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Bone Marrow Harvesting of Allogeneic Donors in an Outpatient Setting: A Single-Center Experience

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A B S T R A C T

The aim of this retrospective study was to assess the safety and efficacy of bone marrow (BM) harvesting of allogeneic donors in an outpatient setting. Data of 226 related and unrelated donors who underwent BM harvest under general anesthesia at our institution from 2002 to 2014 were analyzed. Sixteen patients were a priori planned for admission for social reasons and 210 patients underwent BM harvesting with the intention to perform this procedure on an outpatient basis. To identify factors that predispose for hospital admission, we retrospectively analyzed donor characteristics and collection parameters. Outpatient treatment was performed in 178 of 210 donors (85%), whereas 32 donors (15%) required admission for clinical reasons (mainly clinically relevant anemia and circulatory problems). These individuals were not significantly different in sex distribution, age, donor's body weight, and the proportion of related donors from those who were not admitted. However, we found a significantly higher collection volume per kilogram donor's body weight in inpatients compared with volume for outpatients (16 versus 13 mL/kg body weight, $P < .001$). Severe adverse events or deaths occurred neither in the inpatient nor in the outpatient setting. Our study demonstrated that BM harvest in an outpatient setting is safe and feasible for the majority of allogeneic donors. A high volume of BM represented a major risk factor for inpatient admission.

INTRODUCTION

Despite the increasing use of peripheral blood stem cells (PBSCs) over the last decades, bone marrow (BM) aspirated from the iliac crest has remained an important source of hematopoietic stem cells (HSCs) for allogeneic transplantation [1-5].

Donors undergoing BM harvest under general anesthesia have traditionally been admitted to the hospital for 2 days. With increasing experience of the collection centers in allogeneic BM harvesting and the wish for a shorter stay in the hospital from the donors, there is a clear trend towards outpatient collection. The experience from autologous BM harvesting in the outpatient setting in the early 1990s has indicated a high degree of safety, feasibility, and patient satisfaction of outpatient BM harvest in many centers and paved the avenue for performing outpatient BM harvests in allogeneic donors [6-9].

Since 2002, we have regularly performed BM harvesting from allogeneic donors on an outpatient basis. This report summarizes the long-term experience in a single center. The aim of this retrospective study is to analyze the safety and efficacy of outpatient BM harvesting from allogeneic donors and to identify factors that might predispose for hospital admission.

PATIENTS AND METHODS

BM Donors

Data of 226 related (n = 41) and unrelated (n = 185) consecutive donors who underwent allogeneic BM harvest at our institution from 2002 to 2014 were analyzed retrospectively. Sixteen patients were a priori planned for admission for social reasons (such as the lack of an accompanying person, distance from the place of residence, the explicit wish of the donor for inpatient treatment, or communication problems with donors from abroad requiring a translator) (Table 1) and they were excluded from the statistical analyses. The remaining 210 patients underwent BM harvesting with the intent to perform this procedure on an outpatient basis and their data were

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Table 1
Reasons for Hospital Admission after BM Harvest

Reason for Admission	n
Social (planned admission)	16
No accompanying person	6
Distance to the place of residence	4
Donor's wish	3
Communication problems	3
Medical reasons (no planned admission)	32
Clinically relevant anemia	10
Circulatory problems	16
Postoperative pain	2
Other reasons	4

further analyzed. Medical reasons for admitting a donor as an inpatient included any symptoms indicating poor circulation, anemia-related symptoms, or any signs of prolonged side effects of the anesthesia, eg, nausea, vomiting, and dizziness.

Our institution acted as a collection center for unrelated donors who had been registered in the local donor registries in Heidelberg, Mannheim, Düsseldorf, Hamburg, Dresden, Magdeburg, and Ratingen. In 7 cases, BM harvesting was performed after a prior granulocyte colony–stimulating factor–mobilized PBSC collection attempt had failed to achieve the collection goal. Any signs of pre-existing anemia led to exclusion as BM donor. Autologous red blood cell storage and retransfusion were not performed at our center for allogeneic BM donors.

BM Collection

Since the first reports of allogeneic human BM harvesting in the early 1970s [10], the procedure has been refined and improved in various aspects. In this study, BM collection from the posterior iliac crest was performed as previously described [11] in accordance with standard operating procedures of our institution and Federal General Medical Council guidelines for the preparation of blood and blood components and for the use of blood. As described, before April 2005, a volume of about 10 mL was aspirated and the needle was rotated 90°, followed by another 10 mL aspiration until a full cycle. The time to complete a 360° rotation was only a few seconds to avoid clotting in the syringe. The stylet was reinserted in the needle and introduced a few millimeters deeper into the bone cavity. This collection process was repeated until reaching the opposite cortex. After approximately 100 mL of BM was aspirated, a new insertion side was necessary. Starting in April 2005, a new BM aspiration set was introduced with 5 additional sideholes. With this new aspiration set, the collection volume per needle insertion was approximately 200 mL BM. The needle was rotated 45° after each 10 mL BM aspiration until a full cycle was achieved. Equivalent total nucleated cells (TNC) numbers per aspirated milliliter of BM have been demonstrated with both systems [11].

The yield volume of BM was calculated on the basis of the TNC number requested by the recipient marrow transplantation hospital with a minimum of 2.0×10^8 TNC/kg recipients body weight. According to the National Marrow Donor Program guidelines, a TNC number of $.183 \times 10^8$/mL BM has been assumed up until May 2012. Since June 2012, a TNC count of $.22 \times 10^8$/mL BM was used for the calculation. The maximum amount of BM collected was limited to 20 mL/kg donor's body weight or an absolute volume of 1500 mL. The amount of BM collected was calculated as the difference between the final volume and added media (ACD-A solution 1:10 BM, medium with heparin 20 IE per mL BM). Time for collection was determined as the interval between the first puncture of the BM and the completion of BM harvest marked by pulling out the needle at the end of the procedure. BM was prepared by the marrow collection center IKTZ Heidelberg gGmbH that holds a manufacturing license for stem cell products and keeps complete documentation for all steps of BM transplant manufacturing. The TNC number was determined in a hemocytometer Coulter AcT diff (Beckman Coulter, Fullerton, CA).

Monitoring of Adverse Events and Follow-up Examination

Donors in the outpatient setting were monitored in the hospital for at least 5 hours after the procedure. All donors underwent a medical examination before leaving the hospital. In addition, from 2012 on, all donors were included in an ongoing follow-up program, which includes a medical questionnaire after 6, 12, 24, 60, and 120 months. After 30 days, lab tests including blood count, total protein, ferritin, and renal function at the general practitioner was advised. All donors were instructed to report any symptoms or complaints that might be related to the donation procedure to our institution.

Data Collection and Statistical Analysis

Data collection was performed as a retrospective analysis. Descriptive statistics and comparison between the groups were performed by R studio (Version .99.451, 2009-2015 R Studio, Inc.). Box plots show the maximum, the third quartile, the median, the first quartile, and the minimum. Data are described as median and range. Student's *t*-test was used to determine the significance in TNC numbers, age, donors' body weight, collection time, collection volume, and collection volume per kg donors' body weight between the 2 groups. The gender, related, and foreign donor distribution were compared by chi-square test. Statistical significance was defined as $P < .05$. A receiver operating characteristic (ROC) was performed for comparison of variables that were considered relevant for hospital admission [12]. An optimal cut point analysis was used for cutoff determination for sensitivity, specificity, positive and negative predicted value (PPV, NPV) [13].

RESULTS

BM Harvesting Case Numbers and Reasons for Hospital Admission

A total of 226 BM harvests were performed between 2002 and 2014 at our institution. While in 2002 to 2004 fewer than 10 BM collections were performed per year, the annual quantity rose to 31 in 2012 and 2013 (Figure 1). Sixteen patients planned to be admitted because of problematic social circumstances, which were identified before BM harvesting; thus, treatment as an inpatient was planned for each of the 16. The remaining 210 donors underwent BM harvest with the intent to treat as outpatients, which was reached in 178 (85%) of them. Of these, 32 donors (15%) were admitted to the hospital for medical reasons until the next day. Only 1 related female donor spent 2 nights in the hospital. Most often, circulation problems in terms of hypotension and dizziness led to admission. Other medical reasons were prolonged nausea (n = 1), anxiety attacks in past medical history (n = 1), and BM harvesting after an insufficient attempt of PBSC collection (n = 2). Table 1 provides an overview over the reasons for hospital admission.

Donor Characteristics

To identify factors predicting the need for inpatient admission after BM harvesting, we performed a retrospective analysis of the donor characteristics. No significant

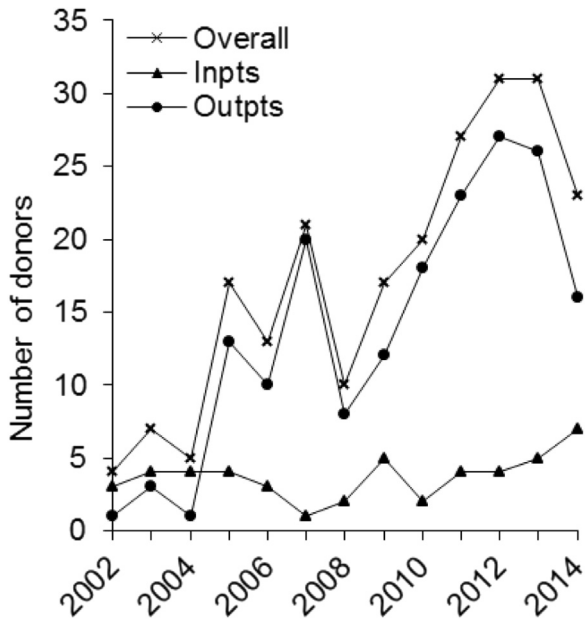

Figure 1. Number of allogeneic BM harvests performed in an inpatient and outpatient setting between 2002 and 2014 at our institution.