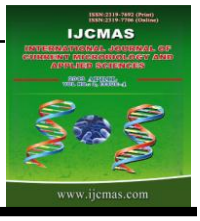
International Journal of Current Microbiology and Applied Sciences
ISSN: 2319-7706 **Volume 2 Number 4 (2013) pp. 183-189**
http://www.ijcmas.com



Original Research Article

Evaluation of Thyroid Nodules Using Ultrasound and Score the Likelihood of Malignancy According To TIRADS

H. Sadashiva Gowda*

Department of Radio diagnosis, VIMS, Bellary, Karnataka, India
*Corresponding author

Keywords

Thyroid nodules, Ultrasound, TIRADS

A B S T R A C T

Multinodular goitre are thought to arise due to differences in response of follicular cells to stimuli such as trophic hormones which in turn result in proliferation of follicular cells which are genetically more sensitive to the effects of trophic hormones. Non-uniform hyperplasia of certain subsets of follicular cells, production of new follicles, non-uniform accumulation of colloid result in stress within the thyroid gland, the end result of increased stress within the thyroid gland results in bleeding into the gland, scar tissue formation and calcifications within the gland. The selection of the study population was independent of the reference standard (histopathology). Personal data and ultrasound findings were entered into a coded – numbered proforma). Informed consent was obtained from the patient / patient`s relative prior to ultrasound in accordance with the ethical guidelines of Helsinki declaration and approved by the Institutional review board of the hospital. The sensitivity, specificity, PPV and NPV of the absent halo sign is -69%, 52%, 67% and 55% respectively. In this study 67% of the nodules with an absent halo sign were found to be malignant.

Introduction

The thyroid gland is an endocrine gland situated in the lower neck extending from the fifth cervical vertebra to the first thoracic vertebra. The thyroid gland is enveloped by the pre-tracheal fascia. The thyroid gland is a midline structure and consists of a right and left lobe connected across the midline by a narrow isthmus. The lobes of the thyroid gland conform to the shape of a cone. The medial or deep aspect of the thyroid gland is closely applied to the larynx and the upper part of closely related to the oesophagus. The thyroid gland occasionally has a pyramidal lobe which usually arises from the isthmus and connects to the hyoid bone (Frates *et al.,* 2003).

The vascular supply of the thyroid gland is via the superior and inferior thyroid arteries with occasional contribution form the arteria thyroidea ima which is a branch of the brachio-cephalic trunk or the arch of aorta(Middleton *et al.,* 2004). The superior thyroid artery is a branch of the external carotid artery, the inferior thyroid artery

arises as a branch from the thyrocervical trunk which is in turn a branch of the first part of the subclavian artery (Brander *et al.,* 2000).

Nerve supply of the thyroid gland: the superior, inferior and middle cervical sympathetic ganglia supply the thyroid gland.

The gland is enveloped by connective tissue with septations which extend into the substance of the gland resulting in the formation of lobules. The basic functional unit of the thyroid gland consists of follicles. The follicle has a core of colloid with a layer of epithelial cells which rest on a basal membrane. The colloid consists of inactive form of thyroid hormone in the form of a glycoprotein which is iodinated (Kuma *et al.,*1994).

The epithelial cells lining the follicles are influenced by TSH levels and change in morphology (squamous, low cuboidal or columnar) under the influence of TSH levels. Follicular cells are responsible for conversion of the inactive colloid to active T3 and T4. The other significant cells seen in the thyroid gland are the C-cells which are responsible for production of calcitonin, a hormone which regulates calcium homeostasis (Shaha JP *et al.,* 1992).

Of the nodular forms of goitre, multinodular goitre is the result of essentially the same pathological process as diffuse simple goitre. Over time, multiple episodes of glandular hyperplasia and involution result in a more nodular, irregular form of thyroid gland enlargement which is termed multinodular goitre (Ahuja *et al.,* 1995).

Multinodular goitre are thought to arise due to differences in response of follicular cells to stimuli such as trophic hormones which in turn result in proliferation of follicular cells which are genetically more sensitive to the effects of trophic hormones. Non-uniform hyperplasia of certain subsets of follicular cells, production of new follicles, non-uniform accumulation of colloid result in stress within the thyroid gland, the end result of increased stress within the thyroid gland results in bleeding into the gland, scar tissue formation and calcifications within the gland. The stromal network of the thyroid gland restricts the hyperplastic follicles and results in the nodular appearance.

Materials and Methods

The prospective study patients were referred from the department of Endocrinology and Endocrine surgery. All patients who fulfilled the inclusion criteria were included in the study. The selection of the study population was independent of the reference standard (histopathology). Personal data and ultrasound findings were entered into a coded – numbered proforma). Informed consent was obtained from the patient / patient`s relative prior to ultrasound in accordance with the ethical guidelines of Helsinki declaration and approved by the Institutional review board of the hospital.

Exclusion criteria

Purely cystic nodules
Nodules < 1 cm
Nodules with gross macrocalcification where the ARFI box cannot avoid areas of macrocalcification.
Patients who do not undergo FNAC / surgery or if the FNAC is inadequate

Performimg the ultrasound examination

Ultrasound scanner

Ultrasound of the neck and thyroid gland was performed using (ACUSON S2000™, Siemens) using a high frequency linear probe (4-9 MHz). Conventional sonography was performed in all patients. The patients were examined in supine position with extension of neck by placing a pillow under the upper back. The images were sent to PACS where another radiologist with 8 years of experience interpreted the findings and was blinded to findings of other radiologist. Gray scale imaging of the thyroid gland was done in both transverse and longitudinal planes and Colour Doppler evaluation of the nodule was done.

Each thyroid nodule was examined for Site (Right lobe, Isthmus, Left lobe), composition (solid, cystic, mixed), Halo (present, absent), echogenicity (hyperechoic, isoechoic, hypoechoic, markedly hypoechoic), margins (well defined, microlobulated, ill-defined, irregular), presence of calcification (microcalcification, macrocalcification), shape of the nodule (wider than tall, taller than wide), vascularity of the nodule (central or peripheral), Presence of background changes of diffuse thyroiditis and lymph nodes.

Nodule with solid component >2/3rd were labelled as solid; cystic nodules had no solid components, mixed nodules had both solid and cystic areas with solid component constituting <2/3rd of the size of the lesion. For mixed lesions echogenicity, margin, shape and presence of calcification was assessed for the solid component. Echogenicity was described in comparison with the thyroid gland and strap muscles.

Results and Discussion

Ultrasound characteristics of nodules

Table.1 Size of the nodule

Size	Benign (%)	Malignant (%)
< 1 cm	1	3
>1cm	72	96
Total	73	99

There is no significant correlation between the size of the nodule and presence of malignancy; Pearson Chi-square value = 0.510, DF =1 and p = 0.475 (p>0.05).

Table.2 Halo sign

Halo	Benign (%)	Malignant (%)
Present	37(55.2)	30(44.8)
Absent	33(33)	67(67)
Total	70	97

Strong correlation was present between the absent halo sign and outcome Pearson Chi-square value= 8.139, DF=1 and p=0.004(p < 0.05).

There is strong evidence that the absent halo sign is associated with malignancy. The sensitivity, specificity, PPV and NPV of the absent halo sign is -69%, 52%, 67% and 55% respectively. In this study 67% of the nodules with an absent halo sign were found to be malignant.

Table.3 Composition

Composition	Benign	Malignant
Solid	54(38.2)	87(61.8)
Mixed	18(66.7)	9(33.3)
Total	72	96

There was moderate correlation between the composition of the nodule and

malignancy Pearson Chi-square value= 7.975, DF=2, p=0.019(p < 0.05).

Table.4 Calcification

Calcification	Benign (%)	Malignant (%)
Microcalcification	7(11.8)	52(88.1)
Macrocalcification	8(72.7)	3(27.3)
Both	3(60)	2(40)
No calcification	55(56.7)	42(43.2)
Total	73	99

There is very strong correlation between the calcification in the nodule and outcome, Pearson Chi -square value- 35.416, DF=3, and p < 0.001 (p < 0.05).

The sensitivity, specificity, PPV and NPV for the presence of calcification were 57%, 75%, 76% and 56 % respectively. In this study 88% of the nodules with microcalcification were malignant. The presence of macrocalcification was not associated with malignancy with 72.7% of the nodules were found to be benign.

Table.5 Echogenicity

Echogenicity	Benign	Malignant
Hyperechoic	5(55.6)	4(44.4)
Isoechoic	46(78)	13(22)
Hypoechoic	15 (26.8)	41(73.2)
Markedly hypoechoic	7(14.5)	41(85.5)
Total	73	99

There is very strong correlation between the hypoechogenecity of the nodule and presence of malignancy. Pearson Chi-square value = 27.747, DF=3 and p<0.001(p < 0.05).

The sensitivity, specificity, PPV and NPV for hypoechogenecity of the nodule were - 82.8%, 69%, 78%, and 75% respectively. In this study 85.5% of the markedly hypoechoic nodules were malignant and 73.2% of the hypoechoic nodules were found to be malignant and 78.9 % of combined hypoechoic and markedly hypoechoic nodules were malignant

Table.6 Margins of the nodule

Margins	Benign	Malignant
Well defined	52(59.1)	36(40.9)
Microlobulated	2(40)	3(60)
Ill defined	14(27)	38(73)
Irregular	5(18.5)	22(81.5)
Total	73	99

There is very strong correlation between absence of a well-defined margin and malignancy. Pearson Chi-square value = 21.450, DF=3 and p <0.001

The sensitivity, specificity, PPV and NPV were 63.6%, 71%, 75% and 59% respectively. 81.5% of the nodules with irregular margins and 73% of nodules with ill-defined margins were malignant.

Table.7 Shape of the nodule

Shape	Benign	Malignant
Wider than tall	62 (56.9)	47 (43.1)
Tall than wide	11(17.4)	52 (82.6)
Total	73	99

There is very strong correlation between the shape of the nodule and malignancy. Pearson Chi-square value- 25.4, DF=1, p < 0.001

The sensitivity, specificity, PPV and NPV of a nodule being taller than wide were 52.5%, 84%, 82% and 56% respectively. In this study 82.6% of taller than wide nodules were malignant compared to only 43% of the wider than tall nodules.

Table.8 Background features of thyroiditis

Background thyroiditis	Benign	Malignant
Present	5 (25)	15 (75)
Absent	68 (44.7)	84 (55.3)
Total	73	99

There is weak statistical correlation between presence of background thyroiditis and the malignancy Pearson Chi-square value= 2.818, DF=1, and p = 0.093 (p >0.05)

Table.9 Nodule vascularity

Vascularity	Benign	Malignant
Central	11(16.2)	57 (83.8)
Peripheral	62 (59.6)	42 (40.4)
Total	73	99

There is very strong statistical correlation between presence of central vascularity and malignancy. Pearson Chi-square value= 31.759, DF=1, and p <0.001 (p < 0.05). The sensitivity, specificity, PPV and NPV for central vascularity were 57.5%, 84%, 83.8% and 59.6% respectively. In this study 83.8% of the nodules with central vascularity were found to be malignant.

Table.10 Lymphadenopathy

Lymph nodes	Benign	Malignant
Present	4 (11.1)	32 (88.9)
Absent	69 (50.7)	67 (49.3)
Total	73	99

There is very strong statistically significant correlation between presence of lymphadenopathy and the outcome Pearson Chi-square value= 31.759, DF=1, and p < 0.001 (p < 0.05).

The sensitivity, specificity, PPV and NPV for presence of cervical lymphadenopathy were 32.3%, 94%, 88.9% and 50% respectively. In this study 83.8% of the nodules associated with lymphadenopathy were found to be malignant

A training set which included 70% of data was used for formulation of the prediction model and 30% of data was used for validation of the prediction model.

Nodules which were included in the study were larger than 5 mm and had been subjected to ultrasound guided FNAC.

Further criteria for nodule inclusion were one or more of the following criteria

Undergone thyroid surgery

At least 2 benign FNAC results

One benign FNAC result with no change or reduction in lesion size on follow up sonography

Results of multiple regression analysis of the training data set (randomly selected 1402 nodule) and odds ratio calculation showed the following sonographic features had statistical significance in predicting presence of malignancy.

Lesion echotexture – Hypoechoic and markedly Hypoechoic lesions were more likely to be malignant

Non-parallel orientation

Margin spiculations

Poorly delineated lesion margins

Presence of micro-calcifications

Of the above features, odds ratio of more than 5 were seen for micro-lobulated or spiculated lesions and lesions with markedly hypoechoic echotexture. Risk scores were assigned to each suspicious ultrasound characteristic based on the odds ratio for each sonographic characteristic which was in turn calculated by logistic regression analysis. The odds ratios were rounded off to the closest integer and denoted as the risk score, the lowest risk score was 0 and maximum risk score was 6.

Risk scores for suspicious ultrasound features were assigned as follows (Shirakawa *et al.,* 2001).

1-Non parallel orientation
2-Hypoechogenecity and microcalcifcations
5-Microlobulated or spiculated margins
6-Markedly Hypoechoic

The total risk score for a particular lesion was the sum of the risk score of individual risk scores for each suspicious sonographic feature the nodule possessed.

Malignancy rates were 59.1 in microlobulated / spiculated lesions and 43.6 in lesions which were markedly hypoechoic.

The malignancy rate was found to be the maximum (95.2) in lesions which had a combination of findings such as being markedly Hypoechoic, of non-parallel orientation with microlobulations / spiculated borders and micro-calcifications.

Validation of the prediction model was then performed by analysing 598 thyroid lesions in 536 individuals. The results obtained during the validation phase of the prediction model showed a 6.2 cancer rate in thyroid lesions with no suspicious sonographic features. Lesions which were of non-parallel orientation and lesions with ill-defined borders had a cancer rate of 8.6, lesions with micro-lobulations or spiculations had a cancer rate of 33.3, lesions which were markedly Hypoechoic had a cancer rate of 34.5.

The authors concluded that the above prediction model which uses suspicious sonographic characteristics may be useful in risk stratification of thyroid lesions.

Jin Young *et al*., thus concluded that a malignancy risk similar to that in BIRADS cannot be assigned to a nodule based on a TIRADS system, on the other hand, calculating the overall risk scores for a thyroid lesion may be more accurate than the TIRADS system in assigning malignancy risk to each individual thyroid lesion. They further concluded that a predictor model which assigns risk scores to thyroid lesions may be contributory in the risk stratification of thyroid lesions.

Real time high resolution sonography of thyroid lesions have been reported in multiple studies to be highly predictive of malignancy only if multiple suspicious sonographic features are present simultaneously, the predictive value of sonography in the diagnosis of cancer in thyroid nodules improves at the expense of its sensitivity and malignancy is predicted in only ~ 20 % of case with a high degree of specificity

Clinicians have however, long relied on palpatory findings in clinical evaluation of thyroid lesions, a hard thyroid nodule being more likely to be malignant as opposed to soft nodules being likely benign (Eleonora Horvath *et al.,* 2009).

Lesion texture on palpation is however subjective and palpation findings vary with the examiner. The palpatory findings are variable depending on the size of the thyroid lesion and the depth at which it is located. Elastography is a relatively new diagnostic modality that has been recently introduced.

It is a modality by which hardness of a lesion can be analysed with greater objectivity when compared to palpation. Elastography is an advanced imaging

technique which enables the sonographer to objectively assess the visco-elasticity of tissues. The image displayed as a result of applying elastography technique to a particular organ is essentially similar to the information obtained by palpation.

The basic concepts involved in Elastography are
Stress
Strain
Elastic modulus

Elastography techniques rely on stress, strain or shear modulus or shear wave velocity imaging. Elastography images are generated by an ultrasound machine along with a simultaneous acquisition of grey scale images enabling comparison between the appearance of a lesion on grey scale and appearance on application of Elastography.

In conclusion, all the nodules were evaluated using ultrasound and graded for a risk of malignancy according to TIRADS. There was no evidence to suggest that sex of the patient and site of the nodule (right lobe, left lobe and isthmus) had an effect on the nodule outcome. The most helpful features in predicting malignancy were

Absence of a well-defined halo around the lesion
Presence of microcalcification
Hypoechogenecity of the nodule – both when the nodule was hypoechoic compared to thyroid parenchyma but more echogenic than the strap muscles and more so when more hypoechoic than the strap muscles
Taller than wide nodule
Presence of irregular or Ill-defined margins of the nodule
Presence of central vascularity
Presence of lymphadenopathy

References

Ahuja AT, Chow L, Chick W, King W, Metreweli C.1995. Metastatic cervical nodes in papillary carcinoma of the thyroid: ultrasound and histological correlation. Clin Radiol. 50(4):229–231.

Brander AE, Viikinkoski VP, Nickels JI, Kivisaari LM.2000. Importance of thyroid abnormalities detected at US screening: a 5-year follow-up. Radiology. 215(3):801–806.

Chan BK, Desser TS, McDougall IR, Weigel RJ, Jeffrey RB Jr.2003. Common and uncommon sonographic features of papillary thyroid carcinoma. J Ultrasound Med.22(10):1083–1090.

Frates MC, Benson CB, Doubilet PM, Cibas ES, Marqusee E.2003. Can color Doppler sonography aid in the prediction of malignancy of thyroid nodules?. J Ultrasound Med. 22(2):127–131.

Kuma K, Matsuzuka F, Yokozawa T, Miyauchi A, Sugawara M.1994. Fate of untreated benign thyroid nodules: results of long-term follow-up. World J Surg. 18(4):495–498.

Middleton WD, Kurtz AB, Hertzberg BS.2004. Ultrasound: the requisites. 2nd ed. St Louis, Mo: Mosby. 244–252.

Shah JP, Loree TR, Dharker D, Strong EW, Begg C, Vlamis V.1992. Prognostic factors in differentiated carcinoma of the thyroid gland. Am J Surg. 164(6):658–661.

Shirakawa T, Miyamoto Y, Yamagishi J, FukudaK, Tada S. 2001. Color/power Doppler sonographic differential diagnosis of superficial lymphadenopathy: metastasis, malignant lymphoma, and benign process. J Ultrasound Med.20(5):525–532.