RESEARCH ARTICLE

Conventional Ultrasonography and Real Time Ultrasound Elastography in the Differential Diagnosis of Degenerating Cystic Thyroid Nodules Mimicking Malignancy and Papillary Thyroid Carcinomas

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Abstract

Background: To evaluate the diagnostic utility of conventional ultrasonography and real time ultrasound elastography in differentiating degenerating cystic thyroid nodules mimicking malignancy from papillary thyroid carcinoma. Methods: We retrospectively analyzed conventional ultrasonographic and elastographic characteristics of 19 degenerating cystic thyroid nodules mimicking malignancy in 19 patients, with 30 surgically confirmed PTCs as controls. Based on size, the nodules had been grouped into less than 10mm (group A) and greater than 10 mm (group B). We evaluated conventional parameters and elasticity pattern. Color-scaled elastograms were graded as to stiffness of nodules using an elasticity pattern from I (soft) to IV (stiff). Results: Degenerating cystic thyroid nodules were similar to PTCs in conventional ultrasonographic findings, but the former frequently showed oval to round in shape (group A, 69.2% vs 18.8%, *P*=0.017; group B, 66.7% vs 7.14%, *P*=0.017) and punctuate hyperechoic foci (group A, 61.5% vs 0, *P*<0.001; group B, 50% vs 0, *P*<0.001). On real time ultrasound elastography, 7 of 13 degenerating cystic thyroid nodules in group A were pattern I, 5 were pattern II, 1 was pattern III. One degenerating cystic thyroid nodule in group B was pattern II, 5 were pattern III. The area under the curve for elastography was 0.98 in group A (sensitivity 92.3%, specificity 100%, *P* = 0.002), and 0.88 in group B (sensitivity 16.7%, specificity 100%, *P* = 0.014). Conclusions: As a dependable imaging technique, elastography helps increase the performance in differential diagnosis of degenerating cystic thyroid nodule and malignancy.

Keywords: Ultrasonography - elastography - thyroid nodule - malignancy - differential diagnosis

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Introduction

Several studies have shown the incidence of thyroid nodules ranged from 41% on ultrasonography (US) to at least 50% on pathology (Mortensen et al., 1955; Tan et al., 1997). The higher detection rate has been attributed to technical improvement in conventional US, leading to the detection of clinically silent nodules (Davies et al., 2006). Certain characteristics on conventional US can be helpful in differentiating benign from malignant nodule, including hypoechoic, poorly defined margin, irregular shape, microcalcification, taller than wide (anteroposterior to transverse diameter ratio greater than 1) (Ahn et al., 2010). However, none of the aforementioned characteristics have a high positive predictive value for malignancy, and some characteristics of benign and malignant nodules overlap (Cappelli et al., 2006; Tamsel et al., 2007; Kim et al., 2008). It has been observed that some benign degenerating cystic thyroid nodules have malignancy-mimicking characteristics during follow-ups (Kim et al., 2011). It is difficult to distinguish the degenerating cystic thyroid nodule with hypoechoic, changed morphologically in the natural course, from papillary thyroid carcinoma (PTC) via conventional US.

Real time ultrasound elastography is an emerging technique. It estimates the tissue stiffness by measuring tissue deformation from returning ultrasonic signals before and after applying an external pressure. The firm tissues show less deformation than soft tissues with compression. The relative elasticity, i.e., strain, in the region of interest is calculated from its deformation rate. A firm stiffness is associated with an increased risk of

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malignancy in thyroid nodules. Several studies have proved that real time ultrasound elastography has a high accuracy for predicting malignancy in thyroid nodules and cervical lymph nodes (Rago et al., 2007; Asteria et al., 2008; Rubaltelli et al., 2009; Friedrich-Rust et al., 2010; Teng et al., 2012). However previous studies have not specifically focused on changes in degenerating cystic thyroid nodule on elastography. The purpose of this study was to evaluate the diagnostic utility of conventional US and real time ultrasound elastography in differentiating degenerating cystic thyroid nodule with malignancy-mimicking characteristics from PTC.

Materials and Methods

Patients

We reviewed the records of 368 patients to our institute for evaluation of nodular thyroid disease from April 2011 to January 2012. All patients routinely underwent conventional US, including B-mode US and Doppler US, followed by real time ultrasound elastography, and ultrasound-guided fine needle aspiration (UG-FNA). Conventional US and elastography were performed independently by two sonographers. Images and dynamic frame captures were stored in the hard drive of the equipment. Off-line analysis was performed retrospectively by other sonographers blindly. All sonographers had more than 15 years of experience in thyroid imaging.

In all 368 patients, 27 patients without consecutive ultrasonographic data were excluded. Nodules that were thought to be technically unsuitable for elastography were excluded. Therefore, 21 patients with cystic nodules or with macrocalcifications in nodules were excluded. 55 patients with histologic findings of chronic inflammation were also excluded. We found a total 265 patients with 281 thyroid nodules. Among them, 19 patients with 19 degenerating cystic thyroid nodules (mean age, 46±11 years; range, 22-69 years; 7 males and 12 females) were ultimately included in this study. The descriptions of "degenerating cystic thyroid nodule" indicated initial cystic nodules underwent degeneration, which had malignancy-mimicking characteristics during follow-up. The patients were followed with a mean interval of 17 months after initial scans (range, 13-25 months). The structure nature of nodules in initial and the size changing during follow-up periods was recorded. 7 nodules proved to be degenerated thyroid nodule, 12 nodules proved to be nodular goiter in histological diagnosis. As a control group, 30 surgically confirmed PTCs (30 patients, mean age, 49±13 years; range, 31-73 years; 9 males and 21 females) were retrospectively reviewed. The local ethics committee at our institute approved the procedures of this study and all patients provided informed consent.

Conventional US

Conventional US examinations were performed by using a 5-12 MHz linear-array transducer (Philips iU22, Philips Healthcare, Bothell, WA, USA). The following parameters were evaluated: size, margin, shape, echogenicity, structure, the presence of microcalcification or hyperechoic spot, vascularity pattern. According to the largest diameter in longitudinal plane, nodules were divided into 2 groups: less than 10 mm (Group A) and greater than 10mm (Group B). The nodular margin was described as poorly defined or well defined. The shape of nodule was classified as taller than wide, oval to round, or irregular. Compared to the normal thyroid parenchyma, the echogenicity of nodule was described as hypoechoic, isoechoic or hyperechoic. Marked hypoechoic was defined as decreased echogenicity compared with strap muscles. The structure of nodule was described as homogeneous or inhomogeneous (if the internal structure distributed as clumps, it was considered as inhomogeneous). Microcalcification was defined as punctuate hyperechoic foci less than 2 mm, without acoustic shadowing; hyperechoic spot was defined as punctuate hyperechoic foci with comet-tail artifact. Vascularity pattern defined as type I absence of blood flow, type II perinodular and absent or slight intranodular blood flow, and type III marked intranodular and absent or slight perinodular blood flow.

Real time ultrasound elastography

Real time ultrasound elastography was performed after the conventional US examination with the same real-time equipment and the same probe. In brief, the probe was placed on the anterior neck. The gentle freehand compression was applied using the probe along the beam axis. To keep the strain distributed evenly, compression was applied with 1 to 2 mm thickness and two to three times per second. The elastogram was displayed over the B-mode image in a color scale that ranged from red, indicating components with greatest elastic strain, to blue, indicating components with no strain. Meanwhile, green indicated moderate strain. The region of interest for the real time ultrasound elastography was selected including the nodule and sufficient surrounding normal thyroid parenchyma. Nodule was evaluated with the probe orientated in both transverse and longitudinal planes. To minimize the inter- and intraobserver variability, the freehand compression was standardized by elastic column displayed on a numeric scale to maintain a stable intermediate level optimal for evaluation (Bhatia et al., 2011). Elasticity was classified in four different patterns as described previously: pattern I: the nodule displays homogeneously in green; pattern II: nodule displays predominantly in green as well as sporadic parts in blue; pattern III: nodule displays predominantly in blue as well as sporadic parts in green, or green displays in the periphery; pattern IV: the nodule displays completely in blue (Rubaltelli et al., 2009).

UG-FNA Procedure

The procedure was performed by the same sonographer. Immediate specimen adequacy evaluation was not provided. UG-FNA was performed with a 23-gauge needles attached syringe. Freehand biopsy and capillary action technique was used. With the nonparallel solution, the needle was inserted adjacent to the side of the midpoint of the transducer and angled minimally back toward the transducer with the degree of angulation varying. Once within the nodule, the needle tip was moved back and forth

Table 1. Data of Degenerating Cystic Thyroid Nodule In Initial

	Group A n=(13)	Group B n=(6)	P
Nature			<0.001
predominantly cystic, n(%)	11(84.6)	0	
mixed, n(%)	2(15.4)	1(16.7)	
predominantly solid, n(%)	0	5(83.3)	
Minimum diameter, mm	14.5	18.4	
Maximum diameter, mm	33.7	35.2	
Decrease in size, mm	17.47±9.07	13.25±8.17	0.033

Table 2. Characteristics of Degenerating Cystic Thyroid Nodules (<10mm) and PTCs (<10mm)

Characteristic	Group A (n=13)	Group C (n=16)	P
Size, mm	8.63±1.91	8.1±2.32	0.623
Shape, n(%)			0.017
Taller than wide	3(23.1%)	12(75%)	
Oval to round	9(69.2%)	3(18.8%)	
Irregular	1(7.7%)	1(6.2%)	
Margin, n(%)			0.073
Poorly defined	9(69.2%)	12(75%)	
Well defined	4(30.8%)	4(25%)	
Echogenicity, n(%)			0.811
Marked hypoechogenicity	2(15.4%)	3(18.8%)	
hypoechogenicity	11(84.6%)	13(81.2%)	
Structure, n(%)			0.22
Homogeneous	12(92.3%)	12(75%)	
Inhomogeneous	1(7.7%)	4(25%)	
Punctuate hyperechoic foci, n(%)			<0.001
Microcalcification	0	7(43.8%)	
Hyperechoic spot	8(61.5%)	0	
Nondisplayed	5(38.5%)	9(56.2%)	
Vascularity pattern, n(%)			0.481
I	8(61.5%)	7(43.8%)	
II	5(38.5%)	8(50%)	
III	0	1(6.2%)	
Elastography pattern, n(%)			<0.001
I	7(53.8%)	0	
II	5(38.5%)	0	
III	1(7.7%)	7(43.8%)	
IV	0	9(56.2%)	

within the nodule 3 to 5 times while needle was rotated on its axis. The specimens acquired were placed on slides. Two direct smears were made for each pass and placed immediately in 95% alcohol for Papanicolaou staining. Two passes were prepared from each nodule.

On principle, we recommended operation in cases when the UG-FNA cytological results are malignant, suspicious for malignancy, or indeterminate. We also recommended repeated UG-FNA for cases with nondiagnostic cytology and follow-up US for those with benign cytology. Repeated UG-FNA was recommended to perform 6 months later. When the cytological results proven benign nodules showed no change on follow-up US after more than a year, they were ultimately included in the benign diagnosis.

Statistical Analysis

Statistical analyses were performed using SPSS 13.0 (SPSS Inc., Chicago, IL). Data were expressed as mean ± SD, a t test was performed to determine whether the data were significantly different between the two groups. The statistical difference between groups was evaluated using the χ^2 test or Fisher exact test. Statistical significance was set at $P < 0.05$. Receiver operating characteristic (ROC) curve analysis was performed to assess the diagnostic value of elastography. The ROC curves were used to determine the diagnostic sensitivity and specificity.

Table 3. Characteristics of Degenerating Cystic Thyroid Nodules (>10mm) and PTC (>10mm)

Characteristic	Group A (n=6)	Group C (n=14)	P
Size, mm	16.17±8.43	22.58±9.68	0.815
Shape, n(%)			0.017
Taller than wide	0	2(14.3%)	
Oval to round	4(66.7%)	1(7.1%)	
Irregular	2(33.3%)	11(78.6%)	
Margin, n(%)			0.091
Poorly defined	0	5(35.7%)	
Well defined	6(100%)	9(64.3%)	
Echogenicity, n(%)			0.329
Marked hypoechogenicity	0	2(14.3%)	
hypoechogenicity	6(100%)	12(85.7%)	
Structure, n(%)			0.329
Homogeneous	0	2(14.3%)	
Inhomogeneous	6(100%)	12(85.7%)	
Punctuate hyperechoic foci, n(%)			<0.001
Microcalcification	0	11(78.6%)	
Hyperechoic foic	3(50%)	0	
Nondisplayed	3(50%)	3(21.4%)	
Vascularity pattern, n(%)			0.004
I	1(16.7%)	0	
II	5(83.3%)	3(21.4%)	
III	0	11(78.6%)	
Elastography pattern, n(%)			<0.001
I	0	0	
II	1(16.7%)	0	
III	5(83.3%)	4(28.6%)	
IV	0	10(71.4%)	

Results

As mentioned above, all degenerating cystic thyroid nodules were divided into two groups according to size in the final conventional US examination, group A and group B, group C and group D were divided in PTCs as well.

As shown in Table 1, more nodules in group A initially represented a predominantly cystic nature in US and the nodular nature was significantly different between the 2 groups (P<0.001). The change of size in group A was greater than in group B (P=0.033).

As shown in Table 2 & 3, there were significant difference between degenerating cystic thyroid nodules and PTCs, in nodule shape (groups<10 mm, P=0.017; groups>10 mm, P=0.017) and punctuate hyperechoic focis (groups<10 mm, P<0.001; groups>10 mm, P<0.001) (Figure 1). Nodules in group A were hypovascular as well as micropapillary thyroid carcinoma. The vascularity pattern was significantly different between group B and group D, vascularity was distributed perinodular in degenerating cystic thyroid nodules, while PTCs were hypervascular (P=0.004). Of the conventional US characteristics, punctuate hyperechoic foci had the highest

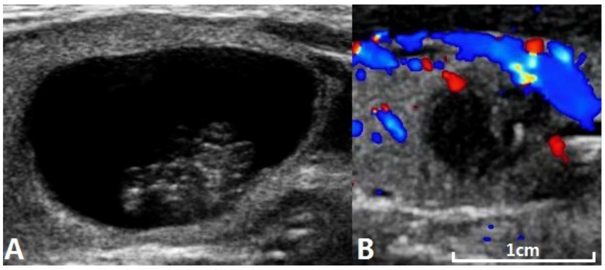

Figure 1. Degenerating Cystic Thyroid Nodule in a 42-year-old Woman. (A) Initial sonogram (longitudinal scan) showing a 21.4mm predominantly cystic nodule in the left thyroid gland. (B) Ten-month follow-up sonogram (longitudinal scan) in color flow mode showing a 9.2 mm hypoechoic nodule with suspicious malignant findings, including poorly defined margin and perinoduler vascularity, however hyperechoic spot with comet-tail artifact and oval to round in shape are differential points from PTC

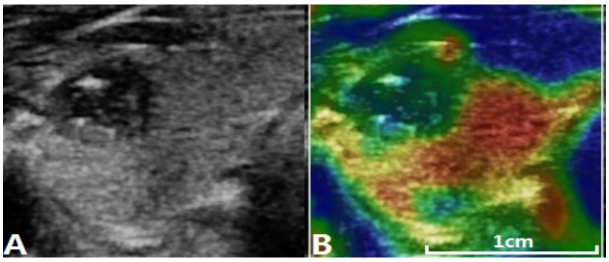

Figure 3. Degenerating Cystic Thyroid Nodule Mimicking Malignancy in a 37-year-old Woman. (A) Transverse sonogram showing suspicious malignant findings, including hypoechoic, poorly defined margin, internal hyperechoic spots mimicking microcalcifications. (B) The nodule displaying predominantly in green and sporadic parts in blue on real time ultrasound elastography (pattern II)

area under the curve (AUROC), at 0.82 and 0.86 in 2 groups, respectively.

Excluding the impact of location and size of nodules on elasticity pattern, 12 of 13 degenerating cystic thyroid nodules in Group A had pattern I&II (Figure 2) (Figure 3), whereas all 16 PTCs in Group C had pattern III&IV (P<0.001). One nodule in pattern III; green band distributed mainly in hyperechoic portion on B-mode US (Figure 4). 1 of 6 degenerating cystic thyroid nodules in group B had pattern I&II, whereas all 14 PTCs in group D had pattern III&IV (P<0.001). When using pattern I&II for the diagnosis of nodules in Group A, sensitivity and specificity were 92.3% (CI 72–91%) and 100% (CI 80–95%), respectively. The diagnostic accuracy (AUROC) of real time ultrasound elastography was 0.98 (P = 0.002). Sensitivity and specificity for the diagnosis of nodules in Group B was 16.7 % (CI 54–78%) and 100 % (CI 80–95%), respectively. The diagnostic accuracy (AUROC) of real time ultrasound elastography was 0.88 (P = 0.014).

Discussion

Cystic thyroid nodules are common. The cystic portion of nodule is considered to be caused by hemorrhage or degeneration of preexisting nodules. Most of them are benign (Choi et al., 2005). Several methods have been introduced for treating benign cystic thyroid nodules,

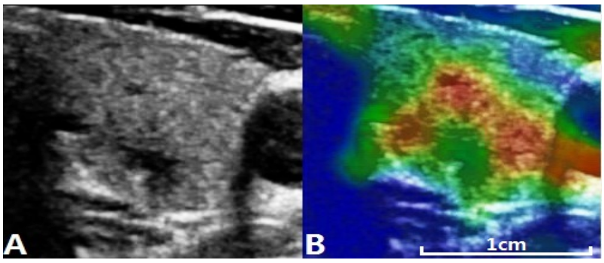

Figure 2. Degenerating Cystic Thyroid Nodule Mimicking Malignancy in a 51-year-old Man. (A) Transverse sonogram showing a 4.9mm hypoechoic nodule with poorly defined margin as well as internal hyperechoic spot, mimicking microcalcification that could be misinterpreted as malignancy. (B) The nodule displaying in green on the real time ultrasound elastography (pattern I)

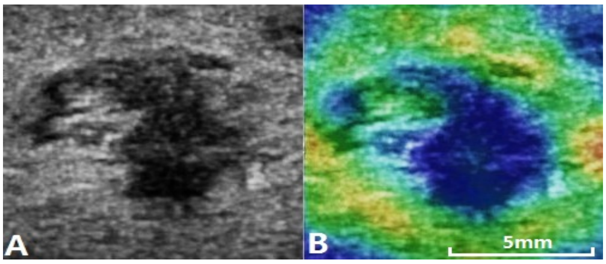

Figure 4. Degenerating Cystic Thyroid Nodule Mimicking Malignancy in a 54-year-old Woman. (A) Longitudinal sonogram of a 8.8mm nodule showing suspicious malignant findings, including hypoechoic, poorly defined margin, irregular shape, inhomogeneous. (B) Hyperechoic portion of nodule displaying in green, while hypoechoic portion displaying in blue on real time ultrasound elastography (pattern III)

such as thyroid hormone suppression therapy, fine-needle aspiration and sclerotherapy with various sclerosants. These treatments lead to morphological changes in cystic thyroid nodules (Park et al., 2008). However, spontaneous collapse may occur in nonaspirated cystic thyroid nodules. The decrease of nodular size and disappearance of the cystic portion in nodules often show in follow-ups of conventional US. Some of these degenerating cystic thyroid nodules show ambiguous characteristics, including hypoechoic. Hypoechoic in PTC is resulted from cellular enlargement and compaction, and accompanying stromal reduction. Although hypoechoic can also been seen in degenerating cystic thyroid nodule, it is caused by the decrease of colloids in follicles when the cystic nodule shrinks. The changes make interface simple, as the nodular echogenicity decreased. However, the specificity of hypoechoic for malignancy is 87%, although the sensitivity is low (15.6%-27%) (Papini et al., 2002; Frates et al., 2005). The ambiguous characteristics can cause confusion.

Taller than wide has both high sensitivity (84%) and specificity (82%) for detection of thyroid malignancy (Kim et al., 2002). Studies have proved that the ratio of the surface area to the volume is maximized by spherical shape, which would optimize exposure of the tumor cells to nutrient delivery (Alexander et al. 2004). So malignant nodules grow across the normal tissue plane, anteroposterior to transverse diameter ratio trends to be or greater than 1. This characteristic has seldom been seen in degenerating cystic thyroid nodules.

In the present study, hyperechoic spots with comet-tail artifact may give a clue in discriminating cystic thyroid nodules from PTCs. Microcalcifications are psammoma bodies, which are 10-100 μm round laminar crystalline calcific deposits. They are one of the most specific characteristics of thyroid malignancy, with a specificity of 85.8%–95%, and a positive predictive value of 41.8%–94.2% (Kim et al., 2002; Iannuccilli et al., 2004). On US, microcalcifications appear as punctate hyperechoic focis without acoustic shadowing. The hyperechoic spots in degenerating cystic thyroid nodule with comet-tail artifact is thought to represent debris composed of cholesterol and keratin. Sometimes, this kind of hyperechoic spots causes color flash artifact on Color Doppler image. However, the definition of microcalcifications and hyperechoic spots are dependent on the cognition and understanding of operator, the performance of equipment and so on.

Palpation is the most frequently used screening method for detecting thyroid nodules. However, it is subjective and depends on the skill of the clinical physician. Elastography could evaluate the tissue stiffness from the deformation rate objectively. It has been proved to be useful in differential diagnosis of thyroid carcinoma. Cell arranged closed in PTC, have complex papillae with a central fibrovascular stalk. Psammoma bodies and fibrosis are often found in them (Carcangui et al., 1985). All these factors increased nodular stiffness.

According to the microscopic features of the histopathology, the main morphologic change in Group A was cystic portion decrease and colloid loss. On the contrary, organizations and scars were shown frequently in Group B, as well as a more compacted solid portion, altering the nodular stiffness. Different from PTC, blue spots were distributed sporadically, suggesting elasticity distribution in degenerating cystic thyroid nodule has a unique feature. In regards to uneven stress distribution, the presence of solid-liquid interfaces within nodules may have interfered with stress distribution. Green spots or bands can go along with solid-liquid fold.

Our study included a relatively small number of cases, especially for group B. Lack of quantitative strain analysis in region of interest is an inherent limitation of the present study, and strain ratios need to be confirmed in further studies with larger samples. Nevertheless, as dense calcification as well as nodules in a background of thyroiditis, are unsuitable for elastography performed in the present study, this technique is likely to be even more limited in routine clinical practice. The accuracy of elastography is influenced by operator technique, or incorrect elastogram interpretation. For it to be established as a useful diagnostic tool, some techniques need to be standardized.

In conclusion, although elastography has some limitations, we found it performs differently in degenerating cystic thyroid nodules and PTCs, mainly for nodules less than 10mm. But it does not add to the ability to distinguish those degenerating complex cystic thyroid nodules from PTCs, particularly nodular size larger than 10mm. Combined with conventional US, it can avoid unnecessary procedures, such as FNAC and surgery.

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References

Ahn SS, Kim EK, Kang DR, et al (2010). Biopsy of thyroid nodules: comparision of three sets of guidelines. *Am J Roentgenol*, **194**, 31-7.

Alexander EK, Marqusee E, Orcutt J, et al (2004). Thyroid nodule shape and prediction of malignancy. *Thyroid*, **14**, 953-8.

Asteria C, Giovanardi A, Pizzocaro A, et al (2008). US-elastography in the differential diagnosis of benign and malignant thyroid nodules. *Thyroid*, **18**, 523-31.

Bhatia KSS, Rasalkar DP, Lee YP, et al (2011). Cystic change in thyroid nodules: A confounding factor for real-time qualitative thyroid ultrasound elastography. *Clin Radiol*, **66**, 799-807.

Cappelli C, Castellano M, Pirola I, et al (2006). Thyroid nodule shape suggests malignancy. *Eur J Endocrinol*, **155**, 27-31.

Carcangui ML, Zampi G, Rosai J (1985). Papillary thyroid carcinoma: a study of its many morphologic expressions and clinical correlates. *Pathol Annu*, **20**, 1-44.

Choi KU, Kim JY, Park DY, et al (2005). Recommendations for the management of cystic thyroid nodules. *ANZ J Surg*, **75**, 537-41.

Davies L, Welch HG (2006). Increasing incidence of thyroid cancer in the United States, 1973-2002. *JAMA*, **295**, 2164-7.

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

Friedrich-Rust M, Sperber A, Holzer K, et al (2010). Real-time elastography and contrast-enhanced ultrasound for the assessment of thyroid nodules. *Exp Clin Endocrinol Diabetes*, **118**, 602-9.

Iannuccilli JD, Cronan JJ, Monchik JM (2004). Risk for malignancy of thyroid nodules as assessed by sonographic criteria: the need for biopsy. *J Ultrasound Med*, **23**, 1455-64.

Kim EK, Park CS, Chung WY, et al (2002). New sonographic criteria for recommending fine-needle aspiration biopsy of nonpalpable solid nodules of the thyroid. *Am J Roentgenol*, **178**, 687-91.

Kim JY, Lee CH, Kim SY, et al (2008). Radiologic and pathologic findings of nonpaplpable thyroid carcinomas detected by ultrasonography in a medical screening center. *J Ultrasound Med*, **27**, 215-23.

Kim SS, Kim MR, Mok JY, et al (2011). Benign cystic nodules may have ultrasonographic features mimicking papillary thyroid carcinoma during interval changes. *Endocr J*, **58**, 633-8.

Mortensen JD, Woolner LB, Bennett WA (1955). Gross and microscopic findings in clinically normal thyroid glands. *J Clin Endocrinol Metab*, **15**, 1270-80.

Papini E, Guglielmi R, Bianchini A, et al (2002). Risk of malignancy in nonpalpable thyroid nodules: predictive value of ultrasound and color-Doppler features. *J Clin Endocrinol Metab*, **87**, 1941-6.

Park JS, Kim DW, Eun CK, et al (2008). Long-term follow-up sonography of benign cystic thyroid nodules after a percutaneous ethanol injection. *J Korean Radiol Soc*, **58**, 21-8.

Rago T, Santini F, Scutari M, et al (2007). Elastography: new developments in ultrasound for predicting malignancy in thyroid nodules. *J Clin Endocrinol Metab*, **92**, 2917-22.
Rubaltelli L, Corradin S, Dorigo A, et al (2009). Differential diagnosis of benign and malignant thyroid nodules at elastosonography. *Ultraschall Med*, **30**,175-9.
Tamsel S, Demirpolat G, Erdogan M, et al (2007). Power Doppler US patterns of vascularity and spectral Doppler US parameters in predicting malignancy in thyroid nodules. *Clin Radiol,* **62**, 245-51.
Tan GH, Gharib H (1997). Thyroid incidentalomas: management approaches to nonpalpable nodules discovered incidentally on thyroid imaging. *Ann Intern Med,* **126**, 226-31.
Teng DK, Wang H, Lin YQ, et al (2012). Value of ultrasound elastography in assessment of enlarged cervical lymph nodes. *Asian Pac J Cancer Prev*, **13**, 2081-5.