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RAPID TRANSPORT AND INFUSION OF HEMATOPOIETIC CELLS IS ASSOCIATED WITH IMPROVED OUTCOME AFTER MYELOABLATIVE THERAPY AND UNRELATED DONOR TRANSPLANT

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Abstract

We evaluated effects of graft transport time on outcomes after transplantation of 938 unrelated donor bone marrow (BM) or 507 peripheral blood progenitor cells (PBPC) in patients with acute or chronic leukemia and myelodysplasia. BM grafts were collected at 107 centers and PBPC, 89 centers. Median time from end of collection to infusion was 14 hours for BM and 15 hours for PBPC. Platelet recovery was less likely in BM recipients when the interval from end of collection to receipt at transplant center was ≥ 20 hours (odds ratio 0.47, p=0.010) and when the interval from receipt to infusion was ≥ 6 hours (odds ratio 0.57, p=0.001). Mortality rates were higher in recipients of HLA-matched BM when the interval from end of collection to receipt at transplant center was ≥ 20 hours (relative risk 2.67, p<0.001) after adjustment for other significant prognostic factors. Mortality after HLA-mismatched BM transplants was not associated with transport time. Transport times had no demonstrable effect on outcomes after PBPC transplants. These data support a general review of current transport procedures, especially for BM grafts requiring longer transport time and every effort made to minimize time from collection to infusion.

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Keywords

transport of unrelated donor grafts; transport times; transplant-outcomes

INTRODUCTION

HLA-matched sibling hematopoietic cell transplantation (HCT) is the treatment of choice for a variety of malignant and non-malignant disorders (1). Only about 30% of candidates, however, will have a suitable unrelated histocompatible or matched-related donor to provide an allogeneic graft.(2) Patients without a related donor must identify a suitable unrelated donor through large international registries. Almost all unrelated donor grafts are collected at a site remote from the site where the recipient is treated. Significant advances, including the discovery of new HLA alleles, the development of precise and efficient HLA typing methods using DNA technology, the implementation of more selective immunosuppressive agents to decrease treatment-related toxicity and graft-versus-host disease (GVHD) and prophylaxis for viral and fungal infections, has enabled more effective identification and use of unrelated donors for HCT. (3–5) Registry data now indicate that more than a third of allogeneic transplants now use unrelated donors and outcomes have improved progressively over the past 20 years.(6)

More than 10 million HLA-typed volunteer donors are available world-wide to donate bone marrow (BM) or peripheral blood progenitor cells (PBPC). Most of these donors are available through the U.S. National Marrow Donor Program (NMDP).(7) The collection and transport of cells for infusion is a complex process coordinated by the NMDP for transplants it facilitates. Grafts are collected at sites accredited by the NMDP and are transported according to specified guidelines. The NMDP recommendations for graft transport are available at www.marrow.org (NMDP Standards, 19th edition, 2004). Since there may be great distances between collection and transplant centers, there is the potential for long delays between collection and infusion that could impact upon graft viability. We studied this issue in more than 1400 transplants facilitated by the NMDP.

PATIENTS AND METHODS

Data collection

Data on transportation and characteristics of PBPC and BM grafts were collected by the NMDP. Detailed demographic, disease and transplant characteristics and outcome data were obtained on all unrelated donor transplant recipients facilitated by the NMDP in the U.S. and participating international centers. Patients were followed longitudinally. Computerized error checks, physician review of submitted data and on-site audits of participating centers were performed to ensure data quality.

Inclusion criteria

The study population includes 938 recipients of BM and 507 recipients of PBPC transplants during the period 2000–2004. This study was restricted to patients receiving HCT for acute leukemia (acute lymphoblastic leukemia [ALL] or acute myeloid leukemia [AML]), chronic myeloid leukemia (CML) or myelodysplastic syndrome (MDS). Only patients in first or second clinical remission, chronic phase and refractory anemia and receiving a myeloablative conditioning regimen were included. Myeloablative conditioning regimen was defined as total body irradiation (TBI) dose greater than 500 cGy (single dose) or greater than 800 cGy (fractionated) with other agents and for non-irradiation regimens, busulfan dose of at least 9 mg/kg or melphalan dose greater than 150 mg/m^2. Excluded were patients who received

regimens of lower intensity to that mentioned above, second or subsequent transplantation, patients with more advanced leukemia, other hematological malignancies and non-malignant diseases, T-cell depleted BM or CD34 selected PBPC transplants, cryopreserved BM or PBPC grafts. Informed consent for surviving patients was obtained in accordance with the declaration of Helsinki. Informed consent was waived by the NMDP Institutional Review Board for all deceased patients. Approximately 12% of surviving patients in the NMDP database did not provide consent for use of data for research. To adjust for the potential bias introduced by the exclusion of 12% of surviving patients and the inclusion of all deceased patients a probability model randomly excluded approximately the same percent of deceased patients (n=166). This probability model uses a biased coin randomization method with exclusion probabilities based on the patient and disease characteristics associated with patients who did provide consent for research (8).

Graft transport

Bags containing BM or PBPC were placed in an outer bag to prevent leakage. Collection bag (s) were enclosed in a rigid container with temperature insulating properties. All products were non-cryopreserved and transported at the temperature specified by the transplant center or the NMDP. NMDP guidelines recommend transportation at ambient temperature for BM and refrigerated for PBPC; transport temperature (ambient or refrigerated for either graft) could also be requested by the transplant center. No product had direct contact with wet ice or frozen gel packs. The temperature at which the grafts were transported was not monitored. All products were hand carried by a courier. The NMDP ensures transportation arrangements for the courier minimizes transit time from collection to transplant centers. Ninety-three percent of BM grafts were transported at ambient temperature and 7% refrigerated at the request of the transplant center; 98% of PBPC grafts were transported refrigerated and 2% at ambient temperature.

Endpoints

The primary outcomes studied were neutrophil and platelet recovery, acute and chronic graft-versus-host disease (GVHD), early (day-100) and overall mortality. Neutrophil recovery was defined as achieving an absolute neutrophil count (ANC)$\geq 0.5 \times 10^9$/L; platelet recovery was defined as achieving a platelet count $\geq 20 \times 10^9$/L, unsupported for 7 days. Failure to achieve an ANC $\geq 0.5 \times 10^9$/L or a decline to $< 0.5 \times 10^9$/L after an initial recovery and without a subsequent recovery was considered graft failure. Incidence of grades 2, 3 and 4 acute GVHD and chronic GVHD were determined in all patients. Diagnosis of acute and chronic GVHD (9,10) was based on local institutional criteria, with overall grade of acute GVHD assigned retrospectively by the NMDP based on stage of involvement reported for each individual organ. Early mortality was defined as death from any cause within the first 100 days after transplantation and overall mortality, death from any cause at any time.

Statistical Analysis

The probabilities of early (day-100) mortality and overall survival were calculated using the Kaplan-Meier estimator (11). For analysis of survival, death from any cause was considered an event and data on surviving patients were censored at time of last follow-up. The probabilities of neutrophil and platelet recovery, and acute and chronic GVHD were calculated using the cumulative-incidence-function method (12). For neutrophil and platelet recovery and GVHD, death without an event (hematopoietic recovery or GVHD) was the competing event. Data on patients without an event were censored at last follow-up. Confidence intervals for odds ratios presented herein were calculated using log-transformation.

Cox regression models were built for analyses of risk factors for GVHD and overall mortality and logistic regression models for analysis of neutrophil and platelet recovery and day-100 mortality (12,13). BM and PBPC transplantations were analyzed separately. All multivariate

models were built using stepwise forward selection, with a p-value of 0.01 or less considered to indicate statistical significance. We used a p-value of ≤ 0.01 to indicate statistical significance due to the number of variables considered in model building (Table 1). Variables were categorized as follows: recipient age (≥ 18 vs. < 18 years), performance score (90–100 vs. < 90), disease (ALL vs. MDS vs. CML vs. AML), disease status (1st complete remission or chronic phase or refractory anemia vs. 2nd clinical remission or chronic phase), total nucleated cell dose at end of collection (≥ 3 vs. <3 × 10^8/kg), interval from end of collection to receipt at transplant center (≥ 20 vs. < 20 hours), shipping temperature (refrigerated vs. ambient), total nucleated cell dose at receipt at transplant center (≥ 3 vs. <3 × 10^8/kg), interval from receipt at transplant center to infusion (≥ 6 vs. <6 hours), processing of graft for ABO incompatibility vs. none, donor-recipient HLA disparity (matched vs. mismatched), donor-recipient cytomegalovirus (CMV) status (donor and recipient negative vs. donor negative/recipient positive vs. donor positive/recipient negative vs. donor and recipient positive), donor-recipient gender match (female donor → male recipient vs. other), conditioning regimen (total body irradiation containing regimens vs. non-irradiation regimens), graft-versus-host disease (GVHD) prophylaxis (tacrolimus vs. cyclosporine) and year of transplant (2000–2002 vs. 2003–2004). As the primary outcome of the study was to access impact of transport times (interval from end of collection to receipt at transplant center and from receipt at transplant center to infusion), these variables were held in all final models regardless of statistical significance.

All variables met the proportional-hazards assumption. Martingale residual plots were constructed for the following variables to determine the appropriate cut-points for inclusion in the model as a binary variable: interval from end of collection to receipt at transplant center and from receipt at transplant center to infusion. These plots were constructed for each outcome of interest to ensure that the cut-point was appropriate for all of the outcomes studied. In addition, we examined the above mentioned time periods by the categories shown in Table 1; the cut-points determined by both methods were comparable. Consequently, we chose 20 hours as the cut-point for time between end of collection and receipt at transplant center and 6 hours, the cut-point for time between receipt at transplant center and infusion. Among BM recipients, there was a first order interaction between donor-recipient HLA match and interval from end of collection to receipt at transplant center and, type of leukemia and disease status at transplantation for overall mortality. We examined for a collection center and transplant center effect on overall survival and found none. P-values are two-sided. Analyses were performed using SAS software, version 9.1 (SAS Institute, Cary, NC).

RESULTS

Patient, disease, graft transport and transplant characteristics are shown in Table 1. Donor high resolution HLA typing (HLA A, B, C and DRB1) were available for 55% of the study population, these data generated by the NMDP's high resolution HLA typing project. For the remaining 45%, HLA data as submitted by transplant centers were used. The classification of donor-recipient HLA compatibility used here-in follows published NMDP guidelines (14). BM transplantations occurred at 115 transplant centers and PBPC transplantations at 89 centers. Five hundred and seven patients received PBPC grafts and transplantations occurred at 80 transplant centers.

Bone marrow grafts

BM grafts were collected at 93 centers in the U.S. and at 14 international locations. All BM grafts involved a single collection. Sixty-one grafts were transported from an international collection center to a U.S. transplant center and 49, from a U.S. collection center to an international transplant center (12% of BM grafts involved international transport). Median

time from end of collection to receipt at transplant center for domestic collection was 9 hours (range <1–47). Median time for international transport was longer at 19 hours (range 9–40). Sixty percent of grafts (n=564) were manipulated for donor-recipient ABO incompatibility. Median time from receipt at transplant center to infusion was 3 hours (range <1–45). The median cell doses prior to shipping from the collection center and receipt at transplant center were 3.8×10^8/kg (range < 1.0–35.5) and 3.6×10^8/kg (range < 1.0–28.6). The cell concentration of almost all of the BM grafts (99%) at collection and shipping was $\leq 5.0 \times 10^7$/ml.

Neutrophil and platelet recovery—Neither the interval from end of collection to receipt at transplant center or from receipt at transplant center to infusion was associated with neutrophil recovery (Table 2A). In contrast, the probability of platelet recovery was lower when interval from end of collection to receipt at transplant center was ≥ 20 hours and when receipt at transplant center to infusion was ≥ 6 hours, adjusted for other significant factors (Table 3A). This effect was independent of cell dose and graft manipulation for donor-recipient ABO incompatibility. Secondary graft failure rate was 9%; a third of graft failures were associated with recurrent leukemia.

Overall mortality—Four hundred and thirty-one of 938 BM recipients are alive with a 1-year probability of overall survival of 58% (95% CI 55–62%). Early mortality (day-100) rates were not associated with interval from end of collection to receipt at transplant center (OR 1.31, 95% CI 0.69–2.50, p=0.413) or from receipt at transplant center to infusion (OR 1.37, 95% CI 0.96–1.95, p=0.087). However, overall mortality was higher when the interval from end of collection to receipt at transplant center of an HLA-matched BM graft was ≥ 20 hours (Table 4A). Mortality rates after mismatched BM transplants were not associated with the interval from end of collection to receipt at transplant center. The interval from receipt at transplant center to infusion was not associated with mortality after either matched or mismatched BM transplants.

We also examined the time from end of collection to infusion (the sum of transport time and time from receipt at transplant center to infusion). After adjusting for significant factors (disease status at transplantation, donor-recipient HLA disparity and year of transplant), patients (n=813) who received BM grafts within 26 hours of collection had a significantly lower rate of mortality compared to those (n=125) who received their BM graft beyond 26 hours from end of collection (RR 0.66, 95% CI 0.52–0.84, p<0.001). Among the grafts that travelled for <20 hours or were infused <6 hours after receipt we did not identify a shorter interval that conferred a survival advantage.

Peripheral blood progenitor cells

Collection of PBPC occurred at 89 centers; 81 U.S. centers and the remaining 8 at international locations. Forty-one grafts were collected at an international collection center and transported to the U.S. and 22 were collected in the U.S and transported to an international transplant center (12% of PBPC grafts involved international transport). Two hundred and eleven (42%) PBPC collections involved a single collection and 296 (58%), two collections. When a donor had to be collected twice, products from days 1 and 2 were shipped at the end of the second collection. Median time from end of collection to receipt at transplant center for domestic collection was 10 hours (range < 1–32). Transport time was longer with international transport, 32 hours (range 7–45). Ninety seven (19%) PBPC grafts were manipulated for donor-recipient ABO incompatibility and none CD34 selected. Median time from receipt at transplant center to infusion was 3 hours (range < 1–39). The median cell doses prior to shipping from the collection center and receipt at transplant center were 7.5×10^8/kg (range < 1.0–68.3) and 7.5×10^8/kg

(range < 1.0–53.3). The cell concentration of all PBPC grafts at collection and shipping was $\leq 5.0 \times 10^8$/ml.

Neutrophil and platelet recovery—Neither the interval from end of collection to receipt at transplant center nor interval from receipt at transplant center to infusion was associated with hematopoietic recovery after PBPC transplants (Table 2B, 3B). Seven percent of patients developed secondary graft failure; a third of failures were associated with recurrent leukemia.

Overall mortality—Two hundred and nine of 507 PBPC recipients are alive with a 1-year probability of overall survival of 57% (95% CI 53–61%). Early mortality was not associated with the interval from end to collection to receipt at transplant center (OR 0.88, 95% CI 0.44–1.75, p=0.711) or from receipt at transplant center to infusion (OR 0.98, 95% CI 0.59–1.62, p=0.932). Overall mortality was not associated with transport time or from receipt at transplant center to infusion (Table 4B). Overall mortality was also not associated with time from end of collection to infusion (the sum of transport time and time from receipt at transplant center to infusion). In subset analysis we examined survival after transplantation of PBPC grafts from a single collection and did not find an association between transport time or interval from receipt at transplant center to infusion.

DISCUSSION

This retrospective study using an observational database is one of the first investigations on the impact of long distance transport of a cellular component, such as hematopoietic stem cells, on patient outcomes. For a long time, platelet concentrates have been obtained for thrombocytopenic recipients at specialized blood collection centers and effectively shipped to remote distances by adhering to the Federal Regulatory codes for transportation of this product. (15,16) Few studies and surveys have been published that address collection, storage, processing, and transport of hematopoietic cells. Lazarus and colleagues (17) have shown that autologous hematopoietic stem cells can be stored at 4°C overnight prior to CD34 cell selection, without affecting engraftment or survival. Thus far, no investigators have addressed transport of BM and PBPC grafts from volunteer unrelated donors and correlated with transplant-outcomes (18–24) although Lioznov and co-workers (25) recently reported in a small series that unrelated donor PBPC grafts transported and then frozen were associated with impaired function and engraftment after thawing and infusion.

Our study involved nearly 200 stem cell collection facilities and transplant centers scattered nationally and internationally for almost 1500 unrelated donor transplant procedures. Hematopoietic recovery after PBPC transplants was not affected by transport times. For BM grafts, a longer interval from end of collection of product to infusion was associated with lower likelihoods of platelet recovery but not neutrophil recovery, after adjusting for other factors that influence platelet recovery. A possible explanation in the observed difference between BM and PBPC transplants could be the cell dose of the graft. The nucleated cell dose of PBPC grafts are approximately one log higher than that of BM and the additional cells may have minimized any adverse impact of transport times on platelet viability. It is possible that at ambient temperature, at which most BM grafts were transported, cellular metabolism is raised with accumulation of by-products potentially adversely affecting cell viability. Only 7% of BM grafts (n=64) were refrigerated but without monitoring of temperature during transportation. Small numbers and absence of documentation of temperature during transport prevented us from examining for an effect of temperature on transplant-outcomes. Transport temperatures were not monitored for PBPC grafts either. However, minimal cell losses as measured by consistency in cell concentration before and after shipment for both graft types were documented.

Mortality rates after HLA-matched BM transplants were higher when these grafts took longer than 20 hours to arrive at the transplant center after its collection. Longer transport times, in general, were noted predominantly when grafts were transported to or from locations outside of the U.S. The observed higher mortality in the 22 patients with good risk leukemia and allele-matched donors but longer graft transport times in this analysis must be validated in a larger cohort. Our inability to observe an association between transport time and mortality after HLA-mismatched BM transplants may be explained by the fact that donor-recipient HLA disparity is a key determinant for a successful outcome after unrelated donor transplantation. Mortality rates are high after HLA-mismatched transplants and consequently any effect of longer transit time of the graft may be obscured.[5] Nevertheless, time from collection to receipt at transplant center and from receipt to infusion should be minimized for BM grafts. Manipulation of BM or PBPC grafts for ABO incompatibility was not associated with hematopoietic recovery or mortality rates. Transport times or the interval from receipt at transplant center to infusion were not associated with acute or chronic GVHD (data not shown).

This analysis has several limitations: 1) data on cell viability and sterility were not collected during the study period and 2) total nucleated cell doses reported were obtained from the collection and transplant centers and were subject to use of variable methods. Clearly future studies on the impact of transport time need to collect more detailed data on cellular composition and sterility at collection and receipt at the transplant center. In such investigations, continuous temperature monitoring may be an important maneuver; in our report nearly all BM grafts were transported at ambient temperature while the vast majority of PBPC products were refrigerated during shipping. The ongoing prospective, randomized Blood & Marrow Transplant Clinical Trials Network (BMT CTN) trial 0201 comparing unrelated BM versus PBPC transplants prescribes that both products be transported at 2–8°C. The United Network for Organ Sharing (UNOS) policy requires that all organs and tissue typing materials be transported at 2–8°C.

Despite these limitations, this is the first attempt to examine BM and PBPC transport time and its impact on outcome after unrelated donor HCT. Prolonged transport times were primarily though not exclusively associated with international transport. It is important to note that 30% of grafts with a prolonged transport time also had a delay to infusion of longer than 6 hours after receipt at the transplant center. Delays encountered at transplant centers are not readily explained by graft processing as only a third of manipulated grafts were infused ≥6 hours after their receipt at the center. The findings of this analysis suggest for BM grafts, delays in transport and delays at the transplant center are important and review of current practices is encouraged. While transport times for BM grafts influence transplant outcomes, selection of an unrelated donor should be dictated by the most suitably matched donor regardless of geographic location of the donor/collection center with care taken to minimize delays during transport and at the transplant center.

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Table 1

Patient, disease and transplant characteristics

	Bone marrow	Peripheral blood
Variables	**Number (%)**	**Number (%)**
Total number	938	507
Sex, male	539 (57)	288 (57)
Recipient age		
< 18 years	284 (30)	80 (16)
≥ 18 years	654 (70)	427 (84)
Performance score		
90–100	705 (75)	356 (70)
< 90	139 (15)	97 (19)
Unknown	94 (10)	54 (11)
Disease		
Acute myeloid leukemia	315 (34)	220 (43)
Acute lymphoblastic leukemia	309 (33)	160 (32)
Chronic myeloid leukemia	281 (30)	88 (17)
Myelodysplastic syndrome	33 (4)	39 (8)
Disease status		
First clinical remission or chronic phase or refractory anemia	534 (57)	312 (62)
Second clinical remission or chronic phase	404 (43)	195 (38)
Collection center		
Domestic	877 (93)	466 (92)
International	61 (7)	41 (8)
Total nucleated cell dose at end of collection		
$< 3 \times 10^8$/kg	234 (25)	16 (3)
$\geq 3 \times 10^8$/kg	699 (75)	478 (94)
Unknown	5 (<1)	13 (3)
Time from end of collection to receipt at transplant center		
<5 hours	69 (7)	31 (6)
5–9 hours	470 (50)	206 (41)
10–19 hours	345 (37)	205 (40)
≥20 hours	54 (6)	65 (13)
Temperature of graft during shipping		
Ambient	874 (93)	10 (2)
Refrigerated	64 (7)	496 (98)
Total nucleated cell dose at receipt at transplant center		
$< 3 \times 10^8$/kg	291 (31)	20(4)
$\geq 3 \times 10^8$/kg	641 (68)	446 (88)
Unknown	6 (<1)	41 (8)
Manipulation of graft prior to infusion		
None	374 (40)	409 (81)
ABO incompatibility	564 (60)	97 (19)

	Bone marrow	Peripheral blood
Variables	**Number (%)**	**Number (%)**
Unknown		1 (<1)
Time from receipt at transplant center to infusion into patient		
<3 hours	421 (45)	269 (53)
3–5 hours	283 (30)	102 (20)
6–9 hours	55 (6)	26 (5)
≥ 10 hours	179 (19)	110 (22)
Total transport time, median (range) hours	14 (3–51)	15 (2–55)
Donor age		
18–30 years	344 (37)	163 (32)
31–40 years	342 (36)	189 (37)
41–60 years	252 (27)	155 (31)
Donor-recipient cytomegalovirus serostatus		
Donor (−)/recipient (−)	302 (32)	160 (32)
Donor (−)/recipient (+)	257 (27)	161 (32)
Donor (+)/recipient (−)	151 (16)	67 (13)
Donor (+)/recipient (+)	210 (22)	103 (20)
Unknown	18 (2)	16 (3)
Donor-recipient sex match		
Male donor → male recipient	351 (37)	188 (37)
Male donor → female recipient	222 (24)	118 (23)
Female donor → male recipient	188 (20)	100 (20)
Female donor → female recipient	177 (19)	101 (20)
Donor-recipient ABO match		
Matched	386 (41)	194 (38)
Minor mismatch	248 (26)	131 (26)
Major mismatch	227 (24)	139 (27)
Bi-directional	65 (7)	42 (8)
Unknown	12 (1)	1 (<1)
Donor-recipient HLA match[†]		
Well matched	516 (55)	334 (66)
Partially matched	297 (32)	119 (23)
Mismatched	125 (13)	54 (11)
Conditioning regimen		
Cyclophosphamide + total body irradiation	694 (74)	333 (66)
Total body irradiation + other	19 (2)	29 (6)
Cyclophosphamide + busulfan	193 (21)	126 (25)
Busulfan + fludarabine +antithymocyte globulin	21 (2)	12 (2)
Busulafan + cytosine arabinoside	1 (<1)	___
Melphalan + fludarabine +antithymocyte globulin	10 (1)	7 (1)
Graft-versus-host disease prophylaxis		

	Bone marrow	Peripheral blood
Variables	**Number (%)**	**Number (%)**
Tacrolimus ± other	378 (40)	246 (49)
Cyclosporine ± other	560 (60)	261 (51)
Year of transplant		
2000–2002	606 (65)	202 (40)
2003–2004	332 (35)	305 (60)
Follow up of surviving patients, median (range) months	48 (6–85)	36 (3–76)

† Well-matched includes: 8/8 allele-level matched(BM n=355, PBPC n=244); allele-level matched A, B, DRB1 and low resolution matched at HLA-C (BM n=31, PBPC n=15); low resolution matched at A, B and C and allele-level DRB1 (BM n=126, PBPC n=69); allele-level matched at A, B, DRB1, and HLA-C unknown (BM n=4, PBPC n=6)

Partially matched includes: single locus antigen or allele-level MM at A, B, C or DRB1 (BM n=238, PBPC n=108); matched at low resolution A, B, C and DRB1(BM n=2, PBPC n=3); 1 allele mismatch at high-res A, B and DRB1 and HLA-C unknown (BM n=1); matched at low resolution A, B and high resolution DRB1 and HLA-C unknown (BM n=56, PBPC n=8)

Mismatched includes: >1 allele or antigen MM at A, B, C, DRB1 (BM n=111, PBPC n=48); 1 antigen MM when low resolution available at A, B, C, DR (BM n=1, PBPC n=1); 1 antigen or ≥2 allele mismatch at high-res A, B, DRB1, and HLA-C unknown (BM n=3); 1 mismatch at low resolution A, B, high resolution at DRB1 and HLA-C unknown (BM n=10, PBPC n=3); Matched at low-res A, B, DRB1, and HLA-C unknown (PBPC n=2).

Table 2

Table 2A. Probability of neutrophil recovery at 28 days after BM transplants

Variables	N	Odds ratio for recovery (95% Confidence Interval)	P-value
Time from end of collection to receipt, hours			
< 20	880	1.00	
≥20	53	0.55 (0.22–1.34)	0.186
Time from receipt to infusion, hours			
< 6	699	1.00	
≥6	234	0.90 (0.50–1.60)	0.711
Total nucleated cell dose at end of collection			
$< 3 \times 10^8$/kg	234	1.00	
$\geq 3 \times 10^8$/kg	699	2.24 (1.32–3.78)	0.003

Table 2B. Probability of neutrophil recovery at 28 days after PBPC transplants

Variables	N	Odds ratio for recovery (95% Confidence Interval)	P-value
Time from end of collection to receipt, hours			
< 20	442	1.00	
≥20	65	0.36 (0.13–0.95)	0.039
Time from receipt to infusion, hours			
< 6	371	1.00	
≥6	136	0.59 (0.24–1.46)	0.257

Table 3

Table 3A. Probability of platelet recovery at 60 days after BM transplants

Variables	N	Odds ratio for recovery (95% Confidence Interval)	P-value
Time from end of collection to receipt, hours			
< 20	883	1.00	
≥20	54	0.47 (0.26–0.83)	0.010
Time from receipt to infusion, hours			
< 6	703	1.00	
≥6	234	0.57 (0.41–0.80)	0.001
Performance score			
90–100	705	1.00	<0.001[a]
< 90	139	0.42 (0.28–0.62)	<0.001
Unknown	93	0.72 (0.43–1.22)	0.221
Year of transplant			
2003 – 2004	331	1.00	
2000 – 2002	606	0.57 (0.40–0.79)	<0.001

Table 3B. Probability of platelet recovery at 60 days after PBPC transplants

Variables	N	Odds ratio for recovery (95% Confidence Interval)	P-value
Time from end of collection to receipt, hours			
< 20	441	1.00	
≥20	65	0.68 (0.36–1.29)	0.235
Time from receipt to infusion, hours			
< 6	370	1.00	
≥6	136	0.59 (0.36–0.97)	0.036
Donor-recipient HLA disparity			
Well matched	333	1.00	
Partially matched or mismatched	173	0.50 (0.31–0.79)	0.003

[a] 2-degree freedom test

Table 4

Table 4A Risk factors for overall mortality after BM transplants

Variables	N	Relative Risk (95% Confidence Interval)	P-value
Time from receipt to infusion, hours			
< 6	704	1.00	
≥ 6	234	1.18 (0.97–1.44)	0.107
Donor recipient HLA disparity and time from collection to receipt, hours*			
Well matched, < 20 hours	494	1.00	
Well matched, ≥ 20 hours	22	2.67 (1.64–4.35)	<0.001
Partially matched/mismatched, < 20 hours	390	1.00	
Partially matched/mismatched, ≥ 20 hours	32	0.88 (0.55–1.43)	0.611
Disease and disease status*			
CML 1st chronic phase	223	1.00	
AML 1st clinical remission	153	2.06 (1.54–2.76)	0.001
ALL 1st clinical remission	125	1.58 (1.15–2.18)	0.005
MDS refractory anemia	33	1.75 (1.05–2.92)	0.033
CML 2nd chronic phase	58	1.00	
AML 2nd clinical remission	162	0.72 (0.50–1.05)	0.091
ALL 2nd clinical remission	184	0.81 (0.56–1.16)	0.245
Year of transplant			
2003–2004	332	1.00	
2000–2002	606	1.51 (1.23–1.84)	<0.001

Table 4B Risk factors for overall mortality after PBPC transplants

Variables	N	Relative Risk (95% Confidence Interval)	P-value
Time from end of collection to receipt, hours			
< 20	441	1.00	
≥ 20	65	0.95 (0.67–1.34)	0.751
Time from receipt to infusion, hours			
< 6	371	1.00	
≥ 6	135	0.92 (0.71–1.19)	0.532
Manipulation for ABO incompatibility			
None	409	1.00	
Yes	97	1.48 (1.12–1.95)	0.005

*First order interaction