Biol Blood Marrow Transplant 20 (2014) 118–127

Health-related Quality of Life of Bone Marrow versus Peripheral Blood Stem Cell Donors: A Prespecified Subgroup Analysis from a Phase III RCT—BMTCTN Protocol 0201

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Article history:
Received 2 July 2013
Accepted 26 October 2013

Key Words:
Marrow versus peripheral blood stem cell donation
Unrelated hematopoietic stem cell donation
Randomized trial

A B S T R A C T

Hematopoietic stem cells can be procured from unrelated donors via either the bone marrow (BM) aspiration or peripheral blood stem cell (PBSC) collection methods. There is no evidence from prospective randomized trials in the unrelated donor setting about the relative health-related quality-of-life (HRQoL) benefits/costs to donors. The goals of this prospective longitudinal investigation were to describe and compare the donation-related HRQoL experiences of 332 BM and PBSC donors. Donors were interviewed before donation, 48 hours after donation, weekly until fully recovered, and at 6 and 12 months after donation. Before donation, BM donors had lower confusion, fewer concerns, and were more prepared for donation. Shortly after donation, BM donors reported more physical side effects. BM donors also reported more donation-related impact on their social activities. However, BM donors reported somewhat better psychological status and were more likely to indicate that the donation made their lives more meaningful. There were virtually no longer term differences in the experiences of the 2 donor groups, including no recovery time difference beginning 3 weeks after donation. Although BM donors may experience the process as more physically stressful and more psychologically beneficial in the short term, the longer term HRQoL consequences of BM and PBSC donors are similar.

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INTRODUCTION

Hematopoietic stem cell (HSC) transplantation is increasingly used to treat leukemia or other blood-related diseases for which other forms of therapy are ineffective or would be less effective. Because a minority of patients requiring transplants can find a matched related HSC donor, approximately 14,000 patients each year search international registries for unrelated donors [1].

When unrelated potential donors preliminarily match a patient, they are contacted to undergo additional testing to confirm eligibility. If selected, they then donate via either the traditional bone marrow (BM) aspiration procedure or the more recent peripheral blood stem cell (PBSC) procedure. Donors who donate BM undergo general/regional anesthesia, and HSCs are collected percutaneously from the posterior iliac crests of the pelvis. Donors who donate PBSCs receive a 5-day course of recombinant human granulocyte colony-stimulating factor (rhGCSF), after which HSCs are collected from the peripheral blood on 1 or 2 consecutive days in 4- to 5-hour apheresis sessions.

Rates of adverse events in donation vary across investigations, primarily depending on whether or not both related and unrelated donors are included [2,3]. Strict guidelines mean that unrelated donors are, on average, younger and healthier than their related donor counterparts and, therefore, experience fewer adverse events. Published data indicate that for unrelated donors, both BM and PBSC donation are generally safe with a low incidence of serious adverse events—1.34% in BM donors and .6% in PBSC donors [4-8]. Therefore, the decision about which type of product is requested is left to the transplantation physician managing the patient. In recent years, the use of PBSC donation has increased because of more rapid hematopoietic engraftment, more reliable engraftment when reduced-intensity conditioning is used, and the potential for greater graft versus

Contributions to the Donor Quality of Life ancillary study were made by The Health Resources and Services Administration contract no. HHSH234200637020C. The authors of this publication alone are responsible for reporting and interpreting the data and all or part of the data used to compile this publication were collected pursuant to a contract with the Department of Health and Human Services, Health Resources and Services Administration, Healthcare Systems Bureau, Division of Transportation.
Financial disclosure: See Acknowledgments on page 127.

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1083-8791/$ – see front matter Published by Elsevier Inc. on behalf of American Society for Blood and Marrow Transplantation.
http://dx.doi.org/10.1016/j.bbmt.2013.10.024

tumor effect because of the larger number of immune cells in PBSC versus BM. PBSC now accounts for 75% of all adult-derived unrelated donations (National Marrow Donor Program statistics) [9]. Until recently, there was no evidence from prospective randomized trials in the unrelated donor setting that 1 product or the other conferred a survival advantage to recipients, nor was there conclusive evidence about the relative health-related quality-of-life (HRQoL) benefits/costs to donors.

There have been several investigations of donor experiences of BM versus PBSC donation. These investigations focused on the physical experience and physical side-effects of the donation process and found that (1) both BM and PBSC donors experience side effects of the donation process, most commonly pain and fatigue [10]; (2) BM donors have a longer recovery time than do PBSC donors [10,11]; and (3) serious adverse events are very rare, but more common in BM donors [10]. Other findings were mixed, including the questions of whether BM or PBSC donors experience similar pain severity and duration [10,11], overall symptom burden [10,12], and emotional stress related to donation [10,13]. Many of these investigations were limited by small numbers of donors, inclusion of donors only from a single transplant center, nonrandomized designs, and/or exclusive focus on physical rather than psychosocial factors.

To address questions about the relative advantages/disadvantages to both patients and donors of the 2 HSC collection and transplantation procedures, the Blood and Marrow Transplant Clinical Trials Network recently completed a phase III trial randomizing patients to receive either marrow or PBSC grafts. Findings for transplant recipients indicated that there were no statistically significant differences in patient survival at 2 years between the 2 procedures [14]. Here, we present findings from a planned subanalysis of the trial, examining the physical and psychosocial experiences of the 2 types of donors. The goals were to describe the donation-related experiences of BM and PBSC donors and to determine whether there were group differences before donation and at and multiple points after donation.

MATERIALS AND METHODS

Human Subjects Research Protection

This investigation was approved by the institutional review boards at the University of Pittsburgh, the National Marrow Donor Program (NMDP), and individual donor centers. All participants signed informed consent before completing the study interview.

Participants and Study Design

Our investigation was a prespecified subgroup analysis of Blood and Marrow Transplant Clinical Trials Network protocol 0201 (ClinicalTrials.gov Identifier: NCT00075816). The prospective, longitudinal investigation included NMDP donors enrolled in the parent randomized clinical trial (RCT) and randomized to donate PBSC or BM from March 2004 through October 2009.

To be eligible, potential participants were required to (1) meet the standard NMDP requirements for donation; (2) be selected for participation in the RCT; (3) consent to participate in both the RCT and the donor substudy; and (4) be enrolled in the parent RCT. Potential participants were excluded from the study if they did not read, write, and speak English; were unable to complete a telephone interview because of cognitive or linguistic difficulties; or if they did not have access to a telephone. Department of Defense donors (after February 6, 2007) and German Registry donors were also excluded from the donor substudy on the basis of logistical issues and language respectively.

NMDP donor center coordinators obtained consent from the participants for the study and passed contact information of enrolled donors to University of Pittsburgh staff. Interviewers from the University of Pittsburgh contacted participants by phone to complete data collection. Within 4 weeks before marrow donation or initiation of rhGCSF administration for PBSC donors, participants completed a baseline interview. PBSC donors only were interviewed on day 4 of rhGCSF administration to assess current pain levels. All donors were interviewed again 48 hours after donation and weekly until symptom free for 3 consecutive weeks. Participants were also interviewed 6 and 12 months after donation. The baseline and 48 hours postdonation interviews required 20 minutes to complete—other interviews required 15 minutes. A computer-assisted telephone interview system was used to collect and enter interview data. Data were stored on a secure server in a proprietary data file.

Study Measures

Four categories of participant characteristics were assessed: (1) socio-demographic, (2) physical status, (3) psychological status, and (4) donation-related characteristics. Measures were previously validated scales/items with established measurement properties either created for, or used in, other donation-related settings. Donor height and weight and experience of an adverse event (AE) or a serious adverse event (SAE) were collected directly from the NMDP.

Socio-demographic characteristics

Age, sex, marital status, education level, employment status, and race were assessed.

Physical status

Overall physical status was assessed with the physical status summary scale of the SF-8 [14]. Scores range from 0 to 100, with higher scores indicating better physical health. *Current symptoms* assessed as present/absent in the past 48 hours included tiredness, muscle aches, problems sleeping, bone pain, light headedness, pain where the needles were inserted, difficulty walking, bleeding, nausea, infection, chills, and fainting [12]. *Current pain* was assessed with 4 items indicating highest pain intensity, average pain, amount of pain, and effect of pain on sleep during the past 48 hours. Pain was rated on a scale from 0 to 10 with a higher score indicating more pain. A composite pain index was also created by averaging the 4-item scores [10].

Psychological status

Overall psychological status was assessed with the psychological status summary scale of the Short Form (SF)-8 [15]. Scores range from 0 to 100 with higher scores indicating better psychological health. *Mood disturbance* was assessed with the Profile of Mood States-Short Form (POMS-SF) [16]. The POMS-SF is a 30-item measure that produces scores on 6 subscales: depression, tension-anxiety, anger, confusion, fatigue, and vitality (range, 0 to 4) and an overall distress score (calculated as the sum of the means of each of the POMS-SF subscales; range 0 to 24) [17]. For all POMS scales other than vitality, a higher score indicates greater distress—higher vitality scores indicate more vitality.

Donation-related characteristics

At the predonation interview, *interactions with others* were assessed with 4 items, asking whether donors consulted family/friends or professionals about donation and whether they had been encouraged/discouraged from donating (yes or no) [18,19]. Concerns about donation were assessed with 13 concerns in 3 categories—medical, work/family, and other (yes or no) [18-20]. Preparedness for donation was assessed with 3 items, asking whether donors felt informed about donation (1 = not at all, 4 = very well), prepared for donation (no, mostly, totally) and whether they felt they needed more information before donating (1 = need much more information, 4 = do not need any more information) [12]. All items were dichotomized to "totally prepared/informed" versus other categories. *Health concerns* were assessed with 2 items asking about worry about longer term health impact of donation (1 = definitely will have impact, 4 = definitely will not have impact) and worry about never feeling 100% well again after donation (1 = very often, 4 = never) [12]. The 2 items were dichotomized to lowest concern about health impact (eg, definitely will not have impact) versus other categories. *Satisfaction with the donation decision* was assessed with 2 items asking about overall satisfaction with the decision (1 = not at all, 4 = extremely) and whether they would volunteer and/or donate again if asked (1 = no, 4 = definitely), and an additional 4 items at postdonation time points asking whether donors would encourage others to donate (1 = discourage strongly, 5 = encourage strongly), felt like a better person after donating (1 = not at all, 3 = a lot), felt proud about donating (1 = not at all, 3 = very), and whether donating made their life seem more meaningful (1 = not at all, 4 = very much). All items were dichotomized to highest satisfaction (eg, extremely satisfied) versus other categories [21]. At 48 hours after donation only, *the social impact of donation* was assessed with 6 items asking whether work, school, and/or leisure activities were affected by donation, and whether the donor needed to make travel, childcare, financial, or home care arrangements (yes or no) [10]. *Donation experience*

was assessed with 2 items asking about the physical/emotional stress of donation (1 = not at all stressful, 4 = very stressful) [12]. Items were dichotomized to no stress versus any stress. Recipient-related variables included whether the donor knew the recipient's health status (yes or no), frequency of thoughts about the recipient (≥once per/day versus all other frequencies), whether they felt they had a special bond with (not at all versus a little, somewhat, and very much) and were worried about the recipient (very and pretty versus not very and not at all) [12]. *Postdonation recovery* was evaluated in 2 ways. Donors were assessed weekly after donation for the presence or absence of 12 key symptoms [12] and were considered fully recovered after 3 consecutive symptom-free weeks. Symptoms were assessed without asking donors to make an attribution of the symptoms specifically to donation. This is a conservative definition of recovery and necessarily means that no donor can be recognized as fully recovered until at least 3 weeks post donation. Recovery was calculated both as the proportion of donors recovered versus not at 6 and 12 months and as a continuous variable (week of full recovery) across the 52 weeks following donation.

Clinical

Donor height (cm) and weight (kg) and the presence or absence of an AE or SAE were assessed.

Statistical Analysis

Data were cleaned and exported from the computer-assisted telephone interview system to PASW Statistic 18, Release Version 18.0.3 (IBM Corporation, Somer, NY) for analysis. Cross-sectional differences in donor HRQoL by donation type at each key time point were examined using odds ratios for categorical variables and *t*-tests for continuous variables. To account for multiple comparisons, we applied the Holm-Bonferroni correction to each of the 4 classes of variables separately for each time point [22]. When the correction was applied, comparisons significant at .001 remained significant, but those with *P* values >.001 no longer reached statistical significance. In the tables, we noted which comparisons were significant at .05, .01, and .001. In the text, we refer to comparisons with differences of $P \leq .001$ as significant and those with differences of $P \leq .05$ and $P \leq .01$ as marginally significant.

To examine longitudinal differences in physical and mental health (SF-8 physical and mental health summary scores) by donation type, we used linear mixed models analyses. Main effects for donation type and time and the donation type by time interaction were examined. We used Kaplan Meier (log rank chi-square) analyses to examine potential differences in recovery time by donation type using week of full recovery as the primary outcome.

RESULTS

Participants

Of the 551 donors who participated in the parent RCT, 335 were eligible for the substudy. The primary reason for ineligibility was registration in the Department of Defense (n = 25) or German registries (n = 154). An additional 34 potential donors were ineligible because of issues related to the recipient or because they were non-English speaking. Three donors declined participation. A total of 332 donors contributed data.

Table 1 lists interview completion rates by cross-sectional time point. A total panel of 236 (71%) completed the baseline, 48 hours postdonation, and 6- and 12-month postdonation interviews. There were no differences between panel and nonpanel members by gender, race, age, marital status, or employment status.

Predonation Characteristics

The predonation interview was completed by BM and PBSC donors an average of 10.6 and 11.5 days respectively before donation (7 and 6 days, respectively).

The majority of participants were in their 30s, white, male, married, and employed—about one half had completed a bachelor's degree (Table 2). There were no group differences in demographic characteristics, clinical variables, physical/psychological status (although BM donors were marginally more likely to report infection and less likely to report confusion), or any of the variables related to interactions with others.

Table 1
Interview Completion Rates at Cross-sectional Time Points

Time Point	Interviews Completed at Time Point	Percent of Total (N = 332)
Before donation	331	99%
48 hours post donation	273	82%
Weekly until fully recovered	318	96%
6 months post donation	294	89%
12 months post donation	288	87%

The most prevalent concerns were that the procedure would be painful and that the donor's family would worry (>50% of donors for each concern). Groups differed marginally on concern about potential damage to the donors' health (BM = 26% versus PBSC = 39%). There were no group differences in health concerns.

Although the majority of donors felt well informed (81%) and fully prepared (80%), PBSC donors felt marginally less prepared (BM = 85% versus PBSC = 75%) and were marginally more likely to indicate that they needed more information (BM = 20% versus PBSC = 30%). More than 90% of donors were satisfied with the decision to donate and would volunteer again—there were no group differences in satisfaction.

Characteristics Forty-eight Hours Post Donation

There were no differences in AE or SAE by donor type (Table 3). BM donors reported lower overall physical health at this time point. The most commonly reported donation-related symptoms were tiredness and muscle aches, and BM donors were significantly more likely to report experiencing multiple current symptoms. Table 3 reports pain for PBSC donors on day 4 of rhGCSF administration and for BM donors within 48 hours post donation, as these are the time points when the 2 groups are likely to experience the most pain. BM donors' worst pain was marginally higher than that of PBSC donors, but the 2 groups did not differ on other pain indicators. BM donors reported better overall psychological status. There were no other group differences in psychological status.

Two thirds of donors reported that the donation was physically stressful and ~60% reported that the donation was emotionally stressful. More than half were worried about longer term health effects, and approximately one third were worried that they might never feel physically 100%. There were no group differences in these variables.

The most frequently endorsed social impacts of donation were effects on leisure and/or recreation and work and/or school. BM donors reported more impact on leisure and/or recreation activities and a marginally greater need to make child care arrangements. There were no other group differences in donation inconveniences.

The majority of donors were satisfied with the donation decision and there were no group differences in these variables. BM donors were marginally more likely to report that donation had made their lives more meaningful (BM = 48% versus PBSC = 35%).

Weekly Assessments for the First Three Weeks Post Donation

BM donors reported significantly more symptoms ($P \leq .001$) in each of the first 3 weeks after donation. Four key

Table 2
Predonation Comparison of Marrow and PBSC Donors

Study Variable	Marrow (n = 161)	PBSC (n = 170)	Test Statistic (t or Odds Ratio)	*P* Value
Sociodemographic				
Age, mean (SD)	33.6 (9.18)	35.1 (10.29)	−1.45	.148
Women	34	34	1.03 (.65-1.62)	.912
Married	63	53	.67 (.43-1.04)	.071
≥Bachelor's degree	46	53	1.32 (.86-2.04)	.204
Employed	93	91	1.32 (.59-2.97)	.501
Race				
Caucasian/White	86	83		
Hispanic	6	8		
African American	4	4		
Asian American	1	2		
Other	2	2		
Physical Status				
Overall physical status				
SF-8 physical health, (SD) (29-68)*	56.47 (3.71)	55.86 (4.79)	.78	.436
Current physical symptoms				
Tiredness	49	52	1.10 (.70-1.74)	.685
Muscle aches	17	24	1.54 (.86-2.74)	.145
Problems sleeping	15	16	1.07 (.57-2.00)	.845
Bone pain	6	8	1.49 (.59-3.76)	.397
Light headedness	6	5	.85 (.32-2.27)	.747
Difficulty walking	4	4	.97 (.30-3.07)	.952
Bleeding	7	3	.37 (.11-1.21)	.087
Nausea or vomiting	1	4	6.00 (.71-50.47)	.062
Infection	3	0	.48 (.43-.55)	.041†
Chills	2	2	.97 (.19-4.87)	.966
Fainting	1	1	.97 (.06-15.60)	.981
Current physical symptoms				
Psychological Status				
Overall psychological status				
SF-8 mental health, mean (SD) (28-69)	55.68 (4.83)	55.12 (5.37)	.94	.350
Profile of mood states				
Depression, mean (SD) (0-4)	.10 (.29)	.11 (.24)	−.28	.784
Vitality, mean (SD) (0-4)	2.40 (.82)	2.46 (.67)	−.60	.548
Confusion, mean (SD) (0-4)	.23 (.34)	.31 (.40)	−2.04	.043†
Tension, mean (SD) (0-4)	.44 (.51)	.45 (.47)	−.11	.911
Anger, mean (SD) (0-4))	.22 (.38)	.22 (.32)	.06	.951
Fatigue, mean (SD) (0-4)	.46 (.61)	.55 (.62)	−1.36	.174
Total distress, mean (SD) (0-24)	4.21 (1.91)	4.19 (1.91)	.07	.941
Donation-related				
Interaction with others				
Consulted family/friends	58	56	1.08 (.68-1.72)	.738
Consulted professionals	29	35	.75 (.46-1.22)	.242
Encouraged to donate	26	30	.80 (.48-1.33)	.390
Discouraged from donating	26	27	.91 (.54-1.53)	.727
Medical concerns				
Pain	58	55	.89 (.56-1.40)	.604
Anesthesia	35	33	.91 (.56-1.48)	.709
Damage health	26	39	1.81 (1.10-2.97)	.018†
Use of needles	13	16	1.33 (.69-2.58)	.391
Work/family concerns				
Family will worry	56	49	.78 (.49-1.23)	.286
Missing work/school	43	41	.92 (.58-1.46)	.714
Reimbursement for missed work	19	19	1.00 (.56-1.80)	.993
Missing family activities	15	15	1.06 (.56-2.02)	.857
Child/family care	15	11	.66 (.33-1.32)	.239
Other concerns				
Patient's chances are low	43	38	.83 (.52-1.33)	.443
Payment for medical treatment	18	14	.74 (.40-1.38)	.343
Transportation to donor center	14	12	.85 (.43-1.67)	.629
Against religious beliefs	0	1	.51 (.45-.57)	.164
Overall health concerns				
Worry about longer term health impact of donation	63	66	1.13 (.70-1.82)	.615
Worry will never feel physically 100% again	29	27	.89 (.54-1.49)	.658
Preparation				
Feel very well informed	84	79	.70 (.39-1.27)	.239
Feel totally prepared	85	75	.55 (.31-.99)	.045†
Need much more information	20	30	1.70 (.99-2.91)	.051†
Satisfaction with donation decision				
Extremely satisfied with decision	90	91	1.05 (.48-2.30)	.894
Would definitely volunteer again	92	91	.80 (.35-1.82)	.590

(*Continued*)

Table 2
(*Continued*)

Study Variable	Marrow (n = 161)	PBSC (n = 170)	Test Statistic (t or Odds Ratio)	*P* Value
Clinical				
Weight, mean (SD), kg	88.12 (18.64)	85.07 (17.33)	1.52	.128
Height, mean (SD), cm	174.48 (9.15)	173.92 (10.26)	.52	.607

PBSC indicates peripheral blood stem cells.
Data presented are % unless otherwise indicated.
* Response range.
† $P \leq .05$.

symptoms—pain at needle insertion sites, bone pain, muscle aches, and difficulty walking—were reported by BM donors at significantly higher levels ($P \leq .001$) across each of the first 3 weeks post donation (data not shown). Tiredness, lightheadedness, nausea, problems sleeping, and chills were reported by BM donors at marginally higher rates ($P \leq .05$) in the first week after donation, but these differences disappeared by the second week post donation.

Characteristics Six Months Post Donation

There were no group differences in overall physical or psychological status (Table 4). The most common current symptoms were tiredness (45%) and muscle aches (22%). The only marginally significant symptom differences were lightheadedness (BM = 6% versus PBSC = 1%) and pain where the needles entered (BM = 6% versus PBSC = 1%).

Forty percent of donors knew the health status of their recipient and 84% said that they had a special bond with the recipient. Fifteen percent of donors indicated that they thought about the recipient more than once each day and 33% were worried about the recipient's health. There were no group differences in recipient-related variables.

Eighty-one percent of donors had reached 3 consecutive symptom-free weeks by 6 months post donation and there were no group differences in recovery.

Characteristics Twelve Months Post Donation

PBSC donors had marginally better physical health status at this time point than the BM donors (Table 5). However, this was due to 3 extreme outliers (SF-8 physical mean < 40) in the BM group. When we compared the distributions with extreme outliers removed ($t = -1.28$; df = 279; $P = .20$) and with Kruskal-Wallis nonparametric tests ($P = .29$) there was no significant difference in overall physical health. All 3 BM donors with very low physical status scores at 12 months post donation were female, ages 32 to 46. One donor had experienced an SAE but was fully recovered (defined as 3 symptom-free weeks) by 6 months post donation. Both that donor and a second donor had higher SF-8 physical health summary scores at 6 months post donation than before donation and then declines between 6 and 12 months post donation. There was no obvious link between donation and the lower physical scores at 12 months post donation.

The third donor reported ongoing pain where the needles entered, difficulty walking, problems sleeping, bone pain, and muscle aches throughout the 52-week follow-up period and was still reporting symptoms at 12 months. This donor had consistently poorer physical health scores at 6 and 12 months post donation.

Overall, the most common symptoms were tiredness (55% of all donors) and muscle aches (23% of all donors). There were no significant symptom differences. There were no group differences in overall psychological status or distress. Nearly half of donors remained concerned about the longer term health effects of donation and 13% worried that they might never feel physically 100%. There were no group differences in these variables.

The majority of donors were extremely satisfied with their decision to donate (91%), would donate again if asked (86%), and would encourage others to donate (81%). There were no group differences in satisfaction variables.

Forty-one percent of donors knew the health status of their recipient. Eleven percent of donors indicated that they thought about the recipient more than once per day, 77% reported that they had a special bond with the recipient, and 30% were worried about the recipient's health. There were no group differences in recipient-related variables.

Eighty-seven percent of donors had reached 3 consecutive symptom-free weeks by 12 months post donation and there were no group differences in recovery. Among the group still reporting weekly symptoms at 12 months post donation, the most commonly reported symptoms across the entire postdonation period were tiredness (~85% of the group consistently reported this symptom), muscle aches (~50%), and problems sleeping (~40%).

Longitudinal Comparisons of Physical/Mental Status and Recovery

Mean values for the physical and mental status components of the SF-8 health survey are presented in Figure 1. Mixed models analyses indicated that there were main effect differences for donation type (physical: F = 30.2, df = 1589, $P < .001$; mental: F = 8.9, df = 1,058, $P = .003$) and time (physical: F = 678.8, df = 3643, $P < .001$; mental: F = 291.7, df = 3539, $P < .001$). In addition, there were significant donation type by time interactions for both physical and mental status (physical: F = 15.6, df = 3643, $P < .001$; mental: F = 3.2, df = 3539, $P = .023$). Both groups experienced declines in physical status immediately following donation and then scores higher than baseline levels at 6 and 12 months. At 48 hours post donation, BM donors reported poorer physical status and PBSC donors reported poorer mental status. Figure 2 presents the Kaplan Meier recovery curves for BM and PBSC donors. There was no significant group difference in recovery (log rank chi-square = 1.85, $P = .18$).

DISCUSSION

This investigation is 1 of the first to systematically and comprehensively examine HRQoL experiences of BM and PBSC donors in the context of a Phase III randomized trial. A central finding of this investigation is that there do not appear to be longer term differences in the HRQoL experiences of the vast majority of BM and PBSC donors.

The pattern of findings before donation indicate that BM donors are slightly advantaged over PBSC donors in

Table 3
Forty-Eight Hours Post-donation Comparison of Marrow and PBSC Donors

Study Variable	Marrow (n = 131)	PBSC (n = 142)	Test Statistic (*t* or Odds Ratio)	*P* Value
Physical Status				
Overall physical status				
SF-8 physical health, mean (SD) (29-68)*	35.38 (9.75)	43.37 (9.75)	−6.59	.000§
Current physical symptoms				
Tiredness	92	92	.98 (.40-2.40)	.972
Muscle aches	75	56	.42 (.25-.71)	.421
Problems sleeping	50	39	.66 (.41-1.07)	.091
Bone pain	58	60	1.09 (.67-1.77)	.717
Light headedness	50	34	.50 (.31-.82)	.006‡
Pain where needles inserted	83	55	.25 (.14-.44)	.000§
Difficulty walking	87	39	.10 (.05-.18)	.000§
Bleeding	41	10	.16 (.08-.30)	.000§
Nausea or vomiting	28	25	.86 (.51-1.48)	.590
Infection	0	0	–	–
Chills	20	9	.41 (.20-.83)	.012†
Fainting	3	0	.47 (.42-.54)	.036†
Current pain‖				
Pain index, mean (SD) (0-10)	4.23 (1.86)	3.84 (1.94)	1.68	.094
Average pain, mean (SD) (0-10)	4.04 (1.98)	3.63 (2.00)	1.69	.093
Worst pain, mean (SD) (0-10)	5.55 (2.45)	4.80 (2.26)	2.60	.009‡
Time with pain, mean (SD) (0-10)	4.77 (2.42)	4.57 (2.58)	.66	.513
Interfered with sleep, mean (SD) (0-10)	2.53 (2.40)	2.35 (2.34)	.62	.535
Psychological Status				
Overall psychological status				
SF-8 mental health, mean (SD) (28-69)	55.40 (7.24)	52.23 (6.24)	3.85	.000§
Profile of mood states				
Depression, mean (SD) (0-4)	.10 (.42)	.12 (.24)	−.61	.541
Vitality, mean (SD) (0-4)	1.23 (.93)	1.46 (.88)	−2.12	.035†
Confusion, mean (SD) (0-4)	.26 (.69)	.25 (.42)	.13	.900
Tension, mean (SD) (0-4)	.46 (.69)	.47 (.51)	−.19	.848
Anger, mean (SD) (0-4)	.12 (.48)	.14 (.25)	−.50	.615
Fatigue, mean (SD) (0-4)	1.31 (1.02)	1.23 (.91)	.69	.491
Total distress, mean (SD) (0-24)	5.01 (2.75)	4.75 (2.28)	.85	.396
Donation-related				
Donation experience				
Donation physically stressful	76	75	.91 (.53-1.59)	.746
Donation emotionally stressful	55	58	1.12 (.69-1.81)	.643
Health concerns				
Worry about longer term health impact of donation	55	58	1.10 (.68-1.78)	.695
Worry will never feel physically 100% again	27	32	1.30 (.75-2.13)	.389
Social impact				
Leisure/recreation affected	87	51	6.46 (3.52-11.86)	.000§
Work/school affected	75	70	1.29 (.75-2.20)	.359
Transportation arrangements	58	47	1.55 (.96-2.50)	.073
Child care arrangements	28	16	2.04 (1.13-3.66)	.016†
Financial arrangements	18	13	1.55 (.80-3.00)	.197
Home care help	7	4	1.67 (.58-4.83)	.338
Satisfaction with donation decision				
Extremely satisfied with decision	92	92	.90 (.37-2.15)	.804
Would definitely donate again	79	78	.94 (.53-1.68)	.843
Would strongly encourage others	82	82	1.00 (.53-1.86)	.992
Feel a lot like a better person	76	76	1.02 (.58-1.78)	.958
Feel very proud	63	65	1.06 (.65-1.75)	.806
Made life much more meaningful	48	35	.58 (.35-.94)	.026†
Recipient-related				
Know health status of recipient	7	10	.67 (.28-1.60)	.365
Think about recipient ≥ once/day	79	78	.92 (.52-1.65)	.784
Have special bond with recipient	82	79	.80 (.43-1.46)	.457
Very/pretty worried about recipient	66	61	.80 (.49-1.32)	.385
Clinical				
Adverse event	15	16	1.12 (.61-2.06)	.705
Serious adverse event	6	2	.30 (.08-1.13)	.061

PBSC indicates peripheral blood stem cells.
* Response range.
† $P \leq .05$.
‡ $P \leq .01$.
§ $P \leq .001$.
‖ For PBSC donors, pain was assessed on the fourth day of rhGCSF administration. For BM donors, pain was assessed 48 hours post donation.

terms of experiencing lower levels of confusion, fewer concerns about the donation procedure, and higher levels of preparedness for donation. Existing literature is mixed on whether there are predonation psychological and preparedness differences between BM and PBSC donors, but when such differences have been found—eg, in predonation anxiety—they have also favored BM donors [23,24]. It is possible that donor center staff were more

Table 4
Six Months after Donation Comparison of Marrow and PBSC donors

Study Variable	Marrow (n = 141)	PBSC (n = 153)	Test Statistic (*t* or Odds Ratio)	*P* Value
Physical Status				
Overall physical status				
SF-8 physical health, mean (SD) (29-68)*	65.18 (4.51)	64.96 (3.85)	.45	.651
Current physical symptoms				
Tiredness	42	48	1.30 (.82-2.06)	.262
Muscle aches	24	20	.80 (.46-1.39)	.427
Problems sleeping	10	15	1.61 (.79-3.26)	.187
Bone pain	9	5	.54 (.22-1.35)	.184
Light headedness	6	1	.22 (.05-1.06)	.039†
Pain where needles inserted	6	1	.12 (.01-.89)	.013†
Difficulty walking	5	5	.92 (.31-2.69)	.876
Bleeding	1	2	2.80 (.29-27.23)	.355
Nausea or vomiting	1	3	1.87 (.34-10.35)	.469
Infection	0	2	.52 (.46-.58)	.095
Chills	0	1	.52 (.47-.58)	.336
Fainting	0	0	-	-
Current pain				
Pain index, mean (SD) (0-10)	.60 (1.38)	.67 (1.23)	−.44	.663
Average pain, mean (SD) (0-10)	.57 (1.38)	.61 (1.17)	−.25	.802
Worst pain, mean (SD) (0-10)	.87 (1.83)	.95 (1.64)	−.41	.685
Time with pain, mean (SD) (0-10)	.69 (1.58)	.82 (1.66)	−.68	.500
Interfered with sleep, mean (SD) (0-10)	.29 (1.12)	.31 (.94)	−.15	.879
Psychological Status				
Overall psychological status				
SF-8 mental health, mean (SD) (28-69)	65.49 (5.81)	65.03 (5.98)	.66	.510
Profile of mood states				
Depression, mean (SD) (0-4)	.10 (.27)	.11 (.25)	−.37	.716
Vitality, mean (SD) (0-4)	2.16 (1.01)	2.22 (.98)	−.59	.555
Confusion, mean (SD) (0-4)	.26 (.42)	.30 (.80)	−.44	.660
Tension, mean (SD) (0-4)	.31 (.45)	.36 (.83)	−.57	.566
Anger, mean (SD) (0-4)	.19 (.37)	.22 (.78)	−.42	.676
Fatigue, mean (SD) (0-4)	.45 (.63)	.23 (.95)	−.81	.417
Total distress, mean (SD) (0-24)	3.15 (2.24)	3.10 (2.01)	.22	.826
Donation-related				
Donation experience				
Donation physically stressful	74	75	1.04 (.62-1.75)	.883
Donation emotionally stressful	63	69	1.28 (.79-2.07)	.319
Health concerns				
Worry about longer term health impact of donation	41	51	1.51 (.95-2.40)	.81
Worry will never feel physically 100% again	14	9	.65 (.31-1.35)	.241
Satisfaction with donation decision				
Extremely satisfied with decision	92	88	.70 (.32-1.51)	.357
Would definitely donate again	87	84	.78 (.40-1.51)	.461
Would strongly encourage others	82	78	.79 (.44-1.41)	.426
Feel a lot like a better person	75	75	.97 (.57-1.64)	.895
Feel very proud	56	62	1.27 (.80-2.03)	.312
Made life much more meaningful	31	28	.86 (.52-1.42)	.561
Recipient-related				
Know health status of recipient	39	41	.93 (.58-1.48)	.756
Think about recipient ≥ once/day	16	14	.85 (.45-1.63)	.631
Have special bond with recipient	83	84	1.09 (.59-2.03)	.776
Very/pretty worried about recipient	35	31	.87 (.53-1.41)	.563
Recovery				
Recovered at 6 months	81	82	1.11 (.63-1.95)	.720

PBSC indicates peripheral blood stem cells.
* Response range.
† $P \leq .05$.

thorough in preparing BM donors, or that BM donors were more likely to seek out donation-related information on their own, given the more invasive nature of this HSC collection procedure. It is also possible that the administration of rhGCSF, for which the longer term risks are likely to be low but at the time of this investigation had not been fully examined in healthy donors, may have heightened health-related concerns in the PBSC group. Regardless of the source of these concerns among PBSC donors, a review and potential revision of the predonation counseling process for PBSC donors may be warranted to ensure that all donors are fully informed about the donation and recovery process.

Findings from 48 hours post donation indicate that BM donors had experienced more physical side effects and pain within the past 48 hours although the pain profiles of BM donors at 48 hours post donation and PBSC donors on day 4 of rhGCSF administration were generally similar. BM donors also reported that the donation had a greater impact on their social activities. Despite these findings, BM donors were more likely to report better psychological status and that the donation had made their lives more meaningful at this time point. This finding may be due to the greater physical intensity of the BM donation process leading to more positive psychological outcomes shortly after donation. It is also possible that those close to BM donors may have viewed the

Table 5
Twelve Months Post-donation Comparison of Marrow and PBSC Donors

Study Variable	Marrow (n = 137)	PBSC (n = 151)	Test Statistic (*t* or Odds Ratio)	*P* Value
Physical Status				
Overall physical status				
SF-8 physical health, mean (SD) (29-68)*	63.95 (6.41)	65.21 (3.91)	−2.03	.043†
Current physical symptoms				
Tiredness	53	56	1.16 (.73-1.85)	.525
Muscle aches	25	22	.85 (.49-1.46)	.552
Problems sleeping	19	21	1.15 (.64-2.05)	.640
Bone pain	12	9	.72 (.34-1.53)	.391
Light headedness	4	7	1.87 (.62-5.62)	.257
Pain where needles inserted	5	0	.99 (.96-1.01)	.742
Difficulty walking	11	5	.46 (.19-1.11)	.077
Bleeding	2	0	.47 (.42-.53)	.136
Nausea or vomiting	4	4	1.09 (.33-3.66)	.886
Infection	4	3	.90 (.26-3.19)	.876
Chills	2	2	.91 (.18-4.56)	.904
Fainting	1	0	.48 (.42-.54)	.293
Current pain				
Pain index, mean (SD) (0-10)	.97 (1.72)	.88 (1.40)	.48	.632
Average pain, mean (SD) (0-10)	.86 (1.60)	.84 (1.43)	.11	.910
Worst pain, mean (SD) (0-10)	1.24 (2.08)	1.28 (2.01)	−.18	.855
Time with pain, mean (SD) (0-10)	1.19 (2.12)	1.01 (1.72)	.81	.420
Interfered with sleep, mean (SD) (0-10)	.59 (1.64)	.40 (1.16)	1.17	.245
Psychological Status				
Overall psychological status				
SF-8 mental health, mean (SD) (28-69)	64.94 (6.16)	64.86 (6.18)	.11	.916
Profile of mood states				
Depression, mean (SD) (0-4)	.11 (.28)	.11 (.29)	.11	.912
Vitality, mean (SD) (0-4)	2.19 (.99)	2.19 (.86)	.02	.986
Confusion, mean (SD) (0-4)	.28 (.40)	.25 (.39)	.61	.545
Tension, mean (SD) (0-4)	.36 (.45)	.34 (.48)	.22	.828
Anger, mean (SD) (0-4)	.19 (.32)	.18 (.36)	.40	.691
Fatigue, mean (SD) (0-4)	.51 (.71)	.55 (.71)	−.45	.657
Total distress, mean (SD) (0-24)	3.26 (2.38)	3.24 (2.27)	.08	.940
Donation-related				
Donation experience				
Donation physically stressful	66	68	1.05 (.64-1.72)	.839
Donation emotionally stressful	60	58	.94 (.59-1.50)	.786
Health concerns				
Worry about longer term health impact of donation	43	50	1.30 (.82-2.08)	.264
Worry will never feel physically 100% again	17	10	.55 (.27-1.10)	.086
Satisfaction with donation decision				
Extremely satisfied with decision	91	91	1.03 (.45-2.34)	.949
Would definitely donate again	88	85	.74 (.37-1.46)	.379
Would strongly encourage others	79	82	1.23 (.69-2.21)	.481
Feel a lot like a better person	72	71	.94 (.56-1.58)	.823
Feel very proud	66	58	.71 (.44-1.14)	.155
Made life much more meaningful	31	29	.93 (.56-1.54)	.779
Recipient-related				
Know health status of recipient	43	40	1.14 (.71-1.82)	.598
Think about recipient ≥ once/day	10	11	1.05 (.49-2.24)	.901
Have special bond with recipient	78	77	.96 (.55-1.67)	.876
Very/pretty worried about recipient	34	26	.69 (.41-1.16)	.160
Recovery				
Recovered at 12 months	87	87	.95 (.50-1.82)	.876

PBSC indicates peripheral blood stem cells.
* Response range.
† $P \leq .05$.

process as entailing greater risk to the donor and may, therefore, have been more engaged with and congratulatory of the donor. Differences in physical side effects persisted for at least 3 weeks post donation, with BM donors experiencing significantly greater adverse effects in these areas than PBSC donors.

There were few longer term differences in the experiences of the 2 donor groups. At 6 months post donation, BM donors were slightly more likely to report continued lightheadedness and pain where the needles entered than were PBSC donors, and at 12 months, BM donors reported marginally poorer physical status. However, the former results are not statistically significant after correcting for multiple comparisons, and the latter was entirely due to 3 outliers in the BM group with very low physical status scores. For 2 of these outliers, there was no apparent link between donation and the lower 12-month physical scores. The third donor reported ongoing symptoms in addition to lower 6- and 12-month physical scores.

Nearly half of donors overall had at least some lingering concerns about the longer term health impact of donation at 12 months post donation. It is possible that this is a natural side effect of any important nonrequired medical procedure, but it suggests that predonation information sessions and postdonation follow-up could better emphasize the very low probability that BM or PBSC donation will have longer term

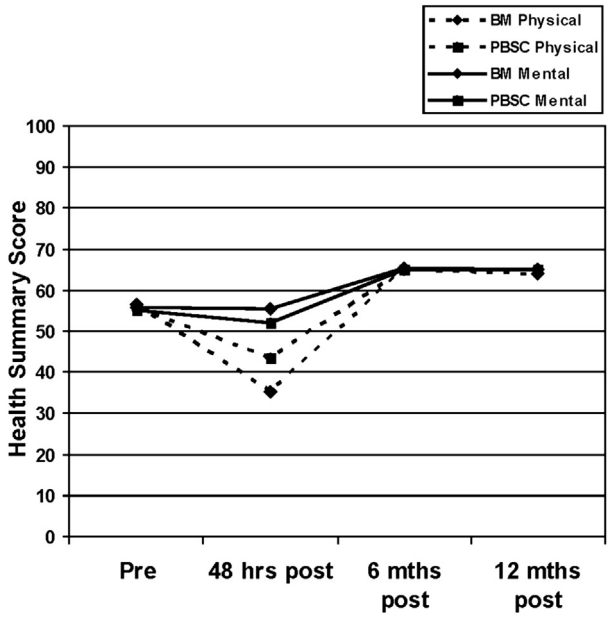

Figure 1. Longitudinal pre- and postdonation physical and mental states for bone marrow and peripheral blood stem cell donors. Physical and mental health summary scores were assessed with the Short Form–8; higher scores indicate better physical or mental health.

health effects. In addition, in concordance with recommendations from the World Marrow Donor Association about longer term donor follow-up, these residual health concerns should be the subject of ongoing assessment beyond the first year post donation [25].

Longitudinal group differences in physical and psychological status were the result of declines in physical status—and psychological status for PBSC donors—immediately following donation, but then gains to levels above predonation levels at 6 and 12 months post donation. Longitudinal group by time physical and psychological status interactions were primarily due to 48-hour postdonation differences when BM donors reported poorer physical status but better psychological status than did PBSC donors. There was no recovery time difference between the 2 groups as assessed starting 3 weeks post donation, the first point at which a donor could be recorded as fully recovered.

It is interesting that approximately 13% of donors had not met our definition of recovery by 12 months post donation. This is likely partly a result of our conservative definition of recovery—3 consecutive symptom-free weeks and assessment of all symptoms, regardless of whether they were attributable to donation—but may also indicate that there are other interesting characteristics about this subgroup. The most commonly reported symptoms by this group were fatigue, muscle aches, and problems sleeping, which are less likely to be an ongoing result of donation than some other symptoms. We are currently analyzing predictors of recovery—including predonation physical and psychological status—for a separate manuscript. Other investigations that asked donors specifically about their recovery from the donation process, rather than reporting all symptoms regardless of whether they are attributable to donation, find that the majority of donors report feeling recovered within

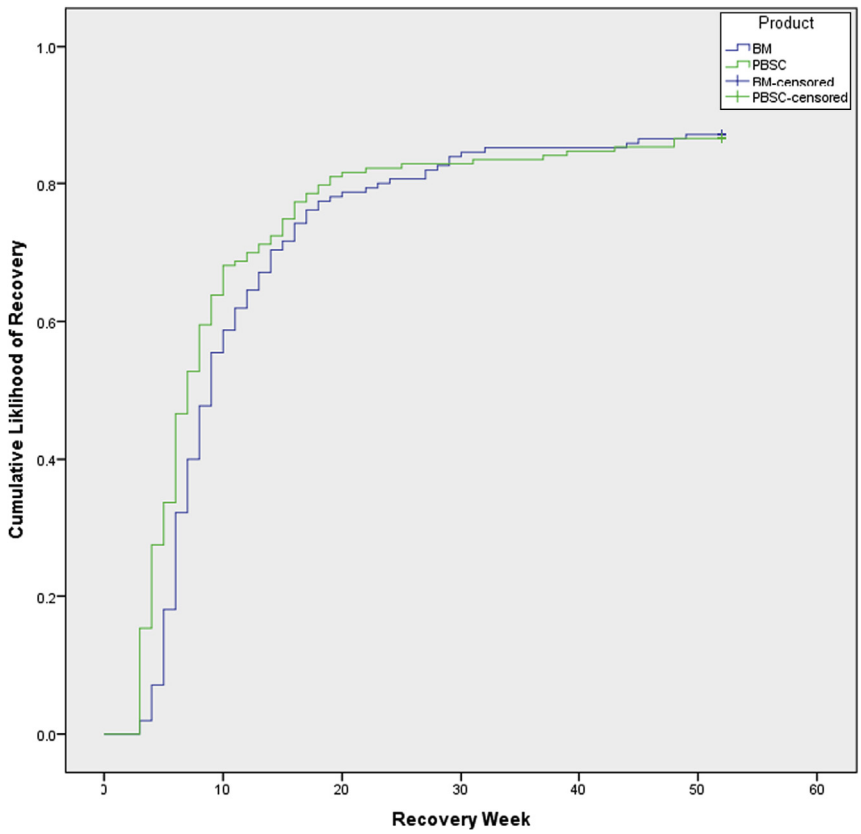

Figure 2. Time to full recovery by product donated.

4 weeks, and virtually all report feeling recovered by 6 months post donation [26].

Overall, these findings suggest that although BM donors may experience the process as more physically uncomfortable in the short term, the physical impact of donation resolves relatively quickly and there are few longer term differences, in aggregate, between the 2 groups. Conversely, BM donors may experience greater short-term psychological gains from donation, particularly in terms of feeling like the donation made their lives more meaningful, but there are no longer term differences between the 2 groups in terms of psychological benefit.

A key limitation of the investigation is that donors were primarily white, and all were required to be able to write, read, and speak English. Given the randomized study design and inclusion criteria, this was expected. However, it may limit generalizability to broader groups of donors. In addition, all participants were unrelated donors belonging to the NMDP registry. Their characteristics—young, self-selected, knowledgeable, healthy, and highly motivated—may make it difficult to extrapolate these findings to other groups of donors, particularly related donors. We are currently conducting an NIH-funded investigation that will compare the HRQoL experiences of donors who are related to the recipient and those who are unrelated.

Despite these limitations, this investigation improves our understanding of HRQoL issues involved in the HSC donation process, provides a stringent comparison of these 2 methods of donation, and indicates that the longer term HRQoL consequences of BM and PBSC donation are similar in the vast majority of donors.

ACKNOWLEDGMENTS

Financial disclosure: Supported by a grant from the National Heart, Lung, and Blood Institute and the National Cancer Institute (U10HL069294), by the Office of Naval Research, and by the National Marrow Donor Program.

Authorship statement: All authors participated in the design of the research, selection of the analytic strategy, and manuscript preparation. J.G.B. and D.H. collected and managed data at the University of Pittsburgh, assisted with data analysis and contributed to the conceptual organization of the manuscript. R.D., A.F., and D.C. facilitated and managed sampling and participant recruitment at the NMDP. All authors interpreted data and reviewed and approved the final manuscript.

Conflict of interest statement: There are no conflicts of interest to report.

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