Review Article

Transfusion practice in allogeneic hematopoietic stem cell transplantation: a narrative review of clinical guidelines and evidence gaps

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Background and Objective: Transfusion support is a cornerstone of care for patients undergoing allogeneic hematopoietic stem cell transplantation (HSCT), yet many aspects of transfusion practice remain controversial due to limited high-quality evidence. Conditioning regimens induce profound cytopenias, making red blood cell (RBC) and platelet (PLT) transfusions essential. Transfusion requirements vary according to transplant modality, with cord blood and haploidentical transplants associated with higher needs. ABO incompatibility, present in up to 50% of transplantation procedures, is not a contraindication but may lead to immunohematological complications such as passenger lymphocyte syndrome and pure red cell aplasia. The objective of this review is to summarise the current guidelines on transfusion management for HSCT patients focusing on evidence gaps and unresolved issues.

Methods: PubMed database was used to carry out the literature search. Search terms used were: "allogeneic hematopoietic stem cell transplantation, blood transfusion, platelet transfusion, transfusion guidelines", from January 2000 to February 2026. All articles were reviewed and those references that did not include the term allogeneic stem cell transplantation or hematological patients were discarded.

Key Content and Findings: Transfusion strategies in ABO-incompatible HSCT must account for the dynamic transition from recipient to donor blood group, requiring careful selection of RBCs, PLTs, and plasma during different transplant phases. While general recommendations exist, PLT transfusion remains particularly challenging because of limited product availability and weak evidence supporting ABO-based selection. Prophylactic PLT transfusion at a threshold of 10×10^9/L is currently recommended for stable patients, with higher thresholds for bleeding risk or invasive procedures. Restrictive RBC transfusion strategies (hemoglobin <7 g/dL) are favoured in hemodynamically stable patients. The optimal duration of irradiated blood component use after HSCT is uncertain, and practices vary widely among institutions. Overall, substantial variability in transfusion practices reflects the lack of robust evidence, underscoring the need for further research to standardize transfusion support in HSCT.

Conclusions: Although blood component transfusion is a critical supportive therapy in HSCT, some transfusion decisions rely on low-quality evidence, resulting in wide variability in clinical practice among centers.

Keywords: Allogeneic hematopoietic stem cell transplantation (HSCT); blood transfusion; platelet transfusion (PLT transfusion); transfusion guidelines

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Introduction

Transfusion is one of the most important supportive treatments for patients undergoing allogeneic hematopoietic stem cell transplantation (HSCT) (1-3). Conditioning chemotherapy produces severe but transient cytopenias that are palliated with the administration of blood components. Transfusion requirements vary greatly, depending on the transplantation platform, with cord blood and haploidentical being the transplantation modalities with higher requirements as compared to HLA identical sibling donor HSCT (4,5). Over the last decade, new transplantation platforms including post-transplantation cyclophosphamide have been introduced leading to delayed engraftment and increased transfusion burden (6). Platelet (PLT) and red blood cell (RBC) concentrates are the blood products that are usually required, while only a minority of patients receive fresh frozen plasma (5). ABO incompatibility is not a barrier to perform HSCT. In fact, HSCT with some grade of ABO incompatibility is performed in up to 50% of patients (7,8). Major, minor and bidirectional ABO incompatibility have been related to development of specific immunohematological complications as passenger lymphocyte syndrome or pure red cell aplasia (9-11). ABO incompatibility is divided into major when the recipient has isoagglutinins (IAs) against the donor ABO antigens, minor when the donor has the IAs against the recipient ABO antigens and bidirectional when both conditions are present. After the transplantation, the recipient-derived IAs disappear as a result of conditioning chemotherapy and are progressively replaced by ABO antibodies produced by engrafted donor B cells. Then, IAs titers may reflect the immunohematological reconstitution status after HSCT. As the engraftment occurs, the appearance of donor RBCs is detected about a month after transplantation (12).

Patients undergoing HSCT must receive blood products tailored to their clinical situation and ABO status, especially those cases with some degree of ABO incompatibility. There is considerable variability in transfusion practices among blood banks as shown in previous reports (13,14), largely due to the lack of evidence in this clinical setting. This review focuses on some critical questions raised from the transfusion practice in HSCT and considered relevant by the author. The objective is to review some relevant unresolved aspects of the current guidelines on blood components transfusion of patients undergoing HSCT and detect evidence gaps. To our knowledge there are no published reviews analysing controversies in HSCT transfusion guidelines. This article is presented in accordance with the Narrative Review reporting checklist (available at https://aob.amegroups.com/article/view/10.21037/aob-2025-1-54/rc).

Methods

PubMed database was used to carry out the literature search (*Table 1*). All articles were reviewed and those references that did not include the condition of allogeneic stem cell transplantation were discarded.

Transfusion support guidelines on patients undergoing HSCT

Specific recommendations for transfusion support in patients receiving HSCT (both autologous and allogeneic) have been published (15-20). These guidelines focus on characteristics of blood products to be transfused, indications for PLT and RBC transfusions, and relevant issues of ABO incompatibility. In addition, recommendations for transfusion support in patients with cancer that includes patients undergoing HSCT are also available (21).

Table 1 The search strategy summary

Items	Specification
Date of search	First search: January 20th, 2026. Second search: March 1st, 2026
Database searched	PubMed
Search terms used	Blood transfusion, platelet transfusion, blood transfusion guidelines, allogeneic hematopoietic stem cell transplantation
Timeframe	From January 2000 to February 2026
Inclusion criteria	English-language peer-reviewed articles were included
Selection process	Selection was conducted independently

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In general, transfusion support thresholds for blood components, especially RBC and PLT are similar to other patients with anemia or thrombocytopenia. However, HSCT is a well-known clinical condition in which cytopenias are anticipated and maintained during at least 2–4 weeks. Some patient-specific factors as $CD34^+$ dose and ABO match of the graft have been shown to influence on transfusion requirements (3). Given that patients undergoing HSCT are hospitalized and closely monitored, transfusion needs can be assessed based on daily blood counts. Then, unnecessary transfusions should be avoided to decrease adverse effects as iron overload. Each institution must develop its own procedures to choose the characteristics and ABO group of blood products to transfuse, based on available scientific evidence and its own experience.

Next, I am going to discuss some topics that I consider more relevant for the clinical practice and that lack, to some degree, robust scientific evidence.

Immunohematology laboratory tests that should be routinely performed in donors and recipients before HSCT

ABO/Rh(D) and antibody screen must be performed before HSCT, in order to assess the degree of ABO/Rh(D) incompatibility between donor and recipient and to detect clinical significant or insignificant alloantibodies against non-ABO RBC antigens (22). Which other determinations should be performed that could be useful for the post-transplant monitoring assessment is unclear. Some authors recommended to phenotype pre-transplant donor and recipient samples for the most important RBC minor antigen systems (Rh, K, Fy, Jk, Ss) to prevent hemolytic complications after bone marrow transplantation (19,23). And even more, respecting donor and recipient CcEe compatibility has been considered as mandatory if possible (19). Since peripheral blood is mostly used as source of hematopoietic progenitor cells and has a low RBC content, immediate hemolytic complications have become rare (24). In La fe University Hospital, in the past we performed extended RBC phenotype but it was never useful to resolve any immunohematological event, then we changed the procedure and performed only Rh and K phenotype. We did not respect Rh CcEe phenotype, since alloimmunization in HSCT is very rare in La fe Hospital.

Non-ABO blood group alloantibodies can cause immediate or delayed hemolytic complications, delayed RBC engraftment and prolonged RBC transfusion dependence. Development of non-ABO RBC alloantibodies in patients undergoing allogeneic HSCT has been reported between 1% and 8.6% (25,26). When alloantibodies against donor or recipient RBC are detected, antigen phenotype must be performed in donor or recipient and cross-match compatible antigen negative RBC must be transfused. The level of alloantibodies can be reduced after HSCT due to the immunosuppressive therapy but the transfusion of positive antigen RBC can stimulate the immunity and produce hemolysis. However, the impact of non-ABO alloantibodies in HSCT is mostly insignificant (22,27).

In ABO incompatible HSCT, the pre-existing levels of recipient anti-donor IAs have been related to delayed PLT engraftment and unfavourable outcome (28). According to these results, titration of recipient derived IAs should be performed before HSCT and taken into account to adopt prophylactic treatment. IAs titration twice a week from day 0 to day 15 after HSCT has been recommended (19). However, it is a not a widespread practice and its usefulness and impact on post-transplantation complications are not clearly established.

First-choice of ABO group for RBCs, PLTs and plasma components to be transfused in case of ABO incompatibility

Transfusion support in HSCT, especially in ABO incompatible HSCT is challenging and must consider both the donor and recipient ABO group. Since the ABO change is dynamic, a close monitoring of patient forward and reverse blood group must be assessed while transfusion is required (16). In the *Table 2* below the different possibilities of ABO incompatibility are detailed.

There are four periods in HSCT in which transfusion practice must be assessed, although these phases are dynamic and cannot be strictly separated in the real practice.

(I) Before HSCT, blood products to transfuse must respect recipient ABO group.

(II) From day of HSCT until engraftment occurs selection of blood products is critical. The *Table 3* below shows the transfusion support recommendations gathered in the most guidelines for this interim period according to the ABO group of donors and recipients (16,17,22,27,29).

Transfusion guidelines for ABO selection of blood components in ABO incompatible HSCT has not changed for decades. In a general manner, the donor and recipient ABO group must be taken into account to choose the ABO type

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Table 2 Types of ABO incompatibility in HSCT

Type of ABO incompatibility	IAs	Donor ABO	Recipient ABO
Minor	Donor IAs against recipient ABO antigens	O	A, B, AB
		A	B, AB
		B	A, AB
Major	Recipient IAs against donor ABO antigens	A	B, O
		B	A, O
		AB	O, A, B
Bidirectional	Donor IAs against recipient ABO antigens + Recipient IAs against donor ABO antigens	A	B
		B	A

HSCT, allogeneic hematopoietic stem cell transplantation; IAs, isoagglutinins.

Table 3 Recommendations for transfusion support in ABO incompatible HSCT

Donor	Recipient	RBCs	PLTs and plasma (in order of choice)
O	A	O	A, AB, B, O
	B	O	B, AB, A, O
	AB	O	AB, A, B, O
A	O	O	A, AB, B, O
	B	O	AB, B, A, O
	AB	A	AB, A, B, O
B	O	O	B, AB, A, O
	A	O	AB, B, A, O
	AB	B	AB, B, A, O
AB	O	O	AB, A, B, O
	A	A	AB, A, B, O
	B	B	AB, B, A, O

HSCT, allogeneic hematopoietic stem cell transplantation; PLTs, platelets; RBCs, red blood cells.

of the blood products to transfuse, in order to minimize the risk of hemolysis of recipient and donor derived RBCs (16). RBCs to be transfused must be compatible between donor and recipient, until blood group changes to donor status. Fresh frozen plasma must also be compatible among donor and recipient, to avoid infusion of IAs directed against donor RBCs and to decrease the risk of acute hemolysis and delayed engraftment (16). PLT concentrates are considered plasma containing blood product and are chosen following the same compatibility criteria as fresh frozen plasma (FFP). However, PLT transfusion in ABO incompatible HSCT is still challenging, since there is limited evidence-based guidance supporting the PLT product selection in this clinical setting. It is well known that PLTs can be transfused without respecting ABO compatibility, but ABO compatible PLTs are preferred to transfuse because they produce improved corrected count increments (30). PLT ABO antigens that are incompatible with recipient ABO IAs may have accelerated clearance from circulation and decrease post-transfusion yield. In addition, ABO IAs that are passively transferred from donor plasma contained in PLT products may result in hemolysis and may delay the RBC engraftment. In a general way, the current recommendations for PLT transfusions focus on avoiding hemolysis. But there are some issues that have to be taken into account. In first place, there is little information about the PLT transfusion in real-world practice and since PLTs are a limited resource it is most likely that many transfusions in HSCT patients do not comply with the recommendations. In addition, B and AB PLT products are often not available. Therefore, the real impact of plasma incompatible PLT transfusions on hemolysis and engraftment is unknown. In addition, PLT products, both pooled random or single-donor are suspended in additive solutions in many centers decreasing the anti-A and anti-B levels as compared to plasma suspended PLTs (31). Hemolytic reactions due to ABO incompatible PLT transfusions have been reported to be rare and non-fatal (1/9,000 PLT transfusions over a period of 10 years) (32,33). Most of the cases have occurred in A patients transfused with O single donor plasma suspended PLTs. The IAs of PLTs are diluted in the plasma volume of recipient, lowering the hemolytic risk.

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In the last years, pathogen reduction technologies have been implemented to enhance safety of blood products. Pathogen reduction using the INTERCEPT® Blood System effectively reduces ABO IAs titers in apheresis PLTs, decreasing the hemolytic risk in case of plasma-ABO incompatible PLT transfusion (34). In addition, it has not been proven that passively transfused IAs delay engraftment. Therefore, and taking these previous comments into account, the current recommendations may not be the most suitable for the current available PLT products.

(III) When engraftment occurs and patient ABO group has changed to donor status, transfusion can be done with donor ABO group blood products. However, the complete conversion of ABO blood group must be clearly determined, mainly for RBC transfusion. For major incompatibility full conversion is achieved when blood type is consistent between forward and reverse test and anti-donor RBC IAs are not detectable. For minor incompatibility, full donor type in forward test must be achieved, while reverse type remains similar to recipient group. This phenomenon has been explained by the development of a donor lymphocyte tolerance to the recipient's antigens and therefore the IAs against recipient's ABO antigens are not usually produced (10). For bidirectional incompatibility full donor type in forward and absence of IAs must be confirmed (35,36). In addition, for all cases the direct antiglobulin test must be negative to confirm the absence of anti-recipient IAs and no transfusions needs to have been performed at least during the past 3 months. Complete achievement of donor ABO group occurs within 90–120 days after HSCT (12). Reverse and forward ABO typing must be assessed with two independent and consecutive blood samples. However, in some cases the persistence of recipient type ABO antigen expressions remains that is detected by mixed-field agglutination reactions, despite complete chimerism of donor white blood cells (20). Blood group chimerism can persists for a prolonged time period after myeloid engraftment (20). Then, the donor and recipient ABO compatibility must be respected in some cases for a long time.

(IV) After relapse: unluckily, some patients relapse and ABO recipient donor group reappears. After establishment of full donor ABO group, the detection of a mixed erythrocyte field may be the signal of relapse or graft loss. In these cases, different approaches have been reported for transfusion support. Transfusion with donor ABO blood products cannot be performed anymore. While some centers transfuse RBC compatible with both donor and recipient ABO group, other institutions change to recipient ABO group in case of minor ABO incompatibility (15). Again, practice is highly variable among hospitals.

Threshold for prophylactic PLT transfusion in patients without hemorrhage

The current evidence from various randomized clinical trials and meta-analyses support the prophylactic PLT transfusion strategy for patients with hematological malignancies receiving chemotherapy and HSCT (37-39). Transfusing PLTs in patients undergoing HSCT decreases in a significant manner the World Health Organization (WHO) grade 2 or greater bleeding complications (40). Prophylactic transfusion strategy respecting a PLT threshold of 10×10^9/L is the current recommendation for hematological patients undergoing chemotherapy or HSCT. Some guidelines recommend that this trigger should be increased to 20×10^9/L if there are some additional risk factors for bleeding (41,42).

However, there is quite a bit of variability in PLT threshold recommendations prior to invasive procedures and surgery according to different available guidelines (43). For instance, to perform a lumbar puncture, recently published association for the advancement of blood and biotherapies (AABB) and international collaboration for transfusion medicine guidelines (ICTMG) guidelines recommend transfusion when PLT counts are below 20×10^9/L (44), while a higher PLT threshold of 40×10^9/L is recommended by British Guidelines (41). Some guidelines as Spanish (45), and British (41) specify thresholds for a higher number of procedures than AABB (44) and American society of clinical oncology (ASCO) guidelines (21), that recommend thresholds only for a few procedures each one. AABB recommends PLT transfusion in patients undergoing interventional radiology when PLT count is less than 20×10^3/μL for low-risk procedures and less than 50×10^3/μL for high-risk procedures (44). It should be emphasized that the evidence quality is low and strength of recommendation weak for most recommendations (39). Possibly due to the lack of robust evidence and other factors, PLT transfusion practice is highly variable among physicians, especially in the pre-procedure indications (46). Results of audits

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on PLT transfusion performed in hematological patients showed a higher grade of inappropriate transfusions that occurred in the prophylactic intention both in inpatient (45%) and outpatient (54%) setting and that inpatients were the most consumers of prophylactic transfusions (46). More randomized studies are needed to clarify PLT needs in specifical procedures.

Hemoglobin threshold for RBC transfusion in stable patients without active bleeding

Hemoglobin threshold for RBC transfusion in stable patients undergoing HSCT without active bleeding has been changing over the years. Hemoglobin threshold for RBC transfusion in HSCT patients was established in 8 g/dL (20). However, in the last years a trend to a more restrictive transfusion has been reported and hemoglobin threshold has been lowered to 7 g/dL in hemodynamically stable patients, otherwise healthy (47). In a randomized clinical trial Tay *et al.* showed similar clinical outcome and health-related quality of life for patients receiving HSCT included in restrictive transfusion strategy (Hb <7 g/dL) as compared to patients transfused following liberal strategy (Hb <9 g/dL) (48). The number of RBC units transfused in the restrictive group was lower than in the liberal group. Chantepie *et al.* carried out a randomized trial in patients with hematological malignancies (including patients receiving a HSCT) in which patients received one or two RBC units. The study concluded that the single RBC unit was not inferior to the double RBC transfusion. However, the number of RBC units transfused per stay was not reduced (49). In a retrospective study other authors have showed the feasibility, non-inferiority and also significant reduction of RBC transfusion of 1 RBC strategy as compared to 2 RBC group in HSCT (50). Therefore, and as a general recommendation, restrictive strategies (Hb threshold <7 g/dL) are preferred for stable patients undergoing HSCT. This trigger should be increased to <8 g/dL in patients suffering cardiovascular disease. Despite these recommendations there is quite variability in threshold for RBC transfusions among institutions in real practice (13). Therefore, the potential for a more restrictive transfusion strategy remains.

How long patients undergoing HSCT should receive irradiated blood products

Transfusion-associated graft-versus-host disease (TA-GvHD) is a rare, mostly fatal, complication of transfusion of blood products containing viable T lymphocytes to immunocompromised patients. It appears usually 2 to 30 days following a blood component transfusion producing a graft versus host disease clinical chart. Although it is a poorly understood chart, some conditions have been related to as the immunosuppression state, the number and viability of T lymphocytes and the degree of HLA incompatibility between donor and recipient (51). Irradiation is the main method used to inactivate lymphocytes in blood products and prevent TA-GvHD. However, different pathogen reduction technologies have been developed during last decade. They use different methodologies as psolaren or riboflavin combined with UV light to reduce the risk of microbiological and are considered irradiation-equivalent (52). Patients undergoing HSCT are immunocompromised and therefore must receive irradiated blood products (RBC and PLTs), from the time of starting the conditioning chemotherapy. What is not clear is which is the current risk of TA-GVHD and how long these patients should receive irradiated components. In fact, there is no consensus on the duration of the use of irradiated blood products in HSCT recipients. According to the British Guidelines, irradiated components should be transfused until all of these criteria were met: more than 6 months from HSCT, lymphocyte count is $>1\times10^9$/L, absence of immunosuppression and free of active chronic graft versus host disease (53). When the patient has an active chronic graft versus host disease irradiation has to be maintained. In the real practice each centre has its own policy that not necessarily fully align with these recommendations and differs among them (54). Other authors have addressed the question whether irradiation is still necessary after implementation of pre-storage leukodepletion of blood components (55). It has been shown that the risk of TA-GVHD has become lower when leukoreduced blood components are transfused (56). In Netherlands, when use of leukodepleted blood components started in 2001, no case of TA-GVHD has been reported since then to the Hemovigilance system. Netherlands guidelines recommend for patients undergoing HSCT to irradiate blood products until 1 year after last medication/intervention (55). It may be difficult for blood Banks to know the patient's condition and the treatment they have received. Therefore, and given the difficulty of knowing the patient's immunosuppression status, some centers as ours decide to maintain the use of irradiated blood components indefinitely (13).

Conclusions

This article provides a comprehensive review of transfusion

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support guidelines in patients undergoing HSCT, highlighting some areas of ongoing uncertainty. Although transfusion thresholds for RBCs and PLTs are broadly similar to those used in other cytopenic patients, HSCT presents unique clinical challenges, such as the predictable and prolonged period of marrow aplasia and the influence of transplant-specific variables like $CD34^+$ cell dose and ABO compatibility between donor and recipient. Since a systematic review has not been performed, this article has some limitations. The literature search carried out could have omitted some articles providing relevant information about transfusion practice in patients undergoing HSCT.

Despite blood component transfusion is a critical supportive therapy in HSCT, many transfusion decisions rely on low-quality evidence, resulting in wide variability in clinical practice among centers. Up to half of HSCT procedures involve some degree of ABO incompatibility, requiring careful and dynamic selection of blood components throughout the different transplant phases to minimize immunohematological complications.

Evidence from recent clinical trials supports lower hemoglobin thresholds and conservative PLT transfusion triggers in stable patients, without compromising clinical outcomes. Nevertheless, significant variability persists across institutions, reflecting both gaps in evidence and differences in clinical judgment, especially for PLT transfusions in the context of invasive procedures.

Uncertainty persists regarding optimal PLT selection in ABO-incompatible HSCT since the influence of passively transferred anti-donor IAs on engraftment is unknown.

Finally, the duration of irradiated blood product use remains controversial. While irradiation is essential to prevent TA-GvHD, there is no consensus on how long it should be continued post-transplant. As a result, institutional policies vary widely.

Overall, this review underscores the need for further prospective studies to strengthen the evidence base and promote more standardized, evidence-driven transfusion practices in the HSCT setting.

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Footnote

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