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# Mobilization and engraftment of peripheral blood stem cells in healthy related donors >55 years old

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**Abstract**

*Background aims.* The increasing scarcity of young related donors has led to the use of older donors for related allogeneic hematopoietic stem cell transplantation (HSCT). This study analyzed the influence of age on the results of mobilization of peripheral blood stem cells (PBSCs) in healthy donors as well as on the engraftment and outcome of HSCT. *Methods.* A retrospective analysis from a single center was performed comparing the results of PBSC mobilization from related healthy donors according to their age. *Results.* The study included 133 consecutive related donors. The median age was 50 years (range, 4–77 years); 70 (53%) donors were males, and 44 (33%) were >55 years old. All donors were mobilized with granulocyte colony-stimulating factor for 5 days. The peak $CD34^+$ cell count in peripheral blood was higher in younger than in older donors (median, 90.5 $CD34^+$ cells/μL [range, 18–240 $CD34^+$ cells/μL] versus 72 $CD34^+$ cells/μL [range, 20–172.5 $CD34^+$ cells/μL], $P = 0.008$). The volume processed was lower in younger than in older donors (16,131 mL [range, 4424–36,906 mL] versus 18,653 mL [range, 10,003–26,261 mL], $P = 0.002$) with similar $CD34^+$ cells collected ($579.3 \times 10^6$ cells [range, $135.14 \times 10^6$–$1557.24 \times 10^6$ cells] versus $513.69 \times 10^6$ cells [range, $149.81 \times 10^6$–$1290 \times 10^6$ cells], $P = 0.844$). There were no differences in time to recovery of neutrophils and platelets or in the incidences of acute and chronic graft-versus-host disease, overall survival, non-relapse mortality and relapse incidence. *Conclusions.* Donors >55 years old mobilized fewer $CD34^+$ cells and required a greater volume to collect a similar number of $CD34^+$ cells. The outcome of HSCT was not influenced by donor age. Donor age should not be a limitation for related allogeneic HSCT.

**Key Words:** *mobilization, old related donors, stem cell transplantation*

## Introduction

Intensive treatments for hematologic malignancies including hematopoietic stem cell transplantation (HSCT) are increasingly employed in elderly patients. Consequently, the probability of finding a related donor decreases, and the donors themselves are frequently old. This situation raises the question of the use of old related donors versus young unrelated donors (1,2). It has been suggested that old donors have more complications during the apheresis process, a lower probability of achievement of the desired number of cells collected, and worse engraftment of the apheresis product in the recipients (3).

The use of peripheral blood stem cells (PBSCs) in apheresis procedures is safe and well tolerated (4–6) and allows old donors to be used as related donors. However, the influence of donor age on HSCT outcomes, such as engraftment, acute and chronic graft-versus-host disease (GVHD), non-relapse mortality (NRM), relapse incidence (RI) and overall survival (OS), has not been extensively studied. The objective of this study was to analyze the influence of age of healthy donors on the results of mobilization and apheresis of PBSCs as well as on the main outcomes of HSCT.

## Methods

From 2001–2012, 133 consecutive healthy donors were referred to our transplant unit to undergo

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mobilization and apheresis of PBSCs for related HSCT. For this retrospective study, donors were divided into two groups according to age: young (≤55 years old) and old (>55 years old). The reasons for choosing this age cut-off (≤55 years vs >55 years) were as follows: (i) this is the upper age limit for selecting unrelated bone marrow donors, and (ii) this age cut-off was used in other similar studies. All donors and recipients provided written consent on use of their data for scientific studies. Demographic and mobilization and apheresis characteristics from all donors were collected. In recipients, demographic data, baseline disease, time to engraftment, HSCT complications, and outcomes were also studied.

### *Mobilization and apheresis*

Donors were mobilized with recombinant human granulocyte colony-stimulating factor (G-CSF) (filgrastim; Amgen, Inc., Thousand Oaks, CA, USA) with subcutaneous doses of 10 μg/kg twice daily for 5 days if the donor weight was less than the patient weight or 5 μg/kg twice daily for 5 days if the donor weight was more than the patient weight. $CD34^+$ cell measurements in peripheral blood (PB) were performed during mobilization with a single-platform method, using an EPICS XL-MCL flow cytometer (Beckman-Coulter, IZASA, Barcelona, Spain) following the International Society of Hematotherapy and Graft Engineering (ISHAGE) guidelines (7). Monoclonal antibodies against CD34 [Phycoerythrin (PE)] clone 581, CD45 (fluorescein isothiocyanate) clone J33 and Flow Count Fluorospheres were purchased from Immunotech (Beckman Coulter, IZASA). The $CD34^+$ cell count in PB was obtained on day 5 after the onset of mobilization. The minimum threshold of $CD34^+$ cell count to perform leukapheresis was established at 5/μL (8).

Collection of PBSCs was carried out with a COBE Spectra Blood Cell Separator (CaridianBCT, Inc., Lakewood, CO, USA). Large-volume leukapheresis were performed in all cases. The $CD34^+$ cell count in the leukapheresis product was also evaluated by flow cytometry using the same method described earlier. The target of mobilization was to achieve at least $4 \times 10^6$ $CD34^+$ cells/kg recipient body weight (BW). The leukapheresis product was cryopreserved in nitrogen until infusion.

### *Engraftment, GVHD and outcome of recipients*

Time to neutrophil engraftment was defined as the first of 3 consecutive days with an absolute neutrophil count $>0.5 \times 10^9$/L after infusion. Platelet engraftment was considered as the first of 3 consecutive days with $>20 \times 10^9$/L without platelet transfusion. In all recipients, the presence of acute or chronic GVHD was recorded. Diagnosis was made by clinical criteria and confirmed by biopsy when possible. Acute and chronic GVHD was classified according to previously published criteria (9,10). HSCT outcomes included OS (defined as time from start of treatment to death, regardless of the cause), NRM (defined as time to death from any cause without relapse or recurrence) and RI (defined as time from HSCT to relapse).

### *Statistical analysis*

Baseline and disease characteristics were described for the whole series and for both groups of donors. Bivariate tests (Student's *t*-test, Mann-Whitney *U* test or median test when appropriate) were used for comparison of quantitative variables, and $\chi^2$ or Fisher exact test was used for categorical variables. The correlation between variables was performed with the Spearman ρ coefficient. Actuarial survival probabilities were estimated with the Kaplan-Meier method (11) and were compared with the log-rank test (12). A competing risk analysis was performed to estimate the cumulative incidence of relapse and NRM. For relapse, death without relapse was the competing event, and for NRM, relapse was the competing event. The Gray test was used for group comparison of cumulative incidences (13). All statistical analyses were carried out using the SPSS (Statistical Package for Social Sciences) package version 15.0 for Windows (IBM, Somers, NY, USA). Cumulative incidence with competing risk was performed in R software version 2.12.2 (Comprehensive R Archive Network [cran.r-project.org]).

## Results

From 2001–2012, 133 donors were referred to our transplant unit to undergo mobilization and apheresis of PBSCs for a related HSCT. The median donor age was 50 years (range, 4–77 years); 44 (33%) donors were >55 years old, and 89 (67%) donors were ≤55 years old. Of the donors, 70 (53%) donors were male.

The main characteristics of the recipients are shown in Table I. The median age of the recipients was 51 years old (range, 15–70 years old), and 72 (54%) were male. Donor and recipient ages were correlated ($\rho = 0.787$, $P = 0.001$). Diseases of recipients were comparable in both groups ($P = 0.593$). Acute myeloid leukemia was the most frequent indication for allogeneic HSCT. The donor was a human leukocyte antigen-matched sibling in 130 HSCTs and a parent in the 3 remaining cases. Recipients from donors ≤55 years old more frequently received myeloablative conditioning regimens