The predictive value of selected ultrasound features in evaluating malignancy in thyroid nodules

Waleed Q. Rajab* FICMS
Ahmed S. Khazaal* FICMS
Mohammed M. Habash** FICMS
Rana Z. Hussien*** GB ridioly

Abstract:

Background: Thyroid ultrasound has been widely used to differentiate benign from malignant nodules; many investigators have tried to point out few ultrasonographic features in order to identify those lesions, which are at a higher risk of malignancy.

Objectives: To evaluate the efficacy of selected conventional ultrasound (US) features of thyroid focal lesions useful for predicting malignancy and establishing indications for fine-needle aspiration cytology (FNAC).

Patients and Methods: Two hundred and four consecutive patients with thyroid nodules who visited the outpatient clinic of the surgical department of Tikrit University teaching hospital for the period from January 2011 to April 2014, and who underwent surgery for clinical suspicion of malignancy; were examined by US before thyroidectomy. Conventional US evaluated the presence of a halo sign, hypochochogenicity and microcalcifications.

Results: On histology, 60 nodules were diagnosed as malignant and 148 as benign nodules. On US, the echographic pattern most predictive for malignancy was microcalcification (P = 0.0001; specificity 78.0%; sensitivity 67.6%). The most specific combination on US, absent halo sign/microcalcifications (P < 0.005; specificity 92.2%; sensitivity 27.6%).

Conclusion: Findings on US become effectively predictive for malignancy only when multiple signs are simultaneously present in a thyroid nodule. Thus the predictive value of these techniques increases at the expense of their sensitivity.

Key words: Ultrasound, Thyroid, Nodule, Malignancy, Feature.

Introduction

It has been estimated that palpable thyroid nodules are present in 4–7% of the population (1), but when examined by ultrasound (US), as many as 50–70% of subjects with no history of thyroid disease have been found to have incidentally discovered thyroid nodules, many of which are not palpable (2–3). Ultrasound is an ideal imaging modality for assessment of the thyroid gland (2). It is readily available, relatively inexpensive, and does not involve ionizing radiation. The superficial location of the gland readily lends itself to sonographic evaluation using high-resolution transducer (with its excellent spatial and contrast resolution).

The role of ultrasound in benign thyroid disease includes: Ultrasound helps confirm benignity of most thyroid nodules and helps to reassure patients and guide subsequent management. In addition, ultrasound also helps to identify the small number of malignant nodules for better preoperative counseling of patients and timely management.

US can be used for follow-up of benign thyroid disease and surveillance to detect any associated malignancy and sequelae/complications.

In addition, ultrasound is easily combined with FNAC which increases its diagnostic accuracy (3). Among several US patterns, hypoechochogenicity of the nodule, microcalcifications and absence of halo sign were reported to be useful in predicting thyroid malignancy (2–4). The Society of Radiologists in Ultrasound consensus panel acknowledged that “although there are certain trends in the ultrasound distinction of benign and malignant thyroid nodules, there is also overlap in their appearances. Because of the inconsistent predictive value of ultrasound features, most agree that FNA and cytopathologic evaluation of a thyroid nodule are usually required before a patient undergoes surgical resection for a possible thyroid malignancy” (5–12).

The aim of this study was to assess the ability of conventional thyroid US, to predict malignancy of thyroid nodules.
Patients and methods:
The study included 208 consecutive patients, with nodular goiter, who visited the outpatient clinic of the surgical department of Tikrit University teaching hospital for the period from January 2011 to April 2014, and who underwent surgery for clinical suspicion of malignancy. All the patients were euthyroid, as assessed by the thyroid function tests mini-VIDAS Lab system. US was performed using an apparatus (Philips ClearVue 850), with a 7.5 MHz linear transducer. The features evaluated; the halo sign, microcalcifications and nodule echogenicity relevant to surrounding glandular tissue. The data were analyzed statistically using the statistical package for Microsoft windows system (XLstat software) using Chi square and sensitivity/specificity tests of Galen.

Results:
From a total of 208 patients there were 140 females (mean age 40.1 ± 15 years, range 17–72 years) and 68 males (mean age 46.8 ± 13.9 years, range 15–68 years). Histological examination demonstrated malignancy in (29%) 60 nodules; while 148 nodules were benign. The size of malignant nodules was 3.2 ± 6.7ml (range 0.4–22); the size of benign nodules was 10.5 ± 12.4 ml (range 0.3–58). The single US pattern that was most predictive of malignancy (Table 1) was microcalcification (P < 0.0001; specificity 78.0%, sensitivity 67.6%). Absent halo sign/ microcalcifications was the most specific double combination (Table 2) of US patterns (P < 0.005; specificity 92.2%, sensitivity 27.6%), no gain in specificity was obtained; when all the three patterns were considered together.

Table (1): ultrasonographic features and histology in thyroid nodules.

| Sonographic pattern       | Malignant | Benign | Significance | Specificity % | Sensitivity % | Positive predictive value % | Negative predictive value % |
|---------------------------|-----------|--------|--------------|---------------|---------------|-------------------------------|-------------------------------|
| Microcalcifications       | 40/60     | 34/148 | P < 0:0001   | 78            | 67.6          | 55                            | 86                            |
| Absent halo sign          | 26/60     | 36/148 | P < 0:05     | 76.6          | 55            | 56.6                          | 77.7                          |
| Hypoechogenicity          | 40/60     | 76/148 | P < 0:15     | 49.6          | 67.6          | 35.4                          | 79.2                          |

Table (2): Combined ultrasonographic features and histology in thyroid nodules.

| Sonographic features       | Malignant | Benign | Significance | Specificity % | Sensitivity % | Positive predictive value % | Negative predictive value % |
|---------------------------|-----------|--------|--------------|---------------|---------------|-------------------------------|-------------------------------|
| Absent halo sign +        | 36/60     | 26/148 | P < 0:0001   | 83.4          | 67            | 59                            | 84.5                          |
| hypoechogenicity          |           |        |              |               |               |                               |                               |
| Absent halo sign +        | 16/60     | 10/148 | P < 0:005    | 92.2          | 27.6          | 62.5                          | 76.8                          |
| microcalcifications       |           |        |              |               |               |                               |                               |
| Hypoechogenicity +        | 18/60     | 30/148 | P < 0:28     | 80.7          | 31            | 27.4                          | 74.7                          |
| microcalcifications       |           |        |              |               |               |                               |                               |

Discussion:
The vast majority of these thyroid nodules are benign hyperplastic nodules; 2–6% of the population have multinodular thyroid with a clinically palpable mass. Compared with the very high prevalence of nodular thyroid disease, thyroid cancer is not common (13). Patients with multinodular thyroid are frequently asymptomatic, but may present with an anterior neck lump or swelling. Occasionally, patients present acutely with compressive symptoms or with a rapidly enlarging neck mass, most commonly caused by hemorrhage into an underlying hyperplastic thyroid nodule. Thyroid ultrasound has been widely used to differentiate benign from malignant nodules and to guide fine needle aspiration cytology (FNAC) (13-14). However, the accuracy and predictive values of sonographic criteria are variable and no single ultrasound feature has both high sensitivity and positive predictive value for prediction of benignity or malignancy. In agreement with other authors, in this study we had found that intranodular microcalcification is the most predictive feature of malignancy on US (15-17); it was found in 67.6% of malignant and in 21.9% of benign. The sensitivity (67.6%) and specificity (78.0%) was higher than in other studies (18). The absence of halo sign had lower sensitivity (55.0%) and specificity (76.6%) than intranodular microcalcifications, in agreement with other authors’ observations (18–22). A hypoechogenic feature was found in 67.6% of malignant nodules and in 52.3% of benign nodules. Hypoechogenicity, absence of halo sign and microcalcifications...
have already been reported as markers suggestive of malignancy in thyroid nodules in previous reports (21, 23–28). In this study we found that the most predictive combination on US was absence of halo sign plus microcalcifications. This combination had a high specificity (92.2%), but a low sensitivity (27.6%); while the predictive value of other combinations was lower. In conclusion, only when multiple signs are simultaneously detected in a thyroid nodule; findings on US become highly predictive for malignancy. However, the predictive value of these features increases at the expense of their sensitivity.

Authors Contribution:
Dr. Waleed Qahtan Rajab: Researcher and supervisor
Dr. Ahmed Salim Khazaal: Researcher, operator and data collection
Dr. Mohammed Mahmood Habash: Researcher, operator and data collection
Dr. Rana Zahim Hussien: Operator and data collection

References
1) Wienke JR, Chon WK, Filding JR, Zou KH & Mittelsköld CA. Sonographic features of benign thyroid nodules. Journal of Ultrasound Medicine 2003 22 1027 1031.

2) Papini E, Guglielmi R, Binchini A, Crescenzi A, Taccagna S, Nardi F, Panuzzi C, Rinaldi R, Toscano V & Pacella C. Risk of malignancy in nonpalpable thyroid nodules: predictive value of ultrasound and color-doppler features. Journal of Clinical Endocrinology and Metabolism 2002 87 1941–1946.

3) Lupoli G, Vite G & Carglia M. Familial papillary thyroid microcarcinoma: a new clinical entity. Lancet 1999 353 637–639.

4) Lyshchik A, Hiashi T, Ašto R, Tanaka S, Ito J, Mai JJ, Pellot- Barakat C, Insana MF, Brill AB, Saga T, Hiraoka M & Togashi KL. Thyroid gland tumor diagnosis at US Elastography. Radiology 2005 237 202–211.

5) Screaton NJ, Braman L & Grant JW. US-guided core-needle biopsy of thyroid gland. Radiology 2003 226 827–832.

6) Tan GH & Ghribi H. Thyroid incidentalomas: management approaches to non-palpable nodules discovered incidentally on thyroid imaging. Annales of Internal Medicine 1997 126 226–231.

7) Hegedus L. The thyroid node. The New England Journal of Medicine 2004 351 1764–1771.

8) Caso MR & Ghribi H. Continuing controversies in the management of thyroid nodules. Annales of Internal Medicine 2005 142 926–931.

9) Kang HW, No H, Chng JH, Min YK, Le MS, Lee MK, Yang JH & Kim KW. Prevalence, clinical and ultrasonographic characteristics of thyroid incidentalomas. Thyroid 2004 14 29–33.

10) Chan BK, Desogol R, Weigel RJ & Brooke JR. Common and uncommon sono graphic features of papillary thyroid carcinoma. Journal of Ultrasound in Medicine 2003 22 1083–1090.

11) Hegedus L. Thyroid ultrasound. Endocrinology and Metabolism Clinics of North America 2001 30 1941–1946.

12) Triton RL, Gervais DA, Boland GW, Mher MM & Mueller PR. Sonography and sonographically guided fine-needle aspiration biopsy of the thyroid gland: indications and techniques, pearls and pitfalls. American Journal of Radiology 2003 14 267–271.

13) Frates MC, Benson CB, Charboneau JW, et al. Management of thyroid nodules detected at US: Society of Radiologists in Ultrasound consensus conference statement. Radiology 2005;237: 794–800.

14) Marqusee E, Benson CB, Frates MC, et al. Usefulness of ultrasonography in the management of nodular thyroid disease. Ann Intern Med. 2000;133:696–700.

15) Nixon JJ, Gany I, Han LE, Yu C, Palmer FL, Whitcher MM, Shah JP, Shaha A, Kattan MW & Patel SG. Nomogram for selecting thyroid nodules for ultrasound guided fine-needle aspiration biopsy based on a quantification of risk of malignancy. Head & Neck 2012 35 1022–1025.

16) Rossi M, Buratto M, Brni S, Fileri C, Tagliati F, Trasforini G, Rossi R, Beccati MD, Degli Uberti EC & Zatelli MC. Role of ultrasonographic/clinical profile, cytology, and BRAF V600E mutation evaluation in thyroid nodule screening for malignancy: a prospective study. Journal of Clinical Endocrinology and Metabolism 2012 97 2354 2361.

17) Ozel A, Erturk SM, Ercan A, Ylmaz B, Bsak T, Cantisani V, Basak M & Karpaz Z. The diagnostic efficiency of ultrasound in characterization for thyroid nodules: how many criteria are required to predict malignancy? Medical Ultrasonography 2012 14 24–28.

18) Takashima S, Fukuda H, Nomra N, Kishimoto H, Kim T & Kobayashi T. Thyroid nodules: re-evaluation with ultrasound. Journal of Clinical Ultrasound 1995 23 179–184.

19) Goldfarb M, Gondek S, Solorzano C & Lew JI. Surgeon-performed ultrasound can predict benignity in thyroid nodules. Surgery 2011 150 436–441.

20) Chen G, Zhu XQ, Zou X, et al: Retrospective analysis of thyroid nodules by clinical and pathological characteristics, and ultrasonographically detected calcification correlated to thyroid carcinoma in South China. Eur Surg Res 2009: 42: 137 – 142.

21) Seiberling KA, Dutra JC, Grant T, et al: Role of intrathyroidal calcifications detected on ultrasound as a marker of malignancy. Laryngoscope 2004; 114: 1753 – 1757.

22) Barbaro D, Simi U, Meucci G, Lapi P, Orsini P &
Pasquini C. Thyroid papillary cancers: microcarcinoma and carcinoma, incidental cancers and non-incidental cancers – are they different diseases? Clinical Endocrinology 2005 63 577–5781.

23) Kwak JY, Han KH, Yoon JH, Moon HJ, Son EJ, Park SH, Jung HK, Choi JS, Kim BM & Kim EK. Thyroid imaging reporting and data system for US features of nodules: a step in establishing better stratification of cancer risk. Radiology 2011 260 892–899.

24) Hong YJ, Son EJ, Kim EK, Kwak JY, Hong SW & Chang HS. Positive predictive values of sonographic features of solid thyroid nodule. Clinical Imaging 2010 34 127 133.

25) Gul K, Ersoy R, Dirikoc A, Korukluoglu B, Ersoy PE, Aydin R, Ugras SN, Belendi OK & Cakir B. Ultrasonographic evaluation of thyroid nodules: comparison of ultrasonographic, cytological, and histopathological findings. Endocrine 2009 36 464–472.

26) 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.

27) Cappelli C, Castellano M, Pirola I, Cumetti D, Agosti B, Gandossi E & Agabiti Rosei E. The predictive value of ultrasound findings in the management of thyroid nodules. Quarterly Journal of Medicine: An International Journal of Medicine 2007 100 29–35.

28) Frates MC, Benson CB, Charboneau JW, Cibas ES, Clark OH, Coleman BG, Cronan JJ, Doublet 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. Society of Radiologists in Ultrasound. Management of thyroid nodules detected at US: Society of Radiologists in Ultrasound consensus conference statement. Radiology 2005 237 794–800.