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BRIEF REPORT

# Pre-harvest CD34$^+$ cell counts predicted peripheral blood stem cell collection yields

Autologous stem cell transplantation (ASCT) after high-dose chemotherapy is part of the treatment for high-risk neuroblastoma, relapsed Hodgkin disease and metastasised Ewing sarcoma. Collecting peripheral blood stem cells (PBSC) can be challenging, as mobilisation failures can delay treatment and increase costs.[1] One widely applied method to predict success and adjust the timing of stem cell collection is monitoring the counts of circulating CD34$^+$ cells before apheresis.[1–5] Collection yields can be further improved using monocyte counts above $1.65\times10^6/\mu L^2$ and increased separator blood flow rates of 42–100 mL/min can be used to optimise harvest outcome.[3] However, we need more accurate methods to optimise the stem cell mobilisation and collection processes and the aim of this study was to identify the factors that predicted the success of the PBSC collection in paediatric patients.

Data were collected from the medical records of paediatric patients who were under 18 years of age at the time of diagnosis and underwent high-dose chemotherapy between January 2000 and April 2021 at Tampere University Hospital, Finland. The clinical data were age, sex, disease status, tumour class and spread of the disease. The PBSC-associated parameters were circulating CD34$^+$ cells, leukocytes and neutrophils and collected CD34$^+$ cells per kilogram. Stem cells were mobilised using granulocyte-colony-stimulating factor (G-CSF) alone, G-CSF after chemotherapy or plerixafor for patients who did not mobilise with other methods. Harvesting was initiated when peripheral blood (PB) CD34$^+$ cell counts exceeded $20\times10^6$/L. However, harvesting was started for 11 poor mobilisers when the minimal threshold was not reached. A minimal target CD34$^+$ cell yield was set at $3\times10^6$/kg in an apheresis session and an optimal yield at $5\times10^6$/kg.

Statistical analyses were performed with R program, version 4.1.2 (R Foundation, Vienna, Austria). Linear regression was applied to model associations between the variables. A joint effect of CD34$^+$ cell and leukocyte counts on the harvest outcome was investigated using multivariate regression with the following covariates: sex, age, diagnosis, bone marrow involvement, mobilisation scheme and PB counts. R's predict() function produced prediction intervals for the models. Pearson's correlation coefficients were calculated to describe linear associations. A $p<0.05$ was considered statistically significant for two-tailed tests.

We studied 26 males and 28 females who received high-dose chemotherapy followed by ASCT at a median age of 6.4 years (range 0.7–17) and median weight of 21 kg (range 9.0–93). Of these, 13% had brain tumours, 13% had lymphomas and 74% had other solid tumours. Bone marrow involvement was detected in 26%.

PBSC mobilisation was performed for 85% patients during their primary tumour treatment and 15% during recurrence: 31% were mobilised using just G-CSF and 69% received chemotherapy followed by G-CSF. Due to poor mobilisation, 20% were given plerixafor, 11% underwent a second course of mobilisation course and 6% had a bone marrow harvest. A total of 97 daily apheresis sessions were performed, with a median of two per patient (range 1–5).

The median pre-harvest PB CD34$^+$ cell count was $39\times10^6$/L, with an interquartile range of 27–88 and the median leukocyte count was $6.5\times10^9$/L (interquartile range 5.3–25). The median CD34$^+$ cell harvest yield was $3.4\times10^6$/kg (interquartile range 1.9–6.7) with a minimal target yield of $3\times10^6$/kg obtained during 61% of the 97 sessions and the optimal yield of $5\times10^6$/kg in 34% of the sessions. Over half (59%) of the patients reached the minimal target level after one session and 76% after two sessions. There were no daily harvest results for seven patients. We found that 87% of the patients reached the minimal target yield in one or several sessions, while 13% did not.

Harvest yields did not differ by the mobilisation method ($p=0.22$), and pre-harvest PB leukocyte counts were not correlated with the yield ($r=-0.12$). Figure 1 shows that the PB CD34$^+$ cell counts alone explained 80% of the variation in the univariate model ($p<0.001$). They remained highly significant in the multivariate regression, while age, diagnosis, leukocyte count and bone marrow involvement did not affect the harvest yield.

We built a multivariable prediction model for harvest yield using the backward stepwise method: the joint effect of pre-harvest PB CD34$^+$ and total leukocyte counts explained 90% of the variation. In a simplified model, the yield was reliably predicted using just the pre-harvest PB CD34$^+$ counts ($y=0.101\times\beta$-0.694), with the minimal target yield of $3\times10^6$/kg achieved when the pre-harvest PB CD34$^+$ cell count reached $36.6\times10^6$/L. Confidence levels of 97.5% were obtained for reaching the minimal target when pre-harvest CD34$^+$ counts were $104\times10^6$/L for the first session.

**Abbreviations:** ASCT, autologous stem cell transplantation; G-CSF, granulocyte-colony-stimulating factor; PB, peripheral blood; PBSC, peripheral blood stem cells.

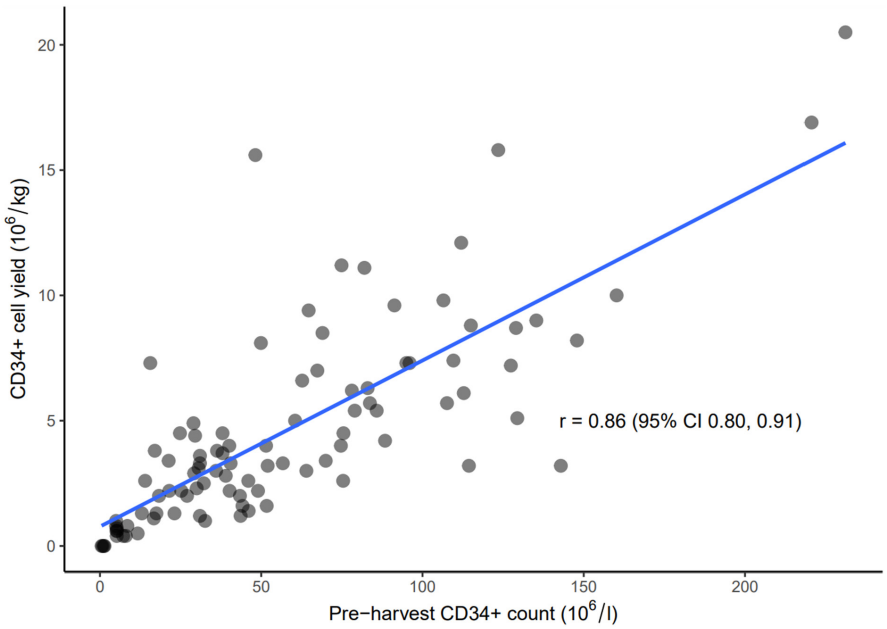


**FIGURE 1** Scatterplot showing correlation between pre-harvest PB $CD34^+$ counts and harvest yields for all harvest sessions.

We built a simplified prediction model that used pre-harvest $CD34^+$ cell counts to estimate harvest outcome:

One study limitation was the relatively small sample size and no validation of the harvest yield formula. Furthermore, we did not have data on the total processed blood volume or the specifics of the blood cell separators, which could have affected the stem cell harvest yield. These limitations may affect the generalisability of the results when applying the formula to external populations.

Pre-harvest PB $CD34^+$ and leukocyte counts predicted 90% of the variation for PBSC collection success, in line with studies that used PB $CD34^+$ cell counts as predictors.[1–5] We also created a simple formula to roughly estimate the harvest potential before the procedure and prevent unnecessary harvest sessions.

## CONFLICT OF INTEREST STATEMENT

None.

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