Osteonecrosis of the Femoral Head: Update Article

Osteonecrose da cabeça femoral: Artigo de atualização

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Abstract

Among the pathologies that affect the hip joint, osteonecrosis of the femoral head (ONFH) is probably the most intriguing and challenging. It consists of a multifactorial disease with a highly-variable spectrum in its clinical presentation. It has a devastating effect, due to disabling painful conditions, both for usual activities and sports. Given the huge range of risk factors, such as prolonged use of corticosteroids (especially in cases of rheumatologic diseases), trauma sequelae, sickle cell anemia, HIV, alcoholism, smoking, blood dyscrasias, and several other diseases that compromise the blood supply to the femoral head, ONFH has a varied clinical presentation and prognosis, which makes it difficult to determine a specific treatment, especially in cases in which chondral involvement has not yet occurred and the hip joint is still preserved. These are the main factors found in the literature that determine the classifications of this pathology. The range of treatments includes several options for cases in which an attempt is made to save the joint: conservative treatment, traditional decompression and/or combined with some type of adjuvant treatment (homologous grafting, synthetic grafting, vascularized grafts, tantalum screws, and bone marrow aspirate injection), and, for cases in which there is already a subchondral fracture and/or collapse of the femoral head and/or a reduction in the joint space, femoral osteotomies or total hip arthroplasty are commonly performed.

Keywords

- femur head/abnormalities
- osteonecrosis
- hip descrompression
- hip prosthesis
- graft

Resumo

Entre as patologias que acometem a articulação coxofemoral, a osteonecrose da cabeça femoral (ONCF) é provavelmente a mais intrigante e desafiadora. Consiste em uma doença multifatorial, com um espectro muito variável em sua apresentação clínica. Tem efeito devastador, devido a quadros dolorosos incapacitantes tanto para atividades habituais quanto esportivas. Dada a gama enorme de fatores de risco, tais como uso prolongado de corticoides (principalmente em casos de doenças reumatológicas), sequelas de trauma, anemia falciforme, HIV, etilismo, tabagismo, discrasias sanguíneas, e várias outras doenças que comprometem a irrigação sanguínea da cabeça femoral, a ONCF tem apresentação

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clínica e prognósticos bem variados, o que dificulta a determinação de um tratamento específico, especialmente em casos nos quais ainda não houve acometimento condral e a articulação do quadril ainda se mantém preservada, sendo estes os principais fatores encontrados na literatura que determinam as classificações desta patologia. No leque de tratamentos, encontramos diversas opções para os casos em que se tenta salvar a articulação: tratamento conservador, descompressão simples e/ou associada a algum tipo de tratamento adjuvante (enxertia homóloga, enxertia sintética, enxertos vascularizados, parafusos de tântalo, e injeção de aspirado de medula óssea), e, para casos nos quais já há fratura subcondral e/ou colapso da cabeça femoral e/ou diminuição do espaço articular, reserva-se, comumente, a realização de osteotomias femorais ou artroplastia total do quadril.

Palavras-chave
- cabeça do fêmur/anormalidades
- osteonecrose
- descompressão do quadril
- prótese de quadril
- enxerto

Introduction

Osteonecrosis of the femoral head (ONFH) usually affects young patients between the third and fifth decades of life.[1] The initial clinical condition is usually insidious, with the patient reporting a pattern of joint pain (inguinal, in the groin region) associated or not with sports activities, with an occasional sudden increase in pain, probably related to the stage of greater ischemia and increased bone edema of the proximal femur,[2] which may later evolve to a pattern of improvement over a few months. Occasionally, the patient may have complaints unrelated to the hip joint, such as low back pain, pain in the peritrochanteric region, or in the knees. It is noteworthy that, during the anamnesis, it is of paramount importance to assess the history of previous diseases, drug treatments, and habits and addictions that may be related to ONFH.

In some cases, patients are initially asymptomatic, and are diagnosed with ONFH lesion as a finding of an exam due to another complaint. In more advanced cases, in which there are degenerative changes (cartilage damage, flattening of the femoral head, reduced joint space) and secondary arthrosis, complaints of pain and functional limitation are more important, and the clinical presentation resembles a case of primary coxarthrosis.

The etiology of ONFH comprises a vast series of pathologies that lead to impairment of the microvascular circulation of the femoral head,[3,4] either by mechanical vascular interruption, as in femoral head fractures, femoral neck fractures (especially displaced neck fractures – Garden III or IV – whose syntheses are maintained)[5] or dislocation of the hip joint, in which there is injury to the medial circumflex femoral artery;[6] intravascular occlusion, such as in blood dyscrasias (sickle cell anemia – probably the hematological condition with the fastest clinical evolution,[7,8] hemophilia – causing repeated intraosseous hemorrhages, Von Willebrand disease, factor V Leiden mutation, deficiency of proteins C and S, and polycythemia vera)[9]; extravascular compression, due to accumulation of fat in the bone marrow, such as with the use of corticosteroids,[10,11] in which there may be a replacement of pluripotent cells by fat cells, alteration of bone homeostasis, and damage to osteocytes; and alcohol abuse.[12,13] As for the use of corticosteroids and alcohol abuse, both have been proven to be dose-dependent, with an increase in the risk with the use of more than 20 mg a day of corticosteroids and an almost 18-fold increase in the risk with an intake of more than 1,000 mL a week of alcohol.

Other less common pathologies,[14–19] such as Gaucher disease, Caisson disease, dysbarism from deep water diving, as well as HIV, radiation therapy, pregnancy, smoking and gout can also lead to ONFH. A current study has shown that, in idiopathic cases, acetabular alterations with less coverage of the femoral head may be related to ONFH.[20]

The most common pathologies and factors are reported in detail in►**Table 1**.

Complementary Exams

The diagnostic investigation of ONFH usually starts with a plain radiograph in anteroposterior and lateral views of the hip, but these exams may be unaltered in the early stages of the disease. Specific incidences such as the Dunn, Lequesne and Ducroquet profiles may be requested, especially if there are other diagnostic hypotheses.[21] On plain radiographs, the findings can range from unaltered images at very early stages, including sclerosis of the femoral head, to the presence of a subchondral fracture (crescent sign – radiolucency in the subchondral area, best seen in lateral view), and eventual late alterations, such as collapse of the femoral head, joint space narrowing, and degenerative acetabular alterations.

In extremely suspicious cases, with a typical clinical picture, previous diseases and factors associated with ONFH, with normal radiographs, it is mandatory to complete the diagnostic investigation. Currently, the most used test, with better accuracy, and 99% of sensitivity and specificity, is hip magnetic resonance imaging (MRI). In addition to being an excellent diagnostic method, it determines the size and location of the lesion, as well as the presence of bone edema in the proximal femur. The typical findings of necrotic lesion are an area with a "geographic" lesion with hyposignal on T1 and hypersignal on T2. In addition,there is a lesion in double line or double contour on T2, which is considered pathognomonic.

Table 1 Risk factors and most common diseases associated with osteonecrosis of the femoral head

- Trauma: femoral neck fracture, deviated or not, traumatic hip dislocation, occasionally inter- and subtrochanteric fractures, repetitive strain injury, pediatric patients undergoing intramedullary osteosynthesis with piriform entry
- Corticosteroids
- Alcoholism
- Smoking
- Hyperlipidemia
- Diabetes
- Pancreatitis and steatonecrosis
- Hemoglobinopathies and coagulation disorders: sickle cell anemia, hemophilia, Von Willebrand disease, factor V Leiden mutation, deficiency of proteins C and S, polycythemia vera, elevated serum lipoprotein levels, hyperhomocysteinemia
- Myeloproliferative disorders: Gaucher disease, leukemia
- Caisson disease and other decompression illnesses
- Systemic lupus erythematosus and its consequences: use of corticosteroids and other cytotoxic drugs, as well as vasculitis caused by the disease
- Antiphospholipid syndrome
- Disbarism
- Radiotherapy or chemotherapy
- Gout
- Acetabular anatomical changes
- HIV and its treatment: use of protease inhibitors
- Pregnancy
- Malignant tumors
- Inflammatory bowel disease
- Idiopathic

Computed tomography may be requested to diagnose a subchondral fracture not detected on MRI, and to determine the extent of the lesion, but it is less requested than hip MRI scans.

Before the routine use of MRI, bone scintigraphy with technetium was a widely used test. It is very useful as a means of assessing the involvement of other joints, but its current use, as well as that of the positron-emission tomography (PET), is more restricted.

The imaging exams are shown in ►**Figure 1**.

Depending on the patient's risk factors and diseases, a search for the etiology can be carried out in idiopathic cases, with complementary tests such as complete blood count, coagulogram, coagulation factors, erythrocyte sedimentation rate, C-reactive protein, rheumatoid factor, urine analysis, and tests to screen for other systemic diseases (hematological and infectious diseases), as well as evaluations of other medical specialties for a coordinated follow-up and better patient care.

Classification

There are several classifications for ONFH, and the ones most commonly used are: [22]

1- **Ficat and Arlet:** based on the clinical picture, imaging findings on radiographs and scintigraphy, and pathological findings. It does not use MRI in its classification, and the downside is that it does not predict prognosis nor measures lesion size. It is the most used classification, and the one most cited in the literature.[23]

2- **Association Research Circulation Osseus (ARCO) classification:** developed in the 1990s based on the classification of the University of Pennsylvania (Steinberg), it includes the location and size of the lesion, with the percentage of collapse and involvement of the femoral head. An updated review of it was recently published.[13,24]

3- **Kerboul:** useful to predict the prognosis, as it involves the measurement of the area of the femoral head injury and its location on plain anteroposterior and lateral radiographs. This classification was extended to measurements in MRIs by Ha et al.[25] In radiographs, angles smaller than 180° had a better prognosis, and those greater than 230°, a worse prognosis. On the MRI, these values changed to 190° and 240°.

►**Table 2** shows the description of the most used classifications.

Treatment

Treatment of ONFH is perhaps the most controversial point involving this pathology.[26,27] Due to numerous peculiarities regarding the etiology and pathophysiology, clinical presentation, and difficulty in defining an exact prognosis, the treatment varies greatly in the literature and, therefore, among hip surgeons, especially in cases in which there is still no involvement of the articular surface and no subchondral fracture in the femoral head.[28–31] In these cases, the following therapeutic options are described:

1) **Non-surgical treatment**

These are measures that encompass conservative treatment, all without significant evidence in the literature regarding prognosis:

- Analgesic medications and use of support for walking and interruption of sports activities according to pain symptoms.
- Physiotherapy activities with muscle strengthening and stretching, as well as treatment with shock waves, electromagnetic stimulation, and hyperbaric oxygen therapy.
  - Shock waves: in early stages, there may be a better response in relation to pain symptoms compared to simple decompression and non-vascularized grafts.[32]
  - Electromagnetic stimulation and hyperbaric chamber: showed encouraging results at early stages, but still without studies with level I of evidence.[33,34]

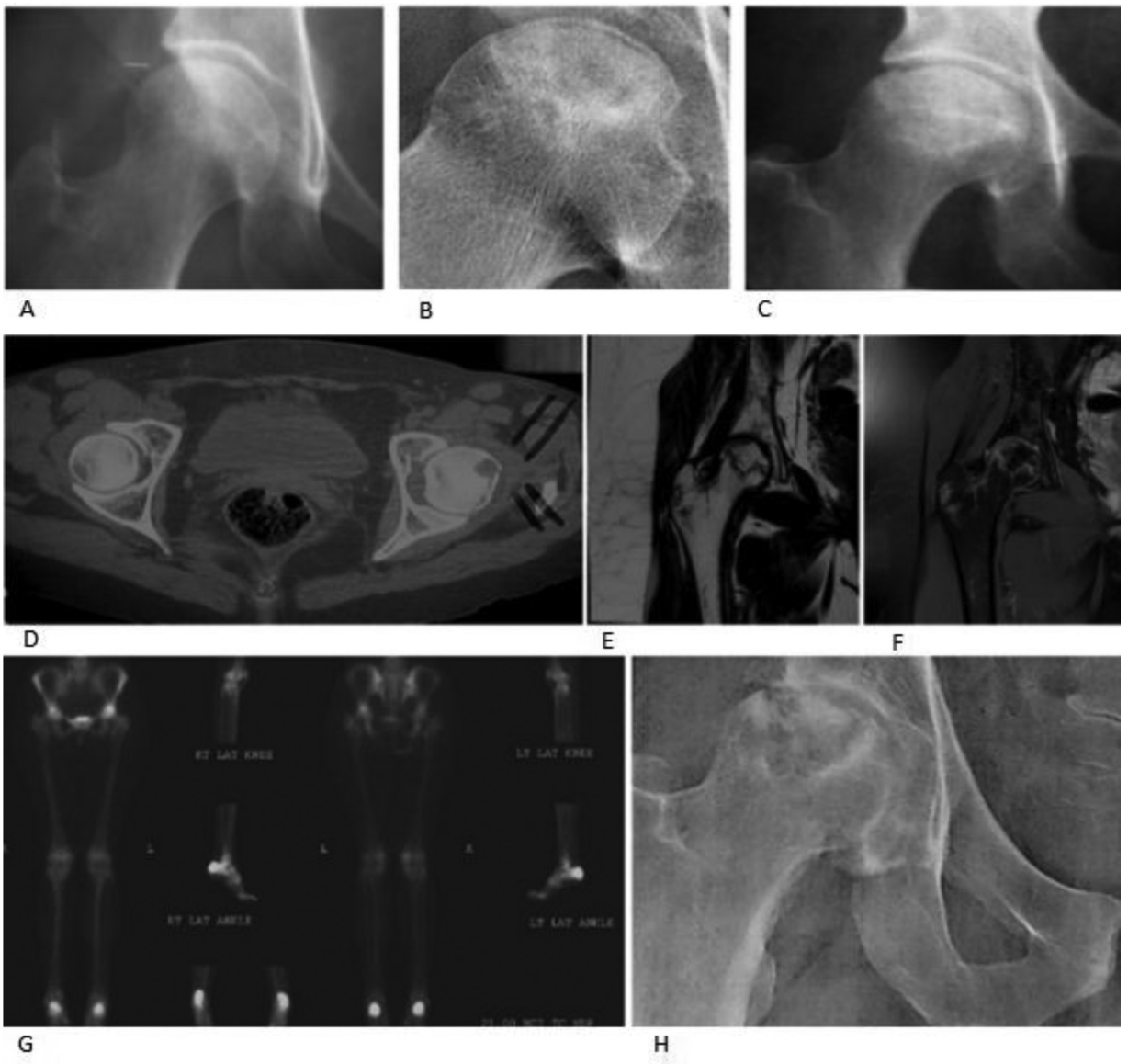

Fig. 1 (**A**) Normal hip radiograph; (**B**) crescent sign; (**C**) flattening of the head; (**D**) tomography with head necrosis; (**E,F**) resonance with T1- and T2-weighted images with necrosis; (**G**) bone scintigraphy of the femoral head; (**H**) secondary degenerative changes.

- Oral medications[35,36] (bisphosphonates, vasodilators, anticoagulants, statins): all with limited statistical support in scientific studies, and none with a recommendation for routine use.
  - Bisphosphonates: in theory, by avoiding bone turnover, they could prevent the collapse of the femoral head. As they have some side effects, such as atypical fracture and osteonecrosis of the jaw, and their use in humans has not been scientifically proven, their use is not routinely indicated.[37,38]
  - Anticoagulants and vasodilators: theoretically, they would be indicated for diseases that cause vascular occlusion and posterior ONFH. There are also no studies that validate its routine use.[39–41]
- Statins: they supposedly have the function of preventing the accumulation of fat in the bone marrow and preventing an increase in intraosseous pressure. However, studies with a higher level of evidence are needed to verify its effectiveness.[42–44]
- Molecular therapy: a recent study[45] with adenovirus associated with anti-mRNA-214, whose importance is to prevent the activation of transcription factor 4, which inhibits the function of the osteoblasts, demonstrated an increase in osteoblastic activity and a decrease in osteoclastic activity, preventing the collapse of the femoral head in mouse models.

2) **Surgical treatment**

- Core decompression: performance of one or multiple perforations of the subchondral bone close to the region of the lesion, in order to provide relief of symptoms and seek an improvement in local blood circulation by

Table 2 Ficat and Arlet, ARCO and Kerboul classifications

Ficat and Arlet	ARCO	Kerboul
0 - Patient without pain, normal radiograph, scintigraphy with decreased uptake	0 - Biopsy results consistent with osteonecrosis of the femoral head; other tests with normal results	Sum of head necrosis angles in coronal and sagittal views on magnetic resonance imaging: $<$ 190° - low risk of head collapse; 190°-240° - moderate risk; $>$ 240° - high risk
1 - Patient without pain, normal radiograph, cold spot scintigraphy in the head, bone infarction in the weight-bearing areas	1 - Positive findings on scintigraphy or magnetic resonance imaging. A: $<$ 15% of the head compromised; B: 15-30%; C: $>$ 30% of the head compromised	
2 - Mild pain, change in radiological density, cysts and sclerosis, but head with preserved contour, hyperuptake scintigraphy, infarcted areas with spontaneous repair	2 - Head sclerosis, cysts and osteopenia on radiographs; without collapse of the femoral head; positive findings on scintigraphy and magnetic resonance imaging; no changes in the acetabulum A: light, up to 15%; B: moderate, 15-30%; C: severe, $>$ 30%	
3 - Moderate pain, radiograph with loss of sphericity and crescent sign – subchondral fracture, hyperuptake scintigraphy	3 - Crescent sign on anteroposterior and profile radiographs: A: $<$ 15% crescent or $<$ 2 mm of head depression; B: 15-30% increasing, 2-4 mm of depression C: $>$ 30% crescent or $>$ 4 mm of head depression	
4 - Moderate/severe pain, acetabular changes and loss of joint space	4 - Flat joint surface; narrowing of the joint space; acetabular changes, cysts, marginal osteophytes	

Abbreviation: ARCO, Association Research Circulation Osseus.

reducing intraosseous pressure. It presents best results in small injuries located outside the weight-bearing area. Complications may include intraoperative joint perforation and postoperative subtrochanteric fracture.[46–48]

- Adjuvant therapies associated or not with core decompression, as a way to prevent the collapse of the femoral head[49]:
  - Homologous grafting, using the Phemister technique, or the "light bulb" or "trap door" procedures. Usually indicated for small or medium injuries.
  - Synthetic grafting, called advanced core decompression in the literature.
  - Microsurgical vascularized graft (fibula, iliac crest, and greater trochanter). The complications encountered involve morbidity due to the surgery, including donor site complications, thrombosis and infection.

All grafting modalities aim to promote a structured bone framework to avoid flattening of the femoral head. They are more indicated in young patients.[50–52]

- Injection of mesenchymal stem cells (bone marrow aspirate): an attempt to promote osteogenesis and necrosis repair.[53] In theory, they decrease the percentage of subchondral collapse in short-term studies.[54–56]
- Tantalum implants: results are still imprecise, and further studies are needed for the correct indication and selection of the ideal patient.[57]
- Femoral osteotomies: the most common in the literature is the Sugioka osteotomy; it consists of an attempt to remove the weight-bearing portion of the joint with the lesion and transfer a healthy area as a new weight-bearing area. The results were not reproduced in all orthopedic centers, and a downside is that there is a possible increase in technical difficulty when patients have to undergo hip prosthesis.[58]
- Arthrodesis: a technique described in literature, but not often used, mainly because it is a pathology that is often bilateral.

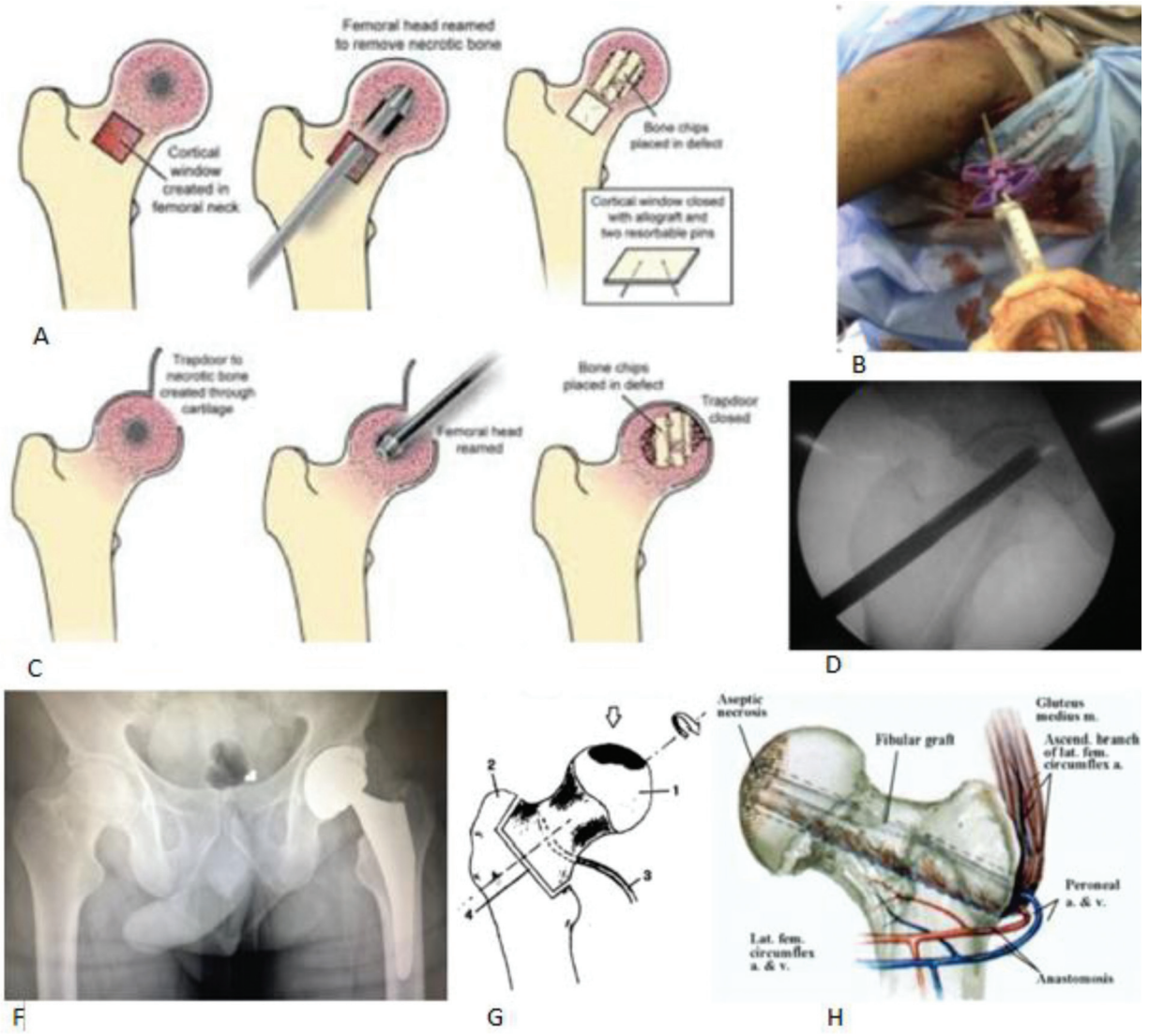

Fig. 2 Treatments: (**A**) "light bulb" procedure; (**B**) decompression and synthetic grafting; (**C**) "trap door" procedure; (**D**) simple core decompression; (**F**) total hip arthroplasty; (**G**) Sugioka osteotomy; (**H**) vascularized graft.

- Arthroplastic resection: as well as arthrodesis and osteotomies, a technique less used nowadays, mainly due to the high success rate of total hip prosthesis.[59]
- Total hip arthroplasty: for cases in which there is already joint involvement, such as the presence of subchondral fracture, flattening of the femoral head and/or joint narrowing, in addition to acetabular changes, the most common treatment is total hip arthroplasty.[60]

►**Figure 2** shows images of the treatments described, and ►**Figure 3** shows the treatment flowchart.

Final Remarks

Osteonecrosis of the femoral head is an extremely intriguing pathology, with several associated factors, multifactorial etiology, and distinct clinical presentations, and there are still divergences regarding the management of each case. A detailed anamnesis and thorough laboratory investigation are of paramount importance to obtain the correct causal diagnosis.

Osteonecrosis of the femoral head has several therapeutic options in its early stages, all for symptom relief, and in an attempt to preserve the joint. In these cases, it is extremely important to elucidate and explain the treatment in order to meet the patient's expectations.

In advanced cases, osteotomies are an option, and total femoral arthroplasty has excellent results, and the procedure should be individualized for each patient.

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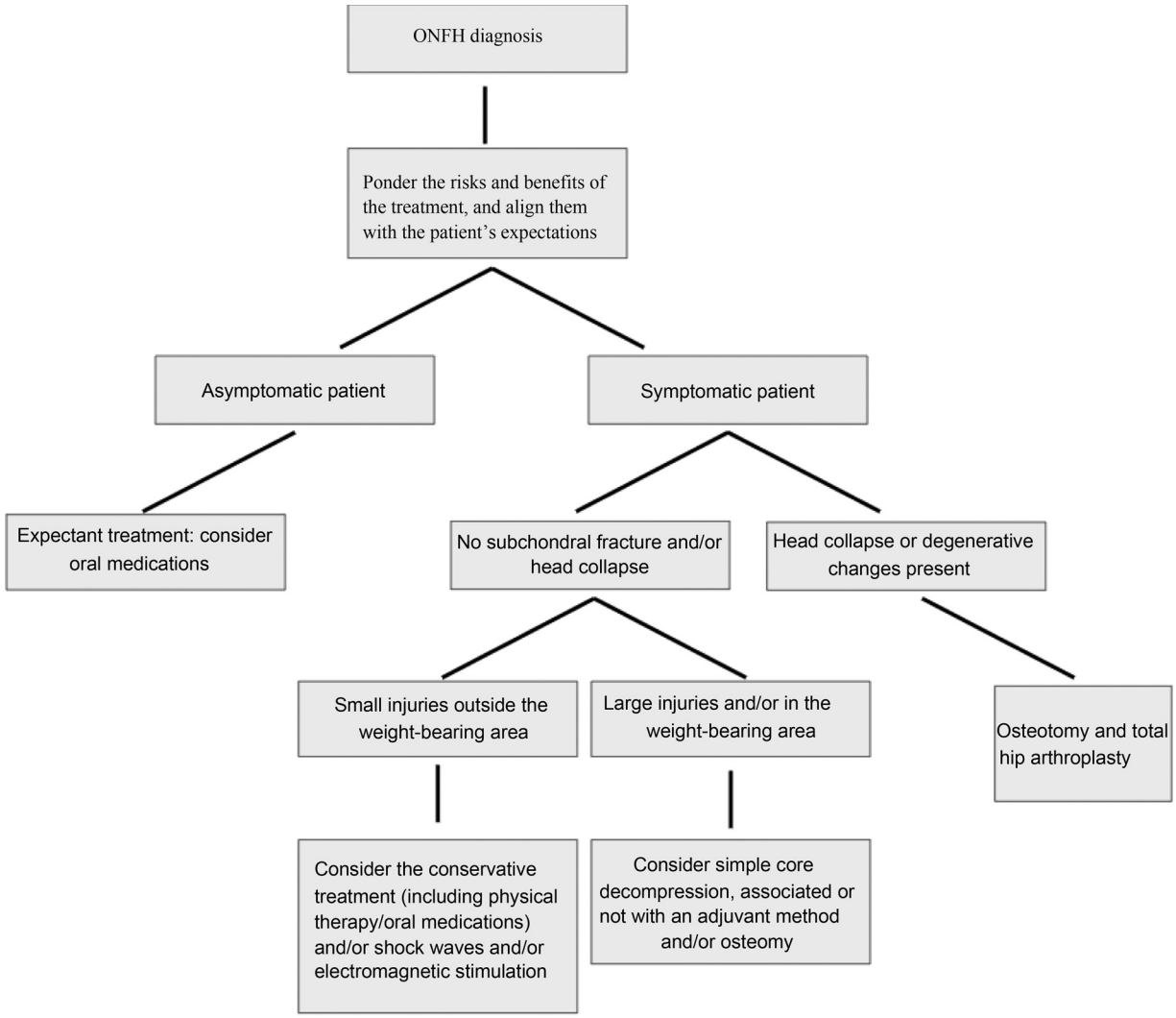

Fig. 3 Treatment flowchart.

Conflict of interests

The authors have no conflict of interests to declare.

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