Original article

Patient Blood Management in pediatric and adolescent bone marrow donors: results from an Italian survey

Claudia Del Fante[1], Francesca Masiello[2], Marco Zecca[3], Ursula La Rocca[2], Simonetta Pupella[2], Vincenzo De Angelis[2]

[1]*Immunohematology and Transfusion Service, Fondazione IRCCS Policlinico "San Matteo", Pavia, Italy;*
[2]*National Blood Center, Italian National Institute of Health, Rome, Italy;*
[3]*Pediatric Hematology/Oncology, Fondazione IRCCS Policlinico "San Matteo", Pavia, Italy*

Background - Current national and international guidelines (Italian Bone Marrow Donor Registry [IBMDR], World Marrow Donor Association [WMDA] standards) provide an indication for preoperative autologous blood donation (PAD) only in adult family and volunteer non-family donors in anticipation of bone marrow (BM) hematopoietic stem cell (HSC) donation to avoid the use of homologous transfusions. In addition, there is no clear guidance from the relevant scientific societies regarding pediatric and adolescent donors.

Material and methods - To assess the actual use of PAD in pediatric (up to 14 years) and adolescent (aged 15-18 years) family donors in relation to BM HSC donation in the five years 2017-2021, a specific online questionnaire was administered to blood establishments and clinical units of pediatric transplantation programs responsible for BM HSC collection.

Results - Adherence to the project was 100% (18/18 centers). During the five-year period considered, 273 BM HSC donors (205 pediatric and 68 adolescent) were registered. Forty percent of the non-trait carrier donors who underwent PAD received iron therapy in preparation for BM HSC donation; only 4.8% of the pediatric and none of the adolescents had hemoglobin values below the age limit at donation. Finally, 66.4% of pediatric donors and 15.4% of non-trait carrier adolescent donors who did not undergo PAD received homologous transfusions during BM harvest.

Discussion - The present study highlights the highly heterogeneous criteria for the use of PAD (including calculating of the volume of whole blood collected) and the lack of a specific policy in preparation for BM HSC donation, either from non-trait carrier donors or those with sickle cell or thalassemia trait, both pediatric and adolescent.

Keywords: *bone marrow, stem cell donors, transplantation, preoperative autologous blood donation, blood transfusion.*

Arrived: 1 July 2024
Revision accepted: 27 October 2024
Correspondence: Francesca Masiello
e-mail: francesca.masiello@iss.it

INTRODUCTION

Despite the scarcity of blood resource worldwide and the development of Patient Blood Management (PBM) programs in adult setting, currently there are no specific guidelines for

optimal management of pediatric patients. In particular, concerning red blood cells (RBC), the transfusion policy in many cases is based solely on the hemoglobin (Hb) value, rather than the patient's overall clinical condition. It follows that several inappropriate transfusions are registered[1-4].

In the last years, there has been an increase in randomized controlled trials (RCTs) aimed at understanding best practice on RBC policy in pediatric setting[5-8]. As a result, even the 2023 AABB guidelines recommend a restrictive transfusion attitude in both adults and children[9].

Pre-operative autologous blood donation (PAD) of 1-2 units in anticipation of bone marrow (BM) harvest for homologous transplantation is a common practice. It was introduced during the 1980s to avoid the risk of homologous transfusions in BM donors and to promote post-harvest recovery[10].

PAD practice in anticipation of BM HSC collection in adult donors is controversial and mostly unnecessary. Several papers published to date have questioned its necessity, the threat of perioperative anemia, the potential risks related to autologous blood transfusion (in particular, clerical errors and bacterial contamination) and over-transfusion and, last but not least, the waste of autologous blood[11-14].

In addition, PAD involves organizational resources, burden on hospitals and costs[15-16].

Despite these premises, the adoption of PBM policy in BM donor setting, primarily by preventing anemia with iron administration, is not routinely practiced. A non-negligible reason may be related to the fact that many national registries still recommend PAD in anticipation of BM HSC donation in adults, even though the WMDA standards, edited in 2020, no longer mention it[17-18].

The results on a recent survey by our group in the adult donor setting highlighted the heterogeneous adoption of PAD and iron supplementation among centers. We highlighted the need for guidelines in this area, for the management of BM HSC donors and donations at best[19]. Subsequently, we also investigated BM donor management in pediatric and adolescent settings in Italy, since to our knowledge, neither national nor international guidelines are available on the subject.

BM HSC donation is considered safe with few side effects: mainly anemia, post-operative pain and anesthesia-related consequences. BM HSC are the most used graft in pediatric setting, both in malignant and non-malignant diseases. In particular, for patients affected with hemoglobinopathies BM HSC from HLA-matched sibling carriers of the trait are frequently used since sibling donors are the gold standard, according to the superior post-transplant outcomes[20].

Pediatric and adolescent settings show peculiar differences from the adult setting based on the assumption that a child is not a small adult. In addition, HSC donations are allowed only for related recipients[21]. Furthermore, the donor's age, a weight disparity with the recipient, concomitant genetic disorders (i.e. sickle cell or thalassemia traits) and the donor's psychological profile, require a multidisciplinary approach (pediatrics, anesthesiologists and transfusion medicine specialists) to avoid any possible risk related to the donation.

The present study presents the results of a national survey carried out by the Italian National Blood Center in collaboration with the Italian Association for Pediatric Hematology and Oncology (AIEOP). The aim was to outline the current utilization of PAD in pediatric bone marrow collection centers (PBMCC) in the PBM age.

MATERIALS AND METHODS

In order to assess the actual use of PAD in pediatric (1 up to 14 years) and adolescent (aged 15-18 years) related BM donors over the five-year period 2017-2021, a specific online questionnaire was sent to blood establishments and clinical units of PBMCC.

The survey was conducted in September 2022, with the support of AIEOP. The main questions concerned the number of donors, whether they were sickle cell or thalassemia traits carriers, the criteria adopted for PAD, the support with iron therapy in preparation for HSC donation and whether the pre-deposited units were transfused in the operating theatre as well as the incidence of anemia. Finally, we asked the centers about the possible usefulness of a PBM approach for the management of this type of donors.

The entire survey is provided in the *Online Supplementary Content* (**Table SI**).

RESULTS

All 18 PBMCC that had received the survey distributed throughout the country, responded: 11 for Northern Italy, 3 for Central Italy, 2 for the South and 1 for both Islands.

Donors

From 2017 to 2021, 273 HSC BM donors were reported: 205 of these were pediatric and 68 were adolescents. Five large centers reported more than 20 donors (21-102 donors). There were no differences between large and small centers: only one large center had a specific policy for healthy and trait donors.

Non-trait carrier HSC BM donors accounted for 84.4% (173 out of 205) of pediatric donors and 80.9% (55 out of 68) of adolescent's donors.

Sickle cell (SC-trait) and thalassemia-trait (Thal-trait) BM HSC donors were equally represented in the pediatric population: 7.8% each (16 out of 205). SC-trait donors accounted for 10.3% (7 out of 68) and Thal-trait donors for 18.8% (6 out of 68) of adolescent donors, respectively.

Preoperative autologous blood donation (PAD) practice

With regard to the criteria adopted for PAD practice in non-trait carrier donors, all centers reported that they considered the donor's age and weight, but the reference values among centers were highly variable for both.

The average age for performing PAD was 9.7 years (standard deviation, SD=3.5) and the average weight was 36.7 kilograms (SD=9.6). There was variability in initial donor hemoglobin (Hb) values: 6 out of 18 centers (33.3% of cases) did not consider it. Among the other centers, the majority (5 out of 18, 27.8%) considered 12.5 g/dL as the minimum acceptable value for donor eligibility for PAD. Finally, 5 out of 18 centers (27.8%) considered weight difference between donor and recipient as a criterion for practicing PAD. Only one center reported having a specific policy for pediatric and adolescent donors with SC-trait and Thal-trait; this center is one of the five largest in the country. No donors with SC-trait underwent PAD.

During the reporting period, 21 out of 173 pediatric (12.1%) and 29 out of 55 adolescent non-trait carrier donors (52.7%) underwent PAD. As a result, the majority (87.9%) of non-trait carrier pediatric donors did not undergo PAD; on the contrary, only 47.3% of non-trait carrier adolescent donors did not undergo PAD.

All centers reported that no adverse events ever occurred during PAD in pediatric and adolescent BM HSC donors (both non-trait carrier and Thal-trait carriers).

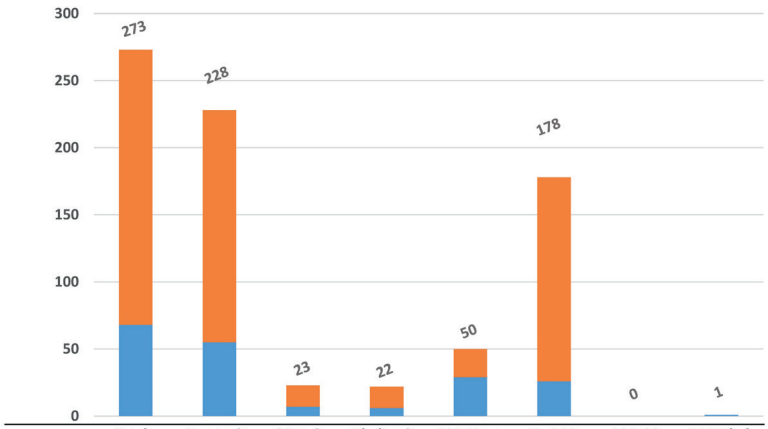
Figure 1 summarizes donors and PAD practice over the period 2017-2021.

Hemoglobin value in BM HSC donation (PAD non-trait carrier donors)

Only 4.8% (1 out of 21) of pediatric and none (0 out of 55) of adolescent non-trait carrier donors who underwent PAD had Hb values below the age limit before BM HSC donation (within 24 hours).

In addition, 9.5% (2 out of 21) of pediatric and 5.5% (3 out of 55) of adolescent donors had Hb values below the age limit after BM HSC donation (within 24 hours).

Out of 18 centers, 3 (16.7%) report that they always observe hemoglobin values below normal limits for age in non-trait carrier donors undergoing PAD immediately after BM HSC donation.



	Total	Non-trait	SC-trait	Thal-trait	PAD Non-trait	No PAD Non-trait	PAD SC-trait	PAD Thal-trait
Pediatric	205 (75%)	173 (76%)	16 (70%)	16 (73%)	21 (42%)	152 (85%)	0	0
Adolescent	68 (25%)	55 (24%)	7 (30%)	6 (27%)	29 (58%)	26 (15%)	0	1 (100%)

Figure 1 - Numbers of donors and PAD practice over the period 2017-2021
PAD: preoperative autologous blood donation; SC-trait: sickle cell trait; Thal-trait: thalassemic-trait.

Iron therapy to support BM HSC donation (without PAD)

47.8% of non-trait carrier pediatric and 36.6% of adolescent donors who did not undergo PAD, supported BM HSC donation with iron therapy (data taken from the 5-year average, **Figure 2**).

13.3% of SC-trait pediatric and 12.2% of adolescent donors who did not undergo PAD were administered iron therapy before BM HSC donation. The same trend was observed for Thal-trait donors: 13.3 % of pediatric and 11.1% of adolescent donors with Thal-trait who did not undergo PAD received iron support before BM HSC donation.

Instead, 77.8% of non-trait carrier pediatric and 50.9% of adolescent donors who did not undergo PAD, received iron supplementation after BM HSC donation (data obtained from the 5-year average, **Figure 3**).

28.9% of SC-trait pediatric and 24.4% of adolescent donors who did not undergo PAD received iron supplementation after BM HSC donation. We observed the same trend for Thal-trait donors: 28.9% of pediatric and 28.9% of adolescent donors with Thal-trait who did not undergo PAD received iron supplementation after BM HSC donation.

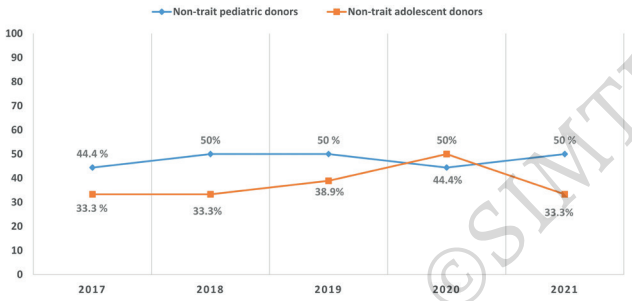


Figure 2 - Iron therapy to support HSC BM donation (without PAD) in pediatric and adolescent non-trait carrier donors, among the 5-years period

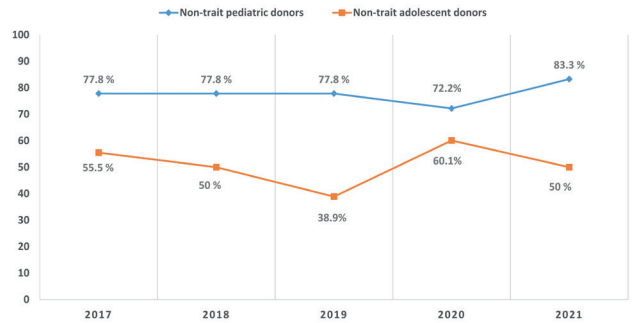


Figure 3 - Iron supplementation after HSC BM donation (without PAD) in pediatric and adolescent non-trait carrier donors, among the 5-years period

PAD units required and transfused

Figure 4 shows the data about operating room requests for PAD units from non-trait carrier pediatric and adolescent donors and the number of PAD units transfused in the operating room (data obtained from the 5-year average).

Three out of 6 large centers (50%) always transfuse PAD units. All centers reported that no side effects had occurred during the transfusion of PAD units in pediatric and adolescent donors (either non-trait carrier or Thal-trait carriers).

Homologous RBC transfusions

We asked about the recurrence of homologous RBC transfusions in HSC BM donors who did not undergo PAD. Ten out of 18 centers (55.6%) stated that a transfusion policy was in place for pediatric donors; whereas, only 5/18 centers (27.8%) had a transfusion policy for adolescent donors. In 8/18 centers (44.5%) a well-defined policy on the subject was absent.

66.4% of non-trait carrier pediatric and 15.4% of adolescent donors, who did not undergo PAD, received homologous transfusions during BM harvest (data taken from the 5-year average).

Among the trait carrier donors, 37.5% and 28.6% of SC-trait pediatric and adolescent donors received homologous transfusions during BM harvest, respectively. On the other hand, 93.7% of pediatric and 66.7% of adolescent donors with Thal-trait who did not undergo PAD received homologous transfusions during BM harvest (data obtained from the 5-year average).

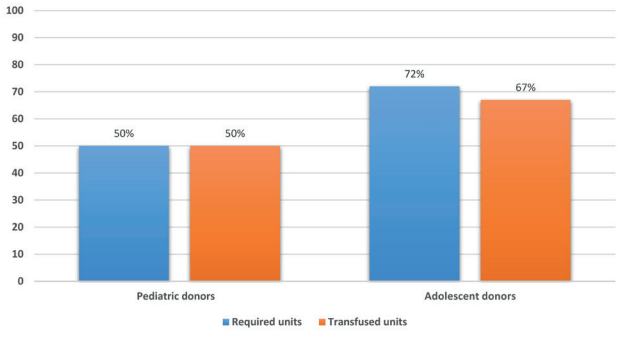


Figure 4 - Percentage of PAD units required and transfused for each donor population

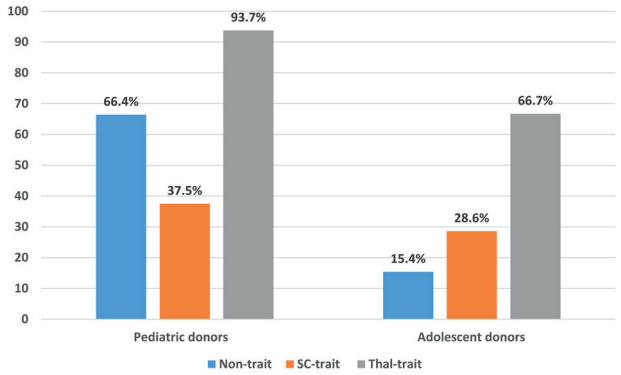


Figure 5 - Homologous RBC transfusions in HSC BM donors who did not undergo PAD, for each donor population

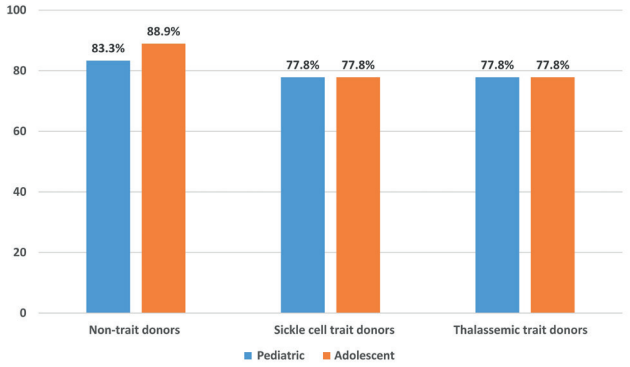


Figure 6 - PBM strategy to manage pediatric and adolescent HSC BM donors

Figure 5 summarizes the results of homologous RBC transfusions for each donor population in both pediatric and adolescent setting.

For non-trait carrier pediatric donors, the decision to administer homologous transfusions to BM HSC donors was mainly influenced by the volume collected (61.1% of respondents). For non-trait carrier adolescent donors, the decision was guided by both the volume collected and the hemoglobin values (33.3% respectively). The responses received regarding trait carrier donors were extremely heterogeneous across the centers.

PBM strategy to manage pediatric and adolescent BM HSC donors

Finally, centers were asked whether a PBM approach could be useful in managing pediatric and adolescent BM HSC donors. The highest percentage of positive responses was for the non-trait carrier adolescent donor category. **Figure 6** explains the responses on the appropriateness of a PBM approach among the centers.

DISCUSSION

The heterogeneous nature of the responses obtained from the present national survey, aimed at investigating the PAD policy in anticipation of BM HSC harvest over 5 years in pediatric and adolescent donors, shows that this practice lacks a standardised approach. We believe these findings are reliable as all 18 Italian PBMCC surveyed responded to the questionnaire (5 of which were large centers) and a significant number of donors (273) was reported.

Although most were pediatric donors, only a minority underwent PAD. In contrast, more than half of the non-trait carrier adolescent donors underwent PAD, with no difference between years. Some studies report that in major surgery, PAD should only be reserved for patients weighing at least 20 kg, where blood loss is expected to exceed 20% of patient's total blood volume with the aim of avoiding homologous transfusion[22-23].

The results of the present study showed that donor age and weight (and not the weight disparity between donor and recipient) guided the decision of most centers to PAD in non-trait carrier donors (both pediatric and adolescent) with different reference values. Moreover, most centers considered 12.5 g/dL the minimum acceptable level to perform PAD.

In our opinion, these results are a cause for reflection because they emphasise that BM harvesting is not considered as other surgical procedures, and therefore subject to recommendations for pediatric PBM, and reflecting an attitude similar to the adult setting[19,24]. The higher use of PAD in non-trait carrier adolescents is not justified and underlines that this outdated practice is frequently utilized even if its use is not supported by evidence. This is probably due to the lack of guidelines on the subject and the absence of a PBM policy in this area, not only in non-trait carriers but also in Thal-trait donors.

Our data show that most PADs were requested in the operating room to support hypovolemia during harvest even though it is well known that both PAD procedure and autologous reinfusion are known to expose the donor to unwanted risks[25,26].

However, as no side effects have been reported during PAD reinfusion, the latter is probably perceived as a

risk-free procedure in BM donors and could sustain PAD wastage, similar to the adult setting[27]. On the other hand, some PADs were transfused only after BM HSC donation or were not even requested, implying that these units were probably not needed. In addition, some studies report that approximately 50% of PAD units intended for major surgery in pediatric patients were discarded, invoking alternatives to transfusion and more restrictive triggers[28-30].

Furthermore, our study shows that only a minority of donors belonging to all categories (children and adolescents, non-trait and trait carriers) who did not undergo PAD were supported with iron therapy prior to BM harvest, and the largest number of donors who were supported with iron after BM donation belonged to the non-trait carrier pediatric setting. Current preparations for iron support are safe and offer the possibility of starting iron therapy easily before BM harvest. This would help optimize body iron stores and Hb levels prior to harvest. Iron therapy should continue also after donation to prevent anemia and to maintain adequate iron levels for growth. Notably, intravenous iron supplementation is only permitted in children of at least 6 years of age; from 6 to 14 years of age, only iron gluconate can be administered[31]. Nevertheless, iron supplementation (either intravenous or oral) has been used proportionally less in adolescents than in children prior to BM collection, as in some ways, they were considered similar to adults[19] and the specific iron requirement of adolescents were not taken into account[32]. These results also underline that the prevention/correction of anemia in pediatric HSC BM donors is not given the importance it deserves, both for donor's health and to avoid homologous transfusions. This is all the more true considering that iron deficiency is prevalent across all pediatric age groups (iron requirement peaks in adolescence) and it is associated with adverse effects on psychomotor and cognitive development[33].

On the other hand, only a minority of pediatric and none of teenagers' Hb values of non-trait carrier donors who underwent PAD, were reported below the age limit: this data highlights that this practice was unnecessary, and the risk of over-transfusion is high. In fact, despite the growing number of published data supporting a restrictive transfusion strategy during surgery in pediatric patients, the practice of maintaining Hb levels higher than recommended is still common[34-36].

Also, in the PAD cohort, the number of donors with lower-than-normal Hb levels increased, confirming what has been reported in the adult setting[37-38].

In the non-trait carriers population, homologous transfusions were reported in 66% of pediatric donors and 15% of adolescents who did not undergo PAD. This finding is probably related to the disproportion in weight between donor and recipient in the pediatric population, which is less common in adolescents. However, half of the centers based their decision of transfusing the donor on the starting Hb values, and this attitude is partially incorrect because it emphasizes that the elective management of anemia could probably avoid unnecessary transfusion in a considerable proportion of donors. A study performed by the European Group for Blood and Marrow Transplantation Pediatric Diseases Working Party showed that the probability of blood transfusion after BM harvest was age related (donors aged 4 years or younger) and associated to a BM harvest volume exceeding 20 mL/kg[39].

Another study demonstrated a significant correlation between homologous transfusion and age at the time of harvest, (particularly in donors aged less than 5 years) and an extremely lower donor weight than the recipient[40]. Furthermore, although homologous transfusions are necessary to treat anemia and improve oxygen delivery, pediatric patients are at higher risk for side effects[41]. Therefore, homologous transfusion should be limited to small donors with a large weight imbalance with the recipient because hypovolemia and anemia can occur more rapidly in small donors during BM collection.

Our study also highlighted that only 3 centers have a specific policy regarding transfusion in trait carrier donors with each center reporting a different one. This is possibly the consequence of the paucity of donors in this setting. However, a specific policy for these donors is also crucial given the increase in transplants in sickle cell anemia and thalassemia patients requiring a family donor with trait[42].

The results about trait population show that no SCT donor and only 3 Thal-trait donors underwent PAD, probably due to the starting low Hb levels. Autologous blood storage in SC-trait may be a potential cause of sickling (15-20% of sickled cells) therefore PAD for auto-transfusion is not allowed and SCT subjects can donate BM HSC if Hb values are normal[43,44].

Moreover, only a minority of SCT donors were transfused, whereas almost all children and about 60% of adolescents with Thal-trait received a homologous transfusion. The high rate of homologous transfusion in the context of Thal-trait may be partly explained by the concern to maintain Hb levels similar to pre-explant, whereas the lower incidence in donors with SCT may be related to the difficulty of transfusing units with the same phenotype. Even in this context, no unambiguous criteria for transfusion emerged with a lack of PBM policy, as reported by other studies[45,46].

Taken together, the results of the present survey underline that PBM is lacking both in non-trait carrier and in trait donors. Hence, a multidisciplinary joint assessment with pre-operative involvement of pediatric anesthesiologists is critical to evaluate the risks/benefits and alternatives to blood transfusion to avoid unnecessary and inappropriate transfusions as well as over transfusion, also given the higher risk of transfusion reactions in children compared to adults[47]. In this regard most centers interviewed gave willingness to develop a specific PBM policy in this setting. For each individual donor, their characteristics should be assessed, taking into account the starting Hb levels, the estimated volume to be collected depending on the donor's weight; the estimated Hb level at the end of the procedure, the speed with which hypovolemia and anemia sets in and how hypovolemia can be corrected managing acute normovolemic hemodilution by infusing crystalloids or colloids as needed[48,49]. Moreover, according to a correct PBM approach, anemic patients should be assessed for hematinics (those nutrients required for hematopoiesis) in order to diagnose and appropriately treat the cause of the anemia.

In addition, specific management of donors with SCT requires the maintenance of an adequate body temperature during harvest (avoiding cold) and good oxygenation to avoid sickling and eventual post-procedure pain control. Although PBM in the pediatric context is more complex than in adults due to variations in weight and blood volume and it is more difficult to draft guidelines, it has been demonstrated that high volumes of RBC transfusions may increase the risk of mortality and post-operative infections in children undergoing non cardiac surgery[41].

As reported in a recent review by Tan *et al.*, the decision to transfuse should be based on the patient's clinical status and not on the Hb value, especially considering that pediatric patients tolerate anemia better than adults without incurring adverse events, as demonstrated by many studies in this field. Improving preoperative anemia will help to improve donor's health, minimize the risk associated with homologous transfusion and reduce the costs[24].

CONCLUSIONS

The present Italian survey on the use of PAD both in non-trait and trait carriers, either in children or adolescent donors before BM HSC harvest, highlights a very heterogeneous policy in the absence of recommendations in the field. Guidelines about PBM in BM HSC in pediatric and adolescent setting are urgently needed to prevent and treat anemia appropriately, and avoid the risk of unnecessary autologous and homologous blood transfusions, resulting in improved outcomes.

ACKNOWLEDGEMENTS

The Authors would like to thank all blood establishments and clinical units of pediatric transplantation programs responsible for BM HSC collection with their respective contact persons:

- Meyer Children's University Hospital, Florence (*Franco Bambi* and *Veronica Tintori*);
- IRCCS Istituto "Giannina Gaslini", Genoa (*Gino Tripodi* and *Maura Faraci*);
- Pescara Hospital, Pescara (*Cecilia Passeri* and *Stella Santarone*);
- Azienda Ospedaliera "S. Maria Della Misericordia", Perugia (*Mauro Marchesi* and *Alessandra Carotti*);
- Institute for Maternal and Child Health-IRCCS Burlo Garofolo, Trieste (*Roberto Simeone* and *Natalia Maximova*);
- University Hospital of Padua, Padua (*Piero Marson* and *Elisabetta Calore*);
- Fondazione IRCCS Policlinico "San Matteo", Pavia (*Claudia Del Fante* and *Marco Zecca*);
- Azienda Ospedaliera Universitaria, Verona (*Aurora Vassanelli* and *Simone Cesaro*);
- Regina Margherita Children's Hospital, Città della Salute e della Scienza di Torino, Turin (*Roberto Albiani* and *Paola Quarello*);
- Azienda Ospedaliero-Universitaria Policlinico, Modena (*Mirco Bevini* and *Paola Bresciani*);
- Hospital Microcitemico "A. Cao", Cagliari (*Rosa Manconi* and *Antonio Piroddi*);

- Rodolico University Hospital, Catania (*Francesco Indelicato* and *Luca Lo Nigro*);
- ASST Spedali Civili of Brescia, Brescia (*Fulvio Porta*);
- IRCCS Ospedale "San Raffaele", Milan (*Milena Coppola* and *Maria Pia Cicalese*);
- Bambino Gesù Children's Hospital, IRCCS, Rome (*Pierpaolo Berti*, *Mattia Algeri* and *Franco Locatelli*);
- Santobono-Pausilipon Children's Hospital, Naples (*Vittoria Mascio* and *Francesco Paolo Tambaro*);
- Azienda Ospedaliero-Universitaria di Bologna, Bologna (*Arcangelo Prete*);
- Fondazione IRCCS "San Gerardo Dei Tintori", Monza (*Chiara Mariadele Scollo* and *Adriana Balduzzi*).

AUTHORS' CONTRIBUTIONS

Conceptualization: CDF, FM, MZ, ULR, and SP. Supervision of the manuscript, VDA. All Authors have read and agreed to the published version of the manuscript.

The Authors declare no conflict of interest.

REFERENCES

1. Roseff SD, Luban NL, Manno CS. Guidelines for assessing appropriateness of pediatric transfusion. Transfusion 2002; 42: 1398-1413. doi: 10.1046/j.1537-2995.2002.00208.x.
2. New HV, Grant-Casey J, Lowe D, Kelleher A, Hennem S, Stanworth SJ. Red blood cell transfusion practice in children: current status and areas for improvement? A study of the use of red blood cell transfusions in children and infants. Transfusion 2014; 54: 119-127. doi: 10.1111/trf.12313.
3. Perrone PM, Milani GP, Dellepiane RM, Petaccia A, Prati D, Agostoni C, et al. Evaluation of six years of appropriateness level of blood transfusion in a pediatric ward. Int J Environ Res Public Health 2023; 20: 1700. doi: 10.3390/ijerph20031700.
4. Del Fante C, Mortellaro C, Recupero S, Giorgiani G, Agostini A, Panigari A, et al. Patient blood management after hematopoietic stem cell transplantation in a pediatric setting: starting low and going lower. Diagnostics (Basel) 2023; 13: 2257. doi: 10.3390/diagnostics13132257.
5. Wang P, Wang X, Deng H, Li L, Chong W, Hai Y, et al. Restrictive versus liberal transfusion thresholds in very low birth weight infants: A systematic review with meta-analysis. PLoS One 2021; 16: e0256810. doi: 10.1371/journal.pone.0256810.
6. Maitland K, Kiguli S, Olupot-Olupot P, Engoru C, Mallewa M, Saramago Goncalves P, et al. Immediate transfusion in African children with uncomplicated severe anemia. N Engl J Med 2019; 381: 407-419. doi: 10.1056/NEJMoa1900105.
7. Maitland K, Olupot-Olupot P, Kiguli S, Chagaluka G, Alaroker F, Opoka RO, et al. transfusion volume for children with severe anemia in Africa. N Engl J Med 2019; 381:420-431. doi: 10.1056/NEJMoa1900100.
8. Akyildiz B, Ulgen Tekerek N, Pamukcu O, Dursun A, Karakukcu M, Narin N, et al. Comprehensive Analysis of Liberal and Restrictive Transfusion Strategies in Pediatric Intensive Care Unit. J Trop Pediatr 2018; 64: 118-125. doi: 10.1093/tropej/fmx037.
9. Carson JL, Stanworth SJ, Guyatt G, Valentine S, Dennis J, Bakhtary S, et al. Red blood cell transfusion: 2023 AABB International Guidelines. JAMA 2023; 330: 1892-1902. doi: 10.1001/jama.2023.12914.
10. Manuel SP, Spitzer TR, Ishizawa Y. Preoperative autologous blood donation in healthy bone marrow donors contributes to pre-procedure anemia. Bone Marrow Transplant 2017; 52: 1191-1193. doi: 10.1038/bmt.2017.84.
11. Arora K, Kelley J, Martinez F, Tholpady A. Preoperative autologous blood collection before bone marrow harvests in haploidentical related donors: is it justified? Transfusion 2018; 58: 1618-1625. doi: 10.1111/trf.14599.
12. Gilli IO, Vigorito AC, Benites BD. Revisiting old practices: more restricted indication of preoperative autologous blood donation in healthy bone marrow donors according to baseline hemoglobin levels. Transfus Apher Sci 2019; 58: 323-325. doi: 10.1016/j.transci.2019.04.001.
13. Spitzer TR, Sugrue MW, Gonzalez C, O'Donnell P, Confer D, Fuchs E, et al. Transfusion practices for bone marrow harvests: a survey analysis from the AABB Bone Marrow Quality Improvement Initiative Working Group. Bone Marrow Transplant 2017; 52: 1199-1200. doi: 10.1038/bmt.2017.92.
14. Lysák D, Hejretová L, Hrabětová M, Jindra P. Should we stop collecting the preoperative autologous blood before bone marrow harvest? J Clin Med 2021; 10: 2134. doi: 10.3390/jcm10102134.
15. Teofili L, Valentini CG, Bianchi M, Pellegrino C, Bellesi S, Chiusolo P, et al. Preoperative autologous blood donation in adult bone marrow donors: reappraisal of a single-centre experience. Vox Sang 2019; 114: 762-768. doi: 10.1111/vox.12834.
16. Fujiwara SI, Ikeda K, Kino S, Tanaka A, Hasegawa Y, Fujino K, et al. Clinical significance of autologous blood transfusions in bone marrow harvest from unrelated donors. Int J Hematol 2020; 111: 833-839. doi: 10.1007/s12185-020-02851-8.
17. Weber M, Sacchi N, Haun S, Tistl I, Thompson S, Sengomona H, et al. Audit of donor centre: guidelines by the World Marrow Donor Association Quality and Regulation Working Group. Bone Marrow Transplant 2022; 57: 466-472. doi: 10.1038/s41409-022-01563-3.
18. International Standards for Unrelated Hematopoietic Stem Cell Donor Registries. World Marrow Donor Association. Available at: https://wmda.info/wp-content/uploads/2021/01/WMDA-2020-Standards_AM1_Jan2021-1.pdf. Accessed on 01/03/2024.
19. Del Fante C, Masiello F, Vaglio S, Lombardini L, Coluzzi S, Rondinelli MB, et al. A survey on preoperative autologous blood donation policy in bone marrow stem cell donors in Italy. Blood Transfus 2023; 21: 337-344. doi: 10.2450/2022.0134-22.
20. Furey A, Rastogi S, Prince R, Jin Z, Smilow E, Briamonte C, et al. Bone marrow harvest in pediatric sibling donors: role of granulocyte colony-stimulating factor priming and CD34+ cell dose. Biol Blood Marrow Transplant 2018; 24: 324-329. doi: 10.1016/j.bbmt.2017.10.031.
21. Styczynski J, Balduzzi A, Gil L, Labopin M, Hamladji RM, Marktel S, et al. Risk of complications during hematopoietic stem cell collection in pediatric sibling donors: a prospective European Group for Blood and Marrow Transplantation Pediatric Diseases Working Party study. Blood 2012; 119: 2935-2942. doi: 10.1182/blood-2011-04-349688.
22. Hibino N, Nagashima M, Sato H, Hori T, Ishitoya H, Tomino T. Preoperative autologous blood donation for cardiac surgery in children. Asian Cardiovasc Thorac Ann 2008; 16: 21-24. doi: 10.1177/021849230801600106.
23. Morley SL. Red blood cell transfusions in acute paediatrics. Arch Dis Child Educ Pract Ed 2009; 94: 65-73. doi: 10.1136/adc.2007.135731.
24. Tan GM, Murto K, Downey LA, Wilder MS, Goobie SM. Error traps in pediatric patient blood management in the perioperative period. Paediatr Anaesth 2023; 33: 609-619. doi: 10.1111/pan.14683.
25. Goel R, Tobian AAR, Shaz BH. Noninfectious transfusion-associated adverse events and their mitigation strategies. Blood 2019; 25: 1831-1839. doi: 10.1182/blood-2018-10-833988.
26. Vassallo R, Goldman M, Germain M, Lozano M, BEST Collaborative. Preoperative autologous blood donation: waning indications in an era of improved blood safety. Transfus Med Rev 2015; 29: 268-275. doi: 10.1016/j.tmrv.2015.04.001.
27. Fujiwara SI, Ikeda K, Kino S, Tanaka A, Hasegawa Y, Fujino K, et al. Clinical significance of autologous blood transfusions in bone marrow harvest from unrelated donors. Int J Hematol 2020; 111: 833-839. doi: 10.1007/s12185-020-02851-8.

28. Willems A, Harrington K, Lacroix J, Biarent D, Joffe AR, Wensley D, et al. Comparison of two red-cell transfusion strategies after pediatric cardiac surgery: a subgroup analysis. Crit Care Med 2010; 38: 649-656. doi: 10.1097/CCM.0b013e3181bc816c.

29. Rouette J, Trottier H, Ducruet T, Beaunoyer M, Lacroix J, Tucci M, et al. Red blood cell transfusion threshold in postsurgical pediatric intensive care patients: a randomized clinical trial. Ann Surg 2010; 251: 421-427. doi: 10.1097/SLA.0b013e3181c5dc2e.

30. Joseph SA Jr, Berekashvili K, Mariller MM, Rivlin M, Sharma K, Casden A, et al. Blood conservation techniques in spinal deformity surgery: a retrospective review of patients refusing blood transfusion. Spine (Phila Pa 1976) 2008; 33: 2310-2315. doi: 10.1097/BRS.0b013e31818047f2.

31. Mantadakis E. Advances in pediatric intravenous iron therapy. Pediatr Blood Cancer 2016; 63: 11-16. doi: 10.1002/pbc.25752.

32. Safiri S, Kolahi AA, Noori M, Nejadghaderi SA, Karamzad N, Bragazzi NL, et al. Burden of anemia and its underlying causes in 204 countries and territories, 1990-2019: results from the Global Burden of Disease Study 2019. J Hematol Oncol 2021; 14: 185. doi: 10.1186/s13045-021-01202-2.

33. Congdon EL, Westerlund A, Algarin CR, Peirano PD, Gregas M, Lozoff B, et al. Iron deficiency in infancy is associated with altered neural correlates of recognition memory at 10 years. J Pediatr 2012; 160: 1027-1033. doi: 10.1016/j.jpeds.2011.12.011.

34. Lacroix J, Hébert PC, Hutchison JS, Hume HA, Tucci M, Ducruet T, et al. Transfusion strategies for patients in pediatric intensive care units. N Engl J Med 2007; 356: 1609-1619. doi: 10.1056/NEJMoa066240.

35. Valentine SL, Bembea MM, Muszynski JA, Cholette JM, Doctor A, Spinella PC, et al. Consensus recommendations for RBC Transfusion practice in critically ill children from the pediatric critical care transfusion and anemia expertise initiative. Pediatr Crit Care Med 2018; 19: 884-898. doi: 10.1097/PCC.0000000000001613.

36. Long JB, Engorn BM, Hill KD, Feng L, Chiswell K, Jacobs ML, et al. Postoperative hematocrit and adverse outcomes in pediatric cardiac surgery patients: a cross-sectional study from the Society of Thoracic Surgeons and Congenital Cardiac Anesthesia Society Database Collaboration. Anesth Analg 2021; 133: 1077-1088. doi: 10.1213/ANE.0000000000005416.

37. Steuer LV, Kondo AT, Cipolletta AN, Sakashita AM, Hamerschlak N, Kutner JM. Predictive factors for the development of anemia after hematopoietic stem cell donation. Transfusion. 2021; 61: 159-166. doi: 10.1111/trf.16124.

38. Fujiwara SI, Ikeda K, Kino S, Tanaka A, Hasegawa Y, Fujino K, et al. Clinical significance of autologous blood transfusions in bone marrow harvest from unrelated donors. Int J Hematol 2020; 111: 833-839. doi: 10.1007/s12185-020-02851-8.

39. Styczynski J, Balduzzi A, Gil L, Labopin M, Hamladji RM, Marktel S, et al. Risk of complications during hematopoietic stem cell collection in pediatric sibling donors: a prospective European Group for Blood and Marrow Transplantation Pediatric Diseases Working Party study. Blood 2012; 119: 2935-2942. doi: 10.1182/blood-2011-04-349688.

40. AlAnazi A, Nadeem A, Siddiqui K, AlAhmari A, Ghemlas I, AlJefri A, et al. Can the bone marrow harvest volume be reduced safely in hematopoietic stem cell transplantation with pediatric sibling donors? Blood Res 2023; 58: 28-35. doi: 10.5045/br.2023.2022167.

41. Goobie SM, DiNardo JA, Faraoni D. Relationship between transfusion volume and outcomes in children undergoing noncardiac surgery. Transfusion 2016; 56: 2487-2494. doi: 10.1111/trf.13732.

42. Brandow AM, Liem RI. Advances in the diagnosis and treatment of sickle cell disease. J Hematol Oncol 2022; 15: 20. doi: 10.1186/s13045-022-01237-z.

43. Romanoff ME, Woodward DG, Bullard WG. Autologous blood transfusion in patients with sickle cell trait. Anesthesiology 1988; 68: 820-821. doi: 10.1097/00000542-198805000-00042.

44. Pinto VM, De Franceschi L, Gianesin B, Gigante A, Graziadei G, Lombardini L, et al. Management of the sickle cell trait: an opinion by expert panel members. J Clin Med 2023; 12: 3441. doi: 10.3390/jcm12103441.

45. Fettah A, Özbek N, Özgüner M, Azik F, Işik P, Avci Z, et al. Factors associated with bone marrow stem cell yield for pediatric allogeneic stem cell transplantation: the impact of donor characteristics. Pediatr Transplant 2017; 21. doi: 10.1111/petr.12841.

46. Al Anazi A, Nadeem A, Siddiqui K, Al Ahmari A, Ghemlas I, AlJefri A, et al. Can the bone marrow harvest volume be reduced safely in hematopoietic stem cell transplantation with pediatric sibling donors? Blood Res 2023; 58: 28-35. doi: 10.5045/br.2023.2022167.

47. Lavoie J. Blood transfusion risks and alternative strategies in pediatric patients. Paediatr Anaesth 2011; 21: 14-24. doi: 10.1111/j.1460-9592.2010.03470.x.

48. Segal JB, Blasco-Colmenares E, Norris EJ, Guallar E. Preoperative acute normovolemic hemodilution: a meta-analysis. Transfusion 2004; 44: 632-644. doi: 10.1111/j.1537-2995.2004.03353.x.

49. Bhananker SM, Ramamoorthy C, Geiduschek JM, Posner KL, Domino KB, Haberkern CM, et al. Anesthesia-related cardiac arrest in children: update from the Pediatric Perioperative Cardiac Arrest Registry. Anesth Analg 2007; 105: 344-50. doi: 10.1213/01.ane.0000268712.00756.dd.