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Quantitative evaluation of diffusion-weighted imaging with multiple b-values in vertebral fractures

Fatma Kulali

Radiology Department, University of Health Sciences, Umraniye Training and Research Hospital, Istanbul, Turkey

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Corresponding Author: Fatma Kulali, MD. Postal address: Adem Yavuz street. No:1, University of Health Sciences, Umraniye Training and Research Hospital, Department of Radiology, Umraniye, 34764, Istanbul, Turkey. Phone: +90 (216) 632 1818*1462; Fax: +90 (216) 6327124
E-mail: ftkulali@gmail.com

Abstract

Aim: Differentiating benign from malignant vertebral fracture is sometimes difficult in geriatric oncology patients. Accurate diagnosis is necessary for treatment planning. Therefore, we aimed to investigate the role of quantitative evaluation of diffusion-weighted imaging (DWI) at multiple b-values of 200, 400 and 600 s/mm2 in differentiating benign from malignant thoracolumbar vertebral fractures and to determine an optimal b-value.

Methods: Forty-four patients with 72 vertebral fractures were enrolled. Magnetic resonance imaging (MRI) findings combined with DWI at b-values of 200, 400 and 600 s/mm2 were evaluated. Apparent diffusion coefficient (ADC) and normalized ADC values were obtained. Radiological and histopathological/follow-up results were compared.

Results: Of 72 vertebral fractures, 22 were benign and 50 were malignant. Mean ADC and normalized ADC values of malignant group were lower than benign group's in all b-values ($p<0.05$). Despite of no significant difference between ADC values at b-values of 200, 400 and 600 s/mm2 within each group, normalized ADC values were lower at b-value of 200 s/mm2 than those of at 600 s/mm2 in malignant group ($p<0.05$).

Conclusion: MRI combined with DWI is a problem solving modality especially in geriatric oncology patients. Performing DWI at b-value of 200 s/mm2 and estimation of normalized ADC value for optimization of data are recommended.

Key words: apparent diffusion coefficient, diffusion-weighted imaging, magnetic resonance imaging, vertebral fracture

ОМЫРТҚАНЫҢ СЫНЫҚТАРЫ КЕЗІНДЕГІ КӨПТЕГЕН B-МӘНІМЕН ДИФФУЗИЯЛЫҚ-ӨЛШЕНГЕН ВИЗУАЛИЗАЦИЯЛАУДЫ САНДЫҚ БАҒАЛАУ

Фатма Кулали
Радиологиялық бөлімі, Медицина ғылымдары университеті, Умрание білім беру және ғылыми-зерттеу клиникасы, Түркия

ТҰЖЫРЫМДАМА

Мақсаты: Кейде гериатриялық онкологиялық науқастарда омыртқаның сынуы кезінде омыртқа сүйектерінің қатерсіз ісіктерін қатерлі ісіктерден ерекшелеу қиынға соғады. Сондықтан, біздің мақсатымыз – 200, 400 және 600 с/мм2 көптеген b-мәнін диффузиялық-өлшенген визуализациялауды сандық бақылаудың рөлін зерделеу және омыртқаның кеуде-белінің сынықтары барысында қатерлі ісіктерден қатерсіз ісікті дифференциациялау үшін тиімді b-мәнін айқындау болып табылады.

Әдістері: Зерттеуге 72 омыртқа сынықтарымен 44 пациент қатысты. 200, 400 және 600 с/мм2 b-мәні кезінде диффузиялық-өлшенген визуализациялаумен үйлестікте магниттік-резонанстық томографияның нәтижелері бағаланды. Диффузияның өлшенетін коэффициентінің мәні және диффузияның өлшенетін коэффициентінің нормаланған мәндері алынды. Радиологиялық және гистологиялық қадағалаудың нәтижелері салыстырылды.

Нәтижелері: 72 омыртқа сынықтарынан 22-уі омыртқа сүйектерінің қатерсіз ісігі және 50-і қатерлі ісік болып шықты. Қатерлі ісіктер тобының диффузиясының өлшенетін коэффициентінің орташа нормаланған мәндері 200 с/мм2b-мәні кезінде қатерсіз ісіктер тобына, қатерлі ісіктер тобында 600 с/мм2 қарағанда, төмен болды.

Қорытынды: магниттік-резонанстық томография диффузиялық-өлшенген визуализациялаумен бірге – бұл әсіресе, гериатриялық онкологиялық науқастардың проблемаларын шешу әдісі. 200 с/мм2 b-мәні кезінде диффузиялық-өлшенген визуализациялауды өткізуге және деректерді оңтайландыру үшін диффузиялау өлшенетін коэфициентінің нормаланған мәнін бағалау ұсынылады.

Негізгі сөздер: диффузияның өлшенетін коэффициенті, диффузиялық-өлшенетін визуализациялау, магниттік-резонанстық томография, омыртқаның сынуы

КОЛИЧЕСТВЕННАЯ ОЦЕНКА ДИФФУЗИОННО-ВЗВЕШЕННОЙ ВИЗУАЛИЗАЦИИ С МНОЖЕСТВЕННЫМ B-ЗНАЧЕНИЕМ ПРИ ПЕРЕЛОМАХ ПОЗВОНКОВ

Фатма Кулали

Радиологическое отделение, Университет медицинских наук, Образовательная и научно-исследовательская клиника Умрание, Стамбул, Турция

РЕЗЮМЕ

Цель: Иногда сложно отличить доброкачественную опухоль костей позвоночника от злокачественной при переломе позвоночника у гериатрических онкобольных. Необходим точный диагноз для планирования лечения. Поэтому, нашей целью является изучить роль количественной оценки диффузионно-взвешенной визуализации множественных b-значений в 200, 400 и 600 с/мм2 и определить оптимальное b-значение для дифференциации доброкачественной опухоли от злокачественной при грудопоясничных переломах позвоночника.

Методы: В исследовании приняли участие сорок четыре пациента с 72 переломами позвоночника. Оценивались результаты магнитно-резонансной томографии в сочетании с диффузионно-взвешенной визуализацией при b-значениях в 200, 400 и 600 с/мм2. Получены значения измеряемого коэффициента диффузии и нормализованные значения измеряемого коэффициента диффузии. Сравнивались результаты радиологического и гистологического наблюдения.

Результаты: Из 72 переломов позвоночника, 22 оказались доброкачественными опухолями костей позвоночника и 50 злокачественными. Средние и нормализованные значения измеряемого коэффициента диффузии группы злокачественной опухоли были ниже, чем в группе доброкачественной опухоли при b-значении в 200 с/мм2, чем при 600 с/мм2 в группе злокачественной опухоли ($p<0.05$).

Заключение: Магнитно-резонансная томография совместно с диффузионно-взвешенной визуализацией это метод решения проблемы в особенности у гериатрических онкобольных. Рекомендуется проведение диффузионно-взвешенной визуализации при b-значении в 200 с/мм2 и оценка нормализованного значения измеряемого коэффициента диффузии для оптимизации данных.

Ключевые слова: Измеряемый коэффициент диффузии, диффузионно-взвешенная визуализация, магнитно-резонансная томография, перелом позвоночника

Introduction

Vertebral fractures are frequently seen due to osteoporosis, trauma and tumor. Incidence of vertebral fractures continues to increase with age [1-5]. The diagnosis and determining the etiology of vertebral fracture are generally made on the basis of history and clinical findings combined with radiological imaging such as conventional radiography, computed tomography (CT) and magnetic resonance imaging (MRI). MRI provides high tissue contrast resolution. Therefore, bone marrow edema, associated soft tissue component and contrast enhancement can accurately be detected on MRI [1-5]. However, some acute osteoporotic and traumatic vertebral fractures can mimic malignant vertebral fractures with increased contrast enhancement and high signal intensity on T2-weighted sequences due to edema and inflammatory reactions. Differentiating benign from malignant vertebral fracture is very important especially in geriatric oncology patients. Existence of bone metastasis changes the management of patient. In patients with bone metastases, conservative treatment is preferred because of reduced probability of being cured. In some patients, additional imaging modality is required for differential diagnosis [1-5].

To the best of our knowledge, quantitative evaluation of diffusion-weighted imaging (DWI) at b-values of 200, 400 and 600 s/mm2 in differential diagnosis of benign and malignant thoracolumbar vertebral fractures has not been investigated before. For this reason, aims of this study were to investigate the role of quantitative evaluation of DWI at multiple b-values in differentiating benign from malignant thoracolumbar vertebral fractures and to determine an optimal b-value for differential diagnosis.

Materials and Methods

The Institutional Review Board approved this retrospective study, and informed consent was waived. Imaging reports of thoracolomber MRI examinations in hospital information system (HIS) were searched retrospectively at a single institution between March 2003 and March 2005. The terms used were vertebral fractures, vertebral tumor, metastasis, lymphoma, multiple myeloma, cancer and carcinoma. There were 51 MRI examinations of consecutive patients. Then, medical imaging records of these patients were reviewed from picture archiving and communications system (PACS). MRI examinations without DWI (n=5) and two patients with insufficient images due to artefacts were excluded. A total 44 patients with 72 vertebral fractures who had undergone thoracolomber MRI combined with DWI were enrolled in this study. There were 22 women and 22 men with a mean age of 45±18 (SD) years (range: 19–78 years).

MRI examinations were performed on a 1.5 Tesla system (GyroscanIntera, Philips Medical Systems, Best, the Netherlands). MRI sequences were as follows; sagittal T2-weighted turbo spin-echo (TSE) (TR/TE: 3500/120, field of view FOV: 325 mm, matrix: 264x512, slice thickness 5 mm), sagittal T1-weighted TSE (TR/TE: 400/11, field of view FOV: 325 mm, matrix: 264x512, slice thickness 5 mm), sagittal T2-weighted TSE spectral presaturation with inversion recovery (SPIR) (TR/TE: 3500/120, field of view FOV: 325 mm, matrix: 216x512, slice thickness 5 mm), axial T2-weighted TSE (TR/TE: 3500/120, FOV: 225mm, matrix: 213x512, slice thickness 5 mm,), sagittal pre-contrast and post-contrast T1-weighted TSESPIR (TR/TE: 400/11, FOV: 325mm, matrix: 264x512, slice thickness 5 mm) sequences, sagittal diffusion weighted single-shot echo-planar imaging (EPI) (TR/TE: 1839/86, EPI factor: 77, FOV: 270mm, image matrix: 77x256, slice thickness 5mm) with b-values 0, 200, 400 and 600 s/mm2.

An experienced radiologist (FK) evaluated the MRI and DWI findings of thoracolumbar vertebral fractures without knowing the history, clinical or surgical results of patients. Signal intensity on T1- and T2-weighted images, convexity of posterior vertebral corpus wall, presence of contrast enhancement, involvement of posterior vertebral elements and associated soft tissue component on MRI were noted. Low signal intensity on T1-weighted sequence and high signal intensity on T2-weighted sequence without contrast enhancement was defined as edema.

Region of interest (ROI) measurements in vertebral fracture and adjacent normal vertebral bone marrow were performed at three different locations inside vertebral fracture in the dedicated workstation (Philips Medical Systems). The measurements of circular ROIs ranged in size between 110 mm2 and 130 mm2. For each vertebral fracture (n=72) and adjacent normal vertebral bone marrow (n=72), the mean value of ROI measurements was estimated on ADC map.The normalized ADC value (ratio of mean ADC value in vertebral fracture to mean ADC value in adjacent normal vertebral bone marrow) was estimated.

Vertebral fractures were classified into two groups as benign and malignant according to follow-up and histopathological results.Vertebral fractures without clinical and radiological progression at least 6 months of follow-up were grouped as benign. All malignant vertebral fractures were histopathologically proven.

Radiological and histopathological/follow-up findings were compared. Kruskal-Wallis test or Mann-Whitney U test were used, where appropriate, and $p<0.05$ was used to determine statistical significance. The diagnostic capabilities of DWI for differentiating malignant from benign vertebral fractures were analyzed by estimation of sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy ratios. Statistical analysis was done by using MedCalc statistical software 12. 1. 4. 0

Results

Forty-four patients with 72 thoracolumbar vertebral fractures were investigated. Of 72 vertebral fractures, 22 were benign and 50 were malignant. Mean follow-up period of benign thoracolumbar vertebral fractures was 13.27±5.38 months (range: 6-24 months). Among benign (n=22) vertebral fractures, 10 were osteoporotic and 12 were traumatic fractures (Figure 1). Of 50 malignant vertebral fractures, there were multiple myeloma (n=1), metastases of invasive ductal breast cancer (n=6), prostate adenocancer (n=15), thyroid papillary cancer (n=18), non-small cell lung cancer (n=5), Ewing sarcoma (n=2) and lymphoma (n=3). Associated soft tissue component (7/50, 14%) and involvement of posterior elements (11/50, 22%) were only seen in malignant fractures (Figure 2). Among 22 benign (osteoporotic and traumatic) fractures, 4 had contrast enhancement. Some qualitative MRI findings such as low signal intensity on T1-weighted sequence, high signal intensity on T2-weighted SPIR sequence, total vertebral corpus involvement, convexity of posterior vertebral corpus wall and contrast enhancement were more frequent in our malignant group. Associated soft tissue component and involvement of posterior vertebral elements were not seen in our benign group. Of 50 malignant vertebral fractures, 3 showed low signal intensity on DWI. Of 22 benign fractures, 2 had high signal intensity on DWI and low signal intensity on ADC map. MRI combined with DWI characteristics of benign and malignant vertebral fractures are shown in Table 1.

The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy of qualitative DWI findings for diagnosing malignant vertebral fractures was 94%, 91%, 96%, 87%, and 93%, respectively.

Mean ADC value of normal adjacent vertebral bone marrow with 0.39 ± 0.07 (0.37-0.41)x10−3 mm2/s at b-value of 200 s/mm2 was significantly lower than those of malignant and benign vertebral fractures ($p<0.05$). Maximum mean ADC value of malignant vertebral fractures was 1.92x10-3 mm2 /s and minimum mean ADC value of benign fractures was 2.68x10-3 mm2 /s at b-value of 200 s/mm2. At b-values of 200, 400 and 600, mean ADC values of malignant vertebral fractures were found statistically lower than benign vertebral fractures' ($p<0.05$). However, there was no significant difference between mean ADC values at b-values of 200, 400 and 600 s/mm2 within each group ($p>0.05$). But, normalized ADC values were found significantly lower at b-value of 200 s/mm2 than those of at b-value of 600 s/mm2 in malignant group ($p<0.05$). Normalized ADC values of benign group was also significantly higher than that of malignant group in all b-values ($p<0.05$). Mean ADC and normalized ADC values of benign and malignant vertebral fractures are demonstrated in Table 2.

Discussion

MRI is an appropriate method to detect bone marrow edema or tumor. Sometimes, additional imaging modalities are needed to make accurate diagnosis because of overlapping MRI findings [1-7].

DWI indicates random movement of water molecules in tissue. Apparent diffusion coefficient (ADC) map is obtained from DWI automatically and also provides opportunity of

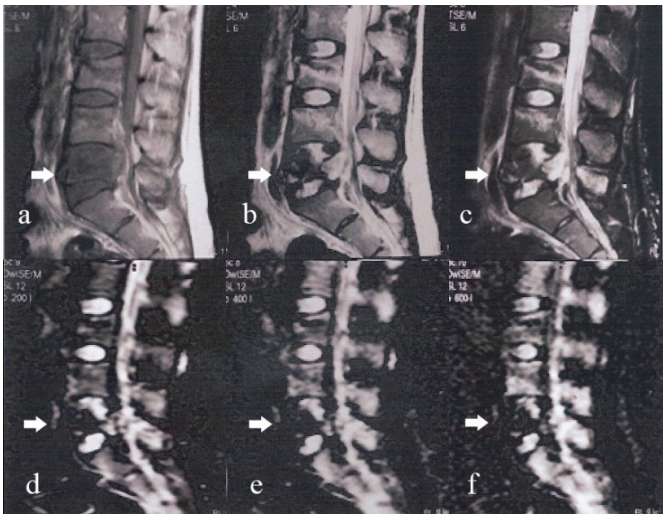

Figure 1. - 19-year-old woman who had traumatic L3, L4 and L5 (arrow) vertebral fractures with bone marrow edema on sagittal T1-weighted sequence (a), on sagittal T2-weighted sequence (b), on sagittal T2-weighted SPIR sequence (c), low signal intensities of fractures and high signal intensities of bone marrow edema on sagittal DWI at b value of 200 (d), 400 (e) and 600 s/mm2 (f).

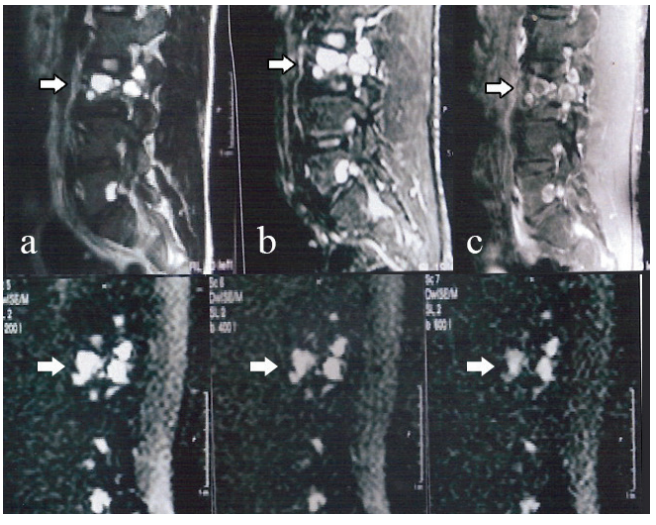

Figure 2. 74-year-old man with prostate adenocancer had metastatic vertebral fractures at L3 (arrow) and L5 vertebra which show low signal intensity on sagittal T1-weighted sequence (a), high signal intensity on sagittal T2-weighted SPIR sequence (b), contrast enhancement on sagittal post-contrast T1-weighted SPIR sequence (c) and high signal intensity on sagittal DWI at b value of 200 (d), 400 (e) and 600 s/mm2 (f).

Table 1 Distribution of qualitative and quantitative characteristics of MRI combined with DWI in benign and malignant vertebral fractures

						High SIon	Low SI							NADCr			
P.Noa	Age	Gb	Me/Bf	Fx(n) g	Etiology	T2-WIh	T2-SPIR1	T1-WIj	CEk	BEl	PEm	TCinvn	Convo	STp	200	400	600
1	55	Fc	B	1	OPs	1	1	1	No	1	No	No	No	No	12.08	12.08	12.08
2	33	Md	B	2	Trauma	2	No	No	No	No	No	1	1	No	15.46	11.17	15.46
3	57	F	B	1	OP	1	1	1	No	1	No	No	1	No	7.63	8.75	7.63
4	52	M	B	2	Trauma	2	No	2	No	1	No	1	1	No	11.59	10.57	11.59
															21.88	12.62	21.88
5	27	M	B	1	Trauma	1	No	No	No	No	No	No	1	No	14.80	11.58	14.80
6	19	M	B	2	Trauma	2	No	No	No	No	No	No	1	No	20.27	18	19.58
															11.51	10.95	11.93
7	65	F	B	4	OP	No	No	No	4	No	No	1	1	No	7.68	7.68	7.97
															12.17	12.17	12.17
															8.12	9.93	8.12
															8.37	8.88	8.37
8	21	M	B	2	Trauma	No	No	No	No	No	No	No	No	No	13.59	13.59	13.22
															12.94	10.16	12.38
9	73	M	B	2	OP	1	No	1	No	No	No	1	1	No	13.27	11.68	13.27
															11.61	9.48	11.61
10	19	F	B	3	Trauma	3	3	3	No	2	No	No	1	No	9.80	9.80	9.57
															14.21	11.78	13.60
															16.62	16.62	15.58
11	61	F	B	2	OP	2	No	1	No	1	No	1	1	No	18	16.70	18.64
															9.73	9.73	9.14
12	70	M	M	4	Prostate ca	4	4	4	4	No	No	3	No	No	3.58	4.13	4.41
															3.81	2.48	4.47
															3.30	4.13	4.13
															4.18	3.57	4.69
13	78	M	M	1	Prostate ca	1	1	1	1	No	1	No	No	No	3.81	3.81	3.81
14	43	M	M	2	Thyroid ca	1	2	1	1	1	1	No	1	2	2.18	2.18	2.18
															1.74	1.74	1.74
15	21	M	M	2	Ewing S.	2	2	2	2	No	1	1	1	1	3.91	3.91	4.04
															3.93	4.14	4.14
16	34	F	M	1	Thyroid ca	1	1	1	1	No	No	1	1	No	1.62	1.62	1.62
17	41	M	M	1	Lung ca	1	1	1	1	No	No	1	1	No	2.25	1.89	1.89
18	78	M	M	1	MM	No	1	1	1	No	No	No	No	No	3.78	4.09	4.39
19	40	F	M	1	Breast ca	No	1	1	1	No	No	1	1	No	3.91	4.35	4.35
20	41	F	M	2	Thyroid ca	1	2	1	1	No	1	1	1	2	2.03	2.03	2.03
															1.50	1.50	1.50
21	42	M	M	1	Lymphoma	1	1	1	1	No	No	No	No	No	4.18	4.40	4.52
22	35	F	M	1	Thyroid ca	1	1	1	1	No	1	No	No	1	3.72	3.93	3.93
23	40	F	M	1	Thyroid ca	1	1	1	1	1	No	No	No	No	2.82	3.04	3.48
24	73	M	M	1	Lung ca	1	1	1	1	No	1	No	No	No	2	1.44	1.44
25	74	M	M	2	Prostate ca	2	2	2	2	No	1	No	1	No	3.76	4.35	4.64
															4.29	4.78	4.78
26	38	F	M	5	Breast ca	No	No	5	5	No	No	3	1	No	1.82	1.82	1.82
															1.39	1.29	1.29
															1.48	1.41	1.41
															1.50	1.50	2.35
															1.48	1.48	1.56
27	33	F	M	1	Thyroid ca	1	1	1	1	No	No	1	1	No	3.65	4.06	4.06
28	74	M	M	1	Lung ca	No	1	No	1	No	No	1	1	No	2.75	3.20	3.42
29	43	F	M	1	Thyroid ca	1	1	No	1	No	1	1	1	No	1.29	1.29	2.25
30	76	M	M	1	Prostate ca	1	1	1	1	No	1	1	1	1	3.42	3.42	3.80
31	45	F	M	1	Thyroid ca	1	1	1	1	No	No	1	1	No	4.30	4.30	4.53
32	41	F	M	1	Thyroid ca	No	1	1	1	No	No	1	1	No	4.25	4.25	4.47
33	19	M	M	1	Lymphoma	1	1	1	1	No	No	No	No	No	4.71	4.71	5.23
34	32	F	M	2	Thyroid ca	2	2	1	2	1	No	No	No	No	3.07	3.56	4.29
															3.70	3.70	3.90
35	31	F	M	1	Thyroid ca	1	1	1	1	No	1	1	1	No	1.31	1.31	1.31
36	40	F	M	1	Thyroid ca	1	1	No	1	No	No	No	No	No	3.77	3.77	4.34
37	41	F	M	1	Lung ca	No	1	No	1	No	No	1	1	No	1.43	1.43	1.54
38	33	M	M	1	Lung ca	No	1	No	1	No	No	No	1	No	3.84	3.60	4.21
39	71	M	M	2	Prostate ca	2	2	1	No	1	1	No	1	No	3.02	3.23	3.45
															4.27	4.27	4.27
40	35	F	M	1	Thyroid ca	No	1	No	1	No	No	1	1	No	4.02	4.02	4.23
41	68	M	M	5	Prostate ca	5	5	5	5	No	No	1	1	No	3.93	4.26	4.26
															3.58	3.79	4
															4.02	4.51	4.75
															4.84	4.84	5.43
															2.84	3.06	3.38
42	21	M	M	1	Lymphoma	No	1	1	1	No	No	No	No	No	2.34	2.52	2.89
43	43	F	M	1	Thyroid ca	No	1	No	1	No	No	1	1	No	3.01	3.36	3.36
44	41	F	M	1	Thyroid ca	No	1	No	1	No	No	1	1	No	2.03	1.89	2.03

P.Noa: Numbers of patients, Gb: Gender, Fc:Female, Md: Male, Me/Bf: Malignant/Benign, Fx(n)g: Number of fractures, High SI on T2-WIh: High signal intensity on T2-weighted image, High SI on T2-SPIR1: High signal intensity on T2- SPIR sequence, Low SI T1-WIj: Low signal intensity on T1-weighted image, CEk: contrast enhancement, BEl: Band like bone marrow edema, PEm: Involvement of posterior vertebral elements, TCinvn: Involvement of total vertebral corpus, Convo:Convexity of posterior vertebral corpus wall, STp: Associated soft tissue, NADCr: Normalized apparent diffusion coefficient, OPs: Osteoporosis, ca: cancer, Ewing: Ewing sarcoma, MM: multiple myeloma.

quantitative measurements. High signal intensity on DWI and low signal intensity on ADC map exhibit restriction of diffusion [1, 5-13]. Degree of DWI is directly related to b-value. The b-value depends on the strength of the gradient, duration of gradient and time between two gradients. Different b-values are mostly achieved due to alterations in strength of gradient. Higher b-value provides stronger diffusion effects and more apparent visualization of diffusion restriction, but decreased signal-to-noise ratio [8, 9]. Therefore, DWI with low (200 s/mm2), intermediate (400 s/mm2) and high (600 s/mm2) b-values was performed in our study group. Although DWI is frequently performed for evaluation of acute cerebral ischemia, it is recommended to use for other diseases of different organs especially when there is a difficulty in differential diagnosis. It is known that MRI combined with DWI increases diagnostic accuracy [1, 5-13]. Increased cellularity due to tumor shows restricted diffusion. Bone marrow edema can be excluded on DWI and ADC map because of non-restriction of diffusion [12].

A number of studies have investigated the diagnostic performance of DWI on differential diagnosis of benign and malignant vertebral lesions and fractures. Castillo et al [14] indicated that qualitative findings of DWI at b= 165 s/mm2 had no advantage in the detection of vertebral metastases compared to T1-weighted sequences in 15 patients. In contrast, qualitative findings of DWI were found valuable in some previous studies [15-17]. The results of these previous studies and ours were summarized in Table 3. In another study, Hamimi et al. [7] demonstrated that osteoporotic fractures (n=80) generally show water line sign and sharp wedging whereas malignant fractures (n=70) frequently have pedicle involvement, homogenous low signal intensity on T1 –weighted sequence and restricted diffusion. However, there was no quantitative assessment of ADC value [7, 14-15]. Similar qualitative findings were observed in our malignant group.

Table 2 Mean ADC and normalized ADC values of benign and malignant thoracolumbar vertebral fractures according to different b-values.

	Mean ADC values (x10 -3 mm2/s)		Normalized ADC valuesa	
	Benign (n=22)	Malignant (n=50)	Benign (n=22)	Malignant (n=50)
	(±SDab) (95%CIc)	(±SD) (95%CI)	(±SD) (95%CI)	(±SD) (95%CI)
b=200 s/mm2*	4.37±1.13 (3.90- 4.85)	1.29±0.54 (1.14- 1.44)	12.78±3.90 (11.14- 14.41)	3.06±1.07 (2.76- 3.36)
b=400 s/mm2*	3.98±0.83 (3.62- 4.32)	1.34±0.59 (1.18 - 1.51)	11.53±2.66 (10.42- 12.65)	3.14±1.17 (2.82- 3.47)
b=600 s/mm2*	4.34±1.13 (3.86- 4.81)	1.44±0.61 (1.27 - 1.60)	12.65±3.84 (11.05- 14.26)	3.40±1.24 (3.05- 3.74)

aNormalized ADC values: ratios of mean ADC value in vertebral fracture to mean ADC value in adjacent normal vertebral bone marrow
abSD: standard deviation, cCI: confidence interval
*Mann Whitney U Test, $p<0.05$ was used to determine statistical significance between benign and malignant group.

Table 3 Diagnostic performance results of qualitative findings on DWI in previous studies and ours

Studies	No of lesions	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
Our study	75	94	91	96	87	93
Bhugaloo15 et al.	68	87	92	90	90	-
Pozzi16 et al.	33	95.6	90	95.6	-	-
Abowarda17 et al.	68	86	91	89	90	-

PPV: Positive predictive value, NPV: Negative predictive value

Previous studies have also suggested that quantitative evaluation of DWI is necessary and lower ADC values (1.0±0.32 - 1.31±0.36 x 10−3 mm2/s) were reported in malignant vertebral fractures with b-value of 1000 s/mm2 [17-18]. Fawsy et al. [19] performed DWI at two b-values of 500 and 800 and found mean ADC values of 1.21±1.94 x 10−3 mm2/s for benign fractures and 0.69±0.92 x 10−3 mm2/s for malignant ones. Zhou et al [20] evaluated mean ADC value with b-values of 0 and 250 s/mm2 for metastases (n=15) (1.9 ± 0.3x10−3 mm2/s) was found significantly lower than that of benign ones (n=12) (3.2 ± 0.5x 10−3 mm2/s). Similar results were found in ours with different b-values.

Padhani et al [3] calculated that maximum mean ADC value in malignant tumors (n=33) was 1.4x10-3 mm2 /s with b-values of 50 and 800 or 900 s/mm2, but they compared only malignant lesions (n=33) and normal bone marrow (n=16) instead of benign lesions or fractures [3]. In our study, maximum mean ADC value of malignant fractures was higher with 1.92x10-3 mm2/s at b-value of 200 s /mm2.

In meta-regression analyses, Suh et al [13] found high sensitivity (92%) and specificity (91%) ratios of ADC values for differential diagnosis of benign and malignant vertebral fractures. Pozzi et al. [16] mentioned that mean ADC value of malignant fractures (1.241 ± 0.4 × 10−3 mm2/s) was higher than osteoporotic fractures (0.646 ± 0.368 × 10−3 mm2/s) at b=800 s/ mm2. In another study, they also supported these findings with accuracy ratio of 76% for DWI with ADC measurement at b values of 0 and 1000 s/mm2 [18]. They estimated mean ADC values of malignant primary tumors as 1.00±0.32x10-3 mm2/s, bone metastases as 1.02±0.25x10-3 mm2/s and benign primary tumors as 1.31±0.36x10-3 mm2/s [18]. In our study, only vertebral fractures were included and ADC values were similarly higher in benign group. Additionally, DWI was performed at multiple b-values.

Luo et al [21] reviewed findings of 12 studies for comparison of DWI at standard (≥500 s/mm2) and low (<500 s/mm2) b-values in differential diagnosis. They noted that ADC value difference between benign and malignant group was more apparent at low-b-value ($p<0.05$). Therefore, they recommended low-b-value DWI (<500s/mm2) for differential diagnosis of benign and malignant vertebral fractures [21]. In contrast, no statistical difference was observed in our study between mean

ADC values at b-values of 200, 400 and 600 s/ mm2 except for normalized ADC values of malignant group at b-values of 200 and 600 s/ mm2.

In some previous studies, cut off points for ADC values were also estimated. Dewan et al. [22] found higher mean ADC value in benign lesions with b-value of 1000 s/mm2 than that of malignant ones ($p < 0.05$). With a cut off ADC value of 1.21x10−3 mm2/s, the sensitivity of 95.12%, specificity of 92.73%, was obtained in differential diagnosis [22]. Wonglaksanapimon et al. [23] found the accuracy of 89.7%, sensitivity of 85.7% and specificity of 90.6% with a cut off ADC value of 0.89 for differentiation malignant (n=7) from benign (n=32) fractures ($p< 0.05$) [23]. Geith et al [24] found that the best diagnostic performance of DWI and ADC measurements is achieved by a combination of b-values of 100, 250, and 400 s/mm2 with a cut off ADC value of < 1.7x10-3 mm2/s for differential diagnosis of acute benign (n=26) and malignant vertebral fractures (n=20) (sensitivity, 85%; specificity, 84.6%; PPV, 81.0%; NPV, 88.0%) [17]. In our study, a cut off value couldn't be estimated because there was a gap between maximum mean ADC value of malignant fractures and minimum mean ADC value of benign fractures. Additionally, our maximum mean ADC value of malignant fractures was near to their cut off value (1.7x10-3 mm2/s) with 1.92x10-3 mm2 /s at b-value of 200 s/ mm2.

We emphasized that some MRI features like low signal intensity on T1-weighted sequence, total vertebral corpus involvement, contrast enhancement, associated soft tissue component and involvement of posterior elements were strongly associated with malignant fractures. We thought that differential diagnosis can be easier with quantitative measurements of mean ADC and normalized ADC values. Malignant vertebral fractures had lower mean ADC and normalized ADC values compared to benign ones.

One of the limitations in our retrospective study was lack of histopathological results in benign fractures. Vertebral fractures without clinical and radiological progression at least 6 months of follow-up were classified as benign. The other limitation is heterogenity of our sample with the etiology of osteoporosis, trauma, primary malignant tumor and metastases secondary to different malignancies. This heterogenity can cause different diffusion behavior and signal characteristics due to content of tissue.

MRI combined with DWI is a problem solving modality especially in geriatric oncology patients. Performing DWI at least two b-values including b-value of 200 s/mm2, quantitative evaluation on ADC map and estimation of normalized ADC value for optimization of data are recommended for differential diagnosis of benign and malignant vertebral fractures.

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