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A Single Center 25-year Experience in Autologous Peripheral Blood Stem Cell Collection: A Focus on the Collection Efficiency

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Authors' contributions

This work was carried out in collaboration among all authors. All the authors contributed significantly to the study and in particular authors DFG, PF and FA performed leukapheresis and recorded patient data. Authors GG and MP carried out the statistical analysis and wrote the manuscript. All authors read and approved the final manuscript.

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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 (CE) 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.

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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, Blood Cells Separators (BCS) , apheresis procedures and PBSC products were collected in our database. In these 25 years different BCS were adopted in our Apheresis Unit (AU). 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 with a shorter apheresis duration. Data related to the PBSC collection demonstrated an increasing CD34+ cell yield and efficiency a raise in CE that was 43% using Fresenius COM-TEC BCS, 49% using Cobe Spectra BCS and 53% using Spectra Optia BCS. .
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, increased experience of the team operating in the Apheresis Unit, improved mobilization protocols, better criteria for patients' selection. Focusing our attention on CE we observed quite satisfactory results with a median which rose from 43% to 53% with an increase of 10% in the observation period.

Keywords: Autologous PBSC collection; CD34 cells; collection efficiency; leukapheresis.

1. INTRODUCTION

Harvest and transplantation of hematopoietic progenitor cells is used increasingly in the treatment of several blood disorders, malignancies, and genetic abnormalities [1-3]. Stem cells are present, with extremely low rate (0.01-0.5% of nucleated cells) in peripheral blood. However, mobilization of cells into 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. Usually, Blood Stem cells are characterized by the expression of the CD34 antigen on the cell membrane [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 20/25 circulating CD34+ cells per microliter 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 for each leukapheresis procedure. However, in some cases, it may be necessary to perform repeated leukapheresis to achieve 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 (BCS) ability to obtain and adequate 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.

2. PATIENTS AND METHODS

2.1 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.

2.2 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' documentation recorded in our AU 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 to leukapheresis procedures: duration, type of BCS used, adverse events, processed volume, CE were also considered. Moreover were considered data regarding PBSC collected units: volume, WBC, HCT, PLT, CD34 yeld. Collections were carried out only for

autologous use. Informed consent was obtained from all patients prior to collection.

2.3 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 as from manufactured recommendations. 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 as from manufactured recommendations. 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 as from manufactured recommendations. The CMNC (Continuous Mononuclear Cell Collection) kit was used, and the collection program was Spectra Optia MNC software V11.30 [20].

2.4 CD34+ Cell Count Determination

CD34+ cell counts was performed , by flow cytometry (FACS Calibur, Becton Dickinson, Heidelberg, Germany) using the protocol of 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].

2.5 Statistical Analysis

Data were analyzed using MedCalc Ver.8.0.0 (Medcalc SW bvda Ostend, Belgium). Categorical data are presented as numbers (percent), the data distribution curves were studied using the Skewness and Courtosi tests, having detected the non-normality of curves we adopted a non-parametric statistical approach and results were reported as median value, first and third Quartiles (IQ and IIIQ), inter Quartile range (IQR). 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 BCS. CE was calculated using following formula [24]:

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

where: Total CD34+ cells in the product were calculated by multiplying CD34+/µL 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.

3. 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 59 -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: problems with vascular access (7) , clots in the extracorporeal line (3), failure of blood cell separator (2); severe hypocalcemia, angor, and loss of consciousness (1 each).

In Table 1 was reported patients' distribution according to diagnosis:. 228 patients (29.9%) had multiple myeloma (MM), 185 (24.2) non-Hodgkin lymphoma (NHL), 143 (18.7%) Hodgkin disease (HD), 106 (13.9%) acute myeloid leukemia (AML), 73 (10.4%) for acute lymphoblastic leukemia (LAL), 13 (1.7%) chronic lymphoid leukemia (CLL) and 9 (1.2%) for other diseases. In Table 2 were reported mobilization's protocols adopted in these patients.

As reported in Table 3, from 1996 to 1999, 118 autologous PBSC collection procedures were

performed in 64 patients (ratio 1.8), using Fresenius Com. Tec BCS Of these 64 patients, 36 (56%) were males, median age was 48 years, median body weight was 72 kg, 6 adverse events were observed (5.1%), of these 3 (2.5%) were serious adverse events requiring to stop the procedure.. Pre- procedural blood count showed a median CD34+ cells value of 39/µL, median HCT was 28.1% , median WBC count was $14.6x10^9$/L , median PLT count was $80x10^9$.

Median volume processed for each leukapheresis was 11.1 L, median procedure duration was 280 minutes. Collected products has a median volume of 340 mL, with a median WBC count of $49.5x10^9$/L, PLT count of $351x10^9$/L , and HCT of 4.3%. Median CD34+ concentration in apheresis product was 620/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).

As reported in Table 3 from 2000 to 2013, 590 autologous PBSC collection procedures were performed in 411 patients (ratio 1.4) using Cobe Spectra BCS blood cell separator in. Of these 411 patients., 223 (54%) were males, median age was 53 years , median body weight was 73 kg , 41 (5.9%) adverse events were observed, of these 9 (1.5%) were seriousadverse events , requiring to stop the procedure. Pre-procedural blood count showed a median CD34+ cells of 54/µL. median HCT was 29.9%, median WBC count was $16.1x10^9$/L, median PLT count was $60x10^9$/L. Median volume processed for each leukapheresis was 12.5 L, median procedure duration was 275 minutes. Collected products has a median volume of 305 mL , with a median WBC count of $113.2x10^9$/L , PLT count of $319x10^9$/L , and HCT of 2.1% . Median CD34+ concentration in apheresis product was 1,150/µL, collection efficiency was 49% (IQ 38% - IIIQ 61%), CD34+ yield was $5.2x10^6$/kg (IQ 2.9 IIIQ $9.1x10^6$/gg).

As reported in Table 3 from 2013 to 2020 318 autologous PBSC collection procedures were performed in 288 patients (ratio 1.1) using Spectra Optia blood cell separator. Of these, 288 patients, 193 (67%) were males, median age was 58 years , median body weight was 71 kg , 14 (4.4%) adverse events were observed, of these 2 (0.6%) were serious adverse events requiring to stop the procedure. Pre-procedural blood count showed a median CD34+ cells of 96/µL, median HCT was 31.1% , median WBC count was of $24.5x10^9$/L, median PLT count was of $73x10^9$. Median volume processed for each leukapheresis was 13.8 L, median procedure duration was 248 minutes. Collected products has a median volume of 180 mL, with a WBC count of $195x10^9$/L, PLT count of 583 10^9/L, median HCT of 1.8%. Median CD34+ concentration in apheresis product was 2,504/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).

When comparing data of the three periods, we observed a progressive increase of median age and male prevalence in patients population. Moreover, we observed a progressive decrease in the number of procedures necessary to reach the PBSC collection target, (ratio from 1.8 to 1.1). As regards the adverse events, a significant reduction was observed in the serious ones, (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 patients' evaluation 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 and a reduction of leukapheresis duration (from 280 to 245 minutes) moreover a significant decrease in collected volume (form 340 mL to 180 mL) was observed.

When considering the PBSC concentrate obtained, we can detect a marked increase in the collection of PLTs and WBCs as well as a better depletion of RBCs. 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 [18-20].

Focusing our attention on collection efficiency, the results obtained have always been satisfactory demonstrating a slight but significant increase. As matter of facts considering the Fresenius COM.TEC BCS the median CE was 43% (IQ 26% - IIIQ 56%) [18,28-29]. Considering the Cobe Spectra BCS the median CE was 49% (IQ 36% - IIIQ 61%) [9,19,21,30-36]. Considering the Spectra Optia BCS the median CE was 53% (IQ 42% - IIIQ65%) [37-42].

Table 1. 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 1 shows the pathologies diagnosed in the 763 patients considered in the present study.

Table 2. 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

Table 2 shows the different mobilization protocols used in the 763 patients considered in the study.

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 3. 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 3 shows data relating to 1026 leukapheresis procedures for the collection of autologous PBCS considered in this study. Results are reported as Median value and interquartile difference.

4. DISCUSSION

In this paper 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 BCS were adopted in our AU. In the first period (1996-1999) we used a Fresenius Com.Tec BCS, in the central period (2000-2013) a Cobe Spectra BCS and, in the last period (2014-2020), a Spectra Optia BCS.

In authors' opinion the main limitation of the study is that it is a retrospective single centre experience and not a polycentric study. 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 decrease in the number of procedures necessary to reach the PBSC collection target (Fig. 1) and a reduction in serious procedure's adverse events. 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 [43-47].

In this paper , we focused our attention about the Collection Efficiency 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 and the number of collected CD 34+ cells. The pool of circulating CD 34+cells should be evaluated taking in consideration the number of CD34+ cells μL and the total blood volume [48-50]. CE2 is an indicator obtained, for each individual procedure, from routine parameters so, in our opinion, it should be sufficiently independent of factors external to it, including methods of quantifying PBSC product, selection criteria of patients, and different mobilization regimes [51-54].

As reported in Table 4 CE2 resulted to be quite satisfactory in our series, substantially in keeping with other previous reports [55-59]. The median value observed by using Fresenius Com.Tec was 43% (IQ 26 – IIIQ 56%) [18, 28,29]. using Cobe Spectra was 49% (IQ 36 IIIQ 61%) [9,19,21,30-36], and using Spectra Optia was 53% (IQ 42 IIIQ 65%) [37-42]. thus we observed a 10% increase in the median values of CE, this increase was statistically significant ($p<0.05$), these data were reported in Fig. 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 4), with median values as low a 29% and as high as 58% [9,19-20,37-53]. Apart from patient's characteristics, type of BCS, 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 [8,40,56,60,61], which caused fluctuation of peripheral CD34+ concentration by recruiting additional cells from the bone marrow during the leukapheresis, when a large volume leukapheresis was 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 for example we performed leukapheresis using the default settings of the BCS, limiting deviations and customizations to a minimum. Moreover the median leukapheresis volumes at our Institution were quite high to harvest an adequate dose in a single procedure, to minimize numbers of procedures and patient discomfort. In literature it is reported than CE tends to decrease, in large volume leukapheresis [8,40,56,60,61]. The CE2 of the blood cell separator is also reflected in its power to extract and concentrate the cells of interest. Matic et al. [56] 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 $18.1x10^9$/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 BCS 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 [54] 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. [58] 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 [53].

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. Internal relationship between these three parameters have not yet been established with absolute certainty; for example, some authors suggest that during a large volume leukapheresis the EC may increase due to the PBSC recruitment linked to the procedure while others suggest an opposite effect. Data reported in this study are unable to clarify the internal relationships of these three parameters. However, we can conclude that, in our experience, an adequate yield of CD34 cells relays on: pre procedure cell count, processed blood volume and the collection efficiency.

Table 4. 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, 2003	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	8 patients	50%
	Fresenius	31 patients	47%

Authors	Type of blood cell separator	Number of procedures/patients	Collection efficiency (CE)
	Com.Tec		
Lee et al, 2017	Cobe Spectra	37 patients	43%
Lisenko et al, 2017	Fresenius Com.Tec	78 patients	45%
	Spectra Optia		
Solmaz et al, 2018	Fresenius Com.Tec	64 procedures	70%
Pandey & Cottler-Fox, 2018	Spectra Optia	59 procedures (LVL)	37%
		28 procedures (non LVL)	53%
	Cobe Spectra	68 procedures (LVL)	39%
		28 procedures (non LVL)	47%
Bojanic et al, 2019	Spectra Optia	67 procedures/ 46 patients	49%
Lopez Pereira et al, 2020	Cobe Spectra	145 procedures/ 86 patients	43%
	Spectra Optia	128 procedures/ 72 patients	50%
Chung et al, 2021	Spectra Optia	56 procedures/ 20 patients	29%

Table 4 shows the collection efficiency data reported in the literature by some authors who used the same cell separators used in this paper, in comparable operative settings. LVL: Large volume leukapheresis.

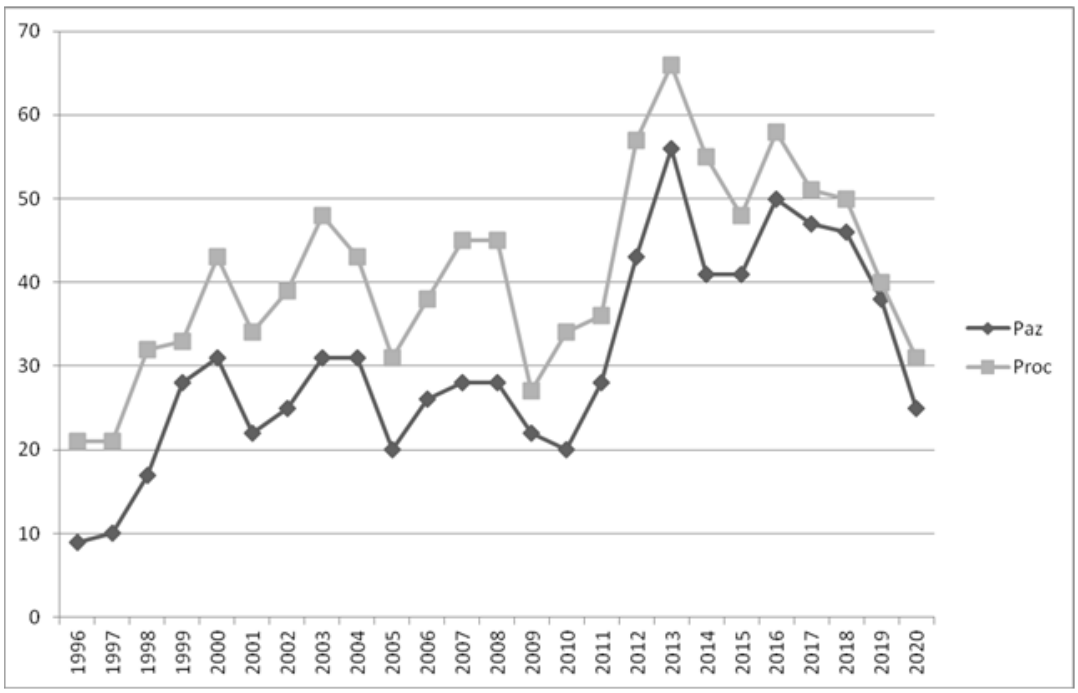

Fig. 1. Patients procedures ratio

Fig. 1 shows the year-by-year trends in the number of patients undergoing autologous PBSC collection and the number of leukapheresis procedures needed to achieve the collection goal set by colleagues in the clinical unit.

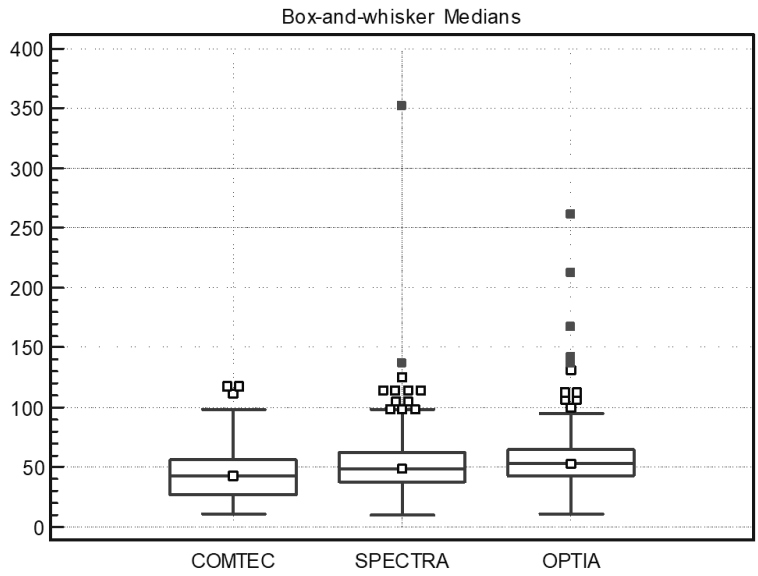

Fig. 2. Box and wiskers diagram for Collection Efficiency

Fig. 2 shows the distribution of collection efficiency data using a box-and-whisker plot. The center line in the box represents the median value, so half of the data is above this value, the other half below. The bottom and top sides of the box show the 1st and 3rd quartiles (interquartile range or IQR). The lines extending from the box are called whiskers. The whiskers represent the expected data variation and extend 1.5x from the IQR from the top and bottom of the box. outlier data is represented as external points.

5. CONCLUSIONS

As conclusive considerations, in our opinion, the take away message should be that, with the improvement of the team's experience and the evolution BCS technology, in our AU we observed series of improvement in leukapheresis for PBSC collection: a reduction in serious adverse events, a decrease in the procedures per patient ratio, an increase in the volume processed with a reduction of leukapheresis duration. Considering the leukapheresis products we observed a lower Hct, a higher CD34+ cells concentration and a raised CD34 yields. Focusing on collection efficiency we observed a significant increase in CE from median value of 45% to 53% ($p<0.05$).

CONSENT

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

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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