BSH position paper on European Society of Intensive Care Medicine (ESICM) guideline: 'Transfusion strategies in non-bleeding critically ill adults'

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Methodology

Each of the recommendations in the ESICM guideline were reviewed and the applicability for practice in the UK considered with reference to relevant published BSH guidelines.

Literature review details

The PubMed database was searched for English language articles with abstracts from 2013 (date of publication of previous BSH guidance on this topic) to 2024 using the following search terms: ‘critical care red cell transfusion; critical care platelet transfusion; acute coronary syndrome red cell transfusion; sepsis red cell transfusion’. References from relevant publications were also searched.

Review of the manuscript

Review of the manuscript was performed by the British Society for Haematology (BSH) Transfusion Task Force and the BSH Guidelines Committee. It was also on the members section of the BSH website for comment.

Introduction

The British Society for Haematology (BSH) published guidelines on the management of anaemia and red cell transfusion in adult critically ill patients in 2013 (1), providing evidence based recommendations for the use of red cells in the management of anaemia in non-bleeding patients suffering critical illness. The recommendations reflected the results of several landmark studies which identified that there was no clear advantage of a liberal transfusion strategy in this patient population.

Anaemia is prevalent among critically ill patients and is associated with inferior outcomes, including poorer recovery following discharge from the intensive care unit. Up to one quarter of patients admitted to ICU receive blood component transfusion (2). This anaemia is multifactorial, with blood loss (including iatrogenic blood loss due to frequent sampling), and inflammation as contributory factors.

In 2020, the European Society for Intensive Care Medicine (ESICM) published up to date guidance on this topic with a similar scope to the previous BSH guidance (3). This BSH position paper will explore the recommendations in the ESICM guideline and consider the applicability for transfusion practice in the UK.

ESICM guideline

Methodology

The ESICM guideline was prepared by a task force with relevant clinical experience using the GRADE methodology. The task force developed a series of questions which were then prioritised to finalise sixteen questions which were addressed by the guideline. Appropriate literature searches were performed, evidence reviewed, and recommendations formulated.

These recommendations were then approved by the task force prior to publication. The recommendations are listed in full in Table 1.

Recommendations

Restrictive versus liberal red blood cell transfusion

General ICU population

The EISCM guideline is divided into sections, the first of which examines the evidence for restrictive versus liberal transfusion thresholds in various scenarios. It recommends a restrictive transfusion threshold, defined as 70g/L in a general ICU population, with or without Acute Respiratory Distress Syndrome (ARDS). The guideline authors acknowledge that at the time of writing a restrictive strategy had become standard practice and that a liberal transfusion strategy, in the absence of further evidence demonstrating substantial benefit would not likely be acceptable to ICU clinicians. An updated literature search performed by the authors of this BSH paper has identified no such evidence and we therefore support the recommendation made by ESICM.

Acute coronary syndromes

When considering the most appropriate transfusion strategy for critically ill adults with acute coronary syndromes, the ESICM task force identified low certainty of evidence but determined that safety signals in the available data support the use of a liberal strategy in this patient group. The more recently published MINT study (4) randomised patients with myocardial infarction and anaemia to a restrictive transfusion strategy (transfusion trigger 70-80g/L) or a liberal transfusion strategy (transfusion trigger 100g/L) and assessed the impact of each on a composite primary outcome of myocardial infarction or death at 30 days. The results of this trial found the rate of the primary outcome was higher in the restrictive group (16.9% vs 14.5%), but this difference was not statistically significant.

Cardiac death was more common in the restrictive group (5.5% vs 3.2%). Safety outcomes including incidence of heart failure at 30 days were similar in both groups, indicating a liberal approach was not associated with additional patient harms. Overall, the results from MINT indicate it is reasonable to continue to support a more liberal transfusion strategy in anaemic patients with myocardial infarction. While this trial did not specifically include patients managed in a critical care setting, it is reasonable to use this data in assessing which transfusion strategy is most appropriate for patients in critical care with acute coronary syndromes. We continue to support the ESICM recommendation for a liberal strategy in this patient group.

Sepsis

The previous BSH guidance made a weak recommendation that in the early stages of sepsis, where there was clear evidence of inadequate oxygen delivery, a transfusion target of 90-100g/L should be considered, but recommended a restrictive approach to the later stages of sepsis (1). The ESICM identified three randomised controlled trials examining this question, all published after the previous BSH guideline. Analysis of these three studies identified minimal differences in outcomes but a decrease in number of blood components transfused and fewer patients transfused. A recommendation is therefore made that a restrictive transfusion threshold of 70g/L is employed. We endorse this recommendation.

Cardiac Surgery

Several studies have examined the effect of a restrictive transfusion strategy in the management of critically ill patients post cardiac surgery. Analysis of these by the ESICM group identified that a restrictive strategy did not significantly impact outcomes including short term mortality, long term mortality and safety outcomes. The recommendation to

adopt a restrictive strategy with a transfusion threshold of 75g/L is therefore made. The taskforce also noted this strategy results in both a lower proportion of patients receiving a transfusion, and a lower mean number of transfusions indicating the positive impact on blood supply and associated resource requirements.

Weaning from ventilation

The role of red cell transfusion in the process of weaning patients from mechanical ventilation was examined in the previous BSH guideline, which recommended a restrictive approach. This continues to be recommended by the ESICM who did not identify new evidence on the topic. We agree with this recommendation.

Areas where no recommendation is made

There are four circumstances where the ESICM do not make recommendations for either a liberal or restrictive transfusion strategy due to uncertainty for outcomes in the available evidence. This was the case for critically ill adults with acute neurologic injury, adults undergoing veno-venous or veno-arterial ECMO, critically unwell adults with malignancy and critically ill elderly adults. Having reviewed the available data, we feel this is reasonable.

Alternative RBC transfusion triggers

This subject was not included in the scope of the previous BSH guideline and examines whether alternatives such as SvO2, acidosis, or presence of arrhythmia should be used to guide transfusion, rather than traditional measures of haemoglobin. There is a paucity of randomised controlled trials examining these parameters and their utility in assessing transfusion requirements and the recommendation is that haemoglobin and haematocrit ought to be used as transfusion triggers rather than physiologic measures.

RBC transfusion prevention

The BSH guideline examined evidence for two potential alternatives to transfusion: erythropoietin (EPO) and iron therapy. It recommended against the use of erythropoietin in this patient population pending further safety and efficacy data, and recommended iron therapy be reserved for patients with clear evidence of iron deficiency. The ESICM guidance reviews up to date evidence for these two therapies individually and in combination and makes conditional recommendations against the use of each. The IRONMAN trial randomised anaemic ICU patients to receive intravenous iron or placebo. While intravenous iron appeared safe, it did not significantly reduce red cell transfusion or length of hospital stay (5). EPO has been examined by a number of studies and the authors conclude there is no clear benefit of EPO or of EPO plus iron therapy in this population. We support this conclusion.

Iatrogenic anaemia due to blood sampling is well recognised in the adult ICU patient population. Opportunities to reduce the blood withdrawn for testing include the use of small volume tubes, or the use of blood conservation sampling devices. The ESICM give a conditional recommendation for the use of small volume tubes, which is consistent with the previous BSH guidance. The data available to inform this recommendation are observational studies. When examining the value of blood conservation devices there are several small, single centre randomised trials which demonstrate a reduction in daily and cumulative blood sampling volume which the ESICM task force felt likely to translate into reduced transfusion requirements and made a conditional recommendation for their use.

It is recognised that anaemia persists for up to one year following hospitalisation for critical illness (6), and that it may impact on recovery, contributing to fatigue and poor health

related quality of life. The management of anaemia following discharge from critical care, and the impact of this is outwith the scope of the ESICM guidance, and is the focus of ongoing clinical trials such as the ABC trial and others.

Transfusion of other blood components

The ESICM guidance makes recommendations on when platelet and plasma transfusions may be appropriate in adult critically unwell patients without bleeding and when invasive procedures were planned. This was outwith the scope of the BSH guideline which focussed on red cell transfusion only, but is the subject of other BSH guidance on the use of platelet transfusions (7) and plasma transfusions (8). The recommendation made for prophylactic platelet transfusion is in line with existing BSH guidance: recommended for patients with a platelet count below $10x10^9$/L. There is less available evidence to guide appropriate platelet thresholds for patients undergoing invasive procedures. The PACER trial reported in 2023 and randomised patients in the haematology ward or ICU with platelet counts between 10 and 50 x 10^9/L to receive platelets or not prior to ultrasound guided central venous catheter insertion. Bleeding rates were increased in patients who did not receive platelet transfusion; however this was most marked in patients being cared for on the haematology ward when compared to ICU patients. Subclavian vein line placement was identified to have a higher bleeding risk than internal jugular or femoral vein placement. Meantime, the ESICM recommend against prophylactic platelet transfusion when the platelet count is above 100 x 10^9/L, and suggests platelet transfusion is not required prior to percutaneous tracheostomy or central line insertion if the platelet count is above 50 $x10^9$/L. Taking into account the results of the PACER study, we feel a platelet threshold for tunnelled central line insertion of 30 x 10^9/L is reasonable, which is the approach endorsed by other BSH guidance (9). This is also the focus of the T4P trial which is ongoing.

The ESICM taskforce also considered the use of prophylactic plasma transfusion in critically ill patients with coagulopathy and suggest against prophylactic transfusion which is in line with BSH guidance and helps prevent adverse events associated with plasma transfusion where there is no clear evidence of benefit. There is little evidence to guide which critically ill patients with coagulopathy undergoing invasive procedures will benefit from prophylactic plasma transfusion and this is reflected in the suggestion against its use in this context.

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Declaration of Interests

The BSH paid the expenses incurred during the writing of this guidance.
All authors have made a declaration of interests to the BSH which may be viewed on request. SJS has been involved in studies and reviews relevant to this topic but has not received direct funding. AR is the Chief Medical Officer of Volition Diagnostics. KH has no conflicts of interest to declare.

Review Process

Members of the writing group will inform the writing group chair if any new evidence becomes available that would alter the strength of the recommendations made in this

document or render it obsolete. The document will be reviewed regularly by the relevant task force and the literature search will be re-run every five years to search systematically for any new evidence that may have been missed. The document will be archived and removed from the BSH current guidelines website if it becomes obsolete. Please check the BSH guidelines website (www.b-s-h.org.uk/guidelines) for any addenda that may be produced after the initial publication.

Disclaimer

While the advice and information in this guidance is believed to be true and accurate at the time of going to press, neither the authors, the BSH nor the publishers accept any legal responsibility for the content of this guidance.

Table 1 ESICM recommendations

ESICM recommendations		BSH Endorsed
1.	We recommend a restrictive transfusion threshold (7 g/dL) vs. a liberal transfusion threshold (9 g/dL) in a general ICU population, with or without ARDS (Strong recommendation, moderate certainty). This recommendation does not apply to patient populations addressed in subsequent recommendations below.	Yes
2.	We suggest a liberal transfusion threshold (9–10 g/dL) vs. a restrictive transfusion threshold (7 g/dL) in critically ill adults with acute coronary syndromes (conditional recommendation, low certainty evidence).	Yes
3.	We suggest a restrictive transfusion threshold (7 g/dL) vs. a liberal transfusion threshold (9 g/dL) in critically ill adults with sepsis and septic shock (conditional recommendation, moderate certainty).	Yes
4.	We suggest a restrictive transfusion threshold (7 g/dL) vs. a liberal transfusion threshold (9 g/dL) in critically ill adults with prolonged weaning from mechanical ventilation (conditional recommendation, low certainty).	Yes
5.	We recommend a restrictive transfusion threshold (7.5 g/dL) vs. a liberal transfusion threshold (8.5–9.0 g/dL) in critically ill adults undergoing cardiac surgery (strong recommendation, moderate certainty).	Yes
6.	We do not make a recommendation for a restrictive (7 g/dL) vs. a liberal (9–11.5 g/dL) transfusion threshold in critically ill adults with acute neurologic injury (traumatic brain injury, subarachnoid haemorrhage, or stroke). Transfusion at either threshold remains appropriate pending further research (no recommendation, low certainty).	Yes
7.	We do not make a recommendation for a restrictive (7 g/dL) vs. a liberal transfusion (9 g/dL) threshold in critically ill adults undergoing veno-venous or veno-arterial ECMO. Transfusion at either threshold would be appropriate pending further research (no recommendation, very low certainty).	Yes
8.	We do not make a recommendation for a restrictive transfusion threshold (7 g/dL) vs. a liberal transfusion threshold (9 g/dL) in critically ill adults with malignancy (haematologic or solid tumour). Transfusion at either threshold would be appropriate pending further research (no recommendation, low certainty).	Yes
9.	We do not make a recommendation for a restrictive transfusion threshold (7 g/dL) vs. a liberal transfusion threshold (9 g/dL) in critically ill elderly patients. Transfusion at either threshold would be appropriate until further research is available (no recommendation, low certainty).	Yes
10.	We suggest using haemoglobin or haematocrit transfusion triggers rather than physiologic transfusion triggers (conditional recommendation, very low certainty evidence).	Yes
11.	We suggest against the routine use of iron therapy (oral or intravenous) in critically ill patients with anaemia (conditional recommendation, low certainty).	Yes
12.	We suggest not using erythropoietin to prevent RBC transfusion (conditional recommendation, low certainty).	Yes

13.	We suggest against the routine use of a combination of EPO and iron in critically ill patients with anaemia (conditional recommendation, very low certainty evidence).	Yes
14.	We suggest using small-volume blood collection tubes to prevent RBC transfusion (conditional recommendation, very low certainty).	Yes
15.	We suggest using blood conservation devices versus conventional blood sampling systems to prevent RBC transfusion (conditional recommendation, low certainty).	Yes
16.	We suggest not using platelet transfusion to treat thrombocytopenia unless the platelet count falls below 10×10^9/L (conditional recommendation, very low certainty).	Yes*
17.	We recommend not giving prophylactic platelet transfusion prior to invasive procedures for platelet counts above 100×10^9/L (strong recommendation, low certainty).	Yes*
18.	We suggest not giving prophylactic plasma transfusion in patients with coagulopathy (conditional recommendation, very low certainty).	Yes**
19.	We suggest against the use of prophylactic plasma transfusion prior to invasive bedside procedures in non-bleeding critically ill patients (conditional recommendation, very low certainty).	Yes**

*see BSH guidelines for the use of platelet transfusions(7)

**see BSH guidelines on the spectrum of fresh frozen plasma and cryoprecipitate products: their handling and use in various patient groups in the absence of major bleeding (8)

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