

Article received on January 19, 2020 and accepted for publishing on March 23, 2020.

ORIGINAL ARTICLES

Diagnostic value of ultrasound in comparison with the pathologic results of fine-needle aspiration of thyroid nodules for rapid diagnosis of thyroid malignancies in patients referred to Baqiyatallah Hospital

Hojjatollah Khajepour¹, Mohammad Ebrahimifar², Efat Naeimi¹, Mortaza Movahed¹

Abstract: Background and Aim: Various studies have reported that 4-7 percent of adults with palpable thyroid nodules that 50-70 percent of it's diagnosed with high-accuracy sonography. Although most thyroid nodules are non-cancerous and do not require treatment, a small percentage of them are associated with a potential risk of malignancy, which is an important early diagnosis by ultrasound or pathology. The present study aimed to compare the ultrasound with the pathologic results of fine-needle aspiration (FNA) of thyroid nodules for the rapid diagnosis of thyroid malignancies in patients referred to Baqiyatallah Hospital.

Methods: The study population consisted of 100 (80 female, 20 male) patients with thyroid nodules in the age range of 19-82 years referred to the radiology ward of Baqiyatallah Hospital who were studied by the cross-sectional method. All patients were first scoring by ultrasound, then fine needle aspiration with thyroid nodule ultrasound was performed, and the specimens were referred to the pathology department for further evaluation.

Results: The pathologic results from fine-needle aspiration showed that only 8 of the 100 patients studied had malignant nodules that, by ultrasound scoring, 7 patients had 4 scores and 1 patient had 3 scores. However, the other 92 patients with benign nodules 57.60% of patients had score 1, 30.43% of patients had score 2 and 11.97% of patients had score 3.

Conclusion: According to the results of this study, it seems that ultrasound scoring is useful in the rapid diagnosis of thyroid nodules and prevent unnecessary thyroid nodule FNA.

Keywords: fine needle aspiration, sonography, thyroid nodule, malignancy

INTRODUCTION

The thyroid gland is one of the largest endocrine glands in the butterfly-shaped transverse section of the larynx. The units that make up the thyroid gland are a sinus or follicles, which are present in the central part of colloidal proteins as a source of thyroid hormone storage [1]. The thyroid gland has several key functions, such as iodine uptake and transfer, thyroglobulin secretion, iodine binding to thyroglobulin to make thyroid hormones, facilitating thyroid hormone secretion into the bloodstream, and interfering with body

metabolism [2].

Thyroid hormones

Thyroglobulin, a large iodized glycoprotein, has been shown by researchers to be the first essential step in initiating the synthesis of thyroid hormones through iodine absorption through the food. Transmission of iodine to the thyroid gland occurs by binding to serum proteins, especially albumin, and

Corresponding author Hojjatollah Khajepour
dr.khajepoor@yahoo.com

¹Chemical Injuries Research Center, System biology and poisoning institute, Baqiyatallah University of medical science, Tehran, Iran

²Student Research Committee, Baqiyatallah University of Medical Sciences, Tehran, Iran

unbound iodine is often excreted in the urine [3]. TSH, which is secreted by the anterior pituitary cells, plays a central role in the control and evaluation of thyroid function, which is regulated by the TRH hypothalamic hormone [4]. Various studies have shown that there is an inverse relationship between thyroid hormone levels and basal TSH production, indicating the role of thyroid hormones as a major regulator of TSH production [5].

Common disorders of the thyroid gland include hypothyroidism, hyperthyroidism, goiter or enlargement of the thyroid gland, thyroid cyst, thyroiditis (Hashimoto's) and thyroid nodules. According to the latest studies, 7-8% of the world population has one of the thyroid disorders [6].

The term thyroid nodule refers to a group of thyroid cells that grow abnormally and fall into a mass, nodule, or node, which are divided into two groups of benign nodules and malignant nodules [7]. Various studies have shown that most thyroid nodules have non-cancerous and benign cells and various reports have estimated 1 in 10 patients as malignant nodules [8].

The types of thyroid nodules are divided into 3 groups of benign (colloidal), malignant (papillary) and suspicious nodules based on pathological findings. Among the types of nodules mentioned, only malignant nodules require further surgery and care.

Symptoms of patients with thyroid nodules include neck, jaw or ear pain, difficulty swallowing, itching or tingling in the throat, shortness of breath, sore throat, hoarseness, and most studies have reported that most patients Thyroid nodules are without symptoms and are often discovered during examination for other causes [9].

Researchers have identified chronic follicular thyroid nodule (Hashimoto's), congenital malformations such as failure to form a lobe, thyroid abscess, simple cyst, and non-thyroid diseases such as lymphoma and teratoma [10].

Tests for the diagnosis of thyroid nodules include measurement of thyroid hormone and thyroid-stimulating hormone, ultrasound, scanning, fine needle aspiration, and pathological examination (cellular aggregation) [12, 11].

Since a rapid diagnosis of malignancy facilitates the process of thyroid nodule healing, therefore, finding the fastest method of diagnosis is important for initiating therapeutic measures.

The present study aimed to compare the ultrasound report only with the pathologic results of fine-needle aspiration of thyroid nodules with the aim of rapid diagnosis of thyroid malignancies in patients referred to Baqiyatallah Hospital.

MATERIAL AND METHOD

Following the approval of the research plan by the University Research Council, informed written consent was obtained from patients' participation and distributed to those who referred to the thyroid nodule interventional ultrasound department and the indication of fine-needle aspiration. No entry and exit criteria were considered for the study.

Finally, 100 patients (80 females, 20 males) from thyroid nodules in the age range of 19-82 years referred to the radiology ward of Baqiyatallah Hospital and the statistical population were selected by census method and studied by the cross-sectional method. After obtaining biographies and demographic information by the student, patients were referred to a skilled sonographer for ultrasound (using Philips Affinity fog) and fine-needle aspiration (with ultrasound guidance) and the specimens were referred to the pathology department for cytological examination.

In thyroid ultrasound, tissue is examined for ultrasound by echogenicity and rate and extent of calcification. 6 modes of Hyper echo nodule (white nodule in ultrasound), Hypo echo nodule (gray and pale nodule in ultrasound), cystic nodule (absolutely Echoless), solid nodule (uniform echo), microcalcification (calcification less than 2 mm) and macro calcification (calcification greater than 2 mm) was determined by scanning ultrasound for scoring from 1-4. The four nodule states were hypo echo, solid, microcalcification, and a 1 cm-high scoring criteria of 1-4. Each of the above was given a score of 1 and the nodule with all four attributes scored 4. In fine needle aspiration, the thyroid tissue is sampled using a fine needle for the microscopic examination of existing cells.

Among the characteristics of malignant nodules can be severe porcelain, cell size and shape variation, dense and double or multilayered cell masses, etc. These features were reported by a skilled pathologist.

Data were analyzed by spss23 software.

RESULTS

The mean age of patients was $48.26 \pm 08/13$ and the results of this study showed that malignant thyroid nodules were more prevalent in 40-49 years old patients and women in our study ($p < 0.05$).

Of the 100 patients with thyroid nodules, 8 (8%) had malignant nodules, indicating that a thyroid nodule may be about 12 times more likely to be benign.

Ultrasound reports showed that of the 92 benign nodules, 58 were hyper echogenic, 22 were hypo echogenic, and 12

were cystic nodular, whereas of the 8 malignant nodules, 5 were hypo and 3 were iso- echogenic.

It was observed that the ratio of solid in malignant nodules was more than benign. The calcification rate in benign nodules was 17% for microcalcification and 2% for macro calcification, which was 40% and 20% for malignant nodules, respectively.

Pathologic reports showed 53 patients with nodular goiter, 28 with adenomatous goiter, 1 with a follicular lesion, 8 with papillary carcinoma, 8 with thyroiditis, and two remained unknown due to insufficient sample that both nodules were cystic.

Of the 8 patients with malignant nodules reported by the pathologist from the side of ultrasound, 7 (87.5%) cases had score 4 and one patient (12.5%) had score 3. While 57.60% of benign nodules had score 1, 30.43% had score 2 and 11.97% had score 3.

From the side of ultrasound scoring, 53 cases received score 1, 28 cases received score 2, 7 cases received score 3 and 12 cases received score 4. In terms of thyroid nodule count were 47 single nodules and 53 multinodular nodules.

From hormonal tests, 4 cases were hypothyroid, 5 were hyperthyroid and 91 cases were normal, 3 cases were hypothyroid or hyperthyroid, and 5 cases were normal. Eleven of the patients had a family history of thyroid disorders, which was found to be 5 out of 11 people and 3 in people with no history of malignancy.

DISCUSSIONS

This study aimed to compare ultrasound only report with pathologic results of fine-needle aspiration of thyroid nodules with the aim of rapid diagnosis of thyroid malignancies in patients referred to Baqiyatallah Hospital. The pathologic results of fine-needle aspiration in the present study showed that only 8 of the 100 patients studied had malignant nodules which, by ultrasound scoring, 7 cases had score 4 and 1 case had score 3. However, the other 92 patients with benign nodules 57.60% had score 1, 30.43% had score 2 and 11.97% had score 3. In other words, by taking into account the pathologic results in this study, it can be concluded that ultrasound results can be used as a quick tool in predicting thyroid nodule malignancy. The reason for the high success of sampling accuracy in this study was the use of ultrasound guidance during biopsy and slide preparation by the pathologist.

In 2015, Siyadati et al investigated the diagnostic value of fine-needle aspiration compared to pathologic results in the diagnosis of thyroid nodules in Babol Shahid Beheshti

Hospital, northern Iran, for 22 years. The researchers said that fine-needle aspiration of the thyroid is a selective method of examining thyroid nodules that have recently been questioned in the management of nodules. This cross-sectional study was performed on cytology specimens of 225 patients who underwent thyroidectomy in Shahid Beheshti hospital of Babol for 22 years (1989-91). Age, sex, physician performing FNA, type, and surgical site, FNA and pathology results were recorded. Pathologic FNA results were classified into four groups of inadequate, benign, malignant and suspicious and pathologic results were also divided into two benign and malignant and compared. The results showed that in the diagnosis of malignant thyroid nodules, sensitivity was 60%, specificity 96%, positive predictive value 65%, negative predictive value 95% and diagnostic accuracy of 81.8%. Of the 225 cytological specimens, 127 were benign (56.4%), 47 suspicious (20.9%), 27 malignant (12%), and 24 inadequate (10.7%). Final pathology was also benign in 150 patients (66.7%) and malignant in 75 patients (33.3%). According to the results of this study, fine needle aspiration can be used to diagnose thyroid nodules [13].

Rosario et al., 2013 in Brazil, designed a study to predict malignancies in thyroid nodules with non-diagnostic cytology and to evaluate the value of ultrasound. The results of this study showed that in patients with thyroid nodules and repeatedly diagnosed cytology findings, ultrasound findings are an excellent parameter for choosing to continue their treatment, which would be useful for periodic ultrasound [14].

In a 2005 study in Taiwan, Lin et al., in the study of thyroid nodules by ultrasound and fine-needle aspiration, concluded that ultrasound combined with fine-needle aspiration detected 10 years earlier than other methods of malignancy [15].

In 2006, in Italy, Baratolata et al. designed a study entitled Quantitative and Qualitative Evaluation of Thyroid Nodule with Ultrasound Contrast. These researchers concluded that quantitative data corroborated the subjective findings and contrast ultrasound of the thyroid gland was a feasible procedure but found other random events during ultrasound may interfere and are one of the reasons limiting the potential of this method for the detection of thyroid nodules [16].

In 2009, Tramaloni et al. evaluated ultrasound and Doppler ultrasound and fine-needle aspiration in thyroid nodules. In this study, microcalcification, hypoechoic nodules, and intra-nodular vascularization were introduced as criteria for malignancy [17]. In our study, as the grayscale ultrasound was used, therefore, vascularization was not used in

malignant scoring.

Rago et al. 2008 evaluated ultrasound and Doppler ultrasound and fine-needle aspiration for malignant patterns in thyroid nodules. In this study, microcalcification, hypoechogenic nodules, and intravascular nodular vasculature were introduced as criteria for malignancy [18]. In our study, as the grayscale ultrasound was used, therefore, vascularization was not used in malignant scoring.

CONCLUSIONS

According to the results of the present study, it seems that ultrasound scanning alone is useful in the rapid diagnosis of thyroid nodules and to suggest a more accurate result, the present study should be designed in a larger statistical population. More accurate and desirable results can be performed on specific types of lesions. Thyroid nodules with scoring 3 and 4 should also be subjected to the fine-needle

aspiration to facilitate faster and more accurate diagnosis and to prevent the progression of malignancy. Among the properties of the nodule used in scoring, nodule size alone may not be a good criterion for nodule malignancy, whereas solidity, hypo echogenic, and microcalcification favor the malignancy of the nodule, and can exclude nodules that score 1 or 2 can be tracked by ultrasound and does not necessarily need to be sampled.

Acknowledgments: This article is excerpted from the thesis of Mohammad Ebrahimi Far, a student of General Medicine, Baqiyatallah University of Medical Sciences. The authors express their gratitude to the research management staff of Baqiyatallah Hospital, Faculty of Medicine and the Radiology Department.

Conflicts of interest: The authors state that there are no conflicts of interest in the present study.

References:

1. Freitag CE, Schoenfield L, Nabhan FA, Naturale RT, Jin M. Fine-needle aspiration cytology of a thyroid nodule: Challenging morphologic considerations. *CYTOJOURNAL*. 2019; 16: 5.
2. Farhat NA, Onenerk AM, Krane JF, Dias-Santagata D, Sadow PM, Faquin WC. Primary benign and malignant thyroid neoplasms with signet ring cells: Cytologic, histologic, and molecular features. *Am J Clin Pathol*. 2017;148:251-8
3. Nikiforov YE, Nikiforova MN. Molecular genetics and diagnosis of thyroid cancer. *Nat Rev Endocrinol*. 2011; 7:569-80.
4. Bhajjee F, Nikiforov YE. Molecular analysis of thyroid tumors. *Endocr Pathol*. 2011; 22:126-33
5. Levy GH, Finkelstein A, Harigopal M, Chhieng D, Cai G. Cytoplasmic vacuolization: An under-recognized cytomorphologic feature in endocrine tumors of the pancreas. *Diagn Cytopathol*. 2013; 41:623-8.
6. Wheeler YY, Stoll LM, Sheth S, Li QK. Metastatic signet ring cell carcinoma presenting as a thyroid nodule: Report of a case with fine-needle aspiration cytology. *Diagn Cytopathol*. 2010; 38:597-602.
7. Jung YY, Kim MK, Lee TJ, Lee CH, Lee CY, Lee H, et al. The unique liquid-based cytologic findings of thyroid signet-ring follicular adenoma: A report of two cases with fine needle aspiration cytology. *Acta Cytol*. 2013;57:100-6
8. Pagni F, Ronchi S, Di Bella C, Serra G, Costantini M, Leone BE. Signet-ring cell differentiation in FNA cytology of a primitive thyroid carcinoma. *Cytopathology*. 2013; 24:274-5.
9. Yang GC, Scognamiglio T, Kuhel WI. Fine-needle aspiration of mucin-producing thyroid tumors. *Acta Cytol*. 2011; 55:549-55.
10. Chiofalo MG, Losito NS, Fulciniti F, Setola SV, Tommaselli A, Marone U, et al. Axillary node metastasis from differentiated thyroid carcinoma with hürthle and signet ring cell differentiation. A case of disseminated thyroid cancer with peculiar histologic findings. *BMC Cancer*. 2012;12:55
11. Bokhari A, Tiscornia-Wasserman PG. Cytology diagnosis of metastatic clear cell renal cell carcinoma, synchronous to pancreas, and metachronous to thyroid and contralateral adrenal: Report of a case and literature review. *Diagn Cytopathol*. 2017; 45:161-7.
12. Esmaili Gourvarchin Galeh H, Meysam Abtahi Froushani S, Afzale Ahangaran N, Hadai SN. Effects of Educated Monocytes with Xenogeneic Mesenchymal Stem Cell-Derived Conditioned Medium in a Mouse Model of Chronic Asthma. *Immunol Invest*. 2018; 47(5):504-520.
13. Siadati S, Moazezi Z, Bayani MA, Mirzapour A, Nikbakhsh N, Ghaemian N, Nabahati M, Shokri S, Sharbatdaran M. The Diagnostic Value of Fine Needle Aspiration as Compared to Pathology Results in Diagnosis of Thyroid Nodules: A 22-Year Followup Study. *J Babol Univ Med Sci*. 2015; 17(9):39-43.
14. Rosário PW, Ward S, Carvalho A, Graf H, Maciel Rui MB, Maciel Z. Thyroid nodules and differentiated thyroid cancer: update on the Brazilian consensus. *Arq Bras Endocrinol Metab*. 2013; 57(4): 240-264.
15. Lin JD, Chao TC, Huang BY, Chen ST, Chang HY, Hsueh C. Thyroid cancer in the thyroid nodules evaluated by ultrasonography and fine-needle aspiration cytology. *Thyroid*. 2005; 15(7):708-17.
16. Bartolotta TV, Midiri M, Runza G, Galia M, Taibbi A, Damiani L, Palermo Patera G, Lagalla R. Incidentally discovered thyroid nodules: incidence, and greyscale and colour Doppler pattern in an adult population screened by real-time compound spatial sonography. *Radiol Med*. 2006; 111(7):989-98.
17. Tramalloni J, Monpeyseen H, Correas JM, Helenon O. Thyroid nodule management: ultrasonography, fine-needle cytology. *J Radial*. 2009; 90 (3 Pt 2): 632-70.
18. Rago T, Vitti P. Role of thyroid ultrasound in the diagnostic evaluation of thyroid nodules. *Best Prac Res Clin Endocrinol Metab*. 2008; 22 (6): 913-28.