

Implementing the »Patient Blood Management« program in everyday clinical practice

Uvedba programa »Skrb za bolnikovo kri« v vsakodnevno klinično prakso

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Abstract

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Transfusion after a surgical procedure elevates risk for perioperative complications, prolongs hospital stay and worsens the outcome of surgical treatment. Undefined and untreated preoperative anaemia presents an independent factor for perioperative complications and transfusion in the perioperative period. Before surgery, we must identify patients at higher risk for anaemia and adjust preoperative preparation, surgical technique and postoperative treatment accordingly.

The "Patient Blood Management" (PBM) programme is established in many European countries and supported by a directorate of the European Commission. It is concerned with the treatment of anemia, optimization of haemostasis and measures to reduce the need for blood transfusion. The three pillars of PBM are: (1) optimal haematopoiesis, (2) reduced iatrogenic blood loss and (3) improved patients' tolerance for anaemia.

In this article we analyse the proportion of patients that came for surgery to the observed surgical institution in an anaemic state in a two-year period and how many of them needed blood transfusion. We also describe the foundations of the PBM program and a plan to implement it in everyday clinical practice.

Neopredeljena in nezdravljena anemija pred operacijo je neodvisni napovedni dejavnik za zaplete ob kirurškem posegu in transfuzijo v obdobju po posegu. Transfuzija krvi po kirurškem posegu poveča tveganje za zaplete po operaciji, podaljša bolnišnično zdravljenje in poslabša izid kirurškega zdravljenja. Pred operacijo moramo anemične bolnike odkriti in zdraviti, prilagoditi pripravo na operacijo, kirurško tehniko in zdravljenje po posegu.

Program »Skrb za bolnikovo kri« (anql. Patient Blood Management, PBM), uveljavljen že v mnogih evropskih državah, podpira pa ga Direktorat Evropske komisije za zdravje, se usmerja v zdravljenje anemije, optimiziranje hemostaze in zmanjšanje potrebe po transfuziji krvi. Trije osnovni stebri so (1) optimalna hematopoeza, (2) zmanjšana iatrogena izguba krvi in (3) izboljšava bolnikove tolerance za anemijo.

Članek analizira, koliko anemičnih bolnikov je prišlo na operacijo, pri kateri je prisotno tveganje za večjo krvavitev, v obdobju med oktobrom 2016 in oktobrom 2018, in kakšne so bile potrebe po transfuziji krvi v opazovani kirurški ustanovi. Poleg tega opisuje elemente programa PBM ter načrt za uvedbo programa v vsakdanjo klinično prakso.

Key words:

transfusion; preoperative anaemia; blood loss; preoperative preparation; haematopoiesis optimisation

Ključne besede:

transfuzija; anemija pred operacijo; izguba krvi; priprava na operacijo; optimiziranje hematopoeze

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1 Introduction

Transfusion after a surgical procedure elevates risk for perioperative complications, prolongs hospital stay and worsens the outcome of surgical treatment. This is especially true for patients who were operated on for a malignant disease (2). Undefined and untreated preoperative anaemia is an independent forecasting factor for complications and the need for transfusion following surgery (3). Before an operation we have to identify the patients with whom the risk for blood transfusion is higher, and tailor the preparations for the operation, surgical technique, and postoperative treatment.

Surgery Bitenc holds pulmonary and urological operations in which blood loss can be greater than 500 ml, making the risk for required blood transfusion higher. In order to improve the results of surgical treatment and lower the risk for required red blood cell transfusion, we followed the route of numerous similar medical centres in Europe and the world (4), and decided to introduce the Patient Blood Management (PBM) programme. In this article we describe the PBM programme and our experience with it.

2 Patient blood management programme

The PBM programme is focused on reducing the need for transfusion of concentrated red blood cells with patient measures: anaemia therapy, haemostasis optimization, reducing iatrogenic blood loss, and improving the patient's anaemia tolerance (5). At the centre of the activities is a patient, and not a safe blood transfusion! That is why Slovenian name for PBM would back-translate as "care for patient's blood".

This is a therapy concept with which every patient receives comprehensive, multidisciplinary and individualised care in order to improve their haematopoietic system (6,7).

In the Republic of Slovenia, the PBM programme is not new, as it has been described already in 2015 in the Slovenian Medical Journal, with authors listing the three pillars of PBM (8). The promotion of the programme in Europe has been undertaken by professional medical organisations, especially those that bring together specialists in anaesthesiology and intensive medicine (9). All experts in this field agree that it is the time to introduce this programme into clinical practice. Recommendation that ease the introduction into clinical practice were issued also by the Directorate-General for Health and Food Safety of the European Commission (6).

3 The first pillar of the PBM programme is treating anaemia and iron deficiency before the operation

The first pillar of the PBM programme includes procedures focused on optimising the haemoglobin concentration in blood, i.e. treating preoperative anaemia. The prevalence of preoperative anaemia is assessed at 5–75%, and depends on the type of operation and the definition of anaemia (10).

World Health The Organisation (WHO) defines anaemia as when the value of haemoglobin (Hb) for men is below 130 g/l, and for women below 120 g/l (11). Experts who treat perioperative anaemia believe that the definition of pre-operative anaemia should be changed or unified, regardless of sex. Both with men and women, the definition of preoperative anaemia should be set at Hb value below 130 g/l (12). There are several reasons for anaemia; however, in the perioperative period, anaemia from iron deficiency is the most frequent (13). Iron deficiency can be either absolute or functional (14). When iron stores in the body are low, this is a case of absolute deficiency, and involves the presence of microcytic anaemia. With functional iron deficiency, its body stores are sufficient. Because of a chronic inflammation with autoimmune diseases, chronic infections, malignant or other modern chronic diseases, the concentration of the regulation hormone hepcidin, which blocks iron absorption from the gastrointestinal system and its transfer from supplies in the liver and macrophages (15). This results in reduced erythropoiesis in the bone marrow. Based on laboratory results, we can define preoperative anaemia and treat it accordingly. Anaemia from iron deficiency should be treated with iron solutions. If there is enough time until the operation, if there is no chronic inflammation and iron absorption from the gastrointestinal system is sufficient, we can prescribe tablet-based iron. This type of anaemia therapy requires at least 6 weeks' time. If there is not enough time before the operation or if the patient's condition does not support sufficient absorption, we supply iron intravenously. In order to establish the cause of anaemia, we have to make a blood image, as well as determine the ferritin concentration, the transferrin saturation, and the inflammation indicators, such as CRP. If this is not a case of an apparent microcytic anaemia, we also determine the vitamin B12, folic acid and

how the thyroid performs. If needed, we consult the haematologist. Based on the laboratory results, we decide appropriate supplemental therapy.

In 2017, an international agreement on treating preoperational anaemia and iron deficiency was published (16). In certain cases, we opt for iron supplementation as well as an erythropoietin therapy, once we weigh the danger of risk for thromboembolic complications, i.e. the impact on tumour growth (17). Less frequently, the reason for anaemia is a deficiency of folic acid, vitamin B12 or hypothyroidism. Anaemia is more frequent with older than with younger patients, and can be often more difficult to determine and treat with the elderly, as it can be the result of a combination of several factors (15,18). Anaemia must also be treated post-operatively.

4 The second PBM pillar is reducing perioperative and postoperative blood loss

Before the operation, we have to identify the patients with whom the risk for haemorrhaging is higher. The main task is a good anamnesis. The anamnesis can surmise whether the patient had severely haemorrhaged after a potential past operation or injury, whether women have stronger menstrual bleeding or whether family members have blood coagulation disorder. According to some experts, the patients who do not have any inclination towards haemorrhaging in their anamnesis, do not require a screening for blood coagulation, as an incorrect selection and assessment of the examination unnecessarily delays the operation (19). If a patient is receiving anticoagulation medication, these are paused or replaced with a low-molecular-weight heparin, when the risk of ischemic events is truly severe.

During the operation, the surgical and anaesthetic techniques are modified as needed. Less invasive surgical techniques, such as laparoscopy and thoracoscopy, which result in lower tissue damage and reduced haemorrhaging, have proven to reduce the need for red blood cell transfusion (20). Maintaining normothermia, permissive hypotension and preventing venal stasis also contribute to reduced haemorrhaging during the operation. Using a cell saver is justified only when the expected blood loss is above 1000 ml, and when the patient has no malignant disease (21).

In the postoperative period, high arterial blood pressure has to be prevented, normal body temperature maintained, and crystalloid or colloid solutions should be prescribed sensibly in order to prevent haemodilution or blood coagulation disorders (5).

In the period during and after the operation, standard haemostasis tests are no longer used for establishing blood coagulation disorders, as so-called bedside or high-elastic tests are used instead, because they are fast and provide the information on the constitution, firmness or dissolution of the blood clot (22). Using antifibrinolytics, such as ε -aminocaproic acid and tranexamic acid, contributes to reduced haemorrhaging during the operation. Utilizing topical skin adhesives that the surgeon applies directly onto a bleeding wound or tissue also contributes to that (20).

5 The third pillar is improving the patient's tolerance for anaemia and a restrictive transfusion approach

In the preoperative period, it is important to optimise the patient's medical condition, especially their cardiovascular and respiratory systems. In the period during and after the operation, an onset of anaemia means we should focus on optimising the minute heart volume and blood oxygenation, as this ensures good tissue oxygenation. Studies have shown that a transfusion of red blood cells does not improve tissue oxygenation for the long term (23). We opt for a transfusion of red blood cells when tissue oxygenation drops and not relying solely on the laboratory results. A recommended threshold for transfusion of red blood cells is the Hb value of 70 g/l_{1} if the patient does not exhibit signs of reduced tissue oxygenation and cardiovascular diseases (24). If possible, we always order only one cell saver unit/time. After each transfusion of one cell saver unit,

	Total	Men	Women
Operations with increased risk of haemorrhaging	639	429 (67,1%)	210 (32,9%)
Age (years)	67	66	70
ASA	2	2	2
Thoracic operations	413	215	198
Urological operations	226	214	12
Preoperative anaemia (Hb < 130 g/l)	90	40 (44%)	50 (56%)

Table 1: Demographic data for age and preoperative anaemia, the average values are listed, and for ASA, the median.

ASA - preoperative risk assessment according to the American Society of Anasthesiologists

the patient's medical condition has to be assessed before ordering additional transfusion.

6 Analysis of PBM-related factors and the need for blood transfusion with patients, who were operated on at our surgical centre, in the twoyear period between October 2016 and October 2018

In our surgical centre, the risk of blood loss in the post-operative period is higher with thoracic and urological operations. For a period of two years, we analysed the data on the need for red blood cell transfusions.

During this period, 639 patients were operated on in thoracic surgery and urology. 413 (64.6%) patients were operated on for pulmonary diseases, and 226 (36.4%) for urological diseases. Demographic data, type of operation and Hb values before operation are collected in Table 1. 458 (71.7%) patients were operated on with less invasive surgical technique, i.e. video assisted video-assisted thoracoscopic surgery (VATS) or laparoscopic surgery for urological surgery. 90 (14.1%) patients suffered from preoperative anaemia, which was defined as Hb concentration < 130 g/l. 67 (74%) patients suffering from anaemia were operated on with the less invasive technique. 31 (4.9%) patients required cell saver transfusion, of which 7 (22.6%) in an operating room, and 24 (77.4%) in intensive care after surgery. Of patients who received transfusion during surgery, 4 (57%) had preoperative anaemia. Of patients who received transfusion at the department after surgery, 12 (50%) had preoperative anaemia. Patients who received a cell saver transfusion at the department were all anaemic when they received the transfusion, with a median Hb value of 93.7 g/l.

7 Implementing the PBM programme

With regard to the recommendations of professional associations (9) and the Directorate-General for Health and Food Safety (6) our monitored surgical establishment has opted to introduce the PBM programme into clinical practice in 2019.

By analysing the patients who were operated on for a thoracic or urological disease, for which a high blood loss was to be expected, we established that 14.1% had preoperative anaemia. No patient had a precisely defined preoperative anaemia, nor was it appropriately treated. During or after the operation, more than 50% of those patients who had preoperative anaemia also needed a cell saver transfusion.

First pillar: The most important measure for introducing the PBM programme is the optimisation of haemoglobin concentration before the operation. Patients who were ready for a thoracic operation at this surgical centre are treated and prepared by pulmonologists from the University Clinic Golnik. Following the agreement with patients with an Hb concentration of < 130 g/l, anaemia was defined and successfully treated (Figure 1) (25). Patients who have urological operation planned are examined by a urologist before the operation. When anaemia is detected, the urologist will launch a diagnostics procedure to define it. During the preoperative period we will treat anaemia, as well as observe any optimisation of the patient's medical condition with an emphasis on the cardiovascular system and pulmonary activity. If the patient is taking anti-coagulation and anti-aggregation drugs, which we will cease and replace with short-term ingredients according to the guidelines for handling anticoagulation therapy (26). Because the patients at the observed surgical institution are most likely operated on for cancer, the preparation before the procedure should not increase the wait time for the operation.

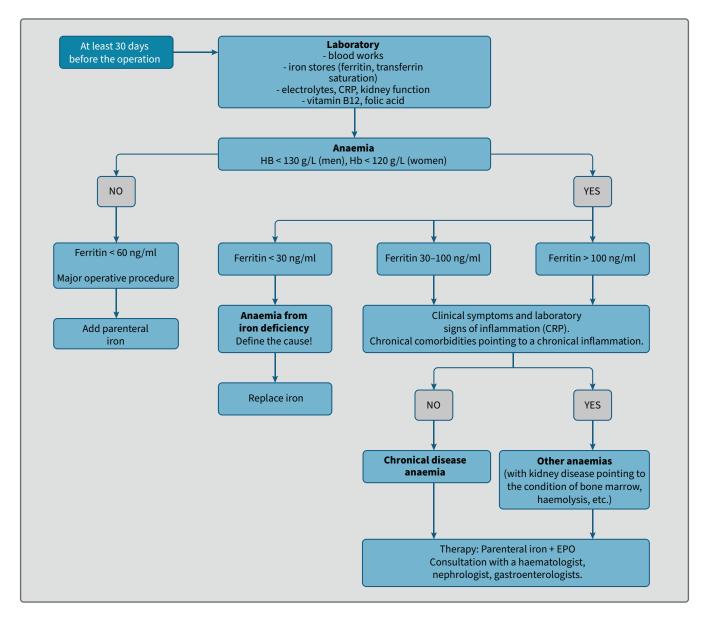


Figure 1: The algorithm for detecting and treating preoperative anaemia (25).

Second pillar: According to our analysis, most patients had been operated on previously with less-invasive surgical techniques. The standard procedure already includes maintaining normal body temperature, reducing the venal stasis, and preventing arterial hypertension. All patients who were scheduled to receive thoracic surgery, and most patients who were scheduled because of urological disease, have their arterial blood pressure measured invasively during the operation and in the early period after it. Using the cell saver device during the operation of a cancerous disease is not recommended.

Because the institution included in the study, as well as some other surgical centres across Slovenia, do not have the option of using high-elasticity tests for determining blood coagulation conditions, we shall continue relying on the anamnesis, the clinical image and the standard tests of blood coagulation. After the operation, we will introduce the prophylactic antico-

Transfusion decision form

The form must be filled in before administering every unit of cell saver (exception: massive haemorrhaging)

Hb < 70g/l

□ Transfusion indicated

Hb 70-80g/l

- Clinical symptoms of anaemic hypoxia (tachycardia, ischemic changes in the ECG, hyposthenia, lactic acidosis)
- Limited option of compensation, risk factors

 (e.g. ischemic heart disease, heart failure, cerebrovascular
 insufficiency)
- □ Other (...)

Transfusion with Hb > 80 g/l do not have a clear advantage from comorbid risks.

□ Individual decision (recommendation level 2C)

Figure 2: Blood transfusion form (27).

agulative therapy according to the recommendations from the Slovenian Medical Association (26).

Third pillar: We opt for blood transfusion with those patients who have Hb values below 70 g/l, or with values of 70-80 g/l, if we detect that along anaemia there are also signs of ineffective tissue perfusion (27). If the attending physician decides for a cell saver transfusion at HB values > 80 g/l, they write a statement with their explanation for this decision on the blood transfusion form. They also take into account the patient's age and comorbidities. The physician details their decision for the transfusion on the form (Figure 2). With patients whose perioperative and post-operative blood loss exceeds 300 ml, laboratory examinations are repeated to establish a potential anaemia, otherwise we generally avoid any excessive laboratory examinations during the post-operative period to help reduce blood loss.

When anaemia from iron deficiency is detected, we introduce appropriate therapy. At discharge from the hospital, the family doctor is informed of the anaemia therapy plan with a note in the release form.

8 Conclusion

Studies have shown that preoperative anaemia is an independent forecast factor of a poor result of surgical treatment even with patients who did not require transfusion. Detecting preoperative anaemia and beginning with the appropriate therapy is the first and most important element of PBM, followed by homoeostasis and a restrictive transfusion approach with the optimisation of the patient's condition.

The European Society of Anaesthesiology (ESA) has set for one of its goals that as many hospitals as possible launch the PBM programme. This approach should also be pursued in Slovenia. In collaboration with the Slovenian Society of Anaesthesiologists, we decided to introduce this programme in 2019, at our surgical centre. The PBM programme will ensure a higher quality and level of safety for patient treatment, which we will also confirm during the upcoming years through prospective data collection and analysis.

A precise definition and therapy of preoperative anaemia will be the main step of our implementation of the programme. Most of the elements from the second pillar of PBM are already a part of the standard patient treatment during surgery. When deciding on a cell saver transfusion, it is important to take into account not only the laboratory values, but also the patient's clinical condition; consequently, we will introduce a form to assist with decision-making.

The PBM programme requires a multidisciplinary approach; therefore, other specialists will be joining anaesthesiologists and surgeons.

References

- 1. Fowler AJ, Ahmad T, Phull MK, Allard S, Gillies MA, Pearse RM. Meta-analysis of the association between preoperative anaemia and mortality after surgery. Br J Surg. 2015;102(11):1314-24. DOI: 10.1002/bjs.9861 PMID: 26349842
- Atzil S, Arad M, Glasner A, Abiri N, Avraham R, Greenfeld K, et al. Blood transfusion promotes cancer progression: a critical role for aged erythrocytes. Anesthesiology. 2008;109(6):989-97. DOI: 10.1097/ ALN.0b013e31818ddb72 PMID: 19034095
- 3. Muñoz M, Gómez-Ramírez S, Campos A, Ruiz J, Liumbruno GM. Pre-operative anaemia: prevalence, consequences and approaches to management. Blood Transfus. 2015;13(3):370-9. PMID: 26192787
- Mueller MM, Van Remoortel H, Meybohm P, Aranko K, Aubron C, Burger R, et al.; ICC PBM Frankfurt 2018 Group. Patient Blood Management: Recommendations From the 2018 Frankfurt Consensus Conference. JAMA. 2019;321(10):983-97. DOI: 10.1001/jama.2019.0554 PMID: 30860564
- Meybohm P, Richards T, Isbister J, Hofmann A, Shander A, Goodnough LT, et al. Patient Blood Management Bundles to Facilitate Implementation. Transfus Med Rev. 2017;31(1):62-71. DOI: 10.1016/j.tmrv.2016.05.012 PMID: 27317382
- Gombotz H, Hofmann A, Norgaard A, Kastner P. Supporting Patient Blood Management (PBM) in the EU A Practical Implementation Guide for Hospitals 2017. Luxemburg: Publications Office of the European Union; 2017. pp. 3-67.
- Althoff FC, Neb H, Herrmann E, Trentino KM, Vernich L, Füllenbach C, et al. Multimodal Patient Blood Management Program Based on a Three-pillar Strategy: A Systematic Review and Meta-analysis. Ann Surg. 2019;269(5):794-804. DOI: 10.1097/SLA.000000000003095 PMID: 30418206
- 8. Poženel P, Zver S, Nikolić B, Rožman P. Klinično vodenje transfuzije sodobni pristopi za optimizacijo transfuzije. Zdrav Vestn. 2015;84(11):743-56. DOI: 10.6016/ZdravVestn.1357
- 9. Shander A, Van Aken H, Colomina MJ, Gombotz H, Hofmann A, Krauspe R, et al. Patient blood management in Europe. Br J Anaesth. 2012;109(1):55-68. DOI: 10.1093/bja/aes139 PMID: 22628393
- Patel MS, Carson JL. Anemia in the preoperative patient. Anesthesiol Clin. 2009;27(4):751-60. DOI: 10.1016/j.anclin.2009.09.009 PMID: 19942178
- 11. WHO. Haemoglobin concentrations for the diagnosis of anaemia and assessment of severity. [cited 2019 Jan 20]. Available from: http://www.who.int/vmnis/indicators/haemoglobin.pdf.
- Muñoz M, Gómez-Ramírez S, Kozek-Langeneker S, Shander A, Richards T, Pavía J, et al. 'Fit to fly': overcoming barriers to preoperative haemoglobin optimization in surgical patients. Br J Anaesth. 2015;115(1):15-24. DOI: 10.1093/bja/aev165 PMID: 26089443
- Kassebaum NJ, Jasrasaria R, Naghavi M, Wulf SK, Johns N, Lozano R, et al. A systematic analysis of global anemia burden from 1990 to 2010. Blood. 2014;123(5):615-24. DOI: 10.1182/blood-2013-06-508325 PMID: 24297872
- 14. Shander A, Javidroozi M, Ozawa S, Hare GM. What is really dangerous: anaemia or transfusion? Br J Anaesth. 2011;107(1):i41-59. DOI: 10.1093/bja/aer350 PMID: 22156270
- 15. Steinbicker AU. Role of anesthesiologists in managing perioperative anemia. Curr Opin Anaesthesiol. 2019;32(1):64-71. DOI: 10.1097/ACO.000000000000000671 PMID: 30531608
- Muñoz M, Acheson AG, Auerbach M, Besser M, Habler O, Kehlet H, et al. International consensus statement on the peri-operative management of anaemia and iron deficiency. Anaesthesia. 2017;72(2):233-47. DOI: 10.1111/anae.13773 PMID: 27996086
- Alghamdi AA, Albanna MJ, Guru V, Brister SJ. Does the use of erythropoietin reduce the risk of exposure to allogeneic blood transfusion in cardiac surgery? A systematic review and meta-analysis. J Card Surg. 2006;21(3):320-6. DOI: 10.1111/j.1540-8191.2006.00241.x PMID: 16684074
- Wawer AA, Jennings A, Fairweather-Tait SJ. Iron status in the elderly: A review of recent evidence. Mech Ageing Dev. 2018;175:55-73. DOI: 10.1016/j.mad.2018.07.003 PMID: 30040993
- 19. Zehnder JL. Clinical use of coagulation tests. [cited 2019 Mar 21]. Available from: https://www.uptodate. com/contents/clinical-use-of-coagulation-tests.
- 20. Desai N, Schofield N, Richards T. Perioperative patient blood management to improve outcome. Anesth Analg. 2018;127(5):1211-20. DOI: 10.1213/ANE.00000000002549 PMID: 29064875
- Carless PA, Henry DA, Moxey AJ, O'Connell D, Brown T, Fergusson DA. Cell salvage for minimising perioperative allogeneic blood transfusion. Cochrane Database Syst Rev. 2010;17(3):CD001888. DOI: 10.1002/14651858.CD001888.pub3 PMID: 20238316
- 22. Whiting D, DiNardo JA. TEG and ROTEM: technology and clinical applications. Am J Hematol. 2014;89(2):228-32. DOI: 10.1002/ajh.23599 PMID: 24123050

- 23. Tsai AG, Cabrales P, Intaglietta M. Microvascular perfusion upon exchange transfusion with stored red blood cells in normovolemic anemic conditions. Transfusion. 2004;44(11):1626-34. DOI: 10.1111/j.0041-1132.2004.04128.x PMID: 15504169
- 24. Padhi S, Kemmis-Betty S, Rajesh S, Hill J, Murphy MF; Guideline Development Group. Blood transfusion: summary of NICE guidance. BMJ. 2015;351:h5832. DOI: 10.1136/bmj.h5832 PMID: 26581483
- 25. Preložnik Zupan I. Pomen predoperativne anemije. 21. Schrottovi dnevi. Zbornik predavanj. 16. in 17. marec 2018; Ljubljana. Ljubljana: Medicinski razgledi; 2018.
- 26. Mavri A, Vene N. Smernice za vodenje antikoagulacijskega zdravljenja. Ljubljana: Slovensko zdravniško društvo; 2009.
- Carson JL, Grossman BJ, Kleinman S, Tinmouth AT, Marques MB, Fung MK, et al.; Clinical Transfusion Medicine Committee of the AABB. Red blood cell transfusion: a clinical practice guideline from the AABB*. Ann Intern Med. 2012;157(1):49-58. DOI: 10.7326/0003-4819-157-1-201206190-00429 PMID: 22751760