Osteonecrosis of the Femoral Head

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Abstract

New cases of osteonecrosis of the femoral head in the United States number between 10,000 and 20,000 per year. This disease usually affects patients in their late 30s and early 40s. Although a number of authors have related specific risk factors to this disease, its etiology, pathogenesis, and treatment remain a source of considerable controversy. This disorder has been associated with corticosteroid use, substance abuse, and various systemic medical conditions. Either direct damage to osteocytes (e.g., by toxin production) or indirect damage (e.g., due to disorders in fat metabolism or hypoxia) may lead to osteonecrosis. Patients at increased risk for osteonecrosis should be monitored closely. Unfortunately, most cases are diagnosed in an advanced stage of disease, when minimally invasive surgical procedures are no longer helpful. Furthermore, patients in the advanced stage of the disease must undergo total hip replacement at a young age, which carries a poor long-term prognosis.

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Osteonecrosis of the femoral head is not a specific diagnostic entity, but rather the final common pathway of a series of derangements that produce a decrease in blood flow, leading to cellular death within the femoral head.[1]

Necrosis of the femoral head is a progressively debilitating lesion, which usually leads to the destruction of the hip joint in patients between 20 and 50 years of age (mean age at presentation, 38 years).[1] In most cases, diagnosis is made at advanced stages of the disorder (Fig. 1), when femoral head–conserving surgical treatment is no longer indicated.[2-4]

This condition was first described by Alexander Munro in 1738. Between 1829 and 1842, Jean Cruvilhier described how the femoral head deformed secondary to an interruption in its blood flow. The first detailed description of idiopathic osteonecrosis of the femoral head is attributed to Freund.

In 1962, Mankin and Brower[5] described 27 cases of osteonecrosis. Since then, there has been a steady increase in the number of cases of osteonecrosis reported annually. Its incidence is estimated to be between 10,000 and 20,000 new cases per year in the United States.[1]

Etiology and Pathogenesis

A number of clinical conditions, both traumatic and nontraumatic, have been associated with osteonecrosis of the femoral head (Table 1). A disruption of blood flow to the femoral head secondary to an injury, such as a femoral neck fracture, has been clearly identified as the leading pathologic factor in posttraumatic osteonecrosis.[1] The exact mechanism leading to atraumatic osteonecrosis is unclear. Some factors are believed to produce direct damage to osteocytes; others are thought to increase the risk of osteonecrosis when associated with an underlying disease process. Approximately 10% to 20% of cases have no clearly identifiable risk factor and are classified as idiopathic osteonecrosis.

Most etiologic factors in atraumatic osteonecrosis are related to underlying pathologic conditions that alter blood flow, leading to cellular necrosis and ultimately to collapse of the femoral head. This damage can occur in one of five vascular areas around the femoral head, classified as arterial extraosseous, arterial intraosseous, venous intraosseous, venous extraosseous,

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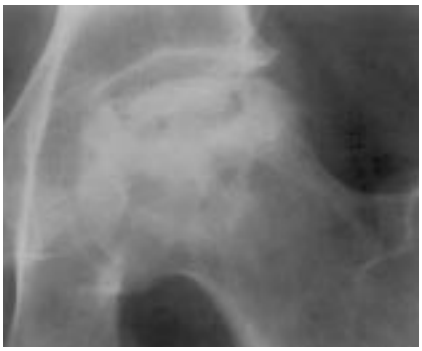

Fig. 1 Collapse of the femoral head due to osteonecrosis.

and extravascular extraosseous.[6] Involvement of inflow or outflow compartments can lead to a dramatic decrease in blood flow to the femoral head, leading to cell death.

Corticosteroid Use

The high-dose corticosteroid therapy used for immunosuppression after organ and bone marrow transplantation, as well as for the treatment of rheumatologic and autoimmune diseases, has been implicated as a risk factor for development of atraumatic osteonecrosis of the femoral head. As many as 90% of new cases of atraumatic osteonecrosis have been associated with steroid use and alcohol abuse.[1,7,8]

The cause-and-effect relationship between steroid use and osteonecrosis has been difficult to establish due to the multiplicity of confounding factors. Most patients who take steroids also have other risk factors. It is still unclear whether the resulting osteonecrosis is due to the underlying disease or the steroid use.[9] The results of initial studies indicated that high doses (>30 mg/day) and longer duration of treatment were the most important predictors of development of osteonecrosis.[9,10] Recent studies have shown that certain clinical findings, such as a change in body habitus, deep vein thrombosis and vasculitis, and certain laboratory findings, such as immunoglobulin G aCL levels in a patient with systemic lupus erythematosus, are also associated with osteonecrosis.[11]

Furthermore, nonrheumatologic conditions treated with long-term low-dose corticosteroid therapy (e.g., ulcerative colitis, asthma, skin disorders) do not present with a high incidence of atraumatic osteonecrosis. Colwell et al[9] reported on 142 hips followed for 10 years in patients with asthma or inflammatory arthritis treated with steroids. The average dose in the asthma group was 2,201 mg/year (6 mg/day); in the inflammatory arthritis group, it was 1,967 mg/year (5.3 mg/day). None of their patients had radiographic or clinical evidence of osteonecrosis. The authors suggest that chronic low-dose steroid treatment for the treatment of asthma or inflammatory arthritis is not associated with an increased risk of osteonecrosis. It is more likely, however, that high-dose therapy (>30 mg/day), such as that needed for transplant recipients, plays a major role in the etiology of this disease.

The mechanism postulated for steroid-induced osteonecrosis is unclear. A disorder in fat metabolism has been implicated as a possible mechanism. In 1964, Johnson[12] proposed that fat cells within the bone marrow increase in size, leading to the disorder. Cell hypertrophy increases pressure inside the femoral head, resulting in sinusoidal vascular collapse and finally necrosis of the femoral head. The exact mechanism of the cell hypertrophy remains elusive. Experimental studies using mouse bone-marrow pluripotential cell lines have demonstrated a dramatic decrease in their osteogenic properties. These cells also tend to differentiate into adipocytes when treated with increasing dexamethasone levels. These findings differed from those in untreated control cells, which continued to exhibit their osteogenic properties.[13]

Jaffe et al[14] consider patients undergoing steroid treatment to be in a hyperlipidemic state, which can increase the fat content within the femoral head and increase intracortical pressure, producing sinusoidal collapse and necrosis. Other investigators have proposed that this hyperlipidemic state may lead to fat embolism directed toward the femoral head, which occludes the microvasculature and initiates the pathophysiologic process.[15]

A recent study in rabbits suggests that the use of steroids can also damage endothelial and smooth muscle cells within the vasculature.[16] This may result in interruption of the venous drainage from the femoral head, leading to blood stasis, an increase in intraosseous pressure, and osteonecrosis.

Alcohol Consumption

A number of published studies have documented the high incidence of alcohol-related osteonecrosis.[1,7,8,17] The exact amount of alcohol intake that can induce osteo-

Table 1
Risk Factors for Osteonecrosis

Trauma
Corticosteroid use
Alcohol abuse
Smoking
Sickle cell anemia
Coagulopathies
Systemic lupus erythematosus
Hypercholesterolemia
Organ transplantation
Gaucher disease
Caisson disease
Radiation therapy
Arterial disorders
Intramedullary hemorrhages
Chronic pancreatitis
Hypertriglyceridemia
Other rare associations

necrosis is not known. When compared with nondrinkers, patients who consume less than 400 mL of alcohol per week have a three times greater risk of osteonecrosis. The risk increases to 11 times if the patient consumes more than 400 mL of alcohol per week.[1,7,8]

The pathophysiologic process of alcohol-induced osteonecrosis is not completely understood. Excess alcohol changes fat metabolism significantly. Small fat emboli from the liver can occlude the vasculature of the femoral head, decreasing blood flow and leading to osteonecrosis. Some investigators suggest that alcohol consumption produces an accumulation of lipids inside the osteocytes of the femoral head.[17] These cells hypertrophy and compress the nuclei of the osteocytes, resulting in cell death. Other proposed mechanisms are related to the direct toxic effects of alcohol. Continued exposure of osteocytes to high blood levels of alcohol can cause chronic cellular lesions that are unable to heal, which can lead to cell death and eventual collapse of the femoral head.[16,18]

Transplantation

The incidence of osteonecrosis in organ transplantation patients has been reported to range from 5% to 29%.[19,20] The time of presentation of osteonecrosis after transplantation appears to be variable, with some researchers reporting that osteonecrosis (manifested by joint pain) may start early after transplantation (<3 months), and others reporting that it occurs later.

Certain bone disorders, such as benign bone edema and bone pain secondary to the use of cyclosporine, should always be included in the differential diagnosis when evaluating bone pain in transplant recipients.[19] A complete clinical and radiologic evaluation, including magnetic resonance (MR) imaging, is necessary to rule out these conditions.

The mechanism underlying this disorder is unclear, but multiple risk factors are usually involved. Some investigators believe that prolonged treatment with corticosteroids and other immunosuppressive agents is responsible for the production of osteonecrosis. Case-control studies suggest that renal transplant recipients in whom osteonecrosis developed had received higher doses than other patients matched for age, sex, and time and type of transplant.[20] Since immunosuppressive agents other than steroids have been used, the incidence of transplantation-associated osteonecrosis has decreased dramatically. Landmann et al[21] reported an incidence of 8.6% before the use of cyclosporine, compared with 1.04% after the use of cyclosporine. Predisposing factors prior to transplantation (steroid use, trauma, rheumatologic or hematologic disorders) may also play an important role in predicting osteonecrosis in transplant recipients.

A direct detrimental effect of the transplanted organ has also been demonstrated. Renal transplantation induces osteocyte necrosis due to the production of toxins by the kidney. This has been shown in autopsy specimens from renal transplant recipients, which display histologic evidence of decreased numbers of osteocytes in subchondral bone.[17]

Patients with solid organ transplants are not the only population at risk for osteonecrosis. An increased incidence of the disease has also been demonstrated in bone marrow transplant patients. In a recent study by Fink et al,[22] osteonecrosis developed in 96 of 1,939 patients who received a bone marrow transplant between 1976 and 1993. The mean time to diagnosis was 26.3 months after transplantation. More than one site was involved in over half of the patients, and more than 60% had osteonecrosis of the hip. The authors reported a 14-fold increase in risk associated with receiving steroids but no variance in risk according to duration of steroid use. They also reported no relationship between cyclosporine therapy and the incidence of osteonecrosis, after adjusting for steroid use and other possible confounding variables.

Thrombophilia and Hypofibrinolysis

Hereditary thrombophilia and hypofibrinolysis have an autosomal dominant inheritance pattern. These disorders have been reported to be the major pathophysiologic causes of osteonecrosis of the jaw and of Legg-Perthes disease in children and have recently been implicated in osteonecrosis of the hip.[23] The coagulation pathways described include (1) decreased levels of tissue plasminogen activator (the major stimulator for fibrinolysis) and high levels of plasminogen activator inhibitor (the major inhibitor of fibrinolysis); (2) high levels of the hypofibrinolytic lipoprotein Lp(a); and (3) activated protein C resistance, which results in production of abnormal factor Va in the coagulation cascade, which in turn leads to thrombophilia.

Venous occlusion by fibrin clots due to thrombophilia (increased tendency toward intravascular thrombosis) and hypofibrinolysis (reduced ability to lyse thrombi) can lead to venous hypertension and higher intramedullary pressures, which will reduce arterial blood flow to the femoral head and cause hypoxic death of bone. Glueck et al[23] reported that some of their cases of osteonecrosis of the hip that had been thought to be idiopathic were actually due to these inherited disorders of coagulation. Furthermore, of 13 patients with secondary disease thought to be due to underlying diseases or corticosteroid use, 8

also had an associated heritable disorder of coagulation.

The association of these disorders with superimposed factors (e.g., corticosteroid use, rheumatologic or hematologic disease, transplantation, sickle cell disease, alcoholism) may increase the risk of developing osteonecrosis. Glueck et al[23] proposed that assessing for these coagulation defects with specific laboratory tests—resistance to activated protein C, lipoprotein Lp(a), antigens to proteins C and S, tissue plasminogen activator and inhibitor, and antiphospholipid antibodies—may help in predicting which patients are at risk for development of this disease.

Other Factors

Caisson disease, or dysbaric osteonecrosis, is a form of osteonecrosis that occurs in deep-sea divers and miners who have been exposed to hyperbaric conditions. This disorder is thought to be produced by occlusion of blood vessels by circulating nitrogen bubbles that are induced in response to a reduction in ambient pressure during decompression.[24]

An animal model for dysbaric osteonecrosis was recently reported.[24] Six sheep were exposed to compressed air for 24 hours at a time 12 or 13 times within a 2-month period, with a 1- to 8-day recovery period between exposures. All six animals had clinical evidence of limb bends (limb lifting for periods of time) immediately after the exposure. In the five surviving sheep, radiographic evidence of disease was present within 5 months in the long bones, specifically, in the metaphyseal and diaphyseal, but not the periarticular, regions. However, histologic evidence of bone marrow necrosis was present in all regions. The histologic and radiographic findings were found to be very similar to those reported in humans.

Although most reported cases of dysbaric osteonecrosis have been a result of continuous exposure, such as occurs in caisson workers, aviators, astronauts, and divers, single-exposure induction of dysbaric osteonecrosis has also been documented. Therefore, orthopaedic surgeons should consider this entity when assessing hip pain of apparently idiopathic origin.

Sickle cell anemia has been reported to be an important risk factor for the development of osteonecrosis. The prevalence of osteonecrosis in patients with sickle cell anemia has been estimated to range from 3% to 41%.[25,26] Patients with sickle cell trait can also be affected, and higher prevalence rates are encountered when asymptomatic patients with radiographic evidence of disease are included in the cohort. Intravascular sickling within sinusoids associated with a hyperviscosity syndrome produced by high hemoglobin concentrations produces short, temporary occlusions of blood flow to the femoral head, which leads to osteonecrosis and eventually to collapse of the femoral head.[26] The distinctive histologic pattern is characterized by rows of necrotic bone separated by fibroadipose tissue.

Fat emboli that arise as a result of an alteration in lipid metabolism can also be responsible for microvascular obstruction. Furthermore, investigators have proposed that hypercholesterolemia can also play an important role in the pathogenesis of osteonecrosis.[27] Disorders in fat metabolism may also lead to immune-complex deposition, which can result in hemorrhage and death of bone.[16,17]

Type I Gaucher's disease is an autosomal recessive genetic disease that affects primarily Ashkenazi Jews and is caused by an enzymatic deficiency of glucocerebroside hydrolase.[28] It results in accumulation of sphingolipids within macrophages and other reticuloendothelial cells and can affect bone as well as other solid organs. Compression of the cellular and vascular elements and increased pressure within the rigid cortical bone of the femoral head decrease blood flow, leading to osteonecrosis.[29]

Arterial disorders have also been associated with osteocyte and bone marrow necrosis. The specific mechanism that results in damage to the tunica intima and tunica media is unknown. However, investigators have noted pathologic changes in arteries in hemorrhagic zones surrounding areas of necrosis.[30,31]

Many etiologic factors and clinical conditions have been proposed as causes of osteonecrosis. For this reason, this entity should not be considered a simple lesion, but rather a multifactorial disease process that can be produced by a diverse group of disorders leading to a common finding: necrosis and the inevitable collapse of the femoral head.

Pathologic Findings

Although there are many causes and risk factors that can lead to osteonecrosis of the femoral head, the resulting pathologic findings are similar in all patients. In early stages of the disease, histologic examination of the diseased femoral head shows bone marrow necrosis. This can be due to a single insult, but most probably results from multiple instances of minor damage over a period of weeks to months. Resorption of dead osteocytes results in the appearance of empty lacunae within bone. Pluripotential cells within the femoral head are recruited in the repair process. Osteoclasts are stimulated to resorb dead bone, and osteoblasts lay down new bone over necrotic areas, creating the characteristic appearance termed "creeping substitution."

Early histologic examination in a canine model has shown that the process of osteonecrosis may begin approximately 3 days after vascular damage. In this model, surgical devascularization of the femoral head was performed in 25 dogs, and dislocation of the hip was maintained for 9 hours to study the initial histologic changes. The dogs were sacrificed 3 days or 1, 2, or 4 weeks after the procedure. In the 4 dogs studied at 3 days, edema with a decreased cell population and bleeding within the bone marrow were observed, but no histologic findings of necrosis were noted. Of the 7 dogs studied 1 week after surgery, 3 showed histologic changes consistent with necrosis of the femoral head, but no evidence of creeping substitution was observed. Of the 7 dogs sacrificed at 2 weeks, 6 showed histologic changes of necrosis of the femoral head, with 4 showing appositional bone. Osteonecrosis was observed in all 7 dogs studied at 4 weeks. These changes included empty lacunae and appositional bone in trabecular bone and mature fibrous tissue in the bone marrow.[13]

When the affected site is small, reparative processes are initiated rapidly, replacing dead bone with normal new bone. However, as the necrotic area enlarges, the histologic appearance changes. At the periphery of the lesion, a zone of vascular ingrowth is produced, with replacement of bone and bone marrow, leading to marked thickening and increased density of its borders. Because vascular structures cannot penetrate deep inside the avascular lesion, repair is interrupted. The dead bone then fractures, although the superior articular surface does not collapse, owing to the strength of the subchondral bone. The radiolucent space produced under the subchondral bone is called the "crescent sign." In time, this fragile structure collapses, and the femoral head flattens. After deformation of the femoral head, abnormal stresses on the acetabular cartilage and subchondral bone lead to sclerosis, cyst formation, and marginal osteophyte formation. Advancing degeneration of the acetabulum and femoral head leads to obliteration of the joint space.

Clinical Presentation

Osteonecrosis can be clinically silent or can present with any of a number of clinical manifestations. The chief complaint of a patient with osteonecrosis is pain, usually localized to the groin area but occasionally to the ipsilateral buttock and knee. It has been described as a deep, intermittent, throbbing pain, with an insidious onset that can be sudden. Physical examination reveals pain with both active and passive range of motion, especially with passive internal rotation.

Initially, the plain-radiographic appearance may be normal. Therefore, the physician should always suspect osteonecrosis of the femoral head in patients who present with hip pain and any associated risk factors. A complete evaluation of the contralateral hip should always be undertaken, as a 40% to 80% incidence of bilaterality has been reported.[1,32]

Diagnosis and Classification

Successful treatment of osteonecrosis is directly related to its stage at diagnosis. The earlier the diagnosis, the greater the chance of influencing the natural history of the disease. Clinical symptoms usually precede radiographic changes; therefore, a high index of suspicion is important to make the correct diagnosis in a timely fashion.

Radiography

Plain radiography should be the next step after the history and physical examination. Anteroposterior and frog-leg lateral views should always be obtained.

Various systems have been proposed for the radiographic staging of this disease. The first was the Arlet-Ficat staging system (Fig. 2),[33] which is based on radiographic

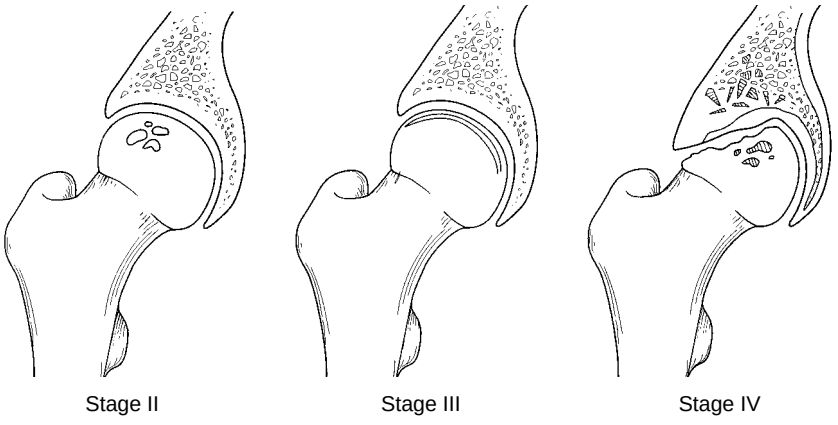

Fig. 2 The Arlet-Ficat staging system is based on the radiographic appearance of the femoral head.[33] In stage I (not shown), there are no changes on x-ray films, but clinical symptoms are suspicious. In stage II, there is radiographic evidence of bone remodeling without changes in the shape of the femoral head; subchondral sclerosis and cysts are present. Stage III is characterized by the crescent sign. Stage IV is characterized by narrowing, osteophyte development, and deformation of the femoral head.

changes in the femoral head. Arlet and Ficat described four stages in the natural history and progression of the disease. In stage I (preradiographic), there are no changes on x-ray films but suspicious clinical symptoms. In stage II, there is radiographic evidence of bone remodeling without changes in the shape of the femoral head; subchondral sclerosis and cysts are present. In stage III, the transition from stage II is heralded by the crescent sign; a sequestrum and partial collapse of the osteonecrotic segment are present (Fig. 1). In stage IV, deterioration of the joint space is characterized by narrowing, osteophyte development, and deformation of the femoral head.

Other classification systems are variations of the Arlet-Ficat staging system. That of Marcus and Enneking[34] is based on clinical symptoms and radiographic abnormalities (Table 2). The staging system of Steinberg et al[32,35] (Table 3, Fig. 3) is highly specific and combines abnormalities observed not only on plain radiographs but also on MR images and bone scans.

Table 2
Radiographic Classification of Marcus and Enneking[34]

Stage	Radiographic Findings
I	Mottled areas of increased density
II	Infarct demarcated by zone of increased density
III	Crescent sign
IV	Depression of lateral edge of infarct
V	Flattening and compression of infarct
VI	Progressive compression and erosion of the head, degenerative changes

Table 3
Staging System of Steinberg et al[32,35]

Stage	Radiologic Features
I	Normal x-ray findings; abnormal bone scan and/or MR findings IA: Mild (<15% of femoral head affected) IB: Moderate (15% to 30% of femoral head affected) IC: Severe (>30% of femoral head affected)
II	Cystic and sclerotic changes in the femoral head IIA: Mild (<15% of femoral head affected) IIB: Moderate (15% to 30% of femoral head affected) IIC: Severe (>30% of femoral head affected)
III	Subchondral collapse (crescent sign) without flattening IIIA: Mild (<15% of femoral head affected) IIIB: Moderate (15% to 30% of femoral head affected) IIIC: Severe (>30% of femoral head affected)
IV	Flattening of femoral head IVA: Mild (<15% of surface and <2-mm depression) IVB: Moderate (15% to 30% of surface or 2- to 4-mm depression) IVC: Severe (30% of surface)
V	Joint narrowing and/or acetabular changes (this stage can be graded according to severity)
VI	Advanced degenerative changes

The Japanese Investigation Committee established a classification based on the size and location of the infarct in the femoral head in relation to the weight-bearing dome of the acetabulum[36] (Fig. 4). Anteroposterior radiographs of the hip joint taken with the patient standing are used for evaluation. Type 1 is characterized by the presence of a necrotic segment involving the zone of the femoral head that is in contact with the weight-bearing surface of the acetabulum (in type 1A, less than the medial third of the weight-bearing surface is involved; type 1B, more than one third but less than two thirds; type 1C, more than two thirds.) Type 2 is characterized by flattening of the weight-bearing surface without radiographic evidence of degeneration. Type 3 is characterized by the presence of a cystic lesion: in type 3A, the lesion does not involve the subcortical area; in type 3B, the lesion is located just beneath the lateral two thirds of the weight-bearing zone.

The Association Internationale de Recherche sur la Circulation Osseuse recently proposed a new classification[1] (Table 4). This staging system combines radiographic, MR imaging, bone scanning, and histologic findings and appears to be the most complete and useful classification scheme. It combines the radiographic staging of Arlet and Ficat, the quantification system of Steinberg et al,[32,35] and the location of involvement, as described by the Japanese Investigation Committee.[36]

Kerboul et al[3] described a method for determining the extent of the radiographic area involved. Both anteroposterior and lateral radiographs are used to calculate a composite angle, which is then used to suggest the prognosis. For exam-

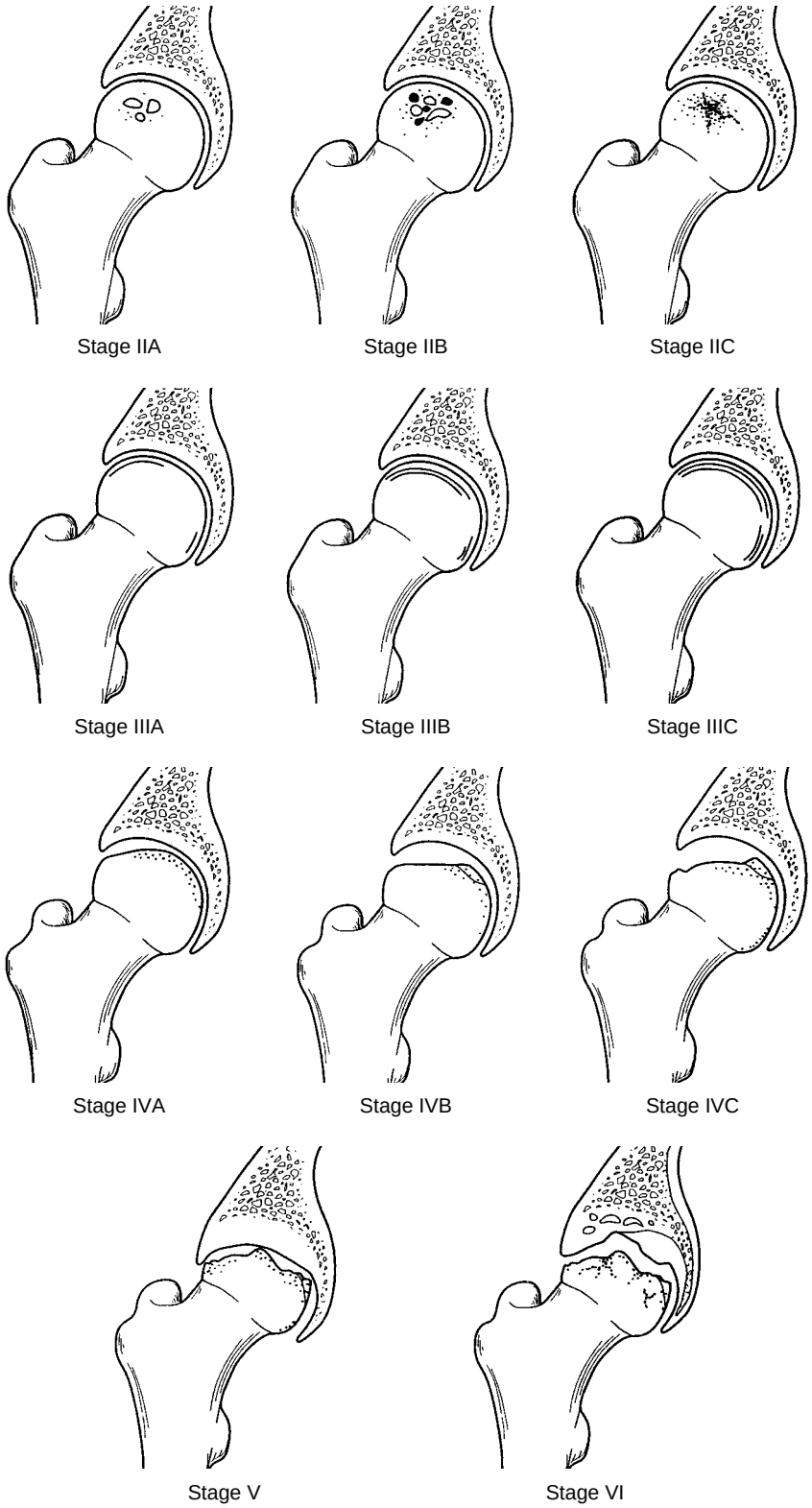

Fig. 3 Radiographic appearance in the staging system of Steinberg et al.[32,35] Stage I disease is not illustrated because the radiographic appearance is normal. See Table 3 for descriptions of other stages.

ple, an angle greater than 200 degrees is considered to indicate a poor outcome.

Magnetic Resonance Imaging

Magnetic resonance imaging is the most accurate imaging modality used for the diagnosis of osteonecrosis of the femoral head. Its sensitivity is thought to be between 88% and 100%, which is higher than that for plain radiography, computed tomography, or bone scanning in detecting early disease (10% to 20% higher than scintigraphy).[13,37,38] Its specificity in differentiating osteonecrosis from other hip disorders is also very high.

When bone marrow cells—osteocytes, hematopoietic cells, and marrow fat cells—are exposed to an ischemic insult, cell death occurs at different intervals.[38] Hematopoietic cells die within 6 to 12 hours, followed by osteocytes at 12 to 48 hours and marrow fat cells 5 days later. The normal high signal intensity seen on T1-weighted images and the intermediate signal intensity seen on T2-weighted MR images of the femoral head change with osteonecrosis, reflecting the death and replacement of marrow fat cells. Although death of osteocytes (depicted as empty lacunae) is not universally present, a peripheral band of low signal intensity depicted on both T1- and T2-weighted images usually demarcates the area of osteonecrosis from the surrounding normal marrow.[38,39] On T2-weighted images, this line, which has been called the "double-line sign," is present in 80% of cases. This sign represents concentric low- and high-signal-intensity rims surrounding the area of necrosis.

The MR imaging findings in animal models of osteonecrosis show that the death of marrow cells determines the changes in signal intensity seen on T1- and T2-weighted images. However, this might not

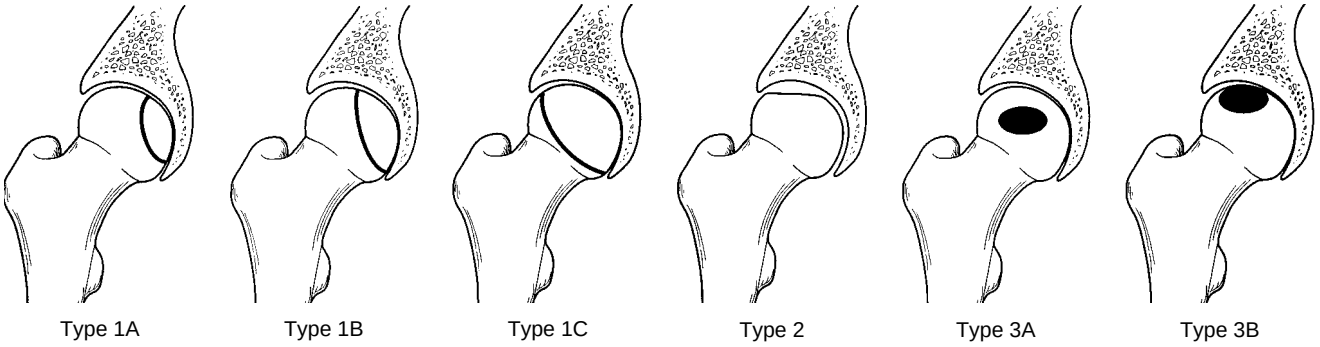

Fig. 4 The Japanese Investigation Committee classification[36] is based on the size and location of the infarct in the femoral head. Type 1 is characterized by the presence of necrosis in the portion of the femoral head in contact with the weight-bearing surface of the acetabulum. Type 2 is characterized by flattening of the weight-bearing surface. Type 3 is characterized by the presence of a cystic lesion.

occur until 5 days after arterial interruption.[40] Therefore, before this period, osteonecrosis may not be represented by any distinctive abnormalities on MR imaging. To increase the early sensitivity of MR imaging, some investigators have suggested the use of gadolinium; however, there is no conclusive evidence supporting this practice.

Sakamoto et al[39] reported that the relationship of the location of the necrotic area to the weight-bearing area of the femoral head and the extent of the necrotic area could be used as predictors of collapse (Fig. 5). In their system, the weight-bearing area is divided into thirds. Lesions that extend across less than one third of the medial area are designated grade A; those that extend across more than one third but less than two thirds, grade B; those that extend across two thirds or more, grade C; those that extend beyond the acetabular edge, grade D. Shimizu et al[41] added to this classification a third criterion for determining prognosis: the image intensity of the necrotic area.

With the objective of identifying a predictor of future collapse, Koo and Kim[42] used MR imaging to quantify the extent of osteonecrosis of the femoral head in 37 hips with early-stage osteonecrosis. The extent of the necrotic area in the weight-bearing portion of the femoral head was measured on midcoronal and midsagittal sections. The authors then calculated an index of necrosis with the following formula: $(A/180) \times (B/180) \times 100$, where A represents the arc (in degrees) of the necrotic portion on the midcoronal image and B

Table 4
International Classification of Osteonecrosis of the Femoral Head[1]

Stage	Characteristics*
0	Bone biopsy results consistent with osteonecrosis; other tests normal
I	Positive bone scan or MR study or both IA: <15% involvement of the femoral head (MR) IB: 15% to 30% involvement of the femoral head (MR) IC: >30% involvement of the femoral head (MR)
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 bone scan and MR study; no changes in acetabulum IIA: <15% involvement of the femoral head (MR) IIB: 15% to 30% involvement of the femoral head (MR) IIC: >30% involvement of the femoral head (MR)
III	Presence of crescent sign lesions classified on basis of appearance on anteroposterior and lateral radiographs IIIA: <15% crescent sign or <2-mm depression of femoral head IIIB: 15% to 30% crescent sign or 2- to 4-mm depression of femoral head IIIC: >30% crescent sign or >4-mm depression of femoral head
IV	Articular surface flattened; joint space shows narrowing; changes in acetabulum with evidence of osteosclerosis, cyst formation, and marginal osteophytes

* Lesions can also be subdivided according to location (medial, central, or lateral).

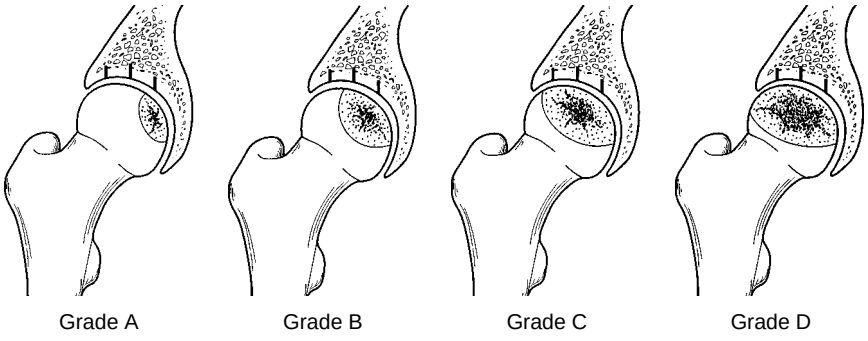

Fig. 5 Classification devised by Sakamoto et al[39] for staging of osteonecrosis on the basis of the extent of lesions as visualized on MR imaging.

represents the arc on the midsagittal image. The values obtained were used to characterize the extent of necrosis as small (<33), designated grade A; medium (34 to 66), grade B; or large (67 to 100), grade C. In their study group, the collapse rate for grade A disease was 13%; for grade B, 95%; and for grade C, 100%.

Sugano et al[43] described another staging system based on the appearance of coronal T1-weighted MR images (Table 5, Fig. 6). This system can be useful in determining the risk of femoral head collapse when lesions are not apparent on plain radiographs.

Bone Scanning

Because of its low cost, some surgeons recommend bone scanning with the use of technetium-99m methylene diphosphonate as an alternative to MR imaging. A common indication for its use is a symptomatic hip with a normal radiographic appearance and no risk factors. Similarly, the surgeon treating a patient with unilateral symptoms may wish to evaluate the contralateral hip to rule out "silent" osteonecrosis; in that situation, it has been proposed that if the bone scan is negative, no treatment other than observation is necessary.[1]

In diseased femoral heads, a zone of increased activity, representing increased bone turnover, will be visualized between the area of necrosis and the area of reactive bone. As the isotope accumulates at that site, the area is visualized as a "hot," or higher-density, zone, which is surrounded by a "colder," or lower-density, zone. Early after the ischemic insult, a bone scan may not show isotope accumulation; once remodeling has begun, however, a cold spot becomes a hot spot. The interval between these two events is from 10 to 14 days; until the end of that period (called the "crossover point"), a bone scan may be false-negative.[38]

Other Diagnostic Methods

Alternative diagnostic methods have been introduced to identify early-stage osteonecrosis, which is not detected with routinely used imaging studies. Histologic studies that reveal empty lacunae in bone trabeculae provide a definite diagnosis of osteonecrosis. Although usually used to confirm disease after core decompression, biopsy has also been used as a preoperative diagnostic method.[1]

Measurement of medullary pressure and venography are specific tests for evaluation of bone function but are no longer used for the diagnosis of osteonecrosis. Computed tomography can be useful for detecting early stages of disease (II or III) without collapse; however, as it has little place in staging the disorder, it is not used routinely.

Management

The treatment of osteonecrosis has been a problem for many years.

Table 5
Staging System of Sugano et al[43]

Type	Appearance on T1-Weighted MR Images
I	Demarcation line appears in the femoral head
	IA: The outer end of the demarcation line is located in the medial third of the weight-bearing surface
	IB: The outer end of the demarcation line is located in the central third of the weight-bearing surface
	IC: The outer end of the demarcation line is located in the lateral third of the weight-bearing surface
II	Early flattening of weight-bearing surface with no demarcation line
III	Cystic radiolucent lesion with no demarcation line
	IIIA: Cystic lesion is located anteriorly or medially, far from the weight-bearing surface
	IIIB: Cystic lesion is under the lateral weight-bearing surface

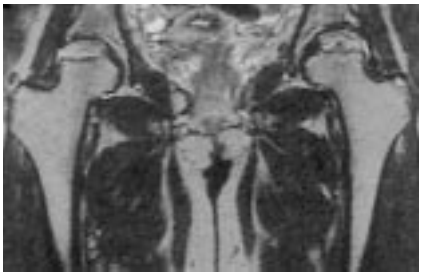

Fig. 6 MR image of a 35-year-old woman receiving corticosteroids for systemic lupus erythematosus. Although the patient had clinical symptoms suggestive of osteonecrosis of both femoral heads, radiographs showed no pathologic changes. MR image clearly demonstrates osteonecrosis of both femoral heads (Sugano stage IC).

No single method or combination of methods has been demonstrated to universally prevent disease progression. The natural history of this devastating disease is one of sclerosis and subchondral fractures leading to collapse and painful disabling arthrosis. Studies have shown that when management is limited to observation alone or restricted weight bearing, collapse of the femoral head will eventually occur in at least 80% of cases. Several treatment modalities are currently available. Their use is based on the stage of the disease: in the early stages, prophylactic measures are instituted to prevent further progression of disease; in later stages, when collapse and significant distortion of the head are present, a reconstructive procedure is the treatment of choice.

Early Stages

Conservative treatment involving only maintenance of nonweight-bearing status with the use of crutches or a cane has proved ineffective except for the treatment of small, asymptomatic lesions located outside the major weight-bearing areas. It is also appropriate for patients with contraindications against surgery and for older patients and those with limited life expectancy.

An appropriate pharmacologic treatment for osteonecrosis is still being sought. Antihypertensive, lipid-lowering,[50] fibrinolytic, and vasoactive agents have been proposed for the treatment of early stages of disease.

Core decompression, as described by Arlet and Ficat in 1964, was first used as part of a diagnostic protocol in which a portion of the femoral head (8 to 10 mm) was removed to obtain tissue for histologic studies.[1] Because patients who underwent this procedure reported lessening of pain, it was instituted as a treatment modality, with the rationale that elevated intraosseous pressure was reduced when holes were drilled into the diseased femoral head. In addition, removal of one or more cores may stimulate repair of the sclerotic areas by promoting vascular ingrowth. Success rates of 96% for stage I disease, 74% for stage II disease, and 35% for stage III disease have been reported.[10] However, these encouraging results have not been obtained by other investigators. Camp and Colwell[44] concluded that core decompression is an ineffective procedure with significant morbidity. Smith et al[45] reported a failure rate of 16% for stage I disease (in the modified Arlet-Ficat staging system), 53% for stage IIA, 80% for stage IIB, and 100% for stage III. The poor outcome in that study could be due to the fact that it reflected the experience of 14 surgeons and the use of various operative techniques.

Although the effectiveness of core decompression continues to be controversial, the larger, better controlled series report a low incidence of complications and superior results when compared with conservative management. Patients who undergo core decompression benefit from pain relief, preservation of the femoral head, and delay of arthroplasty.

Bone-grafting procedures are used as treatment for osteonecrosis, alone or in combination with other procedures, such as core decompression. Both cortical bone and cancellous bone are used for structural support, to promote vascular ingrowth in the healing bone. One of the procedures that has been studied is vascularized fibular bone grafting. This procedure is technically difficult and time consuming and requires a microvascular anastomosis between the vessels of the graft and the branches of the femoral artery that supply the hip joint. There is some morbidity at the graft donor site. In the 103 patients studied by Sotereanos et al,[46] complications included peroneal nerve sensory neuropathy (in 7.6%), contractures of the flexor hallucis longus (in 12.3%), and deep venous thrombosis (in 9.2%). The most commonly reported complication is postoperative ankle discomfort when walking. The superiority of these procedures over simpler surgical techniques has not been established.[46,47]

Osteotomies of the proximal femur are aimed at shifting the affected areas of the femoral head away from the major weight-bearing regions of the joint. These are technically complicated procedures that should be done only by experienced surgeons. Their effectiveness is still under evaluation. They should be done only in carefully selected individuals in whom total hip replacement is not appropriate, with the acknowledgment that a subsequent reconstructive surgery will be more difficult.[3,48]

Later Stages

When collapse and deformation of the femoral head occur and painful arthrosis is refractory to medical treatment, reconstruction is the procedure of choice. Early reports of the results of total hip arthroplasty in young patients

were disappointing when compared with those in older patients, with failure rates of up to 26%.[1,49] However, recent studies suggest otherwise. Garino and Steinberg[35] followed up 123 patients for 2 to 10 years. Only 4% required revision, and 2% showed radiographic evidence of loosening.

Summary

Although the body of knowledge regarding the etiology, pathogenesis, diagnosis, and treatment of osteonecrosis continues to grow, important questions remain unanswered. Differences in study results, the complexity of data collection, and the low incidence of the disease have hindered investigators from reaching consensus on many issues. Multicenter studies are necessary to provide the larger patient numbers that will allow a clearer understanding of this condition.

Appropriate pharmacologic and femoral head–sparing surgical treatments for the early stages of osteonecrosis are being evaluated. Although the benefits of core decompression in the treatment of osteonecrosis of the femoral head continue to be controversial within the orthopaedic community, in the authors' opinion, this procedure provides a reasonable solution for the treatment of early-stage osteonecrosis. For the symptomatic patient with severe disruption of the joint architecture, total hip arthroplasty remains the treatment of choice.

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