What Risks are Associated with Primary THA in Recipients of Hematopoietic Stem Cell Transplantation?

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Abstract

Introduction As patients who receive hematopoietic stem cell transplantation are at increased risk of avascular necrosis (AVN) and subsequent degenerative arthritis, THA may be considered in some of these patients, particularly as overall patient survival improves for patients undergoing stem-cell transplants. Patients receiving hematopoietic stem cell transplantation theoretically are at increased risk of experiencing complications, infection, and poorer implant survivorship owing to the high prevalence of comorbid conditions, immunosuppressive therapy regimens including corticosteroids, and often low circulating hematopoietic cell lines; however, there is a paucity of studies elucidating these risks.

Questions/Purposes We asked: (1) What is the overall mortality of patients with hematopoietic stem cell transplantation who have undergone THA? (2) What is the complication rate for these patients? (3) What are the

revision and reoperation rates and implant survivorship for these patients?

Patients and Methods Between 1999 and 2013, we performed 42 THAs in 36 patients who underwent stem-cell transplants. Other than those who died, all were available for followup at a minimum of 2 years; of the patients whose procedures were done more than 10 years ago and who are not known to have died, two (5%) had not been seen in the last 5 years and so are considered lost to followup. All patients underwent thorough evaluation by the transplant team before arthroplasty; general contraindications included active medical comorbidities or evidence of unstable end-organ damage, active rejection, and critically low circulating hematopoietic cell lines. Underlying primary diseases leading to hematopoietic stem cell transplantation included lymphoma (14/42; 33%), plasma cell disorders (10/42; 24%), leukemia (9/42; 21%), and amyloidosis (3/42; 7%). Complications, reoperations, revisions, and implant and patient survivorship, were recorded from chart review and data from the institutional total joint registry. Mean followup was 5 years (range, 2–15 years).

Results Patient survivorship free of mortality was 91% (95% CI, 81%–100%) and 82% (95% CI, 68%–96%) at 2 and 5 years, respectively. Complications occurred in four of 42 THAs (10%); these complications included an intraoperative fracture and a venous thromboembolism. Revisions occurred in two of 42 (5%) THAs; there were no reoperations. Implant survivorship free of component revision for any reason or implant removal accounting for death as a competing risk was 93% (95% CI, 83%–100%) at 5 years.

Conclusion With appropriate medical evaluation and comanagement by transplant specialists, carefully selected patients with hematopoietic stem cell transplants may undergo elective primary THA, although complications do

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Each author certifies that his or her institution approved the human protocol for this investigation, that all investigations were conducted in conformity with ethical principles of research, and that informed consent for participation in the study was obtained.

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occur in this relatively fragile patient population. Although implant survivorship was modest at 93% at 5 years, there was not a high risk of revision for infection. Improved outcomes for these patients may be expected as their medical management advances and additional comparative studies may clarify other important patient factors.

Level of Evidence Level IV, therapeutic study.

Introduction

The number of people receiving autologous and allogeneic hematopoietic stem cell transplants in the United States continues to increase, with nearly 20,000 hematopoietic stem cell transplants having been performed in 2013 [10]. Given increasingly successful treatment and improved life expectancy, multiple factors increase the likelihood that more patients having hematopoietic stem cell transplantation may become candidates for THA in the years to come. From 2006 to 2011 patients 60 years or older represented 39% of the total recipients of hematopoietic stem cell transplantation [10]. Given these demographics, more patients with hematopoietic stem cell transplants are likely to have degenerative joint disease develop. Graft versus host disease, a known complication of hematopoietic stem cell transplantation, is a known risk factor for avascular necrosis (AVN) of the hip [1, 12]. Compounding the substantial risk for AVN are immunosuppressive therapies, including corticosteroids, used to treat graft versus host disease or other hematopoietic malignancies [1].

With multiple medical comorbidities, immunosuppressive therapy regimens, and frequently diminished levels of erythrocytes, leukocytes, and platelets, patients receiving hematopoietic stem cell transplantation can be at increased risk of perioperative medical and surgical complications, including deep periprosthetic joint infection [11, 12]. Historical studies have shown a high risk of complications and infections in such patients undergoing surgical reconstruction of proximal femoral pathologic fractures [2, 4, 9, 12]. Although some studies have analyzed the perioperative outcomes, patient mortality, and implant survivorship in recipients of solid organ transplants undergoing THAs and/or TKAs [3, 5–8], there is a paucity of studies regarding elective THA outcomes in recipients of hematopoietic stem cell transplants [1, 12].

The purpose of our study was to review our results in patients undergoing THA after hematopoietic stem cell transplantation. Specifically, we asked: (1) What is the overall mortality of patients with hematopoietic stem cell transplants who have undergone THA? (2) What are the complication rates for these patients? (3) What are the revision and reoperation rates and implant survivorship for these patients?

Patients and Methods

We performed a retrospective study of patients who received hematopoietic stem cell transplantation and who underwent primary THA at one academic institution from January 1999 to December 2013 (Table 1). We first identified patients who had hematopoietic stem cell transplantation at our institution via a search of diagnoses codes through our transplant department; we then cross-referenced that patient population with the institution's total joint registry to identify patients with a prior hematopoietic stem cell transplant who underwent elective primary THA during the study period. Patients were included if they were between 18 and 80 years old and underwent elective primary THA. Patients who underwent THA before hematopoietic stem cell transplantation were excluded. Patients were followed until death, revision surgery, or most recent followup. Other than those who died, all patients were available for followup at a minimum of 2 years; of the patients whose procedures were done more than 10 years ago and who are not known to have died, two of 36 patients (6%) had not been seen in the last 5 years and so are considered lost to followup. Mean followup was 5 years (range, 2–15 years). The study was initiated after approval from the institutional review board.

Indications for THA were degenerative joint disease (19/42; 45%) and AVN (23/42; 55%). Surgical procedures were performed after surgical clearance from the transplant specialists. Specifically, the transplant team performed a thorough medical evaluation, analyzing for any signs of graft versus host disease, end-organ damage, significant medication side effects, active medical comorbidities, critically low circulating hematopoietic cells, and general medical health. Each patient was analyzed on a case by case basis given their individual comorbidities, primary disease, and other factors. Each patient who received

Table 1. Clinical demographics

Variable	Number
Total number of THAs	42
Number of patients	36
Age at arthroplasty (years)(range)	52 years (25–74)
Male/female (number)	26 (72%)/10 (28%)
Mean followup (years)(range)	5 (2–15)
Underlying diagnosis	
Lymphoma	14 (33%)
Plasma cell disorders	10 (24%)
Acute leukemia	5 (12%)
Chronic leukemia	4 (10%)
Amyloidosis	3 (7%)

hematopoietic stem cell transplantation remained on their recommended immunosuppressive medication regimen throughout the perioperative period. Although the regimen varied for each patient, it primarily was a low-dose oral corticosteroid and various immunosuppressive medications such as mycophenolate or tacrolimus.

Patient demographics and clinical outcomes were collected through medical records including: multispecialty preoperative consultations (orthopaedic surgery, general medicine, hematopoietic stem cell transplantation physicians, and anesthesia), operative reports, hospital summaries, and routine outpatient clinical followup notes. The information was obtained via individual chart review by a researcher (BPC) not involved in the initial surgery. We analyzed patient mortality rates of the patients who underwent THA after hematopoietic stem cell transplantation. Perioperative complications, including all medical and orthopaedic perioperative complications, reoperations, revisions, and implant survivorship were reviewed separately by type of arthroplasty. For patients with more than one arthroplasty, the mortality rate was calculated from the index arthroplasty.

Thirty-six patients undergoing 42 THAs after hematopoietic stem cell transplantation were identified. Three (8%) patients died before 2 years of follow-up. Eleven (26%) THAs in 10 patients were performed greater than 10 years ago; two of these patients who are not known to have died have not been followed up during the last 5 years and are considered lost to followup. These five patients (5 THAs) were included in survivorship analyses and calculation of complications. Of the 37 THAs analyzed at final clinical follow-up, 13 (31%) THAs were analyzed at 2 years, 20 THAs (47%) were analyzed at 5 years, 3 THAs (7%) were analyzed at 10 years, and 1 THA (2%) was analyzed at 15 years. Of the 36 patients, 10 (28%) were female and 26 (72%) were male, with a mean BMI of 27 kg/m² (range, 21–42 kg/m²). Patients underwent hematopoietic stem cell transplantation for the following underlying primary diseases: Hodgkin's or non-Hodgkin's lymphoma (14/42; 33%), plasma cell disorders (10/42; 24%) (most commonly multiple myeloma), acute leukemia (5/42; 12%), chronic leukemia (4/42; 10%), and amyloidosis (3/42; 7%) (Table 1). All nine THAs in patients who underwent hematopoietic stem cell transplantation for acute or chronic leukemia received allogeneic hematopoietic stem cell transplantation, whereas 31 of 33 (94%) THAs in patients who received hematopoietic stem cell transplantation for all other diagnoses in this series underwent autologous hematopoietic stem cell transplantation. The mean age of the patients at the time of the arthroplasty was 52 years (range, 25–74 years), with a mean interval between hematopoietic stem cell transplantation and index arthroplasty of 5 years (range, 1 year–18 years).

All procedures were completed by six high-volume lower-extremity arthroplasty surgeons using contemporary techniques and implants. Twenty-seven (27/42; 64%) THAs were done from the posterior approach and (15/42; 36%) were done via an anterolateral approach. All THAs had a primary, uncemented acetabular component implanted. Four (10%) of 42 THAs had cemented femoral stems implanted and 38 (90%) of 42 THAs had uncemented primary femoral stems inserted. All patients were made weightbearing as tolerated and placed on a rapid rehabilitation protocol according to institutional protocol.

Statistical Analysis

Dichotomous variables were analyzed with two-tailed Fisher's exact square tests. Complication, revision, and reoperation rates were presented as percentages. Kaplan-Meier survivorship curves were constructed to analyze patient survivorship free from mortality and implant survivorship free of revision or component removal. Cox regression analysis was used to compare survivorship in subgroups of patients. A significance value was set at alpha less than 0.05. Statistics were performed using JMP[®] version 10.0 (SAS[®], Cary, NC, USA).

Results

Patient Mortality

The overall 1-, 2-, and 5-year mortality rates were 8%, 8%, and 15%, respectively, for patients with hematopoietic stem cell transplantation undergoing primary THAs. One patient (3%) died within 90 days of an elective THA for complications related to congestive heart failure. Estimated patient survivorship free from mortality was 91% (95% CI, 81%–100%) at 2 years and 82% (95% CI, 68%–96%) at 5 years (Fig. 1).

With the numbers available, there was no difference in mortality rates among patients with underlying primary diagnoses (ie, lymphoma, leukemia, or plasma cell disorders) at 1, 2 years, or 5 years. There also was no significant difference in mortality between the preoperative indications of AVN versus degenerative joint disease ($p > 0.05$).

Complications

Four patients with THAs (11%, four of 36 patients, 10% four of 42 THAs) experienced perioperative medical or orthopaedic complications (Table 2). One patient (3%) had an intraoperative greater trochanter fracture during femoral

Fig. 1 The Kaplan-Meier curve shows patient survivorship from mortality secondary to all causes, most commonly primary disease-related complications, after undergoing primary THA with a prior hematopoietic stem cell transplantation. Patient survivorship was 91% (95% CI, 81%–100%) and 82% (95% CI, 68%–96%) at 2 and 5 years, respectively.

Table 2. Overall results

Variable	Results
Patient survivorship (95% CI)	
2 years	91% (81%–100%)
5 years	82% (68%–96%)
Implant survivorship (5 years, 95% CI)	
THAs	92% (81%–100%)
Implant survivorship, accounting for competing risk of death (5 years, 95% CI)	93% (83%–100%)
Component revisions	2/42, 5%
Reoperations	0/42, 0%
Procedure-related complications	4/42, 10%
Deep periprosthetic joint infection	0/42, 0%

preparation that required cerclage cable fixation. The fracture had united without issue at 4 years of radiographic followup. One patient (3%) experienced a postoperative deep venous thromboembolism that was treated effectively with 3 months of anticoagulation without chronic sequelae. Another patient (3%) with an uncemented femoral stem had intraoperative hypotension thought to be attributable to intraoperative fat emboli and was transferred to the intensive care unit for one night for monitoring. A fourth patient (3%) who had undergone a posterior approach without significant leg lengthening (< 5 mm) experienced a transient femoral nerve palsy diagnosed postoperatively with new onset of thigh numbness and weakness that completely resolved at 3 months postoperatively.

There were no joint infections noted in this group.

Fig. 2 This Kaplan-Meier curve shows implant survivorship free of revision THAs in patients with prior hematopoietic stem cell transplantation. Survivorship free of implant revision or component removal for any indication was 98% (95% CI, 94%–100%) and 92% (95% CI, 81%–100%) at 2 and 5 years, respectively.

Fig. 3 This Kaplan-Meier curve shows competing risk survival (with death as the risk) free of revision for any indication in patients undergoing primary THA with prior hematopoietic stem cell transplantation. Competing risk was 98% (95% CI, 92%–100%) and 93% (95% CI, 83%–100%) at 2 and 5 years, respectively.

Implant Survivorship

Estimated Kaplan-Meier implant survivorship free of any revision or component removal for THAs was 98% (95% CI, 94%–100%) at 2 years and 92% (95% CI, 81%–100%) at 5 years (Fig. 2). Estimated implant survivorship free of any revision or component removal accounting for death as a competing risk was 98% (95% CI, 92%–100%) and 93% (95% CI, 83%–100%) at 2 and 5 years, respectively (Fig. 3). There were no reoperations with component retention in this cohort. Two (5%) THAs required component revision. One hip (2%) underwent revision with implantation of a constrained liner for recurrent instability at 10 months postoperatively. The other hip (2%) underwent an acetabular revision for iliopsoas impingement.

Discussion

There is an increasing population of patients 60 years or older who have undergone hematopoietic stem cell transplantation [10]. Among the risks of degenerative joint disease that increases with age, the increased risk of AVN from immunosuppressive medications and/or graft versus host disease, and the growing number of patients undergoing stem-cell transplantation, it seems likely that the number of such patients undergoing elective THA will increase. However, with a high incidence of medical comorbidities, immunosuppressive regimens, and often diminished numbers of circulating hematopoietic cell lines, these patients undergoing THA are at a potentially greater risk for perioperative complications [2, 11, 12]. We sought to determine the mortality, complications, and implant survivorship in this difficult-to-treat cohort undergoing THA at our institution.

We acknowledge several limitations in the current study. Foremost, although patients were subdivided based on their underlying primary disease process and surgical indication, the cohort represents a heterogeneous population with varying medical comorbidities, medication regimens, and the extent, stage, and chemotherapy sensitivity of their primary disease. Second, although our study is one of the only to have a cohort of patients with prior hematopoietic stem cell transplantation undergoing joint arthroplasty, it has a relatively small number of patients. Third, this group is highly selected in the sense that specialists in hematopoietic stem cell transplantation and other medical specialists preoperatively screened patients who were considering THA, and these specialists helped manage their preoperative, perioperative, and postoperative course. Finally, there was no control group of patients with hematopoietic stem cell transplants with similar medical management who did not undergo THA, patients with other tumor types who underwent THA, or patients without hematopoietic stem cell transplants but with similar comorbidities undergoing THA for comparison. As our focus was on patient and implant survivorship and perioperative complications, we did not collect patient-reported outcomes which might certainly be influenced by the patients' underlying disease processes.

In the literature, 2- and 5-year survivorship for patients with lymphoma as a primary disease were 86% and 80%, respectively [10]. Likewise, 2-year patient survivorship for patients with leukemia was 92% [10]. Five-year survival for patients after hematopoietic stem cell transplantation for chronic myelogenous leukemia is as much as 65% [10]. Although patient survivorship is widely variable depending on the specific type of primary disease and the sensitivity to chemotherapy regimens, the survival rates of patients in our series are similar to these reported by Pasquini and Zhu

[10]. Given the extensive medical evaluation process before elective arthroplasty, our patient cohort likely represents a more-vetted cohort compared with the general population with hematopoietic stem cell transplants for similar underlying primary diseases. Preoperative screening and medical optimization before elective arthroplasty and coordinated medical comanagement are critical in this patient cohort.

There was high rate of perioperative medical and orthopaedic complications [10] in this series. This is consistent with the numbers reported in similar studies of patients with prior solid organ transplants undergoing elective joint arthroplasty [3, 5–8]. In addition, this complication rate is consistent with those of two other studies reporting rates of 4.5% to 7.4% in patients with THAs for AVN after hematopoietic stem cell transplantation [1, 12]. The higher rate of perioperative complications in patients with hematopoietic stem cell transplants undergoing elective hip arthroplasty is concerning and should be discussed with patients before surgery.

Implant survivorship free of any revision or component removal was lower than expected at 93% for THAs at 5 years. However, there were no revisions for aseptic loosening in this series of modern implants and techniques. Zadegan et al. [12] similarly reported a lower rate of implant survivorship, but the majority of revisions were for implant loosening. Their survivorship free of any component loosening was 74% at 10 years in patients undergoing THA for AVN. However, their patient cohort was younger (mean, 33 years), consisted of older implant designs, and included alumina bearing surfaces no longer used. There were no deep periprosthetic joint infections in the current series. In contrast, Zadegan et al. [12] reported a 4.2% deep periprosthetic joint infection rate requiring component revision. Interestingly, all of the patients in their series had late infections occurring greater than 5 years from the index arthroplasty. Given these patients' prolonged immunosuppressed state, the potential for late periprosthetic joint infection may be greater than that of the general population; as such, these patients should be followed closely and monitored with time.

For patients with prior hematopoietic stem cell transplantation undergoing primary elective THA, patient survivorship was 82% (95% CI, 71%–85%) at 5 years, the complication rate was 10% for four of 42 (10%) THAs, and implant survivorship free of revision or component removal at any indication was 93% at 5 years. There was not a high risk of infection in this patient cohort. With appropriate medical evaluation and comanagement by transplant specialists, carefully selected patients with hematopoietic stem cell transplantation may undergo elective primary THA, although complications do occur in this relatively fragile patient population. Given the pre-arthroplasty evaluation process, the effect that elective

THA has on patient mortality is unclear; future studies controlling patient factors may further elucidate this.

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