Orijinal Araştırma / Original Investigation
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Diagnosis of Thyroid Carcinoma; Dynamic Magnetic Resonance Imaging as a Problem Solver

Tiroid Karsinomu Tanısı; Problem Çözücü Olarak Dinamik Manyetik Rezonans Görüntüleme

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ÖZET

AMAÇ: Tiroid kanseri olgularının ayırıcı tanısında dinamik manyetik rezonans görüntülemenin (MRG) renkli Doppler US ve İnce İğne Aspirasyon Biyopsisi (İİAB) ile tanısal doğruluğunun karşılaştırılması.

GEREÇ VE YÖNTEM: Bu prospektif çalışmada 28 kadın ve 6 erkek hastanın toplam 38 tiroid nodülü incelendi. Radyolojik incelemelerin ardından İİAB ve tiroidektomi uygulandı.

BULGULAR: Dinamik MR inceleme ile elde edilen zaman-sinyal yoğunluk eğrilerinin, malignite teşhisinde renkli Doppler US ve İİAB modalitelerine göre yüksek sensitivite ve spesifiteye sahip olduğu bulundu. Malign lezyonlarda kontrast madde yavaş yıkanma hızı gösterirken, benign lezyonlarda yıkanmanın daha hızlı olduğu gözlemlendi.

SONUÇ: Malign tiroid nodülleri tipik zaman-sinyal yoğunluk eğrileri göstermekte olup, dinamik MRG'nin radyoloji-patoloji uyumsuzluğu gibi belirli durumlarda tiroid nodüllerinin ameliyat öncesi değerlendirilmesi için değerli olabileceğine inanıyoruz.

Anahtar Kelimeler: tiroid kanseri, dinamik MRG, Doppler US

ABSTRACT

OBJECTIVE: Comparison of the diagnostic accuracy of dynamic magnetic resonance imaging (MRI) with color Doppler US and Fine Needle Aspiration Cytology (FNAC) in the differential diagnosis of thyroid carcinoma cases.

MATERIALS AND METHODS: In this prospective study, a total of 38 thyroid nodules of 28 women and 6 men were examined. After radiologic examinations, FNAC and thyroidectomy were applied.

RESULTS: Time-signal intensity curves obtained by dynamic MR examination were found to have higher sensitivity and specificity in the diagnosis of malignancy compared to color Doppler US and FNAB modalities. Slow washout of the contrast material in malignant lesions and rapid washout of the contrast material in malignant lesions were observed.

CONCLUSION: Malignant thyroid nodules show typical time-signal intensity curves, and we believe that dynamic MRI will be valuable for preoperative assessment of the thyroid nodules in certain conditions like radiology–pathology mismatch.

Keywords: thyroid carcinoma, dynamic MRI, Doppler US

INTRODUCTION

Preoperative differentiation of benign and malignant thyroid nodules possesses great importance for treatment and surgical planning. Several methods like scintigraphy, ultrasound-Doppler examination, and fine-needle aspiration cytology are available to evaluate thyroid nodules. In routine practice, fine-needle aspiration cytology (FNAC) is accepted to be the gold standard in the preoperative evaluation of solitary nodules, especially in multinodular goiter (1). Because of sampling inaccuracy, FNAC may not be adequate for the absolute distinction of malignant and benign nodules. In our study, we compared the diagnostic value of Doppler ultrasound, FNAC, and time-intensity curves obtained from dynamic contrast-enhanced magnetic resonance imaging, and as a result, we found that with dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) it might be possible to distinguish malignancy by the simultaneous evaluation of multiple nodules in certain conditions like the radiology–pathology mismatch.

MATERIAL & METHODS

This prospective study group comprised 34 cases, 28 women (82.3 %) and 6 men (17.7 %). Our patient group was aged from 26 to 73 years, and the mean age was 45.1. While 58.8 % of our patients had multinodular goiter (MNG), 41.2 % had solitary nodules.

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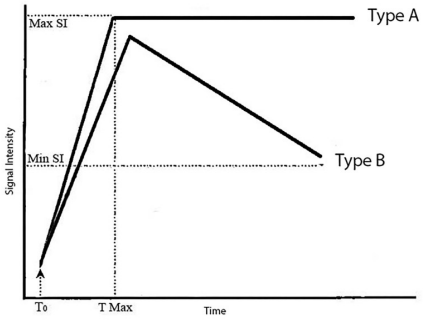
Patients were informed in detail about the purpose of the study, interventional diagnostic modalities to be applied, potential complications of different treatment regimes, and benefits expected from different modalities, and their written informed consent was obtained. Institutional ethics committee approval was obtained prior to the study. All the patients were primarily evaluated by the same endocrinology clinician and found to have incidental thyroid hormone disorders with or without a palpable nodule.

DCE-MRI was performed in patients who were scheduled for thyroid surgery for any reason (suspicion of malignancy, compression effect, family history, patient preference) after the sonographic examination. US and MRI scans were performed by different radiologists who were kept blind to the results of each examination. FNAC was performed with US guidance before thyroidectomy. Histopathological examination results of the thyroidectomy materials were the gold standard for the final diagnosis.

GE Logiq P6 US device with a 12 MHz linear probe was used for the sonographic examination. All the sonographic examinations were performed by the same physician. After evaluating the whole gland, color-Doppler ultrasound was performed. Both the B-Mode (Echogenicity, margins, microcalcifications, and nodule structure) and the color-Doppler findings were considered for the final diagnosis, and the nodules were classified as benign or malignant (2). The vascularity pattern of the nodules was the only color-Doppler criterion that was considered. The nodules that were found to have greater vascularity centrally and, those showing only central vascularity were considered malignant. Because there is no accepted consensus on the correlation between the spectral parameters and pathology results, these parameters were not considered as the diagnostic criteria (3).

For magnetic resonance imaging, a device with a magnetic field of 1.5 Tesla and gradient power of 32 mTesla was used (Intera, Philips Healthcare, Best, The Netherlands). SENSE-parallel imaging was performed with SflexM-surface coils. T2 TSE coronal, T2 TSE SPIR axial, T1 SPIR axial, dynamic-contrast FFE axial, T1 post-contrast axial, and T1 SPIR post-contrast axial images were obtained. The same contrast material with gadolinium-DTPA (Multihance®, Bracco, USA) with a concentration of 469.01 mg/dl gadopentetic acid was used on all the patients for preventing disturbances that may be caused by using different agents. The total dose used was limited to 0.1 mmol/kg. Axial-plane T1-weighted dynamic fast-field echo-sequence was used for the dynamic imaging protocol (TR / TE / FA / NEX = shortest / 5.4 / 20 / 1 matrix: 64x240, field of view (FOV): 200 mm2, slice thickness: 2.0 / 1.0 mm). To avoid vascular pulsation artifacts the front–rear phase encoding was preferred. Image acquisition was initiated simultaneously by the administration of a contrast agent, and 10 s successive sequences were acquired. Dynamic sequence duration was limited to 600 s (10 min) for evaluating late-phase enhancement patterns. All the dynamic sequence series were subtracted from the first series by the default-processing program of the scanner. As a result, only the images with tissues showing contrast enhancement were acquired. Conventional post-contrast series were acquired after the dynamic examination. In the dynamic MR imaging, 2–5 mm circular region-of-interest (ROI) points were placed over each nodule. Time-signal intensity–curves (TSC) were automatically generated from the corresponding ROI's by the scanner's default image-analysis program. Maximum (MaxSE) and minimum (MinSE) signal intensity values were noted for each TSC and the contrast washout ratio was calculated by (MaxSE – MinSE)/MaxSE formula. TSC's were classified as Type A and B (Fig. 1).

Figure 1. *Time–Signal Intensity Curve Types.*



After DCE-MRI imaging US-guided fine-needle biopsy was performed by using a 21G syringe. Biopsies were guided to the suspected zones that were imaged with Doppler-US and dynamic-MR imaging as much as possible. All targeted nodules were successfully sampled, and at least three passes were made for each nodule. Definite diagnoses of all the cases were acquired by the histopathological examination of the thyroidectomy materials.

All nodules were classified as malignant and benign separately with each imaging modality and FNAC while the equivocal findings were considered malignant. SPSS (SPSS

for Windows, Version 16.0. Chicago, SPSS Inc.) Program was used for the statistical analysis. All the data were summarized with tables and graphics while being analyzed.

Results were classified as statistically significant for $p < 0.05$ level and statistically insignificant for $p > 0.05$ level at a confidence interval of 95 %. Additionally, specificity, sensitivity values, PPV, and NPV were calculated for MRI, Doppler US, and FNAC.

RESULTS

Results of the Doppler-US imaging, dynamic MR time-intensity curves, FNAC results, and histopathological diagnosis of the 38 nodules were obtained.

Calculated specificity and sensitivity values of color-Doppler US imaging for differentiating malignant and benign nodules were 83.3 % and 76.9 %, respectively. These results were like that of most of the studies performed on this issue in the literature.

While specificity values for FNAC were very high, sensitivity values were significantly lower. These low-sensitivity values may be owing to the equivocal findings that were considered malignant, as the surgeons tend to choose thyroidectomy when these findings are reported in the cytologic examination.

Slow washout of the contrast material was observed in all 12 nodules (100 %) that were diagnosed as malignant; hence the calculated washout percentage of contrast was less than 25 % after 10 min with an average value of 21.4 % (Fig. 2). Rapid washout of contrast material pattern was observed in 24 of 26 (80 %) benign tumors (Fig. 3). As a result of the 10-min observation, an average percentage of 50 % washout of the contrast media was observed in benign nodules (Figs. 4–6).

Figure 2. *Sample dynamic enhancement curve of a malignant nodule.*

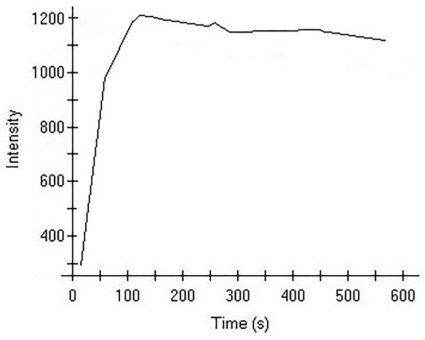


Figure 3. *Sample dynamic enhancement curve of a benign nodule.*

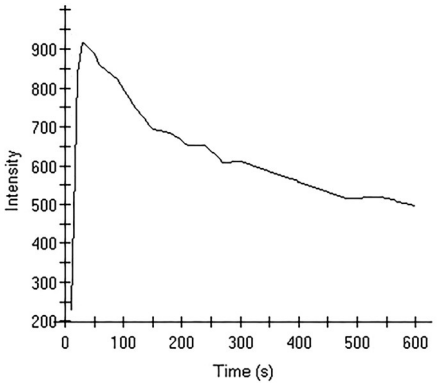


Figure 4. *Malignant characteristics observed in DCE-MR and Doppler US. The pathological examination result was follicular adenoma based on Hashimoto thyroiditis. (Straight arrow: Malignant (?) nodule, Warped arrow: Benign nodules in the right lobe).*

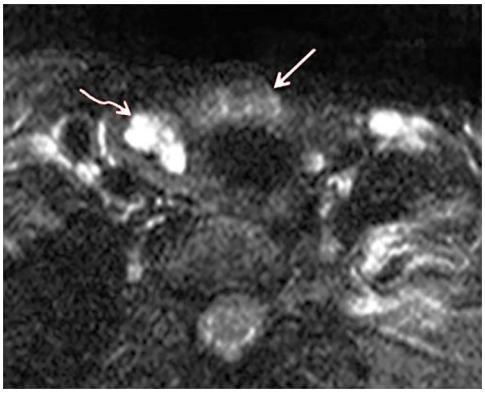


Figure 5. *Malignant characteristics observed in the DCE-MR and Doppler US. The pathological examination result was follicular carcinoma.*

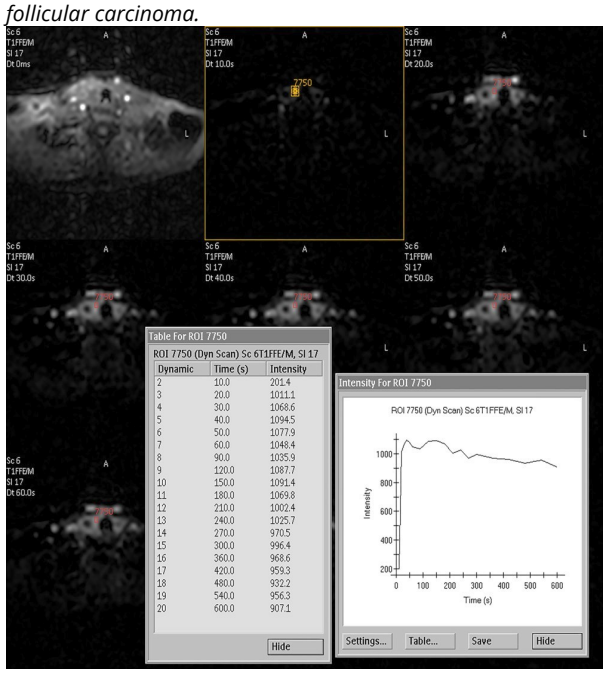
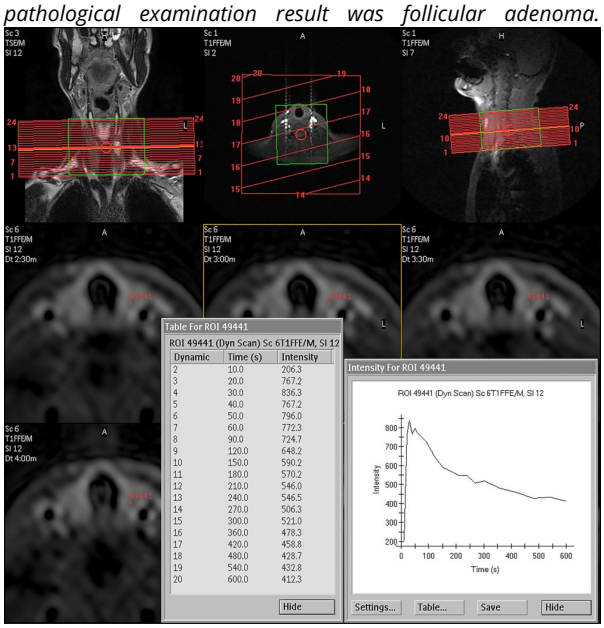


Figure 6. *FNAC results in follicular neoplasm, benign characteristics observed in the DCE-MR and Doppler US. The pathological examination result was follicular adenoma.*



Histopathologic diagnosis of Hashimoto's thyroiditis based on nodular hyperplasia was reported in one nodule, which showed a 5 % of washout of the contrast material and was reported to be malignant with the dynamic MR imaging. A re-evaluation of this specimen was requested from the pathology department, but the preparations could not be reached, and this case was placed under the false positive list for DCE-MRI.

Histopathological examination on the 12 nodules diagnosed as malignant showed peak-enhancement times between 90 to 150 s with a mean value of 101.67 ± 24.01 s. In the benign nodules group, these values were 60 to 100 s with a mean value of 91.54 ± 10.68 s.

For malignant tumors, the peak enhancement in the signal intensity values ranged between 900 and 1200 with an average value of 1116.67 ± 112.54, and for benign tumors, the signal intensity values ranged between 900 and 1100 with the average value calculated as 996.15 ± 37.97. The average minimum value of the signal enhancement was calculated as 419.23 ± 184.32 in the benign nodules.

In the histopathologically proven malignancy cases, diagnosis of follicular carcinoma was reported in 10 of the 12 patients and 2 patients as medullary carcinoma. Apart from the follicular carcinoma cases, showing time to peak intensity ranging from 90 to 100 s (average 92 s), medullary carcinoma cases showed 150 s of peak enhancement time. Slow washout of the contrast agent was observed in the medullary carcinomas as seen in patients with follicular carcinoma.

No significant difference was found between the time-to-peak enhancement of benign and malignant nodules. However, a statistically significant difference was detected between the time-intensity curve's peak signal intensity values (p = 0.018) and the minimum signal intensity values (p = 0.023) observed at the end of 10 minutes (Table 1).

Table 1. *Histopathological results and signal intensity curve characteristics*

	Benign (n=26)	Malignant (n=12)	p
Max SI	996.15±37.97	1116.67±112.54	0.018*
Min SI	419.23±184.32	923.33±60.55	0.023*
Time to Peak	91.54±10.68	101.67±24.01	0.831

** p<0.05 statistically significant (Mann-Whitney Test) SI: signal intensity*

DISCUSSION

Contrast washout pattern evaluation using dynamic-MR imaging was the diagnostic modality with the highest sensitivity and specificity of 100 % and 80 %, respectively. These values were 83.3 % and 76.9 % for the color-Doppler US and 100 % and 61.5 % for the FNAC (Table 2).

Table 2. *Sensitivity, specificity, positive and negative predictive values*

	Doppler	MRI	FNAC
Sensitivity	%83.3	%100.0	%100.0
Specificity	%76.9	%80.0	%61.5
PPV*	%62.5	%83.3	%54.4
NPV*	%90.9	%100.0	%100.0

** PPD: Positive Predictive Value, NPD: Negative Predictive Value*

Being a non-invasive diagnostic modality and possessing the ability of simultaneous multiple nodule examination are the advantages of DCE-MR imaging. In conjunction with the dynamic-contrast enhancement curves obtained from a single ROI point, contrast washout maps can also be used to quickly define the suspected areas. As the image data is stored for later use, the operator dependency issue can be resolved, and a second look examination can be performed if needed. The disadvantages of MRI imaging are higher cost and longer examination times compared to ultrasound imaging.

As our findings show similarities with those few studies about the dynamic MRI evaluation of the thyroid nodules in literature (4–7), to our knowledge, no other study compares

the diagnostic accuracy of the DCE-MRI with other modalities. Dynamic curve patterns showing early contrast washout in benign nodules and delayed washout in malignant nodules are described by Tezelman et al. Diagnostic specificity and sensitivity values of 100 % and 84 % respectively, in the preoperative assessment are also described in this study (4). In another study by Kusunoki et al., besides the delayed contrast washout pattern observed in 12 of 14 carcinoma cases, the typical early contrast washout pattern is shown only in 18 of 24 benign nodule cases. In this study, DCE-MR showed high specificity in terms of the preoperative assessment of thyroid nodules (5). Ying Yuan reported that while rapid washout of contrast material was observed in all the benign thyroid nodules, the plateau pattern with a relatively prominent increase slope of contrast enhancement and late contrast enhancement peaks were observed in the malignant group (6).

Fine-needle aspiration cytology is routinely and widely used in the preoperative evaluation of thyroid nodules. FNAC is the gold standard for diagnostic studies, but this examination alone has some shortcomings. On large nodules, the focus of malignant transformation may not be sampled or because of focusing on large nodules, small malignant nodules may be missed in the multinodular goiter cases. This situation may result in inadequate treatment of malignancy (subtotal thyroidectomy and skipping of metastatic lymph nodes). Especially in small nodules, non-diagnostic pathology results, and re-sampling is frequent. In the case of plunging goiter, the aspiration needle may not be directed to the nodules in the retro-sternal region. While with FNA, most of thyroid malignancies can be diagnosed, and follicular adenoma and follicular carcinoma cannot be distinguished leading to the need for surgical excision of the nodule.

In the past years, color-Doppler US is widely used in the preoperative assessment of thyroid nodules. Vascularity patterns, RI–PI values of the peri nodular and Intra nodular vascular structures, and the relationship of these findings with the malignancy were evaluated in many studies. Chammas' comprehensive study stated that the malignancy rate increases as the nodules' central vascularity increases as opposed to peripheral vascularity (8). The diagnostic value can be improved through findings correlated with the malignancy and by evaluating with the Doppler US (9,10). Doppler ultrasound is vastly used for many years and there are accepted guidelines for its daily use. Despite vascularity patterns related to malignancy being specified with Doppler ultrasound, lately, it is shown that these vascularity patterns and the RI–PI values obtained from these vascular structures specified with the Doppler ultrasound may be inadequate for the absolute distinction of the malignant and benign nodules. By the nature of ultrasound examination, operator dependency is another shortcoming of Doppler imaging. In very large goiter cases, especially in the plunging goiter, a complete examination of the gland may not be possible. Besides findings in our study show similarities with the literature; the US with color Doppler alone cannot fully meet the need for a definitive assessment of nodule structure in the preoperative evaluation (11).

Quantitative DCE-MRI using perfusion data and diffusion-weighted imaging (DWI) techniques are getting popular for the differentiation of thyroid malignancies in recent years. There are studies suggesting the combined usage of these methods may improve overall diagnostic performance (12–14)

Unlike previous study results, in their study on 19 patients Ben-David E. et al., stated that signal-intensity curves and quantitative MRI were not effective in differentiating benign and malignant thyroid nodules, as different types of dynamic contrast enhancement curves (rapid washout, slow washout, and plateau) were observed in malignant nodules (15).

As for the limitations of our study, each diagnostic modality was performed by the same radiologist, deteriorating the in-class correlation. Our results may differ from the normal population since an MRI examination was performed only on the thyroidectomy candidates and the included patient number in our study is limited.

Accurate diagnosis and treatment of thyroid nodules can only be achieved by the combined usage of different diagnostic methods. As a result of our study, we consider that dynamic MRI may be a valuable non-invasive alternative for FNAC, especially in preoperative assessment of multiple thyroid nodules in the case of a radiology-pathology mismatch, and where, the standard diagnostic modalities cannot be applied.

Etik: Bu çalışmanın etik kurulu alınmıştır.

Ethics committee approval had been taken.

Yazar katkı durumu; Çalışmanın konsepti; EA, NE, EU, dizaynı; EA, NE, EU, Literatür taraması; EA, NE, EU, verilerin toplanması ve işlenmesi; EA, NE, EU, istatistik; EA, NE, EU, yazım aşaması; EA, NE, EU.

Author contribution status; The concept of the study; EA, NE, EU, design; EA, NE, EU, literature review; EA, NE, EU, collecting and processing data; EA, NE, EU, statistics; EA, NE, EU, writing phase; EA, NE, EU.

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