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Patient Blood Management in the Intensive Care Unit

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ABSTRACT

Patient Blood Management underscores a fundamental shift from a product-centered approach to a patient-centric approach through timely application of evidence-based medical and surgical concepts designed to maintain hemoglobin concentration, optimize hemostasis, and minimize blood loss in an effort to improve patient outcome. In this concept, allogeneic blood transfusion is not viewed as the treatment of default for anemic patients, but one among many treatment modalities that should be weighed based on its merits—potentials risks and benefits—for the individual patient in the context of other alternatives. Patient blood management provides a multidisciplinary framework for patient-centered decision making with strategies focusing on the management of anemia, optimization of coagulation and hemostasis, and utilization of blood conservation modalities. Among the critically ill patients, Patient Blood Management can be particularly effective given the extremely high prevalence of anemia, variable and unjustified transfusion practices, high frequency of coagulation disorders, and avoidable sources of blood loss such as unnecessary diagnostic blood draws. Proper management of anemia—prevention, screening/monitoring, diagnostic workup, and treatment including hematinic agents—is the key to effective implementation of patient blood management. Blood transfusions should be used in accordance of current guidelines, which are supportive of more restrictive transfusion strategies in most critically ill patients. Emerging studies report on the success of Patient Blood Management programs in reducing transfusion utilization, reducing the burden of anemia in patients, and improving patient outcomes including shortened length of hospital stays, less frequency of complications and lower risk of mortality.

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Definition and History of Patient Blood Management

Changing views on the role of allogeneic blood transfusions in the management of patients—including the critically ill—can perhaps be best portrayed by the emergence of Patient Blood Management (PBM). At its core, PBM marks a fundamental transition from a "product-based" approach to a "patient-based" approach when it comes to blood transfusion [1]. The key questions here is not about transfusing or not transfusing blood, but doing what is best for the patient, be it transfusion or other appropriate treatment modalities.

Patient Blood Management is defined by the Society for the Advancement of Blood Management (SABM) as "the timely application of evidence-based medical and surgical concepts designed to maintain hemoglobin concentration, optimize hemostasis, and minimize blood loss in an effort to improve patient outcome" [2,3]. Alternatively, it is

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defined by the AABB as "an evidence-based, multidisciplinary approach to optimizing the care of patients who might need transfusion."[1] These definitions have undergone a number of revisions, and what sets the current SABM definition apart from the earlier versions is the emphasis on improved patient outcomes as the end point. There is no mention of blood transfusion, underscoring the patient-centered approach and fundamental focus on the medical condition, diagnosis and proper treatment [1].

For decades, blood transfusion was recognized as the unchallenged mainstay treatment for anemia across patient populations, and issues such as transfusion-transmitted infections were viewed rather as temporary nuisances that could be adequately controlled with various testing and screening strategies [4]. First calls for an alternative came from patients for whom blood was not an option for religious or personal reasons and those who could not be transfused for medical reasons [5], and who often suffered grave consequences including long-lasting sequelae and increased risk of death when faced with severe anemia [6]. Strategies were developed to preserve and improve the clinical outcomes of these patients without the help of allogeneic blood transfusions. These "alternative" approaches included proactive optimization of hemoglobin levels in anticipation of a high blood loss scenario, maximizing hematopoiesis during the acute anemic episode to ameliorate the severity of anemia and improve the odds of recovery, avoiding and minimizing blood loss, maintaining adequate oxygen delivery to the tissues, and minimizing tissue oxygen demand and consumption. These strategies collectively became known as "Bloodless Medicine and Surgery" [7,8].

Two large studies have looked at the outcomes of severely anemic (hemoglobin ≤8 g/dL) critically ill patients who were managed without transfusion at centers without and with Bloodless Medicine and Surgery programs. In the study by Carson et al on 300 patients [6], the adjusted odds ratio (OR) of mortality in patients with postoperative hemoglobin level ≤8 g/dL increased 2.5 times for every 1-g/dL drop in the hemoglobin level, reaching highest in hemoglobin levels below 5 to 6 g/dL [6]. In another study performed at a referral center with an established Bloodless Medicine and Surgery program on 293 patients [9], the adjusted odds of death increased by 1.82 (95% confidence interval [CI] 1.2-2.59) for every 1 g/dL drop in nadir hemoglobin level. The proportion of patients with extremely low hemoglobin levels was much lower compared with the study by Carson et al [6], an observation which is attributed to improved care for these patients under the Bloodless Medicine and Surgery program which might have helped patients recover from their severe anemia more effectively [9]. In a follow-up study comparing the outcome of these patients with a matched cohort of severely anemic patients who were managed with transfusion, the overall mortality rates were not statistically significantly different [10]. This observation supports the positive impact of Bloodless Surgery and Medicine programs on outcomes in patients who cannot be transfused.

Individual strategies employed in Bloodless Medicine and Surgery are relatively simple and routinely available and can be applied in many other patients. This, alongside with the revelations that allogeneic blood transfusions can be associated with harm that go much beyond the transmission of dangerous infections gave rise to the idea of Blood Conservation—placing the main focus on conserving patient's blood as a valuable and limited resource [11].

Anemia, Transfusion and Outcomes in Critically ill Patients

Critically ill patients are among the leading recipients of allogeneic blood transfusions. Risk factors of transfusion in perioperative setting include low hemoglobin level, excessive blood loss, and inappropriate transfusion practices [12]. All these factors are also common in the critical care setting.

Anemia reduces oxygen carrying capacity of blood, which could result in tissue ischemia. Blood transfusion is considered as a quick and simple way to increase hemoglobin level, restore oxygen carrying capacity and hemodynamic stability. Nonetheless, allogeneic blood is a complex allograft which interacts in many ways with the recipient, going further beyond simple increasing of oxygen delivery [13,14].

Anemia is common in patients admitted to intensive care units (ICUs), and it is often multi-factorial, with anemia of inflammation being the leading etiology [15]. Iron deficiency is the other commonly present etiology [16,17]. As many as two-third of patients admitted to ICU are anemic at admission, and the prevalence reaches up to 95% by the third day of ICU stay [16,18-23]. Many patients leave the ICU while still anemic and it persists in as many as half of the patients six months later [24]. Anemia is an independent risk factor for morbidity and mortality during hospital stay [16,25-27] and long-term mortality following discharge from the ICU [28].

Given the high prevalence of anemia in the ICU, it is not surprising that transfusion rates are also exceptionally high among the critically ill patients. Analysis of data from critically ill patients admitted to 139 centers across the US hospitals has shown that anemia more than doubles the odds of blood transfusion [29]. The reported transfusion rates in the ICUs vary from the center but usually range from 33% to 75% (Table 1) [18,23,30-35].

There are many reasons for being concerned about the high and variable transfusion rates in the ICUs, ranging from economic issues and availability to the unresolved safety and efficacy concerns [36-39]. Red blood cell (RBC) transfusion is associated with risks despite limited evidence of benefit [40]. While the new and emergent infections that are not being screened for remain a potential threat [41], the risk of transmission of widely recognized infections such as viral hepatitis and human immunodeficiency virus has been greatly reduced to less than 1 per 10 million units of blood in developed nations [42]. Non-infectious risks of transfusion have become the leading concern and they include transfusion-related acute lung injury (TRALI) [43], transfusion-associated circulatory overload (TACO) [44], immunomodulation [45], alloimmunization [46], febrile reactions [47], bacterial contamination (mostly in platelet units) [41] and rarely graft-versus-host disease (GVHD) [48].

An even greater concern comes from a multitude of studies that have linked allogeneic blood transfusions with a long list of unfavorable outcomes such as sepsis and infection, multi-organ dysfunction, thromboembolic events, cardiac complications, stroke, respiratory distress and failure, renal injury, need for prolonged care, and mortality [25,49]. When these events occur in critically ill patients, they may not always be linked directly to transfusion, but when cohorts of patients are studied, it is often seen that the risk of occurrence of these events is higher in those who had received transfusion [50].

A common shortcoming of many of these studies is the uncontrolled retrospective design that can introduce bias. For the results to be reliable, patients who are transfused and those who are not should be otherwise comparable with similar baseline risk profile, an issue which is often not the case [51]. While this concern has some validity, it is noteworthy to point to the documented highly variability in transfusion practices which greatly undermines this notion that transfused patients are invariably sicker than their non-transfused peers [36,51]. On the other hand, randomized controlled trials on "liberal" versus "restrictive" transfusion strategies have their own limitations [51,52]. In either study arm, some patients may benefit for the allocation while other may be harmed suggesting that a unified transfusion strategy (rather than individualized approach) may be akin to collective punishment. Our search should be directed toward identifying those who will benefit from transfusions whilst others might achieve better outcomes with other therapies. To this end, well-designed observational studies can provide as much valuable evidence as randomized controlled trials [51,52].

[1] AABB, Patient Blood Management, available at: http://www.aabb.org/pbm/Pages/default.aspx (Last accessed on May 17, 2017).