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Algorithms utilizing peripheral blood hematopoietic progenitor cell counts in lieu of some CD34⁺ cell counts predict successful peripheral blood stem cell collections with substantial time and cost savings

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Abstract

Background and Objectives—Hematopoietic progenitor cell (HPC) counts from Sysmex hematology analyzers have been shown to correlate with peripheral blood (PB) CD34⁺ cell counts by flow cytometry. Algorithms utilizing HPC counts to guide stem cell collections have been proposed but rarely tested. This study describes the development and validation of algorithms utilizing HPC and PB CD34⁺ cell counts to predict adequate peripheral blood stem cell (PBSC) collections for chemomobilized and cytokine-mobilized individuals.

Materials and Methods—Utilizing a test set of 83 PB samples from chemomobilized or cytokine-mobilized PBSC collection patients, PB CD34⁺ counts were correlated with HPC counts and a receiver operating characteristic curve was constructed. Cut-offs of 0.5 HPC/ μ l and 7 HPC/ μ l were established to maximize sensitivity and specificity for using HPC to predict PB CD34⁺ 10 cells/ μ l. These cut-offs were subsequently validated using a separate prospective validation set of 88 HPC/CD34⁺ cell sample pairs.

Results—Using the algorithms, all patients in the prospective validation data set achieved adequate collections of 1×10^6 CD34⁺ cells/kg, and a 67% reduction in the number of CD34⁺ cell counts performed was achieved. This led to a direct cost savings of at least \$18,700 USD over a 21-month period (88% reduction in direct costs).

Conclusion—Use of the algorithms provides significant time and cost savings for the laboratory while accurately predicting (i) timing of PBSC collections to obtain adequate CD34⁺ product yields for chemomobilized patients and (ii) when to administer plerixafor to cytokine-mobilized patients to improve the likelihood of achieving adequate collections

Keywords

apheresis; chemomobilized; hematopoietic stem cell; plerixafor; stem cell transplantation; Sysmex

Introduction

Stem cell transplantation has long been used as a ‘rescue’ for individuals with chemosensitive hematopoietic malignancies that require doses of chemotherapy beyond which the bone marrow can readily recover. The stem cells are typically harvested from the peripheral blood (PB) [1], and two major approaches to peripheral blood stem cell (PBSC) mobilization are used in PBSCT: chemomobilization and cytokine mobilization. Appropriate timing of apheresis is imperative in chemomobilized patients to achieve an adequate collection. For cytokinemobilized patients, stem cell collection generally begins on day 5 of growth factor administration. Addition of plerixafor can help patients reach their stem cell collection targets if they mobilize marginal stem cell numbers with growth factor alone [2, 3]. The correlation between PB CD34+ cell count and apheresis product yield is quite good; thus, PB CD34+ is often used to guide timing of PBSC collection [4]. Prior to this study, we initiated PBSC collection for chemomobilized patients when PB CD34+ cells are 10 CD34+ cells/μl, and administered plerixafor on day 4 of filgrastim administration if the PB CD34 count is <10 cells/μl. This PB CD34+ cell threshold for adequate stem cell collection was established using prior studies [4, 5] and is also acknowledged in the recent consensus guidelines [6].

Peripheral blood CD34+ quantification requires flow cytometry and generally requires two or more hours from draw time to result. A hematopoietic progenitor cell (HPC) count performed on an automated instrument (Sysmex) has become an attractive alternative to PB CD34+ cell quantification, and numerous studies have investigated its use in predicting CD34+ product yield [7–16]. This automated method involves quantifying immature hematopoietic cells, which have less lipid in the cell membranes and are thus less susceptible to lysis by a proprietary surfactant [10]. HPC measurement saves considerable time and money when compared with conventional CD34+ measurements [12]. Based on reasonably good correlations between HPC counts and successful PBSC collections, several groups proposed algorithms from retrospective data that utilized HPC counts rather than CD34+ counts to guide PBSC collection strategies [7, 8, 11–13, 15, 16]. Two studies [11, 12] prospectively validated their cutpoints; however, they studied only chemomobilized patients, and their outcomes were defined as successfully reaching the total product yield needed for PBSCT in a series of aphereses. Additionally, our study looked at large volume (24–30 l) apheresis collections, which have not been previously studied in this context.

This study reports our experience in using HPC count as a surrogate for PB CD34+ cell count in the optimizing stem cell collections. Specifically, algorithms utilizing HPC were developed and then studied prospectively for their ability to replace PB CD34+ cell count testing in two situations: (i) to determine whether plerixafor is needed to achieve an adequate collection in cytokinemobilized patients and (ii) to accurately predict when to initiate PBSC collections in chemomobilized patients to achieve an adequate yield in the first collection.

Materials and methods

Patient populations

The HPC count was initially compared to the PB CD34+ cell count using a test set of 35 patients preparing for PBSC collection at University of Iowa DeGowin Blood Center (83 samples, May–August 2012). Based on these results, algorithms were devised for use of HPC rather than PB CD34+ cell count in certain circumstances (described below). These algorithms were subsequently prospectively validated by obtaining simultaneous HPC and PB CD34+ cell values in a second independent validation set of 55 patients (88 samples; January 2013–September 2014). In both the sample and validation data sets, if a patient contributed multiple samples, they were obtained on separate days. Finally, from January 2013 to September 2014, an independent product set (120 patients, 259 samples) was constructed which compared HPC values obtained from the patient on the morning of PBSC collection to CD34+ cell counts on the product collected from the patient on that day. Forty-five patients and 74 HPC values from the validation data set were also included in the product set. This study was approved by the University of Iowa Institutional Review Board.

Characteristics of the patients and samples in the test, validation and product sets are shown in Table 1. For the test and validation sets, consecutive samples collected on all patients prior to the first day of stem cell collection were included, as the goal was to determine HPC thresholds to guide clinical decisions that could be easily applied to all patients presenting for PBSC collection in our centre. The product set was analysed retrospectively and included all pairs of HPC and product CD34+ cell counts that were available for analysis.

Stem cell enumeration

HPC counts were performed in duplicate on the Sysmex XE-5000 (Sysmex Corporation, Kobe, Japan), and the values were averaged. CD34+ cell counts were performed on PB drawn at the same time as the HPC sample and were also performed on the PBSC product by dual platform flow cytometry on a Beckman Coulter FC 500 (Beckman Coulter, Inc., Brea, CA, USA) according to ISHAGE protocol [17]. White blood cell counts used to calculate absolute PBSC product yield were obtained on the Sysmex XE-5000.

Stem cell mobilization and collection

For the test set of patients, PB CD34+ cell count ≥ 10 CD34+ cells/ μ l resulted in initiation of PBSC collection for chemomobilized patients, or no plerixafor administration prior to PBSC collection for cytokine-mobilized patients as described previously [18]. For the validation set, these decisions were made according to the algorithm utilizing PB CD34+ cell and/or HPC measurements described in Results. HPC and PB CD34+ count information was obtained on healthy donors per National Marrow Donor Program (NMDP) protocol for informational purposes only.

Chemomobilized patients collected PBSC following recovery of hematopoiesis. When the white blood cell count exceeded 1000/ μ l following the nadir from chemotherapy (generally about day +13), HPC and/or PB CD34+ cell measurement began, to determine whether the patient was ready to begin PBSC collection. If PBSC collection did not begin by day +15

post chemotherapy, the patient began receiving 10 µg/kg filgrastim (5 µg/kg, twice daily dosing) until collections were complete. If PBSC collection did not begin by day +17, 24 mg plerixafor was given on the evening prior to anticipated collection, dose reduced by 50% if the creatinine clearance was <50 ml/min, and continued until collections were complete (patients receiving plerixafor in this setting were still required to demonstrate adequate circulating stem cells the next morning by HPC or CD34+ cell measurement to begin collections.)

Cytokine-mobilized patients received 10 µg/kg/d filgrastim in a single morning dose, starting 4 days prior to collection and continuing at that dose until PBSC collections were complete. These patients received plerixafor (same dosing as myeloma patients) on the evening prior to each PBSC collection based on their HPC and/or PB CD34+ cell counts.

Peripheral blood stem cell collection

An automated blood cell separator (Cobe Spectra, MNC procedure or Spectra Optia, MNC procedure, Terumo BCT, Lakewood, CO, USA) was utilized. Adult apheresis procedures were performed per DeGowin Blood Center protocol for 5 h or 30 l blood volume (BV) processed, whichever came first. At least 24 l were processed for each adult procedure. For NMDP donors, 24 l were processed per their guidelines. For paediatric patients, five BV were processed.

HPC algorithm construction

A receiver operating characteristic (ROC) curve was constructed using EP Evaluator (Data Innovations, LLC, South Burlington, VT, USA), comparing the HPC count to the PB CD34+ cell count using a cut-off of 10 CD34+ cells/µl. Based on this ROC curve, algorithms for collection of chemomobilized patients and administration of plerixafor to cytokine-mobilized patients were constructed.

Testing costs

A cost analysis was performed as detailed in the discussion. The cost of the HPC testing is \$4.69 (\$3.10 labour and \$1.59 supplies). The cost of the weekday flow cytometry testing is \$32.40 (\$20.82 labour and \$11.58 supplies). Weekend testing adds \$0.13 to the labour cost for HPC testing, and \$126.00 to the labour cost of CD34+ cell testing (assuming only one sample needs to be performed on a weekend day, because there is no technologist in house on weekends who can perform this test).

Statistical analysis

Correlations between HPC values and PB and product CD34 values were calculated using Microsoft Excel software (Microsoft Corporation, Redmond, WA). ROC curves (with corresponding statistics) were constructed using EP Evaluator (Data Innovations, South Burlington, VT, USA).

Results

Correlation of PB HPC and CD34+ cell counts

To determine whether HPC correlation with PB CD34+ cells was sufficient for development of clinical management algorithms at our institution, these two values were compared in the initial test data set. The HPC showed reasonable correlation with the PB CD34+ cells in both populations, with $R = 0.67$ (Fig. 1a) for chemomobilized patient samples ($n = 62$) and $R = 0.63$ (Fig. 1b) for cytokine-mobilized patient samples ($n = 21$). These are comparable to R values that have been reported in the literature for comparison of HPC vs. PB CD34+ cells [8, 9, 14].

Development of HPC-based algorithms for PBSC collection management

Using the data from Fig. 1, ROC curves were constructed comparing the HPC values to the cutoff of 10 PB CD34+ cells/ μ l (Fig. 2). HPC ≥ 0.5 cells/l predicted a sample would have <10 CD34+ cells/ μ l 93% of the time. HPC ≥ 7 cells/l predicted a sample would have ≥ 10 CD34+ cells/ μ l 100% of the time. Between these two values (0.5–7 cells/ μ l), the HPC could not reliably predict what the PB CD34+ count would be, with positive predictive values ranging from 73 to 100% and negative predictive values ranging from 66 to 92%. The predictive value of these cutoffs was identical regardless of whether the analysis was performed on the entire test set (Fig. 2a), or on the chemomobilized patient subset (Fig. 2b), suggesting the form of mobilization and the underlying patient characteristics do not have a substantial impact on the correlation between the HPC and PB CD34+ count.

Based on these results, it was determined that a single HPC cut-off could not solely be relied upon to predict a PB CD34+ count of >10 cells/ μ l, so two values were chosen for the algorithms, to maximize sensitivity (HPC ≥ 0.5 cells/ μ l) and specificity (HPC ≥ 7 cells/ μ l). (In the test data set, 36% of the HPC counts fell into the intermediate zone, requiring PB CD34+ counts to determine the appropriate course of action.) These thresholds were then used to predict appropriate management strategies for chemomobilized and cytokine-mobilized patients, as shown in Fig. 3. For cytokine-mobilized patients, the HPC count was used to determine whether or not to administer plerixafor on the evening prior to collection (Fig. 3a). For the chemomobilized group, HPC count was used to determine when stem cell collection initiation would occur following recovery of hematopoiesis (Fig. 3b). For patients whose HPC fell between 0.5 and 7 cells/ μ l, a PB CD34+ count was still performed to determine management, as per the previous practice at our institution. Once collections started for a particular patient, they continued regardless of HPC or PB CD34 counts on subsequent days. These algorithms were implemented in January 2013.

Validation of algorithms

To determine how often the algorithms in Fig. 3 were failing to predict PB CD34 results correctly (and thereby leading to less than optimal patient management), HPC and PB CD34+ cell concordance was studied in 88 samples (55 patients) who had both tests drawn after the algorithms were in place, and had HPC ≥ 0.5 / μ l or ≥ 7 / μ l. Clinical decisions for these patients were made based on HPC results. This validation data set demonstrated ~80% concordance with both low and high level cut-offs for HPC (Table 2). The PB CD34+ cell

values that were discordant with the low level HPC cut-off were just above the predicted threshold of 10 CD34+ cells/ μ l (11.1–11.7/ μ l).

In contrast, no trend in the PB CD34+ cell values that were discordant with the high HPC cut-off was observed. The median PB CD34+ cell value in these samples was 0 cells/ μ l, and even HPC values that were quite elevated sometimes had corresponding PB CD34 counts of 0 cells/ μ l. For example, one lymphoma cytokine-mobilized patient had multiple HPC values above 7/ μ l (26 and 29/ μ l), yet when PB CD34+ cell counts were performed in both instances, the result was 0 cells/ μ l. The linearity of the HPC test has been validated up to 86 cells/ μ l. The reason for the wide variability in CD34 counts in a few of the samples with high HPC values is currently unclear. Identification and evaluation of additional patients with similar HPC/CD34+ cell pairs is ongoing.

Ultimately, the ability to predict the yield of the PBSC collection from the HPC value may be of more interest than the ability of the HPC to predict PB CD34+ cells ≥ 10 / μ l. Thus, the correlation between the HPC value and the product CD34+ cell yield was determined for both chemomobilized and cytokine-mobilized patients following institution of the algorithms, using 259 HPC samples obtained January 2013–September 2014. For this analysis, HPC values determined on the morning of PBSC collection were correlated with product yield. HPC samples from cytokine-mobilized patients showed better correlation with product CD34+ cell counts than did HPC samples from chemomobilized patients ($R = 0.573$ vs. $R = 0.284$; upper panel).

However, of perhaps, more importance was whether the patients achieved an adequate collection (defined as a product yield of $\geq 1 \times 10^6$ CD34+ cells/kg) when the algorithms were utilized. Figure 4 lower panel shows that of the 258 samples for which both HPC counts and corresponding product yields were available, all but eight (3%) of the collections were adequate. These were all cytokinemobilized patients who were being collected on d. 5 of filgrastim administration regardless of HPC count. The eight collections came from five patients, one of whom had an allergic reaction to plerixafor and was unable to receive additional doses (three specimens), and the rest had received plerixafor prior to PBSC collection. Thus, maximal efforts to mobilize these patients had already occurred. Four samples in the validation data set had HPC values ≥ 0.5 / μ l on the day of collection, and all of these collections had adequate yields (all of these collections were on the second or later day of PBSC collection for that patient; thus, the algorithm was not being utilized for the patient on that day). Thus, there were no instances of algorithm failure to predict a series of adequate collections, in patients where additional interventions to enhance collection were available.

Cost efficiencies resulting from use of the algorithms

Utilization of the HPC value in lieu of the PB CD34+ cell count resulted in a two-thirds reduction in CD34+ cell assays performed by flow cytometry (67% of HPC values run were either ≤ 0.5 HPC/ μ l or ≤ 7 HPC/ μ l). In our laboratory, the cost of PB CD34+ cell count performed on a weekday is \$32.40 – nearly seven times more than the HPC count (\$4.69). Weekend testing adds greatly to the labour cost of CD34+ cell testing (detailed in Materials and Methods), particularly if only one sample needs to be performed on a weekend day.

Seventeen per cent of HPC counts in the validation data set were performed on weekend days, and only one test/day was performed for 57% of the Saturday or Sundays where testing occurred. Ultimately, use of the algorithms resulted in direct cost savings of \$18,700 over a 21-month period (January 2013–September 2014) and would be expected to save two-thirds of patients over \$650 in direct costs on each day of algorithm-driven testing.

Regarding time savings for the laboratory, the HPC test takes about 4 min of technologist time to perform, and PB CD34 testing takes about 28 min. Thus, on weekdays, running HPC rather than PB CD34 test results in an 86% savings of technologist time. On weekends, the time savings (and technologist satisfaction) is much greater at our institution, because of the need to bring in a technologist to run the PB CD34 test but not the HPC test. The use of HPC testing did not result in significant delays in other aspects of patient care (e.g. timely central line placement, completing a large volume PBSC collection during normal clinic hours) relative to our previous practice of making decisions based solely on PB CD34+ testing, even if such testing was ultimately required due to an HPC result between 0.5/ μ l and 7/ μ l.

Discussion

The goal of this study was to determine whether HPC testing could be utilized in lieu of PB CD34+ testing, to guide decisions about when to initiate PBSC collections in chemomobilized patients and whether plerixafor administration is warranted in cytokine-mobilized patients. The results indicate that HPC testing can reliably replace PB CD34+ testing when the HPC value is quite low ($< 0.5/\mu$ l), or relatively high ($> 7/\mu$ l), to predict an adequate collection, defined as at least 1×10^6 CD34+ cells/kg in the product. When the HPC value is in the intermediate range ($> 0.5/\mu$ l but $< 7/\mu$ l), HPC testing cannot reliably substitute for PB CD34+ testing. Because the HPC test can be run quickly on the Sysmex XE-5000 hematology analyzer, the turnaround time for the test is much shorter, and the direct and indirect costs of testing are substantially less than performing CD34+ cell enumeration via flow cytometry. This results in increased patient and technologist satisfaction and reduces the testing costs associated with initiation of PBSC collection.

The use of HPC to predict PB CD34+ cell counts and potentially guide PBSC collection has been proposed in the literature multiple times over the past two decades. Several groups have demonstrated reasonably good correlations between HPC counts and PB CD34 counts [7–10, 13–16, 19]. Algorithms to guide PBSC collections using HPC counts have been proposed for certain patient populations [7, 8, 11–13, 15, 16]. However, very few of these algorithms have been tested prospectively, and none addressed when to begin large volume PBSC collections in chemomobilized patients, or whether HPC values could be used to guide administration of plerixafor to optimize PBSC collections in cytokine-mobilized patients who would be predicted to otherwise collect poorly. This study describes the development of HPC-based PBSC collection algorithms for these populations, and evaluation of their effectiveness following implementation.

The correlation between PB CD34+ cell counts and HPC counts has shown much variability from study to study. Although most prior studies have shown that HPC counts are generally

1.5–4.0 times higher than PB CD34+ cell counts [9, 10, 13–15, 19], in our laboratory, the HPC counts were generally less than the PB CD34+ cell counts (HPC median = 4 cells/ μ l vs. CD34+ median = 26.9 cells/ μ l) which also has been reported previously [7, 8]. The reason for these differences is likely multifactorial. Park et al. [19] recently highlighted the differences in HPC measurements between two Sysmex models, and HPCCD34+ cell correlations with the model used in the current study (XE-5000) have not been previously reported. White blood cell count is another variable that could affect an HPC value; however, no good correlation was seen between WBC and HPC in our study ($R = 0.1877$; data not shown). This is not surprising, as WBC has been shown to correlate poorly with PB CD34+ cell counts [5]. Similar variation could be postulated for CD34+ counts using different flow cytometers and single vs. dual platform methods; however, the use of single vs. dual platform flow cytometry is not the sole factor contributing to this variability as both of these approaches have been reported to give CD34+ cell values that are on average either higher or lower than the corresponding HPC value [7, 10, 15].

Several studies have proposed algorithms to use HPC in lieu of CD34+ cell counts to optimize PBSC collections. The proposed cut-offs have varied from 5 to 55 HPC/ μ l (median of 20 HPC/ μ l) [7, 8, 10, 11, 13]. However, none of these studies was performed in patients who underwent large volume (24–30 l) PBSC collections. Large volume PBSC collections have emerged as a valuable method to achieve higher stem cell yields and can achieve nearly twofold higher collection efficiencies over standard volume collections [20]. Another unique aspect of the current study is the patient population, which contains many multiple myeloma patients being chemomobilized with dexamethasone/cisplatin/doxorubicin/cyclophosphamide/etoposide (DPACE). No prior study of HPC utility has examined patients who were treated with this commonly used chemotherapeutic regimen. Finally, only two of the published studies prospectively validated their choice of HPC cut-off in their proposed PBSC collection algorithm [11, 12]. These studies focused on how well their algorithm was able to predict the total number of PBSC required for PBSCT, utilizing 1–5 apheresis sessions yielding $2\text{--}5 \times 10^6$ CD34+ cells/kg or 10×10^6 CD34+ cells/kg [11, 12]. In contrast, the current study evaluated algorithms (Fig. 3) designed to predict 1.9×10^6 CD34+ cells/kg collected in a single PBSC collection. These algorithms are applicable across many autologous treatment plans requiring variable targets for PBSC numbers that must be collected prior to PBSCT. The algorithm for cytokinemobilized collections was not specifically tested for allogeneic donors, as all of the donors in the data sets had HPC $> 7/\mu$ l.

The gold standard for stem cell enumeration in PBSC products is the CD34+ count. The correlation between HPC value and CD34+ count in the PBSC product is better for patients who were cytokine-mobilized than for chemomobilized patients (Fig. 4). The rate of haematologic recovery from chemomobilization is quite variable (ranging from 12 to 22 days in this study) and dependent on multiple factors including the nature of the chemotherapy, prior chemotherapy regimens that the patient has received, concurrent antibiotic administration and other comorbidities. Thus, it is possible that in some chemomobilized patients, rapid haematologic recovery is occurring during PBSC collection, and a HPC value obtained 5–7 h prior to completion of the collection may not reflect the average PB value during the collection. In contrast, cytokine-based stem cell mobilization has very predictable kinetics [21], and stem cell collection is routinely performed on day 5

of filgrastim administration. Even in cytokinemobilized patients, the correlation between HPC value and CD34+ product cell count in this study is not high enough to support an accurate HPC-based algorithm to predict product yields, that would allow real time adjustment of blood volumes processed during apheresis, as has been demonstrated for PB CD34 counts [22, 23].

Despite the better correlation between HPC value and CD34+ product cell count in cytokinemobilized patients than in chemomobilized patients, there were a few examples of cytokinemobilized patients whose HPC count on the morning of PBSC collection would have predicted an adequate collection but did not achieve that value. In these examples, the PB CD34+ count was also $>10/\mu\text{l}$, also predicting an adequate collection. The reason for the discrepancy between PB stem cell counts by either method, and the collection yield, is currently not understood. No significant technical issues were noted in any of these collections.

There are several limitations to this study. First, it is likely that the algorithms cannot be directly applied to standard volume PBSC collections. However, to our knowledge, it provides the first published data supporting HPCbased algorithms that are applicable to large volume PBSC collections. Another limitation is that the chemomobilized study group was heavily weighted with adult multiple myeloma patients who received DPACE chemotherapy, and thus, the data are not as robust in support of the algorithm for other chemomobilization regimens, including those used in paediatric patients. Additionally, because all available samples from our varied patient population were included in the analyses, potential differences in the correlation between HPC and CD34+ cell counts based on patient demographics or treatment regimens cannot be excluded. However, the algorithms performed well in the validation data set and the product data set, and the few failures that were encountered, for which an alternate option for mobilization was available, did not fall into any clear patient demographic or treatment regimen. Finally, the instrument-dependent variability inherent in both HPC and CD34+ cell counts indicates that use of this algorithm should be validated with institution-specific data to determine appropriate HPC cut-offs prior to use for patient management.

In summary, this study reports validated algorithms for the use of HPC measurements as a replacement for CD34+ cell counts, at HPC values $0.5/\mu\text{l}$ and $7/\mu\text{l}$. Use of the algorithms provides significant time and cost savings for the laboratory while accurately predicting the timing of PBSC collections to obtain adequate CD34+ product yields for chemomobilized patients, and when to administer plerixafor to cytokine-mobilized patients who are otherwise likely to have less than adequate collections.

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Figure 1.

Correlation between PB CD34+ cell counts and HPC for test set of (a) chemomobilized patients and (b) cytokine-mobilized patients. PB CD34+ cell counts were determined by flow cytometry and HPC counts on Sysmex XE-5000. Best-fit equation for chemomobilized patients is $y = 0.52x + 20.4$; $R = 0.67$. (If the two outliers with very high HPC values are excluded, the best-fit equation is $y = 1.18x + 14.7$; $R = 0.62$.) Best-fit equation for cytokine-mobilized patients is $y = 1.0x + 12.8$; $R = 0.63$.

Figure 2.

ROC curves used to determine cutpoints for when HPC testing can reliably predict PB CD34+ cells $\geq 10/\mu\text{l}$. (a) All samples in the test set. (b) Only samples from chemomobilized patients in the test set. The cutpoints established ($\geq 0.5/\mu\text{l}$ and $\geq 7/\mu\text{l}$) are marked on the curves. Other possible cutpoints are shown below the curves, with corresponding sensitivities and specificities.

Figure 3.

Algorithms using HPC values to determine management of PBSC collections. (a) Determination of whether to administer plerixafor (cytokine-mobilized patients). (b) Determination of when to begin PBSC collection (chemomobilized patients).

Figure 4.

Correlation between HPC (PB) and product CD34+ cell yield, from data in the product set. Best-fit equation for cytokine-mobilized patients is $y = 0.44x - 0.96$; $R = 0.57$. Best-fit equation for chemomobilized patients is $y = 0.28x + 6.40$; $R = 0.20$. Lower panel: enlargement of the area containing products from inadequate collections (< 19106 CD34 + cells/kg).

Table 1

Characteristics of patients and samples in the data sets used for algorithm construction and analysis

	Test set <i>N</i> = 35 patients			Validation Set <i>N</i> = 55 patients			Product Set <i>N</i> = 120 patients		
Age	59 (4–72) ^a			55 (2–79)			58 (2–79)		
Gender (Male:Female)	22:13			29:26			73:47		
Diagnosis		Patients	Samples		Patients	Samples		Patients	Samples
Multiple myeloma/amyloidosis	16		58	36		59		92	215
Lymphoma	7		12	10		18		19	34
Healthy donor	9		9	5		6		6	6
Solid tumour ^b	3		4	4		5		3 ^c	4
Mobilization strategy									
DPACE ^c	16		58	33		54		84	201
Other Chemotherapy ^b	3		4	4		5		3	4
Cytokine	16		21	18		29		25	54

^aMedian (range).

^bAll paediatric patients are in this group.

^cDPACE, dexamethasone/cisplatin/doxorubicin/cyclophosphamide/etoposide.

Table 2

Ability of low and high range HPC to predict PB CD34 in the validation set

	Number of HPC samples in designated range		PB CD34 result in agreement with HPC prediction	Concordance
Low (HPC 0.5 cells/ μ l; Expect CD34 10 cells/ μ l)	14		11 ^a	79%
High (HPC 7 cells/ μ l; Expect CD34 10 cells/ μ l)	74		59 ^b	80%

^aRange of the three CD34 values that were above threshold of 10 cells/ μ l = 11.1–11.7 cells/ μ l.

^bRange of the fifteen CD34 values that were below threshold of 10 cells/ μ l = 0–8.76 cells/ μ l; median 0 cells/ μ l.