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RESEARCH ARTICLE

The Relationship Between Preoperative Anemia and Morbidity and Mortality in Patients Undergoing Open Heart Surgery

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ABSTRACT

Objectives: Anemia is prevalent in the surgical population. Since anemia and blood transfusion are associated with increased mortality, optimizing patient blood management and treating anemia may improve patient outcomes. This study aims to determine the impact of preoperative anemia on postoperative morbidity and mortality in patients undergoing open-heart surgery.

Methods: Our prospective observational study included 200 patients scheduled for elective open-heart surgery, divided into two groups: 100 with preoperative anemia and 100 without. The two groups were compared in terms of morbidity and in-hospital mortality.

Results: In our study, postoperatively, sepsis was observed in 11% of the anemia group, acute kidney injury (AKI) in 22%, and cerebrovascular disease (CVD) in 4%, while in the control group, sepsis was observed in 4%, AKI in 15%, and CVD in 2%. No significant association was found between the incidence of sepsis, AKI, and CVD in the two groups. Mortality rates were 7% in the anemia group and 4% in the control group, indicating that anemia was not a decisive factor in mortality.

Conclusion: Although the duration of MV was longer in the preoperative anemia group, there was no difference in ICU and hospital stay durations. Despite higher incidences of sepsis, AKI, CVD, and mortality in the anemia group, anemia was not found to be a determining risk factor. We conclude that managing anemia, a treatable condition, in elective cases such as high-mortality open-heart surgeries is essential to minimize risk factors.

Keywords: Acute kidney injury, cerebrovascular disease, open heart surgery, preoperative anemia, sepsis

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Introduction

Open-heart surgery is one of the major surgeries with high morbidity and mortality rates in the postoperative period. A thorough analysis of the risk factors for complications developing in the postoperative period contributes to reducing morbidity and mortality. According to the World Health Organisation (WHO), haemoglobin levels below 12 g/dl in women and 13 g/dl in men are defined as anaemia.[1] In arterial blood, 97% of oxygen is bound to haemoglobin, and 3% is dissolved in plasma.[2] The change in haemoglobin concentration affects the amount of oxygen reaching the tissue.[3] According to the results of various studies, the prevalence of anemia is high in cardiac surgery patients during the preoperative period. While the incidence of preoperative anemia in the general population ranges from 25% to 75%, this rate is between 26% and 30% in patients undergoing cardiac surgery.[4–6] These patients, with limited coronary reserves, have a reduced tolerance for acute blood loss, and the presence of anemia in the preoperative period further diminishes this tolerance. Additionally, the presence of anemia is the strongest predictor of perioperative transfusion. In one study, the frequency of blood transfusion during the intraoperative period in cardiac surgery was reported to be 54% in patients with anemia, compared to 22% in those without anemia.[7] The primary goals of preoperative assessment and treatment in cardiac surgery are to identify and mitigate patient risk during surgery and in the postoperative period. Given that both anemia and blood transfusion are associated with increased mortality,

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optimizing patient blood management and treating anemia can improve patient outcomes. Therefore, in our study, we aimed to determine the relationship between preoperative anemia and postoperative morbidity and mortality in patients undergoing open-heart surgery.

Methods

Our study was conducted between 1 October 2021 and 1 October 2022 after approval (HNEAH-KAEK 2021/223) from the local ethics committee on 06.09.2021. A total of 100 patients with preoperative anemia and 100 patients without anemia, who were scheduled for elective open-heart surgery (coronary artery bypass grafting, valve surgery, or a combination of both, as well as Bentall procedures), were included in the study after obtaining their informed consent. Pregnant patients, those undergoing emergency surgery, and patients under the age of 18 were excluded from the study. This study was conducted in accordance with the principles of the Declaration of Helsinki. The patients' age, gender, body mass index (BMI), EuroScore levels, hemoglobin and hematocrit levels, creatinine levels, and comorbidities were recorded. Intraoperative variables such as the type of surgery, aortic cross-clamp time (minutes), cardiopulmonary bypass time (minutes), and the type and amount of transfused blood and blood products were also documented.

Postoperative mechanical ventilation times were recorded as less than 8 hours, 8–12 hours, and more than 12 hours, with durations over 12 hours considered prolonged mechanical ventilation. The length of stay in the intensive care unit (ICU) was categorized as normal if it was within the first 48 hours and prolonged if it exceeded 48 hours. The length of hospital stay was considered normal if within the first 7 days, and prolonged if it exceeded 7 days. Complications such as sepsis, acute kidney injury (AKI), cerebrovascular disease (CVD), and patient outcomes (discharge or death) were recorded during the hospital stay.

In our study, patients with hemoglobin levels below 12 g/dL in women and below 13 g/dL in men were classified as anemic, according to the World Health Organization (WHO) criteria. The enrolled patients were divided into two groups: anemic and non-anemic. Patients in the anemia group were further classified into mild, moderate, and severe anemia based on their hemoglobin levels (in men, mild anemia: 13>Hb≥11, moderate anemia: 11>Hb≥8, severe anemia: Hb<8; in women, mild anemia: 12>Hb≥11, moderate anemia: 11>Hb≥8, severe anemia: Hb<8). However, since only one patient was in the severe anemia group, our evaluations were based on two groups: mild anemia (13>Hb≥11 in men, 12>Hb≥11 in women) and severe anemia (Hb<11 in men, Hb<11 in women). Additionally, any medical treatment or blood products administered for anemia during the perioperative period were recorded.

Statistical Analysis

The data obtained in this study were analyzed using the licensed SPSS 25 software package. The Shapiro-Wilk test was employed to assess whether the variables followed a normal distribution due to the sample sizes. To examine differences between groups, the Mann-Whitney U Test was used, and the Chi-square test was applied to analyze the relationships between categorical variables. A significance level of 0.05 was used for interpreting the results, with $p<0.05$ indicating a statistically significant difference, and $p>0.05$ indicating no significant difference.

Results

A total of 200 patients were included in the study, with 100 patients in the anemic group (study group) and 100 patients in the non-anemic group (control group). Among these patients, 68.5% underwent coronary artery bypass grafting (CABG), 20.5% had heart valve surgery, 8.5% underwent a combination of CABG and valve surgery, and 2.5% underwent Bentall procedures. Of these patients, 66.5% were male, and 33.5% were female. Among the male participants, 47.37% were anemic in the preoperative period, while 55.22% of the female participants were anemic preoperatively (Table 1). From a sociodemographic perspective, the preoperative anemic group was significantly older than the non-anemic group (p=0.015) (Table 1), and the EuroSCORE level was statistically higher in the anemic group (p=0.001) (Table 2).

The duration of mechanical ventilation in the preoperative anemic group was significantly longer compared to the non-anemic group (p=0.004) (Table 2). In the anemic

Table 1. Anaemia distribution according to gender and demographic data of the patients

	Gender			
	Male		Female	
	n	%	n	%
Anaemia				
Anaemic	63	47.37	37	55.22
Non-anaemic	70	52.63	30	44.78
	Anaemia		**t-test**	
	Mean	**SD**	**t**	**p**
Age (years)				
Anaemic	63.21	9.55	2.462	0.015*
Non-anaemic	59.79	10.09		
BMI				
Anaemic	27.88	5.07	-0.925	0.356
Non-anaemic	28.52	4.70		

*: p<0.05. SD: Standard deviation; BMI: Body mass index.

Table 2. Comparison with anaemia status

	Anaemia conditions		Mann Whitney U	
	Mean	SD	z	p
Duration of MV (hour)				
Anaemic	28.42	55.04	-2.856	0.004*
Non-anaemic	15.97	43.05		
Stay in ICU (hour)				
Anaemic	53.78	79.67	-1.825	0.068
Non-anaemic	35.41	62.82		
Stay in hospital (day)				
Anaemic	10.22	7.37	-1.553	0.120
Non-anaemic	8.30	5.63		
Cross-clamp time (minutes)				
Anaemic	89.54	43.09	-1.857	0.063
Non-anaemic	76.14	29.66		
CPB time (minutes)				
Anaemic	133.4	54.32	-1.62	0.105
Non-anaemic	118.5	39.36		
EuroSCORE				
Anaemic	3.51	2.89	-3.619	0.001*
Non-anaemic	2.55	2.84		

*: p<0.05. SD: Standard deviation; MV: Mechanical ventilator; ICU: Intensive care unit; CPB: Cardiopulmonary bypass.

Table 3. Comparison with anaemia levels

	Anaemia level		Mann Whitney	
	Mean	SD	z	p
EuroSCORE point				
Severe	3.79	3.60	-0.142	0.887
Mild	3.34	2.36		
Duration of MV (hour)				
Severe	39.47	75.45	-0.939	0.348
Mild	21.64	36.60		
Stay in ICU (hour)				
Severe	70.59	111.39	-0.274	0.784
Mild	43.48	49.92		
Stay in hospital (day)				
Severe	11.63	8.01	-1.549	0.121
Mild	9.35	6.88		
Cross-clamp time (minutes)				
Severe	86.73	46.68	-0.879	0.379
Mild	91.21	41.10		
CPB time (minutes)				
Severe	132.55	61.79	-0.774	0.439
Mild	133.98	49.73		

SD: Standard deviation; MV: Mechanical ventilator; ICU: Intensive Care Unit; CPB: Cardiopulmonary bypass.

group, 20% had a short duration of mechanical ventilation, 49% had a normal duration, and 31% had a prolonged duration, compared to the control group, where 20% had a short duration, 64% had a normal duration, and 16% had a prolonged duration.

The mean ICU stay for the study group was recorded as 53.78 hours, with 78% having a normal ICU stay and 22% having a prolonged ICU stay. In the non-anemic group, the mean ICU stay was 35.41 hours, with 91% having a normal ICU stay and 9% having a prolonged stay; however, no significant relationship was found between anemia and ICU stay duration (p>0.05) (Table 2).

Regarding the length of hospital stay, the mean duration was 10.22 days in the anemic group and 8.30 days in the non-anemic group. In the anemic group, 60% had a normal hospital stay, while 40% had a prolonged stay, compared to 70% with a normal stay and 30% with a prolonged stay in the non-anemic group. No significant relationship was found between anemia and the length of hospital stay (p>0.05) (Table 2).

There were no significant differences in cross-clamp time (minutes) or cardiopulmonary bypass (CPB) time (minutes) between the two groups (p>0.05) (Table 2). No relationship was found between the severity of anemia and the duration of mechanical ventilation, ICU stay, or hospital stay (Table 3).

Among the 100 anemic patients, 11 developed sepsis, compared to 4 out of 100 non-anemic patients. Although sepsis was more frequent in the anemic group, no significant association was found between preoperative anemia and the development of sepsis (p>0.05) (Table 4).

Acute kidney injury (AKI) occurred in 22 patients in the study group and 15 patients in the control group. No significant relationship was found between anemia and the development of AKI (p>0.05) (Table 4).

Acute cerebrovascular disease (CVD) was observed in 4 patients in the anemic group and in 2 patients in the non-anemic group. The study did not find a significant association between the presence of anemia and the development of CVD (p>0.05) (Table 4).

Only one patient in the preoperative anemic group received medical treatment, and after the anemia was corrected, the patient underwent surgery. No other patients received preoperative medical treatment or blood transfusions. During the intraoperative period, 5% of the anemic patients received complete blood, 68% received red blood cell (RBC) transfusions, and 40% received fresh frozen plasma (FFP). In contrast, none of the non-anemic patients received complete blood, 27% received RBC transfusions, and 6% received FFP. All patients who received complete blood intraoperatively were anemic (p=0.02). Among those who received RBC transfusions, 71% were anemic (p=0.00). Additionally, 87% of those who received FFP were anemic (p=0.00). In our study, complete blood, RBC, and

Table 4. Association of anaemia with postoperative morbidity and mortality

	Anaemia conditions				Chi-Square	
	Anaemic		Non-anaemic			
	n	%	n	%	z	p
Sepsis						
+	11	11.0	4	4.0	f	0.052
–	89	89.0	96	96.0		
AKI						
+	22	22.0	15	15.0	f	0.137
–	78	78.0	85	85.0		
CVD						
+	4	4.0	2	2.0	f	0.341
–	96	96.0	98	98.0		
Discharged	93	93	96	96	0.866	0.332
Mortality	7	7	4	4		

AKI: Acute kidney injury; CVD: Cerebrovascular disease; f: Fisher exact.

Table 5. Frequency of blood product administration with anaemia

	Anaemia condition					
	Anaemic		Non-anaemic		Total	
	n	%	n	%	n	p
İntraoperative CB						
+	5	100	0	0	5	0.02*
-	95	48.7	100	51.3	195	
İntraoperative RBC						
+	68	71.6	27	28.4	95	0.00*
-	32	30.5	73	69.5	105	
İntraoperative FFP						
+	40	87	6	13	46	0.00*
-	60	39	94	61	154	
Postoperative CB						
+	11	50	11	50	22	1.0
-	89	50	89	50	178	
Postoperative RBC						
+	61	72.6	23	27.4	84	0.00*
-	39	33.6	77	66.4	116	
Postoperative FFP						
+	36	80	9	20	45	0.00*
-	64	41.3	81	58.7	155	

*: p<0.05. CB: Complete blood; RBC: Red blood cell; FFP: Fresh frozen plasma.

FFP transfusions were significantly more common in the anemic group during the intraoperative period ($p<0.05$).

In the postoperative period, 11% of the anemic patients received complete blood, 61% received RBC transfusions, and 36% received FFP. In the non-anemic group, 11% received complete blood, 23% received RBC transfusions, and 9% received FFP. Of the patients who received complete blood postoperatively, 50% were anemic and 50% were not ($p>0.05$). Among those who received RBC transfusions, 72.6% were anemic, while 27.4% were not ($p=0.00$). Additionally, 80% of those who received FFP were anemic, and 20% were not ($p=0.00$). The need for RBC and FFP transfusions in the postoperative period was significantly higher in the anemic group ($p<0.05$) (Table 5).

During the hospital stay, 7% of patients in the anemic group and 4% in the non-anemic group died. However, the presence of preoperative anemia was not found to be a significant predictor of mortality (p>0.05) (Table 4).

Discussion

This single-center, prospective, non-randomized observational study included 200 patients scheduled for open-heart surgery: 100 with preoperative anemia (study group) and 100 without anemia (control group). These two groups were compared in terms of the incidence of postoperative sepsis, cerebrovascular disease (CVD), acute kidney injury (AKI), and in-hospital mortality.

Rubino et al.,[8] in a retrospective observational cohort study of 409 redo cardiac surgery patients (58.4% anemic), demonstrated that patients with preoperative anemia had a longer duration of mechanical ventilation, consistent with the findings of our study.

De Santo et al.[9] reported that preoperative anemia was an independent factor in predicting ARH in a single-center prospective observational study conducted in 1214 consecutive patients undergoing coronary artery bypass grafting. In a retrospective observational cohort study by Rubino et al.,[8] preoperative anemia was associated with a 2.5-fold increase in the risk of severe kidney injury and a 3.3-fold increase in the risk of requiring renal replacement therapy. In our study, no significant association of anemia with ARH developing after open-heart surgery was observed. Our different conclusion may be due to many reasons, because the pathogenesis of ARI (toxins, metabolic factors, ischemia and reperfusion, neurohormonal activation) is complex.

While our study found no association between anemia and sepsis, a meta-analysis by Padmanabhan et al.,[10] which included 114,277 patients and analyzed the outcomes of 23,624 anemic patients, concluded that preoperative anemia was associated with increased sepsis, AKI, CVD, and mortality. Conversely, a study by Riera et al.[11] involving 623 patients undergoing isolated CABG, found results similar to ours, with no statistically significant differences in the rates of postoperative adverse events related to the presence or absence of preoperative anemia. The pathogenesis of perioperative stroke is multifactorial, and despite strong evidence supporting a relationship between stroke and the severity of hemodilution—potentially leading to inadequate oxygen delivery and increased embolic load to the brain—different studies might yield varying results even when optimized.[12] Our study observed a higher incidence of CVD in the anemic group, but the association between anemia and CVD was not statistically significant. Contrary to our findings, Karkouti and colleagues[6] demonstrated that even moderate anemia was associated with worse postoperative outcomes. In a retrospective study of consecutive patients undergoing cardiac surgery in seven hospitals in 2004, preoperative anemia was significantly associated with adverse outcomes, including death, stroke, or acute kidney injury, compared to non-anemic patients.[6]

In this study, we found that the presence of preoperative anaemia was a determinant in the intraoperative blood transfusion decision. Similar results to our study were reported in the study conducted by Williams et al.[13] in 182,000 patients who underwent isolated CABG surgery, in the single-centre cohort study conducted by Hung et al.[7] and in the meta-analysis published by Padmanabhan et al.[10] In the meta-analysis published by Padmanabhan et al., 33.3% of anaemic patients and 11.9% of non-anaemic patients received blood transfusion.

Zindrou et al.,[14] comparing the in-hospital mortality of 62 anaemic patients (haemoglobin≤10.0 g/dL), 15 of whom were severely anaemic, with the mortality rate of 2075 non-anaemic patients (haemoglobin>10.0 g/dL), found that anaemia was associated with an approximately 3-fold increase in the likelihood of in-hospital death.

In the study by Cladellas et al.,[15] in-hospital morbidity and mortality of 42 anaemic patients (haemoglobin<12.0 g/dL) were compared with 15,932 non-anaemic patients (haemoglobin≥12.0 g/dL). After adjustment for several preoperative comorbidities, anaemia was associated with a >3-fold increase in the odds of death (OR=3.2; 95% CI, 1.1 to 9.55) and a >5-fold increase in the risk of major complications (OR=5.2; 95% CI, 2.2 to 1.44). In a study conducted by Saracoğlu et al.[16] in 333 patients undergoing cardiac surgery, no significant difference in mortality was observed between the anaemic and non-anaemic patient groups, similar to our study. The results of our study were affected by the fact that the number of patients in our study was smaller compared to other studies and the haemoglobin value, which we determined by following the WHO diagnostic criteria and considering the gender factor in the definition of anaemia, was used differently and without gender discrimination in some studies.

Conclusion

In our study, although sepsis, ARD, LVO, and mortality were observed more frequently in the postoperative period in patients with preoperative anaemia, these values were not statistically significant. Although the patient group with anaemia in the preoperative period had a longer mechanical ventilator stay in the postoperative period, the duration of intensive care unit and hospital stay was not different from the patient group without anaemia. It was also found that the presence of preoperative anaemia was associated with increased blood transfusion in the postoperative period. Despite the recommendations of guidelines and the results of observational studies, the frequency of anaemia in cardiac surgery patients is high. With this study, we wanted to draw attention to the relationship between preoperative anaemia, which we frequently encounter as anaesthetists, and postoperative outcomes.

While it is easy and inexpensive to detect anaemia in the preoperative period, the reason for the low rate of patients treated for anaemia and the fact that haemoglobin values of these patients are mostly increased by blood transfusion may be that allogeneic blood transfusion is considered an easier and faster method by most clinicians. In order to minimise the risk factors of anaemia, which is a treatable condition, especially in surgeries such as open heart surgery with high mortality, we believe that it would be correct to follow the treatment process after diagnosing anaemia as anaesthesiologists, to postpone elective cases during this process, and to allow the operation after the haemoglobin values are corrected with anaemia treatment. This will both reduce the risks caused by blood transfusion and lower the cost. However, delaying surgery to correct preoperative anaemia may carry risks in critically ill patients. The balance between the risks of anaemia and transfusion and the risks of delaying surgery should be considered and evaluated on a case-by-case basis.

Disclosures

Ethics Committee Approval: The study was approved by The Haydarpaşa Numune Training and Research Hospital Clinical Research Ethics Committee (no: 2021/223, date: 06/09/2021).

Authorship Contributions: Concept – Ö.Y.K., T.K.; Design – Ö.Y.K., T.K.; Supervision – Ö.Y.K., T.K.; Data collection &/or processing – Ö.Y.K.; Analysis and/or interpretation – Ö.Y.K.; Literature search – Ö.Y.K.; Writing – Ö.Y.K., T.K.; Critical review – Ö.Y.K., T.K.

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