Prediction of Risk of Malignancy in A Solitary Thyroid Nodule by Sonographic Characteristics

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ABSTRACT

INTRODUCTION: The thyroid is an endocrine gland situated in the infrahyoid compartment of neck in a space outlined by muscle, trachea, esophagus, carotid arteries and jugular veins. It lies against C5 to T1 vertebral levels. 4-7% of adult population has palpable thyroid nodule, prevalence being higher in females than in males. In autopsy, 50% of adults older than 60y have thyroid nodule. Though nodular thyroid disease is relatively common, thyroid cancer is rare and accounts for less than 1% of all malignancies indicating that overwhelming majority of thyroid nodules are benign. About 80% of nodular thyroid disease is due to hyperplasia of the gland and it occurs in 5% of any population. Many cystic thyroid lesions are hyperplasic nodules that have undergone extensive liquefactive degeneration.Colloid nodule and papillary ca are most common benign and malignant lesion respectively. The purpose of this study was to assess the sonographic characteristics in a solitary thyroid nodule and predicting risk of malignancy

METHODE: This prospective study was conducted in a tertiary care hospital in Kathmandu.62 patients with palpable thyroid nodule were evaluated for sonographic characteristics including color Doppler study. USG guided FNA for cytopathological examination was then performed.

RESULTS: 15 male(24.2%) and 47 female(75.8%) patients in the age group of 20-79 years with palpable solitary thyroid nodule were evaluated. 56 patients(90.4%) had benign nodule and 6 patients(9.6%) had malignant nodule. Colloid goiter was the most common benign nodule where as papillary carcinoma was the most common malignant nodule. Amongst 6 malignant nodules, 3 (50%) were heterogenous, 2 (33.3%) were hypoechoic and 1 (16.7%) was isoechoic. All hyperechoic nodules were benign. All 6 malignant nodules (100%) in this study had ill-defined margin whereas only 7 benign nodules (12.5%) had ill-defined margin.

CONCLUSION: This study has shown that ill-defined margin and non hyperechogenicity are good predictors of malignancy (sensitivity 100% each, specificity 87.5% and 17.9%, PPV 46.2% and 11.5%, NPV 100% each, p value 0.009 and 0.023 respectively). Combining these two parameters increases the predictability (sensitivity 100%, specificity 92.7%, PPV 60% and NPV 100%, P value<0.001).

KEY WORDS: Thyroid nodule, fine needle aspiration, ultrasonography

INTRODUCTION

The thyroid is an endocrine gland situated in the infrahyoid compartment of neck in a space outlined by muscle, trachea, esophagus, carotid arteries and jugular veins. It lies against C5 to T1 vertebral levels.[1] 4-7% of adult population has palpable thyroid nodule prevalence being higher in females than in males.[2, 3] Exposure to ionizing radiation increases the incidence of both benign and malignant nodules with 20-30% of ionizing radiation exposed population having palpable thyroid nodules.[4,5] In autopsy, 50% of adults >60y have thyroid nodule.[6] Though nodular thyroid disease is relatively common, thyroid cancer is rare and accounts for less than 1% of all malignancies indicating that overwhelming majority of thyroid nodules are benign.[7]

The most common lesions are colloid nodules, cysts and thyroiditis (in 80 percent of cases); benign follicular neoplasms (in 10 to 15 percent); and thyroid

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carcinoma (in 5 percent). About 80% of nodular thyroid disease is due to hyperplasia of the gland and it occurs in 5% of any population.[8] Many cystic thyroid lesions are hyperplasic nodules that have undergone extensive liquefactive degeneration. In the course of this degeneration, calcification, which is often coarse and perinodular may occur.[9,10] Sonographically, most hyperplasic nodules are isoechoic. As the size of the mass increases, it may become hyperechoic, owing to the numerous interfaces between cells and colloid substance.[9,11] Among the malignant nodules the approximate prevalence of different histologic types are: Papillary carcinoma 75-90% [7,12], Follicular carcinoma 5-15% [7], Medullary carcinoma 5%, Lymphoma 4% (mostly nonhodgkin's type) and Anaplastic carcinoma <2% .[13]

All these neoplasms are more prevalent in female than male.[1] Of these, papillary and follicular carcinomas are well differentiated and they have best prognosis whereas anaplastic carcinoma is poorly differentiated and has worst prognosis.[14] Other indicators of poor prognosis are male sex and age <20 years or >65 years.[15] Papillary carcinoma is a predominant histologic type in children (75%)and those who were exposed to radiation previously (85-90%).[16] Mean age of presentation is 30-40y and male:female ratio is1:2.[16] Intake of high iodine predisposes to papillary carcinoma but follicular carcinoma is more common in area with low iodine content.[17] It has been previously thought that most papillary carcinoma of thyroid less than 10 mm in maximal diameter have low risk of metastases.[18,19] But occult papillary carcinoma of the thyroid as small as 2 mm has been shown in some studies to have already metastasized to cervical nodes[18,19,20,21].

Correlation of ultrasound and palpation findings will provide a comprehensive evaluation of nodular thyroid disease[22,23].Ultrasonography can accurately detect nonpalpable nodules, estimate the size, volume of the goiter, differentiate simple cysts, and guide for FNA. According to multiple studies, among the various sonographic features, microcalcification shows the highest accuracy (76%), specificity (93%) and positive predictive value (70%) for malignancy as a sign, however sensitivity is low (36%) and insufficient to be reliable for detection of malignancy.[24,25,26]. Presence of comet tail in a nodule is highly specific for benign nodule[27].

Although FNA is the most reliable diagnostic method for evaluating clinically palpable thyroid nodules, high-resolution sonography has some clinical applications[28,29,30].

USG guided FNA has been reported to yield higher diagnostic accuracy than fine-needle aspiration alone, even in clinically palpable nodules[31,32,33]. It can be done either by non-aspiration capillary action or by suction aspiration techniques.[34] . In a cystic lesion or one that is a mixture of cystic and solid components, fine-needle aspiration of a possible solid component should be performed, since the risk of cancer is the same as that for a solid nonfunctioning nodule. Sensitivity and specificity of FNA was reported to be >94%. Nondiagnostic material may be present in 20% cases[23].

METHODE

It was a prospective study carried out in a tertiary care hospital. Patients with solitary thyroid nodule referred for US evaluation were studied. USG of the neck was carried out with 7.5 MHZ linear probe. The nodule was detected and size determined. The nodules were interpreted with respect to echogenicity and border characteristics (margin). Nodules in which these characteristics could not be assessed were excluded from the analysis. The echogenecity of each nodule was classified as hypoechoic, isoechoic, mixed echoie or hyperechoic in comparison with the surrounding tissue of the thyroid gland. Under sonographic guidance, FNA was performed by using 23G needle with standard technique using suction aspiration The specific diagnosis for each case was confirmed by cytological examinations. Statistical analysis was performed using SPSS software version 10.0 and statistical calculations were performed with Chi square, Fisher exact and independent samples tests.

Data associations were considered statistically significant at P<0.005.

RESULTS

Out of 66 patients, 4 were subsequently excluded because they didn't fulfill the inclusion criteria. The sonographic features of all nodules were obtained by high resolution USG and FNA was subsequently performed in all of them. Specimens were immediately sent for cytological examination. FNA was considered gold standard.

Of the 62 patients, 47 (75.8%) were females and 15 (24.2%) were males. Among 56 benign nodules, 45 (80.4%) were in females and 11(19.6) were in males. Among 6 malignant nodules, 4(66.7%) were in males and 2 (33.3%) were in females.

3 malignant nodules (50%) were heterogenous, 2 (33.3%) were hypoechoic and 1(16.7%) was isoechoic. None of the malignant nodule was hyperechoic. 37 (66.1%) benign nodules were heterogenous.10 (17.9%) benign nodules were hyperechoic. 5 malignant nodules (83.3%) were solid where as 1 malignant nodule (16.7%) was complex with solid predominance. All 4 cystic nodules (7.1%) were benign. All complex nodules with predomint cystic components were also benign.

Among benign nodules, 49 (87.5%) had well defined margin where as 7(12.5%) benign nodules had ill defined margin. But all 6 malignant nodules (100%) had ill defined margin.

One malignant nodule (16.7%) had snow storm type of microcalcification. None of the benign nodules had microcalcification. Nodule having microcalcification was malignant.

All malignant nodules (100%) had increased internal vascularity where as benign nodules were variable in internal vascularity.

From the aforementioned analysis, ill defined margin and non hyperechogenicity parameters were found to be more predictive of malignancy.

Hence, validity of these parameters was tested and the results are given below:

Table 1

	Sensitivity	Specificity	PPV	NPV	p-value
Ill defined margin	100.0%	87.5%	46.2%	100.0%	<0.001
Non-hyper echogenicity	100.0%	17.9%	11.5%	100.0%	0.577

This table shows illdefined margin, and non hyperechogenicity as more predictive of malignancy. However only illdefined margin was statistically significant with P value of <0.001.

Binomial Logistic Regression Analysis

A binomial logistic regression analysis was performed with presence or absence of malignancy as the dependent variable and the above-mentioned factors as the independent variables. The result is summarized in the following table:

Table 2

Factor	p-value
Ill defined margin	0.009
Non-hyper echogenicity	0.023

This table shows Ill-defined margin and non hyperechogenicity are the statistically significant Predictors of malignancy.

Table 3

	Malignant		benign	
	n	%	n	%
ill-defined & non-hyper	6	100.0%	4	7.1%
others	0	0.0%	52	92.9%
	6	100.0%	56	100.0%

Sensitivity: 100.0%; specificity: 92.9%; p-value: <0.001

Table 3 shows the results of bivariate analysis of illdefined margin and non hyperechogenicity.With this statistical significant analysis with P value of<0.001, the predictability of malignancy is significantly high with sensitivity, specificity,positive predictive value and negative predictive value of 100%,92.9%,60% and 100% respectively.

DISCUSSION

Evaluation of thyroid nodule frequently involves a stepwise performance of clinical evaluation to several imaging techniques. The use of USG in the assessment of nodular thyroid disease has greatly increased the detection rate of small thyroid nodules.[20] Evaluation of thyroid nodule by FNA has been the gold standard. The purpose of present study was to predict the risk of malignancy in a solitary thyroid nodule as assessed by sonographic characteristics. The prevalence of malignant nodule in this study resembles to the prevalence studied by Enrico papini et al 9.2% [20].

The most common benign nodule was colloid goiter (50 of 56, 89.2%) with or without degeneration and most common malignant nodule was papillary carcinoma,(5

of 6, 83.3%).These figures resemble to the prevalence of 80% of colloid goiter. The prevalence of papillary carcinoma also closely resembles to the general prevalence of papillary carcinoma of 75-90 %.[7,12]

Non hyperechogenicity as a single parameter to predict malignancy, has sensitivity, specificity, positive predictive value and negative predictive value of 100%, 7.9%,

11.5% and 100% respectively with P value of 0.577. Many studies have shown that hypoechogenicity is a good predictor of malignancy.

The study by Kim et al [21] showed the presence of any one of the characters (illdefined margin, marked hypoechogenicity or microcalcification) had the sensitivity of 93.8% and specificity of 66%

As a single parameter, ill defined margin had sensitivity, specificity, positive predictive value and negative predictive value of 100%,87.5%,46.2% and 100% respectively to predict malignancy with P value of<0.001.

CONCLUSION

Ill defined margin and non hyperechogenicity are good predictors of malignancy in a thyroid nodule. Therefore non-hyperechoic nodule with ill defined margin should invariably undergo FNA. This study is limited due to small sample size .Further study in large number of cases is recommended.

REFERENCES

1. Solbiati L, Charboneau JW,.Osti V, James EM ,Hay ID.The Thyroid Gland. In:Rumack CM, Wilson SR, Charboneau JW,editors. Diagnostic Ultrasound, 3rd edition.St Louis,Elevier Mosby.volume 1, 2005, p735-770
2. Rojeski MT, Gharib H. Nodular thyroid disease: Evaluation and management. N Engl J Med. 1985;313:428-436
3. Van Herle AJ, Rich P, Ljung B-ME et al. The thyroid nodule. Ann Intern Med. 1992;96:221-232
4. Favus MJ, Schneider AB,Stachura ME,et al. Thyroid cancer occurring as a late consequence of head-and-neck irradiation: Evaluation of 1056 patients. N Engl J Med. 1976;294:1019-1025.
5. Degroot LJ, Reily M, Pinnamenni K, et al. Retrospective and prospective study of radiation-induced thyroid disease.Am J Med. 1983;74:852-862
6. Hegedüs L. The Thyroid Nodule, volume 351:1764-1771. October 21, 2004, Number 17
7. Grebe SKG, Hay ID. Follicular cell-derived thyroid carcinoma.Cancer treat Res. 1997; 89:91-140
8. Hennemann G. Non-toxic goiter.Clin Endocrinol Metab. 1979; 8:167-179
9. Kerr L. High-resolution thyroid ultrasound: the value of color Doppler. Ultrasound Q. 1994; 12:21-43
10. Solbiati L, Cioffi V, Ballarati E. Ultrasonography of the neck.Radiol Clin North Am. 992;30:941-954
11. Muller HW, Schroder S, Schneider C,et al. Sonographic tissue chacterization in thyroid gland diagnosis.Klin Wochenschr. 1985;63:706-710.
12. Schlumberger M-J,Filetti S, Hay ID. In: Nontoxic goiter and thyroid neoplasia. Larsen PR,Kronenberg HM,Melmed S,et al. (eds):Williams Textbook of Endocrinology,10th ed.Philadelphia,WB Saunders,2003,p 457-490.
13. Nel CJC,van Heerden JA,Goellner JR,James EM,et al. Medullary carcinoma of thethyroid :A clinicopathologic study of 82 cases.Mayo Clin Proc 1985;60:51-58
14. Kumar V,Cotran RS, Robbins SL. Diseases of the endocrine system, Basic Pathology.5th edition, W.B Saunders Company.1992,p 643-680
15. Jameson JL,Weetman AP.Disorders of the thyroid gland. In:Braunwald E,Fauci AS,Kasper Dl,Hauser SL,Longo DL,Jameson JL,editors.Harrison's Principles of internal medicine,15th edition. Mc Graw Hill. Volume 2. 2003, p 2063-2081.
16. Sadlor GP, Clarj OH.Vanherden JA, Farley DR. Thyroid and parathyroid. In: Schwartz SI, Shires GT, Spencer FC, DalyJM,.Fischer JE and Halloway AC, editors.Principles of Surgery.7th edition. Mc Graw Hill.p:1661-1713
17. Dudley N. The thyroid gland. In: Peter J Morris PJ. Malt DA,editors. Oxford Text Book of Surgery, International edition, Oxford University Press, volume 1, p731-754
18. Harach HR, Franssila KO, Wasenius V. Occult papillary carcinoma of the thyroid: a "normal" finding in Finland. Cancer.1985; 56:531–538.
19. Monchick JM, De Petris G, De Crea C. Occult papillary carcinoma of the thyroid presenting as cervical cyst. Surgery. 2001; 129:429–432.
20. Papini E, Guglielmi R, Bianchini A, et al. Risk of malignancy in nonpalpable thyroid nodules: predictive value of ultrasound and color-Doppler features. J Clin Endocrinol Metab. 2002; 87:1941–1946.
21. Kim E, Park CS, Chung WY, et al. New sonographic criteria for recommending fine-needle aspiration biopsy of non-palpable solid nodules of the thyroid. AJR Am J Roentgenol. 2002; 178:687–691.
22. Mandel SJ. A 64 year old woman with a thyroid nodule. JAMA, Dec 1.2004;292(21):2632-2642
23. Larsen TC III,Smith MM, Chong WK,Martin WH.Thyroid and parathyroid gland. In:Haaga JR, Lanzieri CF, Gilkeson RC, editors. CT and MR imaging of the whole body. 4th edition. Mosby. Volume 1, 2003, p 663-681.

24. Brkljacic B, Cuk V,Tomic-Brjac H,et al. Ultrasound evaluation of benign and malignant nodules in echographically multinoular thyroid.J Clin Ultrasound. 1994;22:71

25. Solbiati L,Lerace T,Lagalla R,et al. Reliability of high frequency US and Color Doppler US of Thyroid nodules:Italian multicenter study of 1,042 pathologically confirmed cases,Which role for scintigraphy or biopsy? Presented at Radiological Society of North America Meeting,1995

26. Kakkos SK, Scopa CD, Chalmoukis AK, et al: Relative risk of cancer in sonographically detected thyroid nodules with calcifications. J Clin Ultrasound .2000;7:347-352.

27. Olliff JFC. Ultrasound of the neck.In: David Sutton, editor. Textbook of Radiology and Imaging. 7th edition.Churchill Livingstone,volume 2, 2003:1512-1513

28. James EM, Charboneau JW. High-frequency (10MHz) thyroid ultrasonography.Semin Ultrasound CT MR 1985; 6:294-309

29. Scheible W,Leopold GR,Woo VL,et al. High-resolution real-time ultrasonography of thyroid nodules.Radiology. 979;133:413-417

30. Simeone JF,Daniels GH,Mueller PR,et al. High-resolution real-time sonography of the thyroid.Radiology. 1982;145:431-435

31. Roddie ME and Kreel L. Endocrine disease. In: Grainger RG and Alison DJ, editors. Diagnostic Radiology, A Text Book of Medical Imaging. 3rd edition.Churchill and Livingstone.1997.vol 2,p 1295-1324.

32. Hatada T, Okada K, Ishii H, Ichii S, Utsunomiya J. Evaluation of ultrasound-guided fine-needle aspiration biopsy for thyroid nodules. Am J Surg.1998; 175:133 –136

33. Yokozawa T, Fukata S, Kuma K, et al. Thyroid cancer detected by ultrasound-guided fine-needle aspiration biopsy. World J Surg. 1996;20:848 –853

34. Titton RL, Gervais DA, Boland GW, Maher MM and Mueller PR, Sonography and Sonographically Guided Fine-Needle Aspiration Biopsy of the Thyroid Gland: Indications and Techniques, Pearls and Pitfalls , AJR. 2003; 181:267-271