Commentary

Implementing first pillar of PBM in the Emergency Area: a missed opportunity?

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Emergency Areas (EAs) are typically characterized by high levels of overcrowding, reflecting their critical role within healthcare systems. In Europe, EAs register an average of 250 visits per 1,000 inhabitants annually[1], while in the United States, this figure rises to 427[2], underscoring the significant demand placed on these services.

Within this substantial patient burden, a significant proportion of individuals access EAs following a diagnosis of anemia or due to anemia-related symptoms, while in other cases, anemia is incidentally detected during admission for unrelated medical conditions.

Two key studies have highlighted its prevalence, reporting rates of 27.5% when applying the World Health Organization (WHO) criteria[3] and 45.8% when using a definition of hemoglobin (Hb) levels below 12.0 g/dL[4]. These findings emphasize the relevance of addressing anemia in this critical healthcare context.

A crucial aspect of anemia management in EAs is the appropriateness of red blood cell (RBC) transfusions. While transfusion is often perceived as an immediate solution for anemia correction, evidence suggests a significant proportion of them in EAs are inappropriate. Approximately one-third of RBC transfusions have been shown to be misaligned with established clinical guidelines, either due to inadequate Hb thresholds or neglect of the underlying pathology, such as iron deficiency anemia (IDA) without cardiovascular instability[3,5-7]. These results underscore the persistent knowledge-to-practice gap regarding the application of Patient Blood Management (PBM)[8] principles in EAs, particularly when alternative treatments, such as intravenous (IV) iron, may be more appropriate in many cases. A decision tree algorithm aimed at improving transfusion appropriateness in chronic anemia was proposed by Beverina *et al.*[9] (**Figure 1**).

An additional reason of transfusion inappropriateness is related to the volume of RBCs administered, leading to post-transfusion Hb levels that exceed therapeutic targets. Over transfusion is a critical aspect of transfusion management because it exposes patients to avoidable risks, such as transfusion-associated circulatory overload (TACO) and other complications. Evidence from EAs has shown that the rate of volume inappropriateness ranges from 16 to 91%, reflecting the widespread nature of this issue[3,5,6,10]. This highlights the need for stricter control of transfusion volume and the implementation of strategies such as single-unit transfusion policies and routine post-transfusion Hb reassessment[11].

In addition to the well-known immediate and delayed adverse effects associated with RBC transfusions[12], it is essential to acknowledge that blood is a finite resource. The

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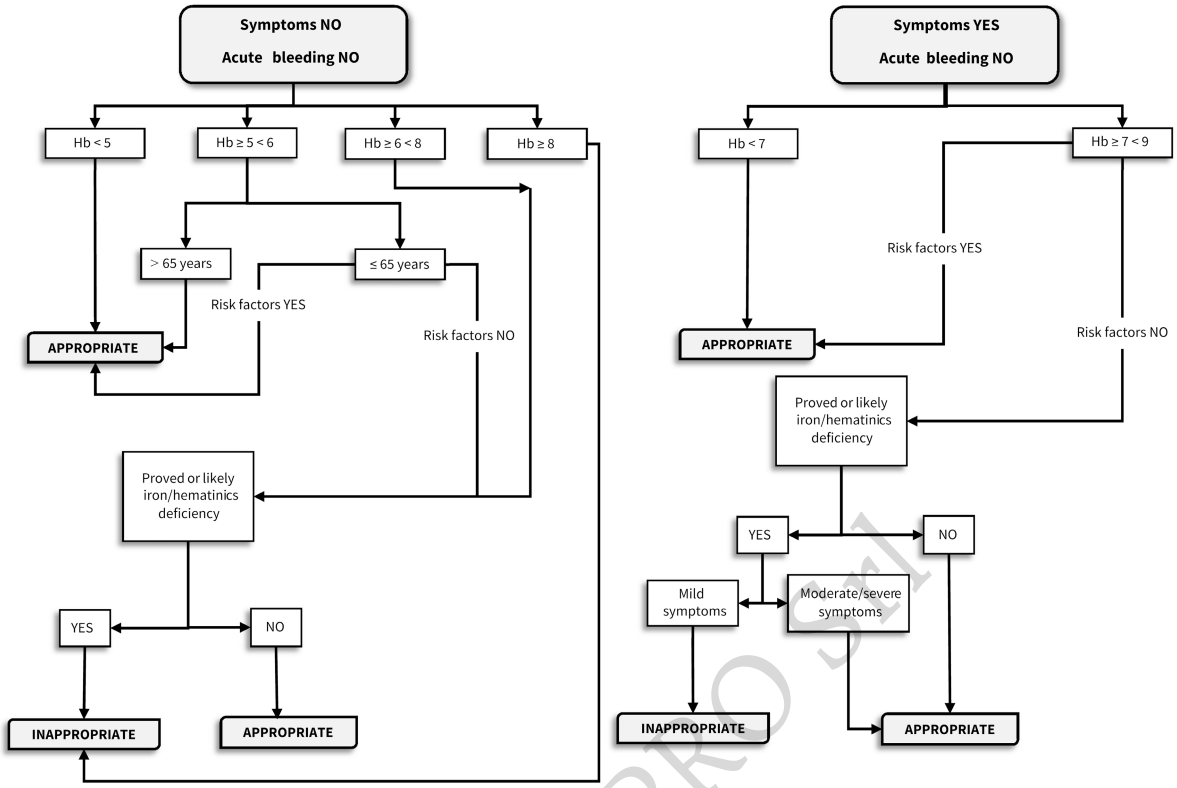

Figure 1 - Transfusion decision algorithm in chronic anemias
From Beverina and Ranzini[18], with permission.

ageing population drives an increase in transfusion-dependent conditions while simultaneously reducing the pool of eligible donors. This strain became particularly evident during the COVID-19 pandemic, which exposed critical vulnerabilities in blood supply chains due to a dramatic shortage of blood reserves. These events underscored the need for broader implementation of PBM strategies to optimise blood use, reduce unnecessary transfusions, and enhance patient safety[13,14].

In the context of chronic anemia due to iron deficiency -the most prevalent cause of anemia in patients admitted to the EA-transfusion thresholds remain a contentious issue. The Association for the Advancement of Blood & Biotherapies (AABB) guidelines recommend restrictive thresholds, typically below 7 g/dL for stable adults[15]. However, this is often misinterpreted as a universal rule, leading to the assumption that transfusions are always appropriate below this threshold. Such an oversimplification overlooks the unique physiology of chronic anemia, where compensatory mechanisms allow patients to tolerate very low Hb levels without symptoms. Consequently, strict adherence to this threshold may result in unnecessary transfusions in patients with chronic anemia[7] who could otherwise be managed with alternative treatments.

A patient-centred approach considering the patient's symptoms, physiological adaptability, comorbidities, and the likelihood of blood loss in the short to medium term is essential for several reasons. Chronic anemia triggers physiological compensations, including increased oxygen extraction and cardiac output, enabling patients to tolerate low Hb levels without clinical symptoms. This adaptation is distinct from acute blood loss, where compensatory responses are insufficient.

Furthermore, none of the RCTs used to develop the AABB guidelines specifically addressed chronic anemia.

Most studies informing the recommendations were conducted in contexts involving acute hemorrhage, surgical patients, or critical care. Therefore, the evidence underpinning these guidelines does not fully account for the clinical and physiological nuances of chronic anemia.

Evidence supports this perspective, as several studies have shown that transfusion thresholds lower than 7 g/dL can be safely applied in this setting. Patients with Hb levels as low as 5 g/dL have been effectively managed with IV iron alone, achieving substantial Hb increases without the need for transfusion[9,16-19]. This was confirmed in a large, retrospective, multicentre Spanish-Italian study by Jericó *et al.*, which included 303 non-transfused IDA patients, 87 of whom were admitted to the EA[19] (**Table I**). Over a median follow-up of 41 days, Hb values increased by 6.0 g/dL [IQR 5.1-6.7], highlighting the efficacy of this approach in restoring hematopoiesis.

In a recent study, Beverina *et al*. demonstrated sustained hematopoietic recovery following IV iron treatment in 47 patients with very severe or extreme anemia. Remarkably, after a median follow-up of 658 days [IQR 444-751], none of them required a transfusion[18].

Table I - *Baseline data and hemoglobin recovery in patient admitted to EA for IDA*

Patients (No.) Female (No.) Male (No.)	87 67 20
Age (years)	45 [36-62]
≤65 (No.) >66 - ≤80 (No.) >80 (No.)	69 (79.4%) 9 (10.3%) 9 (10.3%)
Hb (g/dL) [IQR]	6.5 [5.9-6.8]
≤5.0 (No.) >5.0 - ≤6.0 (No.) >6.0 - ≤7.0 (No.)	5 (5.7%) 19 (21.8%) 63 (72.4%)
Diagnosis (%) Gynecological bleeding (No.) Gastroenterical bleeding (No.) Malabsorption (No.) Other or undefined (No.)	 48 (55.2%) 28 (32.2%) 1 (1.1%) 10 (11.5%)
Total IV iron dose (mg)	1,500 [1,500-2,000]
Days from diagnosis to therapy	1 [0-4]
Total days from therapy to last Hb assessment	41 [30-65]
Delta Hb from therapy to last Hb assessment (g/dL)	6.0 [5.1-6.7]

*Data in square brackets represent the median [IQR]. Data subset from Jericó *et al.* [19]. EA: Emergency Area; IDA: iron deficiency anemia; IV: intravenous.

Despite the significantly lower risk of anaphylaxis with third-generation IV iron agents like ferric carboxymaltose and derisomaltose, healthcare professionals remain hesitant to use them. This reluctance stems from outdated beliefs about the safety of IV iron, particularly fears of hypersensitivity reactions. However, current evidence shows that severe adverse events are exceedingly rare, with an estimated incidence of less than 1 in 250,000 administrations. Addressing these unwarranted concerns is essential to ensure that eligible patients are not denied effective and safe treatment[20].

Establishing an anemia clinic within the EA poses challenges but offers substantial benefits for patient outcomes and healthcare efficiency. It enables rapid diagnosis, classification, and treatment initiation, minimising delays and supporting early intervention, particularly in severe anemia. The clinic reduces inappropriate RBC transfusions by enabling early diagnosis and treatment with IV iron or other hematological therapies. It also avoids unnecessary hospital admissions for "anemia workup" by facilitating outpatient evaluation and treatment, thereby reducing strain on inpatient resources, bed occupancy, and healthcare costs.

Additionally, the clinic facilitates early referral to specialists for targeted management of anemia linked to chronic disease, malignancy, or gastrointestinal bleeding, thereby improving long-term outcomes. For surgical patients, particularly those with cancer-associated anemia, early treatment favours timely correction of Hb levels, thus reducing perioperative transfusions, enhancing surgical outcomes, and supporting faster recovery.

Post-discharge follow-up care is equally essential. An anemia clinic enables treatment monitoring, assessment of Hb recovery, and completion of IV iron therapy to achieve optimal hematopoietic recovery. Regular follow-up also allows for further diagnostic evaluation, specialist referral, and long-term management to prevent anemia recurrence. This approach enhances patient adherence, reduces EA readmissions, and supports a seamless care pathway, ultimately improving clinical outcomes and optimising resource utilisation[18]. An example of the key steps

Table II - *Key steps for implementing the treatment of iron deficiency anemia in Emergency Area*

Step	Description
1. Education and training of healthcare providers	Educate healthcare providers on Patient Blood Management (PBM) principles, diagnosis and treatment of IDA, and appropriate use of IV iron.
2. Involvement of laboratory services	Ensure collaboration with laboratory services to allow for urgent iron balance tests or other if available, with the option to include hematinics, if deemed potentially useful.
3. Availability of IV iron in the Emergency Area	Establish agreements with the hospital pharmacy to ensure the availability of IV iron formulations in the Emergency Area.
4. Patient assessment	Assess patient history, symptoms, and signs of anemia. Identify potential causes, assess hemodynamic stability, and evaluate the likelihood of blood loss in the short to medium term.
5. Laboratory tests	Order key laboratory tests, including cell blood count, reticulocytes, ferritin, transferrin saturation, folate, and vitamin B12.
6. Diagnosis confirmation	Confirm the diagnosis of IDA based on laboratory findings and clinical evaluation.
7. Determine treatment pathway	Determine the most appropriate treatment pathway, considering the need for IV iron or alternative interventions.
8. IV iron administration	Administer IV iron using standardised protocols. Ensure patient safety and monitor for any immediate adverse reactions.
9. Monitor and reassess	Reassess Hb and iron parameters to monitor treatment efficacy. Adjust treatment as needed.
10. Discharge and follow-up plan	Develop a discharge plan, which may include oral iron supplementation, referrals to anemia clinics, or follow-up with primary care.

IDA: iron deficiency anemia; IV: intravenous: Hb: hemoglobin.

for implementing the treatment of IDA in EA are summarized in **Table II**.

The establishment of an anemia clinic within the Emergency Area (EA) is both clinically effective and economically beneficial. Cost-analysis studies show that managing IDA with IV iron in a fast-track anemia clinic reduces healthcare expenses compared to standard care. Quintana-Díaz *et al.* reported a total treatment cost of €594 per patient in the fast-track clinic, compared to €672 in standard care, yielding an average saving of €78 per patient.

These savings are driven by reduced RBC transfusions, shorter EA stays, and fewer hospital admissions. Beverina *et al*. highlighted that the cost per patient treated with IV iron was 59% lower than for those treated with transfusion alone. The outpatient management of anemia further avoids unnecessary hospital admissions, optimising the use of inpatient resources and lowering the overall financial burden on healthcare systems.

In summary, the introduction of an anemia clinic within the EA represents a cost-effective strategy, reducing healthcare expenditures associated with RBC transfusions, length of stay, and hospital admissions. The financial benefits, combined with improved clinical outcomes and alignment with PBM principles, underscore the value of this model as a sustainable and efficient approach to managing IDA. Therefore, we should not miss the opportunity for implementing the first pillar of PBM at the EA.

The Authors declare no conflicts of interest.

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