The Role of Dynamic Contrast Enhanced Magnetic Resonance Imaging in Differentiation of Soft Tissue Masses

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ABSTRACT

Objective: To show the magnetic resonance imaging characteristics of soft tissue masses, and to evaluate the aid of contrast-enhanced static and dynamic magnetic resonance imaging for the differentiation of benign and malignant lesions. Methods: A total of 35 soft tissue masses (16 benign and 19 malignant) were included in this prospective study. Diagnoses of 32 massses (all malignant and 13 benign masses) were histologically confirmed. Diagnoses of 3 benign masses (hematomas) were confirmed with clinical follow-up. Magnetic resonance (MR) images were performed with a 1.5 T MR system (Philips, Medical Systems, The Best, Netherlands). Body coil or surface coil was used depending on the location and size of the lesion. T1 weighted (W) turbo spin-echo (TSE), T2 -W TSE and short tau inversion recovery (STIR) sequences, dynamic contrast-enhanced (DCE) MR images were performed, followed by static contrast-enhanced MR images. The frequency distribution of the individual magnetic resonance imaging (MRI) parameters in the benign group was compared with that in the malignant group by using the Chi-square test. Results: On non-enhanced images; tumor size, peritumoral edema, bone and neurovascular involvement were statistically significant between benign and malignant lesions. Presence of necrosis was only seen in malignant lesions on static contrast-enhanced images. The sensitivity, spesificity and overall accuracy of DCE images for the differentiation of benign and malignant lesions was 94% 75% 86% respectively (p=0.0001). Conclusion: Our study shows that the use of DCE MRI can help for the differentiation of benign and malignant soft tissue tumors.

Key words: Soft tissue tumors, magnetic resonance imaging

Yumuşak Doku Kitlelerinin Ayırımında Manyetik Rezonans Görüntülemenin Rolü

ÖZET

Amac: Yumusak doku kitlelerinin manyetik rezonans görüntülemenin karakteristiklerini göstermek ve benign ve malign lezyonların ayırımında statik ve dinamik kontrastlı manyetik rezonans görüntülemenin yardımını değerlendirmek. Yöntem: Bu prospektif çalışmaya toplam 35 yumuşak doku kitlesi (16 benign ve 19 malign) dahil edildi. Otuziki kitlenin (tüm malign ve 13 benign kitle) tanısı histolojik olrak doğrulandı. Üç benign kitlenin (hematom) tanısı klinik takiple doğrulandı. Manyetik rezonans görüntüleri 1.5 T MR sistemi (Philips, Medical Systems, The Best, Netherlands) ile yapıldı. Lezyonun yerleşimi ve boyutuna göre vücut sarmalı veya yüzeyel sarmal kullanıldı T1 ağırlıklı (A) turbo spin-eko (TSE), T2 -A TSE and short tau inversion recovery (STIR) sekanslar, dinamik kontrastlı MR görüntülerini takiben statik kontrastlı MR görüntüleri alındı. Frekans dağılımları ve her bir manyetik rezonans görüntüleme parametreleri ki-kare testi kullanılarak malign ve benign gruplar karşılaştırıldı. Bulgular: malign ve benign lezyonlar arasında kontrastsız görüntülerde tümör boyutu, peritümöral ödem, kemik ve nörovasküler tutulum istatiksel olrak anlamlıydı. Nekroz varlığı statik kontrastlı MR görüntülerinde yalnızca malign lezyonlarda görüldü. Benign ve malign lezvonların ayırımında dinamik kontrastlı MR görüntülerinin sensitivite, spesifisite, toplam doğruluğu sırasıyla %94, %75, %86 idi (p=0.0001). Sonuç: Bizim çalışmamız benign ve malign tümörlerin ayırımında dinamik kontrastlı MR görüntülerinin yardım edebileceğini gösterdi.

Anahtar kelimeler: Yumuşak doku tümörleri, manyetik rezonans görüntüleme, kontrast materyal

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INTRODUCTION

Soft tissue sarcomas account for 1% of all malignant tumors. Benign soft tissue masses are more common than malignant ones, but the real incidence is not known (1, 2). The life expectancy of patients with soft tissue sarcomas is linked to the timing of sufficient resection and neoadjuvant chemotherapy. For this reason early, correct diagnosis and staging of soft tissue tumors are crucial in appropriate patient management (3). Magnetic resonance imaging (MRI) is a major radiologic method for evaluation of soft tissue masses due to several advantages including superior contrast resolution and ability to directly image in the axial, sagittal and coronal planes, and the lack of ionizing radiation (4,5). Non-enhanced MRI is enough to show the lesions extent and local staging. Whereas it is insufficient for lesion characterization. Intravenous contrast administration is useful for demonstrating the lesion vascularity. Dynamic contrast-enhanced (DCE) MRI gives important information about tumor vascularity and angiogenesis which is helpful for tumor characterization. Therefore the addition of DCE MRI may improve the differentiation between benign and malignant soft tissue lesions (6,7-11). The aim of this study was to evaluate the non-enhanced, static contrast-enhanced and DCE MRI findings and to seek for the most predictive parameters for differentiating benign from malignant soft tissue lesions.

MATERIAL AND METHODS

Study Patients

This prospective study included patients from other clinical departments sent to Radiology Department for MRI due to suspected soft tissue masses. Patients with inflammatory lesions such as abscess or cellulite (fever, pain, clinical history and positive labaratuary test), or with long term soft consistency, compressible superficial lipomas were excluded from the study. The study was carried out with the permission of the Medical Faculty Ethics Committee in accordance with the principles of the 2008 Helsinki Declaration . All patients underwent MRI including non-enhanced and contrast-enhanced static, and DCE MR images. Patients who had any contraindications to MRI (such as a pacemaker, claustrophobia, noncompatible stents for MRI, allergy to contrast material or severe renal dysfunction) were excluded from the study. Only the lesions have clinically or radiologically indefinite findings were included in this study. Soft tissue lesions that had certain diagnosis according to non-enhanced MRI signal characteristics and typical location (i.e., homogeneous lipomas were signal isointense to subcutaneous fat on all pulse sequences with high signal on T1 weighted (W) turbo spin-echo (TSE) and T2-W TSE sequences and thin septations, hemangioma and hematoma had typical MR appearance, elastofibroma dorsi were found between the inferior scapula tip and the chest wall) were excluded. A total of 35 patients were included in the study. Surgical excision or biopsy were performed for all except 3 patients. The diagnoses of these three patients with hematoma were establised by clinical follow-up. Patients were between 1 and 80 years of age (average 43.46±13.17), 17 male and 18 female. All patients gave informed consent for MRI examination. Patients were informed on the importance of remaining motionless during the MRI examination.

MRI Protocols

All MRI examinations were performed with a Gyroscan Intera 1.5 T model (Philips Medical Systems, Best, The Netherlands [maximum gradient strength, 23 mT/m]). Body or surface coil was used depending on the location and size of the lesion. Standard MRI was performed with axial T1 -W TSE sequence (repetition time msec/ echo time msec, 963/15; section thickness, 4 mm; intersection gap, 0.3 mm; NSA, 3), T2 -W TSE sequence (repetition time msec/echo time msec, 6063/70; section thickness, 4 mm; intersection gap, 0.3 mm; NSA, 3) and short tau inversion recovery (STIR) sequence (repetition time msec/ echo time msec/inversion time msec, 4449/70/170; section thickness, 4 mm; intersection gap, 0.3 mm; NSA, 4). Depending on lesion location and size, coronal or sagittal images were added. The matrix was 256x512, and field of view (FOV) range was 140-400 mm. DCE MRI was performed by using a T1 -W TSE sequence without moving the patient or the table. The contrast material 0.1 mmol /kg gadopentetate dimeglumine (Magnevist, Schering, Berlin) or gadodiamide (Omniscan, Nycomed, Oslo) was injected at a rate of 2 mL/sec through an 18-gauge intravenous line into the antecubital vein, followed by a 20-mL saline flush using by a power injector (Spectris; Medrad, Indianola, Pa). A series of 60-100 of these T1 -W TSE sequence axial images were obtained during the first pass of the bolus of contrast material, temporal resolution, of 3 seconds during at least the first 80 seconds. Total scanning time was 5 minutes. The precontrast T1 -W TSE sequence images were subtracted from all DCE MR images by using commercially available software with MRI system. Time-signal intensity curves were obtained



from the subtraction images. Regions of interest (ROI) that were drawn freehandly were selected without in the most homogeneous, contrast-enhancing part of the lesion.

Static contrast-enhanced MR images were performed by obtaining the T1 -W TSE sequence after performance of the dynamic MR images in axial plane within 10 minutes of administration of the contrast material.

MR Interpretations

All MR images were recorded to a magneto-optical disk and were documented on hard copies. Qualitative evaluations were based on these films. Non-enhanced, DCE and static contrast-enhanced MR images were prospectively interpreted by two musculoskeletal radiologists without knowledge of the histopathologic findings. 2.3.1. Nonenhanced MRI parameters:

Lesion size: largest diameter was measured. Lesion margin: was identified as well-defined, partially defined, illdefined margins, or infiltrating. Peritumoral edema: presence or absence of high signal intensity extending into tissue surrounding well-defined lesion edges on T2 -W TSE images, ill-defined margins were noted. Neurovascular involvement: was evaluated as obliteration of at least half of the fatty tissue around the neurovascular bundle and displacement of neurovascular bundle. Bone involvement: soft tissue mass extending into bone cortex and/ or medulla. Lesion heterogeneity: T1 or T2 -W TSE images were classified as less than 25%, 25-50%, more than 50% and 100% homogeneous. Lesion signal intensity on T1 -W TSE images: Four different T1-W TSE signal intensities were noted: isointense with muscle or slightly hypointense, slightly hyperintense than muscle, intensity between muscle and fat and isointense with fat. Lesion signal intensity on T2 -W TSE images: Three different T2-W TSE signal intensities were noted: Isointense with muscle or slightly hypointense, slightly more hyperintense than muscle and marked hyperintense than muscle.

DCE MRI parameters:

The progression of lesion contrast enhancement was classified according to the shape of the time-signal intensity curves (Figure 1: adapted from reference 3). Type 1 timesignal intensity curve: gradual increase of enhancement. Type 2 time-signal intensity curve: rapid initial contrast enhancement followed by plateau phase. Type 3 timesignal intensity curve: rapid initial contrast enhancement followed by washout.

Static contrast-enhanced MRI parameters:

Contrast enhancement pattern: was evaluated as homogeneous, peripheral and heterogeneous. Necrosis: was



Figure 2. 58-year-old woman with a myxoma. Coronal T1-W TSE image (A) demonstrates homogeneous, isointense to muscle in the upper part of the right arm. Static contrast-enhanced T1-W TSE image (B) shows heterogeneous enhancement of the mass. Coronal STIR image (C) depicts well defined, heterogeneous hyperintense soft-tissue mass without peritumoral edema, necrosis and bone -neurovascular involvement. Type 1 time-signal intensity curve (D) generated by using ROI on DCE images (E) which suggests a benign lesion.

evaluated the area of T1-W TSE iso-hypointense relative to muscle, T2 -W TSE hyperintense, no contrast enhancement on contrast-enhanced images.

Statistical Analysis

Statistical analysis of data was completed using SPSS for Windows version 11.5 (SPSS Inc, Chicago, USA). Chisquare and Fisher's exact tests were used for statistical analysis . Benign and malignant lesions were differentiated based on non-enhanced, DCE and static contrastenhanced MR images parameters. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), overall accuracy and P value of each of the MRI parameters were calculated.

RESULTS

The patients' ages were between 1 and 80 with an average age of 43.4 ± 20.8 . Surgical or biopsy proven histopathologic diagnosis was available for all except 3 hematoma patients whose diagnosises were established by clinical follow-up. Sixteen patients had benign and 19 patients had malignant tumors. Of the benign lesions, 3 were hematoma, 3 were hemangioma, 2 were schwannoma, 1 neurofibroma, 1 nodular fasciitis, 1 angiokeratoma, 1 benign fibrosis histiocytoma, 1 myxoma, 1 desmoid tumor, and 2 lipomas. Malignant lesions included 5 lymphomas, 3 undifferentiated pleomorphic sarcomas, 3 rhabdomyosarcomas, 3 metastatic carcinomas, 1 fibrosarcoma, 1



Figure 3. 62-year-old woman with a undifferentiated pleomorphic sarcoma. Axial T2-W TSE image (A) demonstrates ~4 cm heterogeneous, hyperintense mass relative to that of muscle in the upper part of the right leg. Coronal STIR image (B) depicts peritumoral edema. Coronal static contrast-enhanced T1-weighted MR image (C) shows peripheral enhancement. Type 2 timesignal intensity curve (D) generated by using ROI on dynamic contrast-enhanced images (E).

synovial sarcoma, 1 high-grade pleomorphic sarcoma, 1 plasmocytoma, 1 metastatic malignant melanoma and 1 malignant schwannoma. 3.1. Frequency distribution and correlation with final diagnosis of non-enhanced MRI findings which are listed in Table 1. Frequency distribution and correlation with final diagnosis of DCE and static contrast-enhanced MRI findings which are listed in Table 2. Contrast enhancement pattern: The most encountered enhancement pattern was heterogeneous enhancement which was seen in 22 (Twelve benign and 10 malignant) lesions. Homogeneous enhancement was seen in seven lesions (2 benign and 5 malignant). Peripheral contrast enhancement was seen in 2 benign and 4 malignant lesions (Table 2). Progression of contrast enhancement: Type 1 time-signal intensity curve (gradual increase of enhancement) was observed in 12 benign lesions (Figure 2) and 1 malignant (metastatic malignant melanoma) lesion. Type 2 curve (rapid initial contrast enhancement followed by plateau phase) was not seen in any benign lesions but was observed in 7 malignant lesions (Figure 3). Type 3 curve (rapid initial contrast enhancement followed by washout) was seen in 4 benign and 11 malignant lesions (Figure 4). Benign lesions with Type 3 curve were neurofibroma, nodular fasciitis, desmoid tumor and hemangioma (Table 2).

Statistical Analysis of MRI Type in the Evaluation of Lesion Character Lesion size, peritumoral edema, bone and neurovascular involvement, necrosis and contrast progression evaluated by non-enhanced and DCE MRI were statistically significant while lesion margin features, T1 and T2 -W TSE heterogeneity on non-enhanced images and contrast enhancement pattern were not statistically significant on static contrast-enhanced images (Tables 3).



Figure 4. 20-year-old woman with a synovial sarcoma. Axial T2-weighted MR image (A) shows heterogeneous, hyperintense, ill-defined mass with including necrotis areas. Static sagittal contrast-enhanced T1-weighted MR image (B) shows heterogeneous enhanced mass Type 3 time-signal intensity curve (C) generated by using ROI on dynamic contrast-enhanced images (D).

Imaging Findings		Benign	Malignant	Total
Size (cm)	<5	6	1	7
	>5	10	18	28
Margins	Well-defined	8	4	12
	Partially defined	3	7	10
	İll-defined	5	6	11
	Infiltrating	0	2	2
Peritumoral edema	Not present	12	5	17
	Present	4	14	18
Neurovascular involvement	Not present	16	10	26
	Present	0	9	9
Bone involvement	Not present	16	12	28
	Present	0	7	7
	Isointense with muscle or slightly hypointense	11	15	26
	Slightly hyperintense than muscle	3	2	5
TT signal intensity	Intensity between muscle and fat	0	2	2
	Isointense with fat	2	0	2
T1 signal intensity	Isointense with muscle or slightly hypointense	1	0	1
	Slightly hyperintense than muscle	2	3	5
	Marked hyperintense than muscle	13	16	29
T1 heterogeneity	100% homogeneous	12	10	22
	<25% heterogeneous	1	3	4
	%25-50 heterogeneous	1	1	2
	>%50 heterogeneous	2	5	7
T2 heterogeneity	%100 homogeneous	3	4	7
	<%25 heterogeneous	1	5	6
	%25-50 heterogeneous	5	3	8
	>%50 heterogeneous	7	7	14

Table 1. Frequency distribution and correlation with final diagnosis of nonenhanced MR imaging findings

DISCUSSION

Despite benign soft tissue lesions are more numerous than malignant lesion, in this study malignant soft tissue lesions were more than benign ones. Because clinicians referred only equivocal cases that diagnosis was not able to make the based on the physics examination and clinical history in terms of benign-malignant differentiation.MRI is a basic radiologic technique currently used to evaluate soft tissue masses.

The studies in the literature which try to distinguish benign from malignant soft tissue tumors by using nonenhanced MRI have different results. Some studies found high specificity while the others found low specificity due to non-specific imaging findings of soft tissue tumors on MRI (11).

In this study lesion size that was evaluated on nonenhanced MRI had high sensitivity (94%) and low specificity (37%) for benign-malignant differentiation. Most malignant lesions were greater than 5 cm (18 of 19). However some benign lesions were also larger than 5 cm. The results are statistically significant (p<0.02). Lesion size should not be the only parameter used for lesion characterization because its specificity was low. Similar results on lesion size and soft tissue tumor differentiation exist in the literature (9). The malignant lesions tend to be larger due to autonomous abnormal growth of cells.

Imaging Findings		Benign	Malignant	Total
Necrosis	Not present	16	9	25
	Present	0	10	10
	Homogeneous	2	5	7
Contrast enhancement pattern	Peripheral	2	4	6
	Heterogeneous	12	10	22
Progression of contrast enhancement	Type 1	12	1	13
	Type 2	0	7	7
	Type 3	4	11	15

Table 2. Frequency distribution and correlation with final diagnosis of static enhanced and DCE MR imaging findings

There is controversy in regard to the lesion margin for soft tissue characterization in the literature. This overlapping may be due to variable histopathologic orgin of soft tissue tumors. In this study most benign and malignant lesions had similar margin features. Therefore we think that this parameter is not useful for benign-malignant differentiation. Most benign and malignant lesions had similar margin features in this study (8,9,11,12). Ill-defined high signal intensity area extending from the margin of the lesion into the surrounding tissue on T2-W TSE or STIR images, indicating the presence of peritumoral edema had a very high statistical significance in favour of malignancy (sensitivity 73%, specificity 75%, p<0.005) in this study. This result is consistent with the results of Beltran et al (9) and Moulton (13). However, Crim et al (11) and De Schepper (14) et al did not find this parameter useful. This inconcistency may be due to the study design. Because Crim et al (11) and De Schepper (14) et al did not exclude inflammatory lesions causing distinct edema.

Neurovascular and bone involvement were statistically significant in terms of the determination of the malignancy (p<0.001, p<0.007 respectively). Both had a very high specificity (100%) and very low sensitivity (47%, 36% respectively). The high specificity and coincident low sensitivity may be due to the distance of the lesion from the neurovascular and bone structures. Neurovascular and bone structures can not involve in the presence of the remote localization of the malignant lesion (8, 13).

Malignant tumors grow rapidly and have large size because of autonomous growth potential. Thus vasculature of the tumor can be insufficient for feeding the tumor which causes necrosis (15). Contrast enhanced MRI can help to distinguish alive and necrotic tumor tissues, identifying appropriate location for biopsy and showing the extent of tumor. Therefore MRI contributes to proper staging for surgery or radiotherapy. The use of contrast material is an important contributor for the differentiation of benign and malignant lesions. In this study necrosis was seen in approximately a little over half of malignant tumors whereas, was not seen in any benign lesions. The Specificity and sensitivity of necrosis on static contrastenhanced MRI was 100%, (53%) respectively. Reason of the low sensitivity can be related to the small sized malignant lesions do not contain necrosis as their vasculature sufficient for feeding. Our results suggest that necrosis is highly specific for differentiating malignant lesions.

Malignant lesions generally have greater vascularity and perfusion leading to greater contrast enhancement than benign lesions. For this reason the use of contrast material may be beneficial for the characterization of soft tissue tumors. However Kransdorf et al. found too much enhancement was only significant in specific cases (15). Malignant lesions may enhance more than benign lesions but some enhancement features may overlap. Aggressive fibromatosis, myositis ossificans and other aggressive benign tumors may show similar contrast enhancement to malignant lesions.

Most studies have found that peripheral contrast enhancement is significant for identifying malignancy. De Schepper and Mutlu found no relation between contrast enhancement pattern and malignancy (14, 16). Our study shows that contrast enhancement pattern (homogeneous, heterogeneous, peripheral) were evaluated on static contrast-enhanced images was not significant in characterization of benign and malignant lesions since the majority of benign and malignant lesions showed heterogeneous contrast enhancement.

Imaging Findings	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)	Overall accuracy (%)	p value
Size	94	37	64	85	68.5	0.02
Peritumoral edema	73	75	78	70	74.3	0.005
Bone involvement	36	100	100	57	65.7	0.007
Neurovascular involvement	47	100	100	61	71.4	0.001
Necrosis	53	100	100	64	74.3	0.001
Progression of contrast enhancement	94	75	82	92	86	0.0001

Table 3. Stastically significant MRI findings

Evaluating contrast enhancement progression on DCE MRI is useful because the tumor enhance more quickly than surrounding tissue. Malignant tumors have high vascularity and large interstitial space. For this reason they show rapid and early contrast enhancement. Benign lesions enhance more slowly due to narrow interstitial space and having slow perfusion.

Most studies have found contrast enhancement progression significant for benign-malignant differentiation (3, 17-19). This study defined 3 types of time-signal intensity curves based on DCE MRI. One malignant lesion followed Type 1 (gradual increase of enhancement), 7 followed Type 2 (rapid initial contrast enhancement followed by plateau phase) and 11 followed Type 3 (rapid initial contrast enhancement followed by washout) time-signal intensity curves. Four benign lesions followed Type 3 and 12 followed Type 1 time-signal intensity curves. The sensitivity of contrast enhancement progression in benignmalignant differentiation was 95% while the specificity was 75%, PPV was 92% and NPV was 86%. The result was statistically very significant (p<0.0001). Contrast enhancement progression (time-signal intensity curves) is a very important contributor to benign-malignant soft tissue tumor differentiation by using DCE MRI. In this study, the type 2 curve was observed only in malignant lesions whereas there was overlapping for Type 3 for the malignant and benign lesions. when type 1 curve was seen in the most of the benign tumors, only in one malignant lesion. Therefore type 2 curve should be considered suggestive of malignancy.

Unlike most studies try to differentiate between benign and malignant soft tissue lesions, this study excluded many typical lesions that are not difficult for clinicians or radiologists to make diagnosis on imaging modalities. Such as typical lipomas (all sequences with the same intensity as subcutaneous fat, homogeneous), hemangiomas (serpentine vascular structures and hypointense areas representing phleboliths in all sequences), common periarticular cysts (synovial cysts, ganglion cysts, etc.), clinically diagnosed inflammatory lesions (cellulite, abscess, etc.), and hematomas due to trauma. Only the lesions which have indefinite findings clinically or radiologically were included in this study. Therefore number of the patients was low as limitation.

In conclusion, DCE MRI, especially for soft tissue lesions with ill-defined morphologic features (e.g., small, superficial, smooth-edged malignant lesions), contributes to characterization due to the different contrast enhancement progression of malignant and benign soft tissue lesions.

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