Core Decompression for Avascular Necrosis

Number: 0753

Policy

*Please see amendment for Pennsylvania Medicaid at the end of this CPB.

Aetna considers core decompression medically necessary for the treatment of early/pre-collapse (stage I or II; before X-ray changes are evident) avascular necrosis of the hip (femoral head and/or neck).

Aetna considers core decompression experimental and investigational for the treatment of the following indications (not an all-inclusive list) because its effectiveness for these indications has not been established.

- Late/post-collapse (stage III or higher; when X-ray changes have occurred) avascular necrosis of the hip
- Avascular necrosis of other joints (e.g., the ankle, elbow, knee, mandibular condyle, and shoulder)

Aetna considers the following adjunctive treatments experimental and investigational for the treatment of avascular necrosis of any joint because the effectiveness of these approaches has not been established (not an all-inclusive list):

Policy History

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Review History

Definitions

Additional Information

Clinical Policy Bulletin Notes
- Autologous bone marrow mononuclear cell/bone marrow concentrate
- Autologous platelet concentrate
- Bisphosphonates
- Bone morphogenic proteins
- Demineralized bone matrix
- Erythropoietin
- Growth factors
- Laser therapy
- Mesenchymal stem cells
- Ozone therapy
- Platelet-rich fibrin
- Platelet-rich plasma
- Synthetic bone graft substitute (e.g., calcium sulfate and calcium phosphate)

**Note:** According to the Ficat Classification of Avascular Necrosis of the Femoral Head, the presence of cysts is considered stage II. ([http://roentgenrayreader.blogspot.com/2010/05/ficat-classification-of-avascular.html](http://roentgenrayreader.blogspot.com/2010/05/ficat-classification-of-avascular.html)).

See also **CPB 0287 - Total Hip Replacement ([../200_299/0287.html](http://roentgenrayreader.blogspot.com/200_299/0287.html))** and **CPB 0661 - Joint Resurfacing ([../600_699/0661.html](http://roentgenrayreader.blogspot.com/600_699/0661.html)).**

**Background**

Avascular necrosis (AVN), also known as osteonecrosis, aseptic necrosis and ischemic bone necrosis, is a relatively common disease characterized by death of cellular elements of bone or marrow. Most of the 10,000 to 20,000 Americans who develop AVN annually are between the ages of 20 and 50 years. The hip (femoral head) is the most commonly affected site for clinically significant AVN. There are many risk factors for the disease including hemoglobinopathies, dislocation of the hip, alcoholism, fracture of the femoral neck, use of corticosteroid, as well as collagen vascular disease. With secondary collapse of the femoral head, disabling hip pain may
result in the need for total hip replacement. For non-traumatic AVN, the disease is often bilateral, which further increases the extent of disability. Various approaches have been employed for treating different stages of AVN of the hip. Non-operative treatments include rest, non-weight-bearing exercises, protected weight-bearing, pharmacotherapy (e.g., non-steroidal anti-inflammatory drugs and bisphosphonate medications such as alendronate or residronate), and electrical stimulation. Operative treatments include fusion, osteotomy, hemi-resurfacing, hemi-arthroplasty, debridement and grafting, core decompression with or without grafting, as well as total hip arthroplasty (Shannon and Trousdale, 2004; DeSmet et al, 2005; McKown, 2007).

Core Decompression of the Hip:

Core decompression of the hip is usually employed before collapse and fracture of the femoral head and/or neck to delay or avoid reconstructive surgery of the affected joint. It is generally carried out to preserve the function and the structure of the hip as well as to relieve pain associated with AVN. Core decompression entails repair of the necrotic site by coring, followed by filling the cored area with a bone graft, which is optional. A lateral trochanteric approach is used in this procedure: an 8-mm to 10-mm cylindrical core of bone is removed from the antero-lateral segment of the femoral head, which creates an open cylindrical channel. This open channel serves to relieve pressure. The open channel may be filled with either a vascularized or a non-vascularized bone graft. The former is used to aid in the ingrowth of vascular cellular tissue into the necrotic area; thus enhancing re-vascularization, which may arrest the progression of the necrosis. The latter is used to provide structural stability to the hip during the healing process. There is adequate evidence that core decompression is effective in treating early stages (I or II) of AVN of the hip.

Castro and Barrack (2000) performed a metaanalysis of data on core decompression and conservative treatment for avascular necrosis (AVN) of the femoral head. MEDLINE was
searched from 1966 to 1998 using the MeSH terms 'femoral head necrosis' and 'osteonecrosis', and the reference from retrieved articles were examined for additional studies. The search was restricted to citations in the English language. Studies designs of evaluations included in the reviewStudies with at least 10 participants and a minimum average follow-up of 12 months were eligible for inclusion. Studies where patient selection protocols created sample biases were excluded. The average length of follow-up was 43 months (SE=6 months). Surgical core decompression, i.e. the removal of a single core of bone from the avascular segment of the femoral head, was compared with conservative treatment, i.e. a period of protected weight bearing with crutches. Studies in which participants received additional treatments, such as iliac crest bone graft, vascularised fibular grafting, or pulsed electromagnetic stimulation, in addition to core decompression, were excluded from the analysis. Patients with AVN of the femoral head, as determined by radiographic staging according to the Steinberg classification (stages 0 to V) or an equivalent classification system were included. The three most common causes of AVN were steroid use (344 hips), alcohol abuse (153 hips) and idiopathic (127 hips). The average age of the participants presenting was 40 years (standard error, SE=2 years). Bilateral disease was present in 31% of the participants undergoing core decompression and in 62% of those undergoing conservative treatment. Successful treatment, defined as no further surgical intervention implemented or recommended, was assessed. Radiographic progression from stage I to stage II was not considered a failure, since radiographs significantly lag behind the physiological condition in the femoral head. Steinberg stage 0 outcomes were not compared since prophylactic core decompression of an asymptomatic, normal hip was not recommended by most authors. The stage III hips were not compared because their advanced disease predisposes them to failure, regardless of the intervention. A meta-analysis was performed to compare the success rates for core decompression and conservative treatment for Steinberg stages I and II. A sensitivity analysis was used to compare the 22 studies included in the meta-analysis
with the 9 studies excluded on account of highly selected patient groups; this compared year of publication, distribution of Steinberg stages, and percentage of bilateral cases. The sensitivity analysis was performed in order to determine whether the variables used to select patients were predictive of core decompression failure. Twenty-two studies (n=818) using a single surgical core decompression technique, and 8 studies (n=264) using a conservative technique, were included. Eleven studies were non-randomised prospective, 10 were retrospective, and 1 was randomized prospective. An additional 9 studies that were excluded on account of highly selected patient groups were used in a further sensitivity analysis. The most significant finding was that, with an average follow-up time of 42 months, core decompression was 23% more successful than conservative treatment for hips with Steinberg stage I AVN. The success rates for surgical core decompression were 84, 63 and 29% for Steinberg stages I, II, and III, respectively. Conservatively-treated patients with stage 0, I, II and III AVN demonstrated success rates of 86, 61, 59 and 25%, respectively. Chi-squared analysis showed that for stage I hips only, the success rate of core decompression (84%) was statistically significantly higher than that for conservative treatment (61%) (p=0.001). Several significant differences were found in the sensitivity analyses. Studies with selection biases tended to be performed earlier than non-biased studies (1,986 versus 1,992; p=0.0068). Studies on specific groups also had proportionately fewer patients in Steinberg stage I (21 versus 48%; p=0.02), more patients in Steinberg stage III (42 versus 18%; p=0.03), and more patients with bilateral disease (86 versus 31%; p=0.0001). When 70% or more of the sample patients had bilateral disease, the success rates for Steinberg stages I, II and III were 50, 60 and 44%, respectively. There were 33 (5%) complications in the 688 cases reported in the 13 studies. Reported complications were intertrochanteric fracture (n=14), technical errors in surgery (n=6), seromas and wound infections (n=8), femoral head fractures (n=3), deep vein thrombosis (n=1) and pulmonary embolus (n=1). The authors state that the 23% difference between core decompression and conservatively-treated patients with Steinberg stage I AVN was
interpreted cautiously. Although many authors agree that core decompression provides excellent and immediate pain relief, core decompression did not alter the progression of AVN in Steinberg stage II hips.

Steinberg (1995) evaluated the safety and effectiveness of core decompression in the treatment of AVN of the femoral head. All patients with AVN of the femoral head, stages I to IVA, were included regardless of the cause of the necrosis. A total of 300 hips were available for analysis. The follow-up ranged from 2 to 12 years. Main outcome measures included antero-posterior and lateral radiographs, taken immediately before surgery and at the final follow-up, clinical hip evaluation according to the Harris scoring system, and the need for total hip replacement. One patient sustained a subcapital fracture 1 month after surgery due to a fall. There was 1 case of non-fatal pulmonary embolism, 1 case of pneumonia, and 1 case of thrombo-phlebitis of the thigh. A total of 46% of operatively managed hips showed no radiographical progression of disease compared with only 19% of non-operatively managed hips. Moreover, 35% of the operatively managed hips required total hip replacement compared with 77% of non-operatively managed hips. The results in hips with early (stages I and II) AVN were only slightly better than those of hips with advanced (stages III and IVA) disease. However, the results in hips with small areas of necrosis in both stages I and II were much better than those with larger lesions; only 7% of the former group required total hip replacement after decompression and cancellous bone grafting. The authors concluded that core decompression with cancellous bone grafting is a safe and effective procedure for the treatment of early AVN of the femoral head. Results with this form of treatment are considerably better than those obtained in patients treated non-operatively.

Steinberg et al (2001) reviewed the results of a prospective study of 406 hips in 285 patients treated by one surgeon with core decompression and bone grafting. Patients were followed-up for 2 to 14 years. The outcome was determined by the change in the Harris hip score, quantitative radiographical
measurements, and the need for total hip replacement. These hips were compared with 55 hips in 39 patients treated non-operatively and with historic controls. Five complications occurred after 406 procedures including 2 fractures that resulted from falls during the first post-operative month. Of the 312 hips in 208 patients with a minimum 2-year follow-up, 36% of hips (113 hips in 90 patients) required hip replacement at a mean of 29 months: 18 of 65 hips (28%) with stage I disease; 45 of 133 hips (34%) with stage II disease; 3 of 13 hips (23%) with stage III disease; and 45 of 92 hips (49%) with stage IV disease. Before femoral head collapse (stages I and II combined) hip replacement was performed in 10 of 77 hips (14%) with small lesions, 33 of 68 hips (48%) with intermediate lesions, and 20 of 48 hips (42%) with large lesions. Results as determined by changes in Harris hip scores and radiographical progression were similar. Patients who underwent core decompression and bone grafting have a very low complication rate. In patients treated before femoral head collapse, the outcome is significantly better than in patients who received symptomatic treatment. The results were correlated with the stage and the size of the necrotic lesion.

Simank et al (2001) assessed and compared the results of core decompression and inter-trochanteric osteotomy for non-traumatic osteonecrosis of the femoral head using Cox regression and survivorship analysis. A total of 177 cases with a mean age of 41 years at surgery were treated for osteonecrosis (94 core decompressions and 83 osteotomies). Any further surgery was defined as failure and endpoint. Significant risk factors for treatment failure were age over 40 years at surgery (p = 0.022), corticosteroid intake (p < 0.001), advanced stage of necrosis (Steinberg stage greater than or equal to III, p = 0.04), and core decompression (p = 0.084). To analyze the influence of the surgical procedure, patients with corticosteroid treatment were excluded, and survival analysis was performed. This analysis revealed survival rates of 74% after osteotomy and 78% after core decompression 6 years post-operatively in early, pre-collapse stages (p = 0.819). In advanced stages, the rate of survival for hips after core decompression was lower (56
than in hips after osteotomy (76%) (p = 0.056). These findings indicated that core decompression may be as effective as inter-trochanteric osteotomy in pre-collapse stages but is less traumatizing and is cost-effective. For post-collapse hips, inter-trochanteric osteotomy should be considered.

Bellot and associates (2005) studied retrospectively a series of 32 cases (25 patients) of femoral head osteonecrosis treated by core decompression. These researchers examined the epidemiological and clinical features as well as the laboratory findings, and compared cases requiring secondary hip replacement and those that had a favorable outcome. The series included 32 hips, 1 case was lost to follow-up. Mean age at decompression was 41.3 years (22 to 55). In 8 hips, osteonecrosis was favored by corticosteroid treatment, in 3 by chronic alcoholism, and in 1 by hypertriglyceridemia. No favoring factors were present for 20 hips. According to the Association Research Circulation Osseous (ARCO) classification there were 15 stage I hips, 13 stage II, 3 stage III, and 1 stage IV. Core decompression was centered in 24 hips and mean time to decompression was 6.4 months (14 days to 40 months). These investigators reviewed hips without a total prosthesis using the Postel-Merle-d'Aubigne function score and for the radiological assessment the ARCO stage and the Koo index. Favorable outcome was noted in 12 hips. Total hip arthroplasty was required for 19, 1 hip was lost to follow-up. Mean follow-up in the success group was 82 months (26 to 176) and mean "time of participation" in the failure group was 11 months (1 to 38). Mean survival after core decompression was 14 months. Time between onset of symptoms and decompression did not influence outcome. Lesions that remained asymptomatic before decompression remained stable. Stage I hips did not have more favorable outcome than stage II hips (p < 0.05). Stage III or IV hips had unfavorable outcome. Hips with a Koo index greater than 40 had a poor outcome (p < 0.05). The authors concluded that early disease (stage I or II) is an ideal indication for decompression, but is insufficient alone to guarantee success. Furthermore, they considered late disease (stage III or IV and a Koo index greater than 40) an
contraindication for decompression.

Israelite and co-workers (2005) stated that early treatment of osteonecrosis of the femoral head yielded better results than late treatment. Because osteonecrosis is frequently bilateral, it often is advisable to treat both hips simultaneously. Core decompression is one of the more common methods of treatment; however the safety of doing simultaneous bilateral core decompression has been questioned. These researchers sought to evaluate the safety and effectiveness of simultaneous bilateral core decompression compared with unilateral core decompression. A total of 193 patients (276 hips) who had core decompression with bone grafting were followed up for 24 to 145 months; 124 procedures were unilateral and 152 were bilateral. Patients were evaluated by change in Harris hip score, radiographical progression, post-operative complications, and conversion to total hip arthroplasty. Total hip arthroplasty was required in 56 of 124 (45 %) of hips in the unilateral, and 48 of 152 (32 %) of hips in the bilateral group. Post-operative complications were similar. In the unilateral group there were 2 major and 9 minor complications; in the bilateral group there were 3 major and 10 minor complications. When bilateral core decompression is indicated, it can be done simultaneously on both hips, allowing earlier treatment of the contralateral hip without risk of increased complications and possibly with a better outcome. Simultaneous bilateral decompression required only one hospitalization and decreased recovery time compared with two separate procedures. Therefore, it provided advantages over procedures that can not be done simultaneously on both hips.

Keizer and associates (2006) described the long-term results of core decompression and placement of a non-vascularized bone graft in the management of AVN of the femoral head. These investigators treated 80 hips in 65 patients, 18 by a cortical tibial autograft and 62 by a fibular allograft. The mean age of the patients was 36 years. A total of 78 hips were available for evaluation of which pre-operatively 6 were Ficat-Arlet stage 0, 3 stage I, 31 stage IIA, 16 stage IIB, 13 stage III and 9 stage IV. A
total of 34 hips (44%) were revised at a mean of 4 years (SD 3.8). Survivorship analysis using a clinical end-point showed a survival rate of 59% 5 years after surgery. These researchers found a significant difference (p = 0.002) in survivorship, when using a clinical and radiological end-point, between the 2 grafts, in favor of the tibial autograft. They considered this difference to be the result of the better quality and increased volume of tibial bone compared with that from the trochanteric region used with the fibular allograft. This is a relatively simple, extra-articular and reproducible procedure. In the authors' view core decompression, removal of the necrotic tissue and packing of the cancellous grafts into the core track are vital parts of the procedure.

von Stechow and Drees (2007) stated that osteonecrosis of the femoral head eventually leads to its destruction if it remains untreated. Depending on the location and the extent of the osteonecrosis, several surgical options are available. For early small and medium-sized pre-collapse lesions, core decompression is the treatment of choice. Osteotomies and bone grafting procedures can be utilized in medium pre-collapse, as well as in small post-collapse lesions. Cartilage lesions of the femoral head allow limited femoral resurfacing arthroplasty. If the acetabulum reveals cartilage lesions, a total hip replacement should be performed.

Mont and co-workers (2007) noted that when osteonecrosis of the femoral head is diagnosed in its early stages (before collapse of the femoral head), various procedures such as core decompression (with and without bone grafting), osteotomies, as well as non-vascularized and vascularized bone grafting can be used to preserve the joint. The effectiveness of core decompression has been peer-reviewed in more than 40 studies. In general, this treatment is most successful for patients with early stage, small- and medium-sized lesions, before collapse of the femoral head. Various methods of non-vascularized bone grafting have been used. Results have varied; however, a 60% to 80% success rate has been achieved at 5- to 10-year follow-up.
Other techniques such as infusion/implantation of autologous bone-marrow mononuclear cells (BMMC) have also been used in an attempt to improve the outcomes of core decompression.

Gangji and Hauzeur (2005) studied the implantation of autologous BMMC in a necrotic lesion of the femoral head to determine the effect on the clinical symptoms and the stage and volume of osteonecrosis. They studied 13 patients (18 hips) with stage I or II osteonecrosis of the femoral head, according to the ARCO classification. The hips were allocated to a program of either core decompression (the control group) or core decompression and implantation of autologous BMMC (the bone-marrow-graft group). Both patients and assessors were blind with respect to treatment-group assignment. The primary outcomes studied were safety, clinical symptoms, and disease progression. After 24 months, there was a significant reduction in pain \( (p = 0.021) \) and in joint symptoms measured with the Lequesne index \( (p = 0.001) \) and the WOMAC index \( (p = 0.013) \) within the bone-marrow-graft group. At 24 months, 5 of the 8 hips in the control group had deteriorated to stage III, whereas only 1 of the 10 hips in the bone-marrow-graft group had progressed to this stage. Survival analysis showed a significant difference in the time to collapse between the two groups \( (p = 0.016) \). Implantation of BMMC was associated with only minor side effects. The authors concluded that implantation of autologous BMMC appeared to be a safe and effective treatment for early stages of osteonecrosis of the femoral head. Although the findings of this study are promising, their interpretation is limited because of the small number of patients and the short duration of follow-up. Further study is needed to confirm the results.

Yan and colleagues (2006) assessed the safety and effectiveness of the treatment of osteonecrosis of the femoral head by percutaneous decompression and autologous BMMC infusion. A total of 44 hips in 28 patients with AVN at early stage were treated by percutaneous multiple holes decompression followed by autologous BMMC infusion. Autologous BMMC were concentrated from bone marrow that was taken from the
posterior iliac crest of the patient. Patients were followed-up at least 2 years. Results were determined by the changes in the Harris hip score and the progression in the radiographical stages. No complications were observed after the operation. Before operation, there were stage I of femoral head necrosis in 8 hips, stage II in 15 hips, stage III in 14 hips, stage IV in 7 hips, and the post-operative stages at the most recent follow-up were stage O in 1 hip, stage I in 6 hips, stage II in 13 hips, stage III in 13 hips, stage IV in 7 hips, stage V in 4 hips. The mean pre-operative Harris hip score was 58 (46 to 89), and improved to 86 (70 to 94) post-operatively. All the femoral head collapsed pre-operatively showed that the necrotic size was at least more than 30%. The authors concluded that percutaneous multiple holes decompression combined with autologous BMMC is a new way to treat AVN of the femoral head. The earlier the stage, the better the result. They noted that randomized prospective studies are needed to compare this combination approach with routine core decompression.

Gangji et al (2011) examined the effectiveness of bone marrow cell implantation into the necrotic lesion of the femoral head on clinical symptoms and the progression of osteonecrosis of the femoral head in comparison with core decompression. These investigators studied 19 patients and 24 hips with early stage osteonecrosis of the femoral head. The hips were allocated to either core decompression only or core decompression and implantation of bone marrow cells. Both patients and assessors were blind with respect to treatment group assignment. The primary outcomes were clinical symptoms and disease progression. Bone marrow implantation afforded a significant reduction in pain and in joint symptoms and reduced the incidence of fractural stages. At 60 months, 8 of the 11 hips in the control group had deteriorated to the fractural stage whereas only 3 of the 13 hips in the bone marrow graft group had progressed to that stage. Survival analysis showed a significant difference in the time to failure between the 2 groups at 60 months. Patients had only minor side effects after the treatments. The authors concluded that this long-term follow-up study confirmed that implantation of autologous
bone marrow cells in the necrotic lesion might be an effective treatment for patients with early stages of osteonecrosis of the femoral head.

In a Cochrane review on the treatment for AVN of bone in individuals with sickle cell disease, Mari-Carvajal and colleagues (2009) found no evidence that adding hip core decompression to physical therapy achieves clinical improvement compared to physical therapy alone. However, these investigators highlighted that their conclusion was based on 1 trial with high attrition rates. They stated that further randomized controlled trials are needed to assess the role of hip-core depression for this clinical condition. Endpoints should focus on participants' subjective experience (e.g., quality of life and pain) as well as more objective "time-to-event" measures (e.g., mortality, survival, hip longevity).

Bakhshi and colleagues (2012) stated that osteonecrosis of femoral head (ONFH) is a challenging disease. Regardless of underlying causes, the ultimate result in all cases is disruption of femoral head blood supply. Once the disease starts, it is progressive in 80% of cases. Since the majority of the affected individuals are young, every effort should be focused on preserving the patients own femoral head. In recent years, the role of angiogenic growth factors has been studied with promising results in animal models of ONFH. Erythropoietin (EPO) is a well-known hormone that has been used in treatment of chronic anemia for many years with few side effects. Considering the angiogenic properties of EPO, the authors hypothesized that local delivery of recombinant human EPO during core decompression will enhance bone regeneration in ONFH.

Helbig et al (2012) evaluated patients after core decompression combined with an augmentation by a demineralized bone matrix, and particularly aimed to report long-term conversion rates to total hip replacement (THR). A total of 14 patients with 18 hips suffering from ONFH (Ficat stage I to IIB) underwent this surgical procedure. All patients underwent radiographical and
magnetic resonance imaging (MRI) investigations at baseline and at follow-up periods of 12 and 24 months. The clinical follow-up was done using the Merle d'Aubigné-score for an average period of 9 years after surgery. Fourteen of the 18 subjects (77%) achieved at least a good clinical result after 2 years. The Merle d'Aubigné-score improved significantly after 12 ($p = 0.0001$) and 24 months ($p = 0.0002$). However, the MRI volumetric analysis showed an increased necrotic bone volume from $3.16 \pm 0.54$ to $3.88 \pm 0.62 \text{cm}^3$ ($p = 0.04$). Within 9 years, 13 out of 18 cases (72%) required further surgery by THR. Only 7 out of 18 subjects (39%) reported an ongoing post-operative clinical benefit, and would retrospectively redo the same surgical approach again. The 5 patients who did not require THR were still satisfied after 9 years. The authors concluded that in patients with early-stage ONFH, core decompression combined with the implantation of a demineralized bone matrix leads to a limited, temporary pain relief as seen in core decompression alone. However, long-term results were not encouraging with a high rate of conversion to arthroplasty. Therefore, core decompression with implantation of a demineralized bone matrix may be not appropriate to avoid THR in the long-term.

Wang et al (2012) examined the effectiveness of core decompression surgery for the treatment of steroid-induced femoral head osteonecrosis. The rabbit femoral head osteonecrosis model was established by the administration of steroids in combination with horse serum. Magnetic resonance imaging was applied to screen for the animal femoral head osteonecrosis. The rabbits with bilateral femoral head osteonecrosis were randomly selected to do the one side of core decompression. The other side was used as the sham. Quantitative reverse transcription polymerase chain reaction (RT-PCR) and western blot techniques were used to measure the local expression of bone morphogenetic protein-2 (BMP-2) and peroxisome proliferator-activated receptor gamma (PPAR-gamma) mRNAs and proteins. Bone tissues of femoral head from the normal control group and operation group (with or without lateral decompression) were histologically analyzed by
H and E staining. The comparisons of the local expression of BMP-2 and PPAR-gamma mRNAs and proteins and the bone regeneration were further analyzed between different groups at each time point (2, 4 and 8 weeks post-operation, respectively). The expression of BMP-2 mRNA and protein in the steroid-induced femoral head osteonecrosis with or without core decompression was significantly lower than that in normal animals. And BMP-2 expression in femoral head osteonecrosis with and without lateral decompression both showed the decreasing trend with the increased post-operation time. There was no significant difference of BMP-2 expression between femoral head osteonecrosis with and without lateral decompression. The expression of PPAR-gamma mRNA and protein in steroid-induced femoral head osteonecrosis with and without core decompression both were significantly higher than that in normal animals. The PPAR-gamma expression in the steroid-induced femoral head osteonecrosis with and without lateral decompression both showed a significantly increased trend with the increased post-operation time. However, there was no significant difference of PPAR-gamma expression between the femoral head osteonecrosis with and without lateral decompression at each time point.

Histopathological analysis revealed that new trabecular bone and a large number of osteoblasts were observed in the steroid-induced femoral head osteonecrosis with lateral decompression at 8 weeks after surgery, but there still existed phenomenon of trabecular bone fractures and bone marrow cell necrosis. The authors concluded that although core decompression takes partial effect in promoting bone regeneration in the early treatment of femoral head osteonecrosis, such an effect does not significantly improve or reverse the pathological changes of femoral marrow cell necrosis. Thus, the long-term effect of core decompression in the early treatment of steroid-induced femoral head osteonecrosis is not satisfactory.

Guadilla et al (2012) described a non-invasive arthroscopic procedure as an alternative to open surgery for avascular necrosis of the hip. Patients with grade I or IIA AVN of the hip
were treated by core decompression performed by drilling under fluoroscopic guidance. Liquid platelet-rich plasma (PRP) is delivered through a trocar, saturating the necrotic area. In more severe conditions, the necrotic bone is decompressed and debrided, through a cortical window at the head-neck junction. A composite graft made of autologous bone and PRP is delivered by impactation through the core decompression track. Fibrin membranes were applied to enhance healing of the head-neck window and arthroscopic portals. Platelet-rich plasma was infiltrated in the central compartment. This arthroscopic approach aided in making diagnosis of the labrum and articular cartilage and allowed intra-operative treatment decisions. Visual control provided the precise localization and treatment for the necrotic area allowing cartilage integrity to be preserved. The authors concluded that arthroscopic management of AVN of the femoral head is viable and has significant advantages. They stated that clinical studies should justify the theoretical additional benefits of this approach.

Abrisham et al (2013) examined the value of core decompression in treating the AVN; this study was performed on patients with symptomatic AVN with different etiologies who were treated with core decompression. This study was carried out on 25 patients (with the total number of 37 femoral head) who were diagnosed AVN using X-ray and MRI. Core decompressions for these patients were started soon after the diagnosis. The results were considered as a success if there was no progression of disease confirmed by X-ray or no subsequent operation was required. Modified Ficat staging was used to record changes before and 2 years after core decompression treatment. Twenty five patients were participated in this study in which 68 % (n = 17) were female, 32 % (n = 8) were male, and the average of the age of the patients were 29.58 ± 4.58. Eight of these patients had systemic lupus erythematos (SLE) (32 %), 4 rheumatoid arthritis (RA) (16 %), 3 with kidney transplant (12 %), 1 Takayasu's vasculitis (4 %) and 1 Wegner vasculitis (4 %). Eight of patients had a history of intravenous injection of Temgesic (32 %). In patients using Temgesic the changes in Modified Ficat staging were significantly different before and
after core decompression \(p = 0.03\) in comparison with other groups; and in all 8 Temgesic users AVN progressed to the stage 3 and 4 after core decompression. The authors concluded that this study demonstrated that core decompression to prevent the changes in the femoral head has been more effective in patients with collagen vascular diseases and kidney transplant than patients using intravenous Temgesic. These patients, in spite of early operation, showed no benefit of core decompression to prevent the changes in the femoral head.

Zalavras and Lieberman (2014) stated that osteonecrosis of the femoral head may lead to progressive destruction of the hip joint. Although the etiology of osteonecrosis has not been definitely delineated, risk factors include corticosteroid use, alcohol consumption, trauma, and coagulation abnormalities. Size and location of the lesion are prognostic factors for disease progression and are best assessed by MRI. The effectiveness of medical management of osteonecrosis with pharmacologic agents and biophysical modalities requires further investigation. Surgical management is based on patient factors and lesion characteristics. Preservation of the femoral head may be attempted in younger patients without head collapse by core decompression with vascularized bone grafts, avascular grafts, bone morphogenetic proteins, stem cells, or combinations of the above or rotational osteotomies. The authors concluded that the optimal treatment modality has not been identified. When the femoral head is collapsed, arthroplasty is the preferred option.

**Core Decompression of Other Joints (e.g., Knee, Ankle, and Shoulder):**

The knee is the second most common location for osteonecrosis with about a 10% incidence of the disease in the hip. The disease can be classified into 4 stages—stage I: progression from no radiographical findings; stage II: a slight flattening of the medial condyle; stage III: appearance of a radiolucent lesion; and stage IV: articular cartilage collapse (Soucacos et al, 1997). There are two distinctive entities: (i)
spontaneous osteonecrosis of the knee (SPONK), and (ii) secondary osteonecrosis of the knee. They are differentiated by age of presentation, associated risk factors (e.g., use of corticosteroid and alcoholism), location, laterality, and condylar involvement. Each of these two entities has several distinct surgical treatment options, which include osteotomy, arthroscopic debridement, core decompression, unicompartmental knee arthroplasty, and total knee arthroplasty. It is essential to diagnose these two entities as early as possible, and use appropriate treatment to avoid osteoarthritis, joint destruction, and ultimately joint collapse (Ragland et al, 2004).

While available evidence indicates that core decompression is effective in treating early stages of AVN of the hip, there is currently insufficient evidence that this procedure is effective in treating AVN of the knee, ankle, and shoulder. The quality as well as the quantity of the evidence for core decompression for these joints is poor and limited. In particular, the majority of studies involved a small number of patients and lacked appropriate control groups. Furthermore, several of the studies were published by the same group of investigators. Prospective, well‐designed, randomized, controlled trials are needed to ascertain the clinical value of core decompression for joints other than the hip.

Jacobs et al (1989) performed 28 core decompressions of the distal femur for pathologically confirmed AVN. At a mean follow‐up of 54 months (range of 20 to 140 months) and using the Ficat stages, all 7 cases in stage I and stage II had good results. Of 21 cases in stage III, 11 cases had good results, 4 had poor results, and 6 needed total knee replacement. There were no significant orthopedic complications. The authors noted that core decompression is worthwhile and will be more accurate with new methods of imaging.

Mont and colleagues (1997) reported the long‐term results of core decompression for the treatment of AVN of the distal femur. A total of 79 knees (45 patients) were evaluated. All
patients had a corticosteroid association (had been treated with more than 30 mg of prednisone for over 2 weeks predating by at least 6 months the onset of AVN). A total of 32 knees were managed with rest and protected weight-bearing. Core decompression was performed at a minimum of 3 months after the onset of symptoms in another 47 knees. Knees treated with protected weight-bearing had an average asymptomatic period of only 11 months and all but 6 (18%) proceeded to total knee replacement within 6 years. Core decompression yielded good or excellent results in 73% of the knees at an average follow-up of 11 years (range of 4 to 16 years). Of the 13 knees with failed core decompression, 7 were asymptomatic for greater than 5 years. A subset of 26 knees from each group was matched for age, gender, diagnosis, Ficat and Arlet Stage, and length of follow-up. The matched non-core group had 23% survival as compared with 74% survival in the core group. These long-term follow-up findings suggested that core decompression may slow the rate of symptomatic progression of AVN of the knee. Furthermore, core decompression may extend the symptom-free interval in certain patients and may delay the need for more extensive procedures such as total knee arthroplasty.

Forst et al (1998) reported their findings on early core decompression in patients with spontaneous AVN of the knee/femoral condyle. In 16 patients with an average age of 64.6 +/- 9.8 years and sudden onset of severe knee pain, the initial stage of Ahlbäck disease (spontaneous AVN of a femoral condyle) was verified by MRI and subsequent histology. The first radiological sign of AVN (flattening of the affected femoral condyle) was present in only 1 case. All patients were treated surgically by extra-articular drilling into the affected femoral condyle to achieve core decompression. Knee pain disappeared immediately after surgery in all patients. Successful healing was confirmed by normalization of the bone marrow on MRI (on average, 35.8 months follow-up). Core decompression by extra-articular drilling into the femoral condyle can be recommended as an effective treatment in initial AVN of the knee (still radiologically invisible). However, if radiological
flattening of the affected femoral condyle becomes apparent, progression of this disease can not be avoided.

Mont et al (2000a) defined the clinical, demographical, and radiographical patterns of atraumatic AVN of the distal part of the femur and the proximal part of the tibia at presentation and reported the outcome of treatment of this condition. A total of 248 knees in 136 patients who were younger than the age of 55 years were treated. Results of non-operative treatments, core decompression, arthroscopic debridement, and total knee arthroplasty were evaluated. There were 106 female patients and 30 male patients, and their mean age was 36 years (range of 15 to 54 years) at the time of diagnosis. A total of 101 patients (74 %) had involvement of other large joints, with 18 (13 %) presenting initially with knee symptoms. A total of 101 patients (74 %) had a disease that affected the immune system; 67 of them had systemic lupus erythematosus. A total of 123 patients (90 %) had a history of corticosteroid use. Technetium-99m bone-scanning missed lesions in 16 (29 %) of 56 knees. Eight (20 %) of 41 initially symptomatic knees treated non-operatively had a successful clinical outcome (a Knee Society score of at least 80 points and no additional surgery) at a mean of 8 years. The knees that remained severely symptomatic for 3 months were treated with either core decompression (91 knees) or total knee arthroplasty (7 knees). Seventy-two (79 %) of the 91 knees treated with core decompression had a good or excellent clinical outcome at a mean of 7 years. Efforts to avoid total knee arthroplasty with repeat core decompression or arthroscopic debridement led to a successful outcome in 15 (60 %) of 25 knees. Thirty-four (71 %) of 48 knees treated with total knee arthroplasty had a successful clinical outcome at a mean of 9 years. The authors concluded that atraumatic AVN of the knee affects women predominantly, and was associated with corticosteroid use in 90 % of the patients. Evaluation should include standard radiographical and MRI of all symptomatic joints. Prognosis was negatively related to large juxta-articular lesions. Non-operative treatments should be reserved for asymptomatic knees only. Core decompression was successful (a Knee Society
score of at least 80 points and no additional surgery) in 79 % of the knees in which the disease was in an early stage. Total knee arthroplasty was successful in only 71 % of the knees.

Delanois et al (1998) reported their findings of 37 ankles in 24 patients who were treated for atraumatic AVN of the talus. There were 21 women and 3 men, and their mean age was 40 years (range of 26 to 62) at the time of the diagnosis. Thirteen (54 %) of the 24 patients had bilateral involvement. Sixteen patients (67 %) had a disease that affects the immune system, including systemic lupus erythematosus (n = 13), scleroderma (n = 1), insulin-dependent diabetes mellitus (n = 1), and multiple sclerosis (n = 1). Four patients had a history of regular alcohol use, and 4 patients had a history of moderate smoking. One patient had a protein-S deficiency, 1 patient had had a renal transplant, and 1 patient had a history of asthma. Two patients had no identifiable risk factors for osteonecrosis. Fifteen patients (63 %) had involvement of other large joints. The mean duration of symptoms before the patients were seen was 5.4 months (range of 2 months to 2 years). The mean ankle score at the time of presentation was 34 points (range of 2 to 75) according to the system of Mazur et al. A radiographical review revealed that, according to the system of Ficat and Arlet, 8 ankles had stage III or IV disease of the talus at presentation. The remaining 29 ankles had stage II disease. Osteonecrosis was seen in the postero-lateral aspect of the talar dome (zones III and IV on the sagittal images; and zones II, III, and IV on the coronal images) in 22 of the 23 ankles for which MRI were available. Osteonecrosis was seen in the antero-medial aspect of the talar dome (zones I and II on the sagittal images; and zone I on the coronal images) in the remaining ankle. Bone scans, available for 11 ankles, revealed increased uptake in the talus. All patients were initially managed non-operatively with restricted weight-bearing, an ankle-foot orthosis, and use of analgesics; 2 ankles responded to this regimen. Thirty-two ankles that remained severely symptomatic were treated with core decompression, which was useful in the treatment of pre-collapse (stage II) disease. Twenty-nine of these ankles had a fair-to-excellent clinical
outcome a mean of 7 years (range of 2 to 15 years) post-operatively; the remaining 3 ankles had an arthrodesis after the core decompression failed. Three ankles were treated initially with an arthrodesis for post-collapse (stage III or IV) disease. All 6 of the ankles that had an arthrodesis fused, at a mean of 7 months (range of 5 to 9 months) post-operatively.

Mont et al (2000b) described the epidemiology, clinical and radiographical presentation, treatment, and prognosis of atraumatic AVN of the shoulder/humeral head. Of the 1,056 patients managed for AVN of any joint between July 1, 1974, and December 1, 1996, 127 shoulders in 73 patients were treated for atraumatic AVN of the proximal humerus. There were 47 women and 26 men with a mean age of 41 years (range of 20 to 60). Numerous associated factors were noted: alcohol use (38 %), moderate smoking (30 %), asthma (8 %), and nephrosis (3 %). A corticosteroid association was noted in 60 patients (82 %) and 42 of the patients (58 %) had an immuno-compromising disease. The severity of humeral head AVN did not correlate with dose or duration of corticosteroid therapy. According to the modified Ficat and Arlet radiographical staging system, there were 20 shoulders with Stage I disease, 55 shoulders with stage II disease, and 52 shoulders with Stage III or IV disease. Seventy-four of the shoulders treated with core decompression (78 %) had good to excellent clinical outcomes at a mean follow-up of 6 years (range of 2 to 21). Fourteen of the 16 patients (88 %) treated with hemi-arthroplasty or total shoulder arthroplasty were clinically successful at a mean follow-up 4 years (range of 2 to 11). The authors concluded that there was a low incidence of humeral head involvement in the AVN patient cohort (7 % of all AVN patients), and a high incidence of corticosteroid use (82 %), hip involvement (81 %), and bilateral disease (74 %).

Harreld et al (2009) stated that osteonecrosis of the humeral head is considerably less common than osteonecrosis of the hip. However, as in the hip, the interaction between a genetic predisposition and certain risk factors may lead to increased intra-osseous pressure, loss of circulation, and eventual bone
death. The most common risk factor remains corticosteroid use, which accounts for most reported cases. Radiographical staging and measurement of lesion size are predictive of disease progression and can be used to determine appropriate intervention. Recent studies have reported the use of various treatment modalities such as pharmacotherapy, core decompression with small-diameter drilling, arthroscopic-assisted core decompression, as well as bone grafting. The authors concluded that prospective, randomized trials are needed to determine the effectiveness of these joint-preserving procedures. Hemiarthroplasty and total shoulder arthroplasty are recommended for patients with end-stage disease.

Innes and Strauch (2010) performed a systematic review of the treatment of Kienbock’s disease to test the hypothesis that none of the reported treatments for Kienbock’s disease is superior with respect to outcomes of pain, motion, grip strength, and radiographic measures. These investigators searched PubMed, Medline, and the Cochrane Review for articles published between 1998 and 2008 reporting outcomes of treatment for Kienbock’s disease. Patients were grouped by stage of disease. Early stages were defined as Lichtman stage I, II, and IIIa, and "late" stages as IIIb and IV. The groups were then analyzed on the basis of treatment; procedures performed on subjects in the early group included vascularized bone grafting (VBG), metaphyseal core decompression, and radial osteotomy, whereas the procedures performed on subjects in the late group included VBG, radial osteotomy, partial arthrodesis, proximal row carpectomy, tendon ball arthroplasty, and non-surgical treatment. These researchers found no statistically significant difference between any of the treatment groups for subjective pain outcomes. In terms of objective measures, statistically significant improvement (p < 0.05) was seen in range of motion after radial osteotomy and VBG in early-stage patients and after all interventions, except partial arthrodesis and non-surgical treatment, for late-stage patients. Grip strength was significantly improved in early-stage patients after radial osteotomy and VBG and for all late-stage patients, except
among those managed non-surgically. Changes in Stahl and carpal height index scores were not statistically significant regardless of intervention, except after radial osteotomy in the early group, where they statistically worsened. The authors concluded that based on retrospective data from uncontrolled studies, no active treatment is superior in the treatment of Kienbock's disease and there are insufficient data to determine whether the outcomes of any intervention are superior to placebo or the natural history of the disease.

Chuong et al (1995) stated that deviations of the condylar form are usually ascribed to "degenerative arthritis" or "osteoarthritis". More recently, osteonecrosis has been discussed as a possible cause of condylar degeneration and pain. These researchers presented a review of the literature on osteonecrosis, emphasizing the spectrum of degenerative osseous disease, which includes osteoarthrosis, condylsis, osteomyelitis, and osteonecrosis. Preliminary results of mandibular core decompression with and without bone grafting were presented suggesting a therapeutic benefit. Moreover, the authors concluded that further study is needed to elucidate this process.

Lieberman et al (2014) stated that there is no consensus with respect to the best procedures to preserve the knee joint in patients with osteonecrosis of the knee. These investigators performed a systematic review of the literature between 1999 and 2012. Only 10 of 1,057 studies met inclusion criteria. Core decompression prevented additional surgical treatment in pre-collapse knees with a failure rate of 10.4 % (7 of 67 knees). Autogenous and osteochondral grafts decreased the need for additional surgery in both pre-collapse (0 %, 20 of 20) and post-collapse knees (10.5 %, 8 of 76 knees). The authors concluded that although these results are quite promising, multi-center randomized trials are needed to identify the optimal procedures to treat this disease.

Gross et al (2014) identified and summarized all available evidence for the treatment of talar AVN; provided treatment
recommendations; and highlighted gaps in the literature. These investigators searched Medline and Embase using a unique algorithm. The Oxford Level of Evidence Guidelines and GRADE recommendations were used to rate the quality of evidence and to make treatment recommendations. A total of 19 studies fit the inclusion criteria constituting 321 ankles at final follow-up. The interventions of interest included hind-foot fusion, conservative measures, bone grafting, vascularized bone graft, core decompression, and talar replacement. All studies were Level IV evidence. Due to study quality, imprecise and sparse data, and potential for reporting bias, the quality of evidence is "very low". Studies investigating conservative therapy showed that prolonged protective weight-bearing provided the best outcomes in early talar AVN. The authors concluded that given the "very low" GRADE recommendation, understanding of talar AVN would be significantly altered by higher quality studies. Early talar AVN seems best treated with protected weight-bearing and possibly in combination with extracorporeal shock-wave therapy. If that fails, core decompression may be an attractive treatment option. Arthrodesis should be saved as a salvage procedure. Moreover, they stated that future prospective, randomized studies are needed to guide the conservative and surgical management of talar AVN.

In a Cochrane review, Marti-Carvajal et al (2014) determined the impact of any surgical procedure compared with other surgical interventions or non-surgical procedures, on AVN of bone in people with SCD in terms of safety and effectiveness. These investigators searched the Cochrane Cystic Fibrosis and Genetic Disorders Group Haemoglobinopathies Trials Register, comprising references identified from comprehensive electronic database searches and hand-searches of relevant journals and abstract books of conference proceedings. Additional trials were sought from the reference lists of papers identified by the search strategy. Date of the most recent search of the Group's Haemoglobinopathies Trials Register: March 17, 2014. Randomized clinical trials comparing specific therapies for AVN of bone in people with SCD were selected for analysis. Each
author independently extracted data and assessed trial quality. Since only 1 trial was identified, meta-analysis was not possible. One trial (46 subjects) was eligible for inclusion. After randomization, 8 participants were withdrawn, mainly because they declined to participate in the trial. Data were analyzed for 38 participants at the end of the trial. After a mean follow-up of 3 years, hip core decompression and physical therapy did not show clinical improvement when compared with physical therapy alone using the score from the original trial (an improvement of 18.1 points for those treated with intervention therapy versus an improvement of 15.7 points with control therapy). There was no significant statistical difference between groups regarding major complications (hip pain, RR 0.95 (95% confidence intervals [CI]: 0.56 to 1.60; vaso-occlusive crises, RR 1.14 (95% CI: 0.72 to 1.80; very low quality of evidence); and acute chest syndrome, RR 1.06 (95% CI: 0.44 to 2.56; very low quality of evidence)). This trial did not report results on mortality or quality of life. The authors found no evidence that adding hip core decompression to physical therapy achieved clinical improvement in people with SCD with AVN of bone compared to physical therapy alone. However, they highlighted that the conclusion was based on 1 trial with high attrition rates. They stated that further randomized controlled trials are needed to evaluate the role of hip-core depression for this clinical condition; end-points should focus on participants' subjective experience (e.g. quality of life and pain) as well as more objective “time-to-event” measures (e.g. mortality, survival, hip longevity).

Adjunctive Treatments:

Pan and co-workers (2014) examined the effect of recombinant human bone morphogenetic protein 2/poly-lactide-co-glycolic acid (rhBMP-2/PLGA) with core decompression on repair of rabbit femoral head necrosis. Bilateral femoral head necrosis models of rabbit were established by steroid injection. A total of 48 rabbits (96 femoral head necrosis) were randomly divided into 4 groups: Group A, control group with 12 rabbits, 24 femoral head necrosis; Group B, treated with rhBMP-2/PLGA
implantation after core depression, with 12 rabbits, 24 femoral head necrosis; Group C, treated with rhBMP-2 implantation after core depression, with 12 rabbits, 24 femoral head necrosis; and Group D treated with core depression group without implantation, with 12 rabbits, 24 femoral head necrosis. All animals were sacrificed after 12 weeks. The ability of repairing bone defect was evaluated by X-ray radiograph. Bone mineral density analysis of the defect regions were used to evaluate the level of ossification. The morphologic change and bone formation was assessed by hematoxylin and eosin (HE) staining. The angiogenesis was evaluated by vascular endothelial growth factor (VEGF) immunohistochemistry. The osteogenetic ability and quality of femoral head necrosis in group B were better than those of other groups after 12 weeks by X-ray radiograph and morphologic investigation. And the angiogenesis in group B was better than other groups. Group C had similar osteogenetic quality of femoral head necrosis and angiogenesis with group D. The authors concluded that the treatment of rhBMP-2/PLGA implantation after core depression can promote the repair of rabbit femoral head necrosis. They noted that it is a promising and efficient synthetic bone material to treat the femoral head necrosis.

Yu and associates (2015) reviewed the outcomes of using synthetic bone graft substitute (calcium sulfate and calcium phosphate) for the treatment of late-stage osteonecrosis of the femoral head. From November 2008 to May 2009, a total of 19 hips in 18 patients with osteonecrosis of the femoral head [6 hips in ARCO stage IIC and 13 hips in stage IIIA] were treated with core decompression combined with PRO-DENSE (injectable regenerative graft). The average age of the patients at the time of surgery was 48 years (range of 25 to 67 years); 12 patients (13 hips) overused alcohol, 4 patients (4 hips) were idiopathic, 1 patient (1 hip) used corticosteroids, and 1 patient (1 hip) was post-traumatic. The clinical failure was defined as conversion to total hip arthroplasty or progression in head collapse. At the conclusion of the study, 3 in the 6 stage IIC hips and 8 in the 13 stage IIIA hips were converted to total hip arthroplasty in an average of 8.5 months (range of 4 to 30
months) post-operatively. Advanced collapse of the femoral head awaiting for total hip arthroplasty was observed in the other 6 hips. Of the 19 hips, only 2 hips (10.5 %) survived without further collapse in the 5-year follow-up. This resulted in 89.5 % failure rate with early resorption of the grafting in an average of 5.3 months. The authors concluded that core decompression combined with an injectable calcium sulfate and calcium phosphate composite graft (PRO-DENSE) were associated high failure rates in the early post-operative period. They stated that this approach is not recommended for the treatment of ARCO stage IIC and IIIA osteonecrosis of the femoral head.

Pierce and colleagues (2015) carried out a review of core decompression in the treatment of osteonecrosis of the femoral head. These investigators described the following: (i) how traditional core decompression is performed; (ii) adjunctive treatments; (iii) multiple percutaneous drilling techniques; and (iv) overall outcomes of these procedures. The authors concluded that core decompression has optimal outcomes when used in the earliest, pre-collapse disease stages. More recent studies have reported excellent outcomes with percutaneous drilling. Furthermore, they stated that adjunct treatments combining core decompression with growth factors, bone morphogenic proteins, stem cells, and bone grafting have demonstrated positive results; however, larger randomized controlled trials (RCTs) are needed to evaluate their overall effectiveness.

**Autologous Platelet Concentrate:**

Lopez-Jornet and colleagues (2016) performed a systematic literature review to determine the effectiveness of autologous platelet concentrate (APC) application, for prevention or treatment of medication-related osteonecrosis of the jaw (MRONJ) together with surgical debridement. An electronic search was performed using Medline (PubMed), Embase, and Cochrane databases until January 2015 using the following search terms: osteonecrosis, bisphosphonates, antiresorptive,
antiangiogenic therapy, BRONJ, platelet concentrate, PRP, PRF, and PRGF. Two reviewers assessed the eligibility of articles independently and extracted key data. The methodology used met PRISMA criteria. The Newcastle-Ottawa scale was used to assess the quality of the articles. Preventive applications of PRP were reported in 697 dental extractions in patients taking bisphosphonates (BPs) intravenously, of whom 7 patients developed osteonecrosis (5 mandibular and 2 maxillary). In cases of established osteonecrosis, 8 studies reported treatment by surgery combined with APC (7 with PRP and 1 with leukocyte-rich and platelet-rich fibrin) in 123 patients (34 men and 89 women) with ONJ, who received 157 treatments, of which 135 achieved complete resolution (85.98%). The authors concluded that there are no published scientific data to sufficiently support any specific treatment protocol, including the use of APC together with surgical debridement, for the management of MRONJ. They stated that RCTs of the use of APC are needed.

**Bisphosphonates and Mesenchymal Stem Cells:**

In a retrospective study, Gianakos et al (2016) examined if core decompression with mesenchymal stem cells combined with BP therapy can improve the clinical outcomes and reduce the risk of hip replacement when compared to treatment with BP therapy alone. Between 2006 and 2014, a total of 84 consecutive patients who were diagnosed with ONFH were identified from the authors’ institution's registry. Of these 84 patients, 49 patients (62 hips) fit inclusion/exclusion criteria; 29 patients (40 hips) were treated with BP therapy only; 20 patients (20 hips) were treated with BP, core decompression, and mesenchymal stem cells. Functional outcomes were assessed using the Modified Harris Hip Score (MHHS), the visual analog score (VAS), and evaluation of support system. Clinical failure was defined as deterioration of the MHHS/VAS scores and support system used severe enough to require THR. Radiologic outcome measures included the XR and MR imaging staging of the hip. Survival analysis was performed with total hip replacement as the end-point failure. Collapse was defined
as progression from Ficat stage I or II to stage III and from Steinberg I, II, III to IV, V, VI. Failure requiring THR occurred in 21/40 (52.5%) of BP-treated hips at a mean follow-up of 25.3 ± 11.5 months and 5/22 (22.73%) of BP + CD + MSC-treated hips at a mean follow-up of 22.7 ± 19.5 months. The median (Q1, Q3) time to collapse was 24.9 (7.4, 33.0) months in BP-treated hips and 27.3 (27.3) months in BP + CD + MSC-treated hips. There was no evidence of a difference in functional outcomes between the 2 treatment groups. After adjusting for baseline Ficat stage, age, and sex, an un-replaced hip treated with BP + CD + MSC had 0.42 (95% CI: 0.11 to 1.57) times the risk of being replaced in the next moment compared to an un-replaced hip treated with BP only (p = 0.196). The authors concluded that these findings demonstrated that treatment with BP alone or BP + CD + MSC can postpone the need for total hip arthroplasty (THA) in the first 24 months in patients with ONFH compared to previously reported data, but there is no statistically significant difference between the 2 treatment groups. Combination therapy of BP + CD + MSC may be more effective in delaying the progression of collapse in early stage ONFH. Moreover, they stated that future prospective studies are needed to ascertain the effectiveness of these treatment strategies in the long-term.

**Bone Marrow Concentrate:**

In a prospective and randomized clinical trial, Pepke and associates (2016) examined the safety of injection of bone marrow aspirate concentrate during core decompression and studied its clinical (VAS; HHS) and radiological outcomes (MRI). These investigators evaluated 24 consecutive patients with non-traumatic femoral head necrosis (FHN) during a period of 2 years after intervention. In-vitro analysis of mesenchymal stem cells was performed by evaluating the fibroblast colony forming units (CFU-Fs). Post-operatively, significant decrease in pain associated with a functional benefit lasting was observed. However, there was no difference in the clinical outcome between the 2 study groups. Over the period of 2 years there was no significant difference between the head survival rate
between both groups. In contrast to that, these researchers could not perceive any significant change in the volume of FHN in both treatment groups related to the longitudinal course after treating. The number of CFU showed a significant increase after centrifugation. The authors concluded that this trial could not detect a benefit from the additional injection of bone marrow concentrate with regard to bone regeneration and clinical outcome in the short-term.

Cabrolier and Molina (2016) noted that ONFH leads to degeneration of the head and finally to osteoarthritis of the hip. Decompression is the most widely used treatment, but its effectiveness is limited. These researchers stated that it has been proposed instillation of stem cells in addition to decompression, would lead to better results. Searching in Epistemonikos database, which is maintained by screening 30 databases, these investigators identified 2 systematic reviews including 2 randomized trials. They combined the evidence using meta-analysis and generated a summary of findings table following the GRADE approach. The authors concluded that instillation of bone marrow stem cells at the time of core decompression probably slowed progression to osteoarthritis of the hip in patients with ONFH and might reduce the need of subsequent surgeries. However, they stated that it is unclear whether it has any effect on the functionality because the certainty of the evidence is very low.

Yuan and co-workers (2016) evaluated the clinical outcomes of ONFH after autologous bone marrow stem cell implantation. These investigators searched the PubMed, Embase and Web of Science databases and included all case-control trials that reported on the clinical outcomes of osteonecrosis progression, incidence of THA and improvement in HHS. Overall, 7 case-control trials were included. Compared with the controls, patients treated with the bone marrow stem cells implantation treatment showed improved clinical outcomes with delayed osteonecrosis progression (odds ratio [OR] = 0.17, 95% CI: 0.09 to 0.32; p < 0.001), a lower THA incidence (OR = 0.30, 95% CI: 0.12 to 0.72; p < 0.01) and increased HHS (mean difference =
4.76, 95% CI: 1.24 to 8.28; p < 0.01). The heterogeneity, publication bias, and sensitivity analyses showed no statistical difference significant differences between studies. The authors concluded that the findings of this study suggested that autologous bone marrow stem cells implantation has a good therapeutic effect on ONFH, resulting in beneficial clinical outcomes. However, they stated that trials with larger sample sizes are needed to confirm these findings.

**Laser and Ozone Therapies:**

In a systematic review, Fliefe and colleagues (2015) evaluated the available treatments for bisphosphonate-related osteonecrosis of the jaws (BRONJ) and their outcomes. A literature search of PubMed, Cochrane Library, and Web of Science databases was conducted in accordance with the PRISMA statement, search phrases were “jaw osteonecrosis” OR “bisphosphonate-related osteonecrosis” OR “bisphosphonate osteonecrosis” AND “treatment” OR “outcomes”. A total of 97 articles published between 2003 and February 2014 were reviewed. The studies reported 4,879 cases of BRONJ. The mean age of the patients was 66.5 ± 4.7 years. The male to female ratio was 1:2. The mean duration of BP administration was 38.2 ± 15.7 months. The quality of the publications was good, with some moderate and poor.

Minimally invasive surgical treatment was the treatment most used. Medical treatment was also used. Adjunctive treatments included laser, growth factors, hyperbaric oxygen and ozone. The authors concluded that the articles provided a broad range of outcome variables to assess the treatment of BRONJ and the outcomes of each treatment; considerable heterogeneity was found regarding study design, sample size, and treatment modalities. They stated that clinical trials with larger samples are needed to provide sufficient information for each treatment modality to predict the outcomes of each treatment.

Latifyan et al (2016) noted that ONJ resulting from administration of BP or denosumab is a rare but severe complication in cancer patients. Complete remission depends
on the stage of ONJ; it can be estimated in the range of 20 to 30%
. Low-level laser therapy (LLLT) has been advocated as a logical additional option; LLLT irradiation has anti-inflammatory actions and thus can help to control pain, as well as bio-stimulating properties with favorable actions on bacterial control and wound healing. These investigators reviewed the results of 7 published studies of LLLT in BP-associated ONJ; LLLT resulted in an overall response rate of 55 % superior to that observed in controls (30 %). The findings suggested that there might be an advantage to add LLLT to the "classical" management of ONJ. The authors concluded that further research is needed to remove any doubt of protection or enhancement of carcinogenic processes; they believe that prospective well-controlled studies of LLLT in ONJ are needed. If the positive results are confirmed, it would represent a great improvement for the quality of life of many patients.

Platelet-Rich Fibrin (PRF):

Gonen and Yilmaz Asan (2016) stated that platelet-rich fibrin (PRF) is a second generation platelet concentrate, and has the ability of regulating the inflammation and stimulation of chemotactic agents. These researchers presented the treatment of stage-III BRONJ by PRF. A 77-year old male patient with stage-III BRONJ was treated with minimal surgical operations and PRF membrane. The patient was followed-up for 18 months, and there was no recurrence or exposure. The authors concluded that PRF may promote the healing of both bone and soft tissues even in stage-III patients. They stated that this technique is an alternative treatment modality for the closure of bone exposure and tissue healing in BRONJ patients. The findings of this sing-case study need to be validated by well-designed studies.

Norholt and Hartlev (2016) evaluated the outcome of the surgical treatment of osteonecrosis of the jaw (ONJ) with the additional use of autologous membranes of PRF. The study population consisted of 15 patients with ONJ lesions in the maxilla (n = 3), mandible (n = 11), or both (n = 1); 8 patients had
malignant disease and were treated with high-dose anti-resorptive medication; 7 were treated with low-dose anti-resorptive drugs for osteoporosis; 13 patients had grade 2 ONJ lesions and 2 had grade 3 lesions. The following standardized surgical technique was applied: resection of necrotic bone, mobilization of mucoperiosteal flaps, and multiple layer coverage of bone with PRF membranes. At follow-up of 7 to 20 months after surgery, complete mucosal healing and an absence of symptoms were found in 14 of the 15 patients (93%). The patient with persistent bone exposure had a grade 3 ONJ lesion before surgery. The authors concluded that the findings of this study suggested that the use of PRF membranes in the surgical treatment of grade 2 ONJ may be a contributing factor to a successful outcome. These preliminary findings need to be further investigated.

CPT Codes / HCPCS Codes / ICD-10 Codes

*Information in the [brackets] below has been added for clarification purposes. Codes requiring a 7th character are represented by "+":*

**ICD-10 codes will become effective as of October 1, 2015:**

**There is no specific CPT code for core decompression:**

**CPT codes not covered for indications listed in the CPB:**

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0232T</td>
<td>Injection(s), platelet rich plasma, any site, including image guidance, harvesting and preparation when performed</td>
</tr>
</tbody>
</table>

**Other CPT codes related to the CPB:**

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>20955</td>
<td>Bone graft with microvascular anastomosis; fibula</td>
</tr>
<tr>
<td>27071</td>
<td>Partial excision, wing of ilium, symphysis pubis, or greater trochanter of femur, (craterization, saucerization) (eg, osteomyelitis or bone abscess); deep (subfascial or intramuscular)</td>
</tr>
<tr>
<td>27170</td>
<td>Bone graft, femoral head, neck, intertrochanteric or subtrochanteric area (includes obtaining bone graft)</td>
</tr>
<tr>
<td>Code</td>
<td>Description</td>
</tr>
<tr>
<td>-------</td>
<td>-------------------------------------------------------</td>
</tr>
<tr>
<td>38230</td>
<td>Bone marrow harvesting for transplantation; allogenic</td>
</tr>
<tr>
<td>38232</td>
<td>autologous</td>
</tr>
<tr>
<td>38241</td>
<td>Hematopoietic progenitor cell (HPC); autologous</td>
</tr>
<tr>
<td></td>
<td>transplantation</td>
</tr>
</tbody>
</table>

**HCPCS codes covered if selection criteria are met:**
- S2325 Hip core decompression

**HCPCS codes not covered for indications listed in the CPB:**
- P9020 Platelet rich plasma, each unit

**ICD-10 codes covered if selection criteria are met:**
- M87.051 - M87.059, Osteonecrosis of femur [early/pre-collapse (stage I or II; before X-ray changes are evident)]
- M87.151 - M87.159
- M87.251 - M87.256
- M87.351 - M87.353
- M87.851 - M87.859
- M90.551 - M90.559

**ICD-10 codes not covered for indications listed in the CPB:**
| M87.00 - M87.050; M87.061 - M87.150; M87.161 - M87.166; M87.174 - M87.179; M87.188 - M87.219; M87.231 - M87.250; M87.261 - M87.319; M87.331 - M87.350; M87.361 - M87.366; M87.374 - M87.819; M87.831 - M87.850; M87.861 - M87.869; M87.874 - M87.9; M90.511 - M90.549; M90.561 - M90.58 - M90.59 | Osteonecrosis of bone [excluding femur] |

**The above policy is based on the following references:**

[Core Decompression of the Hip](#):

1. Steinberg ME. Core decompression of the femoral head


Core Decompression of the Other Joints:


Adjunctive Treatments:


2. Yu PA, Peng KT, Huang TW, et al. Injectable synthetic bone


10. Latifyan S, Genot MT, Klastersky J. Bisphosphonate-related osteonecrosis of the jaw: A review of the


AETNA BETTER HEALTH® OF PENNSYLVANIA

Amendment to
Aetna Clinical Policy Bulletin Number: 0753
Core Decompression for Avascular Necrosis

There are no amendments for Medicaid.

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