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Avascular necrosis of hip: Pathophysiology, diagnosis, and treatment

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Abstract

Osteonecrosis, another name for avascular necrosis [AVN] of the hip, is a pathological disorder that results from the femoral head's blood supply being cut off, which kills bone cells and causes joint degradation. Although people of various ages can be affected, young adults, especially those between the ages of 30 and 50, are most frequently affected. A number of risk factors, such as trauma, the use of corticosteroids, alcohol misuse, and specific illnesses like HIV, sickle cell disease, and systemic lupus erythematosus, are linked to AVN. Although AVN is frequently asymptomatic in its early stages, individuals may develop discomfort, stiffness, and restricted hip joint range of motion as the condition worsens. Imaging methods, including CT, MRI, and X-rays have a significant impact on AVN diagnosis, with MRI being the most sensitive test for early identification. Depending on the disease's stage as well as the patient's age, health, and functional needs, treatment choices might range from conservative measures like rest and medication to surgical procedures including core decompression, osteotomy, and total hip replacement. In order to improve long-term results and stop joint collapse, early diagnosis and management are essential. Even with treatment improvements, AVN is still a major contributor to hip impairment, underscoring the need for more investigation into its aetiology and innovative treatment strategies.

Keywords: **A**vascular; Necrosis; Femur; Osteonecrosis; Dysbaric; Cresent

1. Introduction

Disruption of the blood supply to the proximal femur causes avascular necrosis [AVN] of the femoral head, a form of aseptic osteonecrosis that leads to osteocyte demise. Ischemia that develops on a traumatic or non-traumatic background might cause AVN. Among the most frequent etiological causes include corticosteroid therapy, fractures, hip dislocations, and alcohol. "[1]" It mostly effects the people in the age group of 20 to 40 years who are physically active though. In India the average age of men at risk of AVN Hip is at 32 Years and the prevalence of new cases is at around 16000 cases per year which also require a Total Hip replacement [THR]."[2]"

2. Aetiology and risk factors

In cases [15%-30%] the cause is not identified, Idiopathic. Clinicians must look for risk factors, particularly those that are modifiable or treatable. It must be acknowledged that all causes share a large number of mechanisms, most of which are complex. [The most frequent cause is the Steroidal and Alcohol misuse. These both accounts for upto 80% and people who misuse are at. "[3]"

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2.1. Corticosteroids

The most common cause of non-traumatic Avascular osteonecrosis of the femoral head [ONFH] is this. Thirty percent of the 3000 cases of non-traumatic osteonecrosis involved corticosteroids, and twenty percent involved alcohol. Another possible aetiology of ONFH, SARS Covid 2 [COVID-19], systemic lupus erythematosus [SLE], seems to be more sensitive to. "[3]" The incidence of ONFH was 6.7% if corticosteroid treatment surpassed 2 g prednisone-equivalent, and it increased by 3.6% for every 10 mg/d increase, according to a meta-analysis of 57 trials including 23,561 patients conducted by Mont et al. The risk was decreased if the threshold was less than 15 mg/d, but it rose if it was greater than 20 mg. "[3]"

2.2. Alcohol Abuse

About 20–30% of patients who had hip osteonecrosis were found to have excessive alcohol usage. Numerous processes, including osteocyte death, increased lipid deposition, and reduced bone formation, have been proposed as causes of steroid-induced ONFH; many of them seem probably going to be shared. It has recently been reported that alcohol-induced osteonecrosis of the femoral head may be caused by abnormal expression of mi-RNAS, with targets for bone or vascular genes including IGF2, PDGFA, RUNX2, PTEN, and VEGF."[4]" Diabetes, Cushing Syndrome, Pancreatitis, Intravascular Coagulation, Hyperuricemia, HIV, Hemochromatosis, Radiation, Smoking are the other risk factors of AVN of Bone.

3. Gaucher's Disease

One of the classic causes of ONFH is Gaucher disease, which frequently occurs in conjunction with multiple osteonecrosis. The accumulation of glucocerebroside in the lysosomes of mononuclear phagocytes, primarily in the liver, spleen, and bone marrow, is caused by a lack of the lysosomal enzyme glucocerebrosidase. Osteoarticular symptoms are frequently early and play a major role in Gaucher disease morbidity and disability. "[4]"

3.1. COVID-19

Osteonecrosis in COVID has been majorly due to use of corticosteroid therapy which is seemed to be the major risk factor.

3.2. Systemic lupus erythematosus

Osteonecrosis in Lupus has been reported in 3-30% of the cases and as said before, corticosteroids seemed to be a major risk factor. However, the susceptibility to steroids induced osteonecrosis seems to be stronger than for other diseases. Very recently a genetic predisposition has been suggested with some Single Nucleotide Variations [SNVs] in NOS3, COL2A1, and CR2 genes, respectively involved in bone or cartilage formation and for CR2 in autoimmunity. "[4]"

Haemodialysis with chronic renal failure in conjunction with organ transplantation: Between 3 to 41% of organ transplant recipients are thought to have ONFH. The most researched patients are those who have received kidney transplants. With various steroids and immunosuppressive drugs, the majority of the investigations are retrospective. Treatment plan and imaging techniques. In a prospective trial, the incidence was lower, with 11% of the hips showing osteonecrosis of the femoral head. "[4]"

3.3. Sickle cell illness

This aetiology is the subject of a separate chapter in this review. In this context, the ONFH is common because of the intravascular blockage associated with the form of crimson globules. In most cases, the clinical setting aids in the diagnosis. "[4]"

3.4. Lymphoma and leukaemia

Acute myeloid lymphoma, chronic myeloid leukaemia, and acute lymphoblastic leukaemia all carry a higher risk of bone death. The main risk factor appears to be steroids. The primary cause is high corticosteroid dosages. In both adults and children, osteonecrosis can also result from bone marrow transplantation and graft versus host reaction. Three years following transplantation, the frequency has been estimated to be between 6% and 19%. The most prevalent localization is ONFH. The two main risk factors are immunosuppressant and steroids. "[4]"

3.5. Caisson disease or Dysbaric osteonecrosis

In addition to underwater divers and workers inhaling compressed air, this is another extremely common but uncommon cause of ONFH. The most widely accepted explanation is that it results from a chronic case of subclinical decompression sickness [DCS]. Decompression causes the coagulation process to be activated, causing emboli in the bone microcirculation and the breakdown of gas in the blood with the creation of gas bubbles. Osteonecrosis and a rise in intraosseous pressure are the results. The femur and tibia may develop diaphysis osteonecrosis, which can occasionally cause severe discomfort while under stress and have a high risk of fracture. "[5]"

3.6. Elevated cholesterol levels

One well-known cause of osteonecrosis is hyperlipidaemia. Few research, meanwhile, have looked at this subject. In 112 acute lymphoblastic leukaemia patients [young adults and children], 22 people had osteonecrosis symptoms. With elevated triglyceride and cholesterol levels, hyperlipidaemia was linked to a higher incidence of osteonecrosis in this cohort. There appeared to be a negative correlation between osteonecrosis and elevated HDL cholesterol. However, osteonecrosis was not linked to a sustained rise in LDL cholesterol. "[6]"

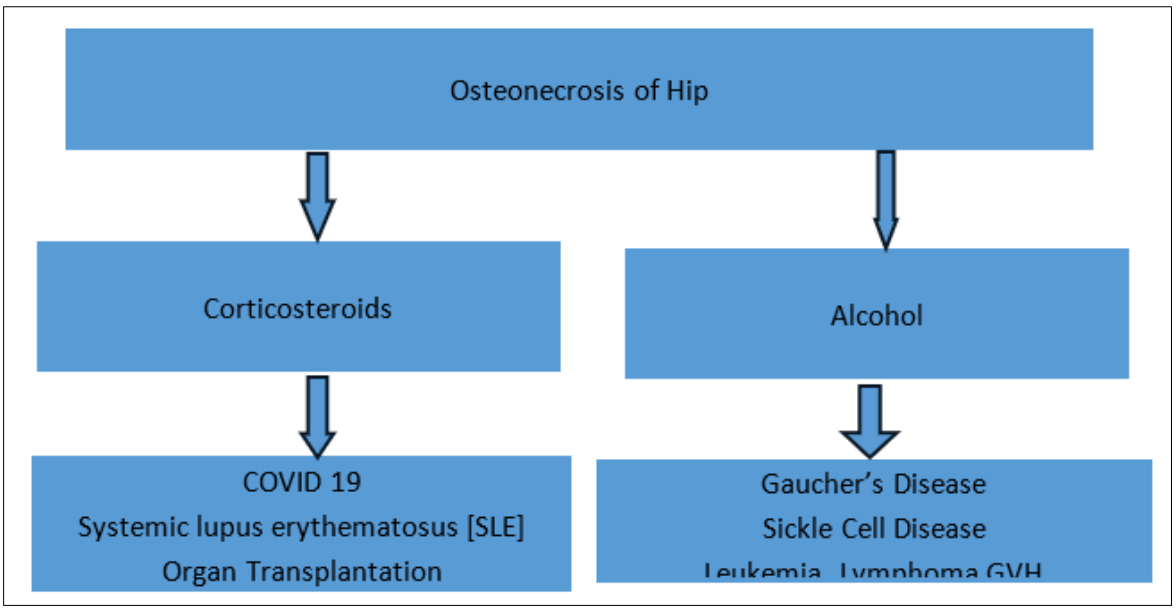

Figure 1 A overview flowchart on etiology of AVN

4. Pathophysiology

Although the clinical appearance is the consequence of the repair process rather than the initial ischemia, osteonecrosis is caused by impaired blood flow or oxygen supply to the bone. Bone resorption by osteoclasts cannot keep pace with bone growth by osteoblasts in osteonecrosis. A zone of structurally unstable bone tissues remains after this remodeling imbalance fails to sufficiently repair the necrotic bone. These changes could be caused by a traumatic or non-traumatic event, or they could result from certain known risk factors. It's crucial to note that, in terms of the traumatic causation, the retinacula arteries that supply the superolateral weight-bearing part of the femoral head provide the majority of the blood flow. The lateral epiphyseal artery, a branch of the medial circumflex arteries, is the source of these retinal vessels. Physical trauma, decompression sickness, or radiation are examples of traumatic causes. Two theories are up for debate in the non-trauma cases: the first posits that an intravascular coagulation occurred, while the second ascribes the ischemia to extravascular compression. Furthermore, it is now acknowledged that the pathophysiological mechanism results from a combination of genetics, risk factors, altered bone-cell physiology, and vascular impairment.14 In hypercoagulable diseases such sickle cell anemia, hereditary thrombophilia, antiphospholipid antibodies, cancer, and inflammatory bowel disease, coagulation abnormalities ultimately lead to vascular damage. It is frequently suggested that the osteonecrosis process involves a changed cell-bone physiology. The theory is that ON develops as a result of poor mesenchymal differentiation, which damages the bone structure. Under normal circumstances, it takes roughly three months to form new bone with useful mechanical qualities, while it takes three weeks for osteoclasts to influence the trabecular bone's mechanical strength. Therefore, the ON of the femoral head would eventually be supported by any mesenchymal cell malfunction that results in changes in osteogenic differentiation and blood flow through an increased

adipogenic volume. Alcohol consumption and the use of corticoids15–18 are the most frequently mentioned risk factors. The administration of corticoids causes vasoconstriction and increases the generation of procoagulant factors. Through the creation of fatty emboli, it also downregulates osseous repair and remodeling, enhances adipogenesis, and lowers osteogenesis. "[7]"

4.1. Traumatic osteonecrosis

The most frequent cause of osteonecrosis is trauma, which causes osteocyte death by altering blood flow. Depending on the type of injury, estimates of the incidence of traumatic osteonecrosis of the femoral head vary.

4.2. Atraumatic osteonecrosis

There are several different causes of atraumatic osteonecrosis. It is significant to remember that systemic risk factors in atraumatic osteonecrosis often cause the illness to be bilateral, with some estimates indicating as high as Disease in the contralateral hip develops in 70% of people with unilateral osteonecrosis. "[8]"Alcohol consumption and the use of corticoids15–18 are the most frequently mentioned risk factors.

4.3. Hyperlipidemia

Through the production of fat emboli and an increase in intraosseous pressure, hyperlipidemia is believed to reduce the blood supply to afflicted areas**.** "[8]"

4.4. Corticosteroids

The administration of corticoids causes vasoconstriction and increases the generation of procoagulant factors. Through the creation of fatty emboli, it also downregulates osseous repair and remodeling, enhances adipogenesis, and lowers osteogenesis. Five main ideas about the pathophysiology of steroid-induced ONFH [SONFH] were enumerated by Wang et al. in a recent review paper. These theories include gene polymorphism, lipid metabolic abnormalities, diminished osteogenesis capacity, inadequate blood supply, and cell death. The authors came to the conclusion that SONFH is the consequence of several steroid-related pathways working together. According to some studies, cortisone can be considered an independent variable, particularly when taken in large quantities, and it can raise the risk of osteonecrosis by up to 20 times**.** "[9]"

4.5. Alcohol

Drinking alcohol would change the way mesenchymal differentiation occurs, and numerous studies have demonstrated that the capacity to differentiate into an osteoblastic lineage is diminished**.** "[9]"In addition, increased serum lipids can also result in marrow packing, which raises intraosseous pressure and reduces blood flow. Alcohol may also be a factor in the mortality of osteocytes**.**

4.6. Coagulation disorders

The risk of AVN is greatly increased by blood coagulation-related conditions such thrombophilia and hypercoagulable disorders. Microvascular thrombosis, which compromises the blood flow to the bone, can result from an imbalance in blood coagulation components in people with coagulation disorders. The pathophysiology of AVN is influenced by thrombotic events that occur in the tiny arteries supplying bone tissue**.** "[10]"

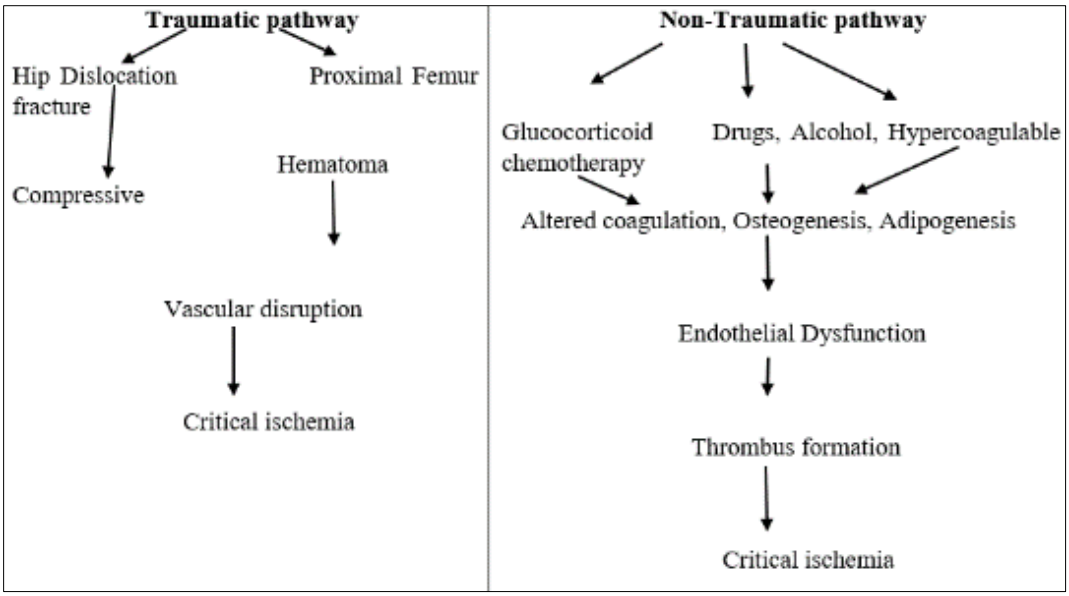

Figure 2 A Brief overview of pathophysiology of AVN

5. Stages of avascular necrosis

Table 1 Stages of avascular necrosis

Stages	Clinical features	Radiological findings	Images
Stage 1	No radiographic abnormalities but pain	Normal radiography, abnormal MRI	
Stage 2	Increased density, and cystic changes	Abnormal radiography without fracture	
Stage 3	Flattening of the femoral head &crescent sign	Subchondral or necrotic zone fracture IIIA:≤2mm flatten IIIB:>2mm flatten	

Stage 4	Full collapse of the femoral head with decreases in joint space	Radiographic evidence of arthritis with joint space narrowing acetabular changes and or join destruction.	

6. Clinical manifestations

- Joint pain that could become worse over time and get really bad if the bone falls out.
- Pain that persists while you're at rest.
- Restricted range of motion.
- If the hip joint is impacted, groin pain
- If the ailment affects the leg, limping.
- If the shoulder joint is impacted, difficulty moving overhead.
- In the early stages, there are no symptoms. The following symptoms could appear when bone degeneration gets worse.
- Joint pain that could become worse over time and get really bad if the bone falls out Even when at rest, there is pain and a restricted range of motion.

The presenting symptom is usually a throbbing, deep, and frequently intermittent pain in the afflicted joint. Patients with femoral head AVN frequently have hip or groin discomfort that can radiate to the knee, anteromedial thigh, or buttocks. This pain is made worse by bearing weight and occasionally by coughing. Although the discomfort may be modest at first, it gradually gets worse with use and time. After a while, the discomfort is felt while at rest and may continue or even get worse at night, in which case it can be linked to stiffness in the morning. "[11]"

7. Diagnosis of AVN hip

A medical professional will apply pressure to your joints during a physical examination to feel for any soreness. In order to determine whether the range of motion is reduced, they may also move the joints into various postures. Imaging examinations Joint pain can be caused by a variety of conditions. Finding the source of discomfort can be aided by imaging testing. X-rays are one type of test. In the final phases of avascular necrosis, they can show changes in the bone. X-rays typically show no issues in the early stages of the illness.

CT and MRI scans: These examinations generate fine-grained pictures that can reveal early bone alterations that may point to avascular necrosis. A vein receives a little injection of radioactive material. This tracer moves to the damaged or healing areas of the bones.

Bone scan with radionuclide: A very tiny quantity of radioactive material is injected into the blood as part of this nuclear imaging approach so that a scanner can detect it. This test demonstrates both bone cell activity and blood flow to the bone.

Bone scintigraphy helps to pick up AVN at an earlier stage. The most sensitive method for AVN diagnosis is MRI. A single density line that shows the division of healthy and osteonecrosis bone is the first noticeable alteration in a T1 picture. Within this line, another line may be visible in the T2 picture, signifying the granulation tissue increased vascularity. The amount and extent of AVN can also be quantified using MRI. If there are several sites involved, the expense of the MRI scan is a disadvantage. "[12]"

MRIs were performed at 7T and 3T on 13 patients with avascular necrosis receiving advanced core decompression treatment. For both field strengths, the same sequence parameters and resolution were used. Two radiologists assessed all MR images [MEDIC, DESS, PD/T2w TSE, T1w TSE, and STIR] for soft tissue contrasts, subjective image quality, B1 homogeneity [four-point scale, higher values indicate better image quality], and representation of femoral head imaging

abnormalities [three-point scale, higher values indicate superiority of 7 T]. Soft tissue contrast ratios were computed and contrasted with subjective information. "[13]"

Avascular necrosis [AVN] of the hip can be diagnosed by MRI, according to a number of studies. But CT and radionuclide bone scanning [RN] can also successfully identify AVN. Plain-film radiography and these methods are currently the main ways to diagnose this illness. Although tomograms can also be helpful in identifying AVN, MRI is more sensitive than both tomograms and radiography in this regard. The theory that MRI is superior to CT and RN in diagnosing AVN. Research conducted by Easton et al. and Thickman et al. demonstrated that MRI was superior to the other methods. "[14]" Numerous imaging methods, such as computed tomography [CT], magnetic resonance imaging [MRI], radionuclide tests, and X-rays, were found to be useful in identifying the symptoms of bone necrosis. The first imaging assessment of AVN should be radiography, which is a widely accessible and reasonably priced method. Subchondral radiolucency, sometimes known as the & quot; crescentsign, & quot; is a symptom of subchondral collapse that can be seen on classic radiography. Later stages of AVN are seen on CT and X-rays, which are less sensitive than MRI. However, AVN symptoms are frequently noticeable enough to not require further radiologic testing. "[15]"

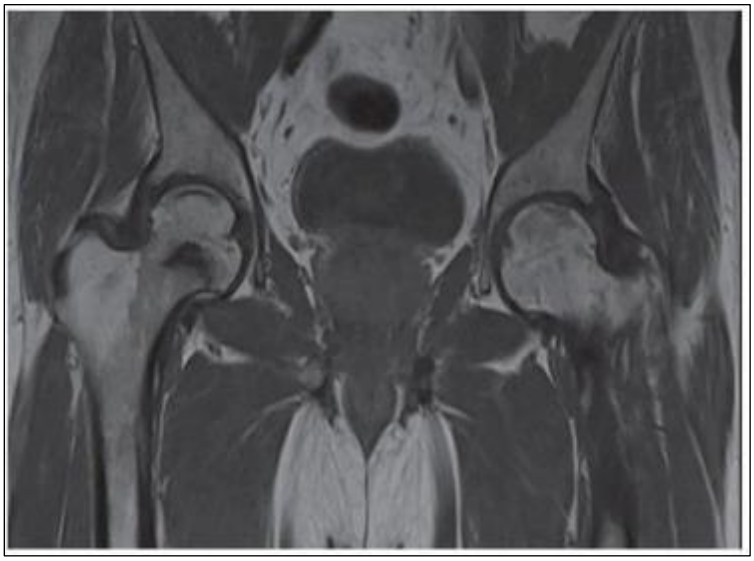

Figure 3 The posteroanterior view shows a right [R] AVN of the femoral head [T1-weighted]. "[1]"

8. Management

8.1. Non-Surgical Management Conservative treatment of AVN

Management Without Surgery Improving hip function, preventing the femoral head from collapsing, relieving discomfort, and delaying necrotic changes are the goals of conservative treatment for AVN. Patients without a history of trauma are typically treated nonoperatively in the early stages of their illness. On the Steinberg scale, the imaging results typically fall between stages 0 and 1. One strategy to slow the progression of the condition is to limit weight-bearing with a walker, crutches, or cane. But according to some research, lowering joint reactive forces doesn't stop the progression of the disease.

8.2. Pharmacological Treatment

For the treatment of AVN, several pharmacological treatments were suggested. These consist of statins, anticoagulants, bisphosphonates, vasodilators, and other medications that are presently being studied. Most often, this type of treatment is applied when the illness is still in its early stages. However, due to a lack of evidence, their usefulness is limited and there are no clear recommendations for its usage in AVN. Many individuals subsequently have surgery following pharmacological treatment.

8.2.1. Bisphosphonates

Bisphosphonates are advised when AVN is first getting started. They prevent woven bone growth by lowering bone turnover and suppressing osteoclastic activity. In individuals with non-traumatic AVN at Steinberg stages II–III, the

effectiveness of alendronate and a placebo was compared in a randomized controlled experiment. Nineteen out of twenty-five evaluated femoral heads collapsed in the placebo group, compared to two collapses in the medication group. Chen et al.'s subsequent prospective, randomized, placebo-controlled research, however, did not support these conclusions. The placebo and therapy arms did not significantly vary in terms of radiographic results, total hip replacement prevention, or quality of life improvement. As a result, the available research findings are not conclusive. The absence of a control group is one of the methodological flaws in some of them. Due to the lack of evidence, guidelines regarding the dosage and duration of bisphosphonate therapy cannot be formed.

8.2.2. Statins

Statin therapy may prevent adipogenesis and femoral head osteonecrosis brought on by corticosteroid use. However, there are no recommendations for the use of statins, just like with bisphosphonate therapy. According to Ajmal et al.'s findings, patients on corticosteroids who are also on statins do not have a different risk of developing osteonecrosis. Conversely, Prichett et al. found that patients using statins and steroids had a much lower AVN rate.

8.2.3. Vasodilators

Iloprost, a vasodilator, has been shown to improve radiological and clinical results in individuals with early-stage AVN. In 108 patients with osteonecrosis, Claßen et al. examined the impact of iloprost; the median patient follow-up was 49.7 months. Subjective complaints improved, and the visual analogue scale showed a decrease, according to the majority of patients [74.8%]. Nonetheless, superior results were obtained by patients with a lower stage of the disease. Although there is currently little information on enoxaparin's efficacy, some writers contend that if treatment is started early in the course of osteonecrosis, it may slow the disease's progression.

9. Other Therapies

In AVN treatment, various shockwave devices were investigated. Extracorporeal shockwave therapy [ESWT] has been used in AVN in a number of studies with encouraging outcomes. Pain reduction was the primary outcome; in certain cases, MRI abnormalities completely disappeared. It is hypothesized that ESWT works by stimulating osteoblastic activity, which raises the density of bone in the pelvic region. According to Russo et al., ESWT is more successful than core decompression and grafting, and its effectiveness is more significant in the early stages of the disease. In addition to lowering intraosseous hypertension and bone edema, hyperbaric oxygen therapy raises the concentration of extracellular oxygen. However, large randomized controlled trials are required to confirm the effectiveness of hyperbaric oxygen therapy because of the limited populations in clinical trials and the limitations in their methodology.

9.1. Surgical Treatment

Joint preservation techniques are part of the surgical treatment for AVN. Young patients at the pre-collapse stage of the illness are typically the only ones eligible for these. Patients with advanced disease should consider THA. The most frequent operation carried out in the first phases of AVN is core decompression [CD]. Restoring circulation in the femoral head and lowering intraosseous pressure are the main goals of this technique. In order to relieve internal pressure and make room for new blood arteries, the technique involves drilling holes into the femoral head. Patients with early illness are advised to have CD as their first line of treatment. In long-term follow-up, the approach yields great outcomes and is cost-effective. As the method developed over time, multiple drilling is now advised. "[15]"

9.2. Nonvascularized

The necrotic area in the femoral head is filled with Non vascularized bone transplants made from various body components [such as allograft, fibular autograft, or tibialautograft]. When CD fails, the procedure is most frequently performed in the early stages of the disease. Trapdoor, lightbulb, and Phemister are the three primary Non vascularized bone grafting procedures. Excellent patient outcomes following Non vascularized bone grafting have been documented in numerous investigations. "[16]"

9.3. Vascularized

In addition to restoring circulation in the injured region of the femoral head, vascularized grafting enhances subchondral architecture. A portion of the fibular bone with a nutrient artery is used in this procedure. The graft is simultaneously anastomosed to the lateral circumflex femoral artery and placed into the decompression core. "[16]"

10. Prevention

10.1. Preventing traumatic ONFH

To assess the femoral head's blood supply and determine whether blood vessels are present in the supporting region, X-ray imaging in conjunction with DSA or computed tomography angiography can be utilized. In the absence of a blood supply, bone flaps with vascular pedicles can be grafted, blood vessels in the supporting region should be explored and anastomosed, and the arterial arch should be maintained during internal fixation to prevent injury. "[17]"

10.2. Prevention of steroid-induced ONFH

Vasodilator medications in conjunction with anticoagulant medications may be given to patients requiring hormone therapy during the course of their medical treatment in order to prevent osteonecrosis. "[17]"

10.3. Prevention of different forms of ONFH

Removing the aetiologic determinants of osteonecrosis can successfully prevent the occurrence of ONFH in a population with high-risk factors for the disease. "[17]"

11. Conclusion

This review's main goal was to present a succinct and useful summary of the state of our understanding of the biology of AVN as well as clinical features such diagnosis, staging, and available treatments. A brief description was also given of a few novel AVN management techniques that are probably going to be used in standard clinical practice. Because they synthesize the evidence presented in numerous systematic reviews and clinical studies—which by definition concentrate on particular populations or management approaches—such thorough overviews created by practicing specialists are valuable to other clinicians, even though they are subject to the narrative review flows. As writers, we hope that this concise synopsis of clinically significant femoral head AVN and its administration would assist in educating working experts. However, we are aware that due to restrictions in the technique of such assessments, narrative synthesis may not be appealing to, say, researchers and academics.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

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