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# Diffusion-weighted magnetic resonance imaging of femoral head osteonecrosis in two groups of patients: Legg–Perthes–Calve and Avascular necrosis

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#### Abstract

*Introduction* The aim of this prospective study was to evaluate the value of diffusion-weighted magnetic resonance imaging (DW-MRI) in patients with osteonecrosis. Patients were divided into two subgroups as avascular necrosis (AVN) of femoral head for adult group and Legg–Calvé–Perthes (LCP) patients for children.

*Patients and methods* Seventeen patients with femoral head AVN (mean age 42.3 years) and 17 patients with LCP (mean age 8.2 years) were included in this study. Diagnosis confirmed with clinical and other imaging procedures among the patients complaining hip pain. DW images were obtained using the single-shot echo planar sequence and had *b* values of 0, 500, 1000 s/mm<sup>2</sup>. The apparent diffusion coefficient (ADC) values were measured from ADC maps in epiphysis of patients with AVN, both from metaphysis and epiphysis in patients with LCP, respectively. Mann-Whitney *U* test was used to compare ADC values.

*Results* The mean ADC value of femoral heads  $(1.285 \pm 0.204 \times 10^{-3} \text{ mm}^2/\text{s})$  was increased in patients

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<sup>2</sup> Okmeydani Education and Research Hospital, Radiology Clinic, Kaptanpasa Mah. Darülaceze Cad. No:27, Okmeydanı - Şişli, 34384 Istanbul, Turkey with AVN when compared to normal bone tissue  $(0.209 \pm 0.214 \times 10^{-3} \text{ mm}^2/\text{s})$  (p < 0.01). The mean ADC values ( $\times 10^{-3} \text{ mm}^2/\text{s}$ ) of both metaphysis ( $0.852 \pm 0.293$ ) and epiphysis ( $0.843 \pm 0.332$ ) were also increased in patients with LCP and differences were statistically significant (p < 0.01).

*Conclusions* As a result, osteonecrosis shows increased ADC values. But it is a controversial concept that DWI offers a valuable data to conventional MRI or not. However, as there are report states, there is a correlation between the stage of the disease with ADC values in the LCP disease. DWI is a fast, without-contrast administration technique and provides quantitative values additional to conventional MR techniques; we believe DWI may play an additional assistance to the diagnosis and treatment for LCP patients. Multicentric larger group studies may provide additional data to this issue.

**Keywords** Diffusion-weighted magnetic resonance imaging · Apparent diffusion coefficient · Avascular necrosis · Legg–Perthes–Calve

# Introduction

Diffusion-weighted magnetic resonance imaging (DW-MRI) is a non-invasive functional technique that evaluates random motion of water protons in body. Since the water molecules show various amount of diffusion according to their interaction with cell membrane, DWI can provide additional information about the tissue characterization by quantitative analysis with the apparent diffusion coefficient (ADC) map obtained from DW-MRI [1, 2].

Osteonecrosis means ischemia, results to death of the bone marrow cellular components. This pathological process is called avascular necrosis when epiphysis is observed. On the other hand, it is named Legg–Calvé– Perthes disease (LCP) when idiopathic osteonecrosis of the proximal epiphysis in children is observed [3]. Osteonecrosis most often affects the hip joint. Incidence is increased depending on the alcohol use, trauma, and exogenous steroids [4]. 5–18 % of the total hip replacement surgery is performed to treat this disease. Early diagnosis delays the implementation of total hip arthroplasty. Therefore, early diagnosis is essential in the treatment of avascular necrosis. There are studies which report that ischemic area shows diffusion limitations and if the treatment begins at this critical period, prognosis could be affected positively in the first 72 h [5, 6].

Furthermore, DWI is used in ischemic issues of neuroradiology efficiently, especially in early diagnosis of cerebrovascular events. However, there are few publications about the use of osteonecrosis [7–9].

The aim of this study was to determine the utility of ADC measurements of ischemic necrosis of the femoral head in both children and adult patients.

#### Materials and methods

## Patients

The study included 17 adult patients diagnosed as AVN and 17 patients diagnosed as LCP in pediatric age group, those admitted to the radiology clinic, because of hip pain between May 2009 and January 2011 in our center.

This study was approved by institutional ethics committee and all persons gave their informed consent prior to their inclusion in the study. Diagnosis performed as a result of further investigation and follow-up.

AVN diagnosis was performed with single line sign which is diagnostic for T1W images and double line sign on T2W images. Additionally, late-stage degenerative changes of AVN were noted such as femoral head circularity loss, crash of femoral head. AVN cases are staged by Mitchell staging system. Pathological diagnosis of 24 femoral head AVN in 17 patients was included in the statistical analysis. Control group was created this way: in bilateral AVN cases, metaphyseal ADC values were obtained from tissue adjacent to the lesion area without any abnormal signals in conventional MRI sequences. For unilateral affected cases, contralateral femoral head ADC values were obtained.

LCP diagnosis of proximal femoral epiphysis was established by monitoring of deformed appearance such as irregularity of contour, height loss, sclerotic appearance, subchondral fracture fragmentation, the existence of the loss of roundness and flattening of the femoral head. In 17 unilateral LCP patients, pathological femoral head metaphyseal and epiphyseal ADC values were used. As a control group, contralateral epiphysis and metaphysis were evaluated for statistical analysis.

In literature, there are not enough data about ADC values in the normal pediatric femoral epiphysis for different age groups and early childhood of up to 5 years, which is considered to be homogeneous. To overcome this issue, we did not include cases of bilateral LCP and patients younger than 5 years. Thus, we were able to compare the ADC values of the affected limb with contralateral healthy side in LCP patients.

## **MRI** technique

Conventional MRI and DWI examinations were performed with Siemens Avanto 1.5 T MR scanner (Siemens Erlangen, Germany). Routine MRI protocol consists of T1W in the axial and coronal and T2W in the coronal and sagittal images.

DWI was obtained when using single-shot echo planar imaging (EPI) sequence in the axial plane. EPI sequence was obtained using TR 4000, TE 76, thickness 5 mm, section spacing of 1 mm, matrix  $156 \times 192$ , FOV = 400, NEX: 3 different "b" value (0, 500 and 1000 s/mm<sup>2</sup>) gradients.

All patients were first assessed visually in terms of signal characteristics. Lesion area on T1W, T2W images was localized. The greatest possible extent region of interest (ROI) was placed on diffusion images with b = 1000 s/ mm<sup>2</sup> using workstation for numerical evaluation. ADC values in the lesion area were measured under T1W and T2W images guidance of ADC maps in accordance with the lesion. Specific mean ADC values were obtained to make separate measurements of each lesion.

For pediatric age, contralateral femoral epiphyseal and metaphyseal head normal ADC values were considered as normal reference.

# Statistical analysis

Data were summarized as mean  $\pm$  standard deviation for continuous variables and frequencies for categorical variables. Mann–Whitney *U* test was used for independent group comparisons depending on the distributional properties of the data. Difference between ADC values of normal and necrotic bone measured with EPI sequence was compared. *p* value <0.05 was considered as statistically significant.

## Results

Seventeen patients with AVN (11 males and six females) with a mean age of 42.3 years (age range 19–62 years) and

Table 1 Demographic data of AVN patients and ADC values

Case	Age	Placement	Stage <sup>a</sup>	EPI of pathological side	EPI of control
1	26	В	R: C	R: 1.390	R: 0.283
			L: C	L: 1.530	L: 0.189
2	30	R	А	1.644	0.102
3	39	В	R: D	R: 1.460	R: 0.174
			L: D	L: 1.531	L: 0.251
4	53	L	А	1.188	0.113
5	46	В	R: D	R: 1.237	R: 0.165
			L: D	L: 1.076	L: 0.230
6	37	В	R: C	R: 1.014	R: 0.109
			L: C	L:1.108	L: 0.293
7	44	R	С	1.369	0.160
8	51	L	С	1.152	0.132
9	57	В	R: A	R: 1.059	R: 0.252
			L: D	L: 1.013	L: 0.125
10	38	В	R: C	R: 1.116	R: 0.232
			L: C	L:1.083	L: 0.189
11	58	В	R: C	R: 1.594	R: 0.194
			L: C	L: 1.477	L: 0.195
12	44	R	А	1.008	0.170
13	31	R	D	1.144	0.198
14	41	R	С	1.431	0.131
15	49	R	С	1.211	0.240
16	62	R	С	1.284	0.720
17	19	L	С	1.604	0.209

EPI: ADC  $\times 10^{-3}$  mm<sup>2</sup>/s

<sup>a</sup> According to Mitchell staging system, R right, L left, B both

**Table 2**Demographic data orLCP cases and ADC values

17 patients with LCP (15 males and two females) with a mean age of 8.2 years (age range 5–13 years) were included in our study. Demographic data of patients with AVN and LCP are summarized in Tables 1 and 2, respectively.

The mean ADC value of patients with AVN was  $1285 \pm 0.204 \times 10^{-3} \text{ mm}^2/\text{s}$  (range  $1.008 \times 10^{-3} - 1.644 \times 10^{-3} \text{ mm}^2/\text{s}$ ) and  $0.209 \pm 0.214 \times 10^{-3} \text{ mm}^2/\text{s}$  for normal bone tissue (p < 0.01) (Figs. 1, 2 and 3).

The ADC value of normal epiphyseal bone was measured as  $0.289 \pm 0.236 \times 10^{-3} \text{ mm}^2/\text{s}$  and normal metaphyseal was measured  $0.418 \pm 0.165 \times 10^{-3} \text{ mm}^2/\text{s}$ , respectively, in the pediatric age group (Fig. 4). The mean ADC value of patients with LCP was measured as  $0.843 \pm 0.332 \times 10^{-3} \text{ mm}^2/\text{s}$  in epiphyseal and  $0.852 \pm 0.293 \times 10^{-3} \text{ mm}^2/\text{s}$ , metaphyseal regions, respectively. In osteonecrotic region, epiphyseal and metaphyseal ADC values were significantly higher than the normal side (p < 0.01) (Table 3; Fig. 5).

# Discussion

DWI is efficiently used in neuroradiology, especially in early diagnosis of cerebrovascular events. In literature, many new and different areas came to agenda. These are in musculoskeletal system, bone marrow and abdominal organs. DWI has also assessed a number of musculoskeletal disorders, including vertebral fractures, bone marrow infection, bone marrow malignancy, primary bone and soft tissue tumors; post-treatment follow-up has also been evaluated [10]. Discrimination between benign and malignant

Case	Age	Placement	Path. eph. EPI	Cont. eph. EPI	Path. meta. EPI	Cont. meta. EPI
1	13	R	0.184	0.135	0.340	0.272
2	5	R	0.926	0.181	0.622	0.456
3	7	R	0.565	0.142	0.787	0.150
4	9	R	0.906	0.106	0.522	0.260
5	7	L	0.772	0.186	0.768	0.306
6	12	L	0.780	0.145	1.015	0.508
7	7	L	0.813	0.102	1.115	0.636
8	10	L	1.452	0.698	0.564	0.389
9	8	L	1.036	0.230	1.390	0.285
10	6	R	1.170	0.590	0.626	0.308
11	7	L	0.973	0.114	0.639	0.520
12	7	R	0.591	0.251	0.956	0.464
13	9	R	0.770	0.132	1.060	0.163
14	10	R	0.232	0.850	0.873	0.571
15	7	R	1.303	0.594	1.386	0.695
16	7	R	0.709	0.219	0.851	0.565
17	9	R	1.069	0.244	0.883	0.561

EPI: ADC  $\times 10^{-3}$  mm<sup>2</sup>/s

R right, L left, eph epiphysis, meta metaphysis, cont contralateral, path pathological

a

C

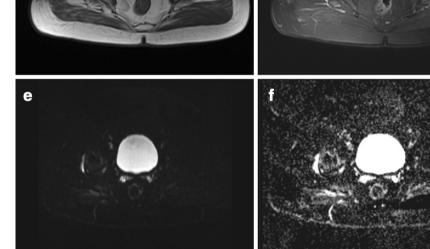
Fig. 1 a-f A 44-year-old male with a diagnosis of right femoral head stage A AVN. Coronal T1-weighted (a), coronal T2 fatsaturated (b), axial T1-weighted (c), axial T2 fat-saturated (d) images demonstrate on the right femoral head double string sign and edematous signal change in medullar bone. Diffusionweighted images (b = 1000 s/mm<sup>2</sup>) show edematous signal change (e). The ADC value of right femoral head was measured as  $1.008 \times 10^{-3} \text{ mm}^2/\text{s}$  (f)

vertebral fractures by DWI and following of therapy response have shown excellent results [10].

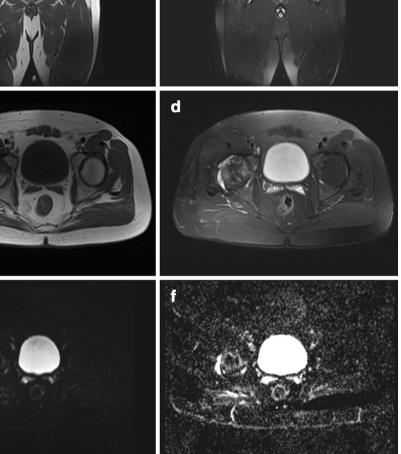
The mean ADC value of muscle tissue was measured as  $1.2-1.7 \times 10^{-3}$  s/mm<sup>2</sup>, the mean ADC value of liver tissue from 1.38 to 1.87  $\times$   $10^{-3}$  s/mm², respectively. Ward et al. reported that normal fat and red bone marrow show low ADC values with minimal diffusion [11].

The mean ADC value of bone marrow is 0.15- $0.59 \times 10^{-3}$  s/mm<sup>2</sup> [12]. It differs with age, gender and changing the bone marrow distribution which is suggested to be dependent on the oil-water ratio. Healthy bone marrow contains 25-70 % oil and shows the rate increase of 7 % each decade lifelong. In the first year of life, all bone marrow is red (cellular) and evolves into yellow (fatty) bone marrow with increasing age. Ward et al. [11] and Nonomura et al. have concluded [13] red (cellular) bone marrow has higher ADC value than yellow (fatty) bone marrow. In early childhood up to 5 years, bone marrow area is considered to be not homogeneous [13, 14]. This situation causes difficulties for the interpretation of ischemic lesions in the femoral head for pediatric age group [15]. To overcome this problem, we did not include cases with bilateral LCP and cases under the age of 5 to our study. Thus, we were able to compare the ADC values with contralateral control side for LCP patients.

Nonomura et al. showed a positive correlation between bone marrow cellularity and ADC values [13]. ADC value increased due to perfusion effect, depended on the large number of bone marrow hematopoietic cells active, and affects microcirculation. Furthermore, for the active hematopoietic, cellular bone marrow has more intracellular diffusion because they contain more free water molecules around. Conversion of hematopoietic bone marrow

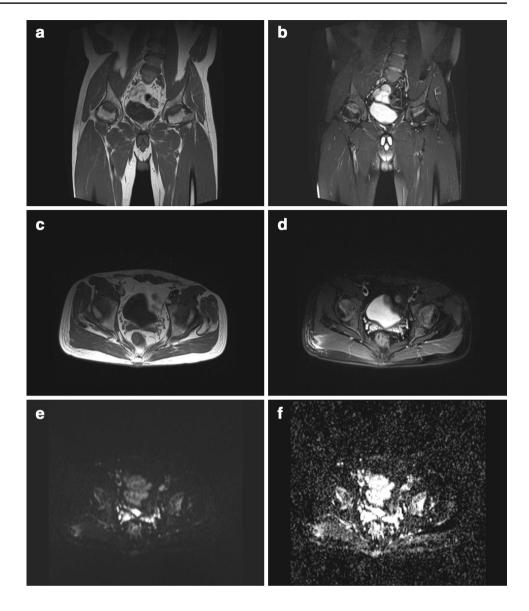






b

Fig. 2 a-f A 26-year-old male with a diagnosis of bilateral femoral head stage C AVN. Coronal T1-weighted (a), coronal T2 fat-saturated (b), axial T1-weighted (c), axial T2 fat-saturated (d) images demonstrate subcortical fissure lines and adjacent medullar edematous signal changes on both femoral head superior anterior regions. Diffusion-weighted images ( $b = 1000 \text{ s/mm}^2$ ) show signal changes in necrotic bone (e, f). The ADC values of right and left femoral heads were measured as  $1.390 \times 10^{-3}$  and  $1.530 \times 10^{-3}$  mm<sup>2</sup>/s, respectively (f)



to fatty bone marrow leads to intramedullary physiological decrease in blood flow [16].

In AVN patients, ischemia results in death and devastation of bone marrow cells such as hematopoietic elements, osteocytes and fat cells. This causes water diffusion to become more effective [14]. Result is increased diffusion and ADC values. This can be one of the factors that can explain the high ADC values determined in avascular necrosis.

Jaramillo et al. and Menezes et al. evaluated the changes of diffusion of the femoral head ischemia with line-scan DWI technique in an experimental animal model. Their studies showed increased diffusion of femoral head with avascular necrosis. Our high ADC values in accordance with the increased diffusion were similar to Jaramillo and Menezes' s findings in the femoral head AVN [17, 18].

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Correlation between ADC values and stage of osteonecrosis of the femoral head is a debatable question. Oner et al. found statistically significant increase of ADC values in patients with AVN in their study that included 21 patients with 35 femoral head involvement. This study also reported that the stage of the disease does not influence the ADC values [19]. However, Boutaulut et al. reported statistically significant increase in ADC values in the pathological side and was correlated with Catterall classification on their study that included 27 children with LCP disease [20]. In addition, Baunin C et al. reported statistically significant increase in ADC values in the pathological side and was correlated with Herring classification on their study with 31 patients with unilateral involvement LCP [21]. Catterall and Herring classifications are two of the five femoral head avascular necrosis disease classification accepted so far and based on femoral areas involved. We were not able to

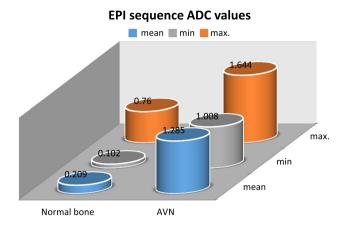


Fig. 3 ADC values of the normal bone tissue and AVN bone lesions

study statistical comparison between the phases of disease because we did not have any patient with stage B. This was one of the limitations of our study.

Fig. 4 a-f A 10-year-old girl with a diagnosis of left Legg-Calvé-Perthes. Coronal T1-weighted (a), coronal T2 fatsaturated (b), axial T1-weighted (c), axial T2 fat-saturated (d) images demonstrate contour irregularity and height loss on the left epiphysis. Additionally, free liquid quantity is slightly increased on the left hip joint space. Diffusionweighted images (b = 1000 s/mm<sup>2</sup>) show edematous signal change (e). The ADC values of left femoral proximal epiphysis and proximal metaphysis were measured as  $1.452 \times 10^{-3}$  and  $0.564 \times 10^{-3}$  mm<sup>2</sup>/s, respectively (f)

Avascular necrosis and repair process begin simultaneously. Capillaries show progress toward the necrotic bone marrow area in the repair process. Increased perfusion can be another factor contributing to the increase in ADC values [22].

Merlini et al. reported, pathological epiphyseal and metaphyseal femoral head ADC values were significantly higher compared with control side in their study including 12 patients with 5–12 age group LCP [15]. In our study, ADC values of normal and pathological bone marrow findings were similar to those previously made studies in literature.

An increase in interstitial bony fluid occurs in bone marrow edema (BME). The exact pathogenetic processes still remain unknown. BME is an unspecific finding that can occur on its own or accompany multiple diseases and pathologies. The differentiation of at least three different etiologies is proposed (mechanic, reactive and ischemic) [23]. As a result of increased interstitial bony fluid, water

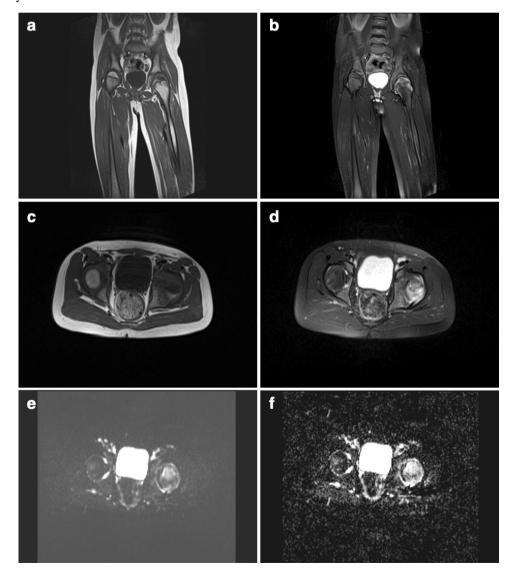


 
 Table 3
 Comparison of normal and pathological epiphyseal/metaphyseal mean ADC values and standard deviation of patients with LCP

	The mean ADC of nor- mal epiphysis	Mean ADC in patients with LCP	Р
Epiphysis	$0.289 \pm 0.236$	$0.843 \pm 0.332$	< 0.01
Metaphysis	$0.418 \pm 0.165$	$0.852\pm0.293$	< 0.01

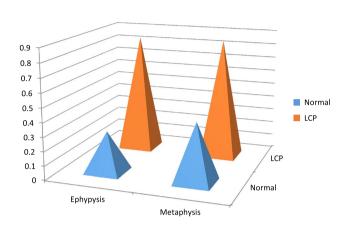


Fig. 5 ADC values of normal and LCP individuals in epiphyseal and metaphyseal regions

molecules can move freely and diffusion coefficient will rise. Increased ADC values can also be explained this way.

Studies related with avascular necrosis report that, in the early stages of the disease before cell death, there is restriction of diffusion means reduction in ADC values. After necrosis, then ADC values will rise. Critical period is this diffusion restriction period.

Menezes et al. and Jaramillo et al. reported that restriction of diffusion was seen with diffusion tensor imaging in early phase of femoral head AVN, similarly to that in the brain [24, 25]. Li et al. reported, after 72 h from ligation of artery surgery, ADC values showed markedly decrease in 25 piglets [6]. In our study, patients have late phase avascular necrosis so we did not see diffusion restriction. It is second limitation of our study.

As a result, osteonecrosis shows high ADC values in late stages. But it is a controversial concept that, how much contribution does this increase offer to conventional MRI, because, stage of disease, prognosis, treatment planning can be performed successfully using conventional MRI techniques. However, there are studies indicating that there is a correlation between the stage of the disease with the ADC value in LCP disease. On the other hand, DWI has advantages such as, it can be completed in a short period of time, no contrast use required and unlike conventional MRI techniques DWI offers quantitative values. Finally, in the early stages, in the restriction of diffusion phase, early treatment prognosis can change in positive direction. Multicenter studies including many patients can make contribution to this issue.

#### Compliance with ethical standards

**Conflict of interest** Author Betul Duran Ozel MD declares that she has no conflict of interest. Author Deniz Ozel MD declares that he has no conflict of interest. Author Fuat Ozkan MD declares that he has no conflict of interest. Author Ahmet M. Halefoglu MD declares that he has no conflict of interest.

**Ethical standards** All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

**Informed consent** Informed consent was obtained from all individual participants included in the study.

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