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Research Article

The Risk of Thyroid Malignancy in a Predominately Older Male Population Based on Sonographic Pattern and Fine Needle Aspiration Cytology

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ABSTRACT

Background: Thyroid cancer is a common malignancy and has an increasing incidence. Thyroid ultrasound is widely used to stratify the risk of malignancy of thyroid nodules and aid decision-making about whether fine needle aspiration biopsy is indicated using the Thyroid Imaging Reporting and Data System (TIRADS). We undertook this study to determine incidence of thyroid cancer in an older, most male population referred for evaluation of a thyroid nodule at a US veterans medical center.

Methods: We performed a retrospective study of all patients undergoing evaluation of a thyroid nodule at the Oklahoma City US Department of Veterans Affairs Medical Center. We recorded sonographic findings, TIRADS score, cytopathology and surgical pathology.

Results: Among 162 subjects undergoing evaluation of a thyroid nodule, 80% were men and average age was >60 years. Only 8 of the 164 had a malignancy diagnosed. Neither age, sex, nor nodule size was associated with malignancy. All with malignancy had a TIRADS score or either 4 or 5, but only a minority of TIRADS 4 (2.4%) or TIRADS 5 (8.8%) had thyroid cancer. Punctate calcifications were found in 6 of the 8 nodules with thyroid cancer and was the only finding statistically associated with malignancy. No malignancy was found in nodules categorized as Bethesda III category.

Keywords: Thyroid cancer; Ultrasound; TIRADS

INTRODUCTION

Thyroid cancer is one of the most common human malignancies. Most thyroid cancer is highly differentiated and can be classified as either follicular or papillary [1]. The latter is the most common histological pattern. Papillary thyroid cancer is more common in younger individuals and more common in women than is follicular thyroid cancer. Differentiated thyroid cancer is generally indolent with long term survival, but there are pathological variants of papillary thyroid cancer that portend a worse outcome [2]. Poorly differentiated thyroid cancer such as anaplastic is rare, while malignancy of the thyroid C cells, medullary thyroid cancer, is also quite uncommon.

In the United States, the diagnosis of thyroid cancer has tripled over the last generation [3]. This rise is mostly due to identification of thyroid nodules on imaging performed for reasons unrelated to the thyroid. For example, a CT of the chest obtained to characterize a pulmonary nodule includes images of the thyroid in which a lesion is noted. Finding of these so called thyroid incidentalomas is the most common manner in which thyroid cancer is ultimately identified [4]. However, how these incidentally found nodules should be approached and treated is not settled [5-7].

Once a thyroid nodule is found, patients typically undergo an ultrasound examination of the thyroid. Several ultrasonographic findings are associated with the presence of thyroid cancer. These include hypoechogenic texture compared to normal thyroid tissue, microcalcifications within the nodules, rim calcifications, and indistinct capsule. In addition, a nodule that is taller than wide is

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more likely cancer [8]. The role of molecular studies of expression of mutant oncogenes is not yet completely defined for thyroid nodules, although recent data suggest improved management of disease with molecular testing [9,10].

Based on the ultrasonographic characteristics relationship to the presence of thyroid cancer, guidelines are promulgated by multiple professional organizations, including the American Thyroid Association and the American College of Clinical Endocrinology, The British Thyroid Society and the American College of Radiology, among others [11-17]. The guidelines give recommendations about which thyroid nodules should be subjected to biopsy, but consensus has not been reached [18,19]. The American Thyroid Association estimates the incidence of cancer with any one of the cancer-associated findings is 70% to 90% [11,20]. The American College of Radiology ultrasonic thyroid nodule scoring system estimates that those with a Thyroid Imaging Reporting and Data System (TI-RADS) score of 5 have a similar rate of cancer - namely, 70% to 90%. These estimates have been validated in independent cohorts [21]. Nonetheless, these recommendations are based on a general population in which papillary thyroid cancer among young women is the most more form of the disease. There are few data concerning the risk of cancer and the need for thyroid biopsy in specialized populations. We undertook this study to determine outcome in an older population consisting of mostly men who were receiving care at a US Department of Veterans Affairs Health Care System.

METHODOLOGY

We performed a retrospective study of all patients undergoing a fine needle aspiration biopsy of a thyroid nodule at the Oklahoma City Department of Veterans Affairs Medical Center. All such patients underwent a thyroid ultrasound and were seen in the Endocrine Thyroid Biopsy Clinic from 1 January 2018 until 31 December 2020. The results of the thyroid ultrasound, biopsy pathology and surgical pathology were recorded in an anonymous manner. In particular, we collected the following data: Age, sex, race/ethnicity, TIRADS score, echogenicity, internal calcifications, Doppler blood flow, taller than wide morphology, Bethesda score of biopsies, surgical pathology results. All data were acquired through chart review using the VA electronic medical record, known as CPRS (Computerized Patient Record System). The study was approved by the University of Oklahoma Health Sciences Center Institutional Review Board as well as the Oklahoma City VAMC Research and Development Committee.

STATISTICS

The results of fine needle aspiration biopsy and incidence of cancer were compiled for each of the ultrasonographic characteristics known to be associated with cancer as well as compared to the overall TI-RADS score. The relationship of the ultrasonographic findings to cancer was assessed by chi square analysis for categorical data or Student's T test for continuous data.

RESULTS

During the three-year study period, 164 patients were evaluated. Of these 164, 131 (81%) were men, as expected from a US Armed Services veteran population. Again, as expected given the demographics of health care in the VA system, the patients were older with an average age of 61 (± 13.8) years. Among these 164 subjects undergoing evaluation of a thyroid nodule, only eight (4.9%) were ultimately diagnosed with thyroid cancer. Among those with cancer seven were men and one (12.5%) was a woman, compared to 30 (16.7%) women among those without cancer (p=NS by chi square testing, see Table 1). One individual without a diagnosis of thyroid cancer was a transgender woman. The average age of those with thyroid cancer was 59.0 years, while those without cancer had an average of 61.5 (p=0.51 by Student's T test). There was no difference in the size of the nodules between the two groups. Among those with cancer, only one of eight (12.5%) had a nodule with one dimension >4 cm while 10 (6.1%) of those without cancer had >4 dimension (p=NS by chi square) (Table 1). We also calculated the volume of each nodule [22], and there was no difference between malignant and benign nodules (Table 2).

Table 1: Features of those diagnosed with thyroid cancer compared to those without thyroid cancer among 164 veterans undergoing a thyroid biopsy.

	Thyroid cancer (n=8)	No thyroid cancer (n=156)	P value
Age	59	61.5	NS
Sex	7 men (88%)	125 men (80%)	NS
	1 woman (12%)	30 women (20%)	
		1 transwoman	
	Nodule size		
>4 cm	1 (14.3%)	10 (6.1%)	0.4†
Volume (ml)	6.3 (± 13.3)	7.33 (1.9)	0.39‡
	TIRADS category		
5	6 (75%)	62 (40%)	0.44†
4	2 (25%)	80 (51.3%)	1.0†
3	0	21 (13%)	0.6†
	Ultrasound features		
Solid	6 (75%)	90 (58%)	0.26†

Mixed	1 (12.5%)	56 (36%)	0.43†
Hypoechoic	6 (75%)	86 (55%)	0.14†
Isoechoic	1 (12.5%)	37 (24%)	1.0†
Hyperechoic Border	0	7 (4.3%)	1.0†
Smooth	2 (25%)	56 (36%)	1.0†
Irregular	5 (62.5%)	49 (31%)	
Calcium*			
None	1 (12.5%)	73 (47%)	0.06†
Punctate	6 (75%)	46 (29%)	0.009†
Rim	0	8 (5.0%)	1.0†
Macro	0	11 (7.0%)	1.0†
Shape			
Wider	6 (756%)	97 (70.8%)	1.0†
Taller	2 (25%)	40 (29.2%)	
Bethesda score			
B6	6	0	0.000001†
B5	1 (14.3%)	3 (2%)	1.0†
B4	1 (14.3%)	5 (3.2%)	0.22†

Note: † By 2-tailed Fisher Exact test, data are given for the 147 patients in whom an ultrasound report specifically mentioned shape of the nodule; ‡ By student's T test.

Table 2: Thyroid cancer and TIRADS scoring.

	Thyroid cancer	No thyroid cancer
TIRADS 5	6 (8.8%)	62 (91.2%)
TIRADS 4	2 (2.4%)	80 (97.6%)
TIRADS 3	0	21

We examined TIRADS score and cancer among these 164 veterans with a thyroid nodule (Table 2). Of the cancers, 6 of 8 had a TIRADS score of 5. However, among those with a TIRADS score of 5, only 5 of 68 (7.3%) were found to be malignant (Table 2). A low rate of cancer was also present with a TIRADS score of 4, with 2 of 82 (2.4%) having malignancy. None of 21 nodules with a TIRADS score of 3 were malignant. There was no statistical difference in the incidence of cancer among these three TIRADS scores (Table 2). Overall, the rate of cancer was about 10 times lower than predicted based on TIRADS score [11,13,21].

We next examined the characteristics of the thyroid ultrasound for factors associated with malignancy in this cohort of older men. Only findings related to calcium within the nodule, or lack thereof, were of interest. Among those with no calcium seen, only 1 of 74 (1.3%) had a malignancy found (Table 1). In addition, 6 of the 8 with cancer had punctate calcification; however, among those with punctate calcification only 6 of 52 (11.5%) had cancer. Nonetheless, punctate calcium was statistically associated with cancer (p=0.009, Table 1), even though this finding was poorly specific.

Almost all patients in whom we found a nodule with a TIRADS score of 4 or 5 underwent a biopsy. Forty-seven of those with a TIRADS score of 5 were classified as Bethesda II and were clinically followed as were 5 patients who were Bethesda I. A total of 8 patients had a Bethesda classification of 3 or 4. One underwent a second biopsy that was Bethesda II. Four had molecular testing that revealed a benign lesion in 3 and metastatic lung cancer in a single person. Two patients underwent thyroidectomy and were shown to have a follicular adenoma. One patient declined surgery and in follow up has not had thyroid cancer diagnosed. One patient with TIRADS 5 and a Bethesda Class IV biopsy results underwent surgery and had a Hurthle cell thyroid carcinoma. Five biopsies were Bethesda Class VI, and all these patients underwent thyroidectomy at which time pathological examination revealed thyroid cancer.

The findings were similar among nodules with a TIRADS score of 4 in that no malignancies were found in those with a Bethesda Classification of 3 or 4. Of 2 patients with Bethesda V classification, one had papillary thyroid cancer at surgery and one had a benign lesion indicated by molecular testing. The single patient with

TIRADS 6 was found to have papillary thyroid cancer.

DISCUSSION

Our cohort of patients being evaluated for a thyroid nodule is markedly different than is generally reported in that about 80% of those with thyroid cancer are women and younger [4]. Of course, we certainly expected that patients obtaining health care within the US Department of Veterans Affairs would be older and more likely male than the general population. However, these differences have marked implications for the evaluation of thyroid nodules.

Ultrasound of the thyroid is an important component of the evaluation of thyroid nodule. Risk related to ultrasonic characteristics of thyroid nodules can be quantified by the TIRADS scoring system. Most studies find a TIRADS score of 5 is highly suspicious for malignancy with incidence of cancer ranging from 35% to 80%. With TIRADS 4, thyroid cancer is less likely but still in the range of 20%. In fact, we found only about 5% of those with TIRADS 5 had cancer and less than 5% of those with TIRADS 4. Guidelines concerning course of action for a given TIRADS score are based on these higher estimates of risk of malignancy found in a general population, and our results indicate that these do not apply well to the demographic of our cohort.

Pathological evaluation of fine needle aspiration biopsy specimens was also markedly different in our cohort. No patient with Bethesda III (atypia of undetermined significance) and only 1 patient with Bethesda IV (suspicious for follicular neoplasm) had thyroid cancer among these patients. The published expected malignancy rate of Bethesda IV is 15%-30% and 5%-15% for Bethesda III. We found only 2 individuals with Bethesda V, one of which had malignancy. Again, guidelines, which suggest thyroid surgery for Bethesda IV and V lesions, do not seem to apply to this group of older men.

We suggest that among older men undergoing evaluation of a thyroid nodule careful consideration should be given to a conservative approach even among those with a TIRADS score of 4 or 5. However, the presence of punctate calcifications may indicate the need for biopsy. Once biopsy is performed, follow up without surgery should be considered for Bethesda III or IV lesions. Molecular testing may be important, however, leading to a recommendation for thyroidectomy in some patients. We had too few patients with Bethesda V pathology to come to a conclusion, but again molecular testing is likely in order prior to surgery.

CONCLUSION

The current recommendations for the evaluation and management of thyroid nodules did not applied to our cohort of older men, a patient group which had far less thyroid cancer than the general population. Currently reported estimates of malignancy in nodules based on TIRADS score may not be applicable to older, predominantly male population. Determination of the need for biopsy and surgery for thyroid nodules should take age and sex into account.

REFERENCES

1. Xu B, Ghossein R. Evolution of the histologic classification of thyroid neoplasms and its impact on clinical management. Eur J Surg Oncol. 2018;44(3):338-347.
2. Nath MC, Erickson LA. Aggressive variants of papillary thyroid carcinoma: Hobnail, tall cell, columnar, and solid. Adv Anat Pathol. 2018;25(3):172-179.
3. Rusinek D, Chmielik E, Krajewska J, Jarzab M, Oczko-Wojciechowska M, Czarniecka A, et al. Current advances in thyroid cancer management. Are we ready for the epidemic rise of diagnoses?. Int J Mol Sci. 2017;18(8):1817.
4. Moubayed SP, Urken ML. Thyroid nodules. CMAJ. 2016;188(17-18):1259-.
5. Kitahara CM, Sosa JA. The changing incidence of thyroid cancer. Nat Rev Endocrinol. 2016;12(11):646-653.
6. Lim H, Devesa SS, Sosa JA, Check D, Kitahara CM. Trends in thyroid cancer incidence and mortality in the United States, 1974-2013. JAMA. 2017;317(13):1338-1348.
7. Kitahara CM, Sosa JA. Understanding the ever-changing incidence of thyroid cancer. Nat Rev Endocrinol. 2020;16(11):617-618.
8. Uliaque CF, Berdún FP, Herrero RL, Lórenz CP. Usefulness of ultrasonography is the evaluation of thyroid nodules. Radiologia (English Edition). 2016;58(5):380-388.
9. Nicholson KJ, Yip L. An update on the status of molecular testing for the indeterminate thyroid nodule and risk stratification of differentiated thyroid cancer. Curr Opin Oncol. 2018;30(1):8-15.
10. Hier J, Avior G, Pusztaszeri M, Krasner JR, Alyouha N, Forest VI, et al. Molecular testing for cytologically suspicious and malignant (Bethesda V and VI) thyroid nodules to optimize the extent of surgical intervention: A retrospective chart review. J Otolaryngol Head Neck Surg. 2021;50(1):1-7.
11. Haugen BR, Alexander EK, Bible KC, Doherty GM, Mandel SJ, Nikiforov YE, et al. 2015 American Thyroid Association management guidelines for adult patients with thyroid nodules and differentiated thyroid cancer: the American Thyroid Association guidelines task force on thyroid nodules and differentiated thyroid cancer. Thyroid. 2016;26(1):1-33.
12. Haugen BR. 2015 American Thyroid Association management guidelines for adult patients with thyroid nodules and differentiated thyroid cancer: what is new and what has changed?. Cancer. 2017;123(3):372-381.
13. Gharib H, Papini E, Garber JR, Duick DS, Harrell RM, Hegedus L, et al. American association of clinical endocrinologists, american college of endocrinology, and associazione medici endocrinologi medical guidelines for clinical practice for the diagnosis and management of thyroid nodules-2016 update appendix. Endocrine practice. 2016;22:1-60.
14. Perros P, Boelaert K, Colley S, Evans C, Evans RM, Gerrard Ba G, et al. Guidelines for the management of thyroid cancer. Clin Endocrinol (Oxf). 2014;81:1-22.
15. Mitchell AL, Gandhi A, Scott-Coombes D, Perros P. Management of thyroid cancer: United Kingdom national multidisciplinary guidelines. J Laryngol Otol. 2016;130(S2):S150-160.
16. Tessler FN, Middleton WD, Grant EG, Hoang JK, Berland LL, Teefey SA, et al. ACR Thyroid Imaging, Reporting and Data System (TI-RADS): White paper of the ACR TI-RADS committee. J Am Coll Radiol. 2017;14(5):587-595.

17. Ha EJ, Na DG, Baek JH, Sung JY, Kim JH, Kang SY. US fine-needle aspiration biopsy for thyroid malignancy: Diagnostic performance of seven society guidelines applied to 2000 thyroid nodules. Radiology. 2018;287(3):893-900.

18. Nabhan F, Ringel MD. Thyroid nodules and cancer management guidelines: Comparisons and controversies. Endocr Relat Cancer. 2017;24(2):R13-26.

19. Liu ZW, Fox R, Unadkat S, Farrell R. A retrospective study of ultrasound and FNA cytology investigation of thyroid nodules: Working towards combined risk stratification. Eur Arch Otorhinolaryngol. 2017;274:2537-2540.

20. Shi LL, DeSantis C, Jemal A, Chen AY. Changes in thyroid cancer incidence, post-2009 American Thyroid Association guidelines. Laryngoscope. 2017;127(10):2437-2441.

21. Tang AL, Falciglia M, Yang H, Mark JR, Steward DL. Validation of American Thyroid Association ultrasound risk assessment of thyroid nodules selected for ultrasound fine-needle aspiration. Thyroid. 2017;27(8):1077-1082.

22. Tuttle RM, Fagin JA, Minkowitz G, Wong RJ, Roman B, Patel S, et al. Natural history and tumor volume kinetics of papillary thyroid cancers during active surveillance. JAMA Otolaryngol Head Neck Surg. 2017;143(10):1015-1020.