ASSOCIATION OF ULTRASONOGRAPHY AND ULTRASOUND -GUIDED FINE NEEDLE ASPIRATION CYTOLOGY IN THE DIAGNOSIS OF THYROID NODULES

Binit Dev[1], Ajay Kumar Yadav[1], Sushil Taparia[2], Roshana Khadka[3], Shripad J. Walavalkar[4]*

Affiliation

1. *Assistant Professor, Radiology, Birat Medical College and Teaching Hospital, Nepal*
2. *Senior Consultant Radiology, Birat Medical College and Teaching Hospital, Nepal*
3. *Assistant Professor Radiology, Birat Medical College and Teaching Hospital, Nepal.*
4. *Senior Consultant Pathology. Birat Medical College and Teaching Hospital, Nepal*

ARTICLE INFO

Received : 25 February, 2021

Accepted : 25 August, 2021

Published : 04 November 2021

ORA 272

DOI: https://doi.org/10.3126/bjhs.v6i2.40562

**** Corresponding Author***

Dr. Binit Dev

Lecturer

Department of Radiology

Email: binit386@gmail.com

ORCID: https://orcid.org/0000-0002-7478-6419

Citation

Binit Dev, Ajay Kumar Yadav, Sushil Taparia, Roshana Khadka, Shripad J. Walavalkar. Association of Ultrasonography and Ultrasound-guided Fine Needle Aspiration Cytology in the Diagnosis of Thyroid Nodules. BJHS 2021;6(2)15. 1573-1578.

ABSTRACT

Introduction

Ultrasound (USG) is the most commonly used imaging method to evaluate thyroid nodules. The sonographic features of thyroid nodules are very important to determine whether the nodule is benign or malignant. Fine Needle Aspiration Cytology (FNAC) is the gold standard to determine whether the nodule is benign or malignant.

Objective

The purpose of this study was to compare ultrasound and color Doppler features of thyroid nodules with ultrasound-guided FNAC results to determine the relative importance of these features in predicting the risk of malignancy.

Methodology

This prospective cross-sectional study was conducted in Birat medical college teaching hospital in Tankisinuwari, Morang, Nepal. The study was conducted from September 2019 to April 2021. In total sixty-one patients with thyroid nodules were evaluated for sonographic characteristics. Finally, USG guided FNA for cytopathological examination was performed. Both descriptive and inferential statistics were used to analyze the result.

Result

Out of the 61 patients, 34 (55.7%) were females and 27 (44.2%) were males. Majority of the malignant nodules were solid 11 (91.6%), whereas cystic and mixed nodules were predominantly seen in benign nodules 18 (36.7%) and 30 (61.2%) respectively. In malignant nodules 10 (83.3%) were heterogeneous and 2 (16.6%) were isoechoic. In benign nodules 29 (59.1%) were heterogeneous and 15 (30.6%) were anechoic with comet-tail artifact and 5 (10.2%) were isoechoic. Among 12 malignant cases, internal and peripheral vascularity were equally present in six cases each. Benign nodules showed peripheral vascularity in 48 (97.9%) and internal vascularity was noted in only one nodule. All of the malignant nodules showed calcification. None of the benign nodules showed micro-calcification. In malignant cases, cervical lymph nodes were present in 7 (58.3%) and absent in 5 (41.6%). In benign cases, cervical lymph nodes were present in 4 (8.1%) and absent in 45 (91.83%).

Conclusion

The ultrasound features associated with malignancy in thyroid nodules are predominantly solid component, presence of micro-calcifications and internal vascularity. Enlarged cervical lymph nodes are good predictors for malignancy. USG guided FNAC confirms the suspicious features of thyroid nodules seen on USG.

KEY WORDS

Diagnosis, Thyroid nodule, Ultrasonography

INTRODUCTION

Thyroid gland is the largest endocrine gland in the human body. Nodules and diseases in the thyroid are common findings and are found mainly in the iodine-deficient areas of the world. According to Surveillance, Epidemiology, and End Results (SEER) data, thyroid cancer constitutes 3.0% of all newly diagnosed cancers.[1]

The extensive use of thyroid ultrasound has led to an increased diagnosis of low-risk thyroid cancer. Therefore, we should pay more attention to risk evaluation and result prediction to minimize morbidity and unnecessary treatment.[2]

Ultrasound (USG) is a reliable and simple diagnostic method with high sensitivity (90%) and specificity (85%) for thyroid nodules.[3] It is suggested that the ultrasonic features of malignant thyroid nodules include hypoechoic, solid structure, irregular margin, micro-calcification, and regional lymph node metastasis.[4-7] Intranodular hypervascularity and nodule size ≥ 2 cm are also consider as indicators of thyroid cancer.[8-10]

Majority of thyroid nodules are due to hyperplasia of glands containing solid and cystic components, in the later stage calcification (micro/macro) occur.[11,12] Lesions that are initially isoechoic may become hyperechoic as the size of the mass increases due to various pathological changes. The approximate prevalence of malignant nodules are Papillary carcinoma 75-90%, Follicular carcinoma 5-15%, Medullary carcinoma 5%, Lymphoma 4%, and Anaplastic carcinoma <2%.[13]

Ultrasound being non-ionizing, fast, easy to perform, cheaper and widely available, and therefore easy to assess the thyroid nodule, and its acceptability to evaluate the thyroid disease has increased day by day. USG is helpful in differentiating solid and cystic lesions, solitary from multinodular lesions, and also from diffuse enlargement of the gland. It is therefore an ideal investigation of choice for evaluating thyroid nodules.[14] Fine Needle Aspiration Cytology (FNAC) is a simple, quick, and well-established first-line diagnostic tool for the evaluation of thyroid disease.[15] USG guided FNAC has much higher sensitivity, specificity, and positive predictive value than palpation guided FNAC.[16] The purpose of this study was to assess the sonographic characteristics in thyroid nodule and predict the risk of malignancy and also compare sonography findings with USG guided FNAC findings.

METHODOLOGY

After getting the approval from institutional ethical committee, this prospective cross-sectional study was conducted from September 2019 to April 2021 in the department of Radiology and Pathology at Birat Medical College Teaching Hospital, Tankisinuwari, Morang, Nepal. During this period, all patients with thyroid nodules referred for ultrasound were considered appropriate for the study. Sample size was calculated using formula $n= z_{\alpha}^{2} * S_N (100-S_N)/ (d^2 * \text{Prevalence})$ and obtained 55.

where z_{α} = 1.96 at 95% confidence level, S_N = Sensitivity = 66.7 taking coarse macro-calcification as a single parameter to diagnose malignancy, d= maximum tolerable error = 4%, prevalence of malignancy in thyroid nodules = 9.6%.

As there could be indefinite cases, we added 10% of the calculated sample size and hence final sample size is 61, which is comparable to sample size taken in various similar published studies.[17] USG of the neck was carried out with a linear high-frequency probe. The nodules were interpreted concerning for echotexture, composition, calcification, vascularity, and presence of cervical lymph nodes. Fine needle aspiration was performed under ultrasound guidance by using a 23 G needle with standard technique using suction aspiration and slides were sent to the department of pathology for cytological study. The definitive diagnosis for each case was determined by cytological examinations.

STATISTICAL ANALYSIS

Statistical analysis was performed using SPSS software version 22.0 and data were analyzed using both descriptive and inferential statistics. Frequency tables, sensitivity, specificity, accuracy, positive predictive value and negative predictive value were calculated. Chi-square test was used to test the level of significance. Data associations were considered statistically significant at P<0.05.

RESULTS

In this study, patients' age was ranged from 20 to 70 years. The mean age for malignant lesions was 39.5 years and for benign lesions was 38.4 years. Out of the 61 patients, 34 (55.7%) were females and 27 (44.2%) were males. Gender variation for malignant thyroid nodules showed female preponderance, which was not evident in benign cases as shown in table 1.

Table 1: Patient's Demography

	Malignant	Benign
Age (years)		
< 20	9 (18.4 %)	1 (8.3 %)
20 – 39	15 (30.6 %)	5 (41.7 %)
40 – 59	20 (40.8 %)	4 (33.3 %)
> 60	5 (10.2 %)	2 (16.7 %)
Gender ratio		
Male	2 (16.6 %)	25 (51 %)
female	10 (83.3 %)	24 (48.9 %)
Location		
Right lobe	3 (25 %)	13 (26.5 %)
Left lobe	5 (41.6 %)	20 (40.8 %)
Isthmus	3 (25 %)	4 (8.1 %)
Both lobes	1 (8.3 %)	12 (24.4 %)

Fisher exact test

Majority of the malignant nodules were solid 11 (91.6%), whereas cystic and mixed (solid and cystic) nodules were predominantly seen in benign. In malignant nodules 10

(83.3%) were heterogeneous. In benign nodules 29 (59.1%) were heterogeneous (figure 1A), 15 (30.6%) were hypoechoic and 5 (10.2%) were isoechoic. In malignant, all cases showed internal and peripheral vascularity (figure 2B). Whereas maximum benign nodules showed peripheral vascularity. Micro-calcification was only noted in the malignant cases hence making it a good predictor for malignancy (figure 1A). In malignant cases, cervical lymph nodes were present in 7 (58.3%). In benign cases, cervical lymph nodes were present in only 4 (8.1%), hence the presence of lymphadenopathy is an indicator for malignancy. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), the accuracy of USG and FNAC findings are illustrated in table 3.

Table 2: Characteristics of USG features for benign and malignant thyroid nodules.

	Malignant (n=12)	Benign (n=49)	*P*-value
Composition			
Solid	11 (91.6%)	1 (2%)	<0.000
Cystic	0	18 (36.7%)	
Mixed	1 (8.3%)	30 (61.2%)	
Echogenicity			
Heterogenous	10 (83.3%)	29 (59.1%)	0.086
Hypoechoic	0	15 (30.6%)	
Isoechoic	2 (16.6%)	5 (10.2%)	
Calcification			
No calcification	0	39 (79.5%)	<0.000
Macrocalcification	6 (50%)	10 (20.4%)	
Microcalcification	6 (50%)	0	
Vascularity			
Peripheral	6 (50%)	48 (97.9%)	<0.000
Intrinsic	6 (50%)	1 (2%)	
Lymph node			
Yes	7 (58.3%)	4 (8.1%)	<0.000
No	5 (41.6%)	45 (91.8%)	

Table 3: Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), accuracy of USG and FNAC findings for malignant and benign lesions.

		FNA result		Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
		Malignant	Benign					
USG result	Malignant	5	2	71.4	95.9	71.4	87	85
	Benign	7	47					

A)

B)

C)

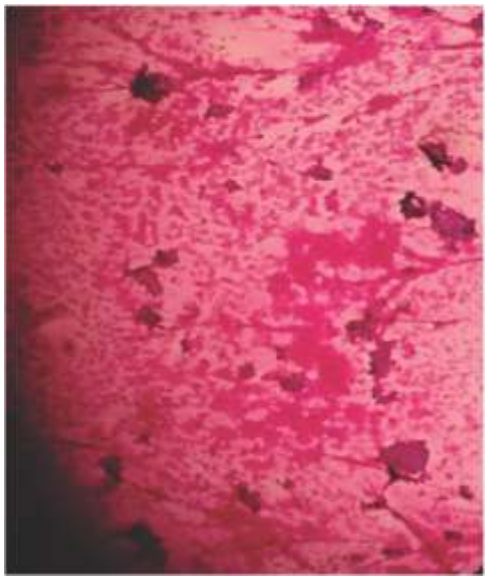
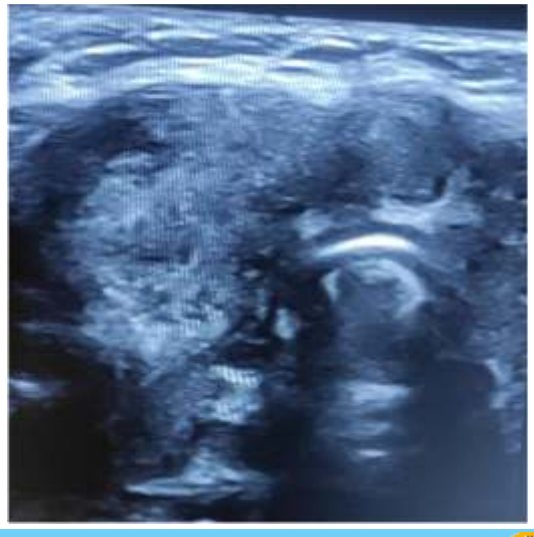
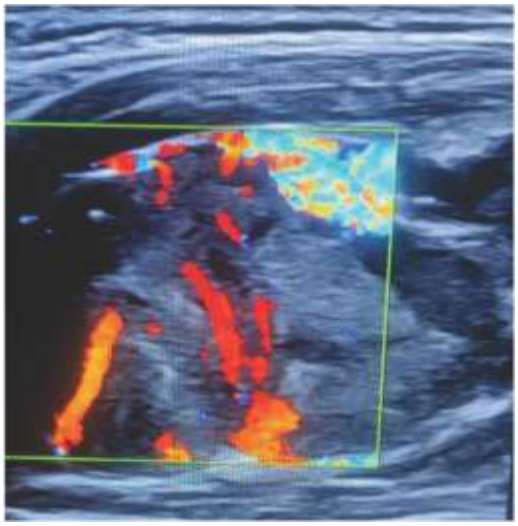


Figure 1.A, B. Heterogeneous nodule with a solid and cystic component with absent vascularity.Macrocalcification was also noted. C. Moderately cellular smears with flat sheets showing evenly spaced follicular cells. Nodular goiter was diagnosed by USG and confirmed by fine-needle aspiration cytology (Pap stain X 40).

A)



B)



C)

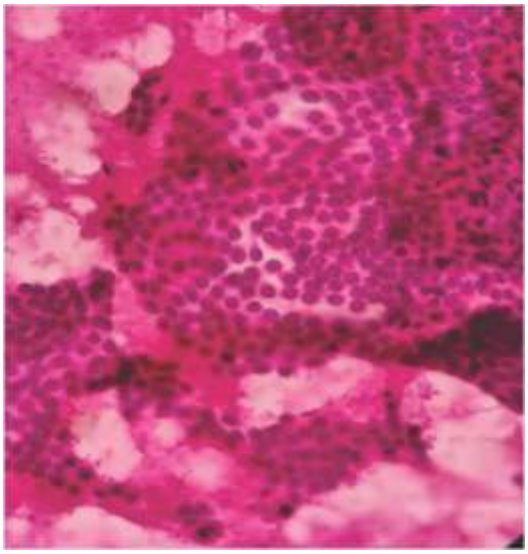


Figure 2. A, B. Ultrasound image shows a heterogenous nodule with predominantly solid component and micro calcifications with intrinsic vascularity. C. Cells arranged in a papillary pattern and in sheets showing nuclear grooves. Papillary carcinoma was diagnosed by US-guided fine-needle aspiration biopsy (Pap stain X 40)

DISCUSSION

This study was conducted to assess the sonographic characteristics in thyroid nodules and predict the risk of malignancy and also compare sonography findings with FNAC findings.

It is generally accepted that when reliably distinguishing malignant nodules from benign nodules, no ultrasound examination feature has sufficient diagnostic accuracy.[18]It is important to emphasize the recognition of complex patterns rather than a single feature to identify malignant thyroid tumors, otherwise the risk of malignant tumors will be incorrectly assessed. Pattern recognition methods have been applied to distinguish malignant thyroid nodules from benign thyroid nodules on ultrasound images because they can effectively capture the nonlinear relationship that exists in most ultrasound features. Assessment of thyroid nodules by FNA has been the gold standard. The overall accuracy of FNA has been shown to exceed 95%, therefore at present, it is the most precise and cost-effective method for initial evaluation of nodular thyroid disease.[19]

Like Reading et al.[20], we found that the echo pattern method for thyroid nodules is highly sensitive and specific to the presence of benignity. In previous studies, the malignant risk of mixed echogenic nodules ranged from 2.3% to 17.6%.[21,22] Our malignant rate is within this range.

The incidence rate of malignant tumors is significantly higher in nodules with solid tumors. In the current study, we have noticed that malignant tumors are associated with larger solid components of the nodules. This may be related to the higher degree of angiogenesis associated with solid thyroid nodules and malignant tumors. The sensitivity and specificity of solid nodules were 91.6% and 98%, respectively (P = 0.000). This result is close to that of Enrico papiniet al.[23], which showed that 87% of malignant nodules were solid hypoechoic

In this study, the incidence of malignant tumors in patients with calcification was significantly higher. About 70.59% of benign nodules had no calcification or micro-calcification. Occurrence of micro-calcification may be a reliable predictor of thyroid cancer which was also demonstrated by Wang et al.[24]that there was a close relationship between micro-calcification detected by ultrasound and thyroid cancer, with a specificity of 96.7%. Chammaset al.[25] reported similar findings, indicating that the presence of micro-calcification may be a specific predictor of thyroid cancer.

In present study, all malignant nodules showed vascularity. Nodules with intrinsic vascularity were more likely to be malignant, while nodules with peripheral vascularity were more likely to be benign. A study by Frateset al.[26] analyzed the relationship between the inherent vascular blood flow pattern of color Doppler imaging and the risk of malignant thyroid nodules and concluded that the possibility of malignancy in solid hypervascular nodules is high. A recent study by Papiniet al.[23] showed that hypoechoic combined with the presence of irregular margins, inherent vascular flow patterns, or micro-calcifications had 87% sensitivity in differentiating malignant nodules in the study population.

In this study, most malignant thyroid nodules were associated with the presence of cervical lymph nodes. For the detection of metastatic thyroid cancer lymph nodes, no single ultrasound feature is sensitive enough. In another recent study, sonographic features obtained 4 days before surgery were directly correlated with the histology of 56 cervical lymph nodes. Some of the most specific criteria were cystic areas (100%), hyperechoic spots with colloidal or microcalcifications (100%), and peripheral vessels (82%). Only peripheral blood supply (86%) was sensitive. The sensitivity of all others was less than 60%, which was not enough to be used as a single standard for differentiating malignant tumors.[27] As shown in the early studies of Frasoldati A et al.[28] and Kuna SK et al.[29], the most sensitive feature was the absence of hilum (100%), but the specificity was low (only 29%).

CONCLUSION

USG features suggesting thyroid malignancy include predominantly solid components, presence of micro-calcifications and internal vascularity. Cervical lymphadenopathy with fine calcifications increases the probability of thyroid malignancy metastasis in the setting of suspicious thyroid nodules. USG guided FNAC confirms the suspicious features of thyroid nodules seen on USG.

RECOMMENDATIONS

All palpable and non-palpable thyroid nodules should be recommended for USG examination. The role of USG is very effective in distinguishing benign from malignant nodules since its high accuracy has been statistically proven. Hence, the clinicians should strongly recommend USG for any suspicious thyroid nodules for better evaluation and proper management.

LIMITATION OF THE STUDY

This study was limited because of its small sample size, a larger sample size would have given us a better understanding. Furthermore, this study was limited to only one hospital. Multi-centered study would have given us better interpretation and a larger sample size.

ACKNOWLEDGEMENTS

We would like to acknowledge everyone who took part in this study.

CONFLICTS OF INTEREST

None

FINANCIAL SUPPORT AND SPONSORSHIP

None

REFERENCES

1. Nambron R, Rosenthal R, Bahl D. Diagnosis and Evaluation of Thyroid Nodules-the Clinician's Perspective. Radiologic Clinics. 2020 Nov 1;58(6):1009-18. DOI: 10.1016/j.rcl.2020.07.007
2. Haymart MR, Banerjee M, Reyes-Gastelum D, Caoili E, Norton EC. Thyroid ultrasound and the increase in diagnosis of low-risk thyroid cancer. The Journal of Clinical Endocrinology & Metabolism. 2019 Mar;104(3):785-92. DOI: 10.1210/jc.2018-01933
3. Brander AE, Viikinkoski VP, Nickels JI, Kivisaari LM. Importance of thyroid abnormalities detected at US screening: a 5-year follow-up. Radiology. 2000 Jun;215(3):801-6. DOI: 10.1148/radiology.215.3.r00jn07801
4. Ginat DT, Butani D, Giampoli EJ, Patel N, Dogra V. Pearls and pitfalls of thyroid nodule sonography and fine-needle aspiration. Ultrasound quarterly. 2010 Sep 1;26(3):171-8. DOI: 10.1097/RUQ.0b0 13e3181efa710
5. Deveci MS, Deveci G, LiVolsi VA, Gupta PK, Baloch ZW. Concordance between thyroid nodule sizes measured by ultrasound and gross pathology examination: effect on patient management. Diagnostic cytopathology. 2007 Sep 1;35(9):579-83. DOI: 10.1002/dc.20714
6. Bonnema SJ, Hegedüs L. Nontoxic Goiter 5. Thyroid Diseases. 2018:127. DOI: https://doi.org/10.1007/978-3-319-45013-1_5
7. Weber AL, Randolph G,Aksoy FG. The thyroid and parathyroid glands: CT and MR imaging and correlation with pathology and clinical findings. Radiologic Clinics of North America. 2000 Sep 1;38(5):1105-29. DOI: 10.1016/s0033-8389(05)70224-4
8. Tay SY, Chen CY, Chan WP. Sonographic criteria predictive of benign thyroid nodules useful in avoiding unnecessary ultrasound-guided fine needle aspiration. Journal of the Formosan Medical Association. 2015 Jul 1;114(7):590-7. DOI: 10.1016/j.jfma.2014.03.015
9. Kamran SC, Marqusee E, Kim MI, Frates MC, Ritner J, Peters H, Benson CB, Doubilet PM, Cibas ES, Barletta J, Cho N. Thyroid nodule size and prediction of cancer. The Journal of Clinical Endocrinology & Metabolism. 2013 Feb 1;98(2):564-70. DOI: 10.1210/jc.2012-2968
10. Smith-Bindman R, 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 internal medicine. 2013 Oct 28;173(19):1788-95. DOI: 10.1001/jamainternmed.2013.9245
11. Kerr L. High-resolution thyroid ultrasound: the value of color Doppler. Ultrasound Q 1994; 12:21-43. DOI: https://doi.org/ 10.1097/00013644-199412010-00002
12. Solbiati L, Cioffi V, Ballarati E. Ultrasonography of the neck. RadiolClin North Am 1992;30:941-954. Available from: https://www.ncbi.nlm.nih.gov/pubmed/1518938PMID: 1518938
13. Nel CJ, van HEERDEN JA, Goellner JR, GHARIB H, McCONAHEY WM, Taylor WF, GRANT CS. Anaplastic carcinoma of the thyroid: a clinicopathologic study of 82 cases. InMayo Clinic Proceedings 1985 Jan 1 (Vol. 60, No. 1, pp. 51-58). Elsevier. DOI: https://doi.org/10.1016/ S0025-6196(12)65285-9
14. Walker J, Findlay D, Amar SS, Small PG, Wastie ML, Pegg CA. A prospective study of thyroid ultrasound scan in the clinically solitary thyroid nodule. The British journal of radiology. 1985 Jul;58(691):617-9. DOI: 10.1259/0007-1285-58-691-617
15. Khafagi F, Castles H, Perry-Keene D, Mortimer R, Wright G. Screening for thyroid malignancy: the role of fine-needle biopsy. Medical Journal of Australia. 1988 Sep;149(6):302-7. DOI: 10.5694/j.1326-5377.1988.tb120629.x
16. Izquierdo R, Arekat MR, Knudson PE, Kartun KF, Khurana K, Kort K, et al. Comparision of palpation versus ultrasound-guided fine needle aspiration biopsies of thyroid nodules in an out-patient endocrinology practice. EndocrPract. 2006;12(6): 609-14. DOI: 10.4158/EP.12.6.609
17. Khadka H, Sharma S, Ghimire RK, Sayami G. Characterization of Thyroid Nodule by Sonographic Features. Nepalese Journal of Radiology. 2017;7(1-2):19-26. DOI: https://doi.org/10.3126/njr.v7i1-2.19365
18. Wolinski K, Szkudlarek M, Szczepanek-Parulska E, Ruchala M. Usefulness of different ultrasound features of malignancy in predicting the type of thyroid lesions: a meta-analysis of prospective studies. Pol Arch Med Wewn. 2014 Jan 1;124(3):97-104. DOI: 10.20452/pamw.2132
19. Woliński K, Stangierski A, Szczepanek-Parulska E, Gurgul E, Ruchała M. Dependence of thyroid sonographic markers of malignancy and its influence on the diagnostic value of sonographic findings. BioMed research international. 2015 Jan 22;2015. DOI: https://doi.org/10.1155/2015/693404

20. Reading CC, Charboneau JW, Hay ID, Sebo TJ. Sonography of thyroid nodules: a "classic pattern" diagnostic approach. Ultrasound quarterly. 2005 Sep 1;21(3):157-65. DOI: https://doi.org/10.21203/rs.3.rs-92155/v1
21. Frates MC, Benson CB, Doubilet PM, Kunreuther E, Contreras M, Cibas ES, Orcutt J, Moore Jr FD, Larsen PR, Marqusee E, Alexander EK. Prevalence and distribution of carcinoma in patients with solitary and multiple thyroid nodules on sonography. The Journal of Clinical Endocrinology & Metabolism. 2006 Sep 1;91(9):3411-7. DOI: 10.1210/jc.2006-0690
22. Nam-Goong IS, Kim HY, Gong G, Lee HK, Hong SJ, Kim WB, Shong YK. Ultrasonography-guided fine-needle aspiration of thyroid incidentaloma: correlation with pathological findings. Clinical endocrinology. 2004 Jan;60(1):21-8. DOI: 10.1046/j.1365-2265.2003.01912.x
23. Papini E, Guglielmi R, Bianchini A, Crescenzi A, Taccogna S, Nardi F, Panunzi C, Rinaldi R, Toscano V, Pacella CM. Risk of malignancy in nonpalpable thyroid nodules: predictive value of ultrasound and color-Doppler features. The Journal of Clinical Endocrinology & Metabolism. 2002 May 1;87(5):1941-6. DOI: 10.1210/jcem.87.5.8504
24. Wang N, Xu Y, Ge C, Guo R, Guo K. Association of sonographically detected calcification with thyroid carcinoma. Head & neck. 2006 Dec;28(12):1077-83. DOI: 10.1002/hed.20481
25. Chammas MC, de AraujoFilho VJ, Moysés RA, Brescia MD, Mulatti GC, Brandão LG, Cerri GG, Ferraz AR. Predictive value for malignancy in the finding of microcalcifications on ultrasonography of thyroid nodules. Head & Neck: Journal for the Sciences and Specialties of the Head and Neck. 2008 Sep;30(9):1206-10. DOI: https://doi.org/10.1159/000478927
26. Frates MC, Benson CB, Doubilet PM, Cibas ES, Marqusee E. Can color Doppler sonography aid in the prediction of malignancy of thyroid nodules?. Journal of ultrasound in medicine. 2003 Feb;22(2):127-31. DOI: 10.7863/jum.2003.22.2.127
27. Leboulleux S, Girard E, Rose M, Travagli JP, Sabbah N, Caillou B, Hartl DM, Lassau N, Baudin E, Schlumberger M. Ultrasound criteria of malignancy for cervical lymph nodes in patients followed up for differentiated thyroid cancer. The Journal of Clinical Endocrinology & Metabolism. 2007 Sep 1;92(9):3590-4. DOI: 10.1210/jc.2007-0444
28. Frasoldati A, Valcavi R. Challenges in neck ultrasonography: lymphadenopathy and parathyroid glands. Endocrine Practice. 2004 May 1;10(3):261-8. DOI: 10.4158/EP.10.3.261
29. Kuna SK, Bracic I, Tesic V, Kuna K, Herceg GH, Dodig D. Ultrasonographic differentiation of benign from malignant neck lymphadenopathy in thyroid cancer. Journal of ultrasound in medicine. 2006 Dec;25(12):1531-7. DOI: 10.7863/jum.2006.25.12.1531.