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Osteonecrosis of The Femoral Head Based on The Ficat and Arlet Classification: A Literature Review

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ABSTRACT

Osteonecrosis is a degenerative bone condition characterized by the death of cellular bone components due to disruption of the subchondral blood supply. Osteonecrosis of the femoral head is the most common location of osteonecrosis. Osteonecrosis causes significant morbidity and impairs quality of life. Early detection of osteonecrosis is important to achieve a good outcome. The Ficat and Arlet classification describes four stages of disease progression based on clinical and radiographic findings. It is generally agreed that the successful treatment of patients with osteonecrosis is directly related to the stage of disease at diagnosis, emphasizing the importance of a reliable classification system. Timely intervention during the early stages of the disease can help in maintaining joint integrity, minimizing pain, and preventing the need for more invasive procedures such as joint replacement. The review focuses on the Ficat and Arlet classification in cases of osteonecrosis of the femoral head.

Keywords: osteonecrosis; Ficat; Arlet.

INTRODUCTION

Osteonecrosis is a degenerative bone condition characterized by the death of cellular bone components due to disruption of the subchondral blood supply. Osteonecrosis also known as avascular necrosis, commonly affects the epiphyses of long bones in weight-bearing joints.[1,2]

The list of risk factors for osteonecrosis is trauma, use of corticosteroids, alcohol abuse, smoking, hemoglobinopathy (e.g. sickle cell anemia), coagulation disorders, myeloproliferative disorders (Gaucher, leukemia), solid organ transplantation, chronic renal failure/hemodialysis, pancreatitis, systemic lupus erythematous, *sindrom cushing,* disease *caisson*, HIV, hyperuricemia, hyperlipidemia, pregnancy, radiation, and smoking. In some cases, the cause of osteonecrosis cannot be identified and is classified as idiopathic osteonecrosis.[3] Osteonecrosis causes significant morbidity and impairs quality of life.[4]

Early detection of osteonecrosis is important to achieve a good outcome. Osteonecrosis is often asymptomatic until it is severe, indicating the importance of monitoring and diagnostic measures. Timely intervention during the onset of the disease can assist in maintaining joint integrity, minimizing pain, and preventing the need for more invasive procedures such as joint replacement. [5]

EPIDEMIOLOGY

Osteonecrosis occurs most often in the *hip joint* (femur head) but can occur in other anatomical structures such as the *shoulder joint*, humerus, knee, and *ankle joint,* and is rarely seen in the smaller bones of the wrist, such as the *lunate*. [6] There is no global prevalence data regarding the incidence of osteonecrosis.

Epidemiological research in England assessed the incidence of osteonecrosis in the British population from 1989 to 2003, finding an increase in cases from 1.4 per 100,000 people to 3.0 per 100,000 people. [7] The majority of cases occur in *hip joints* (75.9% of cases). 2 Analysis of the Japanese population has shown an incidence rate of 1.9 per 100,000. The mean age of affected patients is 47 years and there is a male-to-female ratio of 3:1. [8]

A study in Sweden shows the *incidence rate* of osteonecrosis is 4.7 cases//10,000 people with a *10-year risk* 0.4%. This research shows the strongest risk factors for osteonecrosis are *hip fracture*, solid organ transplantation, dialysis, and osteomyelitis. History *hip fracture* occurs in 21.7% of osteonecrosis cases, but osteomyelitis, dialysis, and solid organ transplantation are present in only 0.5 to 2% of cases. Solid organ transplantation is associated with a high risk of osteonecrosis due to the use of high doses of corticosteroids. The cause of osteonecrosis in dialysis and solid organ transplantation is increased secretion of parathyroid hormone. [9]

PATHOPHYSIOLOGY

Osteonecrosis can have many etiologies. However, all causes of osteonecrosis will ultimately cause disruption of intravascular circulation which results in inadequate oxygen and nutrient supply to the affected area (Figure 1).[10] Intravascular circulation disorders are generally caused by traumatic and non-traumatic causes. Regarding traumatic causes, it is important to note that most of the blood supplied comes from the retinacular artery supplying the superolateral part of the femoral head.[11] This retinacular artery originates from the lateral epiphyseal artery which is a branch of the medial circumflex artery. In non-traumatic cases, two theories are debated: the first concerns the occurrence of intravascular coagulation, and the second attributes extravascular compression ischemia. [6]

Intravascular coagulation can occur due to damage to blood vessels. Blood vessel occlusion occurs due to thrombus formation due to abnormalities in the shape of red blood cells such as in cases of sickle cell anemia or fat or nitrogen embolism. Extravascular compression can arise due to damage to the femoral head blood vessels which allows the accumulation of fat and blood in the extravascular space which causes changes in blood flow through local compression.[6]

The pathophysiological mechanism often used today is osteonecrosis, which is an interaction between blood vessel damage, changes in bone cell physiology, risk factors, and genetic factors. Vascular disorders arise as the end result of coagulation disorders seen in hypercoagulable conditions such as sickle cell anemia, hereditary thrombophilia, antiphospholipid antibodies, malignancy, and inflammatory bowel disease/*inflammatory bowel disease* (IBD). Changes in bone cell physiology are often proposed as part of the osteonecrotic process and the hypothesis is that osteonecrosis arises due to impaired mesenchymal differentiation causing damage to the bone structure. Under physiological conditions, it takes about three months to build new bone with effective mechanical properties, whereas osteoclasts need three weeks to influence the mechanical strength of trabecular bone. Thus, any mesenchymal cell dysfunction that causes altered osteogenic differentiation and altered blood flow through increased adipogenic volume will ultimately favor osteonecrosis. [6]

Corticosteroid use and alcohol consumption are the most common risk factors for osteonecrosis. Administration of corticosteroids induces vasoconstriction and causes increased production of procoagulant factors. It also increases adipogenesis, decreases osteogenesis, and downregulates bone repair and remodeling through the production of fat emboli. Wang et al listed five main theories of pathogenesis *Steroid-induced osteonecrosis of the femoral head* (SONFH), namely lipid metabolism disorders, decreased osteogenesis potential, inadequate blood supply, cell apoptosis, and gene polymorphism.[12] Various reports conclude that corticosteroids can be described as an independent variable, especially at high doses, and increase the risk of osteonecrosis up to 20-fold. Alcohol consumption will alter mesenchymal differentiation and may result in a decreased ability to differentiate towards the osteoblastic lineage. Therefore, both corticosteroids and alcohol have a major influence on bone marrow differentiation and blood supply. There is a hypothesis regarding genetic involvement in the pathogenesis of osteonecrosis; 3 lineages have been described for autosomal dominant inheritance of osteonecrosis. This autosomal dominant gene mutation is mapped to chromosomes 12-13 and is associated with type II collagen abnormalities which contribute to OFNH. However, to date, there are no screening markers available. [6]

Whatever the underlying cause, all forms of ONFH are associated with impaired blood flow. After the onset of ischemia, histological signs of bone marrow necrosis and osteocyte death become apparent within 24 to 72 hours. Then, saponification of free fatty acids occurs in the extracellular matrix as well as the expression of calcium ions leading to an inflammatory response. Eventually, the acellular trabecular bone is replaced by inferior woven bone that cannot withstand normal loading and may collapse. [6]

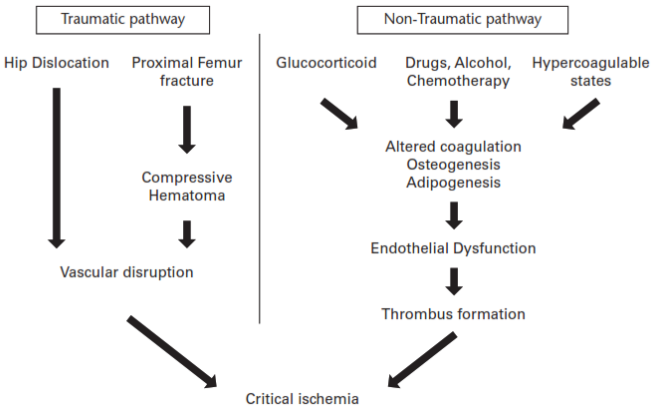

FIGURE 1: Pathogenesis of osteonecrosis of the femoral head (ONFH) [6].

Osteonecrosis is also associated with increased differentiation of mesenchymal stem cells along the adipogenic pathway, and deficiencies in osteogenic and vasculogenic pathways. Anatomic areas experiencing osteonecrosis show chronic inflammation, cell death, and impaired resolution and repair.

Research on mice induced with osteonecrosis by vascular cauterization showed persistent macrophage activation and neutrophil accumulation after 6 weeks of induction.[13] Another study assessing steroid-associated osteonecrosis in mice showed upregulation *pattern recognition receptors* (PRR) that is *Toll-like receptors 4* (TLR4), an adapter protein for most TLRs: Myeloid differentiation factor 88 (MyD88), a major transcription factor for inflammatory proteins: *Nuclear Factor-Kappa B* (NF-κB), and *Monocyte Chemotaxis Protein-1* (MCP-1). [10,14]

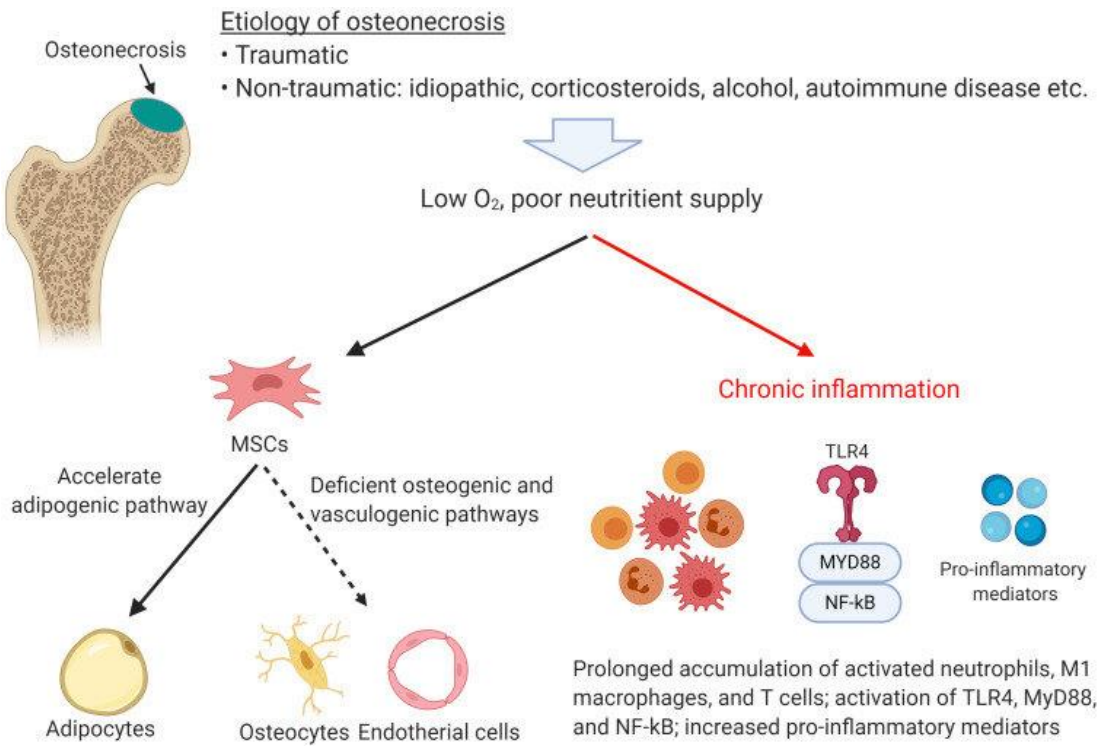

FIGURE 2: Pathogenesis of Osteonecrosis [10].

Molecules associated with acute and chronic inflammation can overlap in triggering osteonecrosis or bone healing, and play a major role in activation of the innate immune system and tissue repair. NF-κB is a major pro-inflammatory transcription factor induced by injury stimuli. NF-κB activates or licenses MSCs. TLR4 is a PRR on the cell surface and is activated by *molecular patterns associated with pathogens* (PAMP), *damage-related molecular patterns* (DAMP), and other compounds. TLR4 has two signaling pathways: the MyD88-dependent pathway (TLR4/MyD88/NF-κB) and the MyD88-independent pathway (TLR4/TRIF/IRF3). The My D88-dependent pathway activates NF-κB and promotes MCP-1 expression. MCP-1 is a chemoattractant for cells of the monocyte-macrophage lineage and the MSC-osteoblast lineage. MCP-1 induces monocyte/macrophage proliferation and promotes osteoclast differentiation and activation. [10,15,16]

DIAGNOSIS AND CLASSIFICATION

The diagnosis of osteonecrosis is primarily based on clinical and radiographic findings. The typical clinical presentation includes increasing pain, stiffness, and crepitus, generally continuing with a period of minimal symptoms. During the physical examination, patients usually complain that range of motion/*range of motion* (ROM) is limited and there is pain.

In cases of osteonecrosis of the femoral head, the pain worsens during forced internal rotation, there is a change in gait, pain at rest, and pain in the hip joint and groin accompanied by referred pain in the buttocks and thighs at an advanced stage.[17]

Early identification of this disease provides better outcomes. Many imaging techniques have proven helpful in detecting signs of bone necrosis, including X-ray, *Magnetic Resonance Imaging* (MRI), *Computed Tomography* (CT), and radionuclide examination. Imaging evaluation of osteonecrosis should begin with X-ray, an inexpensive and widely available technique. CT and X-ray are less sensitive than MRI and show necrotic changes during later stages. Nevertheless, the signs of osteonecrosis are often clear enough to not require additional radiological evaluation.[17]

MRI is the gold standard for the diagnosis of osteonecrosis and allows to exclusion of other differential diagnoses. MRI allows early diagnosis of osteonecrosis and can help identify patients at risk of fracture. Identification of bone marrow edema in the proximal femur and joint effusion is an important prognostic factor. *T1 weighted* shows limited subchondral linear low signal intensity, while T2 shows double line signs/*double dash*.

However, MRI cannot be used after fracture fixation with metal implants, limiting its usefulness, especially in patients who experience bone ischemia after surgical procedures. [18]

Fan et al. compare *single photon emission computed tomography* and CT (SPECT/CT) to determine the risk of bone necrosis in patients after femoral head fracture. The results of the study revealed that SPECT is most useful for determining the prognosis of osteonecrosis in patients aged >58 years and with *displaced fractures*. [19] Diagnostic methods based on nuclear medicine, such as *Positron Emission Tomography* (PET) or *technetium bone scan*, can also be used to detect early-stage osteonecrosis and help predict disease progression. [17]

Although the patient's medical history, clinical features, and radiographic examination may indicate osteonecrosis, the clinician should include other clinical entities in the differential diagnosis. [17]

Osteonecrosis of the femoral head is divided into two classes: traumatic and atraumatic. 70% of atraumatic cases are bilateral. Common classifications that chart the phases of hip osteonecrosis include the Ficat and Arlet, and Steinberg classifications. Ficat and Arlet described four stages of disease progression based on clinical and radiographic findings. [2]

CLASSIFICATION OF FICATES AND ARTLETS

TABLE 1: Femur head Osteonecrosis stages based on Ficat and Arlet [22].

Ficat-Arlet (1964)	Modified Ficat (1984)	X-ray	MRI	*Bone scanner*	Signs and symptoms	Information
Stadium 0	Stadium 0	Normal	+/-	Enhancement *absorption*, decline rarely occurs an *absorption*	Generally absent, known as *hips still*	Patients are generally examined on *hip joint* contralateral to ipsilateral osteonecrosis.
Stadium I	Stadium I	Sometimes normal, patchy osteoporosis, blurred trabecular pattern, slight loss of clarity	+	Decline	+	This stage can generally not be seen on X-ray, increased suspicion is required for early diagnosis.
IIA Stadium	Stadium II	Osteoporosis, sclerosis, cysts	+	Decline	+	
Stadium IIB		Subchondral fracture (*crescent moon sign*), *alignment* segments of the femoral head (*fight-of-round performance*)	+	Decline	++	
Stadium III	Stadium III	Loss of contour of the femoral head, presence of sequestrum, normal joint space	Not needed	Not needed		
Stadium IV	Stadium IV	The femoral head is affected by *alignment* and collapse, reduced joint space, acetabular osteoarthritic changes.	Not needed	Not needed		Advanced stage arthritis

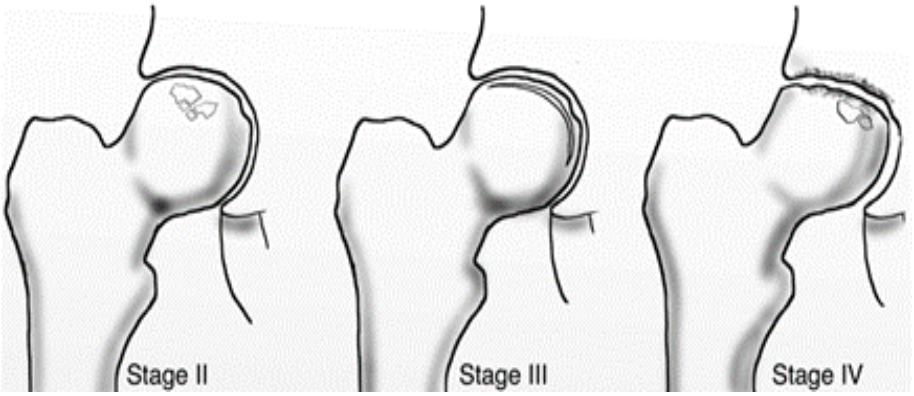

FIGURE 3: Visualization of osteonecrosis of the femoral head based on the Ficat and Arlet classification [20].

The Ficat and Arlet classification was the first classification system developed in the 1960s. This system is most widely reported by studies of osteonecrosis hip joints. This classification has been modified several times, but the version of the classification with division into 4 stages is the most widely used classification. [20] Stage I is a transitional stage and the patient is asymptomatic with normal radiographic findings but with increased uptake bone scanner. Stage II represents the reparative stage and some diffuse sclerotic and cystic lesions can be observed before they occur in alignment with the femoral head. Stage III is characterized by a subchondral fracture (crescent sign). Stage IV involves loss of anatomical sphericity of the femoral head collapse of the femoral head and joint damage. This damage causes further progressive degeneration such as osteoarthritis and acetabular degeneration. There are several weaknesses in this system. First, the description of the various stages is ambiguous and overlapping and does not allow quantifying the size of the lesion, making it impossible to quantify subtle progression. Furthermore, the classification of advanced stages relies on invasive diagnostic techniques, such as core decompression, which can cause secondary trauma. [21]

An ideal classification system should be practical, valid, reliable, and have prognostic importance. This will also help to choose between different treatment options and facilitate communication between researchers. This will provide the basis for uniform reporting of results. There is controversy surrounding the classification of osteonecrosis of the femoral head and the indications and efficacy of various treatment options in preserving the femoral head. Controversy surrounds the natural history of progression and whether intervention is better at preserving femoral head contour than no treatment. The lack of a universally accepted classification system makes it difficult to compare and analyze data coming from different health centers. [23]

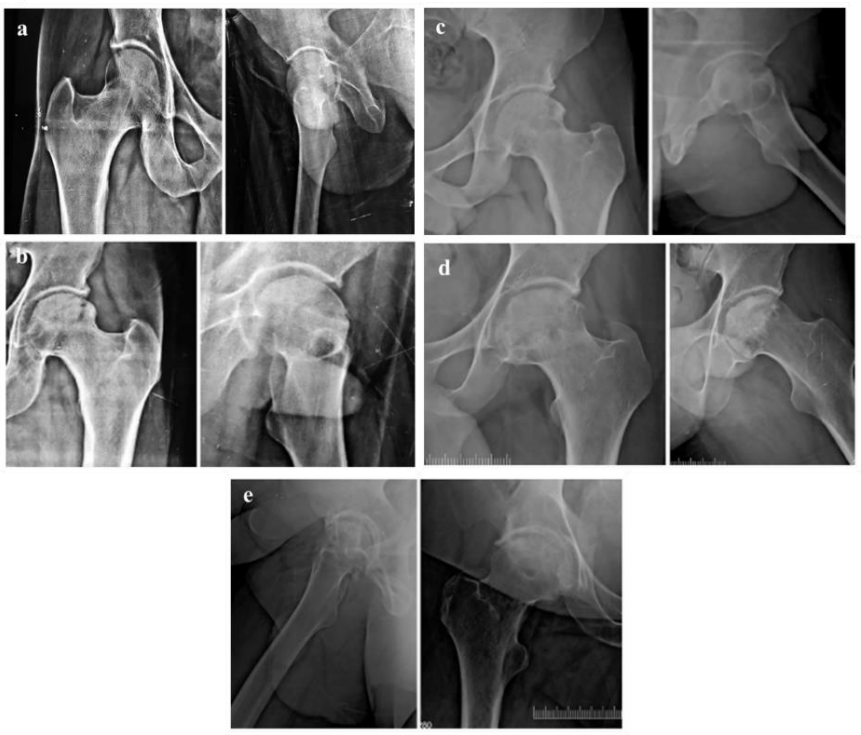

FIGURE 4: Ficat-Arlet stage of femoral head osteonecrosis assessed using X-ray (a) stage I (b) Stage II (c) Stage III (d) Stage IV [22].

Osteonecrosis of the femoral head generally affects patients with an average age in the mid-thirties, this can cause collapse of the femoral head if not treated properly in most patients. Spontaneous resolution of femoral head necrosis has also been reported in patients undergoing renal transplantation. Thus, preserving the femoral head is a primary goal in diagnostic and treatment strategies. Classification systems are useful in outlining criteria for early diagnosis. However, there are no specific radiographic features for osteonecrosis. Every case of osteonecrosis must go through an initial preradiographic stage. Therefore, a useful classification system in assessing osteonecrosis of the femoral head should outline the criteria and methods for early diagnosis at the pre-radiographic stage. [24]

Ficat and Arlet are simple and easy-to-use systems. However, this classification is often criticized because it does not include specific MRI findings. Additionally, there is controversy regarding whether the hip joint which shows a crescent moon sign without chondral flattening should be grouped with the hip joint with chondral flattening. [24] In addition, various studies have questioned the inter- and intra-observer reliability of classification systems. Kay et al evaluated how adequate X-ray was using the Ficat classification. This research shows that there is variability between observers which differs significantly in 36% of the photo reading results pelvis, with a low kappa (K) statistical value of 0.56. Intra-observer variability was similar, as 40% of hips had significant differences, with a kappa (K) statistic of 0.82.[25] They concluded that plain radiography alone is insufficient to evaluate osteonecrosis of the femoral head. Interobserver reliability and intraobserver reproducibility of the Ficat classification were also assessed by Schmitt-Sody et al through X-ray and MRI readings. Results showed mean inter-observer kappa reliability coefficients of 0.39 and 0.32 for the first and second readings, and averages of 0.39 and 0.34 for the first and second readings for MRI. For intra-observer reproducibility, the mean kappa value was 0.52 for X-ray and 0.50 for MRI.26 Poor interobserver reliability and intraobserver variability led them to conclude that Ficat was insufficient to reliably assess osteonecrosis status. Other studies involving the Ficat classification system have shown that the system has inadequate inter- and intra-observer reliability and cannot be used alone to classify and stage hips with osteonecrosis of the femoral head. [24,27]

MANAGEMENT

Management of osteonecrosis of the femoral head consists of conservative and surgical treatment. If based on the Ficat and Arlet classification, Stages 0–II with the femoral head remaining intact are considered early stages, while stages III–IV are considered late stages. It is generally agreed that the successful treatment of patients with osteonecrosis is directly related to the stage of disease at diagnosis, emphasizing the importance of a reliable classification system. [28]

Stages I and II

At this stage, non-operative treatment may have a role although it usually results in a poor prognosis. Most nonoperative treatment methods involve weight-bearing restrictions, pharmacological agents, and various external, biophysical, and nonoperative modalities. [28]

Conservative treatment of osteonecrosis aims to improve hip function, prevent collapse of the femoral head, and delay necrotic changes. Limiting weight using a cane, crutches, or a walker is one way to delay the progression of the disease. However, several papers show that reducing joint reactive forces does not slow disease progression. [17]

Pharmacological interventions in the early stages include: [28]

i. Anticoagulation agents (Enoxaparin) can prevent the development of osteonecrosis hip joint stages I and II.

ii. Bisphosphonates (Alendronate) may interfere with the resorption of necrotic bone, which may delay subchondral collapse and progression of arthrosis.

Other pharmacologic agents proposed as treatments for osteonecrosis are statins, vasodilators, bisphosphonates, and other agents still under investigation. Pharmacological treatment is mostly used in the early stages of the disease. Its effectiveness is limited, and there are no clear recommendations for its use in osteonecrosis due to a lack of evidence. Many patients continue to undergo surgery after pharmacological treatment.[17]

Surgical intervention in the early stages seeks to preserve the femoral head: [28]

i. Core decompression aims to reduce intraosseous pressure and possibly increase in growth of blood vessels, thus delaying or eliminating the need for Total Hip Arthroplasty (THA). This is achieved by creating a tunnel or several small holes drilled through the bone proximal to the femur into the necrotic lesion. This procedure can use bone graft vascularized agents or biologic agents to induce bone repair. Its use, combined with using autologous bone or bone marrow, may increase the success rate. CD is indicated when the etiology is reversible to reduce intraosseous pressure and stimulate bone healing. In meta-analysis studies, it was shown that the success rate is much higher compared with other non-surgical management in early-stage disease. Core decompression is the treatment of choice for early stages, before the crescent moon sign, however, some surgeons may proceed to perform decompression even in asymptomatic cases with large lesions. [28,29]

ii. Corruption Fibular can be used alone or in conjunction with CD or as a treatment option alone. Vascularized and non-vascularized fibula grafts have been used in the past and have provided good results in young patients. [28]

Cellular therapy is one of the osteonecrosis therapy options, cellular therapy is mainly based on mesenchymal stem cells (MSC) originating from bone marrow, adipose tissue, or umbilical cord. MSCs initiate the process of revascularization and regenerate bone tissue. [30] MSC stem cells also play a role in maintaining mitotic multiplication while being able to differentiate into various cellular types, such as osteoblasts, osteocytes, chondrocytes, and adipocytes. MSCs have been shown to increase tissue regeneration when transplanted into necrotic bone areas. Cellular therapy techniques using MSCs are used in conjunction with classic CD procedures and involve the collection of autologous bone marrow aspiration, isolation of the mononuclear cell fraction, and injection into the necrotic zone of the femoral head through the previous CD tract. This treatment strategy is based on the hypothesis that multipotent MSCs in bone marrow aspirate can repopulate the necrotic zone trabeculae within the femoral head, enhancing regeneration and remodeling of necrotic bone. [31]

Stage III and IV

The final stage where the sphericity of the femoral head is affected or even worse, the femoral head has begun to collapse, can only be managed operatively. Total Hip Arthroplasty (THERE IS) Traditional medicine is the treatment of choice. Hemiarthroplasty Resurfacing And total hip resurfacing has been reported as a treatment option but appear to be less reliable than THA. [28] THERE IS should be performed in patients with significant femoral head collapse, loss of hip function, and severe pain. This procedure involves the removal she was and socket of the hip joint and replacing them with artificial implants. THA is a suboptimal option for young patients due to activity restrictions and the possibility of future implant revision. Results are good after THA in most patients, especially pain relief and restoration of hip function. [1,17] Osteotomy and arthrodesis hip joint are a less common option but may be useful as a temporary procedure in certain cases such as very young active patient populations. This procedure is more commonly performed in the intermediate stages and of course in cases where the shape of the femoral head can be maintained. [28]

CONCLUSION

Osteonecrosis is a bone condition characterized by the death of cellular components of the bone due to disruption of the subchondral blood supply. The diagnosis of osteonecrosis is primarily based on clinical and radiographic findings. Typical clinical presentations include increased pain, stiffness, and crepitus. During the physical examination, patients usually complain of limited range of motion and pain. The Ficat and Arlet classification was the first classification system developed in the 1960s. This system is most widely reported by studies of hip osteonecrosis. There are several weaknesses in this system. First, the description of the various stages is ambiguous and overlapping and does not allow quantifying the size of the lesion, making it impossible to quantify subtle progression. Research regarding the validity and reliability of this classification shows that it is not reliable in assessing osteonecrosis of the femoral head inter- and intra-observer. If based on the Ficat and Arlet classification, Stages 0–II with the femoral head remaining intact are considered early stages, while stages III–IV are considered late stages. In the early stages, this non-operative treatment may have a role although it usually results in a poor prognosis. Conservative treatment can include weight limitation and pharmacotherapy. Surgical interventions recommended in the early stages are core decompression, fibular graft, and cellular therapy. Operative interventions that can be carried out at the final stage are: Total Hip Arthroplasty (THA), osteotomy and arthrodesis pelvis joint.

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