Sonographic Differentiation of Thyroid Nodules With Eggshell Calcifications

Byung Moon Kim, MD, Min Jung Kim, MD, Eun-Kyung Kim, MD, Jin Young Kwak, MD, Soon Won Hong, MD, Eun Ju Son, MD, Ki Hwang Kim, MD

Objective. The purpose of this study was to assess the role of known suspicious sonographic findings and to find other additional sonographic findings to differentiate benign and malignant thyroid nodules with "eggshell" calcifications. ***Methods.*** Our Institutional Review Board approved this retrospective study, and informed consent was not required. We reviewed sonographic findings of thyroid nodules in 795 patients who underwent thyroid surgery in our institution between August 2006 and February 2007. Ninety-three thyroid nodules with eggshell calcifications in 92 patients were included in this study. Each lesion was evaluated for known suspicious sonographic criteria, including marked hypoechogenicity, irregular or microlobulated margins, and a taller-than-wide shape, as well as 2 additional sonographic findings: a hypoechoic halo and disruption of eggshell calcifications (halo and disrupted calcification rim). The sensitivity and specificity based on the sonographic criteria were calculated and compared among the 2 types of criteria. ***Results.*** Among the 93 thyroid nodules, 59 were malignant and 34 were benign. The halo and disrupted calcification rim showed higher sensitivity (62.7% and 76.3%, respectively) than any of the known suspicious sonographic criteria (40.7%, 35.6%, and 55.9%). The combination of both the halo and the disrupted calcification rim showed significantly higher sensitivity (93.2%) than the combination of the known suspicious sonographic criteria (78%; $P < .05$), although both had the same specificity (64.7%). ***Conclusions.*** In thyroid nodules with eggshell calcifications but no other calcifications, the findings of a peripheral halo and disruption of the eggshell calcifications may be more useful sonographic predictors of malignancy than hypoechogenicity, microlobulated margins, and a taller-than-wide shape. ***Key words:*** calcifications; sonography; thyroid.

Received April 18, 2008, from the Department of Radiology, Sungkyunkwan University School of Medicine, Kangbuk Samsung Hospital, Seoul, Korea (B.M.K.); and Department of Radiology, Research Institute of Radiological Science (M.J.K., E.-K.K., J.Y.K., E.J.S., K.H.K.), and Department of Pathology (S.W.H.), Yonsei University Health System, Seoul, Korea. Revision requested May 9, 2008. Revised manuscript accepted for publication June 13, 2008.

Address correspondence to Min Jung Kim, MD, Department of Radiology, Yonsei University Health System, 134 Shinchon-dong, Seodaemun-ku, Seoul 120-752, Korea.

E-mail: mines@yuhs.ac

In evaluation of thyroid nodules with macrocalcifications, peripheral or "eggshell" calcifications of the thyroid nodule have been considered an indicator of benignity with a few exceptions[1]; however, several recent investigations suggest that macrocalcifications, as well as microcalcifications, of thyroid nodules should increase the clinical index of suspicion for thyroid carcinoma.[2–6] Kim et al[7] suggested that even in thyroid nodules with macrocalcifications, known suspicious sonographic findings, such as marked hypoechogenicity, irregular or microlobulated margins, and a taller-than-wide shape, would be helpful in distinguishing malignant from benign tumors. Among the types of macrocalcifications, eggshell calcifications lower the sensitivity of sonographic findings for differentiating malignant from benign tumors because of posterior shadowing; therefore, for thyroid nodules with eggshell calcifications, other sonographic findings are needed to help differentiate between benign and malignant nodules.

The purpose of this study was to assess the role of known suspicious sonographic findings and to find additional sonographic findings to differentiate benign and malignant thyroid nodules with eggshell calcifications.

Materials and Methods

Our Institutional Review Board approved this retrospective study, and informed consent was not required.

Between August 2006 and February 2007, 830 patients underwent thyroid surgery at our institution. The patient group consisted of 705 women (84.9%) and 125 men (15.1%). Their ages ranged from 21 to 82 years (mean age, 46 years). The reasons for thyroid evaluation were as follows: a palpable thyroid mass in 166 patients, a palpable lateral neck mass in 7, hoarseness in 7, and discomfort including dysphagia in 42. The remaining 608 patients had incidentalomas found by various imaging modalities, including sonography, computed tomography, magnetic resonance imaging, and positron emission tomography. Preoperative sonographic images obtained in our institution were available for 795 patients.

Preoperative sonographic evaluation was performed with an HDI 3000 or HDI 5000 system (Philips Medical Systems, Bothell, WA) and a linear 7- to 12-MHz probe or an Acuson Sequoia 512 system (Siemens Medical Solutions, Mountain view, CA) and a 5- to 13-MHz linear array probe for evaluation of the thyroid gland and neck. When the HDI 5000 machine was used, compound imaging was performed in all cases. Preoperative real-time sonographic examinations were performed by any 1 of 3 board-certified radiologists with an average of 6.7 years (4, 6, and 10 years, respectively) of experience in thyroid imaging. The time elapsed between sonography and surgery ranged from 27 to 63 days (median, 48 days).

One radiologist (M.J.K), who was blinded with respect to the final pathologic diagnosis and the ratio of malignant to benign lesions, retrospectively reviewed the sonographic data in the 795 patients and identified thyroid nodules with eggshell calcifications. Eggshell calcifications were defined as curvilinear hyperechoic structures parallel to the margin of the nodule and encompassing 120° or more of the circumference. Thyroid nodules with combinations of eggshell calcifications and other types of calcifications such as microcalcifications and macrocalcifications were excluded. Multiple thyroid nodules with eggshell calcifications in the same patient were evaluated independently.

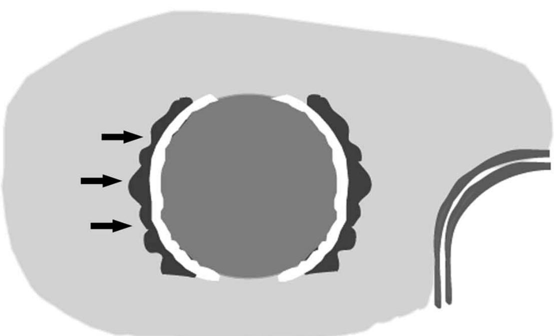
Ninety-three thyroid nodules with eggshell calcifications were found in 92 patients, and these patients constituted our study population. Each nodule with eggshell calcifications was evaluated for size and other suspicious sonographic features according to published data,[2,8,9] including marked hypoechogenicity (decreased echogenicity compared with the surrounding strap muscle), irregular or microlobulated margins, and a taller-than-wide shape (greater in its anteroposterior dimension than its transverse dimension), except for microcalcifications. We referred to these features as the "hypoechogenicity, microlobulated margins, and taller-than-wide shape" criteria. If the imaging findings could not be classified into 1 of the subclasses above because of a calcification shadow cast over the lesion, they were classified as not interpretable. The cases with imaging findings that were not interpretable were classified as negative because they did not show evidence suggesting the possibility of malignancy. Each nodule with eggshell calcifications was also evaluated for whether it had a hypoechoic halo (Figures 1A and 2) or disruption of the eggshell calcifications (Figures 1B and 3). We referred to these additional findings as the "halo and disrupted calcification rim" criteria. A hypoechoic halo was defined as hypoechoic areas outside the eggshell calcifications. Disruption of eggshell calcifications means a simple loss of continuance of linear hyperechoic structures or a loss of approximation in the alignment of the eggshell calcifications. Evaluation of the disruption was limited to the superficial 180° of the nodule circumference because the deep 180° portion was not accessible due to posterior shadowing.

Each nodule was classified by the number of known and additional sonographic features described above. If a thyroid nodule with eggshell calcifications had at least 1 of the 3 known sonographic features (hypoechogenicity, microlobulated margins, and taller-than-wide shape) or 1 of the 2 additional features (halo and disrupted calcification rim), the nodule was considered positive for the respective criteria.

A nodule was considered solitary when there were no other nodules either with or without calcifications in the same gland, and multiple nodules were designated when the thyroid contained more than 1 nodule. Pathologic results were reviewed by another radiologist (B.M.K.) from surgical records and pathology reports, but histologic slides were not reviewed. Sonographic findings and pathologic diagnoses were correlat-

Figure 1. Halo and disrupted calcification rim criteria for eggshell calcifications. **A**, Hypoechoic halo, shown as hypoechoic areas (arrows) outside the eggshell calcifications. **B**, Disruption of eggshell calcifications, shown as a loss of continuance (arrows) of linear hyperechoic structures or a loss of approximation in the alignment of eggshell calcifications.

A



B

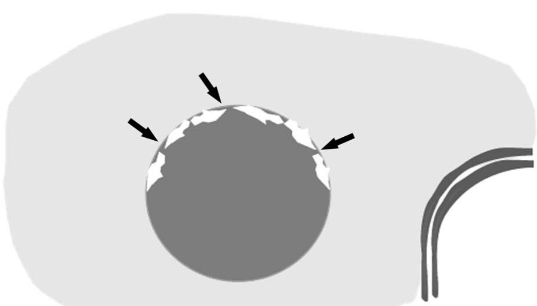
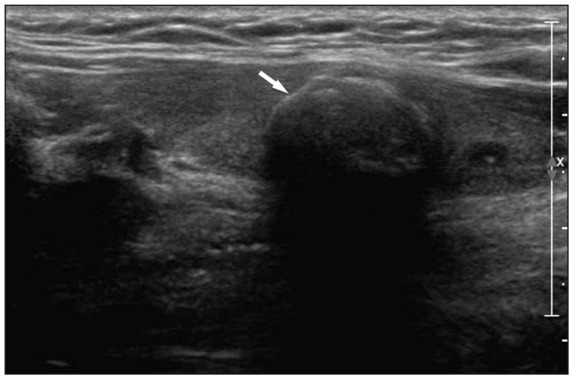
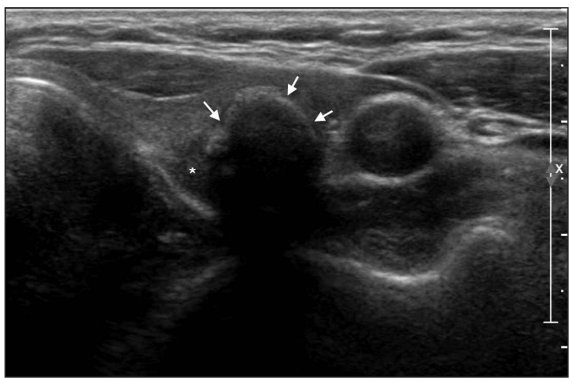


Figure 2. A, Longitudinal sonogram showing a 1.5-cm hypoechoic mass with eggshell calcifications (arrow) but without disruption of the calcifications or a hypoechoic area. **B**, Transverse sonogram showing a hypoechoic area (asterisk) outside the eggshell calcifications (arrows). **C**, Pathologic specimen showing papillary carcinoma (asterisks) outside and inside the calcifications (arrows) (hematoxylin-eosin, original magnification ×12.5).

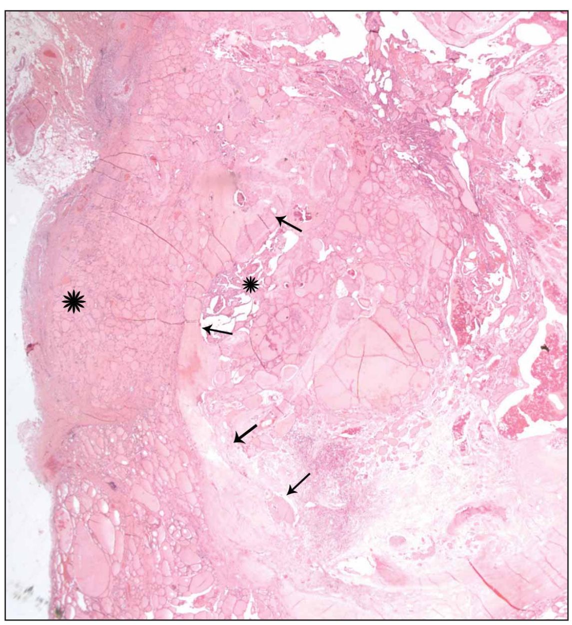
A



B



C

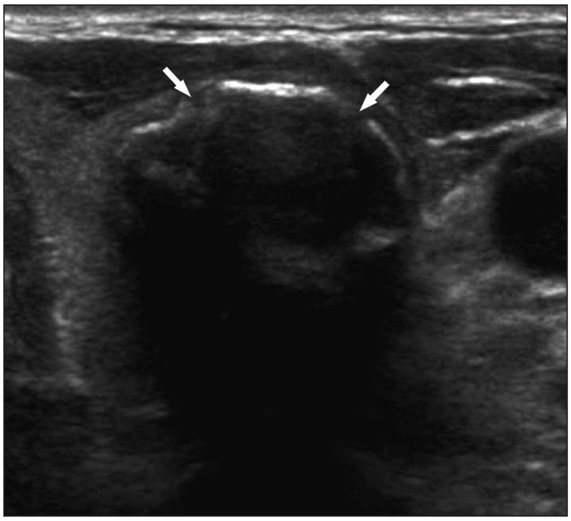


ed according to the size and location of the nodule and the presence of calcifications on the pathologic report.

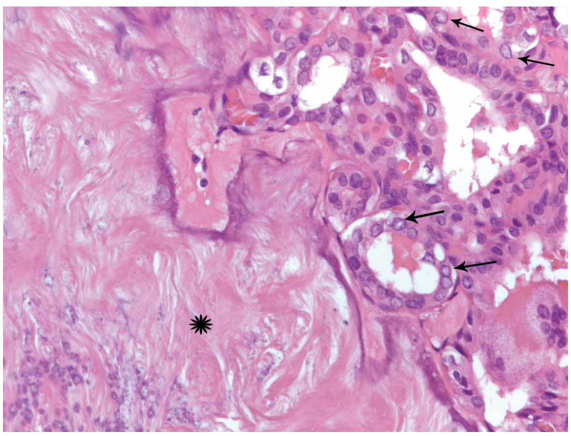
We assessed the sensitivity and specificity of each sonographic feature within both types of criteria for diagnosing malignancy and compared them for the hypoechogenicity, microlobulated margin, and taller-than-wide shape criteria and the halo and disrupted calcification rim criteria. Statistical analyses were conducted with the χ^2 test for nonparametric variables and the t test for parametric inferences. $P < .05$ was considered statistically significant. A 95% confidence interval was calculated. Statistical analyses were performed with SAS version 9.1 software for Windows (SAS Institute Inc, Cary, NC).

Figure 3. A, Transverse sonogram showing a 1.5-cm hypoechoic mass surrounded by eggshell calcifications (arrows) with a loss of continuance. **B**, Pathologic specimen showing tumor cells, including a nuclear groove and nuclear clearing (arrows), in the area of disruption in the calcifications (asterisk) (hematoxylin-eosin, original magnification ×400).

A



B



Results

Among 93 thyroid nodules with eggshell calcifications in 92 patients, 59 nodules were malignant and 34 were benign. All of the malignant thyroid nodules were papillary carcinomas. Benign thyroid nodules included 33 nodules with adenomatous hyperplasia and 1 follicular adenoma. The sizes of the 93 nodules ranged from 4 to 50 mm (mean, 16 mm). There was no statistical difference between the benign and malignant nodules with regard to size ($P > .05$). Among 58 solitary nodules, 20 (34.5%) were benign and 38 (65.5%) were malignant. Of the remaining 35 nodules found in the setting of multiple thyroid nodules within the same gland, 14 (40%) were benign and 21 (60%) were malignant. There was no statistical difference between solitary and multiple nodules in terms of the correlation with benign or malignant nodules ($P > .05$).

Table 1 shows the sensitivity, specificity, positive predictive value, and negative predictive value for predicting malignancy according to each sonographic feature within the 2 types of criteria. The halo and disrupted calcification rim criteria showed higher sensitivity than the hypoechogenicity, microlobulated margins, and taller-than-wide shape criteria. The combination of both the halo and the disrupted calcification rim showed significantly higher sensitivity (93.2% [55 of 59]) than the combination of hypoechogenicity, microlobulated margins, and taller-than-wide shape (78% [46 of 59]; $P < .05$), although both had the same specificity (64.7% [22 of 34]). Table 2 shows the number of sonographic features present within the 2 types of criteria and the pathologic results. Although 22% of the malignant nodules were negative according to the hypoechogenicity, microlobulated margins, and taller-than-wide shape criteria, only 6.8% were negative according to the halo and disrupted calcification rim criteria.

Table 1. Diagnostic Parameters for Each Sonographic Feature

Parameter	Hypoechoic Halo	Disruption of Calcifications	Marked Hypoechogenicity	Irregular or Microlobulated Margin	Taller-Than-Wide Shape
Sensitivity, n (%)	37/59 (62.7)	45/59 (76.3)	24/59 (40.7)	21/59 (35.6)	33/59 (55.9)
Specificity, n (%)	32/34 (94.1)	22/34 (64.7)	27/34 (79.4)	33/34 (97.1)	29/34 (85.3)
PPV, n (%)	37/39 (94.9)	45/57 (78.9)	24/31 (77.4)	21/22 (95.5)	33/38 (86.8)
NPV, n (%)	32/54 (59.3)	22/36 (61.1)	27/62 (43.5)	33/71 (46.5)	29/55 (52.7)

NPV indicates negative predictive value; and PPV, positive predictive value.

Discussion

Although microcalcifications have a well-known association with thyroid malignancy,[8,10,11] peripheral or eggshell calcifications within a thyroid nodule are thought to be an indicator of benign nodules with a few exceptions[1]; however, Taki et al[4] reported that 43% of the thyroid lesions with peripheral calcifications that they examined were associated with cancer. Frates et al[2] reported that rim calcifications doubled the risk of malignancy compared with similar nodules without calcifications, and the risk of malignancy increased when a nodule was solitary and solid. Kim et al[7] suggested that known suspicious sonographic findings other than calcifications would be helpful for distinguishing malignant from benign thyroid nodules with macrocalcifications. They reported, however, that it was difficult to apply these criteria for assessing macrocalcifications to nodules with eggshell calcifications. These difficulties arise from the fact that the calcified margin of the nodule can obscure margin interpretation, and posterior shadowing from the calcifications can obscure the shape (taller than wide) and interpretation of the internal echogenicity.

We suggested that a hypoechoic halo and disruption of rim calcifications may be additional sonographic findings suspicious for malignancy in thyroid nodules with eggshell calcifications. These sonographic findings correspond with tumor invasion through (or over) rim calcifications on pathologic examinations (Figure 2).

Recently, Yoon et al[12] reported that the sonographic features of thyroid nodules with peripheral calcifications did not show any significant differences between benign and malignant groups. As in that study, we evaluated the sonographic size, shape, and internal echogenicity of thyroid nodules. In contrast to the report by Yoon et al,[12] however, which did not differentiate between microcalcifications and macrocalcifications for peripheral calcifications, we clarified the definition of eggshell calcifications to exclude microcalcifications. If the calcifica-

Table 2. Distribution of Suspicious Sonographic Features in Rim-Calcified Nodules Compared With Surgical Pathologic Results

Suspicious Sonographic Features, n	Malignant, n (%)	Benign, n (%)
Hypoechogenicity, microlobulated margin, and taller-than-wide-shape		
0	13 (22)	22 (64.7)
1	24 (40.7)	11 (32.3)
2	12 (20.3)	1 (3)
3	10 (17)	0 (0)
Halo and disrupted calcification rim		
0	4 (6.8)	22 (64.7)
1	28 (47.4)	11 (32.3)
2	27 (45.8)	1 (3)
Total	59 (100)	34 (100)

tions surrounding the nodule were microcalcifications or a combination of macrocalcifications and microcalcifications, we did not consider them peripheral calcifications favoring a benign prognosis because microcalcifications in thyroid lesions are well known to be suspicious sonographic findings for malignancy.[3,8,11,13]

One of the limitations of our study was the small percentage of benign nodules in our population compared with previous reports in the literature. We reviewed consecutive surgical lesions over 6 months. Although we encountered benign calcified nodules frequently during fine-needle aspiration biopsy, nodules referred for surgical excision were more likely to be malignant. This promoted a potential selection bias in our study population. Additional studies that prospectively analyze thyroid nodules with eggshell calcifications during fine-needle aspiration biopsy should be necessary. Second, we did not review the histologic slides to correlate imaging findings with histologic findings in each nodule. Additional studies that correlate the findings of a hypoechoic halo and disrupted calcification rim with histologic findings in benign and malignant nodules may be necessary. Finally, in this study a single investigator reviewed the imaging findings, and we did not evaluate interobserver variability in interpretation of rim calcifications.

In conclusion, in thyroid nodules with eggshell calcifications and no other calcifications, the findings of a peripheral halo and disruption of eggshell calcifications may be more useful sonographic predictors of malignancy than the sonographic features of hypoechogenicity, microlobulated margins, and a taller-than-wide shape.

References

1. Park CH, Rothermel FJ, Judge DM. Unusual calcification in mixed papillary and follicular carcinoma of the thyroid gland. Radiology 1976; 119:554.
2. Frates MC, Benson CB, Doubilet PM, et al. Prevalence and distribution of carcinoma in patients with solitary and multiple thyroid nodules on sonography. J Clin Endocrinol Metab 2006; 91:3411–3417.
3. Wang N, Xu Y, Ge C, Guo R, Guo K. Association of sonographically detected calcification with thyroid carcinoma. Head Neck 2006; 28:1077–1083.
4. Taki S, Terahata S, Yamashita R, et al. Thyroid calcifications: sonographic patterns and incidence of cancer. Clin Imaging 2004; 28:368–371.
5. Seiberling KA, Dutra JC, Grant T, Bajramovic S. Role of intrathyroidal calcifications detected on ultrasound as a marker of malignancy. Laryngoscope 2004; 114:1753–1757.
6. Consorti F, Anello A, Benvenuti C, et al. Clinical value of calcifications in thyroid carcinoma and multinodular goiter. Anticancer Res 2003; 23:3089–3092.
7. Kim MJ, Kim EK, Kwak JY, et al. Differentiation of thyroid nodules with macrocalcifications: role of suspicious sonographic findings. J Ultrasound Med 2008; 27:1179–1184.
8. Kim EK, Park CS, Chung WY, et al. New sonographic criteria for recommending fine-needle aspiration biopsy of nonpalpable solid nodules of the thyroid. AJR Am J Roentgenol 2002; 178:687–691.
9. Tae HJ, Lim DJ, Baek KH, et al. Diagnostic value of ultrasonography to distinguish between benign and malignant lesions in the management of thyroid nodules. Thyroid 2007; 17:461–466.
10. Holtz S, Powers WE. Calcification in papillary carcinoma of the thyroid. Am J Roentgenol Radium Ther Nucl Med 1958; 80:997–1000.
11. Frates MC, Benson CB, Charboneau JW, et al. Management of thyroid nodules detected at US: Society of Radiologists in Ultrasound consensus conference statement. Radiology 2005; 237:794–800.
12. Yoon DY, Lee JW, Chang SK, et al. Peripheral calcification in thyroid nodules: ultrasonographic features and prediction of malignancy. J Ultrasound Med 2007; 26:1349–1355.
13. Takashima S, Fukuda H, Nomura N, Kishimoto H, Kim T, Kobayashi T. Thyroid nodules: re-evaluation with ultrasound. J Clin Ultrasound 1995; 23:179–184.