Avascular necrosis
of the femoral head

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ABSTRACT
Avascular necrosis (AVN) is a disease that may affect several different bones as a result of temporary or permanent loss of the blood supply to these bones. The femoral head is most commonly affected by this disease. Usually, the patients are in their third, fourth or fifth decade of life at the time of diagnose.

Initially, patients are asymptomatic, but, in time, AVN leads to joint destruction, requiring surgical treatment and, in latter stages, total hip replacement. It is essential that AVN of the femoral head is diagnosed early because delaying this disease by joint preserving measures has a much better prognosis and because the results of joint replacement are poorer in young individuals.

There are various conditions than can be incriminated as triggers for this disease. However, almost half of the patients diagnosed present none of these conditions. This type of avascular necrosis is termed primary, or idiopathic. All the other forms of this disease are secondary.

Treatment has been facilitated by using widely accepted international classification systems and by effective earlier diagnosis using MRI and other imaging techniques.

Although treatment has turned more and more towards surgery, no universally satisfactory therapy has been developed, even for early disease.

Key words: avascular necrosis, femoral head, hip pain, ficat-Arlet classification, core decompression, total hip replacement

INTRODUCTION
Avascular necrosis (AVN), also known as osteonecrosis, aseptic necrosis or ischemic bone necrosis is a disease that may affect several different bones as a result of temporary or permanent loss of the blood supply to these bones. The ischemia causes the death and eventual collapse of the bone tissue, with its overlying joint surface (1). Koenig was the first to describe this condition, which he termed osteochondritis dissecans, in 1888. In 1925, Haenish described the first case that involved the femoral head. In 1940, the cause of the necrosis was deemed to be arterial occlusion. Pietrograndi described the first case of femoral head AVN after steroid use in 1957 (2). Ever since, scientists have found out more and more about the complex physiopathology of this disease which to this days remains largely unknown.

The femoral head is most commonly affected by this disease. Usually, the patients are in their
third, fourth or fifth decade of life at the time of diagnose. Men are more prone to this disease than women, the sex ratio being about 4.

Initially, patients are asymptomatic, but, in time, AVN leads to joint destruction, requiring surgical treatment and, in latter stages, total hip replacement (THR) (2). Although treatment has been facilitated by using a widely accepted international classification system, effective earlier diagnosis using MRI, and more aggressive surgical management, no universally satisfactory therapy has been developed, even for early disease.

It is essential that AVN of the femoral head is diagnosed early because delaying this disease by joint preserving measures have a much better prognosis and because the results of joint replacement are poorer in young individuals (2).

ETIOLOGY

There are various conditions than can be considered as triggers for this disease. However, almost half of the patients diagnosed present none of these conditions. This type of avascular necrosis is termed primary, or idiopathic. All the other forms of this disease are secondary (2-8). One of the most common reasons for secondary avascular necrosis is prolonged systemic steroid use in high doses (equivalent to 4000 mg of Prednisone) for extended periods of up to 3 months, or longer. There were cases cited in literature of AVN of the femoral head after relatively brief periods (7 days) of oral steroids. The mechanism of action is not yet fully understood, but it is thought to be linked to the hypercoagulable state, with subsequent impaired fibrinolysis and venous thrombosis in the femoral head. Other common causes include trauma, blood disorders or decompression disease.

Taking these facts into account, AVN can be classified as follows:

- Primary (idiopathic)
- Secondary to:
  - Trauma – Fracture of the femoral neck
  - Slipped capital femoral epiphysis
  - Proximal femoral epiphysiolysis
  - Dislocation of the femoral head
  - Epiphyseal compression
  - Vascular trauma
  - Burns
  - Radiation exposure
  - Hemoglobinopathies
  - Sickle cell disease

- Hemoglobin S or hemoglobin C
- Polycythemia
- Caisson disease – Dysbaric osteonecrosis
- Local infiltrative disease
- Gaucher disease
- Infection
- Neoplasms
- Hypercortisolism
- Corticosteroid medications
- Cushing disease
- Alcohol consumption
- Pancreatitis
- Chronic renal failure
- Cigarette smoking
- Collagen vascular diseases
- Congenital and developmental
- Congenital dislocation of the hip
- Ehlers-Danlos syndrome
- Hereditary dysostosis
- Legg-Calvé-Perthes disease
- Fabry disease
- Giant cell arteritis
- Gout and hyperuricemia
- Hemodialysis
- Hypercholesterolemia
- Hypercoagulable states
- Hyperlipidemia
- Hyperparathyroidism
- Intravascular coagulation
- Organ transplantation
- Pregnancy
- Systemic lupus erythematosus
- Thrombophlebitis
- Hemophilia

PHYSIOPATHOLOGY

Extrarosseous arterial factors are the most important. The femoral head is at increased risk because the blood supply is an end-organ system with poor collateral development. Blood supply can be interrupted by trauma, vasculitis (Raynaud disease), or vasospasm (decompression sickness) (2,3).

Intraosseous arterial factors may block the microcirculation of the femoral head through circulating microemboli. These can occur in sickle cell disease (SCD), fat embolization or air embolization from dysbaric phenomena (2,9).

Intraosseous venous factors affect the femoral head by reducing venous blood flow and causing stasis. These factors may accompany conditions such as Caisson disease, SCD or enlargement of intramedullary fat cells (2,8).
**Intraosseous extravascular factors** affect the hip by increasing the pressure, resulting in a femoral head compartment syndrome (2). For example:

- Fat cells hypertrophy after steroid administration or abnormal cells, such as Gaucher and inflammatory cells, can encroach on intraosseous capillaries, reducing intramedullary circulation and contributing to compartment syndrome.
- Repeated microfractures in the weight-bearing segment of the femur may cause multiple vascular lesions resulting in ischemia within fragile and poorly repaired bone.
- Cytotoxic factors, such as alcoholism and steroid use, have a direct toxic metabolic effect on osteogenic cells (2).
- Decreased concentrations of 1,25 dihydroxyvitamin D3 can cause a quantitative or qualitative deficiency in the bone architecture, causing the bone to deform under pressure.

**Extrasosseous extravascular (capsular) factors** involve the tamponade of the lateral epiphyseal vessels located within the synovial membrane, through increased intracapsular pressure. This occurs after trauma, infection, and arthritis, causing effusion that may affect the blood supply to the epiphysis (2,3).

## CLINICAL DETAILS

### History

Avascular necrosis may be asymptomatic and is occasionally discovered following radiography.

Pain in the affected joint, described as throbbing, deep and often, intermittent (2), is typically the presenting symptom. Patients with AVN of the femoral head often report groin or hip pain that can radiate to the buttocks, anteromedial thigh, or knee that is exacerbated by weight bearing and sometimes by coughing. The pain may initially be mild but progressively worsens over time and with use. Eventually, the pain is present at rest and may be present or even worsen at night (7), in which case, it may be associated with morning stiffness.

### Physical

- Usually the initial findings are unrevealing.
- In the latter stages of the disease, joint function deteriorates and the following signs may be found:
  - The patient may walk with a limp and may experience loss of range of motion, both active and passive, most frequently in flexion, abduction, and internal rotation, especially after collapse of the femoral head.
  - The patient may have tenderness around the affected area.
  - A neurological deficit may be found (7).
  - The Trendelenburg sign may be positive.
  - A click may be heard when the patient rises from a chair or after external rotation of the abducted hip (2).
  - Advanced disease leads to joint deformity and muscle wasting (7).

### Imaging

- Plain film radiographic findings are absent in stages 0 and 1 of AVN. A normal radiograph does not equal a normal hip. A delay of 1-5 years can occur between the first symptoms and the appearance of radiographic modifications (2). In more advanced disease, radiographs show sclerosis and changes in bone density. As the disease progresses, subchondral radiolucent lines (crescent sign), flattening or the collapse of the femoral head may appear (7).
- CT scan is used to determine the extent of involvement, such as subchondral lucencies and sclerosis present in the reparative stage (2) (before the collapse of the femoral head), but it is not as sensitive as MRI in stages 0 and 1. CT is excellent for detecting femoral head collapse, early degenerative joint disease and the presence of loose bodies especially when using multiplanar reconstruction (2).
- MRI is the most sensitive means of diagnosing AVN, representing the gold-standard of noninvasive diagnostic evaluation (FIGURE 1). It has several advantages:
  - It allows accurate staging by clearly depicting the size of the lesion.
  - It detects asymptomatic lesions (7) that are undetectable on plain radiographs, thus facilitating early treatment and better response.
  - It provides multiplanar imaging and excellent soft tissue resolution (10,11).
  - It can demonstrate response of the femoral head to treatment (2).
- Single-photon emission computed tomography (SPECT) is used as an alterna-
tive for MRI when the latter cannot be performed or when MRI results are indeterminate. SPECT is difficult to use because it requires remaining still for long periods of time. Also, bladder artifacts are a frequent problem (2,10).

Scintigraphic imaging reveals a central area of decreased uptake, surrounded by an area of increased uptake (the doughnut sign or cold-in-hot sign) (2). It indicates the reactive zone surrounding the necrotic area. The main disadvantages are that it lacks specificity (2) and that the same image may be encountered in other conditions such as osteoarthritis, fracture, and inflammatory arthritis. Results are difficult to interpret if disease is bilateral.

Bone biopsy is not routinely used because of the availability of sensitive noninvasive tests such as MRI (7). It is a valuable diagnostic tool after analyzing the bony fragment extracted after core decompression.

**CLASSIFICATION**

Ficat and Arlet have developed a staging system using radiographic findings, consisting of four stages. Hungerford and Lennox modified this staging system when MRI became available, adding stage 0 to the classification (2,3).

- **Stage 0** (preclinical and preradiologic) – negative findings on a plain radiograph, in an asymptomatic patient with a positive diagnose in the contralateral hip. The MRI shows a double-line sign, consistent with a necrotic process.
- **Stage I** (preradiologic) – normal findings on radiographs and positive findings on MRI or bone scintigraphy. Stage 1 represents the early resorptive stage. The first radiographic findings appear late in this resorptive stage (minimal osteoporosis and/or blurring and poor definition of the bony trabeculae).
- **Stage II** (reparative stage) occurs before the flattening of the femoral head. It can last for several months or years. The radiographic changes are evident and they are represented by demineralization (early manifestation of the reparative stage, representing resorption of dead bone) and sclerosis (appearing after demineralization, representing apposition of new bone on dead trabeculae). Demineralization may be generalized or patchy or appear in the form of small cysts within the femoral head. Patchy sclerosis appears as increased density on radiographs, usually in the superolateral aspect of the femoral head and may be diffuse, focal, or in a linear arc, which is concave superiorly. These changes are consistent with stage IIA (FIGURE 2). Stage IIB (FIGURE 3) is a transition phase characterized by the presence of the crescent sign, seen as a linear subcortical lucency, situated immediately beneath the subcortical bone, representing a fracture line. It is best seen on a frog leg view. The femoral head remains round, initially, but later collapses, creating a joint-space widening.
- **Stage III** (early collapse of the femoral head) is heralded by the presence of

**Differential diagnose**

- Malignancy
- Hemangioma
- Radiation therapy
- Sympathetic dystrophy
- Bone marrow edema syndrome (2,7)

FIGURE 1. MRI scan of bilateral type II lesion
sequestration and depression, with the appearance of decrochage, without acetabular involvement. The femoral head is no longer round and smoothly contoured. It appears flattened or collapsed. (FIGURE 3)

- Stage IV (progressive degenerative disease) is represented by the severe collapse and destruction of the femoral head along with joint space narrowing, osteophyte and subchondral cyst formation, as definite signs of degenerative joint disease.

Steinberg et al. expanded this staging system, by dividing stage III lesions into femoral heads with or without collapse or hips with or without acetabular involvement. In addition, they quantified the amount of involvement of the femoral head into mild (<15%), moderate (15-30%) and severe (>30%), based on radiographs (TABLE 1).

Ohzono et al. incorporated the concept of location of the lesion, with prognostic value. In type 1 lesions, there is a line separating the normal femoral head from the affected, sclerotic part. Depending on the amount of weight-bearing area involved, they are classified as A

<table>
<thead>
<tr>
<th>Stage</th>
<th>Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Normal radiographs, bone scan, and MR images</td>
</tr>
<tr>
<td>I</td>
<td>Normal radiographs, abnormal bone scan, and MR images</td>
</tr>
<tr>
<td>A: mild</td>
<td>&lt;15% of head involvement</td>
</tr>
<tr>
<td>B: moderate</td>
<td>15% to 30%</td>
</tr>
<tr>
<td>C: severe</td>
<td>&gt;30%</td>
</tr>
<tr>
<td>II</td>
<td>Abnormal radiograph</td>
</tr>
<tr>
<td>A: mild</td>
<td>&lt;15% of head involvement</td>
</tr>
<tr>
<td>B: moderate</td>
<td>15% to 30%</td>
</tr>
<tr>
<td>C: severe</td>
<td>&gt;30%</td>
</tr>
<tr>
<td>III</td>
<td>Subchondral collapse producing a crescent sign</td>
</tr>
<tr>
<td>A: mild</td>
<td>&lt;15% of articular surface</td>
</tr>
<tr>
<td>B: moderate</td>
<td>Crescent beneath 15% to 30%</td>
</tr>
<tr>
<td>C: severe</td>
<td>Crescent beneath &gt;30%</td>
</tr>
<tr>
<td>IV</td>
<td>Average of femoral head involvement, as determined in stage IV and estimated acetabular involvement</td>
</tr>
<tr>
<td>A, B, or C</td>
<td>Average of femoral head involvement, as determined in stage IV and estimated acetabular involvement</td>
</tr>
<tr>
<td>V</td>
<td>Joint narrowing with or without acetabular involvement</td>
</tr>
<tr>
<td>VI</td>
<td>Advanced degenerative changes</td>
</tr>
</tbody>
</table>

TABLE 1. Steinberg classification

FIGURE 2. Crescent sign

FIGURE 3. Ficat-Arlet Stage IV of femoral head avascular necrosis
(<=30%), B (30-60%) or C (>60%). Type 2 is a collapsed head without a separating line and type 3 is represented by the presence of cysts (FIGURE 4). Type 3 A lesions are central, 3 B lesions involve the supero-lateral aspect of the femoral head. Types 1 A, 1 B, 2 and 3 A have a better prognosis than types 1 C and 3 B. More recently, a new classification has been completed by ARCO, which joins the Ficat Arlet staging system, the Hungerford-Lennox modification, the quantification of involvement (Steinberg) and the concept of prognosis based on location (Ohzono) (FIGURE 5).

- Stage 0 – Bone biopsy results consistent with osteonecrosis; other test results normal
- Stage I – Positive findings on bone scan, MRI, or both
  - A – <15% involvement of the femoral head (MRI)
  - B – 15-30% involvement
  - C – >30% involvement
- Stage II – Mottled appearance of femoral head, osteosclerosis, cyst formation, and osteopenia on radiographs; no signs of collapse of femoral head on radiographic or CT study; positive findings on bone scan and MRI; no changes in acetabulum
  - A – <15% involvement of the femoral head (MRI)
  - B – 15-30% involvement
  - C – >30% involvement
- Stage III – Presence of crescent sign lesions classified on basis of appearance on AP and lateral radiographs
  - A – <15% crescent sign or <2-mm depression of femoral head
  - B – 15-30% crescent sign or 2- to 4-mm depression
  - C – >30% crescent sign or >4-mm depression
- Stage IV – Articular surface flattened; joint space shows narrowing; changes in acetabulum with evidence of osteosclerosis, cyst formation, and marginal osteophytes.

**TREATMENT**

The goal of the treatment is to keep joints from breaking down, because severe pain and limitation in movement will occur within 2 years, in the absence of treatment. There are several options that one can choose from and in order to determine the most appropriate treatment, one has to take into consideration the age of the patient, the stage of the disease, the location and amount of bone affected and the underlying cause of avascular necrosis (unless corticosteroid or alcohol use is stopped, treatment may not work) (1).

There are conservative and surgical methods for treating this disease. Conservative treatments have been used experimentally alone or in combination, but they rarely provide lasting improvement. Most patients will eventually need surgery either to delay, or even to repair the joint permanently (1).

**Conservative Treatment**

- Statin therapy, bisphosphonates (6,12,13) or nonsteroidal anti-inflammatory drugs may be helpful.
- In some early cases, reduced weight bearing, limiting activities or using crutches can slow the damage caused by avascular necrosis and permit natural healing (1). However, these patients run a risk of 85% of femoral head collapse (2). Protected weight-bearing may be effective when the involved segment is smaller than 15% and

![FIGURE 4. Ohzono Prognostic Classification](image-url)
<table>
<thead>
<tr>
<th>STAGE</th>
<th>FINDINGS</th>
<th>TECHNIQUES</th>
<th>SUBCLASSIFICATION</th>
<th>QUANTITATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>All present techniques normal or non-diagnostic</td>
<td>X-ray, CT, Scintigraph, MRI</td>
<td>NO</td>
<td>NO</td>
</tr>
<tr>
<td>1</td>
<td>X-ray and CT are normal at least ONE of the below mentioned is positive</td>
<td>Scintigraph MRI *QUANTITATE on MRI</td>
<td>LOCATION medial, central, lateral</td>
<td>% AREA INVOLVEMENT minimal A &lt; 15%, moderate B 15%-30%, extensive C &gt; 30%</td>
</tr>
<tr>
<td>2</td>
<td>NO CREST SIGN! X-RAY ABNORMAL: sclerosis, osteolysis, focal porosis</td>
<td>X-ray, CT, Scintigraph MRI *QUANTITATE MRI &amp; X-ray</td>
<td>LENGTH of CRESCENT a &lt; 15%, b 15%-30%, c &gt; 30%</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>CREST SIGN! on the X-ray and/or flattening of articular surface of femoral head</td>
<td>X-ray, CT ONLY *QUANTITATE on X-ray</td>
<td>% SURFACE COLLAPSE &amp; DOME DEPRESSION</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>OSTEOARTHRITIS! joint space narrowing, acetabular changes, joint destruction</td>
<td>X-ray ONLY</td>
<td>NO</td>
<td></td>
</tr>
</tbody>
</table>

**FIGURE 5.** ARCO International Classification of Osteonecrosis
located far from the weight-bearing region (5).

– Range-of-motion exercises are helpful for maintaining joint function (1).
– Electrical stimulation is thought to induce bone growth (1).

Surgical Treatment

– Core decompression is achieved by removing the inner layer of bone (1) and provides immediate pain relief by reducing pressure in the bone, decreasing vascular engorgement and inflammation and relieving the compartment syndrome (2). It enhances the process of creeping substitution and also encourages the formation of new blood vessels, thereby increasing blood flow to the bone (1). It is indicated in people with early stages of avascular necrosis, before the collapse of the head and when less than 30% of the femoral head is involved (2). Core decompression is also effective for pain relief (11) and helps delay the need for arthroplasty, acting as a joint preserver.

– Bone grafting uses healthy bone from one part of the patient and transplants it to the diseased area. After the failure of nonvascularized grafts, present-day grafts (called vascular grafts) include an artery and veins, increasing the blood supply to the affected area (1). Bone grafting can be combined with core decompression, acting together towards stopping the cycle of ischemia. It is indicated in early stages of the disease and, when it is successful, it can ensure lifelong survival of the femoral head, in the absence of foreign body–associated complications. If unsuccessful, the procedure allows the patient to retain the option of total hip arthroplasty in the future (3).

– Osteotomy is a procedure by which the bone is reshaped to reduce stress on the affected area. It requires a longer recovery period and limited activities for 3 to 12 months after surgery. This procedure is most effective for patients with advanced avascular necrosis and those with a large area of affected bone (1). Intertrochanteric and transtrochanteric rotational osteotomies aim at bringing an intact area of bone and cartilage to the weight-bearing area of the femoral head and, at the same time, at improving blood supply (biotrophic effect) (5,14). The consensus is that femoral osteotomies should be performed in more advanced stages of the disease (II or III Ficat-Arlet), but that they should be limited to patients with Kerboul necrotic angle (sum of angles bordering the sequestrum on antero-posterior and lateral X-ray views) inferior to 200°. Historically, 25-30 years ago, varisation, with or without medialisation osteotomies were thought to be sufficient, but later, flexion (Kempf) or rotational (Sugioka) osteotomies began to gain ground. One possible problem with osteotomies is that they may make conversion to total hip arthroplasty more difficult technically and less successful on a long-term period.

– Arthroplasty. Most patients address an orthopaedic surgeon in advanced stages of the disease, after femoral head collapse. Total joint replacement is the treatment of choice in the final stages of avascular necrosis or when the joint is irreversibly destroyed (1). The procedure can be done in numerous fashions, according to the surgeon’s preference. The surgeon may use various approaches (antero-lateral, Hardinge, postero-lateral, minimal invasive, etc.) and may employ an even broader array of implants. Classic total hip endoprostheses (cemented or, preferably, cementless) account for the majority of implants used but surgeons and patients alike turn more and more towards resurfacing arthroplasty (14), a procedure that holds several advantages. Unlike classic implants that employ a friction couple of metal on polyethylene, or ceramics or, more recently, Oxinium heads on polyethylene cups, resurfacing arthroplasty employs a metal on metal friction couple that is the nearest to the normal hip joint. By this technique, the acetabulum is replaced with a cementless metal cup, very similar to its classic predecessor, but instead of removing the entire head and femoral neck (as is the case with classic implants), the femoral head is prepared by removing its cartilage and a thin layer of bone, thus preserving most of the bone stock. A large diameter femoral implant is cemented (usually larger than 44 mm),
which ensures a superior stability against dislocation. Also, the design of these implants ensures an even better range-of-motion, that can sometimes be crucial for young, active patients. Also, resurfacing arthroplasty preserves more of the patient’s bone stock, a feature that becomes increasingly more important, taking into account the patients’ young age, meaning that he/she will probably require a second and sometimes even a third intervention (15) sometime later. Total hip arthroplasty, be it classic or resurfacing, yields excellent results, with immediate and long-lasting pain relief (4) and allows early mobilization and a quicker return to an active lifestyle. However, several authors have observed that there is an earlier failure of total hip replacement in osteonecrosis than in age-matched patients with other diagnosis. This is probably because of abnormal remodeling of bones and subsidence of prosthesis because of the poor bone quality of the proximal femur. Other factors may include ongoing systemic disease, defects in mineral metabolism, use of steroids, high level of activity in young patients and increased body weight.

Over the years, as our knowledge of this disease has improved, several surgical and conservative methods of treatment have been perfected. Their goal is to preserve the femoral head and prevent its collapse for as long as possible keeping in mind at the same time that the maximal and definitive treatment is total hip replacement. Efforts should be made to delay the moment when arthroplasty is needed, without compromising the chance of a straight-forward hip replacement.

Although there have been extensive studies regarding avascular necrosis of the femoral head, we still know little about its pathogenesis, and therefore about the best method to treat this disease. Future medical treatment should be aimed at the cause of this disease, thus slowing down or even stopping the evolution of avascular necrosis and thus delaying as much as possible the need for surgery.

REFERENCES