

The value of ultrasound examination in Iraqi patients with thyroid nodules: a cross-sectional study

Mohammed Habeeb Hachim

Al-Diwaniyah Teaching Hospital, Al-Diwaniyah, Iraq

Abstract

Background: Nodules in the thyroid gland are frequently seen in the general population, and the rate of their detection is becoming increasingly higher with the current use of ultrasound examination for evaluating thyroid diseases. Some parameters, seen during an ultrasound examination, have been suggested to be associated with increased risk of thyroid malignancy; these include hypoechoogenicity, microcalcifications, increased intranodular vascularity, nodule shape or irregular margins and absence of a halo.

The aim of the study: evaluation of the ultrasound role in a sample of Iraqi patients with thyroid nodules.

Patients and methods: The current cross-sectional study included 112 patients with thyroid nodules. Each patient was evaluated by ultrasound examination for the following parameters: Poorly defined margin, microcalcification, the absence of peripheral halo, taller than full shape, the presence of internal vascularity stable configuration and Hyo-echoic pattern.

Results: The sensitivities of these parameters were 72.7, 72.7, 81.8, 36.4, 90.9, 90.9 and 90.9 %, respectively. The specificities of these parameters were 90.1, 81.2, 8.9, 93.1, 4.4, 9.9 and 84.2 %, respectively. The most sensitive parameters were internal vascularity, solid pattern, and hypoechoogenicity. The most specific parameters were taller than wide shape, poorly defined margin and hypoechoogenicity; however markers with the best combinations regarding sensitivity and specificity were poorly defined margin, calcification, and hypoechoogenicity. When the number of features included in malignancy prediction was increased, the sensitivity was higher; however, the specificity became lower. The combined sensitivity of poorly defined margin, calcification and hypoechoogenicity was 100%.

Conclusion: When the number of features included in malignancy prediction was increased, the sensitivity was higher; however, the specificity became lower. The combined sensitivity of poorly defined margin, calcification and hypoechoogenicity was 100%.

Keywords: ultrasound features, thyroid nodules

INTRODUCTION

Nodules in the thyroid gland are frequently seen in the general population, and the rate of their detection is becoming increasingly higher with the current use of ultrasound examination for evaluating thyroid diseases. The rate of detecting thyroid nodule is in the range of 19 to 67 %, and it was reported that the rate of detecting thyroid nodules becomes significantly more with increasing age reaching more than 50% in people older than 50 [1-4]. From a clinical point of view, the most important target when facing a thyroid nodule is to exclude malignancy. The rate of malignancy in thyroid nodules ranges from 5 to 15 % in different clinical settings regarding the age of the patient, gender, exposure to radiation and other risk factors [4-6]. During the last five decades, the rate of thyroid malignancy increases five times, and this is attributable mainly to increased detection of papillary thyroid carcinoma which is mostly of excellent prognosis [7]. Some parameters, seen during an ultrasound examination, have been suggested to be associated with increased risk of thyroid malignancy; these include hypoechoogenicity, microcalcifications, increased intranodular vascularity, nodule shape or irregular margins and absence of a halo [8]. Nevertheless, it seems that no single parameter can sufficiently alone be reliable to predict malignancy in thyroid nodules. Diagnostic sensitivity ranges from 26.5% to 87.1% for hypoechoogenicity, 54.3% to 74.3% for intranodular vascularity, and 26.1% to 59.1% for microcalcifications, whereas specificity ranges from 43.4% to 94.3%, 78.6% to 80.8%, and 85.8% to 95%, respectively [2, 8, 9]. One recent ultrasound parameter is elastography (US estimation of tissue elasticity) has been suggested to correlate with malignancy in the setting of a thyroid nodule. The sensitivity of this parameter in a meta-analysis study was estimated to be 92% and its specificity to be 90%, but, the number of studies which were selected to carry out the meta-analysis was unfortunately low and a few studies incorporated histopathology for definite characterization of thyroid nodules [10]. Indeed, tissue examination is the standard gold technique to establish diagnosis with certainty in patients with thyroid nodules, and fine needle aspiration cytology (FNAC) stands nowadays as the standard mode of tissue examination method in these clinical settings; however, it has its limitations, and surgical biopsy is extremely costly if considered in all cases of thyroid nodules. Indications to perform thyroid biopsy are now well defined and may include

terms such as “positive family history, radiation exposure and suspicious ultrasound examination”; [4, 8] however, there is no clear incite about the probability of the US features associated with malignancy and which combination would be more clinically useful. In the field of FNAC there is a category of patients that are going to be labeled with either inadequate sample for diagnosis (10 percent) or malignant potential is suspicious but not definite (15 to 30 percent); the risk of malignancy in the latter group being sufficiently high, so the implementation of reliable ultrasound parameters may help to reach final diagnosis or at least to take a decision in these situations [3, 4]. The sensitivity of ultrasound in diagnosing malignancy has been estimated recently to range from 26 to 87 % and specificities to range from 40 to 93% [11]. The presence of sufficient controversy in the available published literature about the role of ultrasound in predicting malignancy in the clinical setting of thyroid nodules beside the very low number of Iraqi studies dealing with this subject justified the conductance of the present study aiming at evaluation of the ultrasound role in a sample of Iraqi patients with thyroid nodules.

PATIENTS AND METHODS

The current cross-sectional study included 112 patients with thyroid nodules. The study was carried out at my private and outpatient clinics Al-Diwaniyah Teaching Hospital, Al-Diwaniyah province, Iraq, starting in January 2017 and ending in January 2018. Each patient was evaluated by ultrasound examination for the following parameters: Poorly defined margin, microcalcification, the absence of peripheral halo, taller than wide shape, the presence of internal vascularity solid configuration and hypo-echoic pattern.

Statistical analysis was carried out using the statistical package for social sciences (SPSS) version 23. Sensitivity, specificity, positive predictive value, negative predictive value and accuracy of each ultrasound parameter was assessed in isolation and also in combination.

RESULTS

Table 1 showed the sensitivity, specificity, positive predictive value, negative predictive value and accuracy of each ultrasound feature in isolation. Poorly defined margin, microcalcification, the absence of peripheral halo, taller than wide shape, the presence of internal vascularity solid configuration and Hyo-echoic pattern

were the main features tested. The sensitivities of these parameters were 72.7, 72.7, 81.8, 36.4, 90.9, 90.9 and 90.9 %, respectively. The specificities of these parameters were 90.1, 81.2, 8.9, 93.1, 4.4, 9.9 and 84.2 %, respectively. The most sensitive parameters were internal vascularity, solid pattern, and hypoechoogenicity. The most specific parameters were taller than wide shape, poorly defined margin and hypoechoogenicity; hover markers with the best combinations regarding sensitivity and specificity were poorly defined margin, calcification, and

hypoechoogenicity. Table 2 showed the sensitivity and specificity of ultrasound features in combination. When the number of features included in malignancy prediction was increased, the sensitivity was higher; however, the specificity became lower. Table 3 showed that the combined sensitivity of poorly defined margin, calcification and hypoechoogenicity was 100%. Distribution of patients according to age and gender is shown in table 4.

Table 1: Sensitivity and specificity of each ultrasound parameter in prediction of malignant thyroid nodule

| Characteristic | | Total | Malignant | Benign | Sensitivity | Specificity | PPV | NPV | Accuracy |
|----------------------|----------------------|-------|-----------|--------|-------------|-------------|------|------|----------|
| Margin | Poorly Defined | 18 | 8 | 10 | 72.7 | 90.1 | 44.4 | 96.8 | 88.4 |
| | Well Defined | 94 | 3 | 91 | | | | | |
| Calcification | Present | 27 | 8 | 19 | 72.7 | 81.2 | 29.6 | 96.5 | 80.4 |
| | Absent | 85 | 3 | 82 | | | | | |
| Peripheral halo | Present | 101 | 9 | 92 | 81.8 | 8.9 | 8.9 | 81.8 | 16.1 |
| | Absent | 11 | 2 | 9 | | | | | |
| Shape | Taller than wide | 11 | 4 | 7 | 36.4 | 93.1 | 36.4 | 93.1 | 87.5 |
| | Not | 101 | 7 | 94 | | | | | |
| Internal vascularity | Present | 46 | 10 | 36 | 90.9 | 64.4 | 21.7 | 98.5 | 67.0 |
| | Absent | 66 | 1 | 65 | | | | | |
| Internal content* | Cystic | 5 | 0 | 5 | 90.9 | 9.9 | 9.9 | 90.9 | 17.9 |
| | Predominantly Cystic | 6 | 1 | 5 | | | | | |
| | Predominantly Solid | 101 | 10 | 91 | | | | | |
| Echogenicity** | Marked Hypo | 8 | 7 | 1 | 90.9 | 84.2 | 38.5 | 98.8 | 84.8 |
| | Hypo | 18 | 3 | 15 | | | | | |
| | Iso | 49 | 1 | 48 | | | | | |
| | Hyper | 37 | 0 | 37 | | | | | |

*sensitivity and other statistics were calculated as cystic versus solid; **sensitivity and other statistics were calculated as hypo versus hyper; PPV: positive predictive value; NPV: negative predictive value

Table 2: Sensitivity of ultrasound parameters when combined together

| Number of parameters | Total | Malignant | Benign | Sensitivity | Specificity | PPV | NPV | Accuracy |
|----------------------|-------|-----------|--------|-------------|-------------|------|-------|----------|
| 2 | 65 | 0 | 65 | 100.0 | 0.0 | 9.8 | | 9.8 |
| 3 | 13 | 0 | 13 | 100.0 | 64.4 | 23.4 | 100.0 | 67.9 |
| 4 | 17 | 2 | 15 | 100.0 | 77.2 | 32.4 | 100.0 | 79.5 |
| 5 | 9 | 3 | 6 | 81.8 | 92.1 | 52.9 | 97.9 | 91.1 |
| 6 | 8 | 6 | 2 | 54.5 | 98.0 | 75.0 | 95.2 | 93.8 |

PPV: positive predictive value; NPV: negative predictive value

Table 3: Sensitivity of margin, calcification, and echogenicity in the prediction of malignant thyroid nodule

| MCE | Total | Malignant | Benign | Sensitivity | Specificity | PPV | NPV | Accuracy |
|------------------|-------|-----------|--------|-------------|-------------|------|-------|----------|
| Positive for any | 40 | 11 | 29 | 100.0 | 71.3 | 27.5 | 100.0 | 74.1 |
| Others | 72 | 0 | 72 | | | | | |

PPV: positive predictive value; NPV: negative predictive value

Table 4: Distribution of patients according to age

| Age | Male | Female | Total |
|-------|------|--------|-------|
| 11-20 | 1 | 5 | 6 |
| 21-30 | 2 | 13 | 15 |
| 31-40 | 8 | 43 | 51 |
| 41-50 | 7 | 24 | 31 |
| 51-60 | 2 | 6 | 8 |
| 61-70 | 0 | 1 | 1 |
| Total | 20 | 92 | 112 |

DISCUSSION

In the present study, it was shown that most parameters had high sensitivity and hence it disagrees with the finding of Moon *et al.* [12] who stated that most ultrasound features were of low sensitivity in a study carried out on 831 patients with thyroid nodules. In Moon *et al.* study, hypoechoogenicity gives the best sensitivity (87.2%), and this is comparable to the sensitivity of this parameter in the current study (90.9%). Also, Moon *et al.*

stated that the specificity of taller than wide shape, poor margins, significant hypoechoogenicity, and the presence of calcifications possessed the highest rates of specificity for malignancy, ranging from 90.8% to 96.1%. Comparable results were obtained in the current study for the latter parameters in the range of 81.2% to 93.1%. In another study, which included a relatively large sample size (672 patients and 1141 nodules) was carried out by Popovic *et al.* and on the contrary to the findings of the present

study, they found low sensitivity for most ultrasound features in detecting malignancy [13]. In Popovich *et al.*, it was found that microcalcifications and taller than wide shape parameters gave the best rates of specificity. Another large study was carried out by Salmaslioglu *et al.* on 550 patients with multinodular goiter and this study it was found that micro-calcifications predicted malignancy with an 89.3% sensitivity [14].

The current results have significant clinical implications. They support the idea that single US features on their own are not sufficient to provide strong evidence to confirm or rule out a diagnosis of malignancy. The utilization of a number of US features in combination to select thyroid nodules that are going to be biopsied is recommended by The American Thyroid Association [4]. Data concerning the possibility of each US characteristic to be accompanied by malignancy would help the ultimate decision to carry out FNA biopsy. The current data also suppose that more certain features are needed to perform surgery in patients with inconclusive cytology which is one of the main problems faced by surgeons in routine daily clinical practice [15, 16]. Some suggestions have been proposed by some authors to combine ultrasound findings with some clinical features and or risk factors to make a better selection of patients. For instance, Moon *et al.* considered an evaluation in which a malignant behavior was suspected when two risk factors are present in addition to the solid configuration as assessed by ultrasound. The accuracy of this combined method reached 96.2%, and the sensitivity and specificity were 87.7 and 97.8% respectively [17]. Similarly, in the present study, we also found that the combination of solid morphological pattern with the other two parameters, namely poor margin and calcification was associated with better accuracy, sensitivity, and specificity. In another case-control study, it was found that the nodular size greater than 2 cm, microcalcification, and solid composition were associated with the highest rate of malignant behavior [18]. Again these findings support our observation that solid configuration and micro-calcification are main predictors of malignancy in a thyroid nodule [19].

REFERENCES

- Remonti LR, Kramer CK, Leitão CB, Pinto LCF, Gross JL. Thyroid Ultrasound Features and Risk of Carcinoma: A Systematic Review and Meta-Analysis of Observational Studies. *Thyroid*. 2015;25(5):538-550.
- Dean DS, Gharib H. Epidemiology of thyroid nodules. *Best Pract Res Clin Endocrinol Metab*. 2008, 22:901-911.
- Hegedus L. Clinical practice. The thyroid nodule. *N Engl J Med*. 2004, 351:1764-1771.
- Cooper DS, Doherty GM, Haugen BR, Kloos RT, Lee SL, Mandel SJ, Mazzaferri EL, McIver B, Pacini F, Schlumberger M, Sherman SI, Steward DL, Tuttle RM. Revised American Thyroid Association management guidelines for patients with thyroid nodules and differentiated thyroid cancer. *Thyroid*. 2009;19:1167-1214.
- Frates MC, Benson CB, Doubilet PM, Kunreuther E, Contreras M, Cibas ES, Orcutt J, Moore FD, Jr., Larsen PR, Marqusee E, Alexander EK. Prevalence and distribution of carcinoma in patients with solitary and multiple thyroid nodules on sonography. *J Clin Endocrinol Metab*. 2006, 91:3411-3417.
- Jin J, McHenry CR. Thyroid incidentaloma. *Best Pract Res Clin Endocrinol Metab*. 2012, 26:83-96.
- Brito JP, Morris JC, Montori VM. Thyroid cancer: zealous imaging has increased detection and treatment of low-risk tumors. *BMJ*. 2013, 347: f4706.
- Frates MC, Benson CB, Charboneau JW, Cibas ES, Clark OH, Coleman BG, Cronan JJ, Doubilet PM, Evans DB, Goellner JR, Hay ID, Hertzberg BS, Intenzo CM, Jeffrey RB, Langer JE, Larsen PR, Mandel SJ, Middleton WD, Reading CC, Sherman SI, Tessler FN. Management of thyroid nodules detected at the US: Society of Radiologists in Ultrasound consensus conference statement. *Radiology*. 2005, 237:794-800.
- Rago T, Vitti P. Role of thyroid ultrasound in the diagnostic evaluation of thyroid nodules. *Best Pract Res Clin Endocrinol Metab*. 2008, 22:913-928.
- Bojunga J, Herrmann E, Meyer G, Weber S, Zeuzem S, Friedrich-Rust M. Real-time elastography for the differentiation of benign and malignant thyroid nodules: a meta-analysis. *Thyroid*. 2010, 20:1145-1150.
- Brito JP, Gionfriddo MR, Al Nofal A, Boehmer KR, Leppin AL, Reading C, Callstrom M, Elraiyah TA, Prokop LJ, Stan MN, Murad H, Morris JC, Montori VM. The accuracy of thyroid nodule ultrasound to predict thyroid cancer: systematic review and meta-analysis. *J Clin Endocrinol Metab*. 2014, 99:1253-1263.
- Moon WJ, Jung SL, Lee JH, Na DG, Baek JH, Lee YH, Kim J, Kim HS, Byun JS, Lee DH. Benign and malignant thyroid nodules: US differentiation—multicenter retrospective study. *Radiology*. 2008, 247:762-770.
- Popowicz B, Klencki M, Lewinski A, Slowinska-Klencka D. The usefulness of sonographic features in the selection of thyroid nodules for biopsy in relation to the nodule's size. *Eur J Endocrinol*. 2009, 161:103-111.
- Salmaslioglu A, Erbil Y, Dural C, Issever H, Kapran Y, Ozarmagan S, Tezelman S. 2008. Predictive value of sonographic features in the preoperative evaluation of malignant thyroid nodules in multinodular goiter. *World J Surg* 32:1948-1954.
- Mehanna HM, Jain A, Morton RP, Watkinson J, Shaha A. Investigating the thyroid nodule. *BMJ*. 2009, 338: b733.
- Langer JE, Baloch ZW, McGrath C, Loevner LA, Mandel SJ. Thyroid nodule fine-needle aspiration. *Semin Ultrasound CT MR*. 2012, 33:158-165.
- Moon HG, Jung EJ, Park ST, Ha WS, Choi SK, Hong SC, Lee YJ, Joo YT, Jeong CY, Choi DS, Ryoo JW. Role of ultrasonography in predicting malignancy in patients with thyroid nodules. *World J Surg*. 2007, 31:1410-1416.
- Smith-Bindman R1, Lebda P, Feldstein VA, Sellami D, Goldstein RB, Brasic N, Jin C, Kornak J. Risk of thyroid cancer based on thyroid ultrasound imaging characteristics: results of a population-based study. *JAMA Intern Med*. 2013, 173:1788-1796.
- Dakhil, A.S, Al-Hajjah, N.N, Shlash, R.F. Identification of factor VIII gene mutations in patients with hemophilia A. *Int. J. Res. Pharm. Sci.*, 2018, 9(2):274-283.