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Patient blood management equals patient safety

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Patient blood management (PBM) can be defined in many ways and may consist of hundreds of single measures to improve patient safety. Traditionally, PBM is based on three pillars and defined as (i) optimization of the endogenous red blood cell (RBC) mass through the targeted stimulation of erythropoiesis and the treatment of modifiable underlying disorders; (ii) minimization of diagnostic, interventional, and surgical blood loss to preserve the patient's RBC mass; and (iii) optimization of the patient-specific tolerance to anemia through strict adherence to physiological transfusion thresholds [1–4]. However, for this review, we have chosen the following three peri-interventional parts: (1) diagnosis and therapy of anemia, (2) optimal hemotherapy, and (3) minimization of hospital-acquired anemia. PBM is an evidence-based, multidisciplinary preventive, and therapeutic approach focusing each patient. The PBM concept involves the use of safe and effective medical and surgical methods and techniques designed to prevent peri-interventional anemia, rationalize use of blood products, and set good blood management measures in an effort to improve patient safety and outcome.

Diagnosis and therapy of anemia

The term “anemia” is derived from ancient Greek and means “bloodless,” and it is represented by the amount of red blood cell (RBC) mass. In clinical practice, hemoglobin levels are used to determine

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anemia. Since 1968, the World Health Organization (WHO) has reported a hemoglobin level of ≥130 g/L for men and ≥120 g/L for menstruating women as normal. In case of lower levels, anemia is present and should be further evaluated and potentially be treated as patient safety, and outcomes are jeopardized during a peri-interventional procedure. Anemia may be the most common abnormal condition worldwide with approximately 30% of mankind being affected [5]. Whether the WHO defined "normal" hemoglobin levels represent a safe margin to perform surgery is unclear and should be evaluated.

In a retrospective trial with >227,000 patients, Musallam el al [6]. have demonstrated that any kind of surgical intervention (cardiac surgery has not been studied) is associated with a higher mortality when anemia is present. Mild anemia was defined as a hematocrit of 30–36% for women and 30–39% for men (hemoglobin level of 100–120 g/L in women and 100–130 g/L in men) and severe anemia as a hematocrit ≤29% for men and women (hemoglobin < 100 g/dL). Non-anemic patients showed a 30-day mortality rate of 0.78% (>158,000 patients), while the mortality of moderately anemic patients increased by a factor of approximately 5 (3.52% in >57,000 patients). However, when patients were severely anemic, the 30-day mortality rate increased by a factor of 13 (>11,000 patients). When corrected for confounding patient- and surgery-related factors, mild anemia was still associated with a 40% increase in mortality and a 30% increase in major morbidity. These numbers are alarming and are usually not explained to patients. In other words, when a patient is suffering from anemia and undergoing elective surgery, patient consent should also be granted for the increased risk of death. A later study by Baron and coworkers confirmed in 39,000 patients that mild anemia (defined as a hemoglobin level of 100–120 g/L in women and 110–130 g/L in men) was associated with increased mortality (+20% in multivariate models) [7]. In addition, they found a longer duration of hospitalization and a more frequent admission to the intensive care unit (ICU) in mildly anemic patients. In both studies, 30% of patients were anemic.

Although anemia is a symptom of various clinical conditions, we postulate for the first time that anemia should be rated as a disease itself. A disease needs evaluation and treatment pathways. Potential causes of anemia are summarized in Fig. 1, where hospital-acquired and malnutrition-related anemia play major roles and their incidence can be reduced by careful planning, diagnosis, and therapy.

Anemia is a serious global health problem with an estimated prevalence of two billion people [5]. As depicted in Fig. 1, the underlying causes can be of various etiologies; the most prominent cause is iron deficiency (approximately 30–50% worldwide) [5]. This frequently underestimated health problem is also often present in the industrialized world [11]. Although the incidence of iron deficiency anemia is lower in the US and in Europe than in the rest of the world, it is still of high relevance.

When focusing on surgeries worldwide in the year 2008 [12], out of 234 million operations, approximately 30% of patients were anemic before the surgery. A third thereof, that is, 23 million patients, may have suffered from iron deficiency or iron-restricted anemia. Postoperative anemia has an even higher prevalence, with up to 32 million patients suffering from iron deficiency (Fig. 2).

When interventions in anemic patients are of so high risk, what is the best treatment before surgery? This question needs to be divided into acute/emergency and elective interventions.

If a patient is suffering from severe anemia and needs urgent surgery, blood transfusion will be the choice of treatment in the case of major bleeding. However, when there is sufficient time to plan an intervention, diagnostics and therapy should be performed before the surgery well in advance. This is underlined by Whitlock et al. [13] who analyzed the association of RBC transfusion with stroke and myocardial infarction in a retrospective study with 1,583,819 patients. A total of 41,421 patients received RBC transfusions. The transfusion of a single unit of RBC already increased the risk of perioperative ischemic stroke or myocardial infarction 2.3-fold.

Iron deficiency anemia (Fig. 3) can be diagnosed when the following parameters are fulfilled ("Frankfurt protocol"):

Anemia caused by nutritional deficiency, primarily iron, is found in approximately one-third of patients and can be treated with oral or intravenous (IV) iron therapy [14–16]. Underlying diseases/chronic inflammation/cancer causes anemia in approximately another third of the patients, and the rest have unexplained anemia and should also be considered as a symptom for another process [14,17]. Patient outcome might improve when anemia is detected as a symptom of an underlying condition, and efforts are made to identify the underlying disorder and to correct or manage it. The