ORIGINAL ARTICLE

DIAGNOSTIC ACCURACY OF ULTRASONOGRAPHY IN DIFFERENTIATING BENIGN AND MALIGNANT THYROID NODULES, TAKING FNAC AS GOLD STANDARD

Ayesha Tareen,[1] Maj Muhammad Omer Aamir,[2] Syed Naseer Ahmed,[3] Javed Anwar,[1] Sami Ullah Khan,[5] Sadia Dilshad,[1] Palwasha Gul,[4] Khalid Shakeel Baber,[6] Baber Khan[1]

[1] Department of Radiology, Combined Military Hospital, Quetta, Pakistan.
[2] Department of Radiology, Combined Military Hospital, Rawalakot, Pakistan.
[3] Department of Radiology, Sheikh Khalifa bin Zayed Hospital, Quetta, Pakistan.
[4] Department of Radiology, Bolan Medical Complex, Quetta, Pakistan.
[5] Department of Neuro-Radiology, Basildon and Thurrock Hospital, UK
[6] Department Interventional Radiology, (Rehman Medical Institute RMI), Peshawar, Paksitan.

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ABSTRACT

BACKGROUND: Ultrasound is the most broadly performed procedure in the thyroid gland screening. It has easy performance and cost effectiveness in determining the size and number of nodules. The aim of this study was to determine the diagnostic accuracy of ultrasonography in differentiating benign and malignant thyroid nodules, taking histopathological findings of FNAC as gold standard. **MATERIAL AND METHODS:** This descriptive, cross-sectional study was conducted from 25th July 2018 to 24th January 2019 in the Department of Radiology, Combined Military Hospital, Quetta. A total of 142 patients with thyroid nodule of any size and duration >3 months, age >15 years & either gender were included. All the patients underwent gray scale ultrasonography. Findings were correlated with FNAC report. **RESULTS:** The data were analyzed and quantitative metric like sensitivity (S_n= 93.15%), specificity (S_p = 89.86%), positive predictive value (PPV = 90.67%), negative predictive value (NPV = 92.54%) and diagnostic accuracy (Acc = 91.55%) of ultrasonography in differentiating benign and malignant thyroid nodules were calculated taking FNAC as gold standard. **CONCLUSIONS:** This study concluded that ultrasound is the non-invasive modality of choice with high diagnostic accuracy in diagnosing malignant thyroid nodules.

Keywords: Thyroid cancer, ultrasound, sensitivity.

Introduction

A thyroid nodule is a solid or cystic lump on the thyroid gland. Thyroid nodule may be involved in various thyroid carcinomas with a noteworthy clinical importance.[1] Thyroid nodules presented commonly as they are found in 4-8% of adults by palpation, in 10-41% by ultrasound either intentionally or incidentally, and in 50% by pathologic examination at autopsy.[2] In spite of high prevalence of nodules, thyroid cancer is relatively rare; however, thyroid cancers generally have good prognosis and fortunately, early diagnosis and treatment is fruitful.[3] Although, most thyroid nodules are benign but Ma JJ et al[4] in his study has found the prevalence of malignant thyroid nodule as 55%.

Correspondence : Dr. Ayesha Tareen
Department of Radiology,
Combined Military Hospital,
Quetta, Pakistan.
Email: dr.ayeshatareen@gmail.com

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After a thyroid nodule is found during a physical examination, a referral to an endocrinologist or a thyroidologist may occur. Most commonly an ultrasound is performed to confirm the presence of a nodule, and assess the status of the whole gland. Measurement of thyroid stimulating hormone and anti-thyroid antibodies will help decide if there is a functional thyroid disease such as Hashimoto's thyroiditis present, a known cause of a benign nodular goiter.6 Measurement of calcitonin is necessary to exclude the presence of medullary thyroid cancer. Finally, to achieve a definitive diagnosis before deciding on treatment, a fine needle aspiration cytology test is usually performed and reported according to the Bethesda system.[7] Fine needle aspiration (FNA) has been widely accepted as the preferred detection technique for the assessment of non-toxic thyroid nodules and aims primarily to triage patients in order to identify those requiring surgery and then to decide on appropriate surgical procedures.[5]

Ultrasound is the most broadly performed procedure in the thyroid gland screening. It has easy performance and cost effectiveness in determining the size and number of nodules. However, the great question is the role of ultrasonography in triage of thyroid nodules.[6] With the increasing detection of thyroid nodules by using high-resolution ultrasound, the rate of detection of asymptomatic thyroid cancers, especially papillary thyroid cancer and PTMCs, has increased.[7] Various recent studies have focused on ultrasonographic (US) features in the diagnosis of benign and malignant thyroid nodules.[8,9] In a study, the overall sensitivity, specificity, positive and negative predictive values for the ultrasound diagnosis of benign and malignant thyroid nodules were 81.8%, 87.2%, 59.0%, and 95.5% respectively.[10] Another study has shown the sensitivity 92%, specificity 34% and positive predictive value (PPV) 85.4% and negative predictive value (NPV) 72.3% and accuracy 73%.[11] In a local study, ultrasound specificity, sensitivity, positive and negative predictive values, and accuracy for differentiating benign from malignant nodules were 93.2%, 93.8%, 81.1%, 98%, and 93.3%, respectively.[12]

As the available local literature on diagnostic accuracy of ultrasound in malignant thyroid nodules is very scarce and also previous studies have shown controversy in the results, so I had planned this study to determine the diagnostic accuracy of ultrasonography in differentiating malignant from benign thyroid nodules. The results of my study will not only be a useful addition in the existing literature but will also help to resolve the controversy. Also if it s diagnostic accuracy will be found high, then we can provide our population with a non-invasive, easily available and cost-effective imaging modality for proper assessment of the thyroid nodules in differentiating between benign and malignant nodules which will further help in taking proper treatment plans accordingly for reducing patient s morbidity.

Material and Methods

This descriptive, cross-sectional study was conducted from 25th July 2018 to 24th January 2019 in the Department of Radiology, Combined Military Hospital, Quetta. After permission from local ethical review committee, A total of 142 patients with thyroid nodule of any size and of duration >3 months of, age >15 years & either gender were included. Patients with already proven histopathology report and previous thyroid surgery were excluded. Gray scale ultrasonography was performed in every patient by using a high-resolution unit with a linear array probe centered at 7.5 MHz. All ultrasonographic examinations were performed by a consultant radiologist. FNAC was performed in the concerned ward by a consultant surgeon and specimen was sent for histopathology to the insti-tutional laboratory where histopathology report was interpreted by the consultant histopathologist. USG Findings were correlated with FNAC report. All this data (age, gender, duration of nodule, size of nodule, benign or malignant nodule) was recorded on a specially designed proforma.

Results

Age range in this study was from 16-80 years with mean age of 47.75 – 11.47 years. Majority of the patients 90 (63.38%) were between 16 to 50 years of age.

Out of these 142 patients, 76 (53.52%) were female and 66 (46.48%) were males with female to male ratio of 1.2:1

Mean duration of disease was 7.18 – 2.61 months. Mean size of nodule was 4.96 – 1.75 cm as shown in (Tab. 1).

Stratification of diagnostic accuracy with respect to size of nodule is shown in (Tab. 3 & 4).

Size of nodule	No. of Patients	% age
≤ 5 cm	88	61.97
> 5 cm	54	38.03

Table 1: Distribution of patients according to size of nodule (n=142).

	Positive result on FNAC	Negative result on FNAC	P-value
Positive result on USG	68 (TP)*	07 (FP)***	0.001
Negative result on USG	05 (FN)**	62 (TN)****	

*-TP=True positive **-FP=False positive ***-FN=False negative ****-TN=True negative

Table 2: Diagnostic accuracy of ultrasonography in differentiating benign and malignant thyroid nodules, taking FNAC as gold standard.

	Positive result on FNAC	Negative result on FNAC	P-value
Positive result on USG	39 (TP)	04 (FP)	0.001
Negative result on USG	04 (FN)	41 (TN)	

Sensitivity: 90.70%, Specificity: 91.11%, Positive Predictive Value (PPV): 90.70%, Negative Predictive Value (NPV): 91.11%, Diagnostic Accuracy: 90.91%

Table 3: Stratification of size of nodule =5 cm (n=88).

	Positive result on FNAC	Negative result on FNAC	P-value
Positive result on USG	29 (TP)	03 (FP)	0.001
Negative result on USG	01 (FN)	21 (TN)	

Sensitivity: 96.67%, Specificity: 87.50%, Positive Predictive Value (PPV): 90.63%, Negative Predictive Value (NPV): 95.45%, Diagnostic Accuracy: 92.59%

Table 4: Stratification of size of nodule ≤5 cm (n=88).

All the patients were subjected to gray scale ultrasonography of the thyroid. USG supported the diagnosis of malignant thyroid nodules in all 75 patients. Histopathology confirmed malignant thyroid nodules in 73 (true positive) cases where as 07 (False Positive) had no malignant lesion on histopathology. In USG negative patients, 62 were true negative while 05 were false negative (Tab. II), (Fig. 1), (Fig. 2)

Overall sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of ultrasonography in differentiating benign and malignant thyroid nodules, taking FNAC as gold standard is 93.15%, 89.86%, 90.67%, 92.54% and 91.55% respectively.

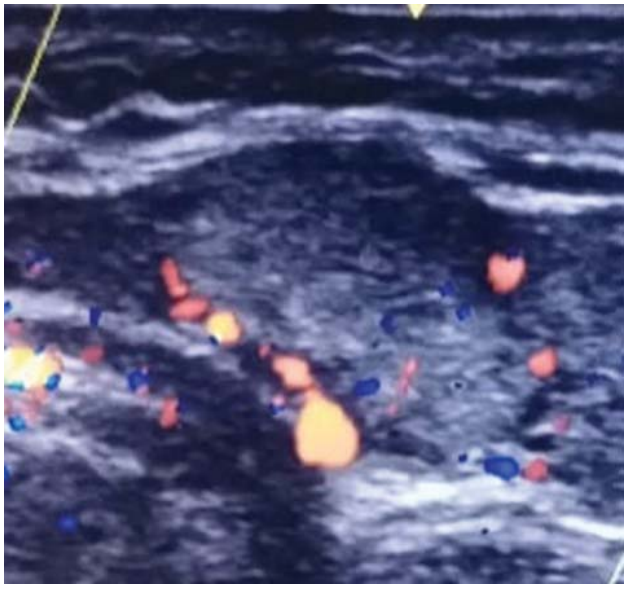

Figure 1: A benign nodule on FNAC

Figure 2: A Malignant Nodule on FNAC

Discussion

Nodular thyroid disease is detected in 3-7% of the adult population worldwide. The majority of these cases are clinically occult but readily detected by high-resolution Ultrasonography (USG).[13-16] Thyroid cancer is rare and accounts for <1% of all malignant neoplasms. It has a good long-term prognosis after

surgical excision. The high prevalence of thyroid nodules in the general population calls for a clear strategy to identify patients in whom surgical excision is genuinely indicated as opposed to those who can be managed conservatively.[14] Current management guidelines (American Thyroid Association) state that diagnostic USG should be performed in all patients with thyroid nodules and fine needle aspiration (FNA) in potentially malignant nodules.[15] Various features seen on USG, such as irregular margins, hypo echogenicity, absence of a surrounding halo, calcifications, and solid internal composition, have been investigated as predictors of malignancy. I have conducted this study to determine the diagnostic accuracy of ultrasonography in differentiating benign and malignant thyroid nodules, taking FNAC as gold standard.

Age range in this study was from 16-80 years with mean age of 47.75 – 11.47 years. Majority of the patients 90 (63.38%) were between 16 to 50 years of age. Out of these 142 patients, 76 (53.52%) were female and 66 (46.48%) were males with female to male ratio of 1.2:1. All the patients were subjected to grey scale ultrasonography of the thyroid. USG supported the diagnosis of malignant thyroid nodules in all 75 patients. Histopathology confirmed malignant thyroid nodules in 73 (true positive) cases where as 07 (False Positive) had no malignant lesion on histopathology. In USG negative patients, 62 were true negative while 05 were false negative. Overall sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of ultrasonography in differentiating benign and malignant thyroid nodules, taking FNAC as gold standard is 93.15%, 89.86%, 90.67%, 92.54% and 91.55% respectively. In a study, the overall sensitivity, spe-cificity, positive and negative predictive values for the ultrasound diagnosis of benign and malignant thyroid nodules were 81.8%, 87.2%, 59.0%, and 95.5% respectively.[10] Another study has shown the sensitivity 92%, specificity 34% and positive predictive value (PPV) 85.4% and negative predictive value (NPV) 72.3% and accuracy 73%.[11] In a local study, ultrasound specificity, sensitivity, positive and negative predictive values, and accuracy for differentiating benign from malignant nodules were 93.2%, 93.8%, 81.1%, 98%, and 93.3%, respectively.[12]

A cross-sectional analytical study[17] was designed to prospectively collect data from December 2010 till December 2012 from the Department of Radiology in Aga Khan University Hospital, Karachi, Pakistan. The subjects comprised 76 (76%) females and 24 males. Mean age was 41.8 – SD 12.3 years. Sensitivity and specificity with 95%CI of ultrasound in differentiating malignant thyroid nodule from benign thyroid nodule calculated to be 91.7% (95%CI, 0.72-0.98) and 78.94% (0.68-0.87) respectively. Reported positive predictive value and negative PV were 57.9% (0.41-0.73) and 96.8% (0.88-0.99) and overall accuracy was 82%. Likelihood ratio (LR) positive was computed to be 4.3 and LR negative was 0.1.[17]

In another study,[18] a total of 831 patients (716 women & 115 men; mean age: 49.5 – 13.8 [SD] years) with 849 nodules (360 malignant, 489 benign) that were diagnosed at surgery or biopsy were included. Statistically significant (P<0.05) findings of malignancy were a taller-than-wide shape (sensitivity: 40.0%; specificity: 91.4%), a spiculated margin (sensitivity 48.3%; specificity 98.1%), marked hypo echogenicity (sensitivity 41.4%; specificity 92.2%), micro calcification (sensitivity 44.2%; specificity 90.8%), and macro calcification (sensitivity 9.7%; specificity 96.1%). The US findings benign nodules were iso-echogenicity (sensitivity 56.6%; specificity 88.1%; P<0.001) and a spongiform appearance (sensitivity 10.4%; specificity 99.7%; P<0.001). The presence of at least one malignant US finding had a sensitivity of 83.3%, a specificity of 74.0%, and a diagnostic accuracy of 78.0%. For thyroid nodules with a diameter of 1 cm or less, the sensitivity of micro calcifications was lower than that in larger nodules (36.6% versus 51.4%, P<0.05).[18]

Avinash B et al[19] in his study, 70 nodules examined, 6 (8.57%) were found to be malignant on cytopathology. The malignant nodules demonstrated solid or predominantly solid composition (sensitivity 100% and specificity 9.37%); presence of micro calcification (sensitivity 66.6% and specificity 98.4%); irregular or poorly defined margins (sensitivity 83.3% and specificity 92.06%); anteroposterior diameter more than transverse diameter (sensitivity 50% and specificity 93.75%); absent or thick incomplete halo (sensitivity 83.3% and specificity 82.8%); markedly hypoechoic character (sensitivity 66.6% and specificity 90.6%).[19]

A descriptive cross-sectional validation study[20] was conducted at Departments of Radiology and Patho-

logy, Shaikh Khalifa Bin Zayed Al-Nahyan Hospital/ CMH, Muzaffarabad from Dec 2014 to Jun 2015. Patients referred for evaluation of thyroid nodules were included in the study. Ultrasound guided FNAC was performed under direct imaging guidance. The imaging findings and FNAC were compared to access the diagnostic accuracy of ultrasound in predicting malignancy in thyroid nodules. A total of 175 patients were studied with age range between 20-70 years. Mean age of the patients was 44.05 – 14.8 years. Of these, 35.4% were males and 64.6% were females. On FNAC, 27.4% cases were positive and 72.6% cases were negative while on thyroid ultrasound 26.3% cases were positive and 73.7% cases were negative. True positive were 24.0%, false positive 2.3%, false negative 3.4%, and true negative were 70.3%. Thyroid ultrasound showed sensitivity 87.5%, specificity 96.8%, diagnostic accuracy 94.2%, positive predictive value 91.3% and negative predictive value 95.3%.[20]

Recently, Ghajarzadeh et al. determined the diagnostic accuracy of US in detecting malignant thyroid nodules, through a systematic review and meta-analysis of all available evidence. They claimed that US can be considered as a reliable screening tool for characterizing thyroid nodules, and detection of benign pathology in almost all cases, thus can be used to exclude many patients from further invasive assessments.[21] Zhuo et al. assessed the performance of acoustic radiation force impulse (ARFI) imaging to differentiate benign from malignant thyroid nodules in 182 patients who needed thyroid surgery. They reported that ARFI imaging may be helpful to differentiate benign thyroid nodules from malignant, and the selecting measurement position is important, as well as it has worthy diagnostic value in clinical applications.[22]

Campanella et al. conducted a study to quantify the risk of malignancy of thyroid nodules using US by conducting a systematic review and meta-analysis of all available studies. They showed the highest risk of malignancy was found for nodule height greater than width, and microcalcifications.[23] Kim et al. investigated the benign thyroid nodules at initial fine-needle aspiration biopsy (FNAB) to determine the percentage of nodules that increased in volume by more than 50% as being an indicator of malignancy in concordance with long-term US, and showed that a positive FNAB result for malignancy is significantly more likely in the presence of suspicious US features.[24]

Yang et al. explored the values of US in differentially diagnosing benign and malignant thyroid nodules, and showed that US can be used to evaluate the malignancy risk of thyroid nodules and help to make the right decision in clinics.[25] Wu et al. evaluated the diagnostic utility of conventional US in differentiating degenerating cystic thyroid nodules mimicking malignancy from thyroid carcinoma, and showed that US contributes to increasing the performance in differential diagnosis of thyroid nodule and malignancy.[26]

Conclusion

This study concluded that ultrasound is the non-invasive modality of choice with high diagnostic accuracy in diagnosing malignant thyroid nodules, and has not only dramatically improved our ability of diagnosing malignant thyroid nodules pre-operatively but also helps the surgeons for proper decision making. So, we recommend that ultrasound should be done routinely in all thyroid lesions for accurate diagnosis of malignant thyroid nodules pre-operatively and opting proper surgical approach.

Conflict of Interest: Authors declared none.

References

1. Tahmasebi M, Dezfouli MRB, Gharibvand MM, Jahanshahi A, Nikpour N, Rahim F. Diagnostic accuracy of sonography in assessment of thyroid masses in comparison with pathology. Russian Open Med J. 2016; **5:** 103.

2. Avinash B, Ahmed N, Sreedevi T, Swapna Ch, Latha RM, et al. Role of ultrasonography to differentiate benign and malignant thyroid nodules in correlation with fine-needle aspiration cytology. Int J Sci Stud. 2016; **4(5):** 81-7.

3. Andrioli M, Carzaniga C, Persani L. Standardized ultrasound report for thyroid nodules: the endocrinologist's viewpoint. Eur Thyroid J. 2013; **2(1):** 37-48.

4. Ma JJ, Ding H, Xu BH, Xu C, Song LJ, Huang BJ, et al. Diagnostic performances of various gray-scale, color Doppler, and contrast-enhanced ultrasonography findings in predicting malignant thyroid nodules. Thyroid. 2014; **24(2):** 355-63.

5. Kim SY, Han KH, Moon HJ, Kwak JY, Chung WY, Kim EK. Thyroid nodules with benign findings at cytologic examination: results of long-term follow-up with US. Radiol. 2014;271(1):272-81.

6. Kwak JY, Kim EK. Ultrasound elastography for thyroid nodules: recent advances. Ultrasonography. 2014; **33(2):** 75-82.

7. Remonti LR, Kramer CK, Leitª o CB, Pinto LC, Gross JL. Thyroid ultrasound features and risk of carcinoma: a systematic review and meta-analysis of observational studies. Thyroid. 2015; **25:** 538-50.

8. Kim JY, Jung SL, Kim MK, Kim TJ, Byun JY. Differentiation of benign and malignant thyroid nodules based on the proportion of sponge-like areas on ultrasonography: imaging-pathologic correlation. Ultrasonography. 2015; **34(4):** 304-11.

9. Maimaiti Y, Sun S, Liu Z, Zeng W, Liu C, Wang S, et al. Diagnostic accuracy of ultrasonographic features for benign and malignant thyroid nodules smaller than 10 mm. Int J Clin Exp Med. 2016; **9(3):** 6476-82.

10. Popli MB, Rastogi A, Bhalla PJS, Solanki Y. Utility of gray-scale ultrasound to differentiate benign from malignant thyroid nodules. Indian J Radiol Imaging. 2012; **22(1):** 63-8.

11. Afifi AH, Alwafa WAHA, Aly WM, Alhammadi HAB. Diagnostic accuracy of the combined use of conventional sonography and sonoelastography in differentiating benign and malignant solitary thyroid nodules. Alexandria J Med. 2017; **53:** 21-30.

12. Zahir ST, Vakili M, Ghaneei A, Sharahjin NS, Heidari F. Ultrasound assistance in differentiating malignant thyroid nodules from benign ones. J Ayub Med Coll Abbottabad. 2016; **28(4):** 644-9.

13. Solbiati L, Charboneau JW, Osti V, James EM, Hay ID. The Thyroid Gland. In: Wilson SR, Charboneau JW, Rumack CM, editors. Diagnostic Ultrasound. 3 rd ed. Missouri: Mosby, Elsevier Inc.; 2005. p. 735-70.

14. Yeung MJ, Serpell JW. Management of the solitary thyroid nodule. Oncologist 2008; **13:** 105-12.

15. Cooper DS, Doherty GM, Haugen BR, Kloos RT, Lee SL, Mandel SJ. Revised American Thyroid Association Management Guidelines for Patients with Thyroid Nodules and Differentiated Thyroid Cancer. Thyroid 2009; **19:** 1167-214.

16. Mortenson J, Woolner L, Benneu W. Gross and microscopic findings in clinically normal thyroid glands. J Clin Endocrinol Metab 1955; **15:** 1270-80.

17. Alam T, Khattak YJ, Beg M, Raouf A, Azeemuddin M, Khan AA. Diagnostic accuracy of ultrasonography in differentiating benign and malignant thyroid nodules using fine needle aspiration cytology as the reference standard. Asian Pac J Cancer Prev. 2014; **15(22):** 10039-43.

18. Moon WJ, Jung SL, Lee JH, Na DG, Baek JH, Lee YH, et al. Benign and malignant thyroid nodules: US differentiation - A multicenter retrospective study. Radiology 2008; **247:** 762-70.

19. Avinash B, Ahmed N, Sreedevi T, Swapna Ch, Latha RM, Babu J. Role of Ultrasonography to Differentiate Benign and Malignant Thyroid Nodules in Correlation with Fine-needle Aspiration Cytology. Int J Sci Stud 2016; **4(5):** 81-7.

20. Nawaz S, Khan MB, Parveen B, Asif M, Rashid M, Azeem M, et al. Diagnostic accuracy of thyroid ultrasound in detection of malignancy in thyroid nodules. Pak J Physiol. 2018; **14(3):** 11-3.

21. Ghajarzadeh M, Sodagari F, Shakiba M. Diagnostic accuracy of sonoelastography in detecting malignant thyroid nodules: a systematic review and meta-analysis. Am J Roentgenol 2014; **202(4):** W379-W389.

22. Zhuo J, Ma Z, Fu WJ, Liu SP. Differentiation of benign from malignant thyroid nodules with acoustic radiation force impulse technique. Br J Radiol 2014; **87(1035):** 20130263.

23. Campanella P, Ianni F, Rota CA, Corsello SM, Pontecorvi A. Quantification of cancer risk of each clinical and ultrasonographic suspicious feature of thyroid nodules: a systematic review and meta-analysis. Eur J Endocrinol 2014; **170(5):** R203-R211.

24. Kim SY, Han KH, Moon HJ, Kwak JY, Chung WY, Kim EK. Thyroid nodules with benign findings at cytologic examination: results of long-term follow-up with US. Radiology 2014; **271(1):** 272-81.

25. Yang C, Han C, Wang LP, Feng N, Wang YF, You XD. Exploration on an ultrasonographic imaging reporting and data system in malignancy grading of thyroid nodules. Zhonghua Zhong Liu Za Zhi 2013; **35(10):** 758-63.

26. Wu HX, Zhang BJ, Wang J, Zhu BL, Zang YP, Cao YL. Conventional ultrasonography and real time ultrasound elastography in the differential diagnosis of degenerating cystic thyroid nodules mimicking malignancy and papillary thyroid carcinomas. Asian Pac J Cancer Prev 2013; **14(2):** 935-40.