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Thyroid Fine Needle Aspiration: Successful Prospective Implementation of Strategies to Eliminate Unnecessary Biopsy in the Veteran Population

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Objective: Thyroid nodules are prevalent in over half the general population. Several multidisciplinary societies have management recommendations. However, the majority of data to support these guidelines are derived from studies of predominantly younger and female populations. This study's aim was to evaluate characteristics of thyroid nodules in a largely older and male Veteran population and apply these findings prospectively to reduce unnecessary thyroid fine needle aspiration (FNA).
Materials and Methods: Over a 4-year period, all ultrasound-guided FNA of thyroid nodules performed in our department were reviewed. Sonographic features, patterns, and histopathology were evaluated. A prospective strategy of avoiding FNA in all lesions matching imaging patterns of benignity was implemented and positive predictive value (PPV) of malignancy was calculated and compared to the retrospective data.
Results: Retrospectively, FNA was performed on 351 successive thyroid nodules, 9 of which were malignant. Statistically significant malignant features include presence of microcalcifications, irregular or amorphous morphology, taller-than-wide shape, spiculated margins, vascularity, and lymphadenopathy. PPV of thyroid FNA was 2.6% in this period. Four sonographic patterns were 100% specific for benignity, including: "spongiform," "cyst with a colloid clot," "giraffe," and "white knight" patterns. Over 23 months, prospective avoidance of FNA of lesions characterized as a benign pattern (159 nodules) was implemented and PPV was calculated as 7.2% resulting in a cost savings of $477,000.
Conclusion: Four sonographic patterns were 100% specific for benignity in the older and predominantly male Veteran population. Strict prospective application of avoiding biopsy in these benign patterns resulted in a decrease of unnecessary biopsies, decrease in patient morbidity, and improved allocation of health care resources.

Introduction

Thyroid nodules are present in about 50%-60% of the general population.[1,2] Biopsy of thyroid nodules in the Veteran population is common, and in our experience, these nodules are almost always benign. Several institutions have reported positive malignancy rates from fine needle aspiration (FNA) of 5%-15%.[1] The Society of Radiologists in Ultrasound (SRU) Consensus Statement in 2005 suggested a framework to approach management of adult patients with a sonographically detected thyroid nodule.[3,4] The SRU recommendations combine nodule size with sonographic features to suggest the need for FNA. Additionally, there are several other studies in the literature, as well as recommendations by the American College of Radiology (ACR Thyroid Imaging, Reporting and Data System or TI-RADS), and endocrine societies such as the American and European Thyroid Associations for thyroid nodule evaluation.[5-7] The central focus for the majority of these studies is to determine which lesions are malignant based on ultrasound criteria, and thus, should warrant investigation with biopsy. However, the lack of consensus in these criteria, combined with conflicting sensitivities and specificities of ultrasound features for the detection of malignancy, has resulted in differing guidance and oftentimes confusion among radiologists as well as the referring clinicians.

Thyroid nodules have also been classified into patterns based on sonographic features.[8] Benign morphological patterns of thyroid lesions have been identified; however, the populations included in these studies were predominantly younger and female, and patterns included: "spongiform," "cyst with a colloid clot," "giraffe," and diffuse hyperechogenicity, which has been described as "white knight" (Fig).[9,10] Furthermore, we are not aware of any study that has evaluated sonographic features or morphologic patterns of thyroid lesions in a predominantly older and male population.

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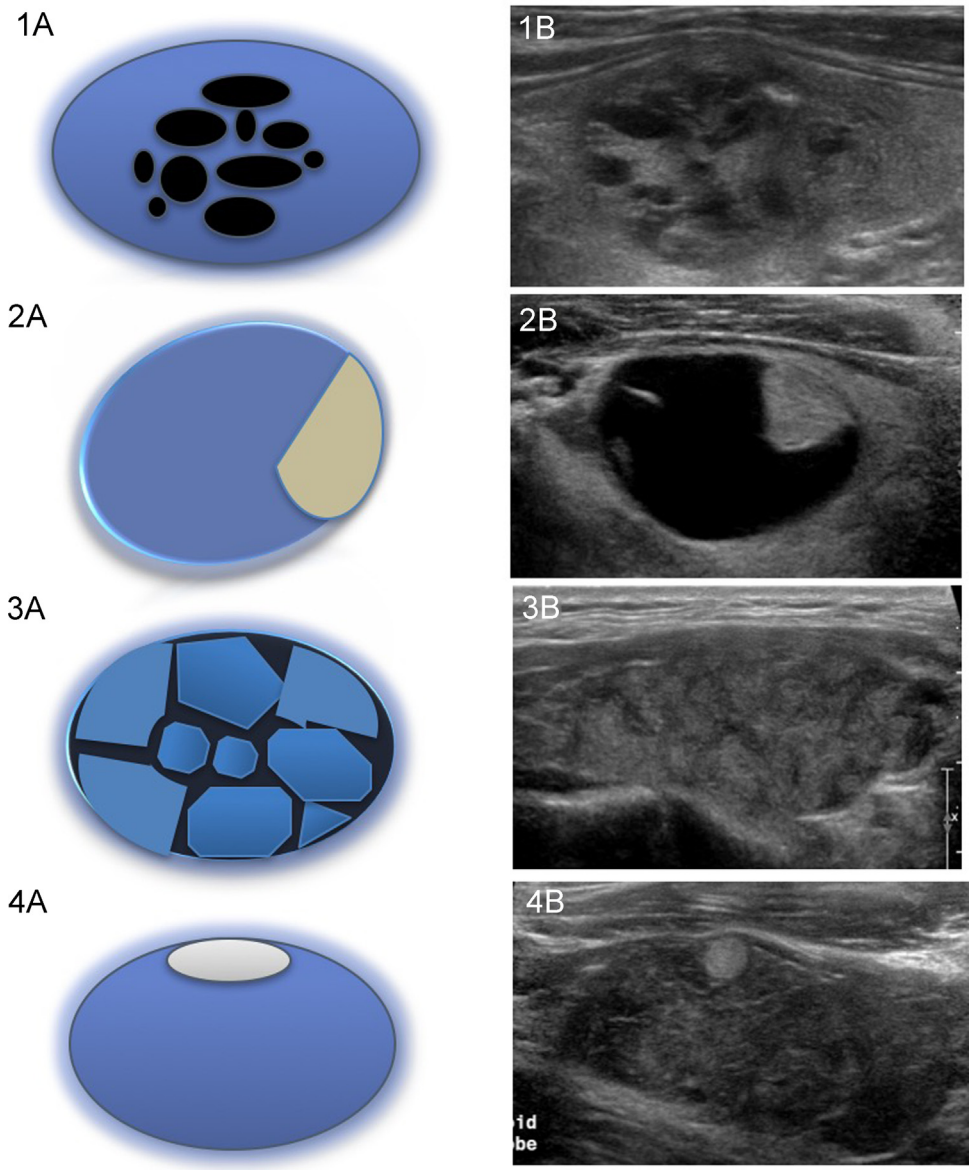

FIG. Patterns of Benign Thyroid Nodules. 1. Spongiform pattern consists of an aggregation of multiple microcystic components in more than 50% of the volume, 1A graphical and 1B sonographic representations. 2. Cyst with colloid clot pattern consists of a cyst with a hyperechoic avascular colloid clot, 2A graphical and 2B sonographic representations. 3. Giraffe pattern appears as hyperechoic blocks separated by hypoechoic stripes, 3A graphical and 3B sonographic representations. 4. White Knight pattern is a hyperechoic nodule in a background of thyroiditis, 4A graphical and 4B sonographic representations. (Color version of figure is available online.)

The initial goal of this study was to better understand characteristics of thyroid nodules in the elderly. Specifically, the purpose was to apply and evaluate criteria from the SRU, as well as other published recommendations retrospectively to a generally older and male Veteran patient population to establish the diagnostic efficacy of these recommended sonographic features as a potential predictor of lesion benignity or malignancy.[11]

After identification of imaging features in the Veteran population that suggested thyroid tissue benignity or malignancy and analysis of our radiologists reporting and recommendations, our prospective strategy focused on eliminating biopsy of lesions determined to have benign sonographic features or patterns, rather than to develop other criteria to distinguish malignancy. Further, education sessions were performed to interpreting radiologists to identify lesions that were sonographically benign and to only recommend FNA of nodules that were thought to be indeterminate or malignant by imaging criteria, thus, increasing the positive predictive value (PPV) for malignancy. Eliminating unnecessary thyroid biopsies could reduce morbidity to the patient, health care costs, and utilization of limited resources.

Materials and Methods

This Health Insurance Portability and Accountability Act (HIPAA)–compliant study was approved by the institutional review board (IRB). The need for informed consent was waived in the retrospective review. The charts and imaging of all patients who underwent thyroid FNA in the Interventional Radiology department between January 2009 and January 2013 were retrospectively reviewed.

Interpreting radiologists practiced with the SRU guidelines as the benchmark for FNA recommendation. SRU recommendations for solitary thyroid nodules at least 1 cm in diameter, include an FNA recommendation for: a lesion with microcalcifications and at least 1 cm, a lesion with coarse calcifications and at least 1.5 cm,

a solid (or nearly solid) lesion and at least 1.5 cm, a mixed solid and cystic lesion and at least 2 cm, or a lesion with substantial growth. If there are multiple nodules, FNA on 1 or more lesions can be considered in order of highest suspicion.

Data collected included the age of the patient, imaging features of thyroid nodules biopsied, laboratory values, procedural images, pathology results, surgical results, any additional imaging results, and complications of biopsy. The sonographic criteria from other previously published strategies for thyroid nodule characterization collected, included: lesion size, microcalcifications, vascularity, taller than wide shape, echogenicity, acoustic shadowing, morphology, margins, growth, borders, multiple nodules, abnormal lymphadenopathy, and diffuse enlargement of the thyroid gland. Lesions which were previously biopsied were excluded from this evaluation. All imaging review was performed by 3 board-eligible, senior radiology residents and 2 fellowship-trained radiologists in the retrospective review. Each lesion was reviewed by at least 3 of the 5 readers to ensure interreader agreement. The FNA pathology results were blinded at the time of radiologist review. Three ultrasound machines were utilized for imaging all patients throughout the duration of both the retrospective and prospective phases of this study (Philips 3 EPIQ 7, software package "Evolution 1.0", manufactured in Bothell, WA).

Nodule pattern was also retrospectively classified into the 10 patterns described by Bonavita et al.[8,9] Four patterns of benignity were specifically evaluated in this study[9,10]: the spongiform pattern is an avascular or isovascular nodule with a collection of microcystic components in more than 50% of the volume. Cyst with colloid clot pattern is a predominantly cystic lesion with a spongiform-appearing avascular colloid clot that can be hyperechoic. A "giraffe" pattern, characteristic of Hashimoto thyroiditis, appears as hyperechoic blocks separated by linear hypoechoic stripes. The "white knight" pattern is a hyperechoic nodule in a background of thyroiditis, often a regenerative nodule in a patient with Hashimoto thyroiditis. Other patterns as previously described had been shown to be indeterminate and require tissue sampling, including: "red light" or central vascularity, "diffusely hypoechoic," "isoechoic without a halo," "isoechoic with a halo," "ring of fire or peripheral vascularity," and others.

Pathology and cytology of the nodules were categorized as benign, indeterminate, malignant, and insufficient cells. Cytologically indeterminate lesions (eg, Hurthle cell neoplasms and follicular lesions) were excluded from the study analysis unless definitive postsurgical histologic characterization as benign or malignant was established.

Determination of sonographic lesion patterns and nodule characteristics as predictors for benignity and malignancy were statistically analyzed for sensitivity and specificity using a chi-square test and odds ratios.

After review and analysis of the retrospective data, we developed strategies to most efficiently reduce the number of unnecessary thyroid FNAs specific to this Veteran population. Prospective implementation of these strategies, specifically avoiding biopsy in lesions found to be retrospectively 100% specific for benignity, was performed from February 2013-December 2014 and statistical analysis was performed. Radiologists were otherwise educated, in departmental lectures, to continue reading with the SRU criteria as the gold standard for FNA recommendations. All lesions with recommendation for FNA were reviewed by at least 2 fellowship-trained radiologists to ensure interreader agreement (and a third, when necessary). Nodules that were determined by strict ultrasound criteria to match a pattern of benignity were medically managed without FNA. PPV for malignancy was also calculated over this time period. Subsequent cost-effective analysis was also performed based on our results.

Results

Retrospective Results

In the retrospective review, 351 nodules were reviewed. The average age of the patient was 65.7 years (range: 28-93 years, SD = 11.2 years), and 81% were male. Pathologic evaluation of the biopsy specimens yielded 307 benign (87.5%), 9 malignant (2.6%), 31 indeterminate (8.8%), and and 4 insufficient (1.1%) etiologies. Benign nodules averaged 2.6 cm in size, whereas malignant nodules averaged 4.1 cm. During this period of time, 2.6% of all nodules with a sonographic recommendation for FNA were positive for malignancy (PPV).

Microcalcification, irregular or amorphous morphology, taller-than-wide shape, spiculated margins, presence of vascularity, and associated lymphadenopathy were all significant ($P < 0.05$) characteristics of malignant nodules. Features which showed no difference between the benign and malignant tissue types ($P > 0.05$), included: coarse calcifications, echogenicity, acoustic enhancement, and presence of multiple nodules.

Four sonographic patterns of nodule benignity were statistically 100% specific for benignity, including: "spongiform" ($n = 95$), "cyst with colloid clot" ($n = 27$), "giraffe" ($n = 1$), and "white knight" ($n = 10$) patterns (Table). All 4 of these patterns which on FNA resulted in indeterminate cytology, subsequently were benign on postoperative histologic analysis or stable on clinical or imaging follow-up. No pathologically proven malignant nodules demonstrated any of these 4 benign sonographic patterns. Other classified patterns were inconsistent in determination of tissue benignity or malignancy.

Prospective Results

After review of the retrospective results with 4 fellowship-trained radiologists and with the referring services of endocrinology and otolaryngology, a proposal to prospectively prevent biopsy of thyroid lesions with 4 sonographic patterns of benignity was implemented with the goal to increase diagnostic efficacy (PPV of malignancy). All lesions that were sonographically recommended for FNA were routinely reviewed by a second radiologist to ensure no lesions demonstrated a benign pattern as identified on retrospective review. If a decision for any lesion lacked consensus regarding pattern benignity, the lesion underwent FNA.

A total of 125 thyroid lesions underwent FNA in this period of time from February 2013-December 2014. A total of 9 lesions proved to be malignant on pathologic review, resulting in a PPV of 7.2%. A total of 159 nodules that met sonographic criteria as 100% specific for benignity were recognized and identification of these specific patterns obviated 56% of potential thyroid biopsies. No specific imaging follow-up was recommended. A chart review—including evaluating clinical notes, imaging findings, and

TABLE
Benign and malignant thyroid nodules and distribution into 4 sonographic patterns of benignity. No pathologically proven malignant nodules exhibit the 4 benign sonographic patterns, including the "spongiform," "cyst with colloid clot," "giraffe," or "white knight" patterns

Sonographic pattern	Pathologically confirmed diagnosis	
	Benign	Malignant
Spongiform	95	0
Cyst with colloid clot	27	0
Giraffe	1	0
White knight	10	0
Other patterns	174	9
Total	307	9

laboratory values—of these 159 nodules in June 2016 (at least 18-month follow-up) after the prospective implementation phase concluded, yielded no development of malignancy on clinical all-cause follow-up, including a review of all clinical notes and any imaging studies in that time period.

Without intervention and implementation of this strategy to avoid biopsy of lesions determined to be 100% specific for benignity, these benign lesions would have undergone unnecessary FNA in this time period resulting in a hypothetical PPV for malignancy of 3.2%, grossly unchanged compared to the preintervention value (2.6%). A cost-effective analysis projected a cost savings of $477,000 to the VA health care system.[12]

Discussion

Approximately 50% of the adult population has sonographically detectable thyroid lesions. This prevalence in combination with numerous recommendations and criteria attempting to distinguish malignant lesions from the overwhelming majority of benign lesions, has led to an excessive oversampling of thyroid nodules and strain on the health care system. Developing strategies to increase diagnostic proficiency by identifying nodules that can confidently be disregarded in this sizeable cohort of patients, resources can be conserved and utilized more efficiently.

Several thyroid nodule sonographic features are significant for malignancy in the Veteran population including microcalcification, irregular or amorphous morphology, taller-than-wide shape, spiculated margins, presence of vascularity, and associated lymphadenopathy. These findings are parallel to features of malignant nodules in studies performed on a younger and predominantly female study population.

Despite our unique patient profile, our findings are in agreement with studies performed by Bonavita et al and subsequently by Virmani et al that when applied strictly, 4 sonographic patterns were 100% specific for benignity and prospective application of this approach significantly increased our PPV for malignancy.[9,10] We also found that educating our fellow radiologists to recognize and specifically avoid FNA of lesions that were characterized on imaging into one of these 4 sonographic patterns of benignity was better received and followed. Common feedback from interpreting radiologists during this period of prospective implementation often included comments relating to ease of avoiding FNA recommendations for these 4 sonographic patterns vs the challenge and onus of attempting to determine if lesion characteristics were worrisome for malignancy and if they met inclusion criteria and management guidelines for FNA. Besides for this change, radiologists otherwise continued to interpret studies with the SRU framework as the suggested recommendations, thus decreasing error often identified when implementing a new interpretation algorithm.

By preventing FNAs for thyroid nodules with a high pretest probability for benignity, the patient will have reduced morbidity, including: elimination of the risk of biopsy-associated complications, emotional and physical trauma from the procedure, and a decreased financial burden from the procedure and associated workup and follow-up visits. Additionally, the overall time spent to perform FNAs and costs to establish a diagnosis would be minimized. This generation of value to the health care system by the conservation of limited resources and improvement in patient-centered quality is aligned with the American College of Radiology's Imaging 3.0 program, in which radiologists are encouraged to promote a more efficient delivery of health care.[13]

Initial retrospective analysis for imaging features is a limitation of this study: radiologists evaluated archived ultrasound images from picture archiving and communication systems , instead of real-time findings. The retrospective review had selection bias as only those patients who were biopsied were evaluated and the study did not include all patients who presented for imaging evaluation of thyroid nodules in the time period. Despite continuing radiologist education, fellowship training, and SRU guidelines posted in the reading room during the time retrospective review was performed, there was no department-wide policies to mandate interpretations of thyroid nodules with defined criteria. The small sample size of malignant nodules is a reflection of the low true positive rate of thyroid cancer in this population and volume of patients we have, and limits evaluation of malignant features of thyroid cancer in this population. In the prospective phase, increased awareness of the interpreting radiologists to current literature and with knowledge of the retrospective results may have partially contributed to an increased PPV. The prospective cohort had a minimum clinical all-cause follow-up at 18 months, however, there are no universally accepted follow-up standards at this time. Further evaluation with larger, multicenter trials in the general patient population, especially in the sparsely studied geriatric population, is warranted. Additionally, this data may continue to be reanalyzed with a higher age cutoff and potentially, looking exclusively at the unstudied older (greater than 65 years old) male population.

Conclusion

The previously proposed criteria to differentiate benign vs malignant thyroid nodules might not apply to a predominantly older and male Veteran population. Four sonographic patterns were determined to be 100% specific for thyroid nodule benignity in the Veteran population on retrospective review. Prospective application of these criteria in this patient population resulted in a significant increase, from 2.6%-7.2%, in PPV for thyroid malignancy by FNA and averted unnecessary biopsy.

Implementation of these strategies in this patient population, specifically avoiding biopsy of lesions with sonographic patterns of benignity, is adaptable to other practice settings while improving patient care and optimizing allocation of clinical resources. This approach and simple modification to thyroid nodule evaluation will improve diagnostic efficacy and result in a marked decrease in patient morbidity, emotional and physical burdens associated with FNA, and minimize health care costs.

Authors' Contribution

All authors had a role in writing the manuscript, including imaging review, and literature search.

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