

Review of Current Concepts Femoral of Head Osteonecrosis

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ABSTRACT

Background: The avascular necrosis (AVN) or osteonecrosis of the femur head (ONFH), an illness with several etiological factors, impacts young populace and otherwise handled prompt, causes the collapse of femur head eventually requiring hip arthroplasty. **Objective:** the present article aims to provide an overview of epidemiology, pathophysiology of osteonecrosis along with diagnosis methods and non-surgical in early stages and surgical treatment methods. **Methodology:** Comprehensive search of the literature was conducted in the following databases; PubMed, and SciVerse Scopus for studies published before November 2017. The PubMed database was searched using an algorithm comprising relevant MeSH terms including “Osteoporosis”, “femoral head osteonecrosis” AND “management” “diagnosis”.

Conclusion: Osteonecrosis is a destructive pathology that eventually results in bone death through loss of blood to the bone, it involves almost every bone including the femoral head while early start of osteoarthritis could ultimately demand hip arthroplasty when non-operative procedures and joint-sparing treatments fail. Nevertheless, recent technological advances in surgical treatment methods have improved outcomes and should help patients recover from this functionally debilitating joint disease.

Keywords: Avascular necrosis, Osteonecrosis, Etiological.

INTRODUCTION

Avascular necrosis (AVN), aseptic necrosis, ischemic necrosis or Osteonecrosis of the femur head (ONFH) is a pathologic condition with several underlying causes that eventually results in the collapse of femur head and hence demanding hip arthroplasty^[1]. Early presentation of AVN is usually painless with nonspecific signs and symptoms, yet pain develops gradually with a profound limitation of hip motion. The pain is not only localized to the groin area, but can also extend to the knee, greater trochanteric region or ipsilateral buttock. Pain has an inverse relationship with rest while it can be aggravated by weight gain^[1,2].

The prevalence of avascular necrosis of the femoral head is not clear however, but each year in the USA there are approximately 10000-20000 new cases diagnosed with AVN. It is considered that a percentage between 5-18% of a total of 500 000 hip replacement surgeries performed in a year are performed on patients diagnosed with avascular necrosis of the femoral head, the cost is estimated to be about 1 billion dollars annually^[3].

meanwhile, in Japan, there is a study revealing a trend of 2500-3000 new cases of avascular necrosis of femoral head every year^[4].

Another retrospective study conducted in England, in 2009, the estimated incidence of disease,

between 1989 and 2003, was from 1.4 to 3 cases per 100 000 inhabitants^[5].

The rise in the number of patients diagnosed with AVN has increased in recent years across the world as a result of the broad use of corticosteroids and the increase in alcohol consumption along with the high incidence of local trauma. Given that the life expectancy of patients with associated diseases has increased led to a higher incidence of this disease. There was an increased number of patients that had access to modern diagnostic imaging, which has helped in the early detection of AVN through MRI and CT^[3].

Noninvasive diagnostic tests used in detecting AVN include Plain radiography, magnetic resonance imaging (MRI), computed tomography (CT), skeletal scintigraphy, and single photon emission computed tomography (SPECT). Location of the affected hip by AVN can be determined by antero-posterior radiographs. Nevertheless, abnormalities in the subchondral area might be missed due to the fact that the former and posterior acetabular margins overlap the exceptional part of the femoral head. Hence, it's crucial to order a very good quality side X-rays of the femoral head. Consequently, a cross table lateral radiograph is not as adequate as a frog

leg side to represent the architectural details of the femoral head ^[4,5].

Furthermore, Technetium 99m diphosphonate imaging serves as a helpful technique for spotting osteonecrosis ^[6]. This was backed up by many researches that have confirmed that MRI is one of the most precise of all imaging methods ^[7].

The double line sign is an MRI finding seen at the periphery of a region of osteonecrosis (avascular necrosis, bone infarct). It is best seen on T2 weighted sequences and consists of an inner bright T2 line representing granulation tissue and an outer dark line representing sclerotic bone. This sign is reported in up to 80% of cases ^[8].

The high spatial resolution and contrast resolution of CT allow analysis of morphologic features. The sensitivity of CT in detecting early AVN is 55%, which is similar to the sensitivity of planar nuclear medicine imaging ^[9]. CT is more appropriate in evaluating the extent of involvement, such as subchondral lucencies and sclerosis during the reparative stage, before the onset of femoral head collapse and superimposed degenerative disease.

The original classification system was described by Ficat and Arlet in 1964 ^[10]. It consisted of Stages 1 through 4. Ficat proposed a modification in 1985 ^[11]. This latter Ficat classification recognized five different stages of bone necrosis from Stage 0 to Stage 4 ^[11].

Stage 0 is known to be the “silent hip” which is preclinical and preradiographic. A Stage I the radiographs are regular. In Stage II the contour of the femoral head is normal however the radiographs show proof of bone remodeling consisting of cystic and sclerotic regions. Stage III is characterized by disruption of the normal round contour of the head and accumulation of sequestrum that might increase or maintain the normal joint space. While A patient with Stage 4 disease presents with complete collapse of the femoral head into a flattened contour and decreased joint space. Stages 3 and 4 of the Ficat classification system originally were grouped together in the Ficat and Arlet classification system as Stage 4 ^[10].

Steinberg *et al.* ^[12] expanded the Ficat system by dividing Stage III lesions into femoral heads with and without collapse or hips with acetabular involvement. The Japanese Investigation Committee introduced the concept of location of the lesions.

Although patients in the advanced stage of AVN most often wind up with hip arthroplasty, hip salvage

surgical treatment has helped manage the disease progression and symptoms of some of these patients when diagnosed at the pre-collapse stage.

Furthermore, recent techniques consisting of range of medicines have additionally been made use of for non-invasive/non-operative management of AVN.

In the present article, we aim to review epidemiology, pathophysiology and highlight diagnosis methods; moreover, overviewed non-surgical in early stages and surgical treatment methods.

METHODOLOGY

Comprehensive search of the literature was conducted in the following databases; PubMed (U.S. National Library of Medicine, USA), and SciVerse Scopus (Elsevier Properties S.A, USA) for studies published before November 2017. The PubMed database was searched using the MeSH (Medical Subject Headings); a term osteoporosis and keywords “femoral head osteonecrosis”, “management”, “diagnosis”. Restriction to English language with human subjects were applied to our search.

The study was done after approval of ethical board of King Khalid university.

DISCUSSION

Epidemiology of AVN

Most AVN cases are secondary to trauma, however non-traumatic AVN can also occur, but the underlying pathology is unclear ^[13].

In the published literature, it has been reported that nearly 5%-18% of all hip arthroplasties are finished on patients with a primary medical diagnosis of osteonecrosis ^[14].

Non-traumatic AVN has been associated with a number of risk factors including ^[13,15]:

- **Drug/Substance use:** Corticosteroid use, alcohol consumption, smoking cigarettes, immunosuppressive therapy.

- **Autoimmune diseases:** particularly systemic lupus erythematosus and rheumatoid arthritis, also vasculitis, sickle cell anemia and malignancies are common.

- **Fematologic/thrombotic disorders:** such as IBD, gout, solid organ or bone transplantation, asthma and metabolic disorders such as diabetes mellitus, and renal failure.

- **Potential etiologies for osteonecrosis** included childhood years; background of slipped funding femoral epiphysis (SCFE), deep sea diving or various

other hyperbaric conditions. In addition to cancer, renal failure or dialysis, osteoporosis, connective tissue disease, and osteoarthritis infections include

- **Viral infections:** human immunodeficiency virus (HIV) infection.
- **Age:** age 35 years to 45 years, and threat elements for 75%-90%.
- **Gender:** Males are affected up to 3 times more than females, and reciprocal femoral head osteonecrosis is discovered in as much as 75% of situations

Incidence of 1.1% in adolescents aged <20 years and 1.5% in patients aged <18 years. The incidence of AVNFH after femoral IM nailing in adolescents reportedly ranges from 1.4 to 2.0% ^[16].

- **PATHOPHYSIOLOGY**

The initial pathologic characteristics of AVN are necrosis of hematopoietic cells and adipocytes followed by interstitial marrow edema. Osteocyte necrosis occurs after nearly 2 to 3 hours of anoxia, but histological signs of osteocyte death do not appear until approximately 24 to 72 h after oxygen deprivation^[17]. The blood supply to the femoral head initiates from the basicervical extracapsular articular ring and ascending branch of the medial and lateral femoral circumflex artery (MFCA). These branches enter the metaphyseal region and the nonarticular portion of the epiphysis of the femoral head, The deep branch of the MFCA has been cited as the most important blood supply to the femoral head ^[18]. The location of these vessels makes them susceptible to direct injury in the setting of trauma.

The disturbance of this blood supply can be multifactorial, either extravascular or intravascular. The mechanism of trauma-triggered extravascular disruption can be explained as follows:

It usually starts with fractures of the proximal femur which in turn result in displacement of the neck affecting the basicervical arterial ring, while hip dislocations can interrupt the ligamentum teres and cause intracapsular hematoma. This renders the integrity of the extracapsular ring an essential element for the survival of the femoral head.

Moreover, Intravascular embolic matter such as clots, lipids, or sickle cells can also occlude the terminal arterioles in the subchondral bone of the femoral head ^[19].

further to infarction, marrow cells and oxygen- and nutrient-deficient osteocytes come to an end unless they can obtain adequate blood supply from collateral circulation. However, since the collateral

blood circulation is already limited, capillary arterIALIZATION turn unable to regain sufficient circulation to the cells. In addition to vascular compromise and programmed cell death, faulty bone fixing is also a crucial element of osteonecrosis^[20].

Steroids has been shown to increase mRNA expression of PPAR- γ and and decrease mRNA expression of Cbfa1 which supports the hypothesis that dexamethasone promotes adipogenesis while inhibiting osteogenesis. Additionally, these studies also suggest that dexamethasone impairs angiogenesis by suppressing the production of VEGF and hence, acts as a factor in steroid- and alcohol-related osteonecrosis, as it results in compression of venous sinusoids and congestion which eventually generate bone infarction^[21].

three families with idiopathic ANFH in which there was autosomal dominant inheritance of the disease and reported that the familial ANFH gene mapped to a 15-cM region between D12S1663 and D12S1632 on chromosome 12q13. In particular cases, hereditary variables, such as mutations in the COL2A1 gene, have been connected with the pathogenesis of osteonecrosis ^[22].

Likewise, weight bearing is a key factor in the emphasis of AVN .Walking generates tons 2 to 3 times body weight on the anterosuperior femoral head articular cartilage and significant acetabular dome and 5 to 6 times body weight throughout running or jumping ^[23] this can significantly affect patients' lifestyle due to the Ischemic disturbance of the weight-bearing surface area in the osteonecrotic hip which limits their capacity to finish day-to-day tasks.

Infarcted subchondral bone has trabeculae that come to be thinned by osteoclastic activity, and the hypoxic atmosphere does not enable osteoblastic fixing or remodeling. The location of bone necrosis becomes surrounded by a reactive, sclerotic edge, and the weakened cancellous bone eventually stops working under the recurring lots of weight bearing, bring about subchondral fracture (the "crescent sign" on radiographs). Subchondral collapse at some point brings about articular deterioration.

- **DIAGNOSIS AND CLASSIFICATION**

Generally, Early stages of the illness are typically asymptomatic, often times some patients present after articular surface collapse has already taken place. nevertheless, Hip prognosis can be markedly

enhanced after early medical diagnosis, prior to articular collapse^[24]

Neither laboratory tests nor radiographic findings can either suggest or confirm the presence of avascular necrosis (AVN). However, the American College of Radiology (ACR) recommends pelvis and hips x-ray of the first and upmost proper diagnostic tool for patients at risk for AVN who typically present with hip pain^[25]. Yet if the results outcome were normal or showing femoral head lucencies doubtful for osteonecrosis, then MRI of the hips without contrast should follow^[25]

Moreover, Median thigh or groin discomfort with limitation of hip movement in patients less than 50 years of age ought to raise the suspicion of osteonecrosis.

Generally, Early stages of the illness can typically be asymptomatic, and some patients present after articular surface collapse has already happened. Hip prognosis can be substantially boosted with early medical diagnosis, prior to articular collapse^[24]

AVN Signs are generally aggravated with weight gain. The pain might extend be in the butts, knees, or anterior and lateral upper leg. Similarly , specific movements including hip abduction and interior rotation, and logrolling triggers excessive pain.

MRI

Because of the closed space of an MRI, patients may experience feelings of claustrophobia, as well as be bothered by the noise. This may be less of a problem with new MRI machines, if available (MIIMAC expert opinion). It has been reported that up to 30% of patients experience apprehension with MRIs and 5% to 10% endure some severe psychological distress, panic, or claustrophobia^[26]. Some patients may have difficulty remaining still during the scan. Patients are not exposed to radiation during an MRI scan, which may be more acceptable to some. Bone scanning (bone scintigraphy) using technetium-99m-labelled methylene diphosphonate (^{99m}Tc-MDP)^[26].

MRI has become the imaging modality of choice, as it is very sensitive and specific for osteonecrosis. T1 pictures on MRI generally show a serpiginous "band-like" lesion with low signal strength in the anterosuperior femoral head, and a "double-line sign" can be seen on T2 series, which depicts a high signal strength reparative interface of vascular responsive bone adjacent to necrotic subchondral bone. Radionuclide bone scans are much less sensitive and

particular compared to MRI however can be utilized to identify inflammatory task in the femoral head when MRI is contraindicated. CT is additionally much less sensitive than MRI in finding osteonecrosis and has a substantial radiation problem. Angiography and biopsy are intrusive approaches to validate osteonecrosis and consequently are only utilized as research study modalities^[6].

CLASSIFICATION AND STAGING OF AVN

An ideal classification system should be practical, valid, reliable, and of prognostic importance. It also would help to choose between different treatment options and facilitate communication between researchers. 3 most common classification systems are used:

1. 1. *Ficat classification*

Radiographs could show typical findings (Ficat phase I) or subchondral cyst formation and sclerosis (Ficat phase II), however more advanced illness entails femoral head flattening and subchondral collapse, as seen with the "crescent indicator" (Ficat phase III). Osteoarthritic joint space narrowing with osteophyte formation are findings of untreated osteonecrosis (Ficat stage IV) . Radiographs are highly specific for advanced osteonecrosis (Ficat II or III) yet not really sensitive for early modifications (Ficat I)^[10]. Descriptive details of the stages are listed in Table 1

2. 2. *Steinberg classification*

Similarly , Steinberg staging of avascular necrosis of hip is a commonly used system (at the time of writing, mid-2016) which differentiates subchondral collapse from femoral head articular cartilage collapse (flattening) (Table 1). Phases I via IV are classified by percent of femoral head participation: A < 15%, B 15%-30%, C > 30%. These dimension modifiers are taken into consideration predictors of femoral head collapse. Small lesion size and more median place are considered prognostically favorable^[6].

3. 3. *ARCO classification*

Another commonly used classification system that utilizes MRI and various other radiographic techniques is the Association Research Circulation Osseous (ARCO) staging system, which was presented in 1992 and is summarized in Table 1^[27].

Table 1. Osteoarthritic joint space narrowing with osteophyte formation findings of untreated osteonecrosis ^[16]

	Ficat ^[10]	Steinberg/U Penn ^[6]	ARCO ^[27]
Stage I	<ul style="list-style-type: none"> • Plain radiograph: normal or minor osteopenia • MRI: oedema • Bone scan: increased uptake • Clinical symptoms: pain typically in the groin 	Normal radiographs	<ul style="list-style-type: none"> • Patient may or may not be symptomatic. • Radiography and CT scan findings are unremarkable. • AVN is considered likely based on MRI and bone scan results (may be subclassified by extent of involvement [see below]). • Histology findings are abnormal.
Stage II	<ul style="list-style-type: none"> • Plain radiograph: mixed osteopenia and/or sclerosis and/or subchondral cysts, without any subchondral lucency (crescent sign: see below) • MRI: geographic defect • bone scan: increased uptake • clinical symptoms: pain and stiffness 	cystic and sclerotic radiographic changes	<ul style="list-style-type: none"> • Patient is symptomatic. • Plain radiography findings are abnormal and include osteopenia, osteosclerosis, or cysts. • Subchondral radiolucency is absent. • MRI findings are diagnostic.
Stage III	<ul style="list-style-type: none"> • Plain radiograph: crescent sign and eventual cortical collapse • MRI: same as Plain radiograph • clinical symptoms: pain and stiffness +/- radiation to knee and limp 	Subchondral collapse without femoral head flattening, "crescent sign"	Femoral head collapse, "crescent sign", no joint space narrowing
IIIA	NA	NA	Crescent is less than 15% of the articular surface. Collapse < 3 mm
IIIB			Crescent is 15-30% of the articular surface. Collapse > 3 mm
IIIC			Crescent is more than 30% of the articular surface. Collapse > 3 mm
Stage IV	<ul style="list-style-type: none"> • Plain radiograph: end-stage with evidence of secondary degenerative change • MRI: same as Plain radiograph • Clinical symptoms: pain and limp 	Subchondral collapse, femoral head flattening, normal joint space	<ul style="list-style-type: none"> • Flattening or collapse of femoral head is present. • Joint space may be irregular. • CT scanning is more sensitive than radiography.
Stage V		joint space narrowing with or without acetabular involvement	Radiography findings include narrowing of the joint space, osteoarthritis with sclerosis of acetabulum, and marginal osteophytes.
Stage VI		Advanced degenerative changes, secondary osteoarthritis	Findings include extensive destruction of the femoral head and joint.

ARCO: Association Research Circulation Osseous, NA: not applicable

TREATMENT OF AVN

Nonoperative treatment

Nonoperative management of ONFH consists of limited weight-bearing, medicinal agents and biophysical methods of treatment. The objective of medication therapy in the precollapsed phase is to improve hip function, give discomfort relief, protect against radiographic progression to subchondral fracture and collapse, and enable recovery of the necrotic lesions^[27].

No weight bearing

Restricted weight-bearing using cane, crutches or a walker is effective in early-stages ON hip (Ficat and Arlet Stage-I and II) when the osteonecrotic lesion is <15% and situated far from the weight-bearing dome (medial lesions)^[28]. Mont et al.^[29] evaluated 21 researches (n = 819 patients) based upon limited weight-bearing treatment and observed satisfactory medical outcome (no further surgical treatment) in 22% patients after 34 months. Radiological development was seen in 74% patients. There was no difference in results amongst patients following complete, partial, and nonweight-bearing programs in the research. In a systematic evaluation (degree II evidence), Mont et al.^[30] once more reported that 59% (394 of 664 hips) of asymptomatic hips had onset of symptoms or disease progression to collapse after 7 years (array, 0.2-20 years). The detectives reported enhanced threat of collapse in sickle cell illness (73%; 29 of 40 hips) and minimal danger of collapse in systemic lupus erythematosus (SLE) (17%; 10 of 59 hips). 32% patients with little or medium-sized lesions (<50% of head involvement) advanced to symptoms or collapse, whereas big lesions had 84% of opportunity of development. It was stressed that development to advanced-stage depends mostly on area, size of the lesion and etiology. Little size lesion could reveal spontaneous regression. In 21st century, this method of treatment could not be accepted as a standard separated modality of treatment and might be an additive therapy to medical or surgical management.

Pulsed electromagnetic therapy

Pulsed electromagnetic therapy is believed to positively impact early-stage ON via stimulation of osteogenesis and angiogenesis much like ESWT. Massari et al.^[31] 37 in their retrospective evaluation of 76 hips treated with electromagnetic field

stimulation in Ficat Stage-I to III, reported that the 94% of hips in Stage-I and II avoided the requirement for THA with a dramatically higher percentage of hips in Stage-III advancing to THA at a mean followup of 2 years. At present, proof in favor of electromagnetic excitement is restricted and additional study is had to discover its possible duty in early-stage AVN.

Hyperbaric oxygen

Hyperbaric oxygen enhances oxygenation, decreases edema by triggering vasoconstriction, and induces angiogenesis; thus creating a reduction in intra osseous pressure and improvement in microcirculation. Reis et al.^[32] observed regular MRI in 13 hips after hyperbaric oxygen treatment (100% oxygen at 2-2.4 atmospheric pressure for 90 min by mask for 100 days) to 12 patients with 16 ONFH, all with Steinberg phase 1 illness. Camporesi et al.^[33] also reported clinical enhancement at followup of 7 years in the research study of 19 patients randomized to obtain 30 treatment doses of either hyperbaric oxygen or hyperbaric air for a total duration of 6 weeks. None of the hyperbaric oxygen team patients needed THA till the moment of final followup. As a result of restricted data, using hyperbaric oxygen in ONFH is controversial.

Operative treatment

Surgical treatment for precollapsed stage ONFH involves hip preserving procedures (CD, nonvascularized bone-graft, vascularized bone-graft) whereas prosthetic hip surgical procedure is reserved for advanced-stage of collapse and arthritic hip.

Core decompression

Core decompression is the most typically performed surgery for therapy of very early ONFH. It decreases the intraosseous pressure in the femoral head and increases blood flow to the necrotic area, thus enhancing neobone formation. It has been taken into consideration as the only cost-efficient surgery for ONFH^[34], yet the success of the treatment is mainly based on the etiology and radiographic criteria such as lesion size, place or collapse of the lesion^[35]. The overall success rate as specified by the need for more surgical procedure has varied between 40% and 80% across numerous research studies at 2-7 year followup^[34]. Conventional core decompression (CD) was carried out utilizing 8-10 mm cannula or trephine which had the prospective threat of subtrochanteric fracture and hip joint penetration.

Mesenchymal stem cells implantation or growth factor based treatment strategies

To augment bony regeneration in the necrotic lesion site, the applications of osteogenic or angiogenic precursor cells with or without development factor is an alluring possibility. Grown-up tissue derived mesenchymal stem cells (MSCs) application represents an extremely appealing alternative for treatment of ONFH in the precollapsed stage^[35]. Many researchers have recorded reduced amount of endothelial progenitor cells and colony creating units in patients suffering from ONFH^[36]. Besides that, there suffers migratory capacity of endothelial progenitor cells and increased cellular senescence leading to reduced angiogenesis in patients of ONFH^[37]. All these reasons justify the potential role of stem cells or development factors in treatment of precollapsed ONFH. MSCs implantation has capability to differentiate into numerous cell lineages including the osteoblast, chondrocytes and adipocytes. This property of stem cells has been observed in a speculative dog model while assessing its effect in AVN. Nonetheless, the efficacy of stem cells in healing AVN lesion is as a result of the osteoblastic distinction capability or additional to release of development factors or cytokines stays vague. In addition, enhancement of neovascularization or angiogenesis property of stem cells have been described by many researchers which ascribes another factor for its possible duty in the therapy of AVN^[38].

CONCLUSION

Osteonecrosis is a destructive pathology that eventually results in bone death through loss of blood to the bone, it involves almost every bone including the femoral head while early start of osteoarthritis could ultimately demand hip arthroplasty when non-operative procedures and joint-sparing treatments fail. Nevertheless, recent technological advances in surgical treatment methods have improved outcomes and should help patients recover from this functionally debilitating joint disease.

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