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A novel predictive model for CD34+ stem cell yield in autologous stem cell collections

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INTRODUCTION

Haematopoietic progenitor cells collected by apheresis (HPC-A) are the most common cell source for haematopoietic stem cell transplantation (HSCT).[1] HPC-A are characterised by surface expression of CD34, enumeration of which determines stem cell collection yield. Accurate prediction of CD34+ yield improves efficiency of stem cell collections, optimises use of healthcare resources and enhances donor safety. Current CD34+ yield predictive models rely on the benchmark collection efficiency (CE) of apheresis systems used.[2-4] However, recent real-life data analysis of 1218 autologous collections at NHS Blood and Transplant (NHSBT) sites demonstrated variable CE between individual procedures, which reduces the utility of current predictive calculations.

AIM

To develop and validate a novel statistical model, not reliant on CE, for the prediction of a target CD34+ yield of ≥ $3x10^6$/kg and to use this model to determine the required total blood volume (TBV) to be processed during apheresis procedures.

METHOD

We used prospectively collected data for autologous collections from the NHSBT Stem Cell Collection Registry between 2016 and 2019. All collections were performed on Spectra Optia devices (Terumo®) using the MNC programme. Patients proceed to collection at a PB CD34+ count of >$10x10^9$/µL with target CD34+ yield ≥ $3x10^6$/kg for single autologous HSCT. A total of 2.5 blood volumes are processed as standard.

Model development:
A multivariable logistic regression analysis with stepwise variable selection was performed on clinical and laboratory parameters of the first HPC-A procedure of the first mobilisation of 1211 patients.

Model validation:
The model was subsequently validated with data from the first HPC-A procedure of the first mobilisation of 462 patients.

To our knowledge, this is the largest dataset used for predictive model development in the setting of autologous HSCT to date.

DEMOGRAPHICS

Patient characteristics at the first HPC-A procedure used in the model development dataset Complete case set (N=1211)		
Collection CD34 ($x10^6$ per kg) Median (IQR)		3.22 (1.52, 6.72)
Target reached	No (%)	575 (47.5)
	Yes (%)	636 (52.5)
TBV processed (L) Mean (SD)		11.62 (2.52)
Sex	Male (%)	747 (61.7)
	Female (%)	464 (38.3)
Age (years) Median (IQR)		60.23 (50.97, 66.30)
Weight (kg) Mean (SD)		80.71 (17.74)
Diagnosis group	Hodgkin's Lymphoma (%)	88 (7.3)
	Multiple Myeloma (%)	743 (61.4)
	Non-Hodgkin's Lymphoma /DLBCL/ Follicular Lymphoma (%)	269 (22.2)
	Solid Tumours (%)	34 (2.8)
	Other (%)	77 (6.4)
Pre-collection CD34 ($x10^3$/µL) – median (IQR)		42.00 (21.80, 93.00)

IQR = interquartile range; SD = standard deviation

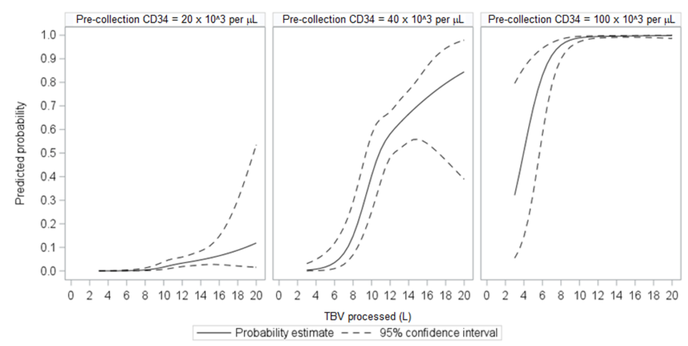
RESULTS

The final multivariable logistic regression model includes the following variables:

1. **Pre-collection CD34+ count** – the strongest predictor of whether target yield is reached or not (p<0.0001)

E.g. with pre-collection CD34+ count of $20x10^3$/µL, the predicted probability of reaching the target yield is ≤0.1 regardless of TBV processed, while for a high pre-collection CD34+ count of $100x10^3$/µL, even a small TBV processed of 5L results in a probability of around 0.7 of achieving the target yield.

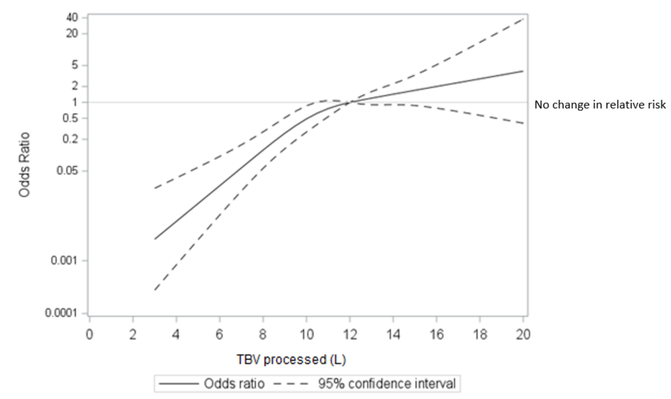
Predicted probability of reaching the target yield by TBV processed at different levels of pre-collection CD34 count*



2. **Total blood volume (TBV) processed** – strong positive association (p<0.0001)

E.g. the odds ratio (95% confidence interval) of reaching the target yield for a TBV processed of 9L compared with 12L (all other variables in the fully adjusted model being equal) is 0.26 (0.13, 0.51).
→ there is a 74.0% decrease in the odds of reaching the target yield for 9L compared with 12L of blood processed for an otherwise equal patient.

Adjusted odds ratios for reaching the target yield by TBV processed compared with a reference value of 12 litres*



3. **Weight** – strong negative association (p<0.0001)

E.g. 1kg increase in weight (for two otherwise similar patients) is associated with a 4.5% reduction in the odds of reaching the target yield.

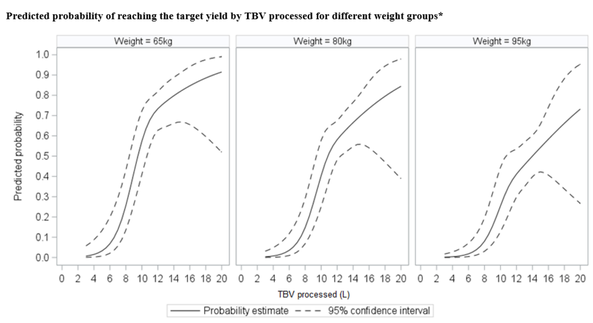
4. **Diagnosis group** – weak association (p=0.02)

Strongest difference between "multiple myeloma" and "other" with a patient in the "other" group having 5.1 (95% CI: 1.8, 14.2) times the odds of reaching the target yield compared with an otherwise similar patient in the "multiple myeloma" group.
But: "other" includes non-haematological & benign conditions and is the second smallest group in the dataset.

5. **Sex** – weak association (p=0.09)

6. **Age** – weak association (p=0.09)

Predicted probability of reaching the target yield by TBV processed for different weight groups*

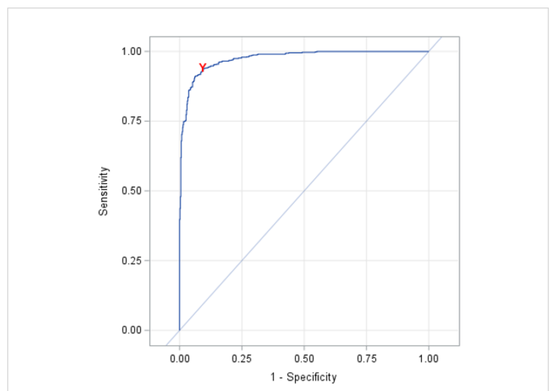


Model is adjusted for patient's age, sex, weight, diagnosis and the logarithm of pre-collection CD34.

Our model demonstrates 94% specificity

The area under the ROC curve for the fully adjusted model was 0.975 which indicates strong ability by the model to discriminate between patients who reach the target CD34+ yield and those who do not. When fitted to the validation dataset, the final multivariable model had an area under the ROC curve of 0.942, again demonstrating strong predictive ability.

ROC curve for fully adjusted logistic regression model showing optimal cut-off point using the Youden index criterion in the model development dataset



CONCLUSIONS

Our novel predictive model demonstrates strong ability to discriminate between patients who will have a successful first HPC-A collection and those who will not. To our knowledge our study analyses the largest dataset on autologous HSCT collections used to evaluate the predictive power of a number of parameters on CD34+ yield. It shows that other parameters in addition to peripheral blood CD34+ count and TBV, such as patient weight and diagnosis, have predictive value. Based on the model presented here, we are planning on developing a tool for our daily practice which we hope will allow us to tailor our procedures more effectively to our patients' characteristics.

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