Original Research Article

A SINGLE CENTER 25-YEAR EXPERIENCE IN AUTOLOGOUS PERIPHERAL BLOOD STEM CELL COLLECTION: A FOCUS ON THE COLLECTION EFFICIENCY.

Abstract

Background: Harvest of hematopoietic progenitor cells via leukapheresis is being used increasingly for autologous transplantation. Adequate yield of cells per kilogram body weight of recipient is required for a successful engraftment. Collection efficiency is a useful parameter to assess quality of peripheral blood stem cell (PBSC) collection program. In this study, we report a 25-year experience in a tertiary care Hospital in Italy.

Patients and Methods: 1,026 consecutives autologous PBSC collection procedure, performed in 763 patients, from January 1996 to December 2020 were retrospectively considered. Data regarding patients, equipments, apheresis procedures and PBSC products were collected in our database. In these 25 years different apheresis collection devices were adopted in our Apheresis Unit. In the first period (1996-1999) we used Fresenius Com.Tec, in the central period (2000-2013) we used Cobe Spectra and in the last period (2014-2020) Spectra Optia.

Results: As regards the evaluation of patients before leukapheresis, the most significant data was the increasing number of CD34+ cells. Considering the PBSC collection procedure, there was a progressive increase in the processed blood volume, accompanied by a reduction in the time required to complete the apheresis session. Data related to the PBSC collection demonstrated an increasing CD34+ cell yield and efficiency.

Conclusions: These results were observed considering a 25-year period, thus a great number of factors likely contributing to the observed results, including technological improvement of the instrumentation for leukapheresis and increased experience of the team operating in the Apheresis Unit. Moreover, we observed an improvement in collection efficiency from 43% to 53%.

Key Words

Autologous PBSC collection, CD34 cells, Collection Efficiency, Leukapheresis.

Introduction

Harvest and transplantation of hematopoietic progenitor cells is used increasingly in the treatment of several blood disorders, malignancies, and genetic abnormalities [1-3]. Progenitor stem cells are present, with extremely low rate (0.01-0.5% of nucleated cells) in peripheral blood. However, mobilization of cells into the peripheral blood using chemotherapy and/or growth factors (G-CSF) results in an increased number of circulating peripheral blood stem cells (PBSCs), facilitating their harvest by leukapheresis, and quantifying them in terms of CD34+ cells [4-6].

The adequacy of a collection is measured by the number of CD34+ cells per kilogram of recipient body weight. Successful engraftment has been observed with an amount ranging from 2 to 5×10^6 CD34+ cells/kg [7-9]. A minimum of 20 circulating CD34+ cells per microliter affords such satisfactory yields and is conventionally considered the threshold for begin the collection procedure [10,11]. These levels of circulating cells are achieved depending on the mobilization regimen, after 5 to 15 days from the beginning of mobilization therapy [12,13]. Usually, two to four blood volumes are processed per leukapheresis procedure, despite which sometimes serial collections may be necessary to attain the appropriate CD34+ cell dose for transplantation [14,15]. Collection efficiency (CE) is one of the objective quality parameters which can be used to assess blood cell separator potential for obtaining high yields of CD34+ cells and, hence facilitating successful transplants. However, data on the CE of cell separators is limited, especially with reference to CD34+ cell collection [16,17].

In this study data recorded during a 25-year experience in autologous PBSC collection, in a tertiary care Hospital in North-East Italy, were retrospectively considered.

Patients and Methods

Study's location: Our institution is located in the Mestre Hospital (Ospedale dell'Angelo), a large tertiary care facility, in Mestre (Venice), North-East Italy.

Data collection: From 01/01/1996 to 12/31/2020 the Apheresis Unit (AU) of Department of Blood Transfusion Medicine performed 1,026 autologous PBSC collection procedures in 763 patients. From patients' clinical records were retrospectively considered personal data including gender, age, weight, volemia; clinical data including diagnosis, mobilization regimen, basal HCT, WBC, PLT and CD34+ counts. Data specifically related with leukapheresis procedures such as instrumentation, time of session, adverse events, processed volume, CE were also considered, as well as data regarding PBSC collected units. Collections were carried out only for autologous use. Informed consent was obtained from all patients prior to collection.

Instrumentations: From 1996 to 1999 autologous PBSC procedures were carried out by using the Fresenius Com.Tec blood cell separator (Fresenius Kabi, Bad Homburg, Germany). The machine was calibrated and worked on its default settings. The P1YA kit (auto MNC stem cells) was used, and the collection program was set to mononuclear cells (autoMNC) software V4.03.07 [18].

From 2000 to 2013 autologous PBSC procedures were carried out by using the Cobe Spectra Apheresis System (Terumo BCT INC, Lakewood, CO). The machine was calibrated and worked on its default settings. The Auto PBSC set (with ISBT labelled bag kit) was used, and the collection program was Cobe Spectra MNC software V6.0 [19]

From 2014 to 2020 autologous PBSC procedures were carried out using the Spectra Optia Apheresis System (Terumo BCT INC, Lakewood, CO). The machine was calibrated and worked on its default settings. The CMNC (Continuous Mononuclear Cell Collection) kit was used, and the collection program was Spectra Optia MNC software V11.30. [20]

CD34+ cell count determination: CD34+ cell counts were determined before procedure in the patients' peripheral blood, and then in the leukapheresis product, by flow cytometry (FACS Calibur, Becton Dickinson, Heidelberg, Germany) using the accepted protocol given by the International Society of Hematology and Graft Engineering (ISHAGE) [21]. Blood cells count was performed using an automated cell counter Sysmex XE 2100 (Sysmex Corporation, Japan) [22]

Statistical Analysis: Data were analyzed using MedCalc Ver.8.0.0 (Medcalc SW bvda Ostend, Belgium). Categorical data are presented as numbers (percent) and continuous data as median and Quartiles (IQ and IIIQ). Alpha defined as $P < 0.05$ was considered statistically significant. Mann–Whitney U-test and Wilcoxon test were used for comparisons between samples, while associations between variables were verified by Fisher's exact test. Linear regression analysis was performed to evaluate the impact of considered parameters on CD34+ CE and CD34+ yield.

CE, also defined as CE2 [23], was calculated to compare the effectiveness of PBSC extraction with different systems. CE was calculated using following formula [23]:

$$\text{CE \%} = \frac{\text{Total CD34+ positive cells obtained by leukapheresis} \times 100}{\text{Peripheral blood (PB) CD34+/µL} \times \text{Blood volume processed (mL)}}$$

where: Total CD34+ cells in the product were calculated by multiplying CD34+/µL in the product and the volume of the product (mL); PB CD34+ cells were the concentration of CD34+ present in the PB before leukapheresis; volumes processed were those processed by the blood cell separator, subtracting the quantity of acid citrate dextrose anticoagulant (ACD) used as anticoagulant.

Results

We retrospectively considered 1,026 consecutives autologous PBSC collections procedures, performed between 1996 to 2020, in 763 patients with a mean of 1.3 procedures per patient (range 1-3). Of these subjects, 452 (59%) were males and 311 (41%) females, median age was 55 years (range 18-79), median body weight was 72 Kg (range 29-125). In 1,026 consecutive procedures we observed 61 (5.9%) adverse events, but only 14 (1.4%) were serious, causing interruption of the apheresis procedure: in 7 cases it was suspended owing to problems with vascular access, in 3 cases owing to the formation of clots in the extracorporeal line, in 2 cases for failure of blood cell separator; moreover, in other 3 cases the procedure was respectively suspended for severe hypocalcemia, angor, and loss of consciousness.

On table I patients' distribution according to diagnosis is reported. In 228 patients (29.9%) autologous PBSC collections procedures were performed for multiple myeloma (MM), in 185 (24.2) for non-Hodgkin lymphoma (NHL), in 143 (18.7%) for Hodgkin disease (HD), in 106 (13.9%) for acute myeloid leukemia (AML), in 73 (10.4%) for acute lymphoblastic leukemia (LAL), in 13 (1.7%) for chronic lymphoid leukemia (CLL) and in 9 (1.2%) for other diseases. On table II mobilization protocols adopted at our institution from 1996 to 2020 in 763 patients were reported.

Between 1996 and 1999 118 autologous PBSC collection procedures were performed by using Fresenius Com.Tec blood cell separator in 64 patients (procedures per patient ratio 1.8). Of these, 36 patients (56%) were males, median age was 48 years (IQ 37 IIIQ 52 years), median body weight was 72 kg (IQ 60 IIIQ 84 kg), prevalence of adverse events were 6 (5.1%), and serious ones, requiring stopping the procedure, were 3 (2.5%). Pre- procedural blood count showed a median CD34+ cells of 39/μL (IQ 21 IIIQ 91 μ/L). Median HCT was 28.1% (IQ 25.5 IIIQ 30.1 %), median WBC count of $14.6x10^9$/L (IQ 8.8 IIIQ 23.7 $x10^9$/L), median PLT count of $80x10^9$ (IQ 47 IIIQ $144x10^9$/L).

Median processed volume for each leukapheresis was 11.1 L (IQ 9.7 IIIQ 12.5 L), median time for each procedure was 280 minutes (IQ 250 IIIQ 303 minutes). Collected products has a median volume of 340 mL (IQ 280 IIIQ 380 mL), with a median WBC count of $49.5x10^9$/L (IQ 34.1 IIIQ $70.9x10^9$/L), PLT count of $351x10^9$/L (IQ 211 IIIQ $643x10^9$/L), and HCT of 4.3% (IQ 3.3 IIIQ 5.6 %). Median CD34+ concentration in apheresis product was 620/μL (IQ 329 IIIQ 1320/μL), collection efficiency was 43% (IQ 26 IIIQ 56 %), CD34+ yield was 2.5 10^6/Kg (IQ 1.6 IIIQ 6.3 10^6/Kg).

Between 2000 and 2013 590 autologous PBSC collection procedures using Cobe Spectra blood cell separator in 411 patients were performed (procedures per patient ratio 1.4). Of these, 223 patients

(54%) were males, median age was 53 years (IQ 43 IIIQ 62 years), median body weight was 73 kg (IQ 62 IIIQ 82 kg), adverse events were 41 (5.9%), and serious ones, requiring stopping the procedure, were 9 (1.5%). Pre-procedural blood count showed a median CD34+ cells of 54/μL (IQ 35 IIIQ 93/μL). Median HCT was 29.9% (IQ 27.4 IIIQ 33.2%), WBC count was $16.1x10^9$/L (IQ 9.3 IIIQ $24.9x10^9$/L), PLT count was $60x10^9$/L (IQ 35 IIIQ $93x10^9$/L). Median processed volume for each leukapheresis was 12.5 L (IQ 11.1 IIIQ 14.5 L), median time for each procedure was 275 minutes (IQ 248 IIIQ 305 minutes). Collected products has a median volume of 305 mL (IQ 255 IIIQ 335 mL), with a median WBC count of $113.2x10^9$/L (IQ 79.9 IIIQ $151.3x10^9$/L), PLT count of $319x10^9$/L (IQ 190 IIIQ $542x10^9$/L), and HCT of 2.1% (IQ 1.5 IIIQ 2.9%). Median CD34+ concentration in apheresis product was 1,150/μL (IQ 595 IIIQ 2,256/μL), collection efficiency was 49% (IQ 38 IIIQ 61%), CD34+ yield was $5.2x10^6$/kg (IQ 2.9 IIIQ $9.1x10^6$/gg).

Between 2013 and 2020 318 autologous PBSC collection procedures using Spectra Optia blood cell separator in 288 patients (procedures per patient ratio 1.1) were performed. Of these, 193 (67%) were males, median age was 58 years (IQ 47 IIIQ 66 years), median body weight was 71 kg (IQ 62 IIIQ 82 kg), adverse events were 14 (4.4%), and serious ones, requiring stopping the procedure, were 2 (0.6%). Pre-procedural blood count showed a median CD34+ cells of 96/μL (IQ 44 IIIQ 220/μL). Median HCT was 31.1% (IQ 29.3 IIIQ 29.3%), median WBC count was of $24.5x10^9$/L (IQ 14.6 IIIQ 39.3 10E9/L), a median PLT count was of $73x10^9$ (IQ 37 IIIQ $124x10^9$/L). Median processed volume for each leukapheresis was 13.8 L (IQ 11.1 IIIQ 15.2 L), median time for each procedure was 248 minutes (IQ 181 IIIQ 290 minutes). Collected products has a median volume of 180 mL (IQ 126 IIIQ 242 mL), with a WBC count of $195x10^9$/L (IQ 166 IIIQ 221 x 10^9/L), PLT count of 583 10^9/L (IQ 323 IIIQ 959 10^9/L), median HCT of 1.8% (IQ 1.2 IIIQ 2.6%). Median CD34+ concentration in apheresis product was 2,504/μL (IQ 1,328 IIIQ 5,231/μL), collection efficiency was 53% (IQ 42% IIIQ 65%), CD34+ yield was 7.2 10E6/Kg (IQ 4.1 IIIQ 10.9 10^6/Kg). All these data were reported on Table III.

When comparing data of the three periods, we observed a progressive increase of median age and male prevalence. Moreover, during the observation period a progressive decrease in the number of procedures necessary to reach the PBSC collection target, as demonstrated by the ratio of procedures per patient reducing from 1.8 to 1.1, was recorded. As regards the adverse events, a significant reduction was observed in the serious ones, namely those needing to stop leukapheresis, decreasing from 2.5% to 0.6%; while the total number of adverse events did not change [25,26].

As regards the evaluation of patients before leukapheresis, the most significant data was the increase in the number of CD34+ cells, from a median of 39/μL to 96/μL [27].

Considering the collection procedure, there is a progressive increase in the processed blood volume which passes from a median of 11.1 to 13.5 L, which is accompanied by a reduction in the time required to complete the procedure, decreasing from 280 to 245 minutes. The collected volume also showed a significant decrease in the median values, lowering from 340 to 180 mL.

When considering the PBSC concentrate obtained, we can detect a marked increase in the collection of PLTs ($p<0.001$) and WBCs as well as a better depletion of RBCs: in fact, median HCT decreased from 4.3% to 1.9%. Data relating to the collection of CD34+ cells appear very good, since their median concentration in the product raised from 620/μL to 2,540/μL, as well as the yield expressed as CD34+ cells/kg of the patient' weight increased from a median value of $2.5x10^6$ to 7.2 $x10^6$/Kg, in keeping also with some technology-based improvement [18-20].

Discussion

In this study a single center 25-year experience (1996-2020) in autologous PBCS collection has been reported. At our Institution PBSC Transplant Program is authorized by Italian National Transplant Authority and our AU is also authorized by National Italian Blood Authority. In this period 1,026 leukapheresis in 763 patients were performed. Obviously, in these 25 years different blood cell separators were adopted in our AU. In the first period (1996-1999) we used Fresenius Com.Tec, in the central period (2000-2013) Cobe Spectra and finally, in the last period (2014-2020), Spectra Optia.

The very conception of the study constitutes its main limitation, being a retrospective evaluation of the activity of a single center. However, the temporal extension of the observation, the large number of patients and procedures included into the study, the completeness of the available data make, at least to our opinion, this experience worthy of being shared and discussed.

In our patients' series we observed: a progressive increase of median age and male prevalence, a decrease in the number of procedures necessary to reach the PBSC collection target (figure 1), a reduction in serious procedure's side effects. Many factors may have contributed to the observed results, including technological advances of blood cell separators for leukapheresis, increased experience of the team operating in the AU, better mobilization regimens, improved patient's clinical condition at enrollment, more clear-cut inclusion criteria, modification of blood cell analyzers and protocol in CD34+ analysis.

Considering all these factors, we mainly focused our attention on the CE (expressed as CE2), that is an index that can be calculated for each individual session, taking into account by a standard formula the pool of circulating CD34+ cells as evaluated from the measurement of circulating CD34+ cells and the total blood volume, as well as the number of collected CD34+ cells. Since it is

an indicator obtained, for each individual procedure, from parameters available at the time of the procedure, it should be sufficiently independent of factors external to it, including methods of quantifying PBSC product, selection criteria of patients, and different mobilization regimes [24, 28-30].

As reported in Table IV CE2 resulted to be quite satisfactory in our series, substantially in keeping with other previous reports [9,19-20,37-53]. The median value observed by using Fresenius Com.Tec was 43% (IQ 26 – IIIQ 56%), Cobe Spectra was 49% (IQ 36 IIIQ 61%) and Spectra Optia was 53% (IQ 42 IIIQ 65%), with a significant increase ($p<0.05$) (Figure 2)

The CD34+ cell yields obtained through leukapheresis are partly determined by the CE, making this an important parameter for successful harvests, as well as a reliable indicator of the quality of the production process. CE values can be highly variable, as seen in the literature (Table IV), with median values as low a 29% and as high as 58% [9,19-20,37-53]. Apart from patient's characteristics, type of collection device, cell separation system, program and operator settings all contribute towards this variability [9,19-20,37-53]. In our experience CE2 varied from 19 to 165%. Values above 100% may be explained by the intra-collection recruitment phenomenon [54], which caused fluctuation of peripheral CD34+ concentration by recruiting additional cells from the bone marrow during the leukapheresis, when a long-lasting procedure is performed. In our study median CE was sometimes slightly lower than the values observed in other studies. To our opinion, this observation may be due to some operative differences, as well as to the fact that the average leukapheresis volumes at our Institution were quite high. Larger volumes were processed to harvest an adequate dose in a single procedure, to minimize numbers of procedures and patient discomfort. The CE2 of the blood cell separator is also reflected in its power to extract and concentrate the cells of interest. Matic *et al*. [34] observed that CD34+ cells were enriched 38-fold in the apheresis product when less than one blood volume was processed, but the efficiency decreased as higher volumes were processed. Moreover, CE2 has been inversely correlated with basal WBC count in previous studies [12-14, 28]. In our experience, a median of 3.1 blood volumes were processed, and median basal WBC count was 18.1×10^9/L. Although multiple collections can be carried out in patients who do not reach the target yield within one procedure, this may be critical due to debilitating conditions on the second or third day of PBSC collection, decrease in CD34+ cell number, cost of additional procedures. Hence attempts should be made to minimize the number of leukapheresis procedures. In the present study, from 1996 to 1999 49 patients (76.5%) required further collection procedures, 71 (17.3%) from 2000 to 2013 and 17 (5.9%) from 2014 to 2020. These results may be due to the technological improvement of blood cell separator technology, as well as to a greater experience of the team operating at the AU [1-3, 18-20].

Optimization of CE requires identification of factors impacting this parameter. In this study multiple regression analysis were carried out to evaluate the impact of age, gender, weight, diagnosis, basal hematocrit, WBC and PLT counts, CD34+ cell concentration and levels, processed blood volume. Correlations were calculated using the Pearson test and were confirmed by the Spearman test. After running a Mann-Whitney U-test the null hypothesis was rejected only for basal CD34+ levels. This result was confirmed also by a multivariable Cox model, resulting this parameter, i.e., the pre-procedure CD34+ cell count, the best predictor factor CD34+ collection yield.

Basal WBC count has been found to be an important independent factor which inversely affects CE in some studies, [4, 7-9] whereas in others it did not show significant correlation with CE [13,14] like our results. Similarly, the role of HCT has also been controversial. Mehta et al [32] and Sarkodee-Adoo et al [8] suggest that there is no correlation between HCT and CE, a finding echoed in the present study as well as in the findings of Ford et al [9], which shows an inverse correlation between the two parameters. Similarly, age was not a significant factor in the present study, a finding supported by Ford et al [9], but at odds with the results of Ikeda et al. [36] No association was found, in our series, between CD34+ yields and gender, weight, type of disease, and basal PLT counts, in keeping with the results of Schwella et al [31].

As results of our multivariate statistical analysis only three parameters were independent markers of CD34+ cell yield: basal CD34+ cell count, CE and processed blood volume. Relationship between these three parameters have not yet been established with absolute certainty. For instance, by increasing the volume of the leukapheresis number of PBSCs processed by the blood cell separator increases and release of CD34+ cells from the bone marrow compartment can also be recruited, however some authors observed a reduction in the collection efficiency [23-26]. Moreover, several studies have also shown a correlation between basal CD34+ cell count and the final yield of collected CD34+ cells per kg weight [1-4]. These results have been confirmed by our data.

As a conclusion, the salient data must be sought in the observation that, with the improvement of the team's experience and the evolution of blood cellular separator technology, a reduction in serious adverse events has been observed, a decrease in the procedures per patient ratio necessary to reach the target collection, an increase in the volume processed with a reduction in the time required to complete leukapheresis.

In addition, over the years we have observed an increase in basal CD34+ cells, namely an improvement in quality of the mobilization regimes and choice of timing of collection accompanied by higher values CE, all these factors enhancing the collected CD34+ yields.

No animal experiments were performed during the study.

Since this is a retrospective study, based on clinical data present in a database, it was not necessary to seek the opinion of the Ethics Committee.

Each patient issued, at the time, written informed consent to undergo the Leukapheresis procedure.

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Table I: Disease distribution in 763 autologous PBSC patients.

Diagnosis	Number	Frequency
Multiple Myeloma	228	29.9%
Non Hodgkin Lymphoma	185	24.2%
Hodgkin Disease	143	18.7%
Acute Myeloid Leukemia	106	13.9%
Acute lymphoblastic Leukemia	79	10.4%
Chronic Lymphoid Leukemia	13	1.7%
Other Diseases	9	1.2%

Table II: Mobilization Protocols in 763 autologous PBSC patients.

Protocol	N°	%
ARA-C	235	30.8
IGEV	154	20.2
CYCLO	151	19.8
DHAP	52	6.8
R-DHAP	56	7.3
G-CSF alone	25	3.3
C + ARA-C	21	2.8
MTX + ARA-C	18	2.4
MTX	6	0.8
Others Protocols	45	5.9

ARA-C: cytarabine;
IGEV: gemcitabine + vinorebeline + ifosfamide;
CYCLO: cyclophosphamide;
DHAP: dexamethasone + high dose cytarabine + cisplatin;
R-DHAP: rituximab + DHAP;
CYCLO + G-CSF: cyclophosphamide + granulocyte stimulating factor;
CYCLO + ARA-C: cyclophosphamide + cytarabine;
MTX + ARA-C: methotrexate + cytarabine;
MTX: metotrexate.

Table III: Data concerning autologous PBSC collection procedures performed between 1996 and 2020, in our Institution.

	FRESENIUS COM.TEC	COBE SPECTRA	SPECTRA OPTIA	FRESENIUS COMTEC versus KOBE SPECTRA	FRESENIUS COMTEC Versus SPECTRA OPTIA	KOBE SPECTRA versus SPECTRA OPTIA
Years	1996-1999	2000-2013	2014-2020			
Patients' number	64	411	288			
Male	36 (56%)	223 (54%)	193 (67%)	NS	P<0.05	P<0.05
Age (years)	48 (37 - 52)	53 (43-62)	58 (47-66)	P<0.05	P<.0.05	NS
Weight (kg)	72 (60 - 84)	73 (62-82)	71 (62-82)	NS	NS	NS
Number of procedures	118	590	318			
Ratio procedures/patients	1,8	1,4	1,1	P<0.05	P<0.01	P<0.05
Totale adverse events	6 (5.1%)	41 (5.9%)	14 (4.4%)	NS	NS	NS
Serious adverse events	3 (2.5%)	9 (1.5%)	2 (0.6%)	P<0.05	P<0.01	P<0.05
Basal WBC count ($x10^9$/L)	14,6 (8.8-23.7)	16.1 (9.3-24.9)	24.5 (14.6-39.3)	NS	P<0.01	P<0.01
Basal HCT value (%)	28.1 (25.5-30.1)	29.9 (27.4-33.2)	31.1 (29.3-34.6)	NS	NS	NS
Basal PLT count ($x10^9$/L)	80 (47-144)	60 (35-93)	73 (37-124)	NS	NS	NS
Basal CD34+ count (/µL)	39 (21-91)	54 (35-93)	96 (44-220)	P<0.05	P<0.01	P<0.05
Processed volume (L)	11.1 (9.7 - 12.5)	12,5 (11,1-14,5)	13.8 (11.1-15.2)	P<0.05	P<0.05	NS
Procedure time (minutes)	280 (250 - 303)	275 (248-305)	248 (181-290)	NS	P<0.05	P<0.05
Product volume (mL)	340 (280-380)	305 (255-335)	180 (126-242)	NS	P<0.01	P<0.01
Product WBC count ($x10^9$/L)	49.5 (34.1-70.9)	113.2 (79.9-151.3)	195 (166-221)	P<0.01	P<0.005	NS
Product HCT value (%)	4.3 (3.3-5.6)	2,1 (1,5-2,9)	1.9 (1.2-2.4)	P<0.05	P<0.01	P<0.05
Product PLT count ($x10^9$/L)	351 (211-643)	319 (190-542)	583 (323-959)	NS	P<0.05	P<0.05
CD34+ CE (%)	43 (26 – 56)	49 (38 -61)	53 (42 -65)	P<0.05	P<0.01	P<0.05
Product CD34+ concentration (/µL)	620 (329-1,320)	1,150 (595-2,256)	2,504 (1,328-5,231)	P<0.005	P<0.001	P<0.005
CD34+ yield ($x10^6$/Kg)	2,5 (1.6-6.3)	5,2 (2,9-9,1)	7.2 (4.1-10.9)	P<0.005	P<0.001	P<0.005

Table IV: Collection efficiency, data from literature

AUTHORS	Type of blood cell separator	Number of procedures/patients	Collection efficiency (CE)
Rowley et al, 1999	Cobe Spectra	28 procedures/ 12 patients	58%
Heuft et al, 2000	Cobe Spectra	102 procedures/ 81 patients	43%
Hitzler et al, 2001	Cobe Spectra	53 procedures/ 29 patients	45%
Ford et al, 2002	Cobe Spectra	61 patients	39%
Adorno et al, 2004	Cobe Spectra	36 procedures	47%
Movassaghi et al, 2007	Fresenius Com.Tec	112 procedures/ 91 patients	42%
Altuntas et al, 2007	Fresenius Com.Tec	20 procedures/ 17 patients	57%
Coluccia et al, 2009	Cobe Spectra	238 procedures	53%
Cooling et al, 2010	Cobe Spectra	35 procedures/ 34 patients	34%
Cousins et al, 2015	Cobe Spectra	174 procedures	51%
Wuchter et al, 2017	Cobe Spectra	60 procedures	47%
Sanderson et al, 2017	Spectra Optia	39 procedures/ 23 patients	49%
Deneys et al, 2017	Cobe Spectra Fresenius Com.Tec	8 patients 31 patients	50% 47%
Lee et al, 2017	Cobe Spectra	37 patients	43%
Lisenko et al, 2017	Spectra Optia	78 patients	45%
Solmaz et al, 2018	Fresenius Com.Tec	64 procedures	70%
Pandey & Cottler-Fox, 2018	Spectra Optia Cobe Spectra	59 procedures (LVL) 28 procedures (non LVL) 68 procedures (LVL) 28 procedures (non LVL)	37% 53% 39% 47%
Bojanic et al, 2019	Spectra Optia	67 procedures/ 46 patients	49%
Lopez Pereira et al, 2020	Cobe Spectra Spectra Optia	145 procedures/ 86 patients 128 procedures/ 72 patients	43% 50%
Chung et al, 2021	Spectra Optia	56 procedures/ 20 patients	29%

LVL: Large volume leukapheresis

Figure 1: Patients procedures ratio

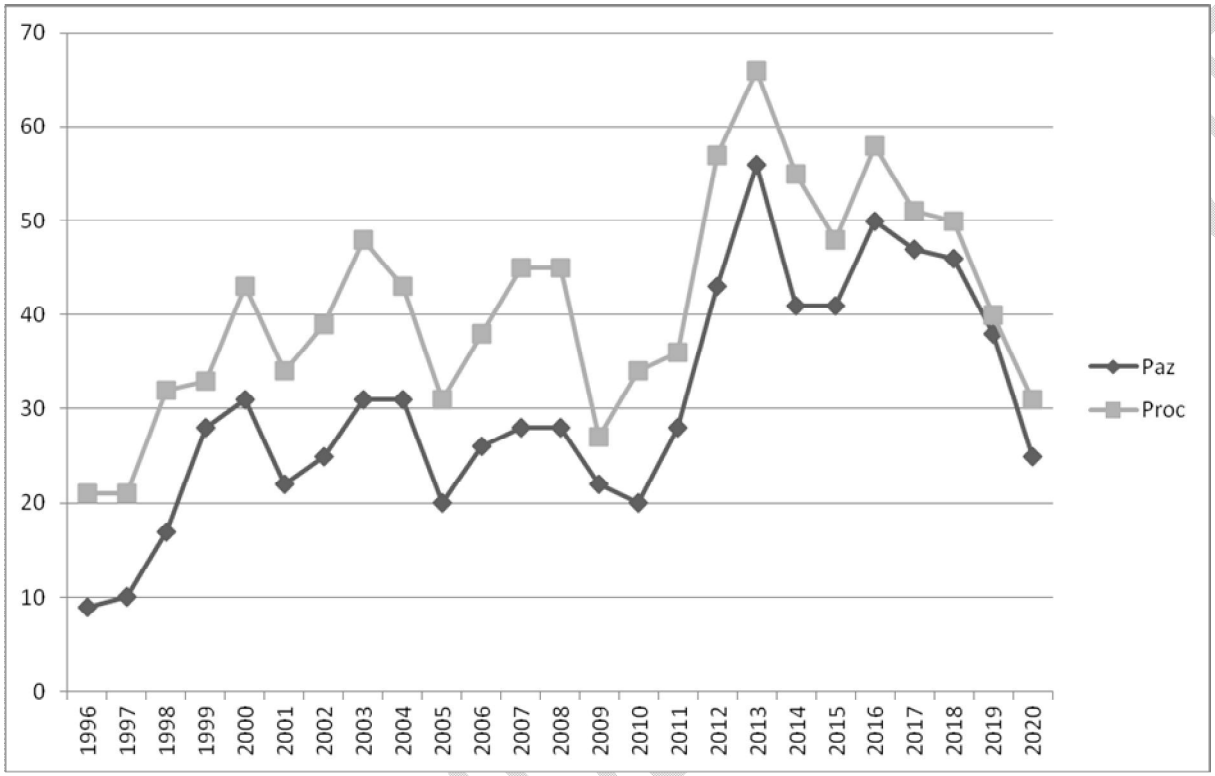

Figure 2: Box and wiskers diagram for Collection Efficiency