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Allogeneic blood transfusions: benefit, risks and clinical indications in countries with a low or high human development index

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The risks associated with allogeneic red blood cell (RBC) transfusions differ significantly between countries with low and high human development indexes (HDIs). In countries with a low HDI, the risk of infection (HIV, HBV, HCV and malaria) is elevated. In contrast, in countries with a high HDI, immunological reactions (haemolytic transfusion reactions, alloimmunization and immunosuppression) are predominant. Therefore the overall risk associated with RBC transfusions in low HDI countries is much more significant than that in high HDI countries. In view of these risks, the limited efficacy of RBC transfusion and its high costs, this procedure should be used sparingly and rationally. Therefore RBC transfusion protocols adapted to the local situation are essential. Such protocols should distinguish between physiological and haemoglobin-based transfusion triggers. In countries with a high HDI, relative tachycardia and hypotension, despite normovolaemia, ST-segment changes suggestive of myocardial ischaemia and an Hb level <6 g/dl can serve as general guidelines for transfusion. Higher haemoglobin transfusion triggers should be used for patients aged >80 years and those with coronary artery or cerebrovascular disease. In countries with a low HDI, clinical signs of circulatory failure or myocardial ischaemia and an Hb level <5 g/dl can serve as transfusion guidelines.

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Introduction

Red blood cell (RBC) transfusions originating from an unrelated donor are known as allogeneic RBC transfusions. In the West, i.e. in countries with a high human development index (HDI), which is an index based on life expectancy, literacy, enrolment in further education and per capita income, >50% of RBC transfusions are used in trauma and surgery to compensate for major blood loss.[1]

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Benefits and risks of RBC transfusions

RBC transfusions are certainly beneficial in specific situations,[2,3] but are accompanied by many risks and side effects (Table 1). Several recent studies have suggested that RBC transfusions are associated with major adverse outcomes[4–7] and high costs.[8–10] In addition, RBC transfusions are a limited resource and blood shortages can occur at times.[11,12]

The risk of viral transmission via RBC transfusions has decreased considerably in recent years in high HDI countries,[13] although new transfusion-transmitted viruses have been discovered.[14] In contrast, in countries with medium or low HDIs, the risk of transmission of infectious diseases may still be extremely high (Table 1).

Risks associated with blood transfusion

Most reviews consider risks on transfusion-transmissible infections and immunological reactions, associated with RBC transfusions, that are only applicable to Western countries, i.e. countries with a high HDI.[13,15] Although 83% of the global population live in countries with medium and low HDIs, they have access to only 40% of the global blood

Table 1 Relevant risks of transfusion of tested blood

Type of risk	Estimate of current risk (infection rate per unit)	
	High HDI countries	Low HDI countries
Infections		
Viruses		
HIV	1:1 468 000[19]–1:4 700 000 [15]	1:50[20]–1:2578[59]
HBV	1:31 000[15]–1:205 000[19]	1:74–1:1000[60]
HCV	1:1 935 000[19]–1:3 100 000[15]	1:2578[59]
Bacteria (contamination)	1:2000–1:8000 (platelet pools) and 1:28 000–1:143 000 (red cells)[15]	?
Parasites		
Malaria	1:4 000 000[15]	Up to 1:3[21]
Prions		
vCJD	? (first possible transmission described[22])	?
Immunological reactions		
Haemolytic transfusion reactions		
Acute haemolytic	1:13 000[15]	?
Delayed haemolytic	1:9000[15]	?
Alloimmunization	1:1600[15]	?
Autoimmunization	? (recently identified as risk[23])	?
Immunosuppression	1:1[61]	?
TRALI	1:70 000[15]	?
Mistransfusion	1:14 000–1:18 000[13]	?

supply.[16,17] Most notably, all blood donations in high HDI countries are screened for transfusion-transmissible infections, whereas only 57% of blood donations in medium and low HDI countries are tested.[16,17] In addition, the tests used for blood screening are not always comparable. For example, only four of the 19 countries participating in the 'Workshop of the Directors of National Blood Transfusion Services', held in Harare, Zimbabwe, in 2000, used p24 antigen testing for HIV blood screening.[18] Moreover, the blood donation rate per 1000 population is almost 20 times higher in developed countries than in countries with a low HDI. Regular non-remunerated volunteers, who are the safest donors, provide 98% of donations in high HDI countries. In contrast, such donors are a minority in low HDI countries where up to 60% of donated blood comes from relatives of the anaemic patient or from paid donors. This leads to a higher incidence and prevalence of transfusion-related transmissible infections. However, the example of Zimbabwe shows that, despite the high seroprevalence (25.8%) of viruses such as HIV in the general population, the establishment of a well-organized voluntary blood donor system can result in a low prevalence of HIV among blood donors (2.3% and 0.7% for new and regular blood donors, respectively).[16,17]

Risks of infection

Viral

The most striking differences in the risks associated with blood transfusion between high and low HDI countries are found amongst viral infections. In recent years, the estimated risk of infection has decreased sharply because improvements in test sensitivity have reduced infectious window periods.[19]

In contrast with Western countries, the predominant risks in low HDI countries are transfusion-transmitted viral infections such as HIV, hepatitis B virus (HBV) and hepatitis C virus (HCV) (Table 1). This is due to the high seroprevalence of these diseases in the general population of these countries, the poorly organized blood donation systems and the low sensitivity of pathogen testing which results in HIV infection rates of up to 1:50 per unit transfused.[20]

Bacterial contamination

Transfusion of contaminated platelets is one of the most common transfusion-related risks in Western countries (1:2000–1:8000).[15] The most important cause is storage of platelets at 20–24 °C, which favours bacterial growth. In contrast, storage of RBCs at 4 °C inhibits the growth of

many bacterial species, resulting in a much lower contamination rate of down to 1:143 000 per RBC unit transfused.[15]

Parasites

Although rare in high HDI countries, transfusion-transmitted malaria is a major problem in highly endemic regions.[21] Only a few studies have addressed this problem, and most have focused on viral infections such as HIV, HBV and HCV.

Prions

The first case of possible variant Creutzfeld-Jakob disease (vCJD) transmitted by an RBC transfusion has recently been reported,[22] although a dietary infection with the agent of bovine spongiform encephalopathy (BSE) cannot be completely ruled out. In view of the probable incubation period of 6.5 years,[22] it will be interesting to observe the evolution of the current risk of transfusion-transmitted vCJD in the future.

Immunological risks

Haemolytic transfusion reactions

According to the data of the Quebec haemovigilance system the risk estimate of acute haemolytic transfusion reactions is about 1:13 000.[15] In this study, about half the cases of acute haemolysis were due to ABO incompatibilities.[15] In contrast, delayed haemolytic transfusion reactions are primarily caused by the presence of previously formed antibodies.

Immunization

A recent study by Young *et al.*[23] strongly suggests that autoimmunization may be added to the risks of allogeneic blood transfusions. The underlying pathomechanism is not currently understood, although conformational changes of RBC epitopes through alloantibody binding may be a possible trigger.[23]

Immunosuppression

Allogeneic RBC transfusions induce immunomodulation in the recipient.[24–26] As a result, the incidence of postoperative infections is elevated in transfused patients[25] and cancer recurrence may be favoured.[25,27]

Transfusion-related acute lung injury (TRALI)

Allogeneic RBC transfusions may cause acute lung injury[13,28,29] characterized by the sudden onset of non-cardiogenic pulmonary oedema,

hypoxaemia, dyspoea and fever, often requiring intensive care treatment including mechanical ventilation.

Mistransfusion

Mistransfusion occurs in 1:14 000–1:18 000 cases,[13,15] with an approximate morbidity and mortality rate of 1:600 000.[30] Approximately 50% of the errors occur at the clinical level and ~30% in the laboratory.[13]

Epidemiology

Three large observational studies indicating that allogeneic RBC transfusions are independently associated with a higher mortality have recently been published.[4,6,31] Sophisticated statistical models were used in these studies, but it is possible that the transfused patients were simply sicker or more severely traumatized and that the increased mortality was not due to a harmful effect of RBC transfusions but to the underlying medical condition of the transfused patients. Indeed, there is some evidence that this was the case. Transfused patients were older, had lower haemoglobin (Hb) and higher lactate levels at admission, had higher morbidity and trauma scores, and were more frequently in shock at admission.[4,6,31]. This potential confounding can only be avoided in prospective randomized trials.[32,33] The largest prospective randomized trial was performed by Hebert *et al.*[32] who compared a restrictive (Hb level <7.0 g/dl) with a liberal (Hb level <9.0 g/dl) transfusion regimen and found a lower 30-day mortality in the restrictive transfusion regimen in patients aged <55 years and patients with a lower morbidity score. Therefore it seems likely that RBC transfusions are efficacious only in very specific situations, such as when pretransfusion oxygen (O_2) delivery is low postoperatively,[34] or that they are associated with enough significant side effects to result in an overall adverse outcome.

Summary

A comparison of transfusion-related risks in high and low HDI countries shows that there are major differences. In low HDI countries transfusion-transmissible infections such as viral infections (HIV, HBV, HCV) and parasitic infections (malaria) strongly dominate. In contrast, although viral infections still occur in high HDI countries, the risk has been significantly reduced by improved laboratory testing and donor screening. The major risks of transfusion in Western countries are immunological reactions (haemolytic transfusion reaction, immunomodulation, mistransfusion) and bacterial contamination of platelets.

RBC transfusion protocols and transfusion triggers

Given the large number of risks and side effects, the high costs of RBC[8–10] and the fact that RBC transfusions are a limited resource, the use of allogeneic RBC transfusion should be restricted (Table 2).

RBC transfusion protocols

Introduction of an RBC transfusion protocol has been reported to reduce transfusion rates significantly.[35] The protocol was very simple, comprising only two rules: blood was only cross-matched for patients

Table 2 Haemoglobin-based and physiological transfusion triggers as a function of patient-related, logistical and geographical factors

Situation	Patients	Hb (g/dl)	Circulation	Myocardial ischaemia	Pvo_2, Ex-O_2, Vo_2
High HDI countries					
Intraoperative, ICU	All patients*	6†	Relative tachycardia/hypotension‡	ST-segment changes§	Yes
	>80 years	7	Relative tachycardia/hypotension‡	ST-segment changes§	Yes
	CAD	8	Relative tachycardia/hypotension‡	ST-segment changes§	Yes
	CVD	7	Relative tachycardia/hypotension‡	ST-segment changes§	Yes
	Fever/hypermetabolism	7	Relative tachycardia/hypotension‡	ST-segment changes§	Yes
Ward	All patients	6†	Relative tachycardia/hypotension‡	Clinical signs¶	NA
	>80 years	8	Relative tachycardia/hypotension‡	Clinical signs¶	NA
	CAD	9	Relative tachycardia/hypotension‡	Clinical signs¶	NA
	CVD	8	Relative tachycardia/hypotension‡	Clinical signs¶	NA
	Fever/hypermetabolism	8	Relative tachycardia/hypotension‡	Clinical signs¶	NA
Low HDI countries					
All situations	All patients	5†	Signs of circulatory failure	Clinical signs¶	NA

NA, not applicable; Pvo_2, mixed venous oxygen partial pressure <32 mmHg; Ex-O_2, oxygen extraction ratio >50%; Vo_2, oxygen consumption >10%; CAD, coronary artery disease; CVD, cerebrovascular disease.

An RBC transfusion is indicated if one of the criteria listed (the Hb threshold, the circulation criterion, myocardial ischaemia or the Pvo_2, Ex-O_2 or Vo_2 criteria) is reached. Normovolaemia is assumed for all triggers, and anaemia should be the only probable cause.

*Includes all patients except the subcategories aged >80 years, those with CAD, those with CVD and those with fever/hypermetabolism.

†One may choose not to transfuse an individual patient without any physiological transfusion triggers.

‡Relative tachycardia is defined as a heart rate >120–130% of baseline (>110–130 bpm), and relative hypotension is defined as a mean arterial blood pressure <70–80% of baseline or <60 mmHg (<55 mmHg in young healthy subjects, <70–80 mmHg in patients with CAD or CVD and in hypertensive patients, and even higher in severely hyperstensive patients).

§A new ST-segment depression >0.1 mV or an ST-segment elevation >0.2 mV.

¶To be confirmed with ECG and/or troponin measurement, if possible, in a timely fashion.

with a preoperative Hb level <11 g/dl, and patients only received allogeneic RBCs if the postoperative Hb level fell below 8.5 g/dl. The introduction of these guidelines resulted in a reduction of the transfusion rate from 35% to 11% and there were no adverse outcomes related to the introduction of the protocol.

Boralessa and colleagues constructed a more complicated transfusion algorithm based on preoperative Hb, postoperative blood loss and clinical signs of anaemia.[36] Particular attention was paid to education of medical and nursing staff, with lectures on the rationale of the protocol. After the introduction of these guidelines the number of patients transfused after total knee replacement was reduced from 64% to 30%. Another important observation was that in the first 24 h after surgery only eight out of 13 patients who received RBC transfusions were transfused according to the guidelines, a compliance rate of only 62%. Improvement of compliance with the algorithm might have reduced the transfusion rate even further.

RBC transfusion triggers

What should rational transfusion triggers be based on? The bulk of literature suggests that transfusion guidelines should not be reduced to a trigger based on Hb levels alone. Physiological triggers rather than Hb levels should guide transfusion therapy. Patient- and procedure-related factors can influence the decision to use allogeneic RBC transfusions, and the possible benefits must always be balanced against the possible risks. Finally, logistical and geographical factors, although not usually discussed in detail, are of major importance when establishing transfusion protocols.

Hb-based RBC transfusion triggers

If the intravascular volume status is normal (normovolaemia), acute anaemia is well tolerated by most individuals. To guarantee adequate tissue oxygenation, the decrease in arterial oxygen content will be compensated by an increase in cardiac output and in oxygen release by the RBCs.[37] In experimental settings volunteers have well tolerated HB levels of 5 g/dl under normovolaemic conditions[38] despite mild and transient cognitive dysfunction,[39,40] although electrocardiographic signs of ischaemia developed in a few subjects who developed tachycardia.[38] All of these adverse effects were readily reversible and resolved without sequelae.

The effect of anaemia on morbidity and mortality in a surgical population has been reported in a retrospective cohort study of 300 patients who refused blood transfusions for religious reasons.[41] Major morbidity

started to increase with postoperative Hb levels <7 g/dl and certainly increased with postoperative Hb levels <6 g/dl. Mortality started to increase with postoperative Hb levels <6 g/dl and certainly increased with postoperative Hb levels <5 g/dl.

Thus an Hb level <6 g/dl seems to be a strong transfusion trigger.[42] However, under the controlled conditions of general anaesthesia and in the absence of physiological and other transfusion triggers one may choose not to transfuse an individual patient. At Hb levels >6 g/dl, the decision to transfuse should be based on physiological signs of inadequate tissue oxygenation, predictability and magnitude of blood loss, and logistical factors.[42]

Physiological RBC transfusion triggers

Physiological transfusion triggers can be divided into signs of inadequate oxygenation of either specific organs or the entire body.[43] The latter include relative tachycardia and hypotension, an exaggerated increase in O_2 extraction, an exaggerated decrease in mixed-venous O_2 partial pressure and saturation, and a decrease in O_2 consumption. Tachycardia and hypotension, related to intraoperative blood loss, can only be considered as transfusion triggers if hypovolaemia has been corrected with crystalloid or colloid fluids. For patients equipped with a pulmonary artery catheter, a mixed-venous O_2 partial pressure <4.3 kPa (32 mmHg) and O_2 extraction >50% are considered to be clear indications to transfuse. Finally, an otherwise unexplained reduction in O_2 consumption of >10% is a reasonable transfusion trigger.[43]

The organs most at risk at critical Hb levels are the heart and the brain. A new ST-segment depression >0.1 mV or a new ST-segment elevation >0.2 mV for more than 1 min and new wall motion abnormalities as detected by transoesophageal echocardiography are indicative of myocardial ischaemia and are triggers for transfusion in the presence of anaemia. All these signs are reversible if the Hb level is increased by only 1–2 g/dl.[43,44]

Cognitive dysfunction is a clear sign of cerebral impairment due to inadequate oxygenation but is of no use in a patient under general anaesthesia. Other means of detecting intraoperative cerebral hypoxia are not available or have not been validated.[43] Therefore more liberal transfusion triggers might be justified for patients with known or suspected cerebrovascular disease.

The adequacy of oxygenation of the splanchnic organs is also difficult to monitor. However, these organs have been shown to support normovolaemic haemodilution very well, and so no specific monitoring is required.[45]

Perioperative and general transfusion guidelines should also take into account patient-related factors such as comorbidities and age. In a review of the literature, Khanna *et al.*[46] found the following characteristics to be

related to perioperative allogeneic RBC transfusion: preoperative anaemia, age, female gender, small body stature, cardiovascular disease, liver disease and other comorbidities such as rheumatoid arthritis and dementia.[46] For most of the factors identified, the evidence of any benefit of transfusion is lacking and transfusions may not be justified. Female gender and small body stature are probably related to a higher transfusion rate because of a smaller circulating blood volume, and loss of similar amounts of blood will lead to severe anaemia sooner than in heavier patients.

Patients with cardiovascular disease deserve special attention. First, impaired contractility, valvular dysfunction or developing myocardial ischaemia due to low Hb may compromise the compensatory increase in cardiac output in anaemia. Carson *et al.*[47] compared the mortality of 1958 Jehovah's Witnesses with and without cardiovascular disease who underwent surgery. The analysis indicated that the overall mortality increased as Hb levels decreased, but the death rate of patients with concomitant cardiovascular disease and preoperative anaemia increased more dramatically for each gram per decilitre of Hb decline. Although this study clearly established the risk of perioperative anaemia for patients with cardiovascular disease, it did not provide conclusive evidence that transfusion diminishes this risk. On the contrary, randomized trials have failed to show any benefit of transfusion in intensive care patients, with or without cardiovascular disease, for Hb levels >7 g/dl.[5,48] Spahn *et al.*[49] found that patients scheduled for coronary artery bypass graft surgery (CBAG), who were chronically β-blocked, tolerate acute normovolaemic haemodilution to a Hb level of 9.9 g/dl. In response to haemodilution they increased their cardiac index without an increase in heart rate and without signs of ischaemia.

A positive correlation between transfusion and short term survival has only been shown for patients with acute myocardial infarction. In a large retrospective cohort study on 78974 patients with acute myocardial infarction, transfusion was related to a reduction in 30-day mortality for patients if the haematocrit on admission was <33%.[50] Conversely, transfusion was related to an increased mortality for patients with haematocrit >36%.

Advancing age is related to a higher probability of coronary or cerebrovascular sclerosis or other concomitant diseases. This is likely to lead physicians to a more liberal use of allogeneic RBCs. However, scientific data indicate that advancing age cannot be considered to be a transfusion trigger. Casutt *et al.*[3] examined the effects of blood transfusion on cardiac index, oxygen delivery index and oxygen consumption index in 170 intensive care patients. They found that individual changes in these parameters were not related to preoperative ejection fraction or age. Elderly patients reacted similarly to younger patients to acute normovolaemic haemodilution (ANH). In a study of the tolerance of ANH in 20 elderly patients (mean age 76 ± 2 years) without known cardiovascular disease,

the preoperative Hb level was decreased from 11.6 ± 0.4 to 8.8 ± 0.3 g/dl without any signs of inadequate oxygenation. Intraoperatively the mean Hb level decreased even further to a mean of 7.7 g/dl, which was equally well tolerated.[51] In a retrospective cohort study of 8787 consecutive hip fracture patients aged from 60 to 106 years, Carson *et al.*[52] matched patients who received RBCs in the perioperative period with patients who did not receive RBCs. They were unable to demonstrate that transfusion was related to a reduced 30- or 90-day postoperative mortality for Hb levels as low as 8.0 g/dl. Almost all patients with Hb levels below this value were transfused, and so no conclusions could be drawn for Hb levels <8.0 g/dl.

Two recently published studies suggest that elderly patients may benefit from relatively high Hb concentrations. Halm *et al.*[53] noted that perioperative transfusion was related to lower re-admission rates after hip fracture repair in a population with a mean age of 80 ± 9 years. This relationship was not valid if patients received RBCs for Hb triggers >10 g/dl. Lawrence *et al.*[54] found that, in patients aged 79 ± 9 years, higher postoperative Hb levels (not necessarily in relation to an RBC transfusion) were associated with a longer walking distance. However, neither study found that morbidity, mortality or length of hospital stay was different between patients with lower or higher Hb levels.

Finally, in patients with increased oxygen consumption, such as those with a high fever or other hypermetabolic states, very low Hb levels (6 g/dl) can theoretically be responsible for an oxygen demand–oxygen delivery imbalance. Scientific data to back this hypothesis are lacking, but higher Hb levels can be justified as a precaution.

Logistical and geographical factors

The Task Force on Blood Component Therapy of the American Society of Anesthesiologists (ASA) conclude in their transfusion practice guidelines that transfusion is rarely indicated when the Hb level is >10 g/dl and is almost always indicated when it is <6 g/dl.[42] The decision as to whether intermediate Hb levels justify or require RBC transfusion should be based on the patient's risk for complications of inadequate oxygenation.

When establishing perioperative transfusion guidelines, one must consider that a patient under general anaesthesia has a decreased oxygen consumption due to muscle paralysis, a hypometabolic state and possibly mild hypothermia. In addition, an anaesthesiologist continuously monitors the patient and strives for an adequate blood pressure, avoids tachycardia and achieves supranormal oxygenation by using supplemental O_2. In the postoperative period oxygen consumption can rise sharply because of shivering, pain and other factors; the heart rate may be less

strictly controlled and the oxygenation less perfect compared with the intraoperative period. When we allow intraoperative Hb levels to fall as low as 5–6 g/dl, close postoperative surveillance and frequent monitoring of vital signs are necessary. Institutional guidelines should take into account local logistical characteristics such as the level of knowledge and availability of physician and nurse staff to guarantee patient safety, possibly justifying higher Hb transfusion triggers postoperatively.

Other logistical factors that may have to be taken into account are the time required for blood products to be prepared and delivered, the safety of local transfusion services and the age of the available RBCs. It has been shown that RBCs that have been stored for >15 days do not augment oxygen transport capacity immediately after transfusion[55] and may even be related to adverse outcome in critically ill patients.[7]

Geographical factors play an important role. Physicians in countries with a low HDI are faced with completely different circumstances than their colleagues in countries with a high HDI. The summary report of the World Health Organization (WHO) Global Database on Blood Safety indicates that the majority of low and medium HDI countries do not have national policies and guidelines on clinical blood usage. The WHO specifically notes that, as most blood in developing countries is donated by a family member or by paid donors, there are compelling social and financial pressures for the use of blood, even if the patient does not require transfusion.[16,17] In view of these risks the WHO advocates that transfusion should only be prescribed for conditions that might result in mortality or significant morbidity, a very restrictive, but necessary, attitude compared with the ASA guidelines.

In addition to problems of safety and access to blood products, physicians in low HDI countries are confronted with many technical problems. Fractioning of whole blood into its various components, storage of blood products and transport of blood in accordance with the 'cold chain' requires expensive equipment, maintenance and trained personnel. Technical instruments to measure Hb levels are often not available. Several strategies to differentiate moderate from severe anaemia have been developed. The degree of pallor of the conjunctiva, tongue, palm of the hand and nailbed has been linked to Hb levels. The severity of pallor is described as definite pallor, probable pallor or none. This technique has a specificity of 99% in detecting severe anaemia (Hb level <5 g/dl), but a sensitivity of only around 50%.[56] The efficacy of this technique is strongly dependent on the experience of the physician and other confounding factors, such as conjunctivitis. In 1995, Stott and Lewis[57] developed the Haemoglobin Colour Scale (HCS) to improve Hb estimation in settings where laboratory facilities are not available. The HCS consists of six standard colours varying from pale to dark red, corresponding to Hb levels of 4, 6, 8, 10, 12 and 14 g/dl. To estimate the Hb level, a drop of blood

is matched against the scale standards. For severe anaemia (<5 g/dl) the HCS has a sensitivity of 92%, a specificity of 90%, a positive predictive value of 49% and a negative predictive value of 99%.[58] These techniques have been developed for screening of patients in rural areas to guide haematological therapy in pregnant woman and children with anaemia due to malnutrition or malaria. The surgical population in low and medium HDI countries consists mainly of trauma victims and young women suffering from postpartum haemorrhage. Transfusion of RBCs can be lifesaving for these patients (worldwide, postpartum haemorrhage is the primary cause of perinatal maternal death). Because of the high risk related to transfusion in these countries, the HCS might be of great use in guiding perioperative fluid therapy but, to our knowledge, has not yet been validated for this purpose.

Owing to the higher risk-to-benefit ratio related to RBC transfusions in low HDI countries a more restrictive RBC transfusion policy is justified, and transfusions are indicated only when clinical signs of circulatory failure or myocardial ischaemia are present or at an Hb level <5 g/dl. In contrast, in high HDI countries where the overall risk associated with RBC transfusions is lower, it is justifiable to administer RBC transfusions more liberally when the patient develops signs of haemodynamic instability, ST-segment alterations suggestive of myocardial ischaemia or an Hb level <6 g/dl. Transfusion may be justified at higher haemoglobin levels if the patient has cardiovascular comorbidities or is aged >80 years.

In conclusion, the decision as to whether to transfuse a patient has to be based on a careful evaluation of the benefits and possible risks. Most importantly, logistical and geographical factors must be taken into account when establishing an individual transfusion strategy based on patient-related, physiological and Hb-based RBC transfusion triggers.

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