Total Hip Arthroplasty in Patients With Avascular Necrosis After Hematopoietic Stem Cell Transplantation

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Abstract

The immunosuppressive regimens required for hematopoietic stem cell transplantation predispose recipients to complications, including avascular necrosis. Cancer-related comorbidities, immunosuppression, and poor bone quality theoretically increase the risk for perioperative medical complications, infection, and implant-related complications in total joint arthroplasty. This study reviewed 20 primary total hip arthroplasties for avascular necrosis in 14 patients. Outcomes were assessed at routine clinical visits and Harris hip scores were calculated. Follow-up radiographs were evaluated for component malposition, loosening, polyethylene wear, and osteolysis. Average follow-up was 44.5 months for all patients. Postoperative clinical follow-up revealed good to excellent outcomes, with significant improvement in functional outcome scores. There were no periprosthetic infections or revisions for aseptic loosening. There was 1 dislocation on postoperative day 40, which was treated successfully with a closed reduction. Two patients with a prior history of venous thromboembolism developed a pulmonary embolus on postoperative day 13 and 77, respectively. Four patients died several months to years after arthroplasty of complications unrelated to the surgical procedure. Total hip arthroplasty can both be safely performed and greatly improve quality of life in recipients of hematopoietic stem cell transplantation who develop avascular necrosis. However, prolonged venous thromboembolism prophylaxis should be carefully considered in this high-risk patient population. [Orthopedics. 2018; 41(2):e257-e261.]

Hematopoietic stem cell transplantation (HSCT) involves the infusion of stem cells derived from bone marrow, peripheral blood, or umbilical cord blood for patients with hematologic disorders. Although the indications for HSCT are diverse, this procedure is most commonly used for the treatment of hematopoietic malignancies. The Worldwide Network for Blood and Marrow Transplantation has reported that more than 50,000 HSCTs are performed each year. Advances in practices and supportive care have led to decreases in transplant-related mortality and a progressive increase in the number of long-term survivors of HSCT. Consequently, the long-term complications of transplantation are becoming more prevalent.

The immunosuppressive regimens required for transplant recipients predispose them to devastating bone complications, including osteoporosis and avascular necrosis. Avascular necrosis (AVN) has been reported in 4% to 19% of HSCT survivors and is diagnosed at a median of approximately 2 years after the transplantation procedure. Risk factors for AVN in this...
patient population include graft-versus-host disease (GVHD) and its treatment with corticosteroids, underlying diagnosis of acute lymphoblastic leukemia, older age, female sex, and use of total body irradiation in conditioning regimen. Several studies have shown that up to half of HSCT recipients who develop AVN eventually require joint replacement.7,8

However, there are no published data on outcomes of total joint arthroplasty (TJA) in HSCT recipients. Specific concerns exist with this patient population because of the intense immunosuppressive effect of the pretransplant conditioning regimen to avoid graft rejection and the posttransplant multidrug immunosuppressive regimen to prevent or treat GVHD when it occurs. Moreover, the 30% to 60% of HSCT recipients who develop acute or chronic GVHD suffer additional compromises to host defenses, and the acute or chronic GVHD after allogeneic HSCT is by itself immunosuppressive.10,11 The purpose of this study was to evaluate outcomes in a series of HSCT recipients who underwent total hip arthroplasty (THA) for AVN.

**MATERIALS AND METHODS**

After institutional review board approval was obtained, 14 HSCT patients who underwent 20 THAs between 2006 and 2014 were retrospectively reviewed. In all patients, the indication for primary THA was AVN.

Data were obtained through a review of patient demographics, preoperative and postoperative multidisciplinary notes (oncology/transplant, anesthesia, and orthopedics), operative reports, discharge summaries, and clinical examinations. Allogeneic HSCT was performed for treatment of hematological malignancies and diseases in all patients. Indications for HSCT were acute leukemia (8 patients), non-Hodgkin’s lymphoma (3 patients), Hodgkin’s disease (2 patients), and myelodysplastic syndrome (1 patient). Treatment prior to the HSCT involved intensive chemotherapy regimens often followed by a myeloablative conditioning regimen in preparation for transplant. Posttransplant immunosuppressive agents used to prevent GVHD most commonly included a combination of tacrolimus or cyclosporine with methotrexate. Despite these measures, all patients in this study had developed chronic GVHD and required prolonged treatment with high-dose systemic corticosteroids. Treatment typically included 1 mg/kg/d of prednisone or methylprednisolone gradually tapered during 1 to 2 years. Each patient subsequently presented for elective joint arthroplasty for AVN with a long-standing history of hip or knee pain that markedly limited function and failed to improve with conservative treatment such as nonsteroidal anti-inflammatory medications, physical therapy, and intra-articular steroid injections. Most patients receiving THA were maintained on an immunosuppressive regimen perioperatively, which included prednisone at a median dose of 20 mg with or without tacrolimus. Additional perioperative glucocorticoid coverage with intravenous hydrocortisone was required in 15 of 20 procedures to avoid potential adrenal insufficiency. Seven procedures (4 hips, 3 knees) were performed while the patients were off all immunosuppressive therapy.

At the time of surgery, intravenous antibiotic prophylaxis with cefazolin, or vancomycin or clindamycin for penicillin allergy, was started. This was continued postoperatively for 24 hours as per Surgical Care Improvement Project guidelines. After surgery, all patients received the institution’s standard deep venous thrombosis prophylaxis, including sequential compression devices, compression stockings, and low-molecular-weight heparin (enoxaparin) or warfarin. Most patients were continued on enoxaparin and/or warfarin for 2 weeks after discharge. Two patients with a prior history of deep venous thrombosis were continued on an anticoagulant for 90 days after discharge.

Total hip arthroplasty was performed using the posterior approach in 17 cases and the anterolateral approach in 3 cases. The acetabular components used included Zimmer (Warsaw, Indiana) Trabecular Metal (18 hips), Continuum (1 hip), and Converge (1 hip). The femoral stems used were the Zimmer M/L Taper (20 hips). Femoral heads ranged from size 32 to 44 mm.

Outcomes were assessed at routine clinical follow-up visits, and standard clinical intake forms were collected to determine Harris hip scores (HHSs). Four patients (29%) died at an average of 2.2 years (range, 0.8-5.1 years) after arthroplasty of causes unrelated to the surgical procedure. Radiographs were performed routinely during the clinical follow-up visits and were evaluated for component malposition, change in component position, loosening, polyethylene wear, and osteolysis.

**RESULTS**

Twenty primary THAs were performed in 14 patients with previous HSCT, including 8 men and 6 women. Indications for HSCT were acute leukemia (8 patients), non-Hodgkin’s lymphoma (3 patients), Hodgkin’s disease (2 patients), and myelodysplastic syndrome (1 patient). Mean age at transplant was 44 years (range, 22-61 years). Mean time between HSCT and TJA was 31.6 months (range, 11.4-78 months). Arthroplasty was performed at a mean age of 46 years (range, 26-63 years). Eleven (79%) patients reported bilateral joint involvement. The patients had multiple preoperative comorbidities associated with their underlying malignancies and/or transplant course, including previous history of respiratory infection (9 patients), other infectious disease (9 patients), venous thromboembolism (5 patients), cardiovascular disease (5 patients), diabetes mellitus (4 patients), and noninfectious pulmonary disease (2 patients). Preoperative comorbidities present in this patient population, including medical complica-
tions associated with underlying malignancy and/or transplant course, are listed in the Table. Average weight and height of the patients were 187 pounds and 69 inches, respectively. Average body mass index was 27.8 kg/m² (range, 20.8-35.0 kg/m²).

Twenty THAs were performed with minimal estimated blood loss and no reported intraoperative complications. Three patients required up to 2 units of packed red blood cells postoperatively. These patients had a history of anemia preoperatively. Average length of hospital stay was 1.7 days (range, 1-3 days), with final disposition of 16 hips returning to home and 4 hips needing extended care facilities. Average postoperative clinical follow-up was 44.5 months (range, 9.5-128 months) for all THA patients. Mean HHS was calculated as 53 preoperatively and 91 postoperatively. Patients subjectively self-reported their overall outcome as good to excellent in all hips. There were no periprosthetic infections or revisions for aseptic loosening. There was 1 dislocation after a fall on postoperative day 40. This was treated successfully with a closed reduction, and no further episodes of instability were reported. Two patients with a prior history of venous thromboembolism (VTE) developed a pulmonary embolus postoperatively despite receiving appropriate prophylaxis. One of these patients was continued on fondaparinux after discharge and developed the pulmonary embolus 13 days postoperatively. The other patient who developed a pulmonary embolus did so 77 days postoperatively. There were no deaths related to the surgery.

For the general population, studies have reported excellent clinical and radiologic results for THA in patients with AVN, with survivorship being comparable to that of patients with other indications for arthroplasty.12-14 Mont et al13 reported similar outcomes for 52 osteonecrotic hips from a single institution. Two revisions were required because of aseptic loosening of the femoral stem and a deep infection. Mean postoperative HHS for the osteonecrotic hips was 92 (range, 69-100) after an average follow-up of 34 months (range, 24-51 months).

Furthermore, the current results resemble those of previous renal, cardiac, liver, and lung transplant cohorts who have undergone TJAs.15-24 Boquet et al16 reported excellent outcomes for 16 primary total knee arthroplasties (6 because of AVN) performed on 12 renal graft recipients. The mean postoperative Knee Society score for AVN was 95.5 (range, 93-100) after an average period of 65 months. There were no deaths related to the surgical procedure, and no knee required revision. Ledford et al24 studied the outcome of TJAs (15 hips, 5 knees) in 14 lung transplant patients. The mean postoperative HHS was 88.7 (range, 71-91) after an average follow-up of 27.5 months (range, 2-56 months). There were no periprosthetic infections, and no revision surgeries performed.

Leonard and Davis18 reported more variable results from their study of 14 primary TJAs (10 hips, 4 knees) in cardiac transplant patients. The mean postoperative HHS was 71.8 for patients with AVN after an average follow-up of 68 months.

### Table

<table>
<thead>
<tr>
<th>Comorbidity</th>
<th>No. of Patients</th>
<th>Description</th>
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<tbody>
<tr>
<td>Respiratory infection</td>
<td>9 (64%)</td>
<td>Bacterial pneumonia (Staphylococcus, Klebsiella, Mycoplasma), RSV infection, Scedosporium infection</td>
</tr>
<tr>
<td>Deep venous thrombosis</td>
<td>5 (36%)</td>
<td>HTN, CAD, atrial fibrillation, pericarditis</td>
</tr>
<tr>
<td>Cardiovascular disease</td>
<td>5 (36%)</td>
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<tr>
<td>Diabetes mellitus</td>
<td>4 (29%)</td>
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<tr>
<td>Renal infection</td>
<td>3 (21%)</td>
<td>Virus-associated hemorrhagic cystitis</td>
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<tr>
<td>Clostridium difficile colitis</td>
<td>2 (14%)</td>
<td></td>
</tr>
<tr>
<td>Viral reactivation</td>
<td>2 (14%)</td>
<td>EBV, CMV</td>
</tr>
<tr>
<td>Pulmonary disease (noninfectious)</td>
<td>2 (14%)</td>
<td>COPD</td>
</tr>
<tr>
<td>Central nervous system infection</td>
<td>1 (7%)</td>
<td>Scedosporium infection, VRE infection</td>
</tr>
<tr>
<td>Septic arthritis</td>
<td>1 (7%)</td>
<td>Klebsiella</td>
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Abbreviations: CAD, coronary artery disease; CMV, cytomegalovirus; COPD, chronic obstructive pulmonary disease; EBV, Epstein–Barr virus; HTN, hypertension; RSV, respiratory syncytial virus; VRE, vancomycin-resistant enterococci.

**Discussion**

Despite the complex medical history and immunosuppressed state, this study shows that good outcomes can be achieved for THA in HSCT recipients who have developed AVN. The mean postoperative functional outcome HHS was 91. Major postoperative complications included 1 hip dislocation from a fall that was managed with closed reduction and 2 pulmonary emboli at postoperative days 13 and 77 in patients with a prior history of VTE. A blood transfusion was required in 3 patients. There were no periprosthetic infections, fractures, loosening, or deaths related to the surgery.

For the general population, studies have reported excellent clinical and radiologic results for THA in patients with AVN, with survivorship being comparable to that of patients with other indications for arthroplasty.12-14 Mont et al13 reported similar outcomes for 52 osteonecrotic hips from a single institution. Two revisions were required because of aseptic loosening of the femoral stem and a deep infection. Mean postoperative HHS for the osteonecrotic hips was 92 (range, 69-100) after an average follow-up of 34 months (range, 24-51 months).
(range, 39-154 months). One patient with bilateral THAs required bilateral revisions because of polyethylene wear, osteolysis, and loosening 7 and 10 years after the index procedure. One patient had multiple dislocations, which were treated with closed reduction. Levitsky et al. studied the outcome of TJA after liver transplantation. They also found no major long-term complications, and no patient had significant pain, dislocation, or infection in the postsurgical period.

The weaknesses of the current study included its retrospective design, small patient population, and short-term follow-up. Nonetheless, although numerous studies have evaluated solid organ transplant populations, there does not appear to be any prior report of outcomes following elective THA and total knee arthroplasty in HSCT recipients. The authors’ institution is a transplant center performing approximately 350 HSCTs annually. Fifty percent of these patients develop GVHD and thus have an increased likelihood of subsequently requiring joint replacement.

Two patients in the current cohort developed pulmonary emboli in the follow-up period despite adequate postoperative anticoagulation therapy. The higher risk of VTE compared with the general population is not surprising given the comorbidities in this high-risk population. Specifically, HSCT patients have a high incidence of VTE because of underlying malignancy, total body irradiation, prolonged hospitalization, administration of conditioning regimens, and GVHD. Previous studies have reported a 1.2% to 4.9% overall incidence of symptomatic VTE in HSCT patients. In the current cohort, 36% of patients had reported VTE events prior to arthroplasty. After surgery, all patients received deep venous thrombosis prophylaxis, including sequential compression devices, compression stockings, and low-molecular-weight heparin (enoxaparin) or warfarin. Most of the patients were continued on enoxaparin and/or warfarin after discharge. Two patients with a prior history of deep venous thrombosis were continued on an anticoagulant for 90 days after discharge; however, 1 of these patients still went on to develop a pulmonary embolus postoperatively. Prolonged VTE prophylaxis should be carefully considered in this high-risk patient population.

CONCLUSION

Despite theoretical risks of high infection rate and inferior bone quality associated with joint arthroplasty in transplant recipients, the current study suggests that THA can be safely performed and can provide good clinical and radiological outcomes in HSCT recipients. No patient developed an infection postoperatively. No episodes of periprosthetic fracture or implant loosening occurred in this group. However, the follow-up period was short for the evaluation of loosening. The inherent risks related to postoperative complications do not appear to be greater than those of other cohorts undergoing arthroplasty. However, larger, randomized, prospective trials and long-term follow-up are needed to confirm these findings and to permit statistical comparisons of the safety and outcome of joint replacement surgery in HSCT recipients vs healthy patients. Until then, other than VTE, there is little evidence that HSCT recipients are at higher risk for perioperative or early postoperative complications than the general population when undergoing arthroplasty. On the basis of these findings, the authors believe that HSCT recipients should not be denied TJA, which can greatly improve their quality of life, but rather that vigilance must be exercised regarding VTE prophylaxis.

REFERENCES


