Analysis of the efficacy of drilling decompression autologous bone marrow and allogeneic bone grafting in the treatment of HIV-positive patients with early osteonecrosis of the femoral head

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Article

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Abstract

Objective

To investigate the efficacy of treating patients with HIV-positive osteonecrosis of the femoral head using drilled decompression autologous bone marrow and allogeneic bone grafting.

Methods

40 patients (44 hips) with early osteonecrosis of the femoral head treated by drilling decompression autologous bone marrow and allogeneic bone grafting since October 2015 were retrospectively analyzed, among which 20 patients (24 hips) were HIV-positive patients with early osteonecrosis of the femoral head, 16 males and 4 females, age 22–43 years, average 39.6 ± 10.18 years, and 20 patients (20 hips) in the same period HIV-negative early osteonecrosis of the femoral head patients, 13 males and 7 females, aged 48–78 years, mean 63.50 ± 7.94 years were negative controls. General information including ARCO stage, Harris score, VAS score, hematological indexes including CD4+ T lymphocyte count, and HIV viral load was recorded for all patients before surgery. All patients were operated on by drilling and decompression of the necrotic area, harvesting autologous iliac bone marrow with allogeneic bone, and bone grafting through the decompression channel. The patients were followed up regularly at 6, 12, and 24 months after surgery and annually thereafter, and the repair of the necrotic femoral head was observed by reviewing the frontal and lateral X-ray, CT or MRI of the hip joint, and the complications and functional recovery of the hip joint was counted and compared between the two groups.

Results

All patients were followed up, and the ARCO stages in the HIV-positive group were stage I 2 hips, stage IIA 6 hips, stage IIB 8 hips, stage IIC 6 hips, and stage III 2 hips, with a follow-up time of 12 to 60 months and a mean of 24.6 months. In the negative control group, there were 3 hips in ARCO stage I, 7 hips in stage IIA, 5 hips in stage IIB, 3 hips in stage IIC, and 2 hips in stage III, and the follow-up time ranged from 13 to 62 months, with an average of 24.8 months. The Harris score and VAS score of the hip in both groups improved significantly at 6-month after surgery compared with those before surgery (P < 0.05). The difference between the Harris score of the hip in the positive group at 2-year after surgery compared with that at 6-month after surgery was statistically significant, but the VAS score at 2-year after surgery compared with that at 6-month after surgery was not statistically significant. In the negative group, there was no statistically significant difference in the Harris score and VAS score of the hip at 2-year after surgery compared with those at 6-month after surgery. In the positive group, there was a trend of continuous increase in hip BMD from the beginning of the postoperative period (P < 0.05). There was no statistically significant difference between the Harris score and the positive group at the 2-year postoperative follow-up except for the Harris score, which was statistically significant (P < 0.05), and the
Conclusion

The treatment of early HIV-positive osteonecrosis of the femoral head patients with autologous bone marrow and allogeneic bone grafting by drilling and decompression to remove the tissue in the necrotic area of the femoral head can effectively stop the process of osteonecrosis of the femoral head and promoting femoral head repair in HIV-positive patients is a safe and effective method for treating HIV-positive patients with early osteonecrosis of the femoral head, and can effectively delay or postpone total hip replacement in patients.

1. INTRODUCTION

With the use of highly active antiretroviral therapy (HAART), the survival of HIV-positive patients is significantly longer, and the number of patients requiring surgery for osteonecrosis of the femoral head (ONFH) is gradually increasing\(^1\). The etiology of HIV-related ONFH is not yet clear, but its incidence has been increasing since the introduction of HAART, especially in patients with protease inhibitors\(^2\). Studies have shown that HIV itself may be an independent risk factor, associated with adrenocorticosteroid use, hypercholesterolemia, hypertriglyceridemia, smoking, excessive alcohol consumption, antiphospholipid antibodies, and megestrol acetate\(^3\). The prevalence of ONFH in HIV-positive patients is statistically 10–100 times higher than in the HIV-negative population\(^4\), and in addition, asymptomatic ONFH is common in HIV-positive patients, with 4.4% of asymptomatic HIV-positive patients showing signs of ONFH on MRI compared with 1.7% of HIV-negative patients\(^4,5\). Drilling decompression autologous bone marrow and allograft bone grafting is an important method for the treatment of early ONFH, in which the necrotic femoral head is drilled to reduce intraosseous pressure, remove tissue from the necrotic area, and improve blood perfusion to the femoral head\(^6\). In the early phases, several surgical procedures have been reported: core decompression, bone grafting coupled with mesenchymal stem cell injection\(^7\). However, there are few reports on the treatment of early ONFH in HIV-positive patients by drilling decompression autologous bone marrow and allogeneic bone grafting, and this study retrospectively analyzed 40 patients (44 hips) with ONFH treated by drilling decompression autologous bone marrow and allogeneic bone grafting admitted to Beijing Ditan Hospital of Capital Medical University, of which 20 HIV-positive cases (24 hips) were the experimental group and 20 HIV-negative cases (20 hips) as the negative control group, comparing the occurrence of intraoperative and postoperative complications and the recovery of hip function in the two groups, are reported below.

2. MATERIALS AND METHOD
2.1. Patient inclusion and exclusion criteria

Inclusion criteria for the experimental group: HIV-positive patients diagnosed according to the AIDS Treatment Guidelines [8], with preoperative CD4+ T lymphocyte counts greater than 200/µL [9]; ONFH diagnosed according to the Chinese Clinical Guidelines for Adult Femoral Head Necrosis (2020) [10], with ARCO staging [11] confirmed by imaging as stage I, II and early stage III(III a) [12]; clear mind, with a strong intention to preserve the hip, agreed to adhere to the follow-up, and signed the informed consent before surgery. Exclusion criteria: patients with HIV-positive ONFH treated with total hip replacement (THR), ARCO stage III end-stage(III b) [12] or stage IV, patients with preoperative CD4+ T lymphocyte count less than 200/µL had elective surgery if not necessary [9]; those who could not tolerate surgery; those with ONFH caused by trauma; those who did not sign informed consenters.

Inclusion criteria for the control group: HIV infection was excluded, and the rest was the same as the experimental group. Exclusion criteria: HIV-negative ONFH patients treated with THR, with ARCO stage III end-stage(III b) [12] or stage IV; those who cannot tolerate surgery; those with trauma-induced ONFH; and those who did not sign informed consent.

2.2 General data

Since October 2015, a total of 40 patients met the above criteria and were included in the study, including 20 HIV-positive cases (24 hips), 2 hips in ARCO stage I, 6 hips in stage IIA, 8 hips in stage IIB, 6 hips in stage IIC, and 2 hips in early stage III. There were 16 males and 4 females, aged 22–43 years, with a mean of 39.60 ± 10.18 years. The follow-up time ranged from 12 to 60 months, with a mean of 24.6 months. The HIV-positive history ranged from 2.4 to 6.0 years, with a mean of 3.9 years, and all were treated with long-term oral tilapia antiviral regimens for 2 to 5 years since the diagnosis of HIV infection, with a mean of about 3 years. Preoperative CD4+ T lymphocyte counts ranged from 201 to 747×10⁶/L, with a mean of 428.25 ± 130.50/L; HIV RNA levels, i.e., viral load (VL), were undetectable to 647 copies/ml, with a mean of < 50 copies/ml. The remaining 20 cases (20 hips) were negative controls, with ARCO stage I. The remaining 20 cases (20 hips) were negative controls, with ARCO stage I 3 hips, stage IIA 7 hips, stage IIB 5 hips, stage IIC 3 hips, and stage III 2 hips. There were 13 males and 7 females, aged 48–78 years, with a mean of 63.50 ± 7.94 years. The follow-up time ranged from 13 to 62 months, with a mean of 24.8 months.

According to the HIV infection classification system of the Centers for Disease Control and Prevention (CDC), which classifies the clinical stages of HIV infection [13], 4 cases in the experimental group were in clinical stage I, 16 cases in clinical stage II, and no patients in clinical stage III, with a history of ONFH of 1 to 5 years, with a mean of 2.9 years. Double hip ONFH patients were operated on in stages, with a surgical interval of 3 to 6 months, with a mean of 3.8 months. The general information of the two groups is shown in Table 1. Figure 1 (AF) shows the preoperative imaging presentation of an HIV-positive ONFH patient. This study was approved by the Ethics Committee of Beijing Ditan Hospital, Capital Medical University.
2.3 Surgical methods

The surgery was performed by the same team of surgeons, and to avoid occupational exposure, the surgeons were required to wear protective equipment. The patient was placed supine on an orthopedic surgical traction bed with continuous epidural or general anesthesia, and the operating area was routinely disinfected and towed. Intraoperative fluoroscopy was performed to verify the position of the guide needle, adjustment was made so that the guide needle reached the preoperative design position, and the 7.2 mm hollow drill was applied under fluoroscopy along with the guide needle to drill through the necrotic area, reaching 5 mm below the cartilage surface as appropriate, withdrawing the hollow drill, scraping the spoon to remove the necrotic area tissue, and the specimen was sent for pathological examination. The bone marrow was extracted from different directions with a 20 ml syringe using a bone puncture needle at the anterior superior iliac spine, and about 20–30 ml was aspirated, and mixed with allogeneic cancellous bone particles from Wuhan Union, sterilized by the instrument dealer (ethylene oxide, valid for 4 years) and set aside. Application of KYPHON V Premium Vertebroplasty System (Medtronic Sofamor Danek USA, Inc.), the bone marrow mud pusher in the instrument kit, pushes the allograft bone particles to implant and filling the decompression channel of the femoral head necrosis area and femoral neck, rams the bone graft particles through the tunnel under C-arm guidance, and after satisfactory fluoroscopy, the incision is sutured and dressed with a sterile dressing. The intraoperative situation is shown in Fig. 2(AL).

2.4 Perioperative treatment and efficacy evaluation

Pre-operative treatment: do safety and protection education for both doctors and patients, psychological preparation, pre-operative visit, preparation of articles, and preparation of protective gear for surgical personnel. VL was effectively controlled in HIV-positive patients who were admitted to the hospital and had their tilai antiviral regimen replaced with a regimen containing an integrase inhibitor and maintenance of CD4+ T lymphocyte counts above 200/µL, with no significant adverse effects in the experimental group; aggressive management of comorbid underlying disease in elderly patients preoperatively. For hypertensive patients, preoperative adjustment of blood pressure was stabilized within 140/90 mmHg; for diabetic patients, perioperative glucose control with mentored insulin was performed with fasting or preprandial glucose 6.1–7.8 mmol/L and 2h postprandial or random glucose 7.8–10.0 mmol/L; for patients with coronary artery disease, perfect cardiac enzymes, electrocardiogram, cardiac ultrasound, coronary CT angiography or coronary angiography, ask the anesthesiology and cardiology departments to assess tolerable surgery, discontinue antiplatelet drugs, and use low-molecular heparin calcium replacement therapy; for patients with hypoproteinemia, preoperative transfusion of human albumin ensured that patients’ serum albumin was greater than 30 g/L; Dual-energy X-ray absorptiometry (DXA) assessment of hip bone mineral density, for osteoporotic patients with DXA bone mineral density T values ≤ -2.5 SD, perioperative and post-discharge long-term oral triple antiosteoporosis drug treatment with alendronate, calcium, and vitamin D.
Special intraoperative treatment in the experimental group: the surgical staff wore protective equipment such as double gloves and eye protection devices, paid attention to not over-pursuing speed during surgical operations, paid attention to intraoperative protection such as strengthening isolation measures, using non-contact techniques for sharp delivery, suction hemostasis, needleless suturing, blunt needle suturing, etc.; AbbVita 160 was given intravenously to strengthen antiviral treatment to reduce the risk of postoperative complications and occupational exposure.

Postoperative treatment: Used disposable items such as masks and gowns were promptly placed in yellow plastic garbage bags, and instruments such as needles and blades were placed in the injurious waste receptacle and labeled "HIV-positive". Spray 70% alcohol into the bag, seal it, and then incinerate it with a person in charge. The patient's blood and secretions are put into containers with special signs and soaked in 70% alcohol for 1h. The operating room equipment is coated with 2% glutaraldehyde, wiped with clean water, and then disinfected. The surgical staff is strictly disinfected after surgery, and once occupational exposure occurs, it is immediately reported to the relevant hospital departments and prophylactic medication is administered in the shortest possible time. Pay attention to the control of blood pressure, blood sugar, and albumin level after surgery, and instruct patients to move their lower limbs to prevent the formation of deep vein thrombosis in the lower limbs. According to individual conditions, partial weight-bearing with crutches for 6 weeks after surgery, gradually to full weight-bearing after 6 weeks, and complete de-crutching in 3 months. Patients in the experimental group continued and adhered to the original HAART protocol after surgery and discharge from the hospital. Long-term postoperative alendronate/zoledronate, vitamin D (1200 U/d) and calcium (1200 mg/d) for those with a clear diagnosis of osteoporosis. The perioperative-related indexes are shown in Table 1. Postoperative outpatient follow-up was performed at 6, 12, 24 months, and annually thereafter, and radiological assessments such as anterior flexion and frog leg lateral radiographs or MRI was performed at each follow-up visit. The values of the visual analog scale (VAS), Harris hip score, and hip bone mineral density (BMD) (measured by dual-energy X-ray) were recorded before surgery, 6 months after surgery, and 2 years after follow-up, as shown in Table 2.

2.5 Statistical methods

SPSS 26.0 statistical software was used for analysis, and the measurement data were expressed as x ± s. When the data were normally distributed, independent samples t-test was used for comparison between the baseline data of the two groups. One-way ANOVA was used to compare the follow-up scores between the two groups at different time points, and the LSD method was used for two-way comparisons. Independent samples t-test was used for comparison between the two groups. The Friedman or Kendall test was used when the data were not normally distributed. p < 0.05 was considered a statistically significant difference.

3. RELUTS

In the experimental group, the follow-up time ranged from 12 to 60 months, with a mean of 24.6 months and the hip Harris score improved from (55.57 ± 3.60) preoperatively to (87.33 ± 2.47) at 6-month
postoperatively and (85.05 ± 4.05) at 2-year postoperative follow-up, with a statistically significant difference (P < 0.05), and the VAS score decreased from (5.19 ± VAS scores decreased from preoperative (5.19 ± 0.98) to postoperative (1.24 ± 0.76) at 6-month and to (0.95 ± 0.74) at the 2-year postoperative follow-up, with a statistically significant difference between preoperative and postoperative VAS scores at 6th month, but not between postoperative and 2-year follow-up. At the 2-year postoperative follow-up, the hip BMD improved significantly, and the difference was statistically significant when compared with preoperative and 6-month postoperative (P < 0.05). In the control group, the follow-up time ranged from 13 to 62 months, with a mean of 24.8 months, and the hip Harris score improved from (56.43 ± 3.10) preoperatively to (88.05 ± 2.31) at 6-month postoperatively and (88.81 ± 2.08) at the 2-year postoperative follow-up, with a statistically significant difference (P < 0.05) when comparing preoperatively and 6-month postoperatively. The difference was not statistically significant (P > 0.05) when comparing 6-month to 2-year postoperatively, and there was no statistically significant difference (P > 0.05) when comparing the rest of the period with the experimental group, except for the statistically significant difference (P < 0.05) when comparing Harris scores at the 2-year postoperative follow-up. The VAS scores decreased from (5.05 ± 0.74) before surgery to (1.14 ± 0.72) at 6-month postoperatively, (1.05 ± 0.74) at the 2-year postoperative follow-up, and the difference was statistically significant (P < 0.05) when comparing preoperative with 6-month postoperative and no statistically significant (P > 0.05) when comparing 6-month postoperative with 2-year postoperative, and the difference in VAS scores was not statistically significant when comparing with all periods in the experimental group.

There were no intraoperative complications such as vascular and nerve injuries and fractures, and no infection-related complications such as incisional infections and pulmonary infections during hospitalization; in the positive group, one case of oral cytomegalovirus infection and one case of Pneumocystis carinii pneumonia, which was cured after treatment; two cases of THR due to aggravation of ONFH on the operated side; three cases of pain due to weight-bearing on the operated side of the limb due to ONFH on the opposite side; And in the negative group, one case of the hip on the operated side due to external environmental, THR was performed in 3 cases due to aggravation of ONFH on the operated side during the follow-up period; 4 cases had pain due to weight bearing on the operated side due to ONFH on the contralateral side; 2 cases had THR on the operated side due to bone graft resorption and femoral head collapse 2 years after surgery. It is noteworthy that the trend of improvement in functional scores and imaging review within two years of follow-up was observed in both groups of patients who underwent borehole decompression osteotomy, while the final time of THR was about 3 to 5 years after 2 years of surgery and the cause of necrosis progression may be related to long-term oral hormone therapy and alcohol consumption. After evaluation, patients treated with THR reached preoperative ARCO stage IIIb or IV, with a preoperative Harris score of 50.71 ± 4.12 in such patients in the positive group and 49.26 ± 5.34 in the control group, with a significant improvement in functional scores after THR treatment. The complications of the patients during the postoperative and follow-up periods are shown in Table 3, and the relevant imaging performances during the follow-up period are shown in Fig. 3 (A&B).

4. DISCUSSION
4.1 Possible mechanisms of ONFH in HIV-positive patients

ONFH is a debilitating disease characterized by increased intraosseous pressure and reduced blood supply to the femoral head leading to progressive bone tissue necrosis, with unknown pathogenesis \cite{14}, in which trauma, hormones, and alcohol are the three main risk factors. In the case of HIV-positive patients, the pathogenesis of ONFH is related to the application of HAART regimens such as tenofovir disoproxil fumarate (TDF), protease inhibitors (PI) and the involvement of HIV itself in cytokine regulation, the effect on differentiation and apoptosis of mesenchymal stem cells (MSCs), osteoblasts, osteoclasts, etc. \cite{15,16,17}, the development of bone metabolism disorders may be multifactorial, such as gender, age, weight, malnutrition, smoking, alcohol consumption, steroid hormones, and lipid metabolism disorders \cite{18}, and the combination of these risk factors with HIV infection and HAART side effects may be the ultimate cause of ONFH in HIV-positive patients. Studies have reported the incidence of ONFH in HIV-positive patients to be 0.4–4.4\% \cite{5,19–21}, with a mean age of 38.1–44.4 years, which corresponds to an ONFH incidence of only 0.010–0.135\% in the general population, with an age of onset of 35–55 years \cite{22,23}, with the advancement of medical technology and the increasing demand for minimally invasive and HIV positive patients are increasing, especially in young and middle-aged patients, it is especially urgent to find new operationally simple, safe and effective surgical methods to reduce occupational exposure of health care workers.

4.2 Surgical methods

Early surgical intervention can effectively delay the progression of necrosis and osteoarthritis \cite{24}, and early treatment before the advanced subchondral bone collapse in ONFH is essential to preserve the structure and function of the joint and prevent the need for THR (a common treatment option for advanced ONFH) \cite{25}. Treatment of patients with early ONFH must address the following four issues to repair the necrotic area \cite{26}: (1) improve blood flow in the femoral head and promote vascular regeneration; (2) effectively remove the necrotic bone; (3) reconstruct the cartilage in the collapsed area of the femoral head to restore its shape and improve the matching relationship between the femoral head and the acetabulum; and (4) improve the mechanical properties of the femoral head and prevent its collapse.

Procedures to preserve the femoral head include marrow core decompression, osteotomy, and bone grafting with or without hematopoiesis \cite{27}, one of the most widely used treatments being marrow core decompression, which involves drilling into the necrotic area to increase blood supply and reduce edema. Marrow core decompression also reduces pain and promotes capillary regeneration, but it does not completely resolve the femoral repair problem \cite{28}; moreover, it is known that the collapse rate is lower in asymptomatic ONFH when the necrotic area is present only medial to the femoral head, and the use of this procedure should be carefully considered for treatment \cite{29}. This procedure has been carried out for a long time with positive efficacy and is mainly divided into fine needle multi-hole drilling decompression and coarse channel medullary core decompression, the difference being the diameter of the decompression channel \cite{30,31}. 
In ONFH, apoptosis of osteocytes and the depression of bone-marrow activity in the femoral head [32] impair the remodelling capability of the bone, leading to femoral head collapse and premature osteoarthritis (OA) [33]. The natural history of ONFH shows a poor prognosis, and up to 80% of conservatively treated patients require THR [34]. Drilling decompression can be used to manage small lesions in their early stages [35], as this procedure can effectively relieve the intraosseous pressure and venous stasis typical of ONFH [36, 37]. However, it alone may not be adequate in more extensive lesions, where insufficient activity of the osteoprogenitor cells does not provide sufficient bone reconstruction [38, 39]. Notably, most of the presented RCTs performed the methods in patients with early-stage lesions and only two papers included patients with ARCO stage III lesions in their trials [40, 41], with variable results. Tabatabaee et al. [41] reported an imaging improvement in the two ARCO III patients treated with this surgical methods in their cohort, while Hauzeur and colleagues [40] did not see sufficient improvement in ARCO III patients undergoing the same treatment. And Migliorini F et al for patients with femoral head osteonecrosis, the methods demonstrated reduced pain and lower rate of progression to total hip arthroplasty compared to core decompression as an isolated procedure. [42] At present, the combination of core decompression with stem cell transplantation (or concentrated autologous bone marrow single nucleus cell transplantation) is clinically effective in domestic medical institutions [43]. Combined stem cell transplantation has a better impact on ONFH outcomes compared to simple drill decompression, as also found by Rajagopal et al. [44] And in a meta-analysis, Sadile F et al thought combining drill decompression with other techniques seems to provide better outcomes in ONFH. Detecting venous stasis and artery insufficiency could be the key to select the right indications for this kind of surgery and to reduce failures. [45]

4.3 Characteristics of ONFH in HIV-positive patients and special management in the perioperative period

HIV-positive ONFH patients have an uneven femoral head surface, most of the cartilage surface has folds, subchondral separation or fibrous tissue proliferation on the cartilage surface, yellowish uniform granular bone in the center of subchondral necrosis, cystic lesion formation, obvious sclerotic zone formation in the repair area, and multifocal granulation tissue proliferation. This group is more specific and requires special management measures in the perioperative period: preoperative HAART treatment is required for at least 1 month, VL is effectively controlled, the CD4+ T lymphocyte count was maintained above 200/µL, and no significant adverse effects were observed; most of the HIV-positive patients were younger than the negative patients (P < 0.05), and the preoperative indexes, such as inflammatory indexes, were not significantly different from those of the negative patients except for HIV-related indexes (Table 1), so the preoperative antiviral treatment was particularly important and had no significant adverse effect on the postoperative hip function. Therefore, preoperative antiviral treatment is particularly important and has no significant adverse effect on postoperative hip function recovery. HIV-positive patients have a significantly longer operative time than negative patients (P < 0.05), so special intraoperative protection measures are needed to reduce the risk of infection among healthcare workers.
For postoperative management, HIV-positive patients also had a longer hospital stay than negative patients (P < 0.05), and postoperative attention was paid to the control of blood pressure, blood glucose, and albumin levels, and patients were instructed to move their lower limbs to prevent lower limb deep vein thrombosis. In this study, the patients with ONFH re-progression in the HIV-positive group may be related to HAART treatment, but in comparison, long-term adherence to HAART treatment is more beneficial. We introduced the concept of enhanced recovery after surgery (ERAS) in the treatment of HIV-positive patients, with emphasis on rapid viral load reduction, immunity enhancement, improvement of nutritional status, control of co-infections, prophylactic antibiotics, and anti-osteoporosis in the perioperative period.

4.4 Advantages, disadvantages, and efficacy of drilling and decompression of HIV femoral head necrosis with autologous bone marrow and allogeneic bone graft

Drilling decompression is important for HIV-positive early ONFH patients: on the one hand, the sclerotic bone is broken open through drilling to reach the necrotic area, so that the lesion area is fully decompressed; on the other hand, it can prevent the destruction of the femoral head cartilage, femoral head deformation and collapse. It works by using a 7.2 mm ring drill to percutaneously bore one or more tunnels from the greater trochanter, through the femoral neck, and into the subchondral bone of the femoral head [46,47]. These tunnels reduce intraosseous pressure and may help restore blood flow to the femoral head, thus allowing for healing and preservation of the joint [48,49]. In this study, combined autologous and allogeneic bone grafts were used to treat early ONFH by filling the bone defect after borehole decompression surgery with bone graft to provide a good carrier for MSC in bone marrow, maintain a high concentration of aggregates, and avoid local loss of MSC. Meanwhile, as a scaffold material, it can improve the local biomechanical strength, achieve the immediate reconstruction of the support of the necrotic area of the femoral head, provide a good scaffold for the formation of new bone, stop or delay the continued necrosis and collapse of the femoral head, and effectively solve the above four problems and good repair effect.

ONFH is not curable. Therefore, it is of particular importance to identify prognostic factors, independent of the treatment, that may lead to adverse clinical outcomes. Veillette et al. and Liu et al. [50,51] found that outcomes are worse for patients with steroid-associated ONFH that were treated with tantalum rod implantation regardless of the disease stage. This was also confirmed by Bozic et al. [52] who found an association between steroid use and survival of hips in patients treated with core decompression. And in a systematic review identified male gender, longer symptom duration before treatment, higher VAS scores and lower HHS scores as negative prognostic factors after treatment for osteonecrosis of the femoral head. However, in their analysis, patients' age and BMI, as well as the aetiology of the osteonecrosis, time from surgery to full-weight bearing, and drill size did not correlate with the clinical outcome after treatment. [53]

The long-term oral tenofovir-containing antiviral regimen of tenofovir in patients in the experimental group in this study [54,55]. For HIV-positive patients who have been diagnosed with osteoporosis, we will prohibit the use of tenofovir-containing antiviral regimen upon admission and replace it with an integrase
inhibitor-containing regimen in combination with anti-osteoporosis therapy, and patients in the experimental group in this study showed a continuous trend of increasing hip BMD during postoperative follow-up. With the development and marketing of new drugs, the current clinical trials of the antiviral regimens of Jefuccane, Pitocin, and injectable Epovetel have all confirmed safety and effectiveness with few adverse effects \textsuperscript{[56–58]}. The use of the Jefukang regimen in orthopedic surgery has been shown to be superior to the tiramis regimen in terms of speed and efficiency of viral load reduction, speed and efficiency of recovery of CD4\(^+\) T lymphocyte counts, and postoperative complication rates as well \textsuperscript{[59]}. It is possible to increase the use of the above-mentioned novel antiviral agents with low impact on BMD in the perioperative period and after discharge in patients with combined osteoporosis. The hip Harris score improved significantly in the HIV-positive group after surgery and at 6-month postoperatively compared to the HIV-positive group \(P < 0.05\), and hip function also improved at 6-month postoperatively versus 2-year postoperative follow-up \(P < 0.05\), and VAS scores were significantly lower postoperatively compared with 6-month postoperatively \(P < 0.05\), but the change was not significant at 6-month postoperatively versus 2-year postoperative follow-up. The Harris score and VAS score were not statistically significant compared with the negative control group at all periods \(P > 0.05\), and the complications during follow-up were similar to those of the HIV-negative control group, during the follow-up period, the patient developed hip pain, which may be related to early weight-bearing and excessive exercise. However, the symptoms were significantly reduced compared with the preoperative period and the previous follow-up, and the imaging CT and MRI showed significant bone repair and improvement compared with the pre-treatment period, and the bone density gradually increased, suggesting that drilling decompression autologous bone marrow and allogeneic bone grafting for HIV-positive patients can achieve similar outcomes to those of the negative population.

**CONCLUSION**

The incidence of ONFH in HIV-positive patients is high and most of them are middle-aged and young, and THR is faced with the problems of limited mobility, wear and tear of the prosthesis, and the need for multiple revisions after loosening, so in principle, hip preservation as much as possible, drilling decompression augmented with autologous bone marrow-derived transplantation or combined with autologous bone graft are effective in reducing symptoms of ONFH (even if it is stage IIIa) and the need for arthroplasty in the adult population \textsuperscript{[60,42]}. The regenerative potential of autologous mesenchymal stem cells have been poorly investigated in the younger HIV population, and further investigations are required.\textsuperscript{[61]} This study is a retrospective study with a small sample size and insufficient observation items, and the results may be biased.

**Abbreviations**

HIV = Human Immunodeficiency Virus; HAART = highly active anti-retroviral therapy; ONFH = osteonecrosis of the femoral head; THR = total hip replacement; BMD = bone mineral density
Declarations

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AUTHORS’ CONTRIBUTIONS

Shengtao Li wrote the main text of the manuscript and prepared Figures 1-3 and Tables 1-3, Jie Wang coauthored the data collection, and Qiang Zhang was involved in the revision and finalization of the paper. All authors reviewed the manuscript.

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AVAILABILITY OF DATA AND MATERIALS

All data generated or analyzed during this study are included in this article.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Not applicable.

CONSENT FOR PUBLICATION

Written informed consent was obtained from all participants.

CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

HUMAN AND ANIMAL RIGHTS

No animals were used in this research. All human research procedures were in accordance with the standards set forth in the Declaration of Helsinki principles of 1975, as revised in 2013 (http://www.wma.net/en/20activities/10ethics/10helsinki/).

References


# Tables

Table 1 General data and perioperative indicators of patients in both groups

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<th>Indicators</th>
<th>Group A (20 cases, 24 hips)</th>
<th>Group B (20 cases, 20 hips)</th>
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</tr>
<tr>
<td>CD4+/CD8+ ratio</td>
<td>0.49±0.22</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>VL (copies/ml)</td>
<td>&lt;50</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>White blood cell count (×109/L)</td>
<td>6.28±1.55</td>
<td>5.68±1.89</td>
<td>0.86</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Neutrophil count (×109/L)</td>
<td>4.19±1.89</td>
<td>3.26±1.50</td>
<td>1.41</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Albumin (g/l)</td>
<td>48.12±11.06</td>
<td>45.63±3.54</td>
<td>0.62</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Hemoglobin (g/l)</td>
<td>138.11±20.48</td>
<td>150.40±26.65</td>
<td>-1.22</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Length of hospitalization (days)</td>
<td>16.17±3.25</td>
<td>8.39±1.65</td>
<td>5.62</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Length of surgery (min)</td>
<td>120.71±57.47</td>
<td>86.58±24.27</td>
<td>1.52</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

Note: Group A - experimental group; Group B - control group

Table 2 Changes in BMD values at different time points in the experimental group and comparison of Harris and VAS scores at different time points in the two groups
**Table 3** Complications during postoperative and follow-up periods in both groups

<table>
<thead>
<tr>
<th>Complications</th>
<th>Group A(24 hips)</th>
<th>Group B(20 hips)</th>
<th>Statistic quantity</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Opportunistic infections(n)</td>
<td>1</td>
<td>0</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Oral cytomegalovirus infection</td>
<td>1</td>
<td>0</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Pneumocystis carinii pneumonia</td>
<td>1</td>
<td>0</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Deep vein thrombosis(n)</td>
<td>0</td>
<td>0</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Hip pain on the operated side(n)</td>
<td>4</td>
<td>4</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>THR for increased necrosis(n)</td>
<td>2</td>
<td>3</td>
<td>-</td>
<td>1.00</td>
</tr>
<tr>
<td>Resorption and collapse of implant THR on the operated side again(n)</td>
<td>1</td>
<td>2</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Contralateral ONFH(n)</td>
<td>3</td>
<td>4</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Total morbidity (%)</td>
<td>37.5</td>
<td>45</td>
<td>X²=0.25</td>
<td>0.42</td>
</tr>
</tbody>
</table>

**Note:** Group A - experimental group; Group B - control group
Preoperative images of an HIV-positive ONFH patient (bilateral); bilateral hip pain for 3 months, aggravated by limited mobility and claudication for 1 month; bilateral hip ARCO stage IIc, treated with bilateral femoral head drilling and decompression combined with bone grafting and autologous bone marrow transplantation. Wear of the femoral head, narrowing of the joint space and uneven surface of the femoral head (X-ray A); significant necrotic area of the femoral head, wear and deformation, narrowing of the joint space and uneven surface of the femoral head (CT B,C,D); mixed signal within the femoral head, depression of the cartilage surface and narrowing of the joint space (MRI E,F);
Figure 2

Intraoperative situation The bone marrow is extracted by puncture at the anterior superior iliac spine, mixed with allograft bone, and the allograft bone mixed with bone marrow is implanted through a bone tunnel into the area of the necrotic cavity, and intraoperative fluoroscopy showed bone drilling through the decompression necrosis area.
Figure 3

Imaging performance at the 24 months postoperatively (bilateral) During follow-up, the patient did not see any significant narrowing and widening of the hip gaps bilaterally, and the X-ray showed bone filling in the capsular area. 2 years later, CT and MRI showed that the necrotic area was slowly replaced by some autologous bone, and the abnormal signal changes of bone and soft tissue were significantly restored compared with before, and the surface of the femoral head was less flat and did not collapse further, without pain and other uncomfortable symptoms, and the patient was satisfied with the treatment: X-ray (A); CT (B,C,D); MRI (E,F)