

Original Article

Prevalence of Anemia in Patients Undergoing Cardiac Surgery and Need for Transfusion During Surgery Regarding Hemoglobin Levels in Rajaie Heart Center

Ali Sadeghi¹, MD; Rasool Ferasatkish¹, MD; Avaz Heydarpour¹, MD;
Rasoul Azarfarin², MD; Mohsen Ziaiefard¹, MD; Zahra Faritous¹, MD;
Fatemehshima Hadipourzadeh^{*1}, MD

ABSTRACT

Background: Bleeding occurs during and after cardiac surgery, resulting in postoperative anemia. If patients have preoperative anemia, the need for blood transfusion increases. Transfusion is associated with several complications.

Methods: In this study, severe anemia was defined as hemoglobin (Hb) < 8 g/dL, moderate anemia was defined as Hb = 8–10 g/dL, and mild anemia was defined as Hb = 10–12 g/dL for women and Hb = 10–13 g/dL for men. In the entire study population, the need for transfusion according to the Hb level and the amount of blood transfusion were evaluated. The study aimed to determine the association between anemia and the patients' age, sex, type of surgery, and weight.

Results: In this study, 306 patients were evaluated in a 3-month period. The mean Hb level of the patients was 13.1 g/dL (12.08–14.2), and the mean hematocrit level was 39.5% (36.17–42.15). Anemia was reported in 32.4% of the patients (Hb < 12 g/dL for women and Hb < 13 g/dL for men). According to the anemia classification, 90.9% of the anemic patients had mild anemia, 8.1% moderate anemia, and 1% severe anemia. Of the 306 patients, 68.6% did not need to receive packed red blood cells. Additionally, of the 207 patients who were not included in the anemia group, 44 (21.2%) cases received packed red blood cells due to surgical bleeding. However, of the 99 patients who were anemic, 52 (52.52%) cases needed packed red blood cells.

Conclusions: In the present investigation, about one-third of the study population had anemia before surgery and these patients required blood transfusion 2.5 times more than those without anemia. (*Iranian Heart Journal 2020; 21(1): 94-102*)

KEYWORDS: Anemia, Transfusion, Cardiac surgery

¹ Rajaie Cardiovascular, Medical, and Research Center, Iran University of Medical Sciences, Tehran, IR Iran.

² Echocardiography Research Center, Rajaie Cardiovascular, Medical, and Research Center, Iran University of Medical Sciences, Tehran, IR Iran.

***Corresponding Author:** Fatemehshima Hadipourzadeh, MD; Fellows of Cardiac Anesthesia, Rajaie Cardiovascular, Medical, and Research Center, Iran University of Medical Sciences, Vali-Asr Ave, Tehran, IR Iran.

Email: shimahadipoorzadeh@gmail.com

Tel: 09166166541

Received: March 15, 2019

Accepted: June 22, 2019

According to the World Health Organization, anemia is defined as hemoglobin (Hb) < 12 g/dL in women and < 13 g/dL in men. Preoperative anemia can be due to several reasons such as iron deficiency or gastrointestinal bleeding. The incidence of preoperative anemia in cardiac surgery ranges between 25% and 32%.¹ Various observational studies have reported that preoperative anemia is related to increased neurological and renal complications.^{2,3} Anemic patients have higher early and late mortality rates than non-anemic patients undergoing cardiac surgery.⁴ During cardiac surgery, because of hemostatic abnormalities, intra- and postoperative bleeding is usually seen, which can result in postoperative anemia. In a previous study, up to 44% of the patients had anemia in the postoperative period.⁵ Another investigation reported that every 1 mg/dL decrease in the Hb concentration was associated with a 13% increase in cardiovascular events and a 22% increase in all-cause mortality.⁶ Although blood transfusion is necessary in cardiac surgery, various studies have found that it also has side effects. In these studies, the transfusion of red blood cells (RBCs) was dose-dependently related to postoperative infections such as mediastinitis, respiratory infection, and sepsis and higher mortality.^{7,8} Moreover, the transfusion of packed RBCs is reported to increase the length of hospital stay.⁹ Some authors have described the importance of a careful preoperative assessment because it can reduce the risk of bleeding and the requirement for blood transfusion during the postoperative period. The evaluation of serum iron and iron administration and preoperative erythropoietin may reduce the requirement for transfusion.¹⁰

The aim of the present study was to determine the prevalence of anemia in

patients undergoing cardiac surgery in Rajaie Cardiovascular, Medical, and Research Center, Tehran, Iran, in 2018 to prevent anemia in preoperative protocols and treatments for anemia and to reduce the need for transfusion.

METHODS

In this study, patients after the admission, blood sample were sent to the laboratory and the hemoglobin level In this study, severe anemia was defined as hemoglobin (Hb) < 8 g/dL, moderate anemia was defined as Hb = 8–10 g/dL, and mild anemia was defined as Hb = 10–12 g/dL for women and Hb = 10–13 g/dL for men. In this study, the demographic and clinical variables and the type of operation of the patients were also considered and anemia relationship with the mentioned cases was considered. During the surgery, the duration of CPB and patient's need for blood transfusion were recorded during surgery, and with this, the need for transfusion was evaluated.

The criteria for entering the plan were all patients 18 years of age and older who were referred for coronary surgery and valve operation or together at the same time (coronary artery bypass graft surgery and valve surgery) for elective surgery.

Exit criteria for this study included patients with congenital heart disease, emergency patients, Patients who have received blood transfusion before surgery, patients treated for anemia, and patients undergoing dialysis.

RESULTS

This research project evaluated 306 patients, comprised of 197 (64.4%) male and 109 (35.6%) female patients, over a period of 3 months. The average age of the patients was 60 (52–67) years, the mean height was 167 (160–173) cm, the mean weight was 74

(65–83) kg, and the mean body mass index was 26 (24–29).

Diabetes mellitus was reported in 5.9% of the patients and hypertension in 5.2%. Of the 306 patients, coronary artery bypass graft surgery (CABG) was performed on 246 (80.4%) patients, 35.9% of whom had 1 graft, 2.9% had 2 grafts, 28.1% had 3 grafts, 12.4% had 4 grafts, and 1% had 5 grafts. Mitral valve replacement was performed on 51 (16.7%) patients, aortic valve replacement on 31 (10.1%), tricuspid valve replacement on 12 (3.9%), and the Bentall surgery on 8 (2.6%). The mean duration of surgery was 6 hours, the mean duration of the pump was 83 (110–160) minutes, and the mean cross-clamping time was 45 (32–61) minutes.

The study population had a mean Hb level of 13.1 (12.08–14.2) g/dL and a mean hematocrit level of 39.5 (36.17–42.15).

Anemia was reported in 32.4% of the study population. According to the classification of anemia based on Hb levels (See Methods), 90.9% of the patients had mild

anemia, 8.1% had moderate anemia, and 1% had severe anemia.

No significant relationships existed between anemia and the variables of age, the body mass index, the duration of surgery, the duration of bypass, and the duration of cross-clamping.

In terms of gender, in the anemia group, 58.6% of the patients were male and 41.1% female; there was no significant relationship between sex and anemia ($P = 0.143$). Additionally, 9.1% of the patients had anemia and diabetes, and there was no significant relationship between diabetes and anemia in this study ($P = 0.099$). Anemia and hypertension were reported in 10.1% of the patients; the relationship between hypertension and anemia was significant ($P = 0.08$). No significant association was, however, found between the type of surgery and anemia, nor was there any significant association between the number of grafts and anemia in the post-CABG patients ($P = 0.878$).

Table 1. Demographic and clinical characteristics of the patients

	Anemic Group (n=99)	Non-anemic Group (n=207)	P value
Age (y)	61(54-69)	59(52-66)	0.105
Median (range)			
Sex(male)	58.6 %	67.1 %	0.143
Sex(female)	41.1%	32.9%	
BMI	26(24.3-29.4)	27(24.4-29.4)	0.283
Median (range)			
Operation time(h)	6(5-6)	6(5-6)	0.671
Median (range)			
CPB time(min)	80(60-110)	85(60-110)	0.741
Median (range)			
Aortic cross-clamp time (min)	44(32-60)	45(31-63)	0.882
Median (range)			
DM	9.1%	4.3%	0.099
HTN	10.1%	2.9%	0.008
CABG	85.9%	77.8%	0.096
MVR	17.2%	16.4%	0.870
AVR	10.1%	10.1%	0.990
TVR	2%	4.8%	0.242
Bental procedure	2%	2.9%	0.652

BMI, Body mass index; CPB, Cardiopulmonary bypass; DM, Diabetes mellitus; HTN, Hypertension; CABG, Coronary artery bypass; MVR, Mitral valve replacement; AVR, Aortic valve replacement; TVR, Tricuspid valve replacement

Of the 207 patients who were not in the anemia group, 44 (21.2%) cases received packed RBCs. Of the 99 patients in the anemia group, 47 (47.47%) patients did not need to receive packed RBCs: 97.9% were in the mild anemia group, 2.1% in the moderate anemia group, and 0.0% in the severe anemia group. Fifty-two (52.52%) of the 99 patients in the anemia group needed blood transfusion. The patients who needed 1 blood unit comprised 82.5% of the mild anemia group, 15% of the moderate anemia group, and 2.5% of the severe anemia group. The patients who needed 2 blood units comprised 90.9% of the mild anemia group, 9.1% of the moderate anemia group, and 0.0% of the severe anemia group. The patients who needed to receive 4 blood units comprised 100% of the mild group. In this study, there was no significant relationship between the severity of anemia and the need for more blood units ($P = 0.362$).

The results revealed that about one-third of the study population had anemia before surgery and those with anemia were in need of blood transfusion 2.5 times more than those without anemia.

DISCUSSION

In this research project, 306 patients were studied over a period of 3 months. Anemia was reported 32.4% of the study population. According to the anemia classification based on the Hb level (severe anemia: Hb < 8 g/dL, moderate anemia: Hb = 8–10 g/dL, and mild anemia: Hb = 10–12 g/dL for women and Hb = 10–13 g/dL for men), of the patients with anemia, 90.9% had mild anemia, 8.1% had moderate anemia, and 1% had severe anemia. Our results demonstrated no relationship between anemia and the variables of gender, the body mass index, the type of surgery, the duration of surgery, the duration of bypass, and the duration of cross-clamping. Our results showed no

relationship between anemia and the underlying disease of diabetes; nonetheless, we found a significant correlation between anemia and hypertension ($P = 0.08$). Our patients with anemia were also more likely to require blood transfusion during the operation, although there was no significant relationship between the severity of anemia and blood intake. The transfusion of blood is commonly performed in heart surgery, but many studies have associated it with such side effects as an increased risk of infectious occurrences (eg, mediastinitis, respiratory infection, and sepsis), atrial fibrillation, acute renal failure, cerebrovascular accident, and acute respiratory distress syndrome, as well as with an increased length of hospital stay.⁹

A study on 502 patients who underwent elective cardiac surgery reported that 60% of the patients had received blood during the first 72 hours of surgery.¹¹ In that study, those who received blood were more likely to be old, to be female, to need re-surgery, to have complicated surgery, to have elevated EuroSCOREs, to have lower levels of Hb and hematocrit, and to suffer the incidence of renal disease. In addition, the patients who received packed RBCs in the first 72 hours after surgery had a higher incidence of complications such as renal failure, cardiogenic shock, acute respiratory distress syndrome, infections, and neurological and inflammatory complications. Also in that study, the length of hospital stay was increased in the patients who received more than 3 units of packed RBCs (nearly 6 days) and in the patients who received fewer or up to 3 units of packed RBCs (up to 1 day) compared with the patients not on packed RBCs.

A recent research on 798 hospitals in the United States for the evaluation of blood and blood products reported that in the hospitals performing at least 100 CABGs on cardiopulmonary bypass ($n = 82\,446$ cases),

the rates of packed RBC transfusion ranged from 7.8% to 92.8% for RBCs, from 0% to 97.5% for fresh frozen plasma, and from 0.4% to 90.4% for platelets.¹² In that study, after adjustments for the patients' risk factors, the amount of transfusion in the hospital varied because of the patients' geographic locations ($P = 0.007$) and academic status ($P = 0.03$), as well as the hospital volume ($P < 0.001$). Also in that investigation, a higher number of packed RBCs was associated with female gender, older age, need for re-surgery or complex operations, elevated EuroSCOREs, renal disease, and previous anemia. This finding highlights the need for further efforts to improve perioperative care in these subgroups of patients to avoid blood transfusion, which leads to complications such as increased lengths of stay in the hospital.¹³

Guidelines from the Society of Thoracic Surgeons and the Society of Cardiovascular Anesthesiologists emphasize the deficiency of evidence on transfusion triggers after cardiac surgery.¹⁴ Most transfusion indications occur in the first 72 hours postoperatively, starting in the operating room, where usually the transfusion indication is due to hemodilution and based on triggers.¹⁵ The principle for implementing a restrictive transfusion strategy is based on the analysis of studies reporting a deficiency of benefits and, at the same time, considerably increased costs and side effects allied to the transfusion of packed RBCs. These side effects include acute hemolytic and non-hemolytic reactions, the transmission of viral and bacterial diseases, transfusion-associated acute lung injury, and transfusion with circulatory overload.¹⁶ Immunosuppression has also been related to transfusion and may explain the higher risk of infection and the recurrence of neoplastic diseases in

transfused patients.¹⁷ In a study on 11 963 patients who underwent isolated CABG, Koch et al¹⁸ explained that the perioperative transfusion of packed RBCs was associated with a dose-dependent increased risk of cardiac complications after surgery, critical infections, renal failure, neurological complications, overall morbidity, prolonged mechanical ventilation, and in-hospital mortality. In a retrospective study, Murphy et al¹⁹ showed that the transfusion of packed RBCs was strongly associated with infections, postoperative ischemic morbidity, hospital stay, early and late mortality, and hospital charges. De Cocker et al²⁰ performed a retrospective analysis on 1566 patients undergoing cardiac surgery and demonstrated that age > 75 years, female gender, New York Heart Association functional class $> II$, arrhythmias, mitral regurgitation, requirement for inotropic support or intra-aortic balloon pumps, non-elective procedures, and aortic surgery were the predictive factors for a prolonged stay in the intensive care unit. Although blood transfusion was not a potential predictor of increased lengths of stay in the hospital in the current study, a prolonged hospital length of stay merits evaluation because of its correlation with increased costs and clinical complications such as exposure to infectious agents.²¹

Previous research has underscored the significance of meticulous preoperative assessments with a view to reducing the risk of bleeding and the need for blood transfusion during the postoperative period.^{22,23} Indeed, an evaluation of serum iron and iron administration and preoperative erythropoietin may lessen the need for transfusion.¹⁰

Recombinant human erythropoietin (rHuEPO) is used for the treatment of anemia related to reduced erythropoiesis

caused by chronic renal disease and some hematological diseases.^{24,25}

Various studies have shown the efficacy of the preoperative administration of rHuEPO for cardiac surgery to lower erythrocyte transfusion in patients having autologous blood donations.^{26,27} Furthermore, rHuEPO has been shown to be safe and effective in correcting preoperative anemia, and it can be used in association with iron therapy in patients with Hb concentrations < 13 g/dL.^{28,29} A typical preoperative regimen of rHuEPO is, however, costly and requires at least 4 days of hospitalization before surgery, limiting a more extensive use of this strategy.³⁰ Outpatient-based repeated subcutaneous injections of rHuEPO may be practical,²⁸ although it may be associated with the increased occurrence of therapy-related complications such as hypertension and thromboembolism.³¹ Moreover, the absorption of subcutaneously administered rHuEPO may not be firm and reliable compared with the intravenous way because of decreased microcirculation in patients with cardiac diseases.³²

In a prospective study, patients with preoperative anemia were randomly allocated to either the erythropoietin group or the control group. The erythropoietin group was given 500 IU/kg of erythropoietin and 200 mg of iron sucrose intravenously 1 day before cardiac surgery, while the control group was given the same volume of normal saline. The initial result was the need for transfusion during surgery and 4 days after surgery. The reticulocyte count and the iron profile were investigated serially and compared preoperatively and on postoperative days 1, 2, 4, and 7.

The results of that study showed that single doses of erythropoietin and supplemental iron injections 1 day prior to cardiac surgery clearly reduced the need for the transfusion of blood after surgery in anemic patients undergoing valvular cardiac surgery. The

complications of erythropoietin injections include hypertension, headaches, tachycardia, nausea, vomiting, hypercalcemia, diarrhea, and thromboembolism; nonetheless, these complications are usually shown in patients receiving chronic erythropoietin treatment.^{28,30} The chronic use in patients with cancer is associated with an increased risk of thrombotic disease, but the short-term use for acute indications even in critical patients can be safe.^{34,35}

Limitations

We conducted a retrospective cohort study using data from the Cardiovascular Surgery Department of Rajaie Cardiovascular, Medical, and Research Center, Tehran, Iran.

CONCLUSIONS

The results of the present study revealed that about one-third of the patients had anemia before surgery and the anemic patients required blood transfusion 2.5 times more than their non-anemic counterparts. Blood transfusion is associated with side effects and increases the length of hospital stay and hospital costs; therefore, diagnostic evaluations before elective surgery may reduce the need for transfusion and complications and, thus, shorten the length of hospital stay.

Conflict of Interest

The authors declare no conflict of interest in this work. This research received no financial support.

REFERENCES

1. David O, Sinha R, Robinson K, Cardone D (2013) The prevalence of anaemia, hypochromia and microcytosis in preoperative cardiac surgical patients. *Anaesth Intensive Care* 41: 316-321.

2. Kulier A, Levin J, Moser R, Rumpold-Seitlinger G, Tudor IC, et al Impact of preoperative anemia on outcome in patients undergoing coronary artery bypass graft surgery. *Circulation* 2007; 116: 471-479
3. Zindrou D, Taylor KM, Bagger JP. Preoperative haemoglobin concentration and mortality rate after coronary artery bypass surgery. *Lancet* 2002; 359: 1747-1748.
4. Van Straten AH, Soliman Hamad MA, van Zundert AA, Martens EJ, terWoorst JF, et al. Effect of duration of red blood cell storage on early and late mortality after CABG. *J Thorac Cardiovasc Surg* 2011; 141: 238-243
5. Westenbrink BD, Kleijn L, de Boer RA, Tijssen JG, Warnica WJ, et al. Sustained postoperative anaemia is associated with an impaired outcome after coronary artery bypass graft surgery: insights from the IMAGINE trial. *Heart* 2011; 97: 1590-1596.
6. Karkouti K, Wijeyesundera DN, Yau TM, Beattie WS, Abdelnaem E, et al. The independent association of massive blood loss with mortality in cardiac surgery. *Transfusion* 2004; 44: 1453-1462.
7. Chelemer SB, Prato BS, Cox PM Jr, O'Connor GT, Morton JR Association of bacterial infection and red blood cell transfusion after coronary artery bypass surgery. *Ann Thorac Surg* 2002; 73: 138-142.
8. Dixon B, Santamaria JD, Reid D, Collins M, Rechnitzer T, et al. The association of blood transfusion with mortality after cardiac surgery: cause or confounding? (CME). *Transfusion* 2013; 53: 19-27.
9. Camila de Christo DORNELES¹, Luiz Carlos BODANESE², João Carlos Vieira da Costa GUARAGNA³, Fabrício Edler MACAGNAN⁴, Juliano Cé COELHO⁵, Anibal Pires BORGES⁶, Marco Antonio GOLDANI⁷, João Batista PETRACCO⁸ The impact of blood transfusion on morbidity and mortality after cardiac surgery *Rev Bras Cir Cardiovasc* 2011; 26(2): 222-9
10. Souza HJB, Moitinho RF. Estratégias para redução do uso de hemoderivados em cirurgia cardiovascular. *Rev Bras Cir Cardiovasc*. 2008; 23(1): 53-9
11. Filomena RBG, Galas¹, Juliano P Almeida^{1*}, Julia T Fukushima¹, Eduardo A Osawa¹, Rosana E Nakamura¹, Carolina MPDC Silva¹, Elisângela Pinto Marinho de Almeida¹, Jose Otavio Costa Auler Jr¹, Jean-Louis Vincent and Ludhmila A Hajjar, Blood transfusion in cardiac surgery is a risk factor for increased hospital length of stay in adult patient, Galas et al. *Journal of Cardiothoracic Surgery* 2013, 8: 54
12. Bennett-Guerrero E, Zhao Y, O'Brien SM, Ferguson TB Jr, Peterson ED, Gammie JS, Song HK: Variation in use of blood transfusion in coronary artery bypass graft surgery. *JAMA* 2010, 304: 1568–1575.
13. Möhnle P, Snyder-Ramos SA, Miao Y, Kulier A, Böttiger BW, Levin J, Mangano DT: Multicenter Study of Perioperative Ischemia (McSPI) Research Group. Postoperative red blood cell transfusion and morbid outcome in uncomplicated cardiac surgery patients. *Intensive Care Med* 2011, 37: 97–109.
14. Society of Thoracic Surgeons Blood Conservation Guideline Task Force, Ferraris VA, Brown JR, Despotis GJ, Hammon JW, Reece TB, Saha SP, Song HK, Clough ER, Society of Cardiovascular Anesthesiologists Special Task Force on Blood Transfusion, Shore-Lesserson LJ, Goodnough LT, Mazer CD, Shander A, Stafford-Smith M, Waters J, International Consortium for Evidence Based Perfusion, Baker RA, Dickinson TA, Fitzgerald DJ, Likosky DS, Shann KG: 2011 update to the Society of Thoracic Surgeons and the Society of Cardiovascular Anesthesiologists blood conservation clinical practice guidelines. *Ann Thorac Surg* 2011, 91: 944–982.
15. Hajjar LA, Vincent JL, Galas FR, Nakamura RE, Silva CM, Santos MH, Fukushima J, Kalil Filho R, Sierra DB, Lopes NH, Mauad T, Roquim AC, Sundin MR, Leão WC, Almeida JP, Pomerantzeff PM, Dallan LO, Jatene FB, Stolf NA, Auler JO Jr: Transfusion

- requirements after cardiac surgery: the TRACS randomized controlled trial. *JAMA*, 2010; 304:1559–1567.
16. Hébert PC, Wells G, Blajchman MA, Marshall J, Martin C, Pagliarello G, Tweeddale M, Schweitzer I, Yetisir E: A multicenter, randomized, controlled clinical trial of transfusion requirements in critical care. Transfusion Requirements in Critical Care Investigators, Canadian Critical Care Trials Group. *N Engl J Med* 1999, 340:409–417.
 17. Vamvakas EC: Perioperative blood transfusion and cancer recurrence: meta-analysis for explanation. *Transfusion* 1995, 35:760–768.
 18. Koch CG, Li L, Duncan AI, Mihaljevic T, Cosgrove DM, Loop FD, Starr NJ, Blackstone EH: Morbidity and mortality risk associated with red blood cell and blood-component transfusion in isolated coronary artery bypass grafting. *Crit Care Med* 2006, 34:1608–1616.
 19. Murphy GJ, Reeves BC, Rogers CA, Rizvi SI, Culliford L, Angelini GD: Increased mortality, postoperative morbidity, and cost after red blood cell transfusion in patients having cardiac surgery. *Circulation* 2007, 116:2544–2552.
 20. De Cocker J, Messaoudi N, Stockman BA, Bossaert LL, Rodrigus IE: Preoperative prediction of intensive care unit stay following cardiac surgery. *Eur J Cardiothorac Surg* 2011, 39(1):60–67.
 21. Gauvin F, Champagne MA, Robillard P, et al: Long-term survival rate of pediatric patients after blood transfusion. *Transfusion* 2008, 48:801–808.
 22. De Santo LS, Romano G, Galdieri N, Buonocore M, Bancone C, De Simone V, Della Corte A, Nappi G: RIFLE criteria for acute kidney injury in valvular surgery. *J Heart Valve Dis* 2010; 19:139 – 47; discussion 148
 23. Surgenor SD, Kramer RS, Olmstead EM, Ross CS, Sellke FW, Likosky DS, Marrin CA, Helm RE Jr, Leavitt BJ, Morton JR, Charlesworth DC, Clough RA, Hernandez F, Frumiento C, Benak A, DioData C, O'Connor GT, Northern New England Cardiovascular Disease Study Group: The association of perioperative red blood cell transfusions and decreased long-term survival after cardiac surgery. *Anesth Analg* 2009; 108:1741–6
 24. Jacobs K, Shoemaker C, Rudersdorf R, Neill SD, Kaufman RJ, Mufson A, Seehra J, Jones SS, Hewick R, Fritsch EF: Isolation and characterization of genomic and cDNA clones of human erythropoietin. *Nature* 1985; 313:806–10
 25. Rizzo JD, Somerfield MR, Hagerty KL, Seidenfeld J, Bohlius J, Bennett CL, Cella DF, Djulbegovic B, Goode MJ, Jakubowski AA, Rarick MU, Regan DH, Lichtin AE: Use of epoetin and darbepoetin in patients with cancer: 2007 American Society of Hematology/American Society of Clinical Oncology clinical practice guideline update. *Blood* 2008; 111:25–41
 26. Kiyama H, Ohshima N, Imazeki T, Yamada T: Autologous blood donation with recombinant human erythropoietin in anemic patients. *Ann Thorac Surg* 1999; 68:1652–6
 27. Gombotz H: Subcutaneous epoetin alfa as an adjunct to autologous blood donation before elective coronary artery bypass graft surgery. *Semin Hematol* 1996; 33:69–70; discussion 71–2
 28. 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; 21:320–6
 29. Weltert L, D'Alessandro S, Nardella S, Girola F, Bellisario A, Maselli D, De Paulis R: Preoperative very short-term, high-dose erythropoietin administration diminishes blood transfusion rate in off-pump coronary artery bypass: A randomized blind controlled study. *J Thorac Cardiovasc Surg* 2010; 139:621–6; discussion 626–7
 30. Yaziciolu L, Eryilmaz S, Sirlak M, Inan MB, Aral AR, Eren NT, Kaya B, Akalin H:

- Recombinant human erythropoietin administration in cardiac surgery. *J Thorac Cardiovasc Surg* 2001; 122:741–5
31. Lippi G, Franchini M, Favaloro EJ: Thrombotic complications of erythropoiesis-stimulating agents. *Semin Thromb Hemost* 2010; 36:537–49
 32. Sowade O, Warnke H, Scigalla P, Sowade B, Franke W, Messinger D, Gross J: Avoidance of allogeneic blood transfusions by treatment with epoetin beta (recombinant human erythropoietin) in patients undergoing open-heart surgery. *Blood* 1997; 89:411–8
 33. Young-Chul Yoo, M.D.,* Jae-Kwang Shim, M.D., Ph.D.,† Jong-Chan Kim, M.D.,‡ Youn-Yi Jo, M.D.,* Jong-Hoon Lee, M.D.,§ Young-Lan Kwak, M.D., Ph.D. Effect of Single Recombinant Human Erythropoietin Injection on Transfusion Requirements in Preoperatively Anemic Patients Undergoing Valvular Heart Surgery, 2011, the American Society of Anesthesiologists, Inc. Lippincott Williams & Wilkins. *Anesthesiology* 2011; 115:929–37
 34. Ziaeeifard. M, Alizadehasl A, Aghdaii N, Sadeghi A, Zarfarin r, Masoumi G, et al. Heparinized and saline solutions in the maintenance of arterial and central venous catheters after cardiac surgery. *Anesthesiology and pain medicine* 2015-5(4):e23963, 5p.
 35. Corwin HL, Gettinger A, Pearl RG, Fink MP, Levy MM, Shapiro MJ, Corwin MJ, Colton T, EPO Critical Care Trials Group: Efficacy of recombinant human erythropoietin in critically ill patients: A randomized controlled trial. *JAMA* 2002; 288:2827–35