ORIGINAL PAPER

How Important Impact of Low Level of Hematocrit Can Be on Outcome in Patients Undergoing Off Pump Coronary Artery Bypass Surgery?

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ABSTRACT

Background: Cardiosurgical patients can be often anemic, and preoperative anaemia is associated with increased postoperative complications, as well as morbidity and mortality. **Objective:** The present study was conducted aiming to determine the influence of lower preoperative hematocrit values on the early postoperative recovery of patients undergoing elective off-pump coronary artery bypass grafting (OPCABG). **Methods:** Our retrospective study included 150 patients who underwent elective OPCABG surgery from September 2021 to December 2022 at the Clinic for Cardiovascular Surgery University of Sarajevo. Patients were divided into two groups, anemic and non-anemic, with anemia defined as hemoglobin level <130g/l males and <120g/l females. Study observed comorbidities and early postoperative data. **Results:** Overall prevalence of anemia in OPCABG patients was 36,6%, more frequent among older patients. Comorbidities as chronic obstructive pulmonary disease, hypertension, ejection fraction was quite similar in both groups, but body mass index was significantly higher in the group of patients with anemia (29.9% vs 28.4%). In early recovery period, vasopressors were more used in patients with anemia (63.6% vs 42.1%) and their doses were higher. Total drainage was higher in patients with anemia (744.45±45.72 ml vs 681.58±349.06 ml). Number of transfusions was higher in the group of patients with anemia: red blood cells (0.89±1.29 vs 0.29±0.84; p<0,05), fresh frozen plasma (0.65±1.13 vs 0.41±1.15; p<0,05) and platelets (0.11±0.57 vs 0,07±0.42; p>0,05). Duration of mechanical ventilation was longer in patients with anemia compared to non-anemic patients (623-91±259.83 minutes vs 469±191.13 minutes). Atrial fibrillation occurred more often in patients with anemia (12.7 vs 7.4%). Length of stay in the intensive care unit was without significant difference. **Conclusion:** Based on our findings, patients who underwent elective OPCABG with lower than normal hematocrit, needed more blood and blood products, more vasopressor drugs in higher doses, longer mechanical ventilation, all which can prolong the patient's recovery and increase the cost of treatment.

Keywords: off pump coronary artery bypass graft surgery, anemia, early postoperative recovery.

1. BACKGROUND

Anemia can be very common among patients undergoing surgery, especially in cardiac surgery. Because of extremely limited coronary reserve, patients undergoing coronary artery bypass grafting surgery represent a group of patients potentially most sensitive to the impact of low hemoglobin level. During surgery it can be aggravated by increased use of fluid, which will cause hemodilution, and by blood loss during surgery, when it is necessary to replace this loss with blood and blood products (1).

As we know, conventional coronary artery bypass graft surgery (CABG) can be executed with the use of cardiopulmonary bypass (CPB) so call on-pump CABG or off-pump coronary artery bypass graft surgery (OPCABG), without CPB, which has been developed to decrease perioperative complications related to the use of CPB. Recent observational and randomized studies have suggested that certain high-risk patient

subgroups are more likely to benefit from an OPCABG approach, avoiding the deleterious effects of CPB (2).

OPCAB has been found to be associated with less bleeding, less renal dysfunction, a shorter length of hospital stay, and less neurocognitive dysfunction, with beneficial effects for patients at high risk for complications. Cardiac surgical procedures are estimated to be responsible for nearly 20% of the annual blood transfusions in the United States, and blood transfusion following CABG has been reported to occur in up to 60% of cases (3).

According to the World Health Organization (WHO) definition of anemia is a hemoglobin (Hb) levels < 120 g/l in non-pregnant adult females and < 130 g/l in adult males. Using WHO definition, the general consensus for preoperative anemia prevalence is around 20–30% and increases with age and the presence of comorbidities. The most common causes of preoperative anemia in cardiac surgery patients are hospital-acquired anemia, iron-deficiency anemia, and anemia of persisting chronic disease (4).

Correcting an anemia, we use allogenic blood transfusion which has been associated with significant adverse patient effects, including the occurrence of transfusion reactions, transfusion related acute lung injury, immunosuppression and immunomodulation, infectious complications, and even reduced long term survival (3).

A significant association of anemia with increased perioperative morbidity and mortality has been established in a multitude of settings and in both cardiac and noncardiac surgery (5).

The relative contribution of preoperative anemia and red blood cells (RBC) transfusion to the adverse outcomes in cardiac surgery patients remains uncertain, however, it has been shown that the interaction of the two increases morbidity and mortality far greater than the additive effects of each exposure individually (6).

2. OBJECTIVE

The present study was conducted aiming to determine the influence of preoperative anemia on the early postoperative recovery of patients undergoing elective OPCABG surgery.

3. PATEIENTS AND METHODS

Our study was retrospective, descriptive, single-center study which enrolled 150 patients in the period from September 2021 to December 2022, at the Clinic for Cardiovascular Surgery Sarajevo. All patients had undergone elective off pump coronary artery bypass surgery (OPCABG).

The inclusion criteria: adult patients (>18 years of age) for the first time on CABG surgery, elective cases, patients with silent, stable, or unstable angina.

The exclusion criteria: patients with a previous history of CABG surgery, emergency surgery, and patients with combined cardiac surgery.

We collected preoperative, intraoperative and postoperative data from our clinical database and hospital charts.

The anesthesia technique was standardized for all patients. In brief, this consisted of intravenous anesthesia with propofol or etomidate. Neuromuscular blockade was achieved with Pancuronium bromide. Anesthesia was maintained by the use of a fentanyl and propofol pump, sevoflurane was used when needed. Intraoperative fluid administration was mainly saline solution. Heparin was given at a dose of 200 IU/kg. It was reversed with protamine sulfate in the proportion of 1:1.

Conventional median sternotomy and preparation of conduits were undertaken by using a standard technique. In all the cases, the left internal mammary artery was anastomosed to the left anterior descending artery. For additional grafts, saphenous vein was used. Cardiac exposure and stabilization was achieved by Octopus Tissue Stabilizer. An intracoronary shunt was used in all cases of to support hemodynamic stability. A cell-saving device was used routinely with frequent infusions of the salvaged blood as collected. Two chest tubes were placed in the mediastinum, and additional tubes were left in the pleura as needed. Additional protamine sulfate was used in relation to the prolonged ACT with excessive bleeding. Patients were weaned from mechanical ventilation (MV) as soon as they were fully awake, hemodynamical stabile, normal body temperature, satisfied diuresis and bleeding and with laboratory tests in normal ranges.

Statistical analysis

Results of the analysis are presented as tables and charts by number of cases, percentage, mean, standard deviation and the range. Statistical comparison was performed using the nonparametric Chi-square and Mann-Whitney test depending on the type of data. Results of the test were considered as significant at the confidence level of 95%. Analysis was performed using the statistical package IBM Statistics SPSS v 23.0.

4. RESULTS

The first table shows sociodemographic data that indicate that the respondents with anemia were older with an average age of 65.29±6.64 years, compared to patients without anemia and average age of 61.8.29±8.29 years (p=0,0023). According to gender there were no statistically significant differences with both groups (p>0,05).

In the group of patients without anemia more present were diabetes mellitus (41.1 vs 38.2%), stroke (6.3 vs 3.6), myo-

Variable		Anemia		p
		Absent (N=95)	Present (N=55)	
Age – Mean±SD (Range)		61,89±8,29 (40-77)	65,29±6,64 (53-80)	0,023
Gender – N (%)	Male	77 (81,1)	41 (74,5)	0,409
	Female	18 (18,9)	14 (25,5)	
Diabetes mellitus – N (%)		39 (41,1)	21 (38,2)	0,433
Stroke – N (%)		6 (6,3)	2 (3,6)	0,384
Myocardial infarction < 6 weeks N (%)		28 (29,5)	9 (16,4)	0,080
Myocardial infarction > 6 weeks N (%)		39 (41,1)	25 (45,5)	0,612
Chronic obstructive pulmonary disease – N (%)		4 (4,2)	4 (7,3)	0,465
Arterial hypertension – N (%)		77 (81,1)	50 (90,9)	0,157
Smoking – N (%)		39 (41,1)	15 (27,3)	0,113
BMI – Mean±SD (Range)		28,48±3,89 (20,2-41,2)	29,95±3,86 (23,1-41,1)	0,040
Ejection fraction – Mean±SD (Range)		44,41±9,32 (25-65)	44,07±9,97 (25-65)	0,834
Percutaneous coronary intervention – N (%)		21 (22,1)	17 (30,9)	0,159

Table 1. Sociodemographic characteristics, comorbidities and risk factors

Variable	Anemia		p
	Absent (N=95)	Present (N=55)	
Hemoglobin – Mean±SD (Range)	145,69±10,12 (124-177)	114,05±12,65 (98-177)	0,0001
Hematocrit – Mean±SD (Range)	42,91±3,52 (37-54)	34,77±2,98 (30-41)	0,0001
Platelets – Mean±SD (Range)	227,96±40,05 (127-331)	221,56±53,69 (118-327)	0,467
Creatinine – Mean±SD (Range)	81,04±20,65 (43-153)	90,69±28,51 (42-173)	0,044
Creatinine >120 – N (%)	3 (3,2)	8 (14,5)	0,019

Table 2. Preoperative values of hemoglobin, hematocrit, platelets and serum creatinine

Variable	Anemia		p
	Absent (N=95)	Present (N=55)	
Transfusion of RBC – Mean±SD (Range)	0,29±0,86 (0-6)	0,93±1,14 (0-3)	0,0001
Transfusion of FFP – Mean±SD (Range)	1,11±1,37 (0-3)	1,81±1,32) (0-4)	0,004
Platelet transfusion – Mean±SD (Range)	0,04±0,07 (0-3)	0,07±0,38 (0-2)	0,576

Table 3. Intraoperative data

cardial infarction less than 6 weeks (29.5 vs 16.4%) and more than 6 weeks before surgery (41.1 vs 45.5%).

Body mass index was statistically significantly higher in the group of patients with anemia (29.95±3.86 vs 28.48±3.89).

Ejection fraction values were higher in average in the group of patients without anemia (44.41±9.32 vs 44.07±9.97 %) and percutaneous coronary intervention (PCI) was more present in the group of patients with anemia (30.9 vs 22.1), all without statistically significant difference (p>0.05).

In the group of patients with present anemia statistically significantly higher mean values of creatinine were recorded (90.69±28.51 vs 81.04±20.62) and more patients with creatinine values above 120 (14.5 vs 3.2%) (Table 2).

Values of blood parameters were higher in the group of patients without anemia, hemoglobin (145.69±10.12 vs 114.05±12.65; p<0,05), hematocrit (42.91±3.52 vs 34.77±2.98; p<0,05) and platelets count (227.96±40.05 vs 221.56±53.69; p>0,05).

The main intraoperative data are shown in the Table 3. Patients with anemia received more transfusions during the surgery – RBC (0.93±1.14 vs 0.29±0.86; p<0.05), FFP (1.81±1.32 vs 1.11±1.37; p<0.05) and platelet transfusion (0.07±0.38 vs 0.04 vs 0.07; p>0,05).

Transfusion of RBC and FFP were significantly different between two groups.

The dose of Cyklokapron was statistically significantly higher in the group of patients with anemia (2.54±0.98 vs 2.25±0.93), unlike Protamine which was statistically significantly more often administered in patients without anemia (28.4 vs 14.5%).

Although without statistically significant difference the insulin was more used in patients with anemia (73.6 vs 28.4%), but its dose was higher in patients without anemia (1.07±4.43 vs 0.44±0.50).

Vasopressors were statistically significantly more often used in patients with anemia (63.6 vs 42.1%) and their dose was higher (0.63±0.49 vs 0.42±0.50).

Variable	Anemia		p
	Absent (N=95)	Present (N=55)	
Dose of Cyklokapron in grams – Mean±SD (Range)	2,25±0,93 (0-6)	2,54±0,98 (2-6)	0,043
Insulin – N (%)	27 (28,4)	24 (43,6)	0,298
Insulin (dose) – Mean±SD (Range)	1,07±4,43 (0-30)	0,44±0,50 (0-1)	0,193
Vasopressors – N (%)	40 (42,1)	35 (63,6)	0,017
Vasopressors – Mean±SD (Range)	0,42±0,50 (0-1)	0,63±0,49 (0-1)	0,011
Total drainage in 48 hours – Mean±SD (Range)	681,58±349,06 (258-2435)	744,45±45,72 (0-2020)	0,115
Transfusion of RBC – Mean±SD (Range)	0,29±0,84 (0-6)	0,89±1,29 (0-6)	0,001
Transfusion of FFP – Mean±SD (Range)	0,41±1,15 (0-6)	0,65±1,13 (0-3)	0,046
Transfusion of platelets – Mean±SD (Range)	0,07±0,42 (0-3)	0,11±0,57 (0-3)	0,856
Minutes of mechanical ventilation – Mean±SD (Range)	469,25±191,13 (80-1289)	623,91±259,83 (0-1200)	0,0001
Occurrence of atrial fibrillation – N (%)	7 (7,4)	7 (12,7)	0,277
Additional dose of Protamine N (%)	27 (28,4)	8 (14,5)	0,039
ICU duration of stay in days – Mean±SD (Range)	3,13±1,15 (2-11)	3,06±1,07 (2-7)	0,467

Table 4. Early postoperative recovery - Intensive Care Unit

Total drainage, although without statistically significant difference was higher in patients with anemia (744.45±45.72 vs 681.58±349.06).

Number of transfusions was higher in group of patients with anemia as follows: RBC (0.89±1.29 vs 0.29±0.84; p<0,05), FFP (0.65±1.13 vs 0.41±1.15; p<0,05) and platelets (0.11±0.57 vs 0,07±0.42; p>0,05).

Duration of MV was statistically significantly longer in patients with compared to patients without anemia (623-91±259.83 vs 469±191.13).

Occurrence of AF was more often in patients with anemia (12.7 vs 7.4%) but without statistically significant difference (p>0.05).

The duration of intensive care unit stay was almost identical in observed groups, longer for patients without anemia (3.13±1.15 vs 3.06±1.07 days).

There were no deaths during early postoperative recovery.

5. DISCUSSION

Conventional CABG with CPB is at increased risk of perioperative blood loss requiring a transfusion of blood products, CPB leads to thrombocytopenia and platelet dysfunction, dilution and consumption of coagulation factors, hyperfibrinolysis, and a residual heparin effect. So, there has been an increasing interest in OPCAB with the suggestion that this may avoid the complication of CPB and reduce postoperative blood loss, usage of blood and blood products, morbidity and mortality. All of which reduces the stay in the intensive care unit, length of hospitalization and thus the total cost of treatment. Preoperative anemia has been identified as the single-most important determinant of transfusion, and many postoperative complications (use of vasoconstrictors, specific drugs to control bleeding and use of allogeneic blood products) (7).

If patient is anemic, in order to avoid donating blood and blood products and thereby reduce postoperative complications, various preoperative blood management strategies have been studied such as iron therapy, erythropoietin administration, dietary supplements of vitamin B12 and folate, or preoperative autologous blood donation. This is particularly relevant since it makes it possible to intervene in patients whose elective cardiac surgery is scheduled (8, 9).

When assessed according to criteria, about 20% - 50% of patients undergoing cardiac surgery suffer from preoperative anemia, with especially high incidences in older patients or in patients with chronic diseases and/or multiple comorbidities. In order to correct anemia, RBC transfusion is indicated and it is another recognized risk factor for adverse events after cardiac surgery. The pathophysiologic mechanism by which transfusions might harm has not been fully elucidated, but it is known that erythrocytes undergo irreversible morphologic and biochemical changes during storage. As a result, after transfusion, they can promote a proinflammatory state, impair tissue oxygen delivery, and exacerbate tissue oxidative stress. This in turn can contribute to organ dysfunction and explain, at least in part, the increased hospital mortality and morbidity (10).

The aging of population, causes an increase of anemia in elderly people. In our study patients with anemia were older than patients without anemia with an average age of 65.29±6.64 years. Same results gave Cappellini MD in his study (11).

Kanic V in his study found that women suffered anemia more than men and that the prevalence of anemia increased rapidly with age in men but not in women. We found no differences between genders in anemic and non anemic group (12).

The prevalence of comorbidities in our patients with anemia is very similar to the data provided by Kulier A et al. and Hung M in their studies (13, 14).

Obesity is linked to a variety of unfavorable outcomes, including anemia, which is a serious global public health problem. The prevalence of obesity along with anemia suggests a relationship between obesity and anemia. Our anemic patients had higher BMI compared to patients without anemia which is the same date from Saad RA et al study (15).

Anand IS in his study showed that anemic patients have a better left ventricular ejection fraction (LVEF) and thus gives the same results as we found in our study (16).

Anemia is often associated with DM. Patients with diabetes need to be screened for anemia along with other risk factors and anemia should be corrected appropriately to improve overall clinical outcomes. Our study had more diabetic patients in non-anemic group, a finding that differs from numerous other studies (17).

Our study confirmed higher dose of vasopressors in anemic patients and that they are used more often. Many studies had the same data, but Pongsuthana S et al. in their study did not find differences in the use of inotropic drugs between anemic and non-anemic patients (18).

Duration of MV in our patients with anemia was significantly longer compared with patients without anemia. The same data was found in the study of Zilberberg MD et al (19).

Zochios V et al in their study found that hypoxemia and anemia on admission to ICU were the only 2 factors independently associated with the need for escalation of respiratory support or prolonged invasive ventilation. Escalation of respiratory support or prolonged invasive ventilation is frequently seen in cardiac surgery patients and is highly associated with increased mortality and morbidity (20).

We found in our study that atrial fibrillation occurred more often in anemic patients which is the same as in the study from Lu Dai et al. and Hanna-Rivero N et al. which confirmed that anemia may be associated with the development of new-onset AF and anemia may also be more likely to experience clinical recurrence of AF (21, 22).

In our study ICU days were almost identical in both groups. Lu Dai et al. showed in their study that anemic patients experienced longer ICU (27 versus 48 hours, $p < 0.001$) and postoperative hospital (6.1 versus 7.4 days, $p < 0.001$) length of stay than non-anemic patients. The same results confirm study from Lorente V et al. that both ICU and hospital stay were significantly longer in patients with anemia (23).

In the investigation made by Sadeghi A it is confirmed that 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 (24). A low preoperative Hct is an independent risk factor for the need for a transfusion, and the mortality rate among patients is directly proportional to the need for a transfusion, regardless of the type of surgery (25).

Defining the subtypes of anemia (iron-deficiency anemia, anemia of chronic disease or anemia due to both conditions) based on laboratory testing seems to be the key for specific and individualized therapy. The optimal treatment strategy remains unclear. Although therapeutic interventions shortly before surgery have been suggested, treatments should be initiated within several weeks before surgery to effectively improve RBC mass and hemoglobin values (26).

Lower pre-operative hemoglobin concentrations are independently associated with increased utilization of hospital resources after cardiac surgery. Each g/dl unit fall in pre-operative hemoglobin concentration is independently associated with increased transfusion requirements of blood products and increased post-operative length of stay in intensive care and in hospital (27).

6. CONSLUSION

Our study showed that patients who underwent elective OPCABG with preoperative anemia, got more units of blood and blood products, had higher doses of inotropic and vasoactive drugs, and longer mechanical ventilation. In order to reduce the use of blood and blood products, which lead to many unwanted complications, it is necessary to correct the existing preoperative anemia in elective OPCABG surgery.

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