Patients who have undergone hematopoietic stem cell transplantation to treat underlying bone marrow pathology represent a unique and potentially high-risk patient population for total knee arthroplasty (TKA). This study retrospectively reviewed 15 TKA procedures performed on 11 patients with a history of hematopoietic stem cell transplantation. The authors analyzed patient survivorship; clinical outcomes, including complications; and implant survivorship. Mean follow-up was 5 years (range, 2-10 years). Patient survivorship free from mortality was 91% (95% confidence interval, 76%-100%) and 55% (95% confidence interval, 25%-85%) at 2 and 5 years, respectively. Patients who underwent hematopoietic stem cell transplantation for multiple myeloma had a significantly higher 5-year mortality rate (100%) compared with patients who had an underlying diagnosis of non-Hodgkin’s lymphoma (0%) (P = .008). Mean Knee Society Score improved to 83 postoperatively (P < .001). Two patients (13%) had postoperative wound healing complications that did not lead to periprosthetic joint infection; however, an additional patient (7%) underwent revision surgery at 5 years for periprosthetic joint infection. Estimated implant survivorship without revision was 80% (95% confidence interval, 60%-100%) at 5 years. Elective primary TKA does not appear to affect survivorship in patients with a history of hematopoietic stem cell transplantation. These patients have modest clinical outcomes, higher complication rates as a result of delayed wound healing, and poorer implant survivorship compared with historical control subjects. [Orthopedics. 201x; xx(x):exx-exx.]

The incidence of primary total knee arthroplasty (TKA) continues to increase, in part because of the expansion of indications in higher-risk populations.1-3 However, with rising health care costs and transparent outcome reporting, there is a critical need to analyze risks, outcomes, and survivorship of primary TKA procedures in these cohorts.1-12 Patients who have undergone hematopoietic stem cell transplantation for the treatment of underlying bone marrow pathology represent a specific high-risk population. These patients often have a compromised immune system secondary to chemotherapeutic or immnosuppressive treatments, multiple medical comorbidities, and low levels of circulating hematopoietic cell lines, which theoretically may increase the risk of perioperative complications and poorer outcomes compared with the general arthroplasty population.4-12 Studies have established the effect of various solid organ transplants and the associated increased complication rate and lower implant survivorship after total joint arthroplasty.6-9 Although little information is available on outcomes among patients undergoing non-solid organ transplantation, a recent report showed a high rate of perioperative complications, modest

The authors are from the Department of Orthopedic Surgery, Mayo Clinic, Rochester, Minnesota.

Drs Chalmers, Ledford, Perry, and Mabry have no relevant financial relationships to disclose. Dr Hансsen receives royalties from Stryker. Dr Abdel is a paid consultant for Stryker.

Correspondence should be addressed to: Matthew P. Abdel, MD, Department of Orthopedic Surgery, Mayo Clinic, 200 First St SW, Rochester, MN 55905 (abdel.matthew@mayo.edu).

Received: March 13, 2017; Accepted: April 10, 2017.
doi: 10.3928/01477447-20170531-01
implant survivorship, and no increased incidence of periprosthetic joint infection compared with the general population in patients with a history of hematopoietic stem cell transplantation undergoing primary total hip arthroplasty (THA). To the authors’ knowledge, no recent reports have described the outcomes of primary TKA in patients with a history of hematopoietic stem cell transplantation.

This study reviewed the outcomes of patients with a history of hematopoietic stem cell transplantation undergoing primary TKA. The study analyzed patient survivorship; clinical outcomes, including complications; and implant survivorship.

### MATERIALS AND METHODS

Patients with a history of hematopoietic stem cell transplantation who underwent subsequent TKA at a single academic institution from January 1, 2001, to December 31, 2013, were identified by cross-referencing the institutional transplant database and total joint registry. Outcome data were collected through retrospective chart review. Patients were followed until death, implant revision, or reoperation, and minimum clinical follow-up was 2 years. Patients who underwent hematopoietic stem cell transplantation after TKA or who underwent TKA for periarticular fracture or stabilization of a periarticular lytic lesion were excluded. In patients who underwent more than 1 TKA, patient survivorship and mortality were determined from the initial TKA. Clinical outcomes were analyzed via Knee Society Score (KSS) and perioperative medical and orthopedic complications. Implant survivorship free of any revision was analyzed. Institutional review board approval was obtained before the start of the research.

#### Patients

A total of 15 TKA procedures in 11 patients with a history of hematopoietic stem cell transplantation met the inclusion criteria and were retrospectively reviewed. Mean follow-up was 5 years (range, 2-10 years) (Table). Of this group, 1 patient (1 TKA) died before the 2-year follow-up period and was included in patient survivorship, complication, and implant survivorship analyses, but was excluded from clinical outcomes analysis. Mean estimated time from transplantation to TKA was 5.5 years (range, 1-18 years). Mean age at index TKA was 64 years (range, 46-76 years), and mean body mass index was 29 kg/m² (range, 22-36 kg/m²). Underlying primary diagnoses for patients undergoing the 15 TKA procedures included non-Hodgkin’s lymphoma (7 of 15 TKA procedures, 46%), multiple myeloma (6 of 15 patients, 40%), chronic leukemia (1 of 15 TKA procedures, 7%), and amyloidosis (1 of 15 TKA procedures, 7%). Each patient underwent autologous hematopoietic stem cell transplantation except for 1 patient (1 TKA) who had chronic leukemia and underwent allogeneic hematopoietic stem cell transplantation. All patients who had underlying multiple myeloma or chronic leukemia were receiving baseline chemotherapeutic treatment with corticosteroids at the time of TKA. The treatment was continued perioperatively. The TKA procedures were performed by 5 different surgeons with experience and training in primary and revision arthroplasty. All patients underwent TKA for degenerative joint disease. Posterior-stabilized designs and cemented fixation were used for all patients. All patients had resurfacing of the patella. All patients were followed by the hematology-oncology department at the study institution. The decision to perform elective TKA was discussed among the patient, the orthopedic surgeon, and the treating hematologist, based on symptoms and a comprehensive preoperative medical evaluation of surgical risk.

#### Statistics

Dichotomous variables were analyzed with Fisher’s exact tests, and continuous variables were analyzed with appropriate Student’s t tests. Kaplan–Meier survivorship curves were constructed to analyze patient survivorship for mortality and implant survivorship free of revision for any reason. Survivorship data are presented
with a 95% confidence interval (CI). Statistics were analyzed with JMP Clinical software, version 10 (SAS, Cary, North Carolina).

RESULTS

Patient Mortality and Survivorship

Overall patient mortality rates at 1, 2, and 5 years were 9% (1 patient), 9% (1 patient), and 36% (4 patients), respectively. No patients died within 90 days of TKA. Patient survivorship free from mortality was 91% (95% CI, 76%-100%) at 2 years and 55% (95% CI, 25%-85%) at 5 years (Figure 1).

Four patients (6 TKA procedures) who underwent hematopoietic stem cell transplantation for multiple myeloma had a 5-year mortality rate of 100% compared with no deaths (0 of 5 patients, 0 of 7 TKA procedures) in those with an underlying diagnosis of non-Hodgkin’s lymphoma (P=.008). Type of transplant (allogeneic vs autologous), age, and sex were not significant risk factors for higher patient mortality (P>.05).

 Clinical Outcomes and Complications

Mean KSS improved significantly from 52 preoperatively to 83 postoperatively (P<.001). Two patients (13%) who underwent TKA had delayed wound healing that resulted in partial wound dehiscence. Both patients were successfully treated conservatively with prophylactic oral antibiotics and wound care without further surgery.

Implant Survivorship

One patient (1 TKA, 7%) underwent revision surgery for periprosthetic joint infection 5 years after index TKA in the setting of pneumococcal sepsis and presumed acute hematogenous spread. This patient underwent irrigation and debridement, polyethylene exchange, and chronic antibiotic suppression until death 1 year later as a result of multiple underlying medical comorbidities. No patient underwent revision or reoperation for any other indication. Estimated implant survivorship free of revision for any reason was 100% (95% CI, 100%-100%) at 2 years and 80% (95% CI, 60-100%) at 5 years (Figure 2). Indications for hematopoietic stem cell transplantation, type of transplant (allogeneic vs autologous), age, and sex were not significant risk factors for poorer implant survivorship (P>.05).

DISCUSSION

With the growing incidence, success, and indications for primary TKA, surgeons must be aware of outcomes in different patient populations, particularly higher-risk populations, such as patients with a history of hematopoietic stem cell transplantation. Theoretically, these patients may be at risk for increased perioperative complications and poorer implant survivorship, especially given their immunocompromised state, low levels of circulating hematopoietic stem cell lines, and associated complex medical comorbidities.4-12 To the authors’ knowledge, the current study is the first to report patient mortality and survivorship.
mortality, clinical outcomes, and implant survivorship for patients with previous hematopoietic stem cell transplantation undergoing primary TKA.

Patient survivorship after hematopoietic stem cell transplantation can be as high as 75% at 3 years and 50% at 5 years for patients with underlying multiple myeloma and 78% at 3 years and 70% at 5 years for patients with chemosensitive follicular lymphoma. The current study, although limited by a smaller number of patients, found survival rates of 91% at 2 years and 55% at 5 years after TKA. In this study, TKA was performed a mean of 5 years after hematopoietic stem cell transplantation. Although patient survivorship after TKA in patients with previous hematopoietic stem cell transplantation was similar at 2 years compared with those undergoing primary elective THA, 5-year survivorship was lower (55% vs 82%, respectively). However, many patients in that series underwent TKA for avascular necrosis at a younger age (mean, 52 years) and may have represented a younger, healthier patient cohort earlier in the disease process. Further, no patients in the current series died within 90 days of TKA, and all patients died of underlying disease-related complications. Therefore, it does not appear that TKA had a significant effect on patient survivorship.

Clinical outcomes improved significantly postoperatively. However, the KSS remained tempered, with a mean of 83 (range, 72-96) compared with traditional knee arthroplasty. The specific reason for lower than expected subjective outcomes in this patient population is unclear. The most common reason for lower scores was continued mild to moderate pain and a low activity level. Studies have shown that patients with multiple medical and psychosocial comorbidities, such as patients who have a history of hematopoietic stem cell transplantation, have a lower perspective of health and often have lower patient-reported outcome scores. These factors may account for only a modest improvement, as seen in the current patient series.

Although no other studies have analyzed perioperative complications of patients with a history of hematopoietic stem cell transplantation, similar high-risk patient cohorts have shown higher complication rates after total joint arthroplasty. In a different study, the authors reported a 10% complication rate in patients with previous hematopoietic stem cell transplantation undergoing elective primary TKA. Ledford et al also reported an even higher 29% complication rate in patients with previous solid organ transplant undergoing total joint arthroplasty. A recent national inpatient database study found significantly higher rates of perioperative complications, including surgical site infection, in patients with multiple myeloma undergoing total joint arthroplasty. In this patient series, the complication rate was 13% (2 of 15), and both complications were the result of delayed wound healing. Although neither patient had a periprosthetic joint infection, the high rate of complications is concerning. When elective primary TKA is considered, patients and surgeons should discuss the necessity of each medication with the treating hematologist and take every step to obtain and maintain a healthy surgical wound.

Implant survivorship free of revision for any reason was very low (80%) at 5 years, primarily because of periprosthetic joint infection, which appears to be consistent with another study of primary TKA in patients with similar disease states, particularly solid organ transplants. However, the literature is not as conclusive about the increased risk of periprosthetic joint infection in patients with previous hematopoietic stem cell transplantation or solid organ transplantation undergoing elective primary THA. The authors previously reported no deep periprosthetic joint infections among 42 THA procedures in patients with a history of hematopoietic stem cell transplantation. Other studies cited a 2% to 4% rate of deep periprosthetic joint infection in patients undergoing THA with previous solid organ transplantation. The difference in the rate of periprosthetic joint infection between patients undergoing TKA and THA is multifactorial and includes discrepancies in age and health at presentation for total joint arthroplasty. In addition, in these studies, a significantly higher number of patients underwent THA compared with TKA because of the risk of avascular necrosis. Nevertheless, the authors recommend discussing the risk of perioperative complications, including infection, with patients and following all precautions to prevent periprosthetic joint infection in these higher-risk patients.

Limitations

The current study had several limitations, including the inherent disadvantages of a retrospective study and a very small patient cohort. This cohort was prone to selection bias, as discussed previously, and was subject to confounding variables that may alter patient outcomes. Additionally, patients with hematopoietic stem cell transplantation have different indications for transplantation, immunosuppressive medication regimens, and ongoing medical comorbidities, factors that cannot be controlled. This study compared patients with different underlying disease processes, but analysis of risk factors for each underlying disease process was limited because of the cohort size. All patients in this series were followed closely by multidisciplinary hematology transplantation teams and medically optimized for surgery. The thorough medical prescreening procedure may have led to selection bias.

Conclusion

Total knee arthroplasty did not affect survivorship of patients with a history of hematopoietic stem cell transplantation compared with historical data on patient survivorship after hematopoietic stem cell transplantation. Postoperative
KSS showed significant improvement; however, the improvement was fair overall. A high proportion of wound healing complications occurred, perhaps increasing the risk of deep periprosthetic joint infection. Finally, an increased rate of deep periprosthetic joint infection (7%) led to relatively poor midterm implant survivorship. Patients with a history of hematopoietic stem cell transplantation undergoing elective primary TKA should be medically optimized by hematopoietic stem cell transplantation teams, and surgeons should discuss the specific risks of complications and potential survivorship.

REFERENCES


