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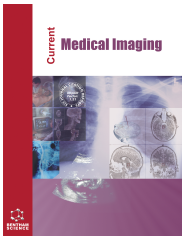

RESEARCH ARTICLE

Diagnostic Reliability of Plain Radiography in Osteonecrosis of the Femoral Head: General Radiological Features Revised

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Abstract:

Background and Objectives:

Osteonecrosis of the femoral head (ONFH) is an incapacitating disease that frequently results in the collapse of the femoral head and secondary osteoarthritis. The diagnosis and staging of this pathology, which usually rely on imaging studies, are challenging. Currently, conventional radiography is the basis of the initial diagnostic assessment. In recent decades, however, radiographs have been considered insensitive to early changes in ONFH and thus, a suboptimal diagnostic tool. Paradoxically, the imaging features of radiographs are often profuse, substantial, and characteristic. This study aimed to elucidate the real limitations of this radiologic tool by assessing the diagnostic reliability of the key radiologic features and staging.

Methods:

This was a retrospective study in which radiographs from 28 idiopathic ONFH confirmed cases who underwent hip arthroplasty were analyzed by eight observers who were asked to identify the presence or absence of ONFH universally reported imaging features in AP hip radiographs.

Results:

Concordance analysis revealed a poor agreement between observers for most of the assessed imaging features. Only the identification of femoral head flattening and osteoarthritis signs exhibited moderate agreement with statistical significance. In contrast, the detection of radiological osteoporosis and the loss of trabeculation showed the lowest reliability, with negative kappa coefficients.

Conclusion:

There is a lack of agreement between qualified observers, even for the identification of the most characteristic ONFH radiographic features. The reliability of plain radiography for the detection of basic radiological elements is even weaker in the early stages of the disease.

Keywords: Osteonecrosis of the femoral head, Avascular necrosis of the hip, Radiological diagnosis, Radiograph, Reliability, Ficat and Arlet classification.

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1. INTRODUCTION

Osteonecrosis of the femoral head (ONFH) is a disabling disease that frequently results in the collapse of the femoral head and secondary osteoarthritis (OA) in middle-aged and young adults [1].

This pathology is defined by the death of the osteocytes and bone marrow and is caused by inadequate blood supply, typically in the subchondral bone, frequently requiring hip

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arthroplasty [2]. In the United States, more than 30,000 new cases are diagnosed annually, with a steady increase in these numbers over the last few years [3]. However, to date, there have been no epidemiological reports of ONFH cases worldwide. Surgery-associated healthcare costs, critical pain, and disability in productive adults imply a significant socioeconomic burden [4].

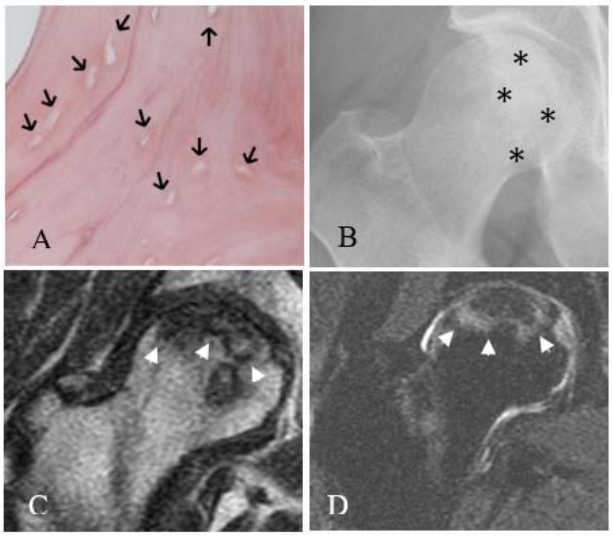

Fig. (1). ONFH histological and radiological findings of the same patient. **A**) Hematoxylin/eosin-stained sections showing partially necrotic trabecula: the bone exhibiting empty osteocytic lacunae (arrows) (40x obj.). **B**) Right hip AP radiograph presenting characteristic radiodensity and trabeculation alterations (asterisks), with preservation of the femoral head sphericity. **C**) MRI coronal view of a T1-weighted image showing typical low-intensity serpiginous lines (white arrows). **D**) MRI coronal view of a T2-weighted image showing typical high-intensity serpiginous lines (white arrows).

The optimal therapeutic approach should include a multimodal treatment regime or a plan specifically tailored for each patient from the moment of hip surgery through rehabilitation [5, 6]. In the early stages, ONFH is usually asymptomatic, although occasionally patients can report groin or knee pain [7]. In the initial stages of the disease, conservative approaches can be used to delay or stop the disease progression. These approaches include physical methods, such as extracorporeal shock wave therapy, drug administration, and the use of biological therapies. Therefore, early diagnosis is the key [8]. However, this initial diagnosis of ONFH is extremely difficult, as both the symptoms and imaging features are subtle [9], leading to diagnostic problems for radiologists and other specialists involved. Misdiagnosis of ONFH can occur when clinicians are unaware of potential difficulties, such as the presence of other pathological processes that can resemble osteonecrosis. These include subchondral cysts, subchondral insufficiency fractures, transient osteoporosis, osteochondral lesions, and metastases. In addition, other features, such as persistent hematopoietic red marrow, fovea centralis, synovial herniation pits, or the existence of pathological processes that can mimic osteonecrosis [10]. Moreover, advanced cases of ONFH may be difficult to differentiate from other conditions, such as osteoarthritis [11]. The complexity associated with the diagnosis of ONFH frequently results in the presentation of cases in advanced stages of this condition, which is when the preservation of the femoral head is no longer advised [12]. The diagnosis of ONFH relies considerably on imaging studies (Fig. **1**), including plain radiography, computed tomography, magnetic resonance imaging (MRI), and bone scintigraphy, although a definitive diagnosis can only be achieved by pathological analysis, which is currently considered the gold standard [13].

Among these modalities, the MRI is considered the most sensitive and noninvasive diagnostic test. Nevertheless, conventional radiography remains the basis for the initial diagnosis of patients with hip pain because of its high availability, safety, and low cost [14]. In recent decades, however, plain radiographs have been widely considered insensitive to early changes in ONFH and thus, a suboptimal diagnostic tool, especially in the initial phases of this condition [2, 15]. Paradoxically, radiographic features are often characteristic. First, bone sclerosis surrounded by osteopenia is common (Fig. **2**).

Fig. (2). Left hip AP radiograph showing typical hypodensity and blurry bone trabeculae found at the femoral head in ONFH initial stages. Region of interest is marked with asterisks.

Nevertheless, the typical radiographic features are patchy areas of lucency and sclerosis [16]. The sclerotic appearance (Fig. **3**) is characteristically within the lesion rim, frequently showing an undulating or "serpentine" morphology, which is more common in metadiaphyseal lesions, and translates the host–bone response to the wall of the necrotic areas [2, 16]. Conventional radiographs can also reveal early areas of articular collapse in ONFH, especially those affecting the anterior and anterolateral epiphysis of the femoral head. An articular collapse normally starts at the confluence of the serpentine sclerotic rim and articular surface, where the maximum mechanical stress occurs. Progressive subsidence may generate an archetypal crescentic subchondral lucency (Fig. **4**) or a "crescent sign," which translates the collapse of the subchondral bone and the splitting from the overlying

cartilage and attached subchondral bone [16, 17]. Consequently, articular fragmentation, progressive femoral head collapse, and secondary degenerative joint disease (Fig. **5**) commonly occur [15]. Hence, this collection of identifiable and characteristic imaging features present in radiographs contrasts with the current underestimation of this technique in the initial stages of the disease.

Fig. (3). Left hip AP radiograph exhibiting characteristic patchy sclerosis present at the femoral head in ONFH initial stages. The region of interest is marked with asterisks.

Fig. (4). Right hip AP radiograph presenting characteristic a subchondral hypodense line or a crescent sign, with an alteration of the femoral head sphericity and loss of the joint space. The region of interest is marked with white arrows.

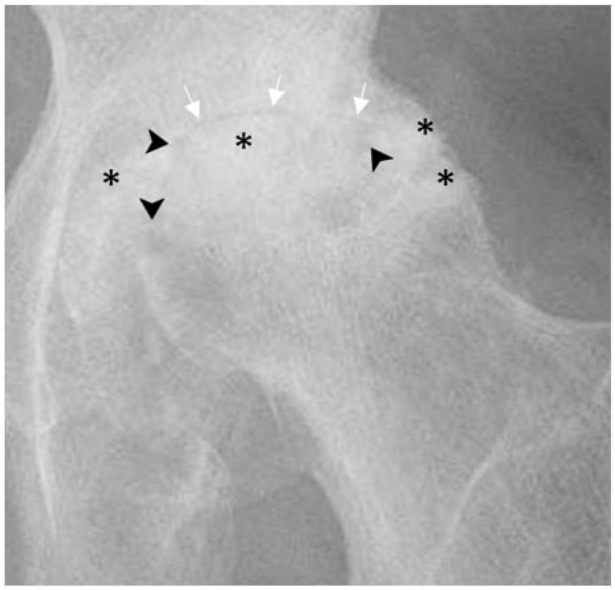

Fig. (5). Left hip AP radiograph exhibiting loss of femoral head sphericity and advanced joint disease. Joint space narrowing is indicated with white arrows; geodes are indicated with arrowheads, and sclerosis is marked with asterisks.

Paradoxically, the first performed test in the diagnostic workup is considered unreliable, as its sensitivity and specificity for ONFH diagnosis range from 52 to 89% and 35 to 97%, respectively, with the weakest performances found in the precollapse phases [14].

Therefore, the diagnostic value of simple radiographs is often underestimated, despite the many useful features that can be identified, especially under an expert look. The goal of this study was to clarify whether this radiologic tool is actually that limited, as popularly considered, through the assessment of diagnostic reliability in key radiological features and staging.

2. MATERIALS AND METHODS

2.1. Study Design

This retrospective study was conducted at a single hospital, in which radiographs from 28 idiopathic ONFH patients who underwent hip arthroplasty were analyzed by radiologists or orthopedic surgeons. The diagnosis was confirmed by MRI or histopathology. Cases lacking a certified report from a radiologist or with below-average histological quality were excluded. The study sample was determined following the guidelines of other studies in this line and made in the field of osteonecrosis [15 - 28].

2.2. Patients

Sixty femoral head specimens were collected from patients who underwent total hip replacement surgery at the Marqués de Valdecilla University Hospital between 2017 and 2020. Of those, 28 met the diagnostic criteria for ONFH, either by preoperative MRI findings, by postsurgical anatomopathological analysis, or by both methods (Table **1**). Since our intention was to study idiopathic cases of ONFH, with no obvious etiologic factor [10, 16] (secondary

osteonecrosis), we applied the following exclusion criteria: (1) systemic glucocorticoids and/or bisphosphonate treatment history, (2) past or present heavy alcohol consumption, (3) hip trauma or radiation history, and (4) storage disorders, pancreatitis, hemoglobinopathies, or dysbarism history. The comorbidities of the patients included in the study that have been identified in the literature as risk factors for this pathology [16] are summarized in Table **2**. A written informed consent was obtained from all patients. The study protocol was approved by the Institutional Review Board (Comité de Ética en Investigación Clínica de Cantabria, February 2018), with Identification Code 2018.014.

Table 1. Clinical data of patients enrolled.

Parameter	Value
Age (years; mean ± SE)	66.46 ± 11.07
Sex (males *vs.* females)	12 *vs.* 16
MRI-confirmed diagnosis	11
Histology-confirmed diagnosis	17
MRI- and histology-confirmed diagnosis	4
Ficat and Arlet stage (mean ± SE)	3.63 ± 0.67
Hip side (right *vs.* left)	18 *vs.* 10

Table 2. Comorbidities in the study sample identified as idiopathic ONCF risk factors.

ONCF Risk Factors in the Study Sample	Percentage (%) of Patients
Overweight or obesity	61
Smoker	53
Hypertension	50
Dyslipidemia	34
Contralateral hip arthroplasty	19
Diabetes mellitus	15
Hyperuricemia	7

2.3. Diagnosis

All patients were originally referred from primary care to the orthopedic surgeon for presenting pain with mechanical characteristics and functional limitation in the hip for at least one month's evolution. Clinico-radiological ONFH diagnosis performed by orthopedic surgeons during the clinical practice was confirmed by a certified-radiologist-reported MRI and/or certified-pathologist-exam of the surgical specimen, as both methods are considered the most reliable to confirm suspected ONFH cases [8, 13, 17]. In our series, the cases of ONFH that were confirmed by MRI were 11 and those confirmed by pathology were 17 (Table **1**). Regarding histology, empty osteocytic lacunae are considered the main diagnostic criterion of bone death. For MRI diagnosis, the initial specific findings are in T1-weighted image areas of low-signal intensity representing edema, which can be bordered by a hyperintense line that represents blood products, and for T2-weighted image, a second hyperintense inner line between the normal marrow and the ischemic marrow, its appearance being highly specific for ONFH, known as the double-line sign [18, 29].

2.4. Reliability Assessment

Each observer was asked to identify the presence or absence of ONFH on universally reported imaging features and universally reported imaging features [2]: 1) osteopenia, 2) blurry bone trabeculae, 3) patchy areas of lucency and sclerosis, 4) crescent sign, 5) femoral head flattening or joint space widening, and 6) secondary degenerative joint disease changes. The observers were also asked to stage all the X-rays according to the Ficat and Arlet classification system. Each radiograph was reviewed and classified by eight observers: two certified orthopedic surgeons, one certified musculoskeletal radiologist, and five certified general radiologists. The participants were unaware of the patient's previous imaging studies or disease stage. All observers were familiar with the radiological characteristics and staging systems of ONFH. Radiographic diagnostic reliability was estimated through interobserver agreement for the six previously cited imaging features and Ficat and Arlet disease stages. The strength of agreement between observers was defined based on the statistic value [30].

2.5. Statistical Analysis

The inter-rater reliability of agreement was calculated using the Fleiss' kappa coefficient for categorical ratings and Kendall's coefficient of concordance for ordinal ratings. Statistical significance was attributed to a P-value probability threshold of less than 0.05. All statistical analyses were performed using the SPSS software (SPSS Inc., Chicago, IL, USA).

3. RESULTS

Of the 60 femoral heads collected in the operating room, nine did not meet our exclusion criteria. Of the remaining 51 samples, only 28 obtained diagnostic confirmation of ONCF, by MRI, histology, or both (Fig. **6**).

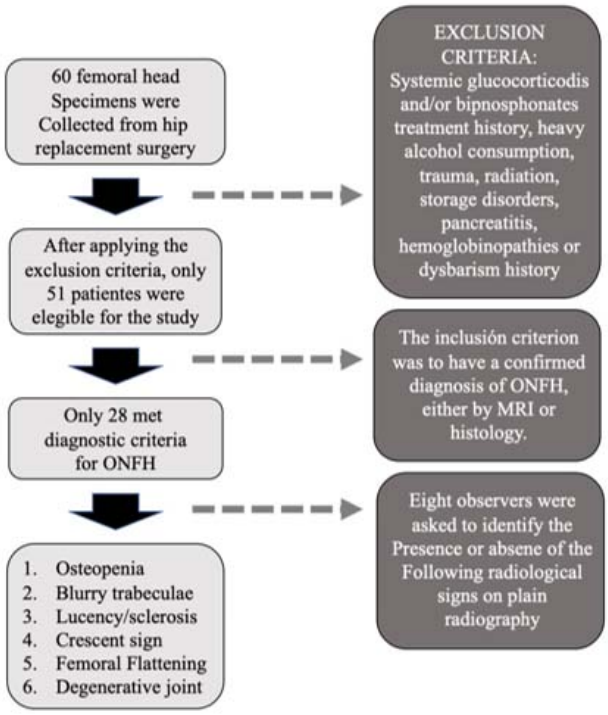

Fig. (6). Flow diagram of our patient's origin, selection and exclusion criteria, and study diagnostic endpoints.

Table 3. Results from the Fleiss' kappa analysis of reliability of imaging feature identification.

-	Kappa	P-value	Lower CI*	Upper CI*	Level of Agreement†
Osteoporosis overall	-0.056	0.124	-0.127	0.015	P
Osteoporosis radiologists	-0.054	0.279	-0.151	0.044	P
Osteoporosis orthopedists	-0.448	0.018	-0.818	-0.077	P
Blurry trabeculae overall	-0.071	0.051	-0.142	0	P
Blurry trabeculae radiologists	-0.076	0.125	-0.174	0.021	P
Blurry trabeculae orthopedists	-0.333	0.078	-0.704	0.037	P
Sclerosis overall	0.111	0.002	0.04	0.182	S
Sclerosis radiologists	0.026	0.599	-0.071	0.124	S
Sclerosis orthopedists	0.253	0.18	-0.117	0.624	F
Crescent sign overall	-0.044	0.227	-0.115	0.027	P
Crescent sign radiologists	-0.092	0.064	-0.189	0.005	P
Crescent sign orthopedists	-0.217	0.25	-0.588	0.153	P
Flattening overall	0.345	0	0.274	0.417	F
Flattening radiologists	0.455	0	0.357	0.552	M
Flattening orthopedists	-0.149	0.431	-0.519	0.222	P
OA overall	0.43	0	0.359	0.502	M
OA radiologists	0.396	0	0.298	0.493	F
OA orthopedists	0.578	0.002	0.207	0.948	M

Note: *:Upper and lower 95% asymptotic confidence interval bounds.†: Level of inter-rater agreement suggested interpretation [30]. Level of agreement: (P) Poor, (S) Slight, (M) Moderate, (F) Fair.

Reliability was assessed using the Fleiss' kappa statistical test. The results of the radiographic feature identification agreement between the eight observers are summarized in Table **3**. Concordance analysis revealed poor agreement between the observers for most of the assessed imaging features. Only the identification of the femoral head flattening and osteoarthritis signs exhibited moderate agreement with statistical significance. On the other hand, the detection of radiological osteoporosis and loss of trabeculation showed the lowest reliability, with negative kappa coefficients.

Regarding the inter-observer reliability for ONFH staging with plain radiographs, Kendall's W coefficient of concordance revealed an important and statistically significant degree of agreement between all raters, especially between orthopedists. The results are summarized in Table **4**.

Table 4. Kendall's W coefficient of concordance for Ficat and Arlet classification staging agreement.

	Kendall's W	P-value	Level of Agreement†
Ficat staging overall agreement	0.675	0.000	Substantial
Ficat staging radiologists' agreement	0.684	0.000	Substantial
Ficat staging orthopedists' agreement	0.883	0.008	Almost perfect

Note:†: Level of inter-rater agreement suggested interpretation [30].

4. DISCUSSION

In daily clinical practice, ONFH diagnosis is usually performed by orthopedic surgeons and/or radiologists, occasionally assisted by the pathologist's report [15]. The need for histopathological confirmation in many suspected cases of the disease has been frequently reported [11, 13]; thus, most of our cases were confirmed by a certified pathologist. With regard to the use of MRI in daily practice, it has been reported that "suspected ONFH despite negative radiographs" remains the main indication for this test [31]. In our sample, one-third of the cases were confirmed by MRI. As previously mentioned, simple radiographs are still considered the cornerstone of the clinical diagnosis of ONFH [14], with most patients undergoing hip replacement surgery being diagnosed using only this technique [31]. Regarding radiographic reliability in ONFH, the literature has focused on studying diagnostic and staging agreements [25, 32, 33], with a mild interest in subchondral fracture detection [34]. To clarify the potential causes of misdiagnosis in ONFH imaging, we analyzed the recognition of the characteristic radiological features. When comparing interobserver reliability in identifying the typical radiographic features of ONFH, we observed poor agreement for most of the assessed characteristics. This lack of reliability was found to be more important in imaging features considered to be initial radiological signs of the disease, such as osteopenia, loss of trabeculation, and patchy sclerosis [16], thus confirming radiographic insensitivity in the early stages of ONFH. These findings are consistent with those of previous studies [29]. Chee *et al.* demonstrated that the sensitivity and specificity of radiographs for diagnosing ONFH are especially reduced in the precollapse stages [14]. On the other hand, moderate agreement was observed in the identification of femoral head flattening and osteoarthritis signs, which is consistent with previous studies [15, 25]. In the present study, when the diagnostic reliability of radiologists and orthopedic surgeons was compared, no substantial differences were found, with a slightly better concordance among radiologists in femoral head flattening identification and a moderately superior agreement between orthopedists in osteoarthritis detection. Literature regarding ONFH reliability for staging correlation has evidenced a poor inter-rater agreement,

especially among the intermediate stages, with average kappa values ranging from 0.39 to 0.56 [15]. In the present work, Kendall's W coefficient of concordance revealed an important and statistically significant degree of agreement between all raters, especially between orthopedists. In this sense, our better results in staging reliability are probably due to our observer's expertise, particularly among orthopedists. In this respect, previous studies have shown the positive effect of expertise in radiographic diagnosis and staging of ONFH [14, 32, 33]. In addition, it must be considered that, although the Ficat and Arlet classification system is not free of controversy, it was originally conceived for plain radiographs [27, 32].

5. STUDY LIMITATIONS

Although the aim of the present study was to highlight the weaknesses of plain radiographs in ONFH diagnosis, some limitations should be considered before drawing conclusions. First, the necessity for diagnostic confirmation *via* histopathology or MRI allowed us to analyze only 28 suitable cases; thus, the limitations of a small sample size and its monocentric nature should be considered. Second, the study did not include control radiographs, because all imaging features were assessed in ONFH-confirmed patients. Third, this was a retrospective study with two orthopedic surgeons and six radiologists; thus, it remains unclear whether the diagnostic performance of these eight raters is representative of all the readers. Fourth, the raters were only allowed to use anteroposterior view of the hip to assess radiographic features, excluding the frog–leg view. Fifth, the accuracy, or how close an experimental observation lies to the true value, was not measured.

CONCLUSION

Even for the most characteristic radiographic feature identification of ONFH, there is a lack of agreement among qualified observers. The reliability of plain radiography for the detection of basic radiological elements is even weaker in the early stages of the disease. Therefore, to enhance the current diagnostic precision of ONFH, we advocate for a multidisciplinary diagnostic approach and the need to use complementary imaging tests, such as CT and MRI.

LIST OF ABBREVIATIONS

ONFH	=	Osteonecrosis of the femoral head
OA	=	Osteoarthritis

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Consent and approval were granted by the Institutional Review Board (Comité de Ética en Investigación Clínica de Cantabria) in February 2018, Identification Code 2018.014.

HUMAN AND ANIMAL RIGHTS

No animals were used in this research. All procedures performed in the studies involving human participants were in accordance with the ethical standards of institutional and/or research committee and with the 1975 Declaration of Helsinki, as revised in 2013.

CONSENT FOR PUBLICATION

An informed consent was obtained from all the subjects involved in the study.

STANDARDS OF REPORTING

The STROBE guidelines were followed.

AVAILABILITY OF DATA AND MATERIALS

The data supporting the findings of the article is readily available to the scientific community by contacting [A. C-P].

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CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

ACKNOWLEDGMENTS

Declared none.

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