Original Article

An Audit Study of the Sensitivity and Specificity of Ultrasound, Fine Needle Aspiration Cytology and Frozen Section in the Evaluation of Thyroid Malignancies in a Tertiary Institution

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Abstract

Introduction: The aim of this study was to conduct an audit of the sensitivity and specificity of ultrasound, fine needle aspiration cytology (FNAC) and frozen section in the evaluation of thyroid malignancies in our practice. Materials and Methods: The medical records of all the patients who underwent thyroid surgery in a tertiary institution's General Surgery Department between January 2005 and December 2007 were retrospectively reviewed using a standardised data collection template. Results of the ultrasounds, FNACs and frozen sections were compared with the final histological diagnosis. Results: A total of 112 patients underwent thyroid surgery in the 3-year study period. Thyroid malignancy constituted 34 (30%) of all patients who underwent thyroid surgery. The most popular diagnostic tools used were ultrasound (81%), FNAC (69%) and frozen section (59%). The sensitivity of ultrasound, FNAC and frozen section were 41.4%, 86.4% and 68.8%, respectively. FNAC was shown to be a superior diagnostic test in detecting malignancy compared to ultrasound. FNAC was able to pick up 53% of thyroid cancers missed by ultrasound. Frozen section was able to pick up 33% of thyroid cancers that were missed by both ultrasound and FNAC. Conclusion: FNAC is the most reliable tool in detecting malignancies and ought to form the mainstay for investigation of thyroid nodules. The utilisation of ultrasonographic features in the evaluation of thyroid nodules might not necessary improve the detection rate of thyroid malignancy. Frozen section helps to improve the detection rate of thyroid malignancy but further studies into its cost-effectiveness ought to be performed.

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Introduction

Thyroid lesions constitute a considerable bulk of surgical practice, majority of which are thyroid nodules. A large population study revealed that clinically apparent thyroid nodules were present in 6.4% of women and 1.5% of men.[1] Although most nodules are benign, there remains a 5% to 14% risk of malignancy.[2-4]

For the period 1998 to 2002, there were 828 reported cases of thyroid carcinoma amongst the Singapore population, with a female-to-male ratio of 3.5:1. It is currently the ninth most common malignancy in Singapore women. Although thyroid cancer rates among males have been relatively stable, there appears to be an upward trend among females.[5]

Differentiating malignant from benign thyroid lesions remains a diagnostic challenge in clinical practice. Doctors are torn between subjecting patients to the morbidity of thyroid surgery and the risk of malignancy in a thyroid nodule. In current day surgical practice, ultrasound, fine-needle aspiration cytology (FNAC) and frozen section form the clinician's main diagnostic tools in assessing a nodule for malignancy. The current American Thyroid Association (ATA) guidelines[6] recommends that ultrasound be performed in all patients with suspected thyroid nodules. FNAC is also regarded as the most accurate and cost effective method for evaluating thyroid nodules. In our practice, the investigative modalities utilised to evaluate thyroid nodules is highly dependent on the surgeon's preference. Although numerous foreign studies have been done regarding the sensitivity and specificity of FNAC, ultrasound and frozen section in evaluating thyroid nodules for malignancy, local data remains scant.[7-14]

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The aim of this study was to audit the sensitivity and specificity of ultrasound, FNAC and frozen section in detecting thyroid malignancy in our centre in Singapore.

Materials and Methods

In our department, most patients with thyroid lesions are managed by the head and neck service. A minority of patients are managed by surgeons in other services due to patients' preferences as well as personal referrals from endocrinologists. The investigations used to evaluate these patients are driven by surgeons' preferences as well as clinical features of the presenting lesion. Patients are then advised to undergo surgery based on their symptoms, the clinical judgement of the surgeon as well as the results of the investigations performed. Intraoperatively, only patients who underwent a hemi-thyroidectomy or subtotal thyroidectomy would have a frozen section performed. The specimens from all thyroid surgeries would eventually be sent to the hospital pathologist for a histological diagnosis.

All the patients who underwent thyroid surgery at the Department of General Surgery of a tertiary institution between January 2005 and December 2007 were identified from hospital records. Our selection criteria included all patients who underwent both diagnostic evaluation and thyroid surgery in the hospital. Our definition of thyroid lesions included thyroid nodules, multi-nodular goitres and diffuse goitres. Patients who underwent diagnostic evaluation in other hospitals were excluded from the study. A total of 112 patients were identified based on our selection criteria.

A retrospective audit of the 112 patients was then carried out. Information was gathered from the case files and supplemented by data within the computerised patient support system (CPSS). All record reviews were performed by the same investigator. For each patient, information regarding the demographics, presenting lesion, diagnostic work up, type of thyroid surgery performed, length of stay in high dependency and intensive care unit, postoperative complications and final histological diagnosis were collected.

We paid particular attention to the investigations utilised in evaluating the thyroid lesions. These investigations included ultrasound, FNAC, thyroid scintigraphy, computed tomography (CT) scan and positron emission tomography (PET) scan. As ultrasound, FNAC and frozen section were the predominant investigative modalities used, these were analysed in further detail.

Ultrasound scan results were divided into 2 categories: suspicious and non-suspicious. Ultrasonographic features that were associated with an increased risk of malignancy included hypoechoic lesions, ill-defined edges and the presence of microcalcifications. However, there were no ultrasonographic findings that were specific for thyroid malignancy and radiologists usually considered a constellation of features before deciding if a lesion was suspicious or not. Suspicious scans were defined as those reported by the radiologist to be suspicious for malignancy or lesions whereby further evaluation by FNAC was recommended. Non-suspicious scans were scans whereby a benign diagnosis was suggested by the radiologist. These included cysts, nodular goitre, thyroiditis and Graves' disease.

Similarly, after excluding FNAC with insufficient cellular yield, the remaining FNAC results were classified into suspicious and non-suspicious categories. Suspicious FNACs were defined as those showing follicular cells, atypical cellular changes or malignant cells. Follicular cells were included under the suspicious category as follicular carcinoma can only be diagnosed from the presence of capsular invasion on histology. Non-suspicious FNACs were defined as those with benign diagnosis suggested such as nodular goitre, cysts and colloid nodules.

Frozen section results were also classified into suspicious and non-suspicious categories after the indeterminate lesions were excluded. The pre- and intraoperative investigation results were then compared to the final histological diagnosis of the postoperative specimens.

Based on the above definitions, the number of true-positive (TP), true-negative (TN), false-positive (FP) and false-negative (FN) ultrasound, FNAC and frozen section diagnoses were determined. Sensitivity was calculated as TP/(TP+FN) and specificity was calculated as TN/(TN+FP). The 95% confidence intervals (95% CIs) for the sensitivity and specificity of ultrasound, FNAC and frozen section were calculated using the Statistical Package for the Social Sciences for Windows version 12.0 (SPSS Inc, Chicago, IL, USA).

Results

Our study population consisted of 97 females (87%) and 15 males (13%). The mean age was 49 ± 13 years. Mean age for males and females were 52 ± 5.9 and 48.5 ± 2.7 years, respectively. Sixty-nine per cent of patients were Chinese, 14% were Malays, 5% were Indians and 12% were of other ethnic groups. Sixty-two patients (55%) underwent a hemi-thyroidectomy while 43 patients (38%) underwent a total thyroidectomy. The remaining 7 patients (6%) underwent procedures such as sub-total thyroidectomy, neck exploration and Sistrunk excision of thyroglossal cyst. Among the patients who underwent hemi-thyroidectomy, 3 subsequently underwent a completion thyroidectomy when histology results indicated malignancy, bringing the total number of surgeries performed for the 112 patients to 115.

Histological diagnosis of the lesions revealed multi-

nodular goitre in 61 patients (54%) and malignancies in 31 patients (28%). Benign cysts and nodules, Graves' disease and thyroiditis accounted for the remaining 18% of patients. Three patients with multi-nodular goitre had incidental papillary carcinoma but were classified according to their presenting lesion.

Among the 34 thyroid malignancies (inclusive of 3 cases of incidental papillary carcinoma), 28 (82%) were papillary carcinomas while 3 (9%) were follicular carcinomas. There were 2 cases of mixed papillary and follicular carcinoma and 1 case of Hurthle cell tumour.

The most commonly used diagnostic modalities were ultrasound (81%), FNAC (69%) and frozen section (59%). The sensitivity of ultrasound, FNAC and frozen section were 41.4%, 86.4% and 68.8%, respectively. The specificity of ultrasound, FNAC and frozen section were 83.9%, 66.7% and 95.5%, respectively. The sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of ultrasound, FNAC and frozen section, with their respective 95% CI, are illustrated in Table 1. The sensitivity of FNAC was shown to be superior compared to ultrasound in picking up malignancy in thyroid lesions.

Out of the 17 thyroid cancers that were misclassified as benign by ultrasound, FNAC was performed for 13 of them. The addition of FNAC as a diagnostic tool managed to detect an additional 7 (54%) cancers missed by ultrasound. In contrast, out of the 3 thyroid cancers misclassified as benign by FNAC, none were detected successfully by ultrasonography.

Six (5%) thyroid cancers were misclassified as benign by both ultrasound and FNAC. Out of these 6 cancers, 3 had an intraoperative frozen section performed. Frozen section managed to pick up an additional 1 (33%) out of the 3 cancers missed by both ultrasound and FNAC.

Table 1. Sensitivity, Specificity, PPV and NPV of Ultrasound, FNAC and Frozen Section

	Ultrasound (N = 91)	FNAC (N = 77)	Frozen section (N = 66)
Sensitivity	41%	86%	69%
95% CI	(24% to 61%)	(65% to 97%)	(41% to 89%)
Specificity	84%	67%	95.5%
95% CI	(72% to 92%)	(51% to 81%)	(85% to 99%)
PPV	55%	56%	85%
95% CI	(32% to 76%)	(38% to 73%)	(55% to 98%)
NPV	84%	91%	89%
95% CI	(64% to 85%)	(76% to 98%)	(77% to 97%)

95% CI: 95% confidence interval; FNAC: fine-needle aspiration cytology; NPV: negative predictive value; PPV: positive predictive value

Discussion

The reported sensitivity of FNAC for thyroid malignancy ranged from 61% to 97.7%.[10,15,16] In our series, the sensitivity of FNAC was comparable at 86.4%.

Our results show that FNAC has high sensitivity in diagnosing malignant lesions and should be considered the first-line investigation in evaluating thyroid lesions for malignancy. This is consistent with the guidelines recommended by the American Thyroid Association.[6] Lesions that failed to be detected by FNAC can usually be attributed to missed sampling.[8] Clinically suspicious lesions should thus be subjected to repeated FNAC or imaging-guided FNAC evaluation.

Various studies have quoted the sensitivity of ultrasound in evaluating thyroid nodules for malignancy to be in the range of 46% to 86.5%.[17,18] However in our series, the sensitivity of ultrasound was only 41.4%. This huge discrepancy can be explained as ultrasound is operator dependant. Studies which quoted high sensitivities of ultrasound were based in high volume centres. These results might not be applicable in our practice. In our series, ultrasound as a sole diagnostic tool was shown to have poor sensitivity in the diagnosis of thyroid malignancies.

There appears to be an increasing popularity in the use of ultrasound as a diagnostic modality. According to figures quoted by a local publication, between 1995 and 2000, only 27% of patients were evaluated by ultrasound.[19] In contrast, our data from 2005 to 2007 indicated that 81% of patients were evaluated with ultrasound. This could be due to influence from practice in Europe as well as recommendations from the American Thyroid Association.[6,20] Despite its popularity, the addition of ultrasound might not necessary increase the detection rate of thyroid malignancy. In our series, thyroid lesions which were misclassified as benign by FNAC were not picked up by ultrasonography as well. The role of ultrasound in evaluating thyroid lesions for malignancy should perhaps be limited to that of ultrasound-guided FNAC where sensitivity of up to 96% have been reported in literature.[21] However, ultrasound does provide information on the location and nature (cystic vs non-cystic) of the nodule. This is clinically relevant as nodules located posteriorly or those with more than 50% cystic contents are poorly evaluated with palpation-guided FNAC.[6] Imaging-guided FNAC should thus be considered for these lesions. The usefulness of frozen section as a diagnostic tool remains controversial. Quoted values of the sensitivity of frozen section range widely from 32.4% to 93%.[22-25] Our sensitivity for frozen section was 68.8% (11 out of 16). Among the 5 false negative frozen section specimens, 2 were due to papillary microcarcinoma while 1 was a minimally invasive follicular carcinoma. This suggests that sampling error may contribute to the false

negative rate in frozen section. Frozen section is also a poor tool in differentiating follicular adenomas from follicular carcinomas. Studies have shown that up to 43% of follicular carcinomas were misclassified as benign on frozen section.[26] This can be explained as frozen section distorts and collapses the blood vessels of the thyroid gland, increasing the difficulty in detecting angioinvasion which is an important feature in differentiating between follicular adenomas and carcinomas.[27]

In order to assess the added benefit of frozen section in detecting malignant lesions missed by preoperative diagnostic modalities, 6 malignant lesions missed by both ultrasound and FNAC were identified. Frozen section managed to detect 2 of the 6 (33%) malignant lesions. Three (50%) of the malignant lesions were wrongly classified as benign and 1 yielded indeterminate results. Two out of the 3 malignant lesions wrongly classified as benign on frozen section were papillary microcarcinoma. Although these figures are too small to establish statistical significance, frozen section seems to improve detection rates of thyroid malignancy when used as a complementary tool to ultrasound and FNAC.

Conclusion

Detecting malignancies in thyroid nodules remains a diagnostic challenge in clinical practice. A highly sensitive diagnostic algorithm would allow early detection of thyroid cancer and improve morbidity and mortality. FNAC remains the most reliable tool in detecting malignancies and ought to be performed in most patients presenting with thyroid nodules. The utilisation of ultrasonographic features in the evaluation of thyroid nodules might not necessary improve the detection rate of thyroid malignancy. Frozen section helps to improve the detection rate of thyroid malignancy but further studies into its cost-effectiveness ought to be performed.

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