

Positive Predictive Value of Ultrasound in Determination of Malignant Thyroid Nodule

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ABSTRACT

Background: Thyroid nodule is a discrete lesion which is ultrasonographically distinct from the surrounding thyroid parenchyma. Overall risk of malignancy in thyroid nodule is 5-10%. Thyroid carcinoma accounts for <1% of all malignant neoplasms. High resolution thyroid ultrasound is used as a screening procedure in clinical evaluation for detecting and characterizing nodular thyroid disease.

Aim: To determine the positive predictive value of ultrasound in determination of malignant thyroid nodules having ultrasonographic features of microcalcification and shape (which is taller than wide) taking histopathology as gold standard.

Methods: It was a Cross-sectional survey which was carried out in 100 patients. Linear array high frequency probes (frequency 7-10MHz) scanning was done at the department of Radiology. Then patients were sent to the department of pathology for histopathological examination.

Results: Most common age group was 46-55 years with mean age of 38.62±13.25 years. Out of 100 patients, 41 patients (41%) were males while 59 patients (59%) were females. Out of 100 positive cases of possible malignant thyroid nodule on sonography, 82 cases were true positive and 18 cases were false positive. Positive predictive value of high resolution thyroid ultrasound was 82%.

Conclusion: High resolution thyroid ultrasound is highly helpful for diagnosis of malignant thyroid nodule.

Keywords: Thyroid carcinoma, Positive predictive value of thyroid sonography, thyroid, microcalcification.

INTRODUCTION

A thyroid nodule is a discrete lesion within the thyroid gland that is sonographically distinguishable from the adjacent parenchyma¹. Thyroid nodules are very common. They are found in 4%–8% of adults by means of palpation, in 10%–41% by means of US, and in 50% by means of pathologic examination at autopsy^{2,3,4}. The prevalence of thyroid nodules increases with age. Malignancy is more common in nodules found in patients who are younger than 20 or older than 60 years of age than in patients between 20 and 60 years of age¹.

Thyroid cancer is the most common endocrine cancer (approximately 1.0%–1.5% of all new cancers diagnosed each year in the USA) and its incidence has continuously increased in the last three decades all over the world^{5,6}.

Thyroid ultrasound and especially high resolution thyroid screening procedures are useful in detecting and characterizing nodular thyroid disease^{7,8,9}.

Thyroid ultrasound features which are associated with malignancy are micro calcifications, hypo echogenicity, irregular margins or absent halo sign, intra-nodular vascularization and shape taller than wide¹⁰⁻¹³. These patterns taken singly are poor predictors^{14,15}. Presence of microcalcification and nodule shape taller than wider detected on thyroid ultrasound should alert the physician for possibility of malignancy^{15,16}. Irregular shape had the highest sensitivity and positive predictive value while microcalcification had the highest diagnostic accuracy¹⁷.

The rationale of performing this study is to determine the positive predictive value of ultrasound in determination of malignant thyroid nodules having ultrasonographic features of microcalcification and shape taller than wide, while taking histopathology as gold standard. Both of these features have p-values less than 0.05 suggestive of their significance and association with malignancy^{18,19}.

MATERIALS AND METHODS

It was a Cross-sectional survey which was carried out from August 2016 to July 2019. In this study 100 patients were included with solitary thyroid nodule and in which thyroid ultrasonography showed microcalcifications and shape taller than wide. The patients with multinodular or diffuse goiter were not included in this study. 100 patients who fulfilled the inclusion criteria were enrolled in the study from Outpatient department. Thyroid ultrasonography was done by using 7-10 MHz linear array superficial probe. Informed consent of positive patients (as per Criteria) was obtained. All basic demographic information of each patient (name, age, sex, address and contact) was also noted. Patients were sent to the Department of Pathology of hospital for histopathological examination. The report of histopathology was assessed for confirmation of positive and negative cases. The collected data was analysed statistically by using SPSS version 10.

RESULTS

This study was conducted on 100 patients who fulfilled the inclusion criteria. Out of these 100 patients 59(59%) were female and 41 (41%) were male.

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Table 1: Frequency distribution of patients gender

| Valid | Frequency | %age |
|-------|-----------|------|
| F | 59 | 59 |
| M | 41 | 41 |
| Total | 100 | 100 |

Table 2: Descriptive statistics of age

| | N | Range | Min. | Max. | Mean | Std. Deviation |
|---------------------|-----|-------|------|------|-------|----------------|
| Age | 100 | 45 | 15 | 61 | 38.62 | 13.251 |
| Valid N (list-wise) | 100 | | | | | |

The age of the patients ranged from minimum age of 15 years to maximum age of 60 years with a mean age of 38.62 with standard deviation of ±13.25. The highest number of patients were aged between 46-55 years i.e. 24 (24%). 18 patients (18%) were aged between 16-25 years. 23 patients (23%) were aged between 26-35 years. 23 patients (23%) were aged between 36-45 years. 12 patients (12%) was aged between 55-60 years (Table 2).

Table 3: Age distribution of patients

| Age(year) | Frequency | Percent | |
|-----------|-----------|---------|-------|
| Valid | 16 – 25 | 18 | 18.0 |
| | 26 – 35 | 23 | 23.0 |
| | 36 – 45 | 23 | 23.0 |
| | 46 – 55 | 24 | 24.0 |
| | 56 – 65 | 12 | 12.0 |
| | Total | 100 | 100.0 |

Out of 100 patients who were included in the study only 82 proved to be positive on histopathology and were declared true positive while 18 patients were declared negative on histopathology and were thus declared false positive.

Following formula was used to calculate the positive predictive value of ultrasonography with 95% confidence level & 10% level of significance for diagnosis of malignant thyroid nodule in patients of thyroid nodule.

$$PPV = \frac{\text{No. of True positive}}{\text{No. of True positive} + \text{No. of false positives}}$$

The positive predictive value of ultrasonography for diagnosis of malignant thyroid nodule in patients of thyroid nodule was found to be 82%.

Table 4; Comparison of thyroid sonography vs histopathology for diagnosis of malignant thyroid nodule

| Thyroid ultrasound | Histopathology (Gold Standard) | | Total |
|--------------------|--------------------------------|----------|-------|
| | Positive | Negative | |
| Positive | 82(TP) | 18(FP) | 100 |
| Total | 82 | 18 | 100 |

TP=True positive, FP= False positive

Table 5: Positive Predictive Value of thyroid sonography

| |
|------------------------------------|
| True positive |
| Positive predictive _____ x100= |
| Value True Positive+False Positive |
| 82 |
| _____ x100=82% |
| 82+18 |

DISCUSSION

Most of the solitary thyroid nodules are benign, yet up to 30% of the solitary nodules may harbour malignancy²³. Thyroid nodules are most commonly found in 20 to 40 years of age group²⁴. The incidence of thyroid nodules is much commoner in females, male to female ratio being 1:6.3. Thyroid malignancy is more common in females but incidence before puberty and after menopause is equal in both sexes. The frequency of solitary thyroid nodule malignancy was found to be 13.33% in another study. Similarly discrete thyroid swellings are 3-4 times more common in women than men²⁵. Malignant nodules are mainly carcinomas, and, less frequently, lymphomas or metastases.

Thyroid cancer is the most common endocrine cancer (approximately 1.0%–1.5% of all new cancers diagnosed each year in the USA) and its incidence has continuously increased in the last three decades all over the world. The increasing incidence is indicated by the annual percent change (APC) that in the USA was 2.4% from 1980 to 1997 and 6.6% from 1997 to 2009 (both genders)^{22,26}.

Presently, high-resolution real-time US not only detects the presence, site, number, and size of thyroid nodules but also clearly shows the characteristics of thyroid nodules. Thyroid ultrasound features which are associated with malignancy are micro calcifications, hypo echogenicity, irregular margins or absent halo sign, intra nodular vascularization and shape taller than wide¹⁰⁻¹³. These patterns taken singly are poor predictors^{14,15}. The major limitations of ultrasonography are the high degree of observer dependency²¹ and the inability to identify retro tracheal, retroclavicular, or intrathoracic extensions of the thyroid because of acoustic shadowing from overlying air or bone.

Some authors have reported US diagnosis of thyroid nodules of all types with relatively high sensitivity ranging from 74% to 81%, but no formulas based on analysis of US characteristics are available to predict malignancy²⁰. Any useful formula should be simple and accurate for clinical use. I therefore evaluated US characteristics of thyroid nodules prospectively and analyzed the probability of malignancy on the basis of microcalcification and shape of thyroid nodule analysis.

In this study, we found no single criterion that could distinguish benign from malignant thyroid nodules with 100% reliability. As individual suspicious findings had low-to-moderate sensitivity, our sonographic classification, by which a nodule is classified as positive if microcalcification and shape taller than wide sonographic finding is present, was found to have high positive predictive value of 82%. Results of the present study are also supported by other international studies^{10,28,29}. These results, if widely reproducible, could have a substantial impact on the evaluation of incidental thyroid lesions.

In this study I included 100 patients with sonographic diagnosis of possible thyroid malignancy. Their selection was random with no gender discrimination or age specification. The age distribution shows the highest number of patients were aged between 46-55 years i.e., 24(24%). 18 patients (18%) were aged between 16-25 years. 23 patients (23%) were aged between 26-35 years.

23 patients (23%) were aged between 36-45 years. 12 patients (12%) was aged between 55-60 years. According/ to national cancer intelligence network data briefing For women diagnosed with thyroid cancer , the incidence rate peaked for ages40-44 years and then remained at about the same level. In men, the incidence rate increased steadily with age. The number of thyroid cancer diagnoses in individuals under 20 years of age was low²⁷.

In Zbigniew Adamczewski and Andrzej Lewiński study positive predictive value of microcalcification and taller than wide shape is 72% and 73% respectively that is comparable to this study²⁸. As well as Anjum Sharma et al. shows positive predictive value of ultrasound 88.4% in determining thyroid malignancy²⁹. Yet in another study positive predictive value of 94.3%is determined³⁰

This shows that the positive predictive value of thyroid ultrasound is high enough to allow reliable diagnosis of malignant thyroid nodule; therefore, it is doubtlessly highly valuable imaging modality for detection of malignant thyroid nodule. Now US is the most common method for the screening of thyroid nodule because of its advantages - simple, non-invasive and real-time observation.

CONCLUSION

High Resolution Thyroid Ultrasonography is a highly accurate, safe, non-invasive and convenient imaging modality for the evaluation of malignant thyroid nodule and is valuable for guiding treatment options thereby decreasing unnecessary intervention. It plays an integral role in early detection, planning management and estimating patient's prognosis.

REFERENCES

- Frates MC, Benson CB, Charboneau JW, Cibas ES, Clark OH, Coleman BG, et al. Management of thyroid nodules detected at US: Society of Radiologists in Ultrasound consensus conference statement. *Radiology*. 2005;237(3):794-800.
- Brander A, Viikinkoski P, Nickels J, Kivisaari L. Thyroid gland: US screening in a random adult population. *Radiology*. 1991;181(3):683-7.
- Bruneton JN, Balu-Maestro C, Marcy PY, Melia P, Mourou MY. Very high frequency (13 MHz) ultrasonographic examination of the normal neck: detection of normal lymph nodes and thyroid nodules. *J Ultrasound Med*. 1994;13(2):87-90.
- Carroll BA. Asymptomatic thyroid nodules: incidental sonographic detection. *AJR American journal of roentgenology*. 1982;138(3):499-501.
- Pellegriti G, Frasca F, Regalbuto C, Squatrito S, Vigneri R. Worldwide increasing incidence of thyroid cancer: update on epidemiology and risk factors. *J Cancer Epidemiol*. 2013;2013:965212.
- Laszlo Hegedüs MD. The Thyroid Nodule. *Clinical Practice*. October 21, 2004;Med 2004;(351):J 1764-71.
- Kim SJ, Moon WK, Cho N. Sonographic criteria for fine-needle aspiration cytology in a Korean female population undergoing thyroid ultrasound screening. *Acta radiologica*. 2010;51(5):475-81.
- Kwak JY, Kim EK, Kim MJ, Son EJ. Significance of sonographic characterization for managing subcentimeter thyroid nodules. *Acta radiologica*. 2009;50(8):917-23.
- Lin JD. Thyroid Cancer in Thyroid Nodules Diagnosed Using Ultrasonography and Fine Needle Aspiration Cytology. *Journal of Medical Ultrasound*. 2010;Vol18(3):91-104.
- Hambly NM, Gonen M, Gerst SR, Li D, Jia X, Mironov S, et al. Implementation of evidence-based guidelines for thyroid nodule biopsy: a model for establishment of practice standards. *AJR Am J Roentgenol*. 2011 ;196(3):655-60
- Popli MB, Rastogi A, Bhalla P, Solanki Y. Utility of gray-scale ultrasound to differentiate benign from malignant thyroid nodules. *Indian J Radiol Imaging*. 2012 ;22(1):63-8.
- Yoon DY, Lee JW, Chang SK, Choi CS, Yun EJ, Seo YL, et al. Peripheral calcification in thyroid nodules: ultrasonographic features and prediction of malignancy. *J Ultrasound Med*. 2007 ;26(10):1349-55.
- Hegedus L, Bonnema SJ, Bennedbaek FN. Management of simple nodular goiter: current status and future perspectives. *Endocrine reviews*. 2003;24(1):102-32.
- Kim SJ, Moon Wk, Cho N. Sonographic criteria for fine-needle aspiration cytology in a Korean female population undergoing thyroid ultrasound screening. *ActaRadiol*. 2010 51(5):475-81.
- Yunus M ,Ahmed Z. Significance of ultrasound features in predicting malignant solid thyroid nodules: need for fine-needle aspiration. *J Pak Med Assoc*. 2010 ;60(10):84.
- Seiberling KA, Dutra JC, Grant T, Bajramovic S. Role of intrathyroidal calcifications detected on ultrasound as a marker of malignancy. *Laryngoscope*. 2004;114(10):1753-7.
- Lü Zh, Zhu HQ, Dou JT, Luo YK, Kong QL, Yang GQ. Predictive value of sonographic features in preoperative evaluation of malignant thyroid nodules. *Zhonghua Yi Xue Za Zhi*. 2010 14;90(46):3272-5.
- Lu Z,Mu Y, Zhu H, Luo Y, Kong Q, Dou J, Lu J. Clinical value of using ultrasound to assess calcification patterns in thyroid nodules. *World J Surg*. 2011;35(11):122-7.
- Vinayak S,Sande JA. Avoiding unnecessary fine-needle aspiration cytology by accurately predicting the benign nature of thyroid nodules using ultrasound. *J Clin Imaging Sci*. 2012;23(2).
- Koike E, Noguchi S, Yamashita H, Murakami T, Ohshima A, Kawamoto H, et al. Ultrasonographic characteristics of thyroid nodules: prediction of malignancy. *Archives of surgery*. 2001;136(3):334-7.
- Peterson S, Sanga A, Eklof H, Bunga B, Taube A, Gebre-Medhin M, et al. Classification of thyroid size by palpation and ultrasonography in field surveys. *Lancet*. 2000;355(9198):106-10.
- Moon WJ, Jung SL, Lee JH, Na DG, Baek JH, Lee YH, et al. Benign and malignant thyroid nodules: US differentiation--multicenter retrospective study. *Radiology*. 2008;247(3):762-70.
- Duek SD, Goldenberg D, Linn S, Krausz MM, Hershko DD. The role of fine-needle aspiration and intraoperative frozen section in the surgical management of solitary thyroid nodules. *Surgery today*. 2002;32(10):857-61.
- Williams NS BC, O'Connell PR. The thyroid and parathyroid gland. . Baile and Love's short practice of surgery 25 ed. London: Hodder Arnold; 2008. p. 771 – 806.
- Sarfraz T UK, Muzaffar M. The frequency and histological types of thyroid carcinoma in northern Pakistan. *Pak Armed Forces Med* 2000;50(2):98-101.
- Gabriella Pellegriti FF, 2 Concetto Regalbuto,2 Sebastiano Squatrito,2 and Riccardo Vigneri3. Worldwide Increasing Incidence of Thyroid Cancer: Update on Epidemiology and Risk Factors. *Journal of Cancer Epidemiology*, 2013;Volume 2013 10 pages.
- Haymart MR. Understanding the relationship between age and thyroid cancer. *The oncologist*. 2009;14(3):216-21.
- Lewiński ZAa. Proposed algorithm for management of patients with thyroid nodules/focal lesions, based on ultrasound (US) and fine-needle aspiration biopsy (FNAB); 2013 [6.08.2014]. Available from: <http://www.thyroidresearchjournal.com/content/6/1/6>.
- Kwak JY KE, Kim MJ, Son EJ. Significance of sonographic characterization for managing subcentimeter thyroid nodules. *ActaRadiol*. 2009 50(8):917-23.
- Kim DW, Park JS, In HS, Choo HJ, Ryu JH, Jung SJ. Ultrasound-based diagnostic classification for solid and partially cystic thyroid nodules. *AJNR American journal of neuroradiology*. 2012;33(6):1144-9