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Development of model for analysing respective collections of intended hematopoietic stem cells and harvests of unintended mature cells in apheresis for autologous hematopoietic stem cell collection

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ABSTRACT

Hematopoietic stem cells (HSCs) required to perform peripheral hematopoietic autologous stem cell transplantation (APBSCT) can be collected by processing several blood volumes (BVs) in leukapheresis sessions. However, this may cause granulocyte harvest in graft and decrease in patient's platelet blood level. Both consequences may induce disturbances in patient. One apheresis team's current purpose is to improve HSC collection by increasing HSC collection and prevent increase in granulocyte and platelet harvests. Before improving HSC collection it seemed important to know more about the way to harvest these types of cells.

The purpose of our study was to develop a simple model for analysing respective collections of intended CD34+ cells among HSC (designated here as HSC) and harvests of unintended platelets or granulocytes among mature cells (designated here as mature cells) considering the number of BVs processed and factors likely to influence cell collection or harvest. For this, we processed 1, 2 and 3 BVs in 59 leukapheresis sessions and analysed corresponding collections and harvests with a referent device (COBE Spectra).

First we analysed the amounts of HSC collected and mature cells harvested and second the evolution of the respective shares of HSC and mature cells collected or harvested throughout the BV processes. HSC collections and mature cell harvests increased globally ($p < 0.0001$) and their respective shares remained stable throughout the BV processes (p non-significant). We analysed the role of intrinsic (patient's features) and extrinsic (features before starting leukapheresis sessions) factors in collections and harvests, which showed that only pre-leukapheresis blood levels (CD34+ cells and platelets) influenced both cell collections and harvests (CD34+ cells and platelets) ($p < 0.001$) and shares of HSC collections and mature unintended cells harvests ($p < 0.001$) throughout the BV processes. Altogether, our results suggested that the main factors likely to influence intended HSC collections or unintended mature cell harvests were pre-leukapheresis blood cell levels. Our model was meant to assist apheresis teams in analysing shares of HSC collected and mature cells harvested with new devices or with new types of HSC mobilization.

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1. Introduction

Autologous peripheral blood stem cell transplantation (APBSCT) to treat malignant diseases such as non-Hodgkin lymphoma (NHL), multiple myeloma (MM) or Hodgkin disease (HD) [1] requires hematopoietic stem cell (HSC) collection by mobilizing them from bone marrow to peripheral blood and collecting them from blood by leukapheresis. Leukapheresis divides blood components in layers and collects blood-mobilized HSC in a particular layer associated to other blood cells. Collected HSC are estimated by counting CD34+ cells considered as intended collected cells while some harvested blood mature cells (granulocytes, platelets) are considered as unintended harvested cells. The performances of HSC collecting process were extensively described while the performances of mature cell harvesting process were not. Therefore, HSC outputs were different in patients with or without risk factors of poor HSC mobilization [2–4] and could be predicted by analysing the levels of pre-leukapheresis blood CD34+ cells alone or combined with the amounts of CD34+ cells collected at mid-point in leukapheresis sessions [5–7]. However, only few studies analysed the role of the number of blood volumes (BVs) processed in CD34+ cells yield outputs [8,9]. According to these, processing higher numbers of BVs not only generates higher amounts of HSC collected but may also generate higher amounts of blood mature cells harvested, which could be deleterious for the patient or the graft. Moreover, large amounts of granulocytes harvested in HSC collections can induce side-effects during APBSCT infusion [10–12]. Similarly, platelet harvests can induce severe thrombocytopenia after leukapheresis. Therefore, if CD34+ cells (intended cells) are collected with G-CSF alone, the main unintended harvested mature cells can be granulocytes or if CD34+ cells are collected after chemotherapy-induced aplasia, the main unintended harvested mature cells can be platelets.

Over the last fifteen years, the conditions in which peripheral HSC were collected experienced insignificant changes. In fact, except with the use of Plerixafor in poor mobilizer patients in the last three years, the conditions of HSC mobilization (after aplasia-induced chemotherapy or after G-CSF mobilization) remained unchanged. Moreover, apheresis devices underwent little upgrade over the last decades. The COBE Spectra device (TerumoBCT) was one of the referent devices used by most apheresis teams to collect peripheral HSC.

We developed a model to estimate the amounts and respective shares of HSC or mature cells collected and harvested after processing 1, 2 or 3 BVs with the COBE Spectra device and determine the factors (patient's and disease features or pre-leukapheresis blood levels of each cell subtype) influencing HSC collections and mature cell harvests. This provided relevant information that will have to be evaluated with other devices and mobilization regimen in identical conditions.

2. Materials and methods

2.1. Study design

This study was a prospective assessment. Approval was obtained from the local ethical committee and written informed consent was obtained from all subjects enrolled in this research.

2.2. Patients' features

59 Autologous leukapheresis were performed in 43 patients, treated for NHL, HD and MM. Disease features and conditions before leukapheresis were recorded (Tables 1 and 2). Risk factors of poor APBSCT mobilization were considered if at least two of the following factors were present: age over 50, marrow infiltrating disease, irradiation history, numerous chemotherapy lines (over 3) and previous chemotherapy courses with platinum or fludarabine.

2.3. Collection of autologous HSC

Autologous HSC were collected by leukapheresis after mobilization either by a minimum five-day granulocyte colony-stimulating factor (rHuG-CSF; filgastrim, Amgen, Thousand Oaks, CA; lenogastrim, Chugaï, Tokyo, Japan) treatment alone or by rHuG-CSF treatment during hematological recovery after chemotherapy. Cytokine was given until full completion of the sessions.

CD34+ cell blood levels were counted in the patient's blood less than two hours before starting leukapheresis by flow cytometry (Facsort, Becton Dickinson, Mountain View, CA). Blood leukocyte populations were stained

Table 1
Characteristics of patients: intrinsic factors.

Parameters	
Numbers of patients	43
Gender (M/F)	25 /18
Median age (range)	56 yo (16-70)
Underlying disease	
NHL	19
HD	3
MM	21
APBSCT for relapse	16
Number of patients with risk factors of poor APBSCT mobilization	11

F = female; HD = Hodgkin's disease; M = male, MM = multiple myeloma; NHL = non-Hogkin lymphoma; yo = years old.

Table 2
Blood parameters during stem cells mobilization and before starting leukapheresis sessions: extrinsic factors.

Parameters	
Numbers of cytapheresis sessions analysed	59
Median level of WBC at collection ($\times 10^9$/mL) (range)	26 (2–60)
Median level of blood platelets at collection ($\times 10^9$/mL) (range)	82 (26–472)
Median percentage of blood CD34+ cells at collection (%) (range)	0.07 (0.01–1.48)
Median level of blood CD34+ cells at collection (/μL) (range)	18 (2–98)

APBSCT : autologous peripheral blood stem cell transplantation.
WBC: white blood cells.