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ORIGINAL RESEARCH

Total Hip Arthroplasty in Very Young Bone Marrow Transplant Patients

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ABSTRACT

Concerns remain about total hip arthroplasty (THA) performed in very young patients, especially those with complex medical history such as allogeneic bone marrow transplantation (ABMT). This study retrospectively reviews the perioperative courses and functional outcomes of ABMT patients <21 years old undergoing primary uncemented THA. Nine THAs were performed in five ABMT patients at an average age of 19.7 years. The interval between ABMT and THA was 73.0 months with clinical follow-up of 25.8 months. Harris Hip Scores (HHS) increased dramatically from preoperatively 44.5 (31.1-53.4) to postoperatively 85.2 (72.0-96.0) and all patients subjectively reported a good (4 hips) to excellent (5 hips) overall outcome. There was one reoperation for periprosthetic fracture fixation but there were no infections or revisions performed. Despite the history of severe hematopoietic conditions requiring ABMT, these very young patients do appear to have improved pain and function following primary THA with short-term follow-up. These results are comparable to prior studies of adult ABMT patients undergoing THA and are encouraging given the complexity of the decision to perform hip arthroplasty in the medically complicated very young patient.

Keywords: Bone marrow transplant, Total hip arthroplasty, Osteonecrosis, Outcomes.

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INTRODUCTION

Allogenic bone marrow transplantation (ABMT), also known as hematopoietic stem cell transplantation (HSCT), has become the life-saving treatment for patients with disorders or malignancies of the hematopoietic system.[1-3] In 2006, 50,147 HSCTs were performed worldwide including 15,082 in the United States.[4] One of the most common complications following this procedure is graft versus host disease (GVHD), which can occur both acutely and chronically.[5-7] Primary management GVHD is high dose corticosteroids given for at least a period of 3 months with some receiving treatment for several years predisposing to the development of femoral head osteonecrosis (ON) as quickly as 12 months or less.[8-10] Additionally, other congenital blood dyscrasias and mucopolysaccharidoses treated with HSCT are often associated with severe hip dysplasia resulting in pain and disability from degenerative arthritis.[11,12]

Total hip arthroplasty (THA) has been to shown to be an effective treatment option in adult ABMT recipients with femoral head ON.[13,14] However, many ABMT procedures are indicated and performed in very young patients who may subsequently present to orthopaedic surgeons with end-stage osteoarthritis secondary to ON or hip dysplasia. Historical concerns exist for performing THA in a young, active population despite recent studies suggesting contemporary THA components provide dramatically improved hip function and secure fixation.[15,16] There appears to be a paucity of data related to outcomes of young ABMT patients undergoing THA.

This study sought to review the preoperative indications, perioperative courses and postoperative complications and functional outcomes of very young ABMT patients (≤21 years old) undergoing primary THA for degenerative hip osteoarthritis at a single academic center. To the authors' knowledge, it represents the first report of this medically unique and very young arthroplasty population and serves as an addition to the results reported for THA in adult ABMT patients.[12,13]

MATERIALS AND METHODS

This study retrospectively reviewed a series of very young ABMT patients who underwent THA at a tertiary referral institution from 2009 to 2012. Nine THAs performed in five transplant recipients were identified through an internal surgical database search for both the ICD-9 code V42.81 (bone marrow replaced by transplant) or V42.82 (peripheral stem cells replaced by transplant) and the corresponding current procedural terminology code 27130 (THA). Exclusion criteria included: patients >21 years old, failure to complete full ABMT regimen, those undergoing previous arthroplasty procedure, or not obtaining standard clinical follow-up locally by the treating surgeon.

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The Institutional Review Board approved the study prior to investigation.

ABMT was performed in these patients for a variety of reasons including common leukemia but also for rare indications, such as hereditary blood dyscrasias or mucopolysaccharidosis. As a result of the HSCT procedure, all five patients were subjected to rigorous pretransplant myeloablative therapies followed by maintenance chronic immunosuppression, commonly high-dose oral steroids for at least 12 months. Each patient presented for elective primary THA after referral from their primary hematologist/oncologist after the hip pain appeared to markedly limit their function. Given the very young age range, each patient was given a complete trial of conservative treatment and all had failed to improve prior to arthroplasty. A multidisciplinary preoperative assessment was undertaken including: medical optimization and clearance from primary bone marrow transplant (BMT) team, standard pediatric and adult anesthesia assessment, and review of risks and benefits by the treating surgeon with informed consent obtained via a parental guardian. A postoperative plan of care was also established to allocate placement on the medical BMT service or to ensure close consultation with the BMT physicians while on the orthopaedic inpatient service.

Two separate fellowship-trained academic adult reconstruction surgeons (SSW, MPB) performed the procedures. THA was performed through a posterior approach in all patients with placement in abduction pillows following the procedure. Postoperative weight bearing status was either full immediately or partial (50%) weight bearing for 4 weeks followed by advancement to full as tolerated pending surgeon's preference. Clinical follow-up was obtained through a retrospective chart review of patient demographics, pre- and postoperative multidisciplinary physician clinical notes (BMT, anesthesia and orthopaedic adult reconstruction), operative reports, discharge summaries, clinical exams and serial radiographs. Specific validated outcome measures were gathered according to standard clinical intake forms including Harris hip scores (HHS) and visual analog scale (VAS). Routine descriptive statistical analysis was undertaken to include the means for appropriate data.

RESULTS

Nine primary uncemented THAs were performed in five patients including 4 males and 1 female who had previously undergone bone marrow transplantation (Table 1). Indications for BMT included: acute or chronic myelogenous leukemia (2 patients), rare genetic disorders causing profound anemia, such as erythropoietic protoporphyria and dyskeratosis congenita (1 patient each), and a mucopolysaccharidosis (Hurler's syndrome in 1 patient). The average age at allogeneic hematopoietic stem cell transplant was 13.8 (2-20) years old with an interval time to THA of 73.0 (8-169) months. Uncemented THA was performed at an average age of 19.7 (14-21) years old for Ficat Stage IV avascular necrosis in seven hips and dysplasia in two hips. The comorbidity profile of the patients was minimal with two exceptions. First, 3/5 patients (5/9 hips) had concurrent hemochromatosis.

Table 1: BMT patient demographics and outcomes

Patient	*Side*	*Indication for BMT*	*Age at THA*	*Interval* from BMT (MOS)*	*Follow-up time (MOS)*	*Reoperation*	*Final HHS*	*Final VAS pain score*	*Final patient-reported outcome*
1	R	Aplastic anemia[#]	21	8	8	No	72.02	0	Good
1	L	Aplastic anemia	21	8	8	No	72.02	0	Good
2	R	AML	21	25	12	No	94.02	0	Excellent
2	L	AML	21	25	12	No	94.02	0	Excellent
3	L	Hurler's syndrome	14	169	42	Yes[+]	78.75	0	Good
3	R	Hurler's syndrome	16	153	58	No	71.87	1	Good
4	L	CML	21	113	40	No	96.02	0	Excellent
5	R	EPP	21	78	27	No	94.02	0	Excellent
5	L	EPP	21	78	27	No	94.02	0	Excellent
AVG			19.7	73	26.0	11.1%	85.19	0.11	

*Interval time between first bone marrow transplant procedure and THA; [+]Patient sustained periprosthetic femur fracture after fall requiring open reduction internal fixation with placement of allograft strut; [#]Aplastic anemia resulting from rare diagnosis of dyskeratosis congenita; MOS: Months; HHS: Harris hip score; VAS: Visual analog scale; AML: Acute myelogenous leukemia; CML: Chronic myelogenous leukemia; EPP: Erythropoietic protoporphyria

Secondly, due to his metabolic genetic condition, patient #5 had also undergone prior hepatic and renal transplantation prior to arthroplasty. The average body mass index was 25.8 (17.3-33.0) kg/m^2 at the time of operation.

Each patient underwent extensive preoperative multi-disciplinary evaluation with surgical clearance provided by the primary BMT team and anesthesia. Specifically, all patients received an American Society of Anesthesiologist (ASA) score of 3, which represents a patient with severe systemic disease. Type of anesthesia chosen varied and included either general endotracheal anesthesia (6 hips) or combined general endotracheal with epidural (3 hips).

Intraoperatively, standard posterior approach was utilized in each case with placement of contemporary uncemented components. Acetabular components were either DePuy Pinnacle© (Warsaw, IN) for the AVN cases or Zimmer Trabecular Metal Natural Cup System© (Warsaw, IN) for the dysplastic hips ranging in sizes from 40-66. Similarly, femoral components were DePuy Summit© or S-ROM Modular© hip systems with head sizes ranging from 22 to 32. There were five hips with metal-on-ceramic articulation and four hips with metal-on-polyethylene. Average estimated blood loss was 321.7 (160-525) ml and there were four hips that received an average of <1 irradiated packed red blood cell transfusion during the procedure. Total anesthesia time, defined from start of preoperative medication administration to patient hand-off in the postanesthesia care unit, averaged 222.5 (156-381) minutes. In patient #3's left dysplastic hip, an intraoperative complication of anterior femoral cortex perforation during stem placement was noted and managed by placing a strut allograft and 2 cerclage wires. Unfortunately, the same patient suffered a periprosthetic fracture at the tip of his left femoral stem approximately 8 months after index procedure requiring reoperation with open reduction internal fixation placement of an allograft strut (Figs 1A to C).

Figs 1A to C: Patient #3 with Hurler's syndrome and radiographic severe hip dysplasia presented for THA after multiple pelvic osteotomies were performed (A) The femoral component perforated the anterior cortex on the left side intraoperatively which was managed with 2 cerclage wires and strut allograft as seen in the AP portable radiograph (B) Patient subsequently fractured after mechanical fall 8 months postoperatively and was revised with open reduction internal fixation and placement of another strut allograft seen in AP (C) radiograph

As described previously, a postoperative care plan was established prior to surgery which placed 7 hips primarily on the orthopaedic inpatient service with BMT physicians in consultation while 2 hips (1 patient) was managed on the BMT service with orthopaedics following with recommendations. The hospital course was complicated by symptomatic postoperative anemia requiring transfusion of 1 unit of irradiated packed red blood cells in 2/9 hips. Further documented complications were thrombocytopenia in the same 2/9 hips. Interestingly, length of stay for all patients was 3 days for all patients on the orthopaedic service while an outlier patient on the BMT service was hospitalized for 29 days secondary to difficult acceptance into an extended care facility given his young age. Final disposition was to an extended care facility in 6 hips with only three hips returning home directly after hospital discharge.

Short-term postoperative clinical follow-up was available at an average of 25.8 (8-58) months in all patients. Patients and/or their guardians subjectively reported their perceived outcome from THA as good (4 hips) and excellent (5 hips). Preoperative HHS of 44.5 (31.1-53.4) significantly increased in every patient to an average of 85.19 (72.03-96.02) representing a 'good' result according to the scoring system.[17] Additionally, pain scores according to the VAS substantially decreased from preoperatively 5.2 (0-10) to 0.1 (0-1) in all patients. There were no periprosthetic infections or revision THA performed, however, there was one reoperation for periprosthetic fracture as described previously. Fortunately, there were no reported deaths at the time of follow-up.

DISCUSSION

The increasing incidence of ABMT globally demonstrates its powerful ability to be a curative treatment in otherwise fatal hematopoietic disorders.[4] Yet, this procedure as associated cost of potential ON related to GVHD and its treatment with long-term steroid use.[18,19] Furthermore, patients with genetic blood disorders and mucopolysaccharidoses also have been associated with hip dysplasia inferring additional risk to that of ABMT for development of degenerative hip disease.[11,12] Either end-stage ON and/or severe hip dysplasia were present in all of the hips reviewed. Although, the options for treatment of resultant OA in these very young ABMT patients are limited, this study presents a case series of successful THA in such population.

Previous studies by Zadegan et al[13] and Petsatodis et al[14] reported their experience with cementless THA after ABMT in a slightly older population (33.0 and 33.6 respectively compared to 19.6 years old in the present study). Patient reported outcomes in those studies were 88 and 96.1% with mid to long-term follow-up in comparison to our 100% good to excellent outcomes with relatively short-term follow-up of 26 months. Average HHS significantly increased to an average of 85.2 from preoperative scores. The final average was lowered by one patient (patient #1) who had a low functional level at baseline secondary to motor and behavioral developmental issues. Other studies that have examined THA in the very young reported equally significant improvements to final HHS of 77-83.[15,16] Similarly, VAS were $\leq$1 in all patients, which we believe to be an important and accurate assessment of the patients' outcomes given the patient's young age and simplicity of the scale.

Despite the encouraging clinical functional outcomes, concerns exist of serious early and late complications in these obvious high-risk patients. Overall, operative time, estimated blood loss, and length of stay (with one previously described exception) were optimized with no acute or chronic septic events including periprosthetic infection. There was only one minor hospital-related complication of thrombocytopenia in one patient (bilateral hips) requiring no specific medical intervention or change of deep vein thrombosis prophylaxis. The multidisciplinary perioperative care plan established for each individual patient between the BMT hematologist-oncologists, anesthesia, and arthroplasty surgeons was critical in leading to a safe and effective overall experience for all of our patients. These results correlate with the first report that early primary THA is a safe, reliable treatment while minimizing potential increased infection risk after undergoing previous conservative procedures.[20]

In general, cemented techniques have been thought to lead to early component loosening in young patients[21-23] but contemporary cementless THA components have been shown to produce nearly equivalent and satisfying results.[24-26] Moreover, Phillips et al described concern of bone-ingrowth during steroid treatment increasing risk of loosening yet demonstrated good fixation with cementless implants.[27] It is normally our practice to perform THA without cement and with use of proximally porous coated femoral stems thus reducing operative time and preserving more bone stock. However, an intraoperative anterior femur perforation treated with cerclage wire likely predisposed to the one major postoperative complication of periprosthetic fracture sustained after mechanical fall 8 months postoperatively in the patient with Hurler's syndrome treated for severe hip dysplasia. Interestingly, although this patient certainly had a history of use of corticosteroids, he had not been on such treatment for a long period before and after arthroplasty. Perhaps the fracture may be more attributable to skeletal manifestations and deformity of the underlying lysosomal storage disorder[11] rather than corticosteroid administration. The patient did undergo open reduction internal fixation with placement of allograft strut graft and despite this devastating complication and modest final HHS of 78.8, the patient still reported a good overall outcome and was pain-free with transfers and ambulation. In contrast, Zadegan et al[13] reported a revision rate of 4.2% for septic loosening, and 5.7% for aseptic loosening with overall survivorship of 74.8% at 10 years. The period of follow-up for that study was significantly longer so it could be predicted that the revision rate would likely rise in the present cohort as time out from index procedure increased.

There were several obvious limitations with this case series. The study population examined was a very specific young ($\leq$21 years old) group of patients who had undergone ABMT, a treatment for infrequent and rare hematopoeitic disorders. Such a demographic is most commonly encountered at a large tertiary referral center and less likely to present to a general orthopaedist. Additionally, the preoperative assessment and postoperative care of our patients required a multidisciplinary approach which included highly specialized BMT physicians who may not be practicing within a community setting. Also, 25.8 (8-58) months follow-up certainly yields only short-term results and longer follow-up is needed to examine implant survivorship and possible trends for revision.

CONCLUSION

Despite the history of severe hematopoietic conditions requiring ABMT, these very young patients do appear to have substantially improved pain and function following primary THA with short-term follow-up. These results are comparable

to prior studies of adult ABMT patients undergoing THA and are encouraging given the complexity of decision to perform hip arthroplasty in the medically complicated young patient. We do recommend multidisciplinary care teams to include BMT medical specialist to optimize the patient preoperatively and continue to follow postoperatively to minimize acute complications and length of stay while maximizing overall outcomes.

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