test for continuous variables. A p value of <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 was calculated after correlating with histopathologic results. False negative FNAC cytology was defined as a benign FNAC found to be thyroid cancer on histology. Time to surgery between the groups was compared using the Mann-Whitney U test and Kaplan-Meier's survival curve.

Results

576 US-FNACs were performed on 402 patients. Median age was 51 years (range 19-91). There were 342 female and 60 male patients. The endocrine surgeons performed 299 US FNAC on 199 patients while the radiologists performed 277 on 203 patients. The age and gender distribution between ES and R groups were similar (Table 1). 134 US-FNACs were repeated within the study period (76 FNAC by the R and 58 FNAC by the ES) and 40 US-FNAC were performed on a different nodule in the thyroid gland of the same patient (24 and 16 FNAC for the ES and R respectively).

Characteristics of the thyroid nodules

The median size of the biopsied thyroid nodules was 18 mm for the endocrine surgeons and 20mm for the radiologists (p=ns). The overall incidence of suspicious and malignant nodules (Bethesda V and VI) was 3.9% (ES =4.6% and R=3.2% p=0.254). The sensitivity, specificity and the false negative cytology of US-FNAC for thyroid cancer for the endocrine surgeons was 87%, 98% and 3.1% respectively while 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 13mm (range 5 - 53mm) 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. Fifteen/299 (5.3%) US FNAC

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

Surgery

Ninety-one patients (22.6%) had thyroid surgery for various indications (Table 1): 63 patients (31%) in the ES group and 28 patients (13.7%) in the radiologists group. More patients whose FNA's were performed by a surgeon went on to require surgery p= 0.001. Patients younger than 45 year 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 goitre with compressive symptoms. Table 3 shows the histopathologic results of the resection specimens.

False negative FNAC's

There were three patients with benign FNAC (Bethesda II) who were found to have cancer at surgery: two in the ES group and one in the radiology group. In these patients, indication for surgery was a high index of suspicion of the treating clinician based on nodule growth or suspicious US findings. There may be other false negatives that were not operated upon 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 had thyroid cancer related surgery in the ES group (13 patients had FNAC Bethesda VI and two patients were Bethesda II but have suspicious US findings of micro-calcifications and abnormal internal vascularity). Eight patients in the R group had a cancer diagnosis following thyroid surgery, 7 patients with Bethesda VI cytology and one patient was Bethesda II but with pressure symptoms was found to have papillary carcinoma. (One patient with papillary ca 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 ES group and 53.3 days for the R group. The difference between the two groups was significant p=0.014 (Figure 2). The wait for an appointment with either of the two participating ES's is 2-3 weeks, while the wait for a thyroid US-FNA in our department of radiology is 4-6 weeks.

Discussion:

FNAC is the investigation of choice for thyroid nodules (8). US-FNAC is preferable to freehand FNAC as it reduces the inadequacy rate and subsequent need for repeat biopsy (9-13). The inadequacy rate of US-FNAC 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% by 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. Our series did not demonstrate this association. The presence of onsite cytology assessment has been shown to increase the adequacy of FNAC samples (20); the presence of a cytology technician may have reduced the incidence of inadequate FNAC for thyroid cysts in this series, as well as the universal use of ultrasound guidance to enable 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 (ES 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 ES had more thyroid cancer, more suspicious nodules and

more symptomatic goitres compared with patients referred to radiology for FNA. Similarly these results do not mean that patients referred to ES will always have surgery, as 69% of patients referred to ES did not undergo thyroid surgery. In addition, two patients in the ES group with false negative FNAC results underwent surgery because the surgeon was concerned about the US appearance. While these two patients were false negative FNAC, they were true positive US findings acted upon by the surgeon. This observation raises the question of whether an experienced ES may be more likely to act on suspicious US findings.

Patients appreciate rapid investigation and management of medical problems. Time to operate on multinodular goitre and benign thyroid nodules is variable and dependent on patient symptoms (1-22). While thyroid cancer typically has a favourable 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 ES rather than a Radiologist. When adding the waiting time to get a biopsy appointment with an Endocrine Surgeon (2-3 weeks) compared to a Radiologist (4-6 weeks,) the difference is 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 should be performed by ES. However, our findings demonstrate US FNAC performed by an experienced thyroid surgeon produces quality samples for cytologic analysis comparable to those performed by the radiologists, while streamlining patient care and reducing time to surgery in patients with thyroid cancer. We recommend that while asymptomatic nodules without suspicious features are appropriately evaluated in a radiology

department, 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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	ES	**R**	**p value**
Number of patients	199	203	
AGE (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 (range)	17.9(5-90mm)	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 U/S	13	2	0.001
	Increase in nodule size	9	5	0.23
	Suspicious or malignant FNAC	14	8	0.001

Table 1 Patients' characteristics and indications for surgery. (ES endocrine surgeons and R radiologists).

		Endocrine surgeons	Radiologists	Total	p 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	

Table 2. Bethesda rating of US FNAC according to operator. 13 Bethesda VI were true positive for cancers in the ER group and 8 in the Radiologists group. Both Bethesda V patients were false positive. Two Bethesda II patients in the ES group and one patient in the Radiologist group were false negative for cancers.

Final pathology			
	Surgeon patients	Radiology 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 CA (including Hurthle cell CA)	2	0	2
Papillary CA	12	7	19
Medullary CA	1	0	1
Metastatic adenocarcinoma	0	1	1
Total	63	28	91

Table 3 Histopathologic for operative cases.

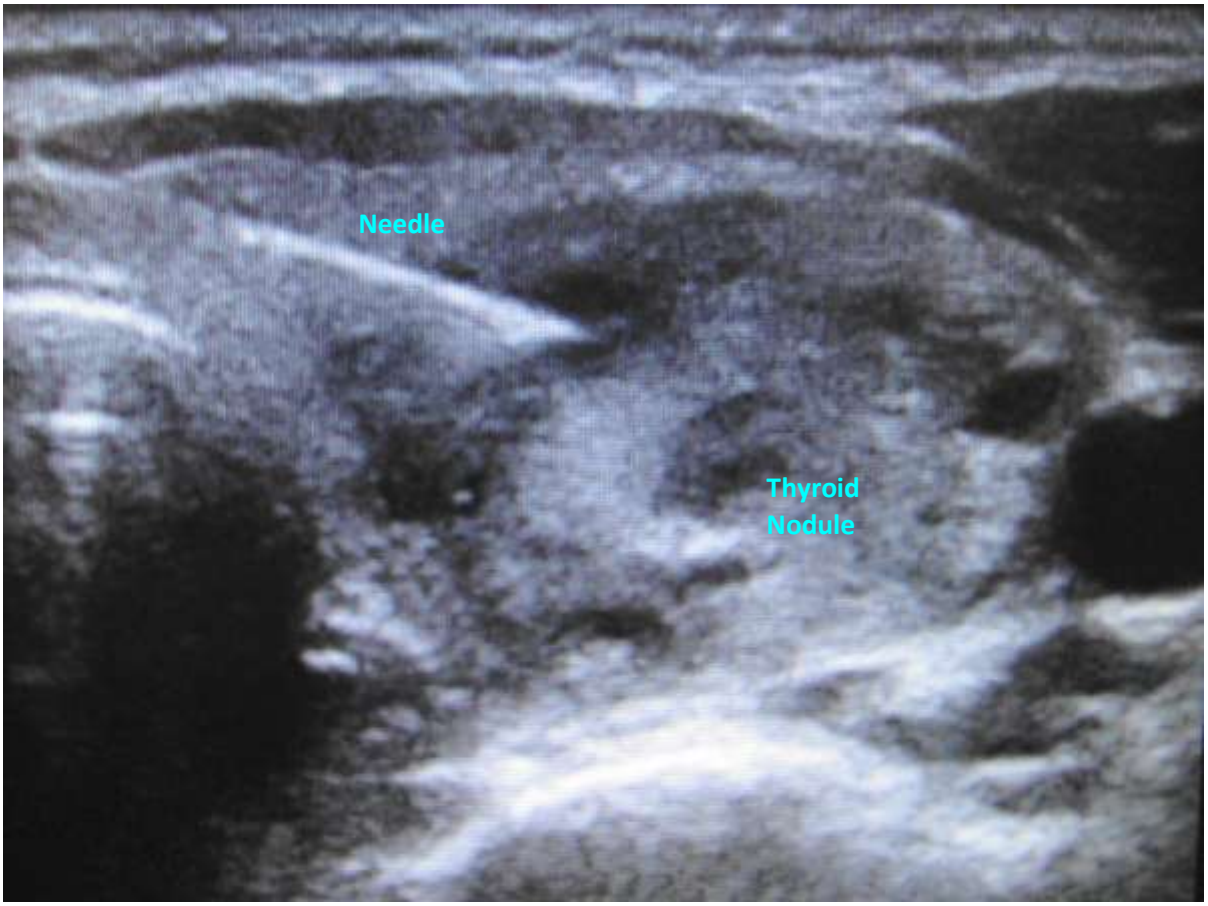
Needle
Thyroid
Nodule

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

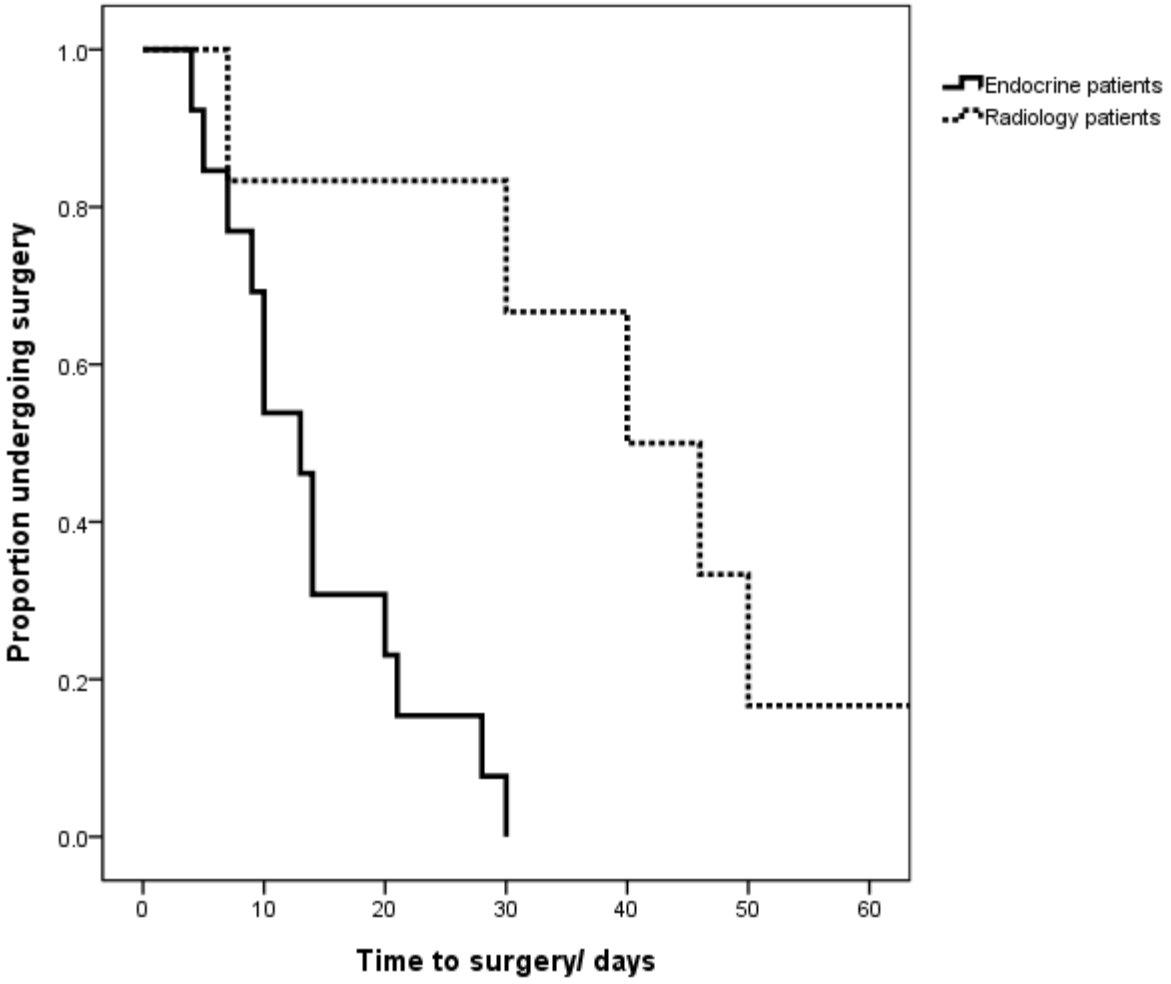

Figure 2 Kaplan Meier curve demonstrating time to surgery calculated from the time of US FNAC to surgery for patients found to have Bethesda V, VI and thyroid cancer following surgery. Patients who had U/S FNAC by ES had shorter time to surgery. P= 0.014

Author/s:
Al-azawi, D; Mann, GB; Judson, RT; Miller, JA

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