Hong Kong Society of Clinical Blood Management recommendations for implementation of patient blood management

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ABSTRACT

Patient blood management (PBM) is a patient-centred, multidisciplinary approach to optimise red cell mass, minimise blood loss, and manage tolerance to anaemia in an effort to improve patient outcomes. Well-implemented PBM improves patient outcomes and reduces demand for blood products. The multidisciplinary approach of PBM can often allow patients to avoid blood transfusions, which are associated with less favourable clinical outcomes. In Hong Kong, there has been increasing demand for blood in the ageing population, and there are simultaneous blood safety and donor issues that are adversely affecting the blood supply. To address these challenges, the Hong Kong Society of Clinical Blood Management recommends implementation of a PBM programme in Hong Kong, including strategies such as optimising red blood cell mass, improving anaemia management, minimising blood loss, and rationalising the use of blood and blood products.

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Introduction

Clinical blood transfusion remains an essential and irreplaceable part of modern medicine, either as an independent therapeutic modality or an additional support to other clinical therapies. Anaemia, a serious disease with a worldwide burden on both hospitalised patients and society,[1-3] is often managed with blood transfusion as part of the treatment. Without a reliable substitute, sourcing of the blood used in transfusion relies solely on donations from voluntary, non-remunerated blood donors. Because blood is a biological substance, it is impossible to completely eliminate adverse outcomes during and after transfusion. Worldwide, particularly in developed countries, the ageing of the population and emerging infectious diseases are the two most important and ongoing threats to the sustainability of the safe blood supply. Ageing populations tend to have increased numbers of complex surgeries and cancer treatments requiring increased blood transfusions.[4] In 2016, the mean per capital blood use in high-income countries was 32 units of red cell components per 1000 population. Moreover, the most frequently transfused patient group is aged >60 years, accounting for up to 79% among these transfusions.[5] Infectious pathogens continue to emerge rapidly, which could adversely affect transfusion safety both directly (if the pathogen is transmitted through blood transfusion) and indirectly (if outbreaks reduce the pool of available donors).[6] Recent examples include the Zika virus outbreak in South America and the dengue, hepatitis E, and chikungunya virus outbreaks in Southeast Asia.[7] Therefore, maintenance of a sustainable and safe blood supply continues to be a challenging task that requires a substantial amount of effort and resources.

There is evidence associating blood transfusion with less favourable clinical outcomes.[8,9] This evidence includes a higher incidence of recurrence in cancer surgeries, higher operative mortality, failure to rescue from sepsis, and other

香港臨床血液管理學會有關實施患者血液管理的建議

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患者血液管理（PBM）是一種以患者為中心的多學科方法，可優化紅細胞質量、把失血量減至最低並管理對貧血的耐受性，以改善患者治療效果。只要推行得宜，PBM可提升醫療成效並減少對血液製成品的需求。PBM的多學科方法可使患者避免輸血，這與臨床效果較差有關。在香港，人口老化使血液需求不斷增加，同時存在血液安全和供血者問題，對血液供應產生不利影響。為了應對這些挑戰，香港臨床血液管理學會建議在香港實施PBM計劃，包括優化紅細胞質量、改善貧血管理、減少失血以及合理使用血液和血液製成品等策略。

serious complications like renal, neurological, cardiac, and pulmonary dysfunction.[10] Patient blood management (PBM) is a patient-centred and multidisciplinary framework that has been rapidly developing throughout the last decade in Western countries to improve the treatment outcomes of patients who may need blood transfusions during their treatment. It refers to evidence-based medical and surgical concepts designed to improve patient outcomes. Commonly, PBM employs a three-pillar approach: (1) optimise red blood cell mass; (2) minimise blood loss; and (3) manage anaemia (Table 1[11-14]). Indeed, PBM optimises the patient's condition before, during, and after the procedure and only recommends transfusion when indicated. It directly addresses the triad of independent risk factors that can affect patient outcomes: anaemia, blood loss, and transfusion. Anaemia is appropriately and timely managed according to its aetiology instead of being bluntly corrected by blood transfusion. Thereby, blood loss is minimised, and the harm associated with inappropriate transfusions is avoided.[15] Therefore, countries that have implemented PBM have shown improvement of patients' outcomes, such as overall survival, disease recurrence, infection rate, length of stay in intensive care unit and hospital, cost, and blood utilisation.[16-22] During the Sixty-third World Health Assembly in 2010, member states were urged to establish or strengthen systems for the safe and rational use of blood products and to provide training for all staff involved in clinical transfusion, to implement potential solutions to minimise transfusion errors and promote patient safety, and to promote the availability of transfusion alternatives including, where appropriate, autologous transfusion and PBM.[23]

TABLE 1. Three pillars of patient blood management (adapted and modified)[11-14]

	Pillar one: Optimise red blood cell mass	**Pillar two: Minimise blood loss**	**Pillar three: Manage anaemia**
Preoperative	Detect/treat anaemia and iron deficiency Treat underlying causes Optimise haemoglobin Cease medications	Identify, manage, and treat bleeding/bleeding risk Minimise phlebotomy Plan/rehearse procedure	Assess patients' bleeding history and develop management plan Estimate patients' tolerance for blood loss Optimise cardiopulmonary function
Intra-operative	Time surgery with optimisation of erythropoiesis and red blood cell mass	Meticulous haemostatic/surgical/anaesthetic techniques Cell salvage techniques Avoid coagulopathy Patient positioning/warming Pharmacological agents	Optimise cardiopulmonary function Optimise ventilation and oxygenation Restrictive transfusion strategies
Postoperative	Manage anaemia and iron deficiency Manage medications and potential interactions	Monitor and manage postoperative bleeding Keep patient warm Minimise phlebotomy Awareness of drug interactions and adverse events Treat infections promptly	Maximise oxygen delivery Minimise oxygen use Treat infections promptly Tolerance of anaemia Restrictive transfusion strategies

Blood supply and transfusion demand in Hong Kong

Although Hong Kong has a long history of self-sufficiency in terms of blood supply, population ageing has brought a significant increase in demand for blood over the last decade.[24] Since 2015, the Hong Kong Blood Transfusion Service has experienced excessive difficulties at mobilising citizens to maintain a stable, safe blood supply. As a result, the Blood Transfusion Service faces a number of blood safety and donor issues that affect the blood supply. Emerging infectious diseases like Zika virus and low pre-donation haemoglobin due to iron deficiency are typical examples that may prevent apparently healthy persons from donating blood.

As blood is irreplaceable and has a limited shelf life, securing a sustainable and safe blood supply is of paramount importance in the modern healthcare system to ensure that patients' transfusion needs are met promptly and appropriately. Strategies to enhance new donor recruitment and existing donor retention should be undertaken by the Blood Transfusion Service to increase the blood supply. However, demand control measures should be simultaneously implemented to reduce the pressure on the supply side. In Hong Kong, there has been increasing awareness of the concept of PBM beginning in the past 2 years, and small-scale projects have been initiated. One local project was able to increase the preoperative haemoglobin concentration and reduce the transfusion rate after implementation of PBM.[25] In the UK, the National Institute for Health and Care Excellence recommended consideration of single-unit transfusions for adults without active bleeding in November 2015.[26] On the basis of this recommendation, some medical departments in Hong Kong have implemented single-unit blood transfusions over the past 2 years, and unpublished audit results demonstrate an overall reduction of red blood cell transfusions in general medical in-patients over that period.

With the objective of improving patients' outcomes and better managing transfusion demand, a group of experienced clinicians from different specialties and hospitals in Hong Kong has established the Hong Kong Society of Clinical Blood Management to continuously promote PBM in Hong Kong. The Society aims to discuss and make recommendations regarding the implementation of PBM in Hong Kong. Below are three areas of focus that the Society intends to address.

I. Optimising patients' red blood cell mass and better managing anaemia

Anaemia is a serious disease burden in both hospitalised patients and society.[1-3] Haematopoiesis and anaemia management are important modifiable risk factors for adverse outcomes.[9,27,28] Beneficial outcomes in this important pillar of PBM are seen in not only surgical patients but also other patient groups, such as those with underlying medical, obstetric, or gynaecological problems. Therefore, clinical guidelines have recommended that anaemia be promptly recognised and the underlying causes identified and managed appropriately.[29] Because some surgical patients have an increased risk of bleeding, haemoglobin measurement well before operation in all patients could provide adequate time to manage any anaemia before surgery and improve outcomes.[29]

Red blood cell transfusion should be restricted to the minimal amount necessary to achieve clinical stability and to patients presenting with severe iron deficiency anaemia and alarming symptoms (eg, haemodynamic instability) and/or risk criteria (eg, coronary heart disease).[30,31] As iron deficiency (whether absolute or functional) is commonly found in anaemic patients, its correction should be promptly instituted. Oral iron supplements, provided as ferrous or ferric salts, are usually the first line of treatment for uncomplicated iron deficiency anaemia because of their availability, ease of administration, and relatively low cost. However, because of these supplements' notorious gastrointestinal adverse effects, intravenous iron should be considered in patients with intolerance to oral iron and when more rapid restoration of the iron store is expected. 'Newer' intravenous iron formulations with safer profiles, such as ferric carboxymaltose or iron isomaltoside, which allow for a short-time (15-60 min) infusion of high iron doses (≥1000 mg), are now available for use in both in-patients and out-patients. Such intravenous iron formulations can rapidly correct iron deficiency and anaemia within a few weeks (vs the few months needed for correction via oral iron). At the University Hospitals Plymouth, UK, intravenous iron is given to successfully treat iron deficiency anaemia when surgery with anticipated blood loss of >500 mL is anticipated within 6 weeks.[32] As a result, intravenous iron has become an important component of PBM management strategies.

In Hong Kong, the Blood Transfusion Service and the Hong Kong Medical Association have recently issued a simple algorithm to aid general practitioners with early and prompt recognition of anaemia and its management.[33] Further work is required to enhance the general population's awareness of anaemia and iron deficiency issues, their diagnosis, and improving their management.

II. Minimising blood loss

Reducing or minimising blood loss in hospitalised patients is another approach to reduce the need for blood transfusion and improve patients' outcomes. Some might consider that this type of planning should only occur in surgical or operative settings, but reducing iatrogenic blood loss in non-operative settings has also been shown to improve patients' outcomes. Table 2[34-43] highlights the measures that have been shown to be effective at minimising blood loss. These measures are safe and have not affected organ function or caused other complications. Instead, they reduce iatrogenic blood loss and avoid blood transfusions.

Temporary cessation of antiplatelet and anticoagulant medications in the perioperative period may lead to reduced blood loss and transfusion requirements if the risks of perioperative thromboembolic events and bleeding are balanced. Meticulous surgical techniques such as performing minimally invasive surgery, judicious use of electrocautery, tourniquets, topical haemostatic agents, and intra-operative blood salvage can minimise surgery-related blood loss.[44-49]

A number of anaesthetic techniques can also help to reduce blood loss. Permissive hypotension refers to the lowering of mean arterial pressure to values between 50 and 65 mm Hg with the goal of reducing blood flow to the surgical field, thereby reducing blood loss and improving visibility in the surgical field.[50] Studies have shown that permissive hypotension during anaesthesia reduced blood loss in spinal surgery, radical prostatectomy, functional endoscopic sinus surgery, and orthopaedic surgery.[51-53] It can also reduce blood loss and blood product utilisation in adult trauma patients with haemorrhagic shock.[54] Organ hypoperfusion is the major drawback, and therefore, this strategy may not be suitable for patients with coronary artery disease, cerebrovascular disease, traumatic brain injury, or spinal injury.

Prevention of perioperative hypothermia is another strategy that can help to reduce blood loss. Hypothermia is defined as a core temperature <36°C and is a common consequence of anaesthesia.[55] Even mild hypothermia, defined as a core temperature between 35°C and 36°C, significantly increases perioperative blood loss and augments the transfusion requirement.[56] Therefore, measures should be taken to prevent inadvertent hypothermia, including identification of high-risk patients, pre-warming before surgery, intra-operative monitoring of body temperature, using warm intravenous/irrigation fluid and forced-air warming devices, and avoidance of unnecessary body exposure.[57]

Another method to minimise blood loss is acute normovolaemic haemodilution. Acute normovolaemic haemodilution involves withdrawal of whole blood with concurrent infusion of fluids to maintain normovolaemia.[58] The autologous blood is re-infused at the conclusion of the surgery. This method has been shown to significantly reduce the incidence and volume of allogeneic blood transfusion, and its use should be considered in adult patients who undergo surgery in which substantial blood loss is anticipated.[44] However, relatively profound anaemia is expected during the surgery, which may induce tissue ischaemia, particularly in the myocardium.[45] Furthermore, the effects of normovolaemic haemodilution on morbidity and mortality are uncertain.

Appropriate patient positioning during the intra-operative period may also help to reduce surgery-related blood loss. Elevation of the surgical site above the right atrium facilitates venous return and reduces venous engorgement. For example, the reverse Trendelenburg position has been shown to reduce intra-operative blood loss in endoscopic sinus surgery.[46]

Using the wide pad support widths of the Wilson frame, when compared with narrow pad support widths, significantly decreased intra-abdominal pressure and intra-operative blood loss in patients undergoing spine surgery in the prone position.[47] Pharmacological agents can also be used to facilitate haemostasis. Tranexamic acid has been studied extensively in a wide range of surgeries and has been shown to reduce blood loss effectively without increasing the risk of thromboembolic events.[48,49] In

TABLE 2. Measures to minimise blood loss in both operative and non-operative settings[34-43]

Surgical/operative settings	Non-operative settings
1. Early management of bleeding risk, such as cessation or alteration of antiplatelet or anticoagulation therapy 2. Anaesthetic techniques to minimise blood loss or the use of allogeneic blood, eg,[38] • Avoidance of hypothermia (core temperature <36°C) • Permissive hypotension (mean arterial pressure 50-65 mm Hg) • Autologous blood pre-deposit • Acute normovolaemic haemodilution[39,40] • Intra- and post-operative cell salvage 3. Guided transfusion therapy through the use of point of care testing 4. Use of antifibrinolytics[41-43]	Strategies to minimise the blood volume taken and thereby reduce iatrogenic blood loss, eg,[34-37] • Small-volume phlebotomy tubes • Closed inline sampling devices • Frequent evaluation of routine blood sampling orders and cumulative daily phlebotomy loss • Bundled scheduling of blood sampling • Use of non-invasive techniques and measurements, such as continuous non-invasive haemoglobin monitoring

case of significant haemorrhage that is refractory to standard treatment, the use of recombinant factor VIIa should also be considered.[59]

Diagnostic phlebotomy for laboratory testing can also be a significant source of blood loss, especially in critically ill patients.[60] Such blood loss has been associated with the development of anaemia and the need for transfusion.[61] Therefore, blood tests should be ordered only when necessary, and the volume of blood collected should be the minimum required. Paediatric bottles can be used to minimise the blood volume collected for testing, which in turn reduces iatrogenic blood loss and transfusion requirements.[60] Point-of-care testing devices require smaller blood volumes for analysis and serve as an alternative to traditional laboratory testing. Blood sampling from arterial and central venous lines traditionally involves discarding the initial blood sample. The method of returning the initial blood sample back to the patients has been used to significantly reduce iatrogenic blood loss,[62] and this measure should be considered.

III. Rationalising use of blood and blood components

As blood transfusion is not without risks, consideration should be given to the balance of benefits against risks. Most would advocate the adoption of a quality clinical transfusion process, ie, "transfusion of the right number of units of blood to the right patient at the right time, in the right conditions, and according to appropriate guidelines".[63] Thus, clinicians should proceed through a chain of related events by making appropriate decisions (Fig).

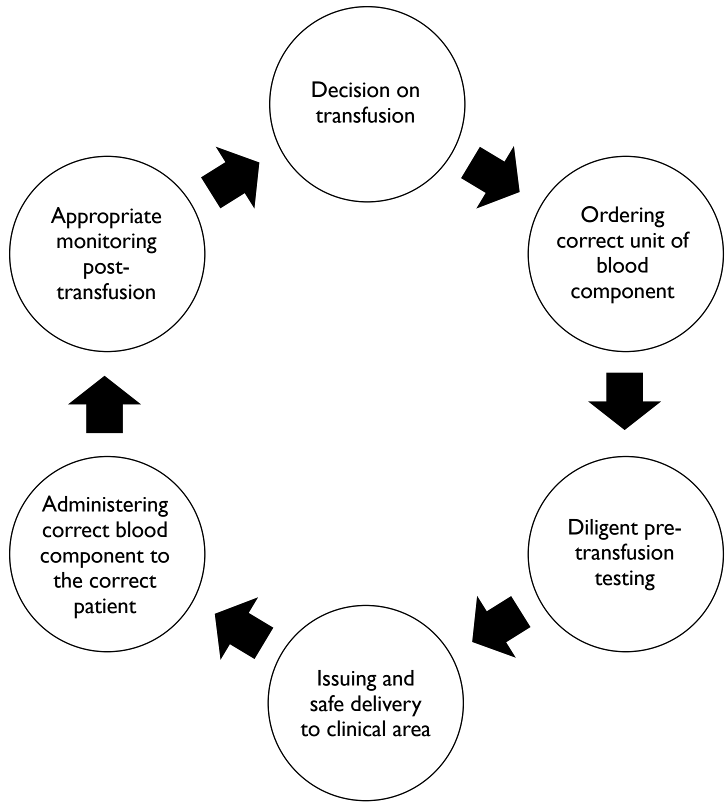

FIG. Key decision-making points in clinical blood transfusion

Recommendations for implementation of patient blood management in Hong Kong

On the basis of the above three areas for consideration, as well as advice from the Joint United Kingdom (UK) Blood Transfusion and Tissue Transplantation Services Professional Advisory Committee[64] and the World Health Organization,[65] the Hong Kong Society of Clinical Blood Management makes the following recommendations:

1. A PBM framework, covering primary, hospital, research, audit, and public health measures, should be developed for use in Hong Kong after engagement of different stakeholders;
2. Healthcare professionals, patients, and the public should be educated on the appropriateness of blood transfusion, and PBM programmes; and
3. A PBM framework should be developed for application in Hong Kong, including early recognition and better management of anaemia and iron deficiency in patients and the general population; optimisation of patients' haematopoiesis and correction of coagulation before surgical procedures; and application of various blood-saving technologies/techniques and point-of-care testing to optimise patients' outcomes with less transfusion.

The proposed PBM framework is a multi-pronged approach that encompasses a wide range of sectors, disciplines, specialties, and departments. Its implementation will include hospitals, clinics, healthcare facilities, and public health measures to provide care to in-patients, out-patients, and the public of Hong Kong. However, a number of barriers exist that may hamper PBM implementation in Hong Kong.[66,67] These include misconceptions related to blood transfusion and difficulties accessing contemporary evidence and data about PBM. There are also existing cultural pressures to retain the status quo, with inadequate incentive for change, as blood is currently delivered freely and efficiently to receivers in Hong Kong. Resources may be inadequate or unequally allocated, such as ferritin assays and intravenous iron preparations for early diagnosis and effective treatment of anaemia, or cell savers and active patient warming equipment for minimising blood loss and conserving blood during surgery. Logistical complexities such as timely investigation and treatment of preoperative anaemia before elective surgery and establishment of point-of-care testing coagulation management programmes may also present obstacles. Finally, PBM lacks specific established quality mechanisms, such as associated policies, standards, guidelines, documentation, performance indicators, coordination, monitoring, evaluation, and feedback.

To overcome these barriers, strong leadership with central steering and empowerment of PBM advocates is required to reinforce and coordinate the current piecemeal and uncoordinated efforts of PBM promotion. The goal of PBM is not simply to reduce the amount of blood transfusion. It is a continuing programme of quality improvement that has the goal of improving patient outcomes via its different measures. With reference to other countries' experiences and the barriers and challenges that could limit the implementation of PBM in clinical practice, an appropriate framework with local interest should be developed to implement PBM practices at the hospital and territory level.[11,68,69]

Conclusion

On the basis of the scientific evidence on the successful implementation of PBM and its improvement of patient outcomes, the Hong Kong Society of Clinical Blood Management strongly recommends that Hong Kong implement PBM as soon as possible. The Society will continue to work with relevant professional bodies, patients, and stakeholders to facilitate the local implementation of PBM.

Author contributions

All authors contributed to the concept or design of the study, acquisition and analysis or interpretation of data, drafting of the manuscript, and critical revision of the manuscript for important intellectual content. All authors had full access to the data, contributed to the study, approved the final version for publication, and take responsibility for its accuracy and integrity.

Conflicts of interest

All authors have disclosed no conflicts of interest.

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