

ORIGINAL ARTICLE

Impact of Preoperative Anaemia on Outcome in Elective On-Pump Cardiac Surgery

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Summary

Introduction. Anaemia is a clinically important and increasingly frequent finding in cardiac surgery. Whether preoperative anaemia is an independent risk factor for adverse outcomes after elective cardiac surgery is still under discussion. We analysed prevalence of preoperative anaemia and its influence to outcome in patients undergoing elective on-pump cardiac surgery.

Aim of the Study. To analyse preoperative anaemia and its influence to outcome in patients undergoing elective cardiac surgery.

Material and Methods. Prospective study was done from October 2013 to January 2014 at the Cardiac Surgery Centre of Pauls Stradins Clinical University Hospital. Data were collected on 192 patients who underwent elective on-pump cardiac surgery. The prevalence of preoperative anaemia was defined as haemoglobin (Hb) for men < 130 g/l, for women < 120 g/l. Surgical bleeding was found for 17 patients during re-operation, those were excluded from future analysis. Consequently, 175 were divided into two groups: anaemic (n=69) and control group (n=106). Anaemia relationships with haemotransfusions, postoperative complications as acute heart failure, infections, atrial fibrillation, acute kidney injury (AKI) and length of mechanical ventilation and stay in hospital were obtained.

Results. The overall prevalence of preoperative anaemia was 39%. Preoperative Hb values were 111 ± 13 g/l, MCHC 329 ± 12 g/l, MCV 86 ± 8 fl in anaemic group and in a control group Hb 140 ± 11 g/l, MCHC 335 ± 8 g/l, MCV 89 ± 9 fl ($p < 0,001$; $p < 0,001$; $p = 0,01$). Anaemic patients in 80% received red blood cell (RBC) transfusions 586 ± 801 ml and 47% in control group, $p < 0,0001$. Fresh frozen plasma (FFP) and Cryoprecipitate (Cryo) transfused volumes did not differ statistically between groups ($p = 0,15$; $p = 0,2$). Sensitivity and specificity of preoperative anaemia to haemotransfusions: area under curve for RBC transfusions 0,71, for FFP 0,57, for Cryo 0,44. Hb levels before and 24 hours after surgery correlated with RBC transfusions ($r = -0,4$, $-0,5$; $p < 0,001$). Anaemia is an independent risk factor for postoperative infection ($p=0,04$; OR 4.2; 95% C.I. 1.2-16.7) and AKI ($p=0,02$; OR 2.3; 95% C.I. 1.1-4.6). RBC transfusion volume is adjusted to postoperative infections and AKI, respectively, $p = 0,004$ and $p = 0,01$. Anaemic patients had statistically longer mechanical lung ventilation ($p = 0,02$) and stay in hospital ($p = 0,04$).

Conclusions. Preoperative anaemia, mainly normocytic normochromic (72%) and microcytic hypochromic (13%), is observed in 39%. Anaemic patients received major RBC transfusions to compare with non-anaemic patients. Preoperative anaemia and volume of RBC transfused are associated with development of AKI and infections postoperatively. Preoperative anaemia prolongs mechanical lung ventilation and in-hospital stay.

Key words: preoperative anaemia; RBC transfusions; elective cardiac surgery; complications

INTRODUCTION

Anaemia is clinically important and increasingly frequent finding in cardiac surgery. Currently, there is no unifying definition of anaemia, however World Health Organization (WHO) definition is well accepted. WHO defines anaemia as a clinical situation where red blood cells count or their ability of transporting oxygen is insufficient for physiological demand (18). Anaemia is defined as haemoglobin (Hb) level under 130 g/l for male and under 120 g/l for female according to the WHO. Preoperative anaemia has been found in 25,2% - 54,4% patients undergoing elective surgery (3, 5, 18). Incidence of preoperative anaemia varies depending on studied population, the definition of anaemia used, as well as on age and chronic co-morbidities like chronic renal and liver insufficiency and usage of some medicines (diuretics, proton pump inhibitors) (3, 13). Anaemia can be a significant clinical sign of chronic illness or inflammation processes in patients after age 65 (3). The relevant algorithm to evaluate etiology of anaemia is offered by GA Hans, shown in Fig.1.

Anaemia				
Low reticulocyte			High reticulocyte	
Microcytic	Normocytic	Macrocytic		
Ferritin; Transferrin saturation; Inflammatory markers; U&E	Vitamin B12; Folate; LFTs		LDH; Serum Iron; Free Plasma Hb; Haptoglobin	
Iron deficiency anaemia	Renal Anaemia; Anaemia of chronic disease; Dimorphic anaemia	Vitamin deficiencies; AED; Thyroid disease; Alcohol abuse; Liver disease	Haemo- lysis	Non Haemo- lytic

Fig.1. Algorithm for the etiological diagnosis of anaemia by GA Hans (6).

Abbreviations: U&E – urea and electrolytes; LFTs – liver function tests; LDH – lactate dehydrogenase; AED – anti-epileptic drugs.

Anaemia is characterized by following parameters: haemoglobin level (Hb, g/l), haematocrit (Ht, %), mean cell haemoglobin (MCH, pg), mean cell volume (MCV, fl) and mean cell Hb concentration (MCHC, g/l) (3, 6). Hb and/or Ht level prior surgery could be used as prognostic markers to predict amount of RBC transfusions and postoperative complications after cardiac surgery (5, 9). At the Cardiac Surgery Center in Pauls Stradins Clinical University hospital are carried out more than 1000 operations with cardiopulmonary bypass (CPB) every year. Majority are coronary artery bypass grafting (CABG), heart valve replacement and mixed (CABG + valve) on-pump operations. Risk for perioperative complications, morbidity and mortality is increased after CPB surgery (2). Average mortality is 2,5% in CABG surgery, it is up to 1,2% in Latvia. Perioperative risk assessment is important for patients planned for cardiac surgery. Widely 2 score systems have been used - EuroSCORE II (*The European System for cardiac operative Risk Evaluation*) (15) and STS (*The Society of Thoracic Surgeons National Cardiac Database*) (4). These scoring systems predict early mortality depending on patient's risk factors and planned surgical intervention (15). Preoperative Hb level is not included in mentioned scoring systems as important risk factor however preoperative anaemia is associated with an increased risk of 30 day postoperative mortality and cardiac events (19). Anaemia can predispose to excessive vasodilatation during CPB causing renal and cerebral hypoperfusion, mainly in elderly patients (6, 10, 13). Furthermore, vasodilatation due to anaemia increases the risk of low cardiac output syndrome and arrhythmias. The risk of major non-cardiac as respiratory, acute kidney injury (AKI), wound, septic and thromboembolic complications is increased either. The adverse impact of anaemia on perioperative outcome is potentially confounded by the receipt of allogeneic red blood cells (RBC) (16). Anaemia notably prolongs length of stay in intensive care unit (ICU) and in hospital, increasing hospital costs after on-pump cardiac surgery (5, 7, 10, 17) and general surgery (14). Therefore, correction of preoperative anaemia would be crucial before elective surgery, thus improving outcome (11).

AIM OF THE STUDY

To analyze prevalence and type of preoperative anaemia and its influence on outcome in patients undergoing elective on-pump cardiac surgery.

MATERIAL AND METHODS

Prospective study was done at the Cardiac Surgery Centre of Pauls Stradins Clinical University Hospital, Riga, Latvia from October 2013 till January 2014. Inclusion criteria were: first time CABG and/or valve replacement under CPB; age > 18, Euroscore II < 10%. Coagulations tests activated partial thromboplastin time (APTT), prothrombin index (PI), fibrinogen, international normalized ratio (INR) were within the normal range before surgery.

In the study were included 192 patients undergoing elective cardiac surgery with CPB. Following parameters

were analyzed: demographical data, surgical and post-surgical parameters and laboratory findings, as presented in Table 1. Hb level were fixed in four time points: prior surgery (T_0), 24 hours after surgery (T_{24}), in the 5th postoperative day and at discharge (T_5 , T_D). Type of anaemia was obtained by analyzing MCH, MCV and MCHC prior surgery. Studied population was divided into two groups: anaemic group $n = 69$ (T_0 Hb male < 130 g/l, female < 120 g/l) and control group $n = 106$.

As primary outcome postoperative complications were observed: acute heart failure (AHF) requiring inotropic support > 48 h, atrial fibrillation (AF), acute kidney injury (AKI) defined as creatinine level increase 2 times from baseline postoperatively, approved wound, blood, catheter or lung infection. As secondary outcomes amount of allogeneic blood component transfusions (ml), duration of mechanical lung ventilation (MLV), length of stay in intensive care unit (ICU) and in hospital were analyzed.

Statistical analysis was performed using SPSS Statistics (Chicago, IL, Ver. 20). Descriptive and comparative statistics were used between groups, displaying mean value $\pm$ standard deviation (SD). Distribution of parameters were evaluated with Kolmogorov-Smirnov test. Data with regular distribution were analyzed with parametrical tests (*Student-t*, *ANOVA*), data with irregular distribution with non-parametrical tests (*Mann-Whitney U*). Binary logistic regression analysis was used to estimate anaemia as a major risk factor to develop postoperative complications. Statistical significance was defined as $p < 0,05$. ROC (*receiver operating characteristic*) curve analysis was performed to demonstrate prognostic efficiency of preoperative anaemia as predictive marker for allogeneic blood cell transfusions.

RESULTS

In presented study 192 patients were analyzed with average age 68 ± 10 years. Excessive postoperative surgical bleeding requiring re-exploration were observed for 23 patients. Those were excluded from further analysis. As surveyed in Table 1, 175 patients were subjected to further analysis. Anaemia was found for 69 patients (39%) prior elective cardiac surgery.

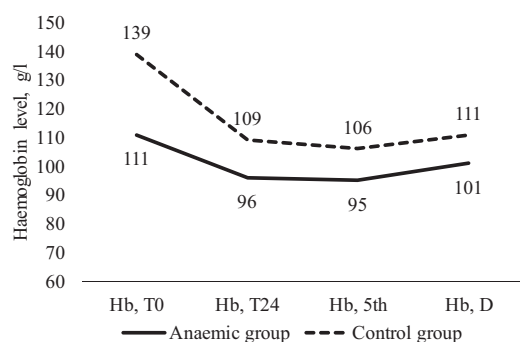
Demographical, laboratory and surgical parameters. In anaemic group 49% were females, with average age 69 ± 10 years, ejection fraction (EF) $57 \pm 7\%$, body mass index (BMI) 27 ± 6 kg/m². The letters most often underwent mixed surgery in 33% and AVR in 36%. Mean CPB time for anaemic patients was $102 \text{ min} \pm 35 \text{ min}$ vs. $101 \pm 34 \text{ min}$ in control group, with statistically lower mean Ht level during CPB $19 \pm 3\%$ vs. $22 \pm 4\%$, $p < 0,0001$. In control group 57% were females with average age 67 ± 10 years, EF $56 \pm 7\%$, BMI 28 ± 5 kg/m². Statistically more often was performed CABG compare to anaemic group in 41%, respectively. Priming volume used for extracorporeal circuit system depended on BMI and cristalloid cardioplegia volume were similar in both groups. Before surgery Hb level, MCHC and MCV was statistically lower in anaemic group compare to control group. Data are presented in the table 1.

Table 1. Demographical and surgical data.

Parameter	Anaemic group n= 69	Control group n = 106	P value
Female, n (%)	34 (49%)	60 (57%)	0,007
Age, y	69 ± 10	67 ± 10	0,2
EF, %	57 ± 7	56 ± 7	0,5
BMI, kg/m ²	27 ± 6	28 ± 5	0,2
Laboratory parameters			
Creatinine, mkmol/l	94 ± 35	89 ± 9	0,13
Hb, g/l	111 ± 13	139 ± 11	0,01
MCHC, g/l	328 ± 12	335 ± 8	0,001
MCV, fl	86 ± 8	89 ± 9	0,02
PI, %	91 ± 14	91 ± 13	0,8
Fibrinogen, g/l	4,2 ± 1,5	4,2 ± 1,4	0,9
INR	1 ± 0,1	1 ± 0,1	0,2
Surgical parameters			
CABG, n (%)	16 (23%)	43 (41%)	<0,001
AVR, n (%)	25 (36%)	21 (20%)	0,5
MVR, n (%)	5 (7 %)	12 (11%)	0,09
Mixed, n (%)	23 (33%)	30 (28%)	0,3
CPB duration, min	102 ± 35	101 ± 34	0,9
Rectal temp. in CPB, C°	35 ± 0,4	35 ± 0,5	0,4
Ht, %, in CPB	19 ± 3	22 ± 4	< 0,0001
Cardioplegia, ml	1781 ± 546	1789 ± 624	0,95

Abbreviations: EF –Ejection fraction; BMI – Body mass index; Hb – haemoglobin; Ht – hematocrit; MCHC – mean cell Hb concentration; MCV –mean cell volume; PI – prothrombin index; INR – international normalized ratio; CABG – coronary artery bypass graft surgery; AVR – aortic valve replacement, MVR – mitral valve replacement; CPB – cardiopulmonary bypass.

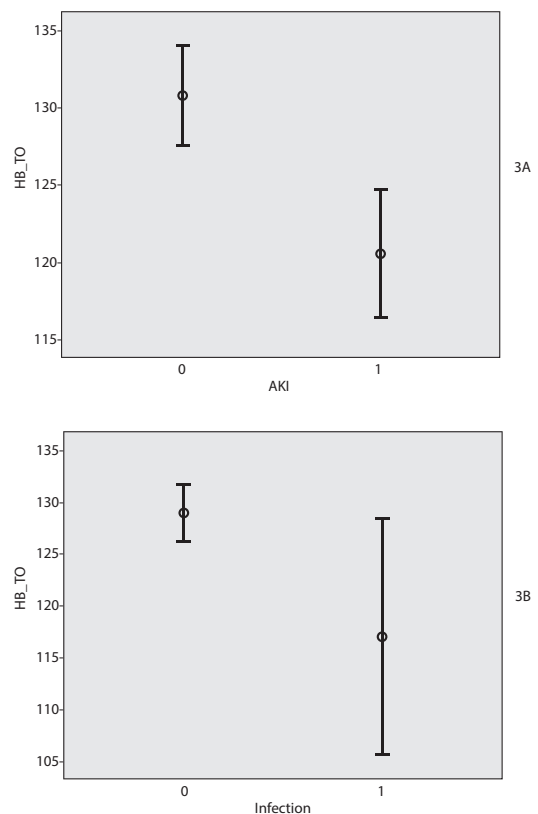
Hb level significantly differed between groups during all analyzed time periods – T₀, T₂₄, T₅, T_D (p < 0,0001), as demonstrated in Figure 2.

**Fig. 2. Haemoglobin level changes during analyzed time points.**

Abbreviations: Hb, T0 – haemoglobin level prior surgery; Hb, T24 – haemoglobin level 24 hours after surgery; Hb, 5th – haemoglobin level 5 days after surgery; Hb, D – haemoglobin level at discharge of hospital.

Postoperative complications. AHF developed for 12 anaemic patients (17%), at least one episode of AF for 25 (36%), AKI was detected for 24 (35%) and infection complications were observed in 8 (12%) anaemic patients. Consequently, in control group the same complications were as follows: AHF 13 (12%), AF 45 (42%), AKI 20 (19%) and approved infection in 4 (4%) cases.

AF statistically more often were fixed in control group (p=0,02). Comparing two groups using binary logistic regression analysis anaemia was found as independent risk factor for postoperative infections (p=0,04; OR 4.2; 95% C.I. 1.2-16.7) and AKI (p=0,02; OR 2.3; 95% C.I. 1.1-4.6) as presented in Figure 3A and 3B.

**Fig. 3A, 3B. Association between preoperative Hb level and development of AKI (3A) and infection (3B).**

Abbreviations: HB_T0 – Haemoglobin level prior surgery; AKI – acute kidney injury.

Impact of anaemia on allogeneic blood component transfusions, MLV and length of stay in hospital. During surgery and/or ICU 80% of anaemic patients received RBC transfusions with an average volume 586 ± 801 ml, 61% received FFP

420 ± 573 ml and 58% Cryo 158 ± 176 ml. Statistically less in 47% of cases RBC transfusions were administered in control group with an average volume 230 ± 336 ml; $p = 0,007$, respectively. FFP was transfused in 49% with mean volume 275 ± 330 ml and in 66% Cryo 175 ± 131 ml without statistical difference between groups ($p = 0,15$; $p = 0,2$). Furthermore, Hb level prior surgery correlates negatively with RBC transfusion volume ($r = -0,52$, $p < 0,0001$).

Preoperative anaemia showed high sensitivity and specificity for RBC transfusions demonstrated by ROC analysis where area under the curve (AUC) was 0,708 as shown in Figure 4.

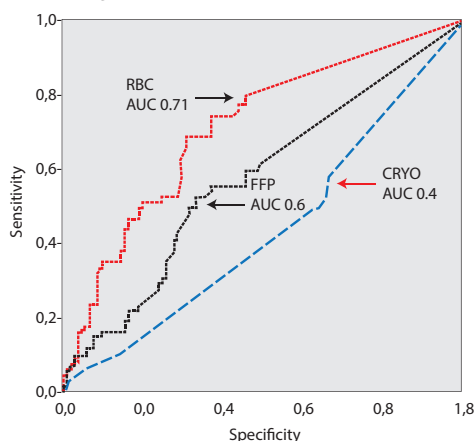


Fig. 4. Sensitivity and specificity of preoperative anaemia in relation to blood component transfusions.

Abbreviations: RBC – Red blood cells, FFP- fresh frozen plasma, Cryo – cryoprecipitate. AUC (Area under Curve) for RBC 0,71; FFP 0,6; Cryo 0,43.

Comparing anaemic with control group related to duration of MLV and length of stay in ICU and in hospital results were as following: MLV duration 14 ± 24 h vs. 7 ± 4 h ($p = 0,02$), length of ICU stay 2 ± 3 vs. 2 ± 1 days, in-hospital stay 18 ± 10 vs. 16 ± 6 days ($p = 0,04$).

DISCUSSION

Nowadays preoperative anaemia is still an actual problem, demonstrated by increasing number of publications in last years (3, 7, 14, 17). Impact of preoperative anaemia to outcome is still disputable. There is no a common way for identification and correction of preoperative anaemia in patients scheduled for elective surgery. Moreover, cardiac surgery belongs to high bleeding risk interventions, where preoperative anaemia can play a crucial role. In present study from 175 patients subjected to further analysis, 69 (39%) were anaemic mostly normocytic normochromic before elective cardiac surgery with CPB. Incidence of preoperative anaemia detected in our study is similar reported in other studies, ranging from 26% to 54% (1, 6, 10). Causes of normocytic normochromic anaemia could be several. The most spread chronic diseases that could induce anaemia are chronic kidney injury or chronic heart failure (6). We speculate chronic heart disease from NYHA II to IV class, could be the main reason for our investigated population

where the mean age was 69 years. After 60 years of age incidence of anaemia increases, and per every 5 years it deteriorates (4). In present study creatinine level didn't differ between groups preoperatively. Although, these patients used to receive diuretics for prolonged treatment period that could increase glomerular ischemia. Second major type of preoperative anaemia was microcytic hypochromic where iron deficiency, chronic alcoholism, some medicines are main reasons. Iron deficiency is the easiest reason to correct and detect preoperatively that could be treated with iron supplement at least 7-10 days before surgery (11). We speculate, both groups were comparable because all preoperative parameters, excepting gender, didn't differ statistically. Mixed surgery could increase bleeding tendency, request of allogeneic blood transfusions and development of complications postoperatively, mostly due to prolonged CPB time. Mixed surgery was performed in the same frequency with similar CPB time in both analysed groups. Preoperative anaemia can influence and significantly augment transfusion volume of RBC as it is shown in our study, where anaemic patients had significantly higher rates and amount of RBC transfused. Also David et al. demonstrated that anaemic patients more often received RBC transfusions 79.8 vs. 46.4% (3), consequently in our study 80% vs. 47%. Preoperative anaemia is an important risk factor in developing major post-surgical complications like AHF, AF, AKI, infections, as well as cerebral strokes and myocardial infarctions (5, 6). Kurfurst et al. demonstrated those complications ranging from 0,5% up to 50% in patients undergoing elective cardiac surgery with CPB and majority of them were for patients older 70 years (12). We were able to show statistically significant association between preoperative anaemia and AKI ($p = 0,02$) and development of infection complication ($p = 0,04$). AF was observed more frequently in control group. Probably anaemic patients received more aggressive therapy of beta adrenergic blockers before surgery for AF prophylaxis. In present study we didn't observe statistical difference in AHF, although there was a notable tendency to develop AHF more often in anaemic patients, that could reach statistical significance by increasing patient sample size.

Preoperative anaemia should be detected early, because allogeneic blood cell transfusions must be restricted as much as possible (11) When to start patient's preoperative inspection for anaemia is unclear. Few authors recommend at least 4 weeks (8), but European Society of Anaesthesiologists (ESA) at least 8 weeks before elective surgery (11). Cardiac surgery consumes up to 40% of blood components from local blood bank in Latvia. Although treatment costs were not calculated in presented study, similar to other reports, duration of MLV and length of stay in-hospital significantly differed between groups, most likely augmenting treatment costs for anaemic patients (6, 9, 17).

CONCLUSION

Preoperative anemia, mainly normocytic normochromic (72%) and microcytic hypochromic (13%), is observed in 39% patients undergoing elective on-pump cardiac surgery.

Anaemic patients received major RBC transfusions to compare with non-anaemic patients ($p < 0,0001$). Preoperative anaemia and amount of RBC transfused are associated with development of AKI and infection complications postoperatively. Preoperative anaemia prolongs mechanical lung ventilation and in-hospital stay.

Conflict of interest: None

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