Transfusion Medicine and Hemotherapy

Research Article

Transfus Med Hemother
DOI: 10.1159/000531236

Received: February 24, 2023
Accepted: May 18, 2023
Published online: June 30, 2023

Predicting Successful Hematopoietic Stem Cell Collection in Healthy Allogeneic Donors

Sabine Kayser[a, b] Richard F. Schlenk[b] Marcus Steiner[a] Harald Klüter[a] Patrick Wuchter[a]

[a]Institute of Transfusion Medicine and Immunology, Medical Faculty Mannheim, Heidelberg University; German Red Cross Blood Service Baden-Württemberg – Hessen, Mannheim, Germany; [b]NCT Trial Center, National Center of Tumor Diseases, German Cancer Research Center (DKFZ), Heidelberg, Germany

Keywords

Hematopoietic stem cell mobilization · Peripheral blood stem cells · Allogeneic donors · Efficacy · Apheresis

Abstract

Introduction: Collection of peripheral blood stem cells (PBSCs) from healthy donors is a well-established process. We aimed to identify factors predictive of successful CD34+ PBSC collection and established a formula capable of predicting CD34+ cell yield. ***Methods:*** We retrospectively evaluated 588 healthy adult donors (median age 29 years, range 18–69 years) at our institution from 2017 to 2022. The predicted minimal number of CD34+ cells was calculated as follows: (peripheral CD34+ cells/μL × adjusted collection efficiency of 30%) × total liters processed. This formula was further modified according to donor and recipient body weight (BW). ***Results:*** Median total collection was 8.0×10^6 CD34+ cells/kg BW (range $1.0–47.1 \times 10^6$ cells/kg BW) with 522 donors (89%) collecting $\geq 5.0 \times 10^6$ cells/kg of recipient BW. A second leukapheresis (LP) was performed in 49 donors. Need for two LPs was more common in female donors (OR 6.68, 95% CI, 2.62–17.05; $p < 0.001$), donors with higher age (OR for 10 years difference 1.53, 95% CI, 1.15–2.03, $p = 0.003$), donors with WBC count $<30 \times 10^9$/L after 5 days of granulocyte-colony stimulating factor (G-CSF) stimulation (OR, 4.33; 95% CI, 1.59–11.83; $p = 0.004$), and a donor/recipient weight ratio <1 (OR 6.21, 95% CI, 2.69–14.34; $p < 0.001$). Predictive factors for optimal LP (i.e., $\geq 5.0 \times 10^6$ CD34+ cells/kg of recipient BW) were peripheral blood (PB) CD34+ cell count >50/μL (OR 12.82, range 6.34–25.92, $p < 0.001$), male donor (OR 2.77, range 1.06–7.23, $p = 0.04$), and a donor/recipient weight ratio >1 (OR 3.12, range 1.57–6.24, $p = 0.001$). WBC, platelets, hemoglobin, and age had no significant predictive value. Predicted versus observed number of CD34+ cells/kg BW collected demonstrated a very strong linear correlation ($r = 0.925$, 95% CI, 0.912–0.936, $p < 0.0001$). ***Conclusions:*** Of the routinely monitored indicators in PBSC donors, CD34+ cell count in PB is the most important factor in predicting G-CSF-induced PBSC yields. Higher age, female sex, WBC $<30 \times 10^9$/L, and a donor/recipient weight ratio <1 are useful indicators for identifying suboptimal mobilizers. The modified formula has shown successful and consistent performance in the prediction of key outcome measures including the minimum CD34+ cell collection, determination of the required length of apheresis, and whether a second day of PBSC collection was necessary to achieve the respective collection goal.

Introduction

Collection of peripheral blood stem cells (PBSCs) after stimulation with granulocyte-colony stimulating factor (G-CSF) for allogeneic hematopoietic stem cell

karger@karger.com
www.karger.com/tmh

Correspondence to:
Sabine Kayser, sabine.kayser@medma.uni-heidelberg.de

transplantation is a routine procedure worldwide that has replaced bone marrow as the major source for allogeneic hematopoietic stem cell transplantation [1–4]. The required minimum cellular content is still a matter of debate. Depending on patient's diagnosis and the type of transplant, a minimum of $\geq 3 \times 10^6$ CD34+ cells/kg body weight (BW) is commonly warranted [5]. However, the European Society for Blood and Marrow Transplantation recommends a minimum of $>4.0 \times 10^6$ CD34+ cells/kg BW for hematological diseases to guarantee timely engraftment and thus successful PBSC transplantation [6]. Since the SARS-CoV-2 pandemic in 2020, transplant centers have regularly requested even higher PBSC transplant doses of $>5.0 \times 10^6$ CD34+ cells/kg BW as a precautionary measure, most likely due to the many unknowns presented during this time (e.g., possibility of further collections, shortage of collection kits). Additionally, a larger proportion of products were cryopreserved than before. In terms of donor safety, it is important to limit the duration and number of leukapheresis (LP) sessions to a minimum, particularly in view of ever-growing requested PBSC numbers. Thus, predictive factors for sufficient mobilization are highly desirable, and a benchmarking system would provide significant value as a mean to ensure both consistent and realistic PBSC collection outcomes for LP events. Regarding PBSC collection, several groups have proposed formulas to predict daily CD34+ cell yields for PBSC products based on parameters such as peripheral CD34+ count and patient blood volume to be processed [7–11]. The collection efficiency coefficient, abbreviated interchangeably as either CEC or CE2, varies from 30% to 50% and depends on the automatic LP system used, the skills of the operators, and the peripheral vein conditions of the donor [11]. The number of CD34+ cells in peripheral blood (PB) is highly predictive for a successful PBSC collection. A variety of additional factors that might influence the PBSC mobilization and collection process have been described, such as biological sex, donor age, and weight, as well as WBC count [11–18]. Nevertheless, studies evaluating predictive factors of successful PBSC collection in healthy donors are scarce. Furthermore, a major challenge that remains is balancing the PBSC collection goal with precollection planning aimed to minimize duration and number of procedures – an effort intended to avoid side effects, particularly those induced by anticoagulation.

Thus, our study aimed to identify factors predictive of successful CD34+ collection. In addition, we propose a refined formula that predicted the minimal CD34+ cell yield and took the donor's and the recipient's BW into account.

Methods

Donor Selection and LP Procedure

Approximately 3 weeks prior to the scheduled collection day, donors were evaluated at our center by trained physicians to determine if donors were suitable candidates for PBSC collection. Donors were required to fulfill German guidelines for hemotherapy (apheresis subsections) [19]. If the peripheral vein status of a donor was judged to be insufficient for a successful LP during the qualification visit, the donor was also excluded from PBSC collection. All donors provided written informed consent, including data collection.

G-CSF (filgrastim) was administered subcutaneously on five consecutive days of the donor, and HSPC was collected via a peripheral venous catheter on the fifth day. Filgrastim dosing is outlined in Table 1. Complete blood cell counts were performed on donors immediately pre- and post-LP using the Sysmex XN-350 automated hematology analyzer (Sysmex GmbH, Norderstedt, Germany). CD34+ cells in PB and collected products were measured by flow cytometry (Becton Dickinson, FACSLyric system, USA) using a protocol based on the guidelines of the International Society of Hematotherapy and Graft Engineering (ISHAGE) [20]. Leukapheresis was performed using a Spectra Optia® (Terumo BCT, Garching, Germany) apheresis machine using the cMNC program, software version 11.3. Collection time was restricted to a maximum of 5 h per LP session, as per German hemotherapy guidelines [19]. Acid-citrate-dextrose was used at an inlet ratio of 14:1, with an inlet flow rate of 40–100 mL/min. The requested number of CD34+ cells varied according to the TC from ≥ 4.0 to $\geq 5.0 \times 10^6$ CD34+ cells/kg BW. A sufficient PBSC collection was defined as $\geq 4.0 \times 10^6$ CD34+ cells/kg BW of the recipient (over no more than 2 LP sessions), whereas a PBSC collection of $\geq 5.0 \times 10^6$ CD34+ cells/kg BW of the recipient was regarded as optimal. No more than two consecutive LP sessions were allowed as per German hemotherapy guidelines [19].

Calcium was substituted orally as needed to prevent symptoms of hypocalcemia as common side effect of citrate. Calcium administration was switched to intravenous infusion, if necessary. Potassium was substituted orally, as needed.

Calculation of Performance Variables

We reviewed data from donors (age, biological sex, and BW), donor laboratory results (CD34+ cells in PB, WBC, hemoglobin, and platelets) before and after LP, recipient data (age and BW), and LP parameters for each LP session, including processed blood volume, collected volume of the product, and number of collected CD34+ cells/μL in the product. We also calculated the collection result (in CD34+ cells $\times 10^6$/kg BW of the recipient) as follows: ([CD34+ cells/μL in the product] × [collection volume of the product in mL] ÷ [BW of the donor in kg] ÷ 1,000).

To predict the minimal CD34+ cell number within the collection and to determine the required blood volume, we used the formula validated by Rosenbaum et al. [9] (2012): {([PB CD34+ cells/μL] × [adjusted CE2 of 30%]) ÷ [donor BW in kg]} × (processed blood volume in L). Since this formula was originally developed for autologous stem cell collection, we adopted it for the allogeneic setting by taking the BW of the recipient into account.

First Step

We calculated the CD34+ cells per kg BW of the donor/L PB (named *S1*) as follows:

S1 = (CD34+ cells per μL PB × CE2) ÷ BW of the donor in kg.

Table 1. Dosage of filgrastim according to BW of the donor

Body weight of the donor, kg	Filgrastim dosage subcutaneously	Dosage, µg/kg BW/day
50	48-0-0	9.6
51	48-0-0	9.4
52	48-0-0	9.2
53	48-0-0	9.1
54	48-0-0	8.9
55	48-0-0	8.7
56	48-0-0	8.6
57	30-0-30	10.5
58	30-0-30	10.3
59	30-0-30	10.2
60	30-0-30	10.0
61	30-0-30	9.8
62	30-0-30	9.7
63	30-0-30	9.5
64	30-0-30	9.4
65	30-0-30	9.2
66	30-0-30	9.1
67	30-0-30	9.0
68	30-0-30	8.8
69	30-0-30	8.7
70	30-0-30	8.6
71	48-0-30	11.0
72	48-0-30	10.8
73	48-0-30	10.7
74	48-0-30	10.5
75	48-0-30	10.4
76	48-0-30	10.3
77	48-0-30	10.1
78	48-0-30	10.0
79	48-0-30	9.9
80	48-0-30	9.8
81	48-0-30	9.6
82	48-0-30	9.5
83	48-0-30	9.4
83	48-0-30	9.3
85	48-0-30	9.2
86	48-0-30	9.1
87	48-0-30	9.0
88	48-0-30	8.9
89	48-0-30	8.8
90	48-0-30	8.7
91	48-0-30	8.6
92	48-0-48	10.4
93	48-0-48	10.3
94	48-0-48	10.2
95	48-0-48	10.1
96	48-0-48	10.0
>96	48-0-48	10.0

Second Step

We calculated the CD34+ cell yield per kg BW of the donor (in CD34+ cells/kg BW of the donor) (named *S2*) as follows:

$S2 = S1 \times$ processed blood volume in liters.

Third Step

We calculated the CD34+ cell yield per kg/BW of the recipient (in CD34+ cells/kg BW of the recipient) (named *S3*) as follows:

$S3 = (S2 \times$ BW of the donor in kg) ÷ BW of the recipient in kg.

This value ultimately predicts the number of collected CD34+ cells/kg BW of the recipient with a CE2 of 30% at a given processed blood volume.

Example

- BW of the donor: 60 kg
- BW of the recipient: 70 kg
- CD34+ cells in PB of the donor: 80/µL
- Processed blood volume: 15 L
- CE2: 30% = 0.3

Step 1: $S1 = ((80 \times 0.3) \div 60) = 0.4$ CD34+ cells $\times 10^6$ per kg BW of the donor/L PB

Step 2: $S2 = (S1 \times 15) = 6.0 \times 10^6$ CD34+ cells per kg BW of the donor

Step 3: $S3 = (S2 \times 60) \div 70 = 5.14 \times 10^6$ CD34+ cells per kg BW of the recipient

In this example, we would expect 5.14×10^6 CD34+ cells/kg BW of the recipient as yield.

As a matter of fact, using a CE2 of 30% delivers the expected minimum number of collected CD34+ cells. This means that in 95% of the cases, the actual CD34+ cell yield will be higher. In clinical reality, obtaining less than the desired minimum CD34+ cell yield presents a significant challenge for transplant, whereas exceeding the expected yield is never a problem. Thus, the rather low CE2 of 30% was intentionally used to ensure the expected yield would be achieved in the majority of cases. In addition, this formula was used to avoid unnecessary long LPs by calculating the required processed PB volume and adjusting it to the respective collection goal.

Upon completion of each LP procedure, the number of collected CD34+ cells were compared with the predicted number and a performance ratio (collected/predicted CD34+ cells in %) was calculated. In addition, the true collection efficiency (CE2 in %) of every LP session (in contrast to the assumed CE2 of 30% as described above) was calculated as follows: {([CD34+ concentration of the product/µL] × [collection volume of the product]) ÷ ([CD34+ cells/µL in PB] × [processed blood volume in L])} ÷ 10.

Statistical Analyses

Comparisons of donor characteristics were performed using the Kruskal-Wallis rank sum test for continuous variables and the Fisher's exact test for categorical variables. Unadjusted and adjusted analyses were conducted using logistic regression models to determine the association of covariates with binary outcome. Unadjusted and adjusted analyses were conducted using linear regression models to determine the association of covariates on a continuous outcome scale. Variables included WBC count, platelet count, hemoglobin level prior to apheresis, age and weight of the donor, as well as biological sex. Linear correlations were evaluated using the Pearson correlation coefficient (*r*). All statistical analyses were performed with the statistical software environment R, version 4.2.1, using the R packages rms, version 6.3.0 [21].

Results

Study Cohort

Data for 637 LP sessions from 588 healthy adult donors were collected from our center between 2017 and 2022. In 49 donors, a second LP was performed to achieve the target CD34+ cell count. Of the 588 donors, 125 donors (21%) were female. Median age of the donors was 29 years (range 18–69 years) with 80% being younger than 40 years of age (n = 471/588). The number of LPs

increased over time with $n = 40$ performed in 2017, $n = 60$ in 2018, $n = 51$ in 2019, $n = 152$ in 2020, $n = 148$ in 2021, and $n = 186$ in 2022. Baseline characteristics are summarized in Table 2.

In 539 (92%) donors, one LP session was sufficient to reach $\geq 4.0 \times 10^6$ CD34+ cells/kg BW, whereas $n = 49$ donors needed two LPs. In 495 (84%) donors $\geq 5.0 \times 10^6$ CD34+ cells/kg, BW were collected after one LP. The necessity of two LPs were more common in female donors (OR 6.68, 95% CI, 2.61–17.05, $p < 0.001$), donors with higher age (OR for 10 years difference 1.53, 95% CI, 1.15–2.03, $p = 0.003$), donors with WBC $<30 \times 10^9$/L after 5 days of G-CSF stimulation at the date of first apheresis (OR 4.33, 95% CI, 1.59–11.83, $p = 0.004$), and a weight ratio donor/recipient <1 (OR 6.21, 95% CI, 2.69–14.34, $p < 0.001$), whereas platelet count and hemoglobin level prior to apheresis had no significant impact.

Pre-LP Conditions and LP Variables

The minimal predicted CD34+ result and the processed blood volume required to reach the collection goal were calculated prior to each LP session based on the pre-LP CD34+ cell count in PB. Prior to first LP ($n = 588$), WBC, hemoglobin, platelet, and CD34+ counts in the PB were 44.3×10^9/L (range 9.5–92.7 $\times 10^9$/L), 14.7 g/dL (range 10.8–17.8 g/dL), 207×10^9/L (range 102–424 $\times 10^9$/L), and 83/μL (range 6.7–322/μL), respectively. In 49 donors, a second LP was necessary. Of those, WBC, hemoglobin, platelet, and CD34+ cell counts before second LP in the PB were 39.8×10^9/L (range, 18.9–58.7 $\times 10^9$/L), 13.3 g/dL (range 11–15.7 g/dL), 134×10^9/L (range, 80–213 $\times 10^9$/L), and 37.8/μL (range 14.2–74.0/μL). Overall, a cell count of ≥50 CD34+ cells/μL in PB could be achieved in $n = 481$ (76%) donors.

The median weight ratio of donor to recipient was 1.04 (range 0.49–19) with no correlation between weights ($p = 0.61$). Median PB CD34+ cell counts at first and second LP were 83.0/μL (range 6.7–322/μL, $n = 588$) and 37.8/μL (range 14.2–74/μL, $n = 49$), respectively. The median processed volume at first LP was 12 L (range 3.8–19.2 L) and was adapted after receipt of CD34+ cell counts in the PB as outlined above [9]. Shown by linear regression modeling (adjusted r^2, 0.41), processed volume during first LP was inversely correlated with CD34+ cells in PB (slope, −0.04; $p < 0.0001$), female donor (slope, −1.83; $p < 0.0001$), and positively correlated with donor weight (slope, 0.02; $p = 0.028$); neither WBC count ($p = 0.97$), platelet count ($p = 0.51$), hemoglobin level ($p = 0.51$) nor age ($p = 0.12$) were correlated with the processed volume. Median processed volume at second apheresis was 11 L (range 1.4–18.1 L).

LP Performance Assessment

Right in the first LP session, a product with $\geq 5.0 \times 10^6$ CD34+ cells/kg of the recipient's BW was collected in 495 of 588 donors (84%). This ratio did not vary among the year of apheresis ($p = 0.14$). In 49 of 93 (53%) donors with CD34+ cell collection below 5.0×10^6 CD34+ cells/kg, a second LP was performed on the next day after ongoing G-CSF stimulation. Of those, median CD34+ $\times 10^6$ cells/kg of recipient BW was 2.2 (range 0.3–5.3) and $n = 27$ achieved $\geq 5.0 \times 10^6$ CD34+ cells/kg of recipient BW if the CD34+ cell count totals of both LPs were combined. Of the remaining 22 of 49 donors having undergone two LPs, the total CD34+ $\times 10^6$ cells/kg of recipient BW was <5.0 and ≥4.0 in $n = 10$ – this cohort fell in the gray zone of what was regarded as the collection goal, as described above. The total CD34+ $\times 10^6$ cells/kg of recipient BW was <4.0 and ≥3.0 in $n = 8$, and <3.0 in $n = 4$ donors, respectively.

Of the remaining 44 donors having undergone one LP, $n = 32$ achieved products containing <5.0 and $\geq 4.0 \times 10^6$ CD34+ cells/kg of recipient BW, $n = 9$ products containing <4.0 and ≥3.0 and $n = 3$ products containing $<3.0 \times 10^6$ CD34+ cells/kg of recipient BW, respectively. Of the latter cases, only one product was transplanted, the other two products were discarded, and the recipients received HPSC from another donor. No cases of failure to engraft were reported.

Overall, median total collection result of the 588 donors was 8.0×10^6 CD34+ cells/kg (range 1.0–47.1 $\times 10^6$ cells/kg) with $n = 522$ (89%) donors collecting $\geq 5.0 \times 10^6$ CD34+ cells/kg of recipient BW (1 LP, $n = 495$; 2 LPs, $n = 27$). A logistic regression model again showed that low CD34+ harvest ($<5.0 \times 10^6$ cells/kg CD34+ of recipient BW) was associated with female sex (OR 2.77, range 1.06–7.23, $p = 0.04$), a weight ratio <1 (OR 3.12, range 1.57–6.24, $p = 0.001$), PB CD34+ cell count <50/μL (OR 12.82, range 6.34–25.92, $p < 0.001$), whereas WBC, platelets, hemoglobin, and age had no significant association.

Based on the collected and processed CD34+ cell count, a CE2 was calculated with a median of 59% (range 29–142%). In only one LP (0.2%), a CE2 below 30% was noted. Referring to the minimal predicted and the actual

Table 2. Baseline characteristics of 637 LPs from healthy donors ($n = 637$)

	n or value	% or range
Female sex	155	26
Median age, years	29	18–69
Peripheral blood values		
Median WBC, $\times 10^9$/L	43.9	9.5–92.7
Median platelets, $\times 10^9$/L	203	80–3,424
Median hemoglobin, g/dL	14.6	10.8–17.8

Results may not add up to 100 due to rounding. WBC, white blood cell count.

CD34+ cell collection result, a performance ratio was calculated that was 195% (range 98–473%). Predicted versus observed data showed a high correlation coefficient of 0.925 (95% CI, 0.912–0.936, $p < 0.0001$), demonstrating a very strong linear correlation (shown in Fig. 1).

Post-LP Conditions

After the first LP ($n = 588$), median hemoglobin and platelets declined marginally from 14.7 g/dL (range 10.8–17.8 g/dL) to 13.6 g/dL (range 9.7–17.2) and more pronounced from 207 × 10^9/L (range 102–424) to 135 × 10^9/L (range 60–290), respectively. In donors with a second LP ($n = 49$), median PB hemoglobin and platelets declined from 13.3 g/dL (range 11–15.7) to 12.2 g/dL (range 9.7–15.9) and from 134 × 10^9/L (range 80–213) to 94 × 10^9/L (range 60–183), respectively.

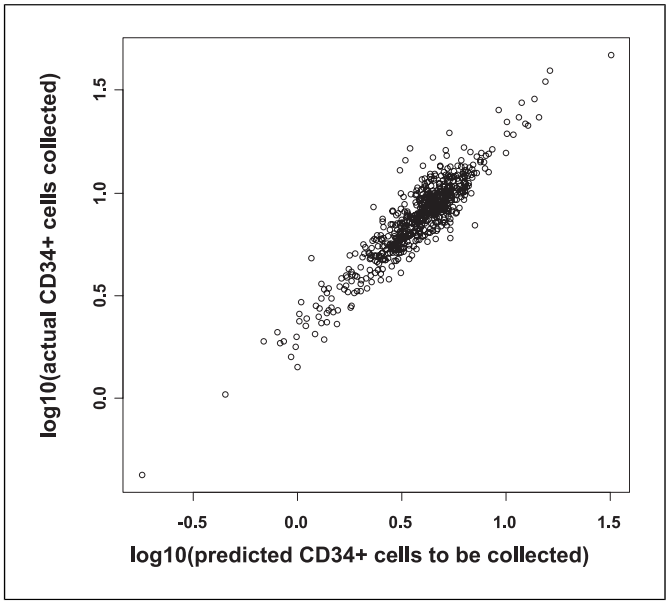

Fig. 1. Predicted versus actual collected CD34+ cells × 10^6/kg BW of the recipient in 588 LP sessions. Equation: log10(actual CD34+ cells collected) = 0.932 × [log10(predicted CD34+ cells to be collected)] − 0.237.

Discussion

The focus of our study was to determine predictive factors for successful CD34+ PBSC collection. We also validated for the first time a modified formula capable of predicting CD34+ cell yield in allogeneic donors that takes BW of the recipient into account [8–10]. In line with the data by de Almeida-Neto, a predictive factor of a successful CD34+ cell collection was >50/μL CD34+ cells in PB [11]. In accordance with other publications, additional predictive factors were male sex [11, 22–24] as well as a donor/recipient weight ratio of more than one [11]. In contrast, WBC was not a predictive factor, when accounting for CD34+ cells in PB [11]. Additional variables influencing G-CSF responsiveness might be related to genetic factors involved in migration and homing of CD34+ cells, such as VCAM1 [25]. Identification of risk factors associated with poor mobilization in healthy donors may help improve donor selection and develop strategies to ensure successful and efficient engraftment in recipients.

In the analyzed cohort, a sufficient number of CD34+ cells could be mobilized and collected in most cases with a G-CSF dosage of >8.5 to ≤11/kg BW/day as outlined in Table 1. Actually, mobilization failure with <2.0 × 10^6 CD34+ cells/kg BW occurred in only 0.45% of donors, which compares favorably to other data [26].

We could demonstrate that the number of predicted CD34+ cells by our formula and the actual number of CD34+ cells collected showed a very strong linear correlation. However, as we used our formula to predict the expected minimum CD34+ cells to be collected, we used a CE2 of only 30% [27] rather than 40% [28] since collecting an insufficient CD34+ stem cell product due to a shortened LP session based on yield overestimation would be detrimental. In contrast, collecting a higher number of CD34+ cells than predicted would be beneficial. Our rather conservative approach of setting the CE2 at 30% proved clinically translational, as only one LP in this study fell below 30%. This CE2 prevents premature stop of the LP collection in the overwhelming majority of procedures. The reliable prediction of the minimal CD34+ cells to be collected by our formula allowed to safely adjust the necessary total blood volume needed for the respective collection goal [27]. From the donor perspective, the use of the formula allowed to stop LP as soon as the predicted minimum cell number was reached. Moreover, our formula helped reduce the uncertainty regarding the need of a second LP session the following day. This represented an important measure to limit the strain of the donor. For transplant centers, a collection result that reached or exceeded the initial request could be achieved in most cases.

The stepwise calculation, as described above, was applied and documented on a regular basis in our institution since 2017. As a result, it allows an instant comparison of the collection yields over the years in relation to the donor BW (*S2*) and the recipient BW (*S3*). In addition, the performance ratio (collected/predicted CD34+ cells in %) allows a quantitative assessment of the efficacy of the individual LP run, thus providing an advanced benchmarking value for quality assurance [27]. These data can be obtained with very low effort and no costs, and represent a valuable tool to expedite measures of quality control and management including product quality reports etc. As a limiting factor, we did not collect data of baseline blood values measured prior to starting G-CSF, potentially limiting the identification of additional predictive factors not covered in this study, which might have an impact on the mobilization result.

In conclusion, the CD34+ cell count in PB is the most important factor in predicting G-CSF-induced PBSC yields. Higher age, female sex, WBC <30 × 10^9/L, and a donor/recipient weight ratio <1 are useful indicators for identifying poor mobilizers. The formula for predicting CD34+ cell yields allowed to determine the required duration of apheresis and whether a second LP session is necessary to achieve the collection goal. This is particularly important if collection time and resources may be limited (e.g., supply chain shortage during pandemics, social factors limiting a donor's ability to return for another collection etc). Thus, our innovative benchmarking system can be implemented easily and without costs and may serve as a blueprint for any stem cell collection center.

Acknowledgments

The authors are grateful for the altruistic generosity of all PBSC volunteer donors. The authors thank the laboratory technicians, the operators, and physicians of the apheresis unit at our Institute for providing excellent medical care to our donors, and the team of the German Stem Cell Donation registry (DSSD Mannheim) for long-term support and cooperation.

Statement of Ethics

The research was conducted ethically in accordance with the World Medical Association Declaration of Helsinki (https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/). All donors provided written informed consent for data collection. This retrospective review of patient data did not require ethical approval in accordance with local guidelines.

Conflict of Interest Statement

All authors declare no competing conflict of interest.

Funding Sources

Research funding was provided by the German Red Cross Blood Service Baden-Württemberg – Hessen, Mannheim, Germany.

Author Contributions

Sabine Kayser, Patrick Wuchter, and Richard F. Schlenk were responsible for the concept of this paper. Sabine Kayser and Richard F. Schlenk contributed to the literature search data collection, analyzed and interpreted data, and wrote the manuscript. Marcus Steiner, Harald Klüter, Sabine Kayser, and Patrick Wuchter contributed donors. Harald Klüter and Patrick Wuchter critically revised the manuscript. All authors reviewed and approved the final manuscript.

Data Availability Statement

Questions regarding data sharing should be addressed to the corresponding author.

References

1 Appelbaum FR. Hematopoietic-cell transplantation at 50. N Engl J Med. 2007;357(15):1472–5.
2 Ballen KK, King RJ, Chitphakdithai P, Bolan CD Jr, Agura E, Hartzman RJ, et al. The national marrow donor program 20 years of unrelated donor hematopoietic cell transplantation. Biol Blood Marrow Transplant. 2008;14(9 Suppl):2–7.
3 Karanes C, Nelson GO, Chitphakdithai P, Agura E, Ballen KK, Bolan CD, et al. Twenty years of unrelated donor hematopoietic cell transplantation for adult recipients facilitated by the National Marrow Donor Program. Biol Blood Marrow Transplant. 2008;14(9 Suppl):8–15.
4 Bolan CD, Hartzman RJ, Perry EH, Trainor L, Miller J, Miller R, et al. Donation activities and product integrity in unrelated donor allogeneic hematopoietic transplantation: experience of the National Marrow Donor Program. Biol Blood Marrow Transplant. 2008;14(9 Suppl):23–8.
5 Pierelli L, Perseghin P, Marchetti M, Accorsi P, Fanin R, Messina C, et al. Best practice for peripheral blood progenitor cell mobilization and collection in adults and children: results of a Società Italiana Di Emaferesi e Manipolazione Cellulare (SIDEM) and Gruppo Italiano Trapianto Midollo Osseo (GITMO) consensus process. Transfusion. 2012;52(4):893–905.
6 Duarte RF, Labopin M, Bader P, Basak GW, Bonini C, Chabannon C, et al. Indications for haematopoietic stem cell transplantation for haematological diseases, solid tumours and immune disorders: current practice in Europe, 2019. Bone Marrow Transplant. 2019;54(10):1525–52.
7 Abuabdou A, Rosenbaum ER, Usmani SZ, Barlogie B, Cottler-Fox M. Analysis of CD34+ cell collection using two mobilization regimens for newly diagnosed multiple myeloma patients reveals the separate impact of mobilization and collection variables. J Clin Apher. 2014;29(5):251–5.
8 Cousins AF, Sinclair JE, Alcorn MJ, H A Green R, Douglas KW. HPC-A dose prediction on the optia® cell separator based on a benchmark CE2 collection efficiency: promoting clinical efficiency, minimizing toxicity, and allowing quality control. J Clin Apher. 2015;30(6):321–8.
9 Rosenbaum ER, O'Connell B, Cottler-Fox M. Validation of a formula for predicting daily CD34(+) cell collection by leukapheresis. Cytotherapy. 2012;14(4):461–6.
10 Lisenko K, Pavel P, Bruckner T, Puthenparambil J, Hundemer M, Schmitt A, et al. Comparison between intermittent and continuous Spectra Optia leukapheresis systems for autologous peripheral blood stem cell collection. J Clin Apher. 2017 Feb;32(1):27–34.
11 de Almeida-Neto C, Rocha V, Moreira FR, Hamasaki DT, Farias MC, Arrifano AM, et al. Validation of a formula predictive of peripheral blood stem cell yield and successful collection in healthy allogeneic donors. Hematol Transfus Cell Ther. 2020;42(2):164–5.e5.
12 Bertani G, Santoleri L, Martino M, Fedele R, Moscato T, Marenco P, et al. Identification of hematopoietic progenitor cell donor characteristics predicting successful mobilization: results of an Italian multicenter study. Transfusion. 2014;54(8):2028–33.
13 Teipel R, Schetelig J, Kramer M, Schmidt H, Schmidt AH, Thiede C, et al. Prediction of hematopoietic stem cell yield after mobilization with granulocyte-colony-stimulating factor in healthy unrelated donors. Transfusion. 2015;55(12):2855–63.

14 Billen A, Madrigal JA, Szydlo RM, Shaw BE. Female donors and donors who are lighter than their recipient are less likely to meet the CD34+ cell dose requested for peripheral blood stem cell transplantation. Transfusion. 2014;54(11):2953–60.
15 Ozkurt ZN, Batmaz L, Yeğin ZA, İlhan Ç. Factors affecting hematopoietic stem cell mobilization and apheresis in allogeneic donors: the role of iron status. Transfus Apher Sci. 2017;56(3):470–3.
16 Pornprasertsud N, Niparuck P, Kidkarn R, Puavilai T, Sirachainan N, Pakakasama S, et al. The use of hematocrit level for predicting the efficiency of peripheral blood CD34(+) cell collection after G-CSF mobilization in healthy donors. J Clin Apher. 2015;30(6):329–34.
17 Hsu JW, Wingard JR, Logan BR, Chitphakdithai P, Akpek G, Anderlini P, et al. Race and ethnicity influences collection of granulocyte colony-stimulating factor-mobilized peripheral blood progenitor cells from unrelated donors, a Center for International Blood and Marrow Transplant Research analysis. Biol Blood Marrow Transplant. 2015;21(1):165–71.
18 Martino M, Gori M, Pitino A, Gentile M, Dattola A, Pontari A, et al. Basal CD34+ cell count predicts peripheral blood stem cell mobilization in healthy donors after administration of granulocyte colony-stimulating factor: a longitudinal, prospective, observational, single-center, cohort study. Biol Blood Marrow Transplant. 2017;23(7):1215–20.
19 Richtlinien zur Gewinnung von Blut und Blutbestandteilen und zur Anwendung von Blutprodukten (Hämotherapie). Aufgestellt gemäß §§ 12a u. 18 Transfusionsgesetz von der Bundesärztekammer im Einvernehmen mit dem Paul-Ehrlich-Institut. Gesamtnovelle 2017.
20 Sutherland DR, Anderson L, Keeney M, Nayar R, Chin-Yee I. The ISHAGE guidelines for CD34+ cell determination by flow cytometry. International Society of Hematotherapy and Graft Engineering. J Hematother. 1996;5(3):213–26.
21 R Development Core Team. R. A language and environment for statistical computing. Vienna, Austria: R Foundation for Statistical Computing; 2014.
22 Ings SJ, Balsa C, Leverett D, Mackinnon S, Linch DC, Watts MJ. Peripheral blood stem cell yield in 400 normal donors mobilised with granulocyte colony-stimulating factor (G-CSF): impact of age, sex, donor weight and type of G-CSF used. Br J Haematol. 2006;134(5):517–25.
23 Fischer JC, Frick M, Wassmuth R, Platz A, Punzel M, Wernet P. Superior mobilisation of haematopoietic progenitor cells with glycosylated G-CSF in male but not female unrelated stem cell donors. Br J Haematol. 2005;130(5):740–6.
24 Hölig K, Kramer M, Kroschinsky F, Bornhäuser M, Mengling T, Schmidt AH, et al. Safety and efficacy of hematopoietic stem cell collection from mobilized peripheral blood in unrelated volunteers: 12 years of single-center experience in 3,928 donors. Blood. 2009;114(18):3757–63.
25 Martín-Antonio B, Carmona M, Falantes J, Gil E, Baez A, Suarez M, et al. Impact of constitutional polymorphisms in VCAM1 and CD44 on CD34+ cell collection yield after administration of granulocyte colony-stimulating factor to healthy donors. Haematologica. 2011;96(1):102–9.
26 Anderlini P, Donato M, Chan KW, Huh YO, Gee AP, Lauppe MJ, et al. Allogeneic blood progenitor cell collection in normal donors after mobilization with filgrastim: the M.D. Anderson Cancer Center experience. Transfusion. 1999;39(6):555–60.
27 Wuchter P, Hundemer M, Schmitt A, Witzens-Harig M, Pavel P, Hillengass J, et al. Performance assessment and benchmarking of autologous peripheral blood stem cell collection with two different apheresis devices. Transfus Med. 2017;27(1):36–42.
28 Pierelli L, Maresca M, Piccirillo N, Pupella S, Gozzer M, Foddai ML, et al. Accurate prediction of autologous stem cell apheresis yields using a double variable-dependent method assures systematic efficiency control of continuous flow collection procedures. Vox Sang. 2006;91(2):126–34.