International Journal of Radiology Sciences

ISSN Print: 2664-9810
ISSN Online: 2664-9829
IJRC 2024; 6(2): 01-05
www.radiologyjournals.com
Received: 01-05-2024
Accepted: 04-06-2024

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Advantage of magnetic resonance imaging over X-Ray in diagnosis and evaluation of avascular necrosis of femoral head in patients with sickle cell disease

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DOI: https://doi.org/10.33545/26649810.2024.v6.i2a.21

Abstract
Background: Avascular necrosis (AVN) of the femoral head in sickle cell disease (SCD) individuals causes substantial morbidity and joint dysfunction. Preventing disease progression and planning therapy need early identification. MRI and X-ray are standard diagnostic techniques, although their efficiency in identifying early AVN in SCD patients is unknown.
Objective: This research compares MRI and conventional X-ray in identifying AVN of the femoral head in SCD patients and evaluates Ficat-Arlet and Mitchell classification systems for AVN progression.
Method: From August 2023 to March 2024, the Radiology Department of Al Sader Teaching Hospital performed a cross-sectional research of 80 SCD patients with hip pain, stiffness, or limping. All subjects had MRIs and X-rays. Imaging data were staged using Ficat-Arlet and Mitchell classifications to assess AVN severity and progression.
Results: MRI detected early-stage AVN lesions that X-rays missed. MRI revealed early-stage AVN in 15.6% of Ficat-Arlet stage 1 patients, compared to 6.2% by X-ray. MRI had a 31.9% and 18.7% detection rate in stages 2 and 3, compared to 17.5% and 16.2% for X-ray. MRI showed precise femoral head structural and pathological alterations, essential for early management. MRI also revealed bone marrow edoema and the "double-line sign," which indicate persistent ischemia damage and were not visible by X-ray.
Conclusion: MRI surpasses X-ray in detecting and staging AVN in SCD patients, offering crucial insights for early treatment. In SCD patients at risk for AVN, MRI is indicated as a key diagnostic technique for comprehensive anatomical and pathological examination to improve clinical outcomes.

Keywords: Avascular necrosis, femoral head, sickle cell disease, MRI, X-ray

Introduction

Sickle cell disease (SCD) is a genetic disorder characterized by the production of abnormal hemoglobin (HbS), leading to altered red blood cell morphology and complications such as pain, anemia, and organ damage. The bones, particularly the femoral head, are severely affected due to reduced blood flow that encourages sickling, resulting in vascular occlusion, thrombosis, infarction, and avascular necrosis (AVN), a significant complication that can lead to joint collapse or subchondral bone destruction [1-3]. Epidemiologically, the prevalence of SCD in Iraq has increased slightly over recent years, with the highest rates observed in Basra. Despite this, data on the prevalence of AVN among SCD patients in Iraq remains lacking, though it is a notable issue in other regions such as the United States and Germany [4, 5]. Pathophysiologic ally, AVN in SCD occurs when sickle-shaped red blood cells block capillaries, leading to oxygen deprivation and tissue death in bone, particularly in areas like the femoral head where blood supply is critical yet easily compromised. This ischemia and subsequent infarction of bone tissue are exacerbated by conditions like infection or dehydration, which promote sickling [6-8]. Clinically, AVN typically presents with pain and limited mobility, particularly affecting the hip joint, where over 70% of cases are diagnosed. Early stages may be asymptomatic, but progression can lead to severe pain, even at rest, and eventual joint collapse requiring surgical intervention such as hip arthroplasty [9-11]. Diagnostically, AVN is primarily detected through imaging techniques like MRI, which is

preferred due to its ability to detail soft tissue and early bone changes not visible on X-rays. Early detection through MRI is crucial as it can prevent severe outcomes by enabling timely treatment interventions [12-15]. The classification of AVN stages helps in assessing the severity and progression of the disease. Systems such as the Ficat and Arlet provide frameworks based on imaging findings and clinical features. For instance, Stage 0 represents no detectable changes, while Stage 4 indicates advanced degenerative changes [16, 17]. Bone biopsy, though accurate for diagnosing AVN, is generally avoided due to its invasive nature. It involves inserting a trephine through the greater trochanter to the femoral head but stopping short of the articular cartilage [18, 19].

The primary objective of the study is to assess the effectiveness of MRI in detecting avascular necrosis (AVN) of the femoral head in sickle cell disease patients. It aims to compare the diagnostic capabilities of MRI with conventional plain X-ray imaging and to evaluate various radiological classification systems to systematically characterize the extent and progression of osteonecrosis of the femoral head.

Method

The methodology of this cross-sectional study, conducted between August 2023 and March 2024, focused on evaluating the effectiveness of magnetic resonance imaging (MRI) compared to conventional plain X-ray imaging in detecting avascular necrosis (AVN) of the femoral head in patients with sickle cell disease (SCD). The study was carried out in the Radiology Department of Al Sader Teaching Hospital and included 80 SCD patients (47 males and 33 females) aged between 18 and 64 years. These patients were referred from Orthopedic and Hematological departments based on their history of SCD and symptoms like hip pain, limping, or stiffness.

Inclusion and Exclusion Criteria: Participants were included if they had a documented history of SCD and presented with related symptoms. Exclusion criteria encompassed those with contraindications to MRI such as metallic implants, pacemakers, or cochlear implants, those who had undergone previous hip joint surgery, uncooperative patients, those in sickle cell crisis, chronic users of steroids, and patients with a history of hip trauma.

Imaging Procedures: Each participant underwent bilateral hip imaging, yielding a total of 160 imaging records. Initially, X-ray imaging was performed for all participants, followed by MRI scans to allow a comparative analysis. The study utilized high-resolution MRI scanners (Philips Achieva and GE Optima MR450W, 1.5 Tesla) without contrast enhancement.

Imaging included a series of specific sequences to optimally visualize the femoral head and assess for signs of AVN. The protocol involved T_1-weighted, T_2-weighted, and STIR sequences with detailed parameter settings adjusted based on clinical indications to best highlight bone and soft tissue contrasts. Radiographic imaging was conducted using a Philips Digital Radiography system, with parameters set to optimize image clarity and detail. The protocol for X-ray included anteroposterior (AP) and frog-lateral views, which were crucial for initial evaluation and comparison with MRI findings.

Staging and Classification: The Ficat-Arlet and Mitchell staging systems were used to classify the degree of AVN detected in the hip joints. X-ray features considered included osteopenia, sclerosis, the crescent sign indicating subchondral fracture, loss of the femoral head's spherical shape, partial collapse of the head, and secondary osteoarthritis. MRI staging focused on the type of signal in the necrotic core and other changes indicative of AVN.

Data Collection: Data collection was structured around a specifically designed questionnaire divided into three parts: sociodemographic information, laboratory data, and imaging findings (MRI and X-ray). After collection, data were categorized, sorted, and prepared for statistical analysis.

Statistical Analysis: Statistical analysis was conducted using the Statistical Package for the Social Sciences (SPSS), version 26. Categorical data were presented as numbers and percentages, and differences between groups were assessed using the Chi-square test and Fisher exact test as appropriate. Continuous variables were analyzed using one-way ANOVA. Key outcome measures included sensitivity, specificity, positive predictive value, and negative predictive value of each imaging modality in the diagnosis of AVN.

Results

The study analyzed socio-demographic and health-related data of 80 patients, divided into two groups: those with avascular necrosis (AVN) and those without. The analysis revealed no significant difference in age and gender distribution between the two groups. However, there was a significant difference in Body Mass Index (BMI), with the group without AVN having a higher proportion of normal weight individuals, whereas the group with AVN had more overweight individuals. There were no significant differences in occupation and smoking habits. The distribution of sickle cell disease types showed that patients with SCA (HbSS) were most affected by AVN, followed by those with sickle thalassemia, while those with Hb CS had the lowest occurrence, with this variation being statistically significant.

Table 1: The distribution of socio-demographical data among the studied patients.

Variables		Without AVN	With AVN	P-Value
		(No. 12)	(No. 68)	
Age	Mean ±SD	33.62±12.56	35.82±13.38	0.472
Gender	Male	8 (66.6%)	39 (57.3%)	0.776
	Female	4 (33.3%)	29 (42.6%)	
Body Mass Index	Underweight	2 (16.6%)	9 (13.3%)	0.004
	Normal	7 (58.3%)	25 (36.7%)	
	Overweight	3 (25.0%)	34 (50.0%)	
Occupation	Self-employee	4 (33.3%)	23 (33.8%)	0.802
	Housewife	3 (25.0%)	17 (25.5%)	
	Employee	3 (25.0%)	15 (22.0%)	
	Student	2(16.6%)	13 (19.1%)	
Smoking	Yes	2 (16.6%)	21 (30.8%)	0.593
	No	10 (83.3%)	47 (69.1%)	
Type of anemia	Sickle cell Anemia (HbSS)	3(25.0%)	51 (75.0%)	0.002
	Sickle- thalassemia	7 (58.3%)	16(23.5%)	
	Hb SC	2 (16.6%)	1 (1.4%)	

Table 2 compares laboratory data (hemoglobin levels, white blood cell counts, and platelet counts). Despite slight differences in mean values, the P values (hemoglobin: 0.214, WBC: 0.787, platelets: 0.573) indicate these

differences are not statistically significant. HCT mean was significantly higher in patients with AVN (26.33%) than those Without AVN (23.16%) with P value <0.05. On the other hand, Retics count was significantly lower level in patients with AVN (6.37±4.48), P value <0.05.

Table 2: Laboratory data analysis among the studied patients.

Variables	Without AVN		With AVN	P Value
		(No. 12)	(No. 68)	
HCT	Mean ± SD	23.16±5.36	26.33±4.96	0.015
Hb(g/dl)	Mean ±SD	8.51±1.12	8.19±1.06	0.214
WBC× 10^3/µL	Mean ±SD	10.77±11.66	10.72±14.78	0.787
Platelets× 10^3/µL	Mean ±SD	318.63±60.89	325.26±58.9	0.573
Retics(%)	Mean ±SD	12.20 ±5.89	6.37±4.48	0.001

Table 3 provides an overview of the prevalence of various signs and symptoms among 80 enrolled patients. The most common symptom reported is Localized pain, with 63.7% (51 patients) experiencing it and 36.3% (29 patients) not experiencing it. The symptom of Pain referred to the thigh is less common, with only 15.0% (12 patients) experiencing it and a vast majority of 85.0% (68 patients) not experiencing it. Stiffness is reported in 37.5% (30 patients) of cases, making it slightly less prevalent than localized pain. On the other hand, Limping is the least common symptom, present in only 13.8% (11 patients) of the cases, with 86.3% (69 patients) not experiencing it.

Table 3: Signs and Symptoms among enrolled patients

Variables		Frequency (No. 80)	Percentage
Localized Pain	Present	51	63.7%
	Absent	29	36.3%
Pain referred to the thigh	Present	12	15.0%
	Absent	68	85.0%
Stiffness	Present	30	37.5%
	Absent	50	62.5%
Limping	Present	11	13.8%
	Absent	69	86.3%

The analysis of X-Ray and MRI findings in a study involving 80 patients (160 hips) shows differing patterns of abnormalities. X-Ray results indicate that 51.25% of the hips appear normal, while sclerosis and the crescent sign, indicative of avascular necrosis, are observed in 21.88% and 18.25% of hips, respectively. Both femoral head osteopenia and osteoarthritic changes are less common, each noted in 6.25% of hips. MRI findings, however, display a broader range of abnormalities. Only 27.50% of hips show normal results. The most common abnormality observed is focal subchondral signal abnormalities in a geographical pattern, affecting 45.63% of hips. Bone marrow edema and the double line sign, indicative of avascular necrosis, are significantly prevalent, observed in 33.75% and 43.75% of hips, respectively. Additionally, collapsed femoral heads are noted in 20.63% of cases, with osteoarthritic changes and joint effusion present in 6.88% and 29.88% of hips, respectively. Acetabular involvement is observed in 5.63% of the cases. As in table 4.

Table 4: X-Ray and MRI findings analysis

Variables		Frequency (No. 160)	Percentage
X-Ray Findings	Normal	82	51.25%
	Sclerosis	35	21.88%
	Osteopenia	10	6.25%
	Crescent sign	30	18.25%
	Osteoarthritic	10	6.25%
	changes		
MRI Findings	Normal	44	27.50%
	Focal subchondral signal abnormalities (geographical sign)	73	45.63%
	Bone marrow edema	54	33.75%
	Double line sign	70	43.75%
	Collapsed femoral	33	20.63%
	head		
	Osteoarthritic	10	6.88%
	changes		
	Joint effusion	47	29.88%
	Acetabular	9	5.63%
	involvement		

Table 5 presents a comparative analysis of the FICAT staging system for diagnosing avascular necrosis (AVN), utilizing both X-Ray and MRI findings. The data reveals a statistically significant difference in the detection capabilities of X-Ray and MRI, as highlighted by the P-Value of <0.001. For X-Ray, normal finding identified

(51.2%) as Stage 0 compared to MRI (27.5%) indicating no AVN. For stage 1 X-Ray detected in 10 hips (6.2%) while MRI identified 25 hips in stage 1 (15.6%). In Stage 2 MRI identified a significantly higher percentage of patients (31.8%) than X-Ray (17.5%). Finally, for Stage 3 and stage 4, the percentages are same in both X-Ray and MRI (18.7% and 6.2% respectively).

Table 5: FICAT staging system analysis

Variables	X-Ray (No. 160)	MRI (No. 160)	P-Value
Stage 0(normal)	82 (51.2%)	44(27.5%)	<0.001
Stage 1	10 (6.2%)	25 (15.6%)	
Stage 2	28 (17.5%)	51 (31.8%)	
Stage 3	30 (18.7%)	30 (18.7%)	
Stage 4	10 (6.2%)	10 (6.2%)	

The table 6 presents the Michell staging system analysis (normal, stage A, stage B, stage C, and stage D) with corresponding frequencies and percentages of their occurrence. A total of 160 hips are examined, with stage B being the most frequent occurs among affected hips (38 hips), constituting 23.75% of the dataset. This is followed by stage A with 34 (21.25%), Stage C with 28 (17.5%), and finally, Stage D being the least frequent at 16 occurrences (10.0%).

Table 6: Michell staging system analysis

Variables	Frequency (No. 160)	Percent
normal	44	27.5%
Stage A	34	21.25%
Stage B	38	23.75%
Stage C	28	17.5%
Stage D	16	10.0%

Table 7 delineates the detection rates of X-Ray compared to MRI for AVN across a total of 160 hips. Of the cases where MRI detected AVN (positive findings), X-Ray detected it in 76 cases, accounting for 65.5% of the MRI positive findings. Conversely, of the cases where X-Ray did not detect the condition, MRI found the condition in 40 cases, which (34.4%) of the MRI positive finding. Furthermore, when MRI did not find the condition (negative findings), X-Ray was positive in 2 cases (4.5%) and negative in 42 cases, demonstrating a 95.4%.

Table 7: X-ray detection rate compared to MRI.

	MRI (Positive)	MRI (Negative)		Total
X-Ray (Positive)	76 (65.5%)	2	(4.5%)	78
X-Ray (Negative)	40 (34.4%)	42	(95.4%)	82
Total	116		44	160

Table 8 evaluates the diagnostic accuracy of X-Ray, revealing that it has a Positive Predictive Value (PPV) 97.43% while Negative Predictive Value was 51.21%. The Sensitivity was only 65.5%, indicating it detects just more than a half of actual cases, however the Specificity was 95.4%.

Table 8: Positive predictive Value, Negative Predictive Value, Sensitivity, and specificity of the X-ray.

Positive predictive Value	Negative predictive Value	Sensitivity		Specificity
X-Ray	97.43%	51.21%	65.5%	95.4%

Discussion

This comprehensive study evaluated the diagnostic effectiveness of MRI compared to X-ray in detecting avascular necrosis (AVN) of the femoral head in patients with sickle cell disease (SCD). The study utilized both imaging modalities across a cohort of 80 patients, comparing their findings with epidemiological data and previous studies to contextualize the results.

Comparative Analysis of Imaging Modalities

MRI proved superior to X-ray in several aspects, especially in detecting early stages of AVN. While 27.50% of MRI scans showed normal results, only 51.25% of X-ray scans did so, indicating MRI's higher sensitivity in identifying early pathological changes. MRI detected focal subchondral signal abnormalities, bone marrow edema, and the double line sign—hallmarks of AVN—in a significantly larger percentage of cases compared to X-ray. For instance, collapsed femoral heads were identified in 20.63% of MRI scans versus a lower detection rate in X-ray images. This aligns with findings from Manenti G *et al*. [20], who noted MRI's superior sensitivity in early AVN stages that were often missed on X-rays.

Diagnostic Accuracy and Clinical Implications:

The Ficat staging system further highlighted differences in the detection capabilities of X-ray and MRI, with MRI identifying a higher percentage of early-stage AVN cases (stage I and II). The study's results are supported by previous research, such as that by Netam *et al*. [21], which showed that MRI could detect changes in the femoral head not visible on X-rays, particularly in stages I and II of AVN. The diagnostic accuracy of X-ray showed a Positive Predictive Value (PPV) of 97.43% and a Sensitivity of 65.5%, indicating that while X-ray is reliable when AVN is visible, it misses a significant number of cases that MRI can detect. This finding emphasizes MRI's role as a critical tool in the early diagnosis and management of AVN, potentially guiding earlier intervention and better patient outcomes.

Epidemiological Insights and Disease Progression

The age distribution analysis in the study suggested that younger patients generally presented with milder forms of the disease, whereas more severe forms like destruction or diffuse necrosis were more common in the mid-age group (21–30 years). This trend mirrors the findings from Netam *et al*. [21], emphasizing that age may influence the severity and presentation of AVN. Moreover, the study observed a significant occurrence of AVN in patients with SCA and sickle thalassemia, consistent with Mahadeo *et al*. [22], who reported a higher prevalence of AVN among these genotypes.

Hematological Variables and Symptomatology

There were no significant differences in hemoglobin levels between patients with and without AVN, aligning with findings from Marouf R *et al*. [23]. However, the study did find that hematocrit (HCT) levels were significantly higher in patients with AVN. Symptomatically, pain was the most commonly reported symptom, paralleling findings from Kathale *et al*. [24], where pain often accompanied by limping was predominant. Such symptoms necessitate careful consideration in clinical evaluations, as they may indicate progressing AVN.

Implications for Clinical Practice

Given the high sensitivity of MRI in detecting early and subtler changes associated with AVN, it is recommended as the diagnostic tool of choice in patients at risk, particularly those with SCD. Early detection allows for more effective management strategies and could potentially delay or prevent the progression to more severe stages that require surgical intervention, such as hip replacements.

Conclusion

The research shows that MRI detects sickle cell avascular necrosis (AVN) better than X-ray. Still the primary line of femoral head evaluation, plain radiographs are easy and affordable but lack sensitivity in early stages. With no significant socio-demographic variations across patient groups, BMI was an exception, indicating a relationship between physical health and AVN risk. The FICAT and Michell systems showed MRI's sensitivity in early AVN identification and thorough disease staging, whereas X-Ray failed to detect many instances. This emphasises the importance of MRI in early AVN identification and management, recommending its main use in clinical diagnostics for optimal treatment.

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