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UNDERSTANDING THE DISEASE

Ten things ICU specialists need to know about platelet transfusions

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Thrombocytopaenia is common in critically ill patients and is associated with higher bleeding risk and worse outcomes [1]. Platelet transfusions are frequently used to prevent or treat bleeding, though often with uncertain benefits and potential harms (Fig. 1).

Take-home message

The use of platelet transfusion in critically ill patients is multifaceted, and should be driven by a personalised transfusion strategy, not only based on platelet count, but also on the underlying condition, the platelet function and the associated risks of bleeding or thrombosis.

Platelet concentrates are scarce collective resources

Platelet concentrates are produced from pooled whole-blood donations or single-donor apheresis and stored at room temperature under slow, continuous agitation. The storage duration is limited to 5–7 days, and hence with a high risk of shortage or waste. While the demand for platelet concentrates has been increasing during the last decade, the donor base in most countries is dropping. Therefore, the focus on alternative products with longer storage duration is increasing, including cold-stored platelets (14 days) and cryopreserved or lyophilised platelets (3 years), although the latter are currently only available in research and combat settings. Cold-stored platelet products exhibit poor post-transfusion platelet count increment, but increased haemostatic capacities and may, therefore, be considered in bleeding patients [2].

Platelet concentrates undergo storage lesions

Manufacturing and storage induce structural and functional changes to the platelets, including the accumulation of bioactive substances and microparticles that may elicit pro-inflammatory reactions. Prolonged storage time has been associated with lower post-transfusion platelet increments, but not with increased risk of bleeding [3].

Prophylactic platelet transfusion reduces the risk of bleeding

A systematic review including hospitalised adult patients found that prophylactic platelet transfusion may reduce the proportion of patients with bleeding, but statistical heterogeneity was large, and the results, therefore, uncertain [4]. Two randomised controlled trials (RCT) assessing the effect of prophylactic versus a therapeutic-only transfusion strategy in patients with haematological malignancies [5, 6] found that the therapeutic-only group displayed an increased risk of significant bleeding, albeit most often of mild severity. An increase in severe bleeding (World Health Organization grade 3–4) in the therapeutic-only group was mainly carried by patients with acute leukaemia with profound and sustained thrombocytopaenia. At the opposite, the benefit of prophylactic platelet transfusion has been challenged by a RCT on platelet transfusion thresholds in neonates (25 vs. 50×10^9 cells/L [G/L]); here, a significantly higher rate of death or major bleeding within 28 days was found in the higher threshold arm [7].

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Prophylactic platelet transfusion thresholds are heterogeneous

Platelet transfusion practices in the intensive care unit (ICU) largely depend on the clinical setting, with higher thresholds typically seen in surgical and bleeding patients [1]. Prophylactic transfusions are often triggered by platelet count thresholds of 10–20 G/L in critically ill patients, with this practice being derived from the haematological setting [5, 6]. Accordingly, current European guidelines suggest prophylactic transfusions at a platelet count threshold of 10 G/L in non-bleeding critically ill adults, though with very low certainty [8].

The dose of prophylactic platelet transfusion does not modulate the risk of bleeding

Considerable practice variation occurs regarding the platelet dose both across and within countries [1]. An RCT in haematological patients assessing doses of prophylactic platelets (1.1×10^{11} vs. 2.2×10^{11} vs. 4.4×10^{11} /m^2 body surface area) triggered by a platelet count ≤ 10 G/L found that the low- and intermediate-dose strategies resulted in lower post-transfusion platelet increments and more transfusions as compared to the high-dose strategy but without effect on the bleeding incidence [9].

Post-transfusion platelet increments are often poor in critically ill patients

The post-transfusion increment is used to assess the yield of platelet transfusion. The corrected count increment (CCI) is the most accurate, since it includes the administered number of platelets and the body surface area. At the bedside, the post-transfusion response is usually assessed by the absolute platelet count increment. Poor post-transfusion platelet responses, commonly defined by an absolute increment less than 15 G/L within 24 h after prophylactic platelet transfusion, are frequent in the ICU, especially in patients with haematological malignancies and sepsis [10]. Pooled and apheresis platelet products resulted in similar increments. In contrast, increased storage time of platelet concentrates was associated with poor post-transfusion increments. Refractoriness to platelet transfusions indicates anti-human leukocyte antigen (HLA) antibody testing and then warrants the use of

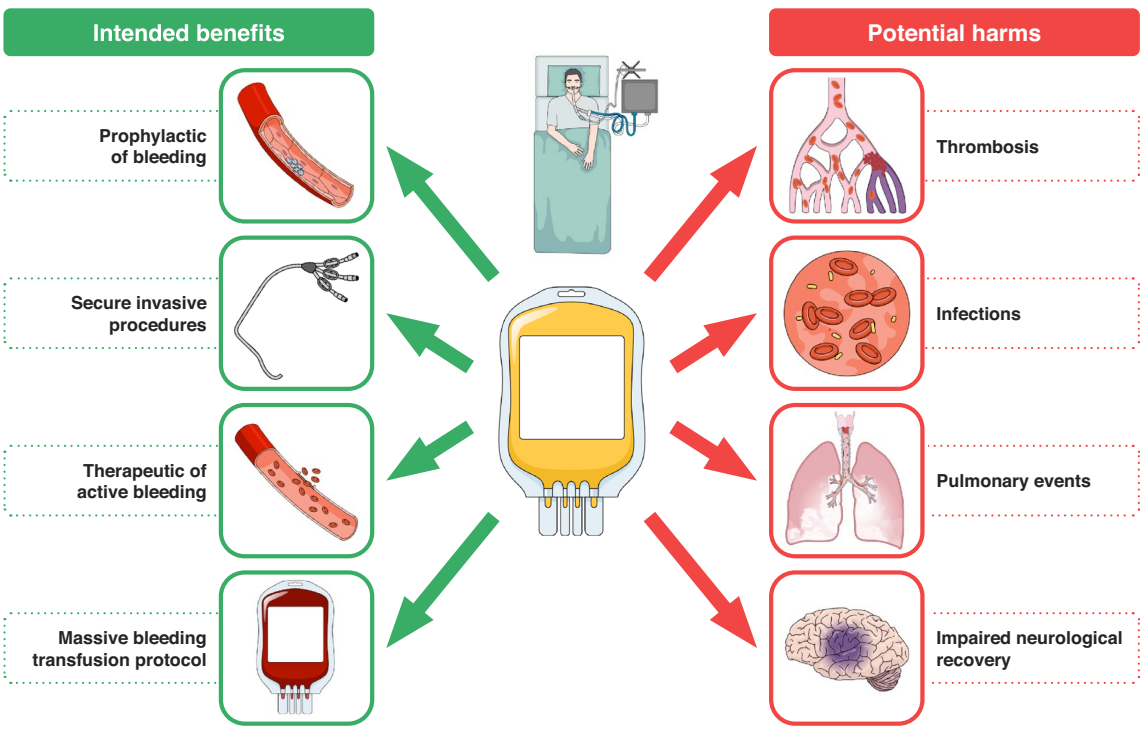

Fig. 1 Benefits and harms of platelet transfusions in critically ill patients. Platelet transfusions are administered to thrombocytopaenic patients for the prevention of spontaneous bleeding, to secure surgery or alternative invasive procedures or to treat active bleeding. In addition, platelet transfusions are components of massive haemorrhage protocols. The administration of platelets concentrates exposes patients to various side effects, including fever and allergic reactions, microvascular and arterial thrombosis, transfusion-transmitted bacterial infections from contaminated stored platelets, increased susceptibility to ICU-acquired infections, acute pulmonary events including transfusion-associated cardiac overload, and transfusion-related acute lung injury. Unexpectedly, platelet transfusions are also associated with long-term impairment in neurological recovery in patients with spontaneous intracranial haemorrhage

HLA-matched platelet concentrates when positive, and otherwise may justify moving from a non-sustainable prophylactic to a therapeutic-only transfusion strategy.

Pre-procedural platelet transfusions: some initial answers

The risk of procedure-related bleeding complications in thrombocytopaenic ICU patients remains unclear. A recent RCT assessed the impact of a single platelet transfusion prior to ultrasound-guided placement of central venous catheters (CVC) in the haematology ward and ICU patients with platelet counts of 10–50 G/L [11]. Although the study did not reach its primary objective of non-inferiority of the no-transfusion strategy, the incidence of severe bleeding remained low in both arms. Furthermore, subgroup analysis suggested that platelet transfusions did not decrease the risk of bleeding among ICU patients or when the CVC was placed in compressible jugular and femoral veins, suggesting that platelet transfusion could be avoided in these settings. However, a pre-procedural platelet transfusion should probably be considered when using the subclavian site.

Platelet transfusions improve outcomes in severely injured bleeding patients

The PROPPR (Pragmatic Randomized Optimal Platelet Plasma Ratio) trial randomised bleeding trauma patients to receive either high or low ratios of platelets and plasma to red blood cells (1:1:1 versus 1:1:2). In a post hoc analysis, early platelet administration was associated with improved haemostasis and decreased mortality [12]. The benefit of early (< 6 h) platelet transfusions on mortality in severe bleeding trauma patients was also found in a large multicentre observational study [13].

Platelet transfusions are not indicated for the reversal of anti-platelet agents

Defective platelet aggregation induced by anti-platelet agents is amenable to antagonisation by platelet transfusion. However, adjuvant platelet transfusions in patients receiving anti-platelet therapy did not improve the outcome of traumatic brain injury [14] and unexpectedly resulted in impaired neurological recovery in spontaneous intracranial haemorrhage [15]. There is currently no evidence to modify the transfusion strategy for the purpose of reversal of anti-platelet agents in the presence of active bleeding [16].

Platelet transfusions harbour potential side effects

There is increasing evidence of the immunomodulatory properties of platelets as part of a complex interplay between haemostasis, thrombosis, and inflammation. Consistent with the well-known immunosuppressive potential of red blood cell transfusions, platelet transfusions have also been associated with ICU-acquired infections [17]. Pulmonary side effects include both transfusion-associated cardiac overload and transfusion-related acute lung injury (TRALI) [18]. In the setting of thrombotic microangiopathies, transfusing platelets might sustain or exacerbate the thrombotic process and have been associated with arterial thrombosis, clinical worsening, and sudden death in patients with thrombotic thrombocytopaenic purpura [19]. Caution regarding the use of platelet transfusion may extend to other microvascular thrombotic disorders such as heparin-induced thrombocytopaenia, catastrophic anti-phospholipid syndrome, and haemolytic uraemic syndrome.

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