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Research Article

Accuracy of non-ultrasound guided thyroid gland fine needle aspiration with biopsy

Abstract

Objectives: The aim of this study was to examine the accuracy of fine needle aspiration with cytology (FNAC) for thyroid gland masses without (US) ultrasound guidance by comparing results with final Histopathological Examination (HPE) findings.

Study Design: Retrospective chart review

Setting: Tertiary Care Medical Center in Montego Bay, Jamaica.

Subjects and Methods: Patient charts were retrospectively reviewed at Cornwall Regional Hospital in Montego Bay, Jamaica. Individuals with thyroid nodules less than 3 cm were excluded. Non-ultrasound guided FNA was performed by the attending otolaryngologist and cytology was analyzed by the attending pathologist. FNAC results were compared to final HPE results. A total of 412 patients were sampled.

Results: The rate of agreement between the results of FNAC and HPE was very high (90%), especially for all benign lesions. Multi-nodular goiter was the most common presentation.

Conclusion: Head and neck disease is difficult to identify in developing nations. Results of non-US guided FNAC for thyroid lesions 3 cm and larger proved to be accurate 90% of the time when compared to final HPE results. These data demonstrate the relative reliability of FNAC without US guidance for the vast majority of thyroid gland masses that were evaluated. The findings also support the active role of the otolaryngologist in the diagnostic process; participation that can be efficiently accomplished in a routine ENT out-patient clinic setting.

Introduction

Thyroid lesions, salivary gland tumors, and head and neck masses are commonly evaluated and treated by endocrinologists and otolaryngologists. Within this context, palpable thyroid nodules are amongst the most frequently presenting pathologies; an occurrence of 5% in women and 1% in men [1]. In the United States, it is estimated that 600,000 nodules are sent for fine-needle aspiration (FNA) alone [2]. The primary concern with these lesions is that they may harbor a thyroid malignancy. In approximately 15% of patients who exhibit palpable thyroid nodules, particularly those with family histories of thyroid disease or radiation exposure, malignant pathology is identified upon further work up [1].

In general, timely diagnosis and treatment of thyroid disease can be challenging to both primary care providers and otolaryngologists. With respect to thyroid nodules, FNA has been shown to result in high degrees of diagnostic accuracy.

Moreover, throughout developing countries this evaluation technique is considered not only reliable, but also a very cost-effective method of differential evaluation and diagnosis. Reports of FNA of thyroid abnormalities date back to the 11th century, with numerous scientific publications on this topic since then [3].

Since the 1980's, FNA has been coupled to ultrasound (US) guidance for appraising the cytology (FNAC) of suspicious thyroid gland lesions [4]. Notwithstanding the inherent value of such technology, in some underdeveloped or underprivileged countries the availability of this imaging equipment is either inadequate or absent owing to prohibitive cost and limited professional diagnostician expertise [5,6].

Ordinarily and ideally, US guided FNAC requires the collaborative efforts of a radiologist, pathologist, and otolaryngologist or endocrinologist. Conversely, palpation guided FNA of large thyroid lesions (>2 cm) can often be

achieved in an outpatient setting by a single practitioner with the assistance of an attending pathologist [7]. The comparative reliability of these two methods (i.e., USFNAC vs. FNAC) for thyroid lesion diagnoses has not been extensively studied [8]. It has been our professional experience that otolaryngologists may be uniquely positioned to not only evaluate but also conduct thyroid diagnostic procedures on an outpatient basis in the clinic setting. To our knowledge no investigation of non-US guided FNAC for palpable thyroid nodules has been conducted in a select large adult cohort population.

The purpose of this investigation is to compare results of thyroid gland FNAC without US guidance with final histopathological examination (HPE) findings. The study population was drawn from patients of African origin living in west Jamaica. The following null hypothesis was employed for analysis: Non-US guided FNAC of thyroid gland masses 3 cm or larger is not a reliable diagnostic methodology.

Methods

In accordance with well documented requirements to conduct retrospective human participant research at our medical center, this investigation was deemed exempt from having to undergo a formal IRB review. A retrospective chart review of patients who presented with thyroid masses to the Otolaryngology/Head and Neck Surgery clinic at Cornwall Regional Hospital (CRH) in Montego Bay, Jamaica between 1999 and 2009 was conducted by two independent judges. Chart extractions focused on several variables, as described below. Patients with thyroid nodules measuring less than 3 cm were excluded. Medical co-morbidity was not considered as an inclusion or exclusion criterion. All charts were independently reviewed by 2 attending otolaryngologists for inter-rater reliability and internal validity purposes.

Each thyroid lesion was clinically evaluated by one of four attending otolaryngologists according to the following rating format: a) overall size b) right or left mass, b) bilateral mass, c) nodular goiter (NG), or d) multi-nodular goiter (MNG). Patients were then sent to the radiology department where ultrasound was done to further evaluate the nodule. Size measurement was appreciated in the longest dimension. Ultrasound interpretation was done by one of two radiologists in the entire Cornwall County/West Jamaica region. Of note, per the hospital's registrar, CRH provides service to a population greater than 500,000 citizens in west Jamaica. These individuals are mainly of low socio-economic status. Ideally, as done in developed nations, patients would have FNA completed at the same time as US evaluation. However, due to the shortage of certified radiologists, associated personnel (i.e. sonographer), and a limited number of US machines, it is common practice to perform palpation guided FNA. This procedure was conducted next by the examining otolaryngologist using a standard palpation technique without US guidance. When patients were evaluated in the otolaryngology clinic they underwent same day FNAC. Cytopathology was immediately determined in the clinic setting by the only certified pathologist in the hospital at the completion of each FNA.

Specifically, the FNAC procedure was conducted by physical palpation of the thyroid mass. Once the mass was adequately appraised following the aforementioned rating format the

procedure began by administering local anesthesia into the subcutaneous tissue layer with 0.5 ml of 1% lidocaine with 1:100,000 epinephrine. Once adequate blanching was established, a 25-gauge needle was used to aspirate material from the suspicious lesion. This procedure was performed at least three times with each mass to ensure satisfactory sampling for cytological analysis. The pathologist confirmed the adequacy of drawn samples prior to microscopic evaluation.

Results of the FNAC were discussed with each subject individually, followed by type-specific treatment recommendations. Current American Thyroid Association (ATA) guidelines preclude surgical intervention for thyroid nodules that are 3 cm or above with benign characteristics (e.g. spongiform appearance/cystic nature). Additionally, the ATA advocates evaluating nodules on their sonographic features for pre-biopsy risk stratification. Because our study was conducted in Jamaica prior to the publication of these existing guidelines we did not adhere to these recommendations. Consequently, many of our patients with benign FNAC results were treated surgically, largely due to obstructive and/or compressive airway symptoms. These individuals underwent one of the following indicated surgical procedures, usually within one month following the FNAC results: hemi-thyroidectomy, subtotal thyroidectomy, total thyroidectomy, or isthmectomy. These procedures were performed by the otolaryngologists who respectively conducted the associated biopsies. Final post-operative HPE was conducted in each case by the hospital's only pathologist. These data were subjected to comparative analyses with the original FNAC findings.

Statistical analysis was accomplished using SPS software. Descriptive statistics including frequency distributions and demographics were conducted. Cohen's kappa analysis was performed to evaluate percentage of agreement between FNAC and HPE results.

Results

Inter-rater agreement was achieved by ensuring zero discrepancies between the two reviewers in all chart extractions. Intra-rater agreement of 100% was also achieved via a second round of chart reviews, wherein 100 charts were re-reviewed by each judge to ensure complete accuracy of all original data extractions. These findings suggest very strong levels of reviewer reliability relative to the contents of all patient charts. A total of 412 patients met the eligibility criteria for participation. Of those, 95.6% were female. Mean patient age was 47.2 years (range: 11-83 years; SD: 14.3 years). The clinical diagnoses frequency and FNAC findings are illustrated in table 1. Clinical presentations included the following: right thyroid mass, left thyroid mass, bilateral thyroid mass, MNG, NG, and other. MNG was the most common diagnosis at 36.7% of the total study population. Findings of right thyroid mass and left thyroid mass were nearly equally frequent at 24.3% and 27.0%, respectively. NG was detected in 6.6%, and bilateral thyroid mass was observed in 4.4% of all patients studied.

As mentioned in the Methods, patients underwent one of the following procedures: right hemi-thyroidectomy, left hemi-thyroidectomy, subtotal thyroidectomy, total thyroidectomy, or isthmectomy; only 2 patients received the latter procedure, as shown in table 1. FNAC and HPE comparative outcomes

frequencies revealed that the most common diagnosis for both procedures was nodular hypoplasia (46.0% and 53.2%, respectively). NG was seen on FNAC 39.1% of the time and reported on HPE at 32.4%. The least common finding on FNAC was normal thyroid/benign tissue at 0.3%, with 0.2% found on HPE.

Of the total sample of 412 patients, 350 individuals underwent both non-US guided FNAC and postoperative HPE analyses. The overall percentage of agreement between these two cytologic diagnostic procedures was 90%, as shown in table 2. To examine the statistical power of such agreements between these two categorical variables, Cohen's Kappa was computed from the observed diagnostic frequencies. Results revealed the proportion of agreement between the non-US guided FNAC findings and the post-operative HPE results was 0.84 ($p < .001$), which represents very strong statistical significance.

Discussion

The vast majority of US-FNAC procedures in the United States are performed by radiologists, with or without the assistance

of the referring endocrinologist or otolaryngologist. Following this procedure the patient is typically sent back to the original referring physician for discussion of pathological results and treatment options [8,9]. This procedural algorithm is slow moving, inconvenient, costly, and inherently disadvantageous to timely diagnosis [10]. It has been long acknowledged by endocrinologists and otolaryngologists alike that the most appropriate and effective method of evaluating a thyroid mass is via the FNAC technique, because it is quick, safe, cheap, and usually accurately yields the cytological characteristics of the tissue samples [11].

The results of this investigation have enabled us to reject the proposed null hypothesis. That is, from our relatively large data base we demonstrated that non-US guided FNAC of thyroid masses 3 cm or larger in size yielded accurate pathologic diagnosis in 90% of patients studied. These findings lend support to the practice of performing in-clinic FNAC without US in select patients with easily palpable thyroid masses. The benefits associated with this strategy include: 1) prompt and accurate diagnoses in most cases, 2) timely initiation of appropriate treatments, and 3) increased healthcare efficiency. Additionally, the anticipated surgeon remains fully engaged in the care of the patient from the initial examination through the postoperative period without the likelihood of sacrificing quality of care or treatment results. Consistent with this latter suggestion are the results reported by Patel and his associates [12]. They discovered that when the surgeon him or herself performed the thyroid FNAC with US there was a notable decrease in the time to diagnosis and treatment in over 100 cases, which in the final analysis translated into significantly fewer office visits and more efficient patient care. Although these clinical researches used US guidance during their FNAC procedures, they demonstrated that the surgeons' participation led to more expeditious diagnostic and treatment outcomes than they normally experienced when they referred their patients outside their practices for such testing. Our results add another dimension to this approach: The ability to proceed in the office setting without the need for US guidance.

On a much smaller data base, Guo et-al found that the sensitivity and accuracy of palpation guided FNA were not lower than those of US FNAC [7]. These findings also corroborate the results of the current investigation. In that earlier study a small percentage of thyroid nodules to be evaluated via FNAC were achieved without US guidance using palpation only. These researchers concluded that relatively large thyroid nodules can be accurately evaluated via FNAC without US guidance in select individuals. They also pointed out the important efficiency and cost saving factors of this alternative examination approach, akin to our own previously mentioned advantages of this procedure modification. Other researchers have similarly supported the cost-effective approach to palpable thyroid mass appraisal, suggesting that even in the presence of US guidance sampling errors do occur with false negative outcomes [13,14]. In the current investigation, the diagnostic accuracy of FNAC without US guidance exceeded 90%, as confirmed by HPE, postoperatively. Whether or not these results could be duplicated with smaller thyroid masses remains unclear and is certainly a limitation of the findings reported. We offer the proposition however, that any adequately palpable thyroid gland mass can be successfully evaluated via FNAC without US guidance. Future

Table 1: Clinical diagnoses and procedures performed.

	%
Presentation Diagnosis	
Right Thyroid Mass	24.3
Left Thyroid Mass	27.0
Bilateral Thyroid Mass	4.4
Multi-nodular Goiter	36.7
Nodular Goiter	6.6
Other	1.0
Procedure	
Right Hemithyroidectomy	28.0
Left Hemithyroidectomy	32.4
Subtotal Thyroidectomy	21.9
Total Thyroidectomy	17.3
Isthmectomy	0.5

Percentages are given to reflect both the clinical diagnoses and the surgical procedures performed on the study population.

Table 2: Overall level of agreement between FNAC and HPE results for each diagnostic categorical variable.

Clinical Findings	Agreement	
	N	% ^a
Nodular Goiter	130	85.0
Follicular lesion	27	90.0
Nodular hyperplasia	174	97.8
Reidels/Hashimotos/Hypothyroidism	8	100.0
Papillary/anaplastic carcinoma	11	78.6
Normal Thyroid/Benign Tissue	0	0.0
Mean Value		90.28%

^aHPE (Histopathological Examination) finding used as the gold standard. Values above represent the number of individuals in each diagnostic sub-category and percentage of agreement between the initial FNAC and final HPE results for each respective sub-group.

investigation of this hypothesis will be required to remove the doubt and support this examination approach. Naturally, non-palpable thyroid nodules, for example, will require US guidance for FNAC accuracy.

Although Voit et al., examined FNAC of lymph nodes for detection of Melanoma, their data provide support for use of FNAC with palpable lesions. In their investigation, the specificity of palpation-guided FNAC's (100%) was similar to that of US guided FNAC's (99.8%); the negative predictive value was 95.2% vs. 96.4% for the both categories [15]. These investigators concluded in their review that palpation guided FNAC is as specific and sensitive as US FNAC in cases of melanoma lymphadenopathy. These findings offer support for the current study design and results.

To our knowledge, this is the only investigation of a large patient cohort whose thyroid gland lesions were evaluated via non-US guided FNAC and then compared for cytological accuracy with postoperative HPE results. Technology and financial limitations in the developing nation where all data were collected serendipitously enabled this analysis, which otherwise might not have been possible for medical-legal or medical-ethical reasons in the United States. To strengthen the results of this investigation a duplicative prospective research design is under consideration, wherein several endocrinologists, otolaryngologists, and pathologists will be independently employed to conduct non-US guided FNAC and US guided FNAC in patients with thyroid gland masses of variable sizes for detailed HPE outcomes comparisons. If blinded results are clinically and statistically equivalent between and within these hopefully more equally gender distributed study groups, and among the examining physicians, additional support would be mounted for in-office non-US guided FNAC of many thyroid gland masses.

Conclusion

The importance of accurate and timely diagnosis of thyroid gland masses is self-evident. The vast majority of patients with such conditions undergo US guided FNAC for such purposes. This is especially true in virtually all developed nations around the world; and in most cases the otolaryngologist (or endocrinologist) defers to the interventional radiologist for the tissue examination and diagnosis. The results of this investigation provide strong preliminary evidence that for palpable thyroid lesions, FNAC without US guidance is a highly reliable alternative evaluation approach, which enables the otolaryngologist to participate in the differential diagnosis and medical-surgical management of the patient from the outset of care to completion. We anticipate that similar investigations of smaller masses may corroborate and extend the results of this study by demonstrating that for most palpable thyroid gland lesions, regardless of suspected size, it may be diagnostically superfluous to include routinely US technology during the FNAC biopsy procedure.

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