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Short-term preoperative intravenous iron replacement: Impact on surgical outcomes in cardiovascular disease

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ABSTRACT

Objectives: This study aimed to compare surgical outcomes between patients scheduled for cardiovascular surgery diagnosed with anemia according to the World Health Organization criteria who received intravenous iron replacement and those who were not anemic.

Patients and methods: This retrospective study analyzed patients who underwent cardiovascular surgery between February 2021 and January 2024. Patients with preoperative anemia treated with intravenous iron replacement were compared with nonanemic patients. Data on demographics, preoperative conditions, surgical details, and postoperative outcomes were analyzed.

Results: Of the 193 patients (142 males, 51 females; mean age: 62±10 years; range, 27 to 82 years) analyzed, 173 survived, and 20 did not. Surviving patients were younger and had a lower body mass index. Comorbidities such as congestive heart failure and a history of cerebrovascular events were associated with mortality. Laboratory results showed significant differences in hemoglobin levels and iron binding capacity between survivors and nonsurvivors. The study found no significant differences in surgical procedures or reoperation rates between the groups. However, nonsurvivors had more postoperative complications. Multivariate analysis identified cardiopulmonary bypass time and new-onset acute renal failure as independent risk factors for 30-day mortality. Anemic patients treated with intravenous iron replacement had comparable perioperative outcomes to nonanemic patients, including similar lengths of intensive care unit and hospital stays and mortality rates.

Conclusion: Treatment of preoperative anemia with intravenous iron replacement in patients undergoing cardiovascular surgery resulted in outcomes comparable to those of nonanemic patients. This suggests that short-term intravenous iron replacement may be an effective strategy to improve surgical readiness and outcomes in anemic patients.

Keywords: Anemia, intravenous iron replacement, mortality, open heart surgery.

Cardiovascular diseases are the primary cause of death globally. Surgical procedures used to treat these diseases have become increasingly advanced, but mortality rates persist. Anemia detected in the preoperative period is a significant risk factor for mortality. Many publications have identified it as a critical factor in determining survival.[1-4] Managing preoperative anemia is crucial.[5] A thorough preoperative assessment of transfusion risk, particularly for low-risk patients who often undergo elective surgery, could improve their transfusion risk profile and reduce surgery-related morbidity and mortality.[6] While transfusion is a quick and easy method, it carries the risk of infection and additional volume, which is a significant concern in patients with heart failure. Therefore, short-term preoperative intravenous (IV) iron treatments are increasingly being emphasized as a safer alternative.

In the preoperative period, patients who received IV iron replacement (IVIR) have shown positive effects on important perioperative outcomes of open heart surgery, according to some publications.[7,8] Most studies use other treatments along with IVIR, and they typically focus on outcomes related to the amount of red blood cell (RBC) transfusions during the perioperative period. However, there are few studies that have compared the data of anemic

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patients receiving IVIR with nonanemic patients, particularly with respect to key surgical outcomes, and that have been conducted in a single center with patients undergoing standard surgical procedures. Hence, this study aimed to compare surgical outcomes between patients scheduled for cardiovascular surgery diagnosed with anemia according to World Health Organization (WHO) criteria who received IVIR and those who were not anemic.

PATIENTS AND METHODS

In this retrospective study, all consecutive patients who underwent open heart surgery at the cardiovascular surgery clinic of the Izmir Bakırçay University Hospital between February 2021 and January 2024 were included. Preoperative preparations, perioperative follow-ups, and surgeries were performed by the same surgical team. All patients were evaluated within the patient blood management protocol applied in the department, and IVIR was administered to patients identified as anemic according to the WHO definition.[9,10] Anemic patients who received IVIR were compared with those who did not have anemia.

The study collected data from the patient records in the hospital information system. The data on the patients' demographic characteristics, treatment history, preoperative data, surgical procedure details, postoperative complications, length of hospital stay, and several factors related to mortality were collected. The severity of heart disease was assessed using the New York Heart Association (NYHA) functional class and Canadian Cardiovascular Society angina grade. EuroSCORE II was calculated for the prediction of the risk of mortality. We excluded patients with incomplete data, those who had not received IVIR despite being anemic, and those who received RBC suspension prior to surgery (Figure 1).

The primary endpoint was 30-day mortality between the anemic and nonanemic groups. Secondary endpoints were the duration of cardiopulmonary bypass (CPB) and aortic cross-clamp, ICU length of stay, hospital length of stay, and in-hospital mortality. Additionally, several features including demographic characteristics, pre-operative measures, surgical procedure, post-operative complications, and survival measures were analyzed between survivors and nonsurvivors.

Statistical analysis

The data collected were analyzed using IBM SPSS version 20.0 software (IBM Corp., Armonk, NY, USA). Categorical variables were presented as frequencies and proportions, while continuous variables were expressed as mean ± standard deviation (SD) (min-max) and medians (interquartile range), depending on the distribution of the data. Comparisons for continuous data were made using the independent samples t-test or the Mann-Whitney U test, depending on whether the data were parametric. The chi-square test was used to compare categorical variables. Variables that were found to be significant in the univariate analysis underwent multivariate analysis using logistic regression. A p-value <0.05 was considered statistically significant.

RESULTS

The study analyzed the outcomes of 193 patients (142 males, 51 females; mean age: 62±10 years; range, 27 to 82 years), of whom 173 (89.6%) survived, and 20 (10.4%) did not. The data are summarized in Table 1. Age was a significant factor, with surviving patients being younger than those who died. Lower body mass index was associated with worse outcomes. Congestive heart failure and a history of cerebrovascular events were significantly

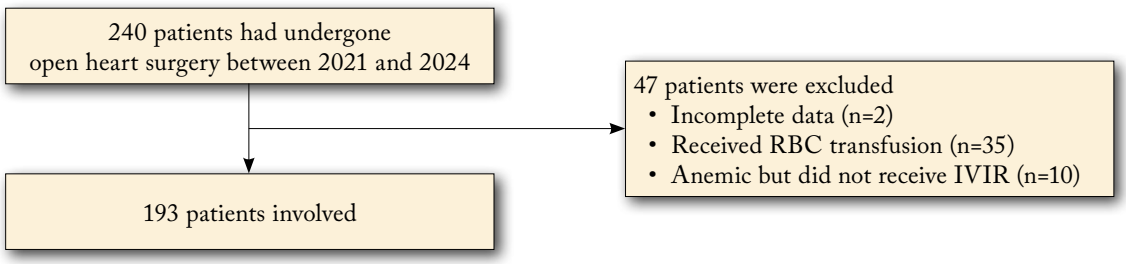

Figure 1. Flowchart on the selection of the patients.
RBC: Red blood cell; IVIR: Intravenous iron replacement.

Table 1
Characteristics of the patients

	Total						Survivors group						Nonsurvivors group						
	n	%	Mean±SD	Median	Min-Max	IQR	n	%	Mean±SD	Median	Min-Max	IQR	n	%	Mean±SD	Median	Min-Max	IQR	*p*
Demographics																			
Age (year)			62±10		27-82				61±10		27-82				69±7		58-82		0.002*
Sex																			0.879**
Male	142						127						15						
Female	51						46						5						
Body mass index (kg/m²)				26.6		24.6-29.7				26.8		25.0-29.7				25.1		23.3-28.0	**0.039†**
Body surface area (m²)			1.9±0.2		1.3-2.5				1.9±0.2		1.4-2.5				1.8±0.2		1.3-2.3		0.356*
Active smoker	55	28.5					50	28.9					5	25.0					0.714**
Comorbidites																			
Hyperlipidemia	153	79.4					138	79.8					15	75.0					0.618**
Hypertension	138	71.5					124	71.7					14	70.0					0.875**
Chronic kidney disease	95	49.2					82	47.4					13	65.0					0.136**
Diabetes mellitus	81	42.0					74	42.8					7	35.0					0.505**
Congestive heart failure	45	23.3					36	20.8					9	45.0					0.015**
Atrial fibrillation	23	11.9					20	11.6					3	15.0					0.875**
History of serebrovascular event	23	11.9					20	11.6					3	15.0					0.012**
Carotis artery disease	22	11.4					19	11.0					3	15.0					0.405**
History of rheumatic heart disease	15	7.8					14	8.1					1	5.0					0.523**
Peripheral artery disease	10	5.2					8	4.6					2	10.0					0.277**
Chronic obstructive pulmonary disease	9	4.7					6	3.5					3	15.0					0.054**
Chronic liver disease	1	0.5					1	0.6					0	0					0.896**
New York Heart Association Functional Classes																			0.077**
I	104	53.9					98	56.6					6	30.0					
II	58	30.1					29	28.3					9	45.0					
III	31	16.1					26	15.0					5	25.0					
IV	0	0					0	0					0	0					
Canadian Cardiovascular Society Angina Grade (of 136 patients)																			**0.021****
I	36	26.5					34	27.6					2	15.4					
II	74	54.4					69	56.1					5	38.5					
III	22	16.2					16	13.0					6	46.2					
IV	4	2.9					4	3.3					0	0					
Hematological medications																			
Acetylsalicylic acid	123	63.7					112	64.7					11	55.0					0.391**
P2Y12 inhibitors	62	32.1					56	32.4					6	30.0					0.830**
Low molecular weight heparin	19	9.8					18	10.4					1	5.0					0.387**
Direct oral anticoagulants	12	6.2					10	5.8					2	10.0					0.359**
Warfarin	7	3.6					7	4.0					0	0					0.459**

Table 1
Continued

	Total						Survivors group						Nonsurvivors group						
	n	%	Mean±SD	Median	Min-Max	IQR	n	%	Mean±SD	Median	Min-Max	IQR	n	%	Mean±SD	Median	Min-Max	IQR	*p*
Preoperative measures																			
Selected laboratory results																			
Hemoglobin (g/dL)				13.4		11.5-14.3				13.6		11.78-14.4				12.5		11.1-13.3	**0.044**†
Hematocrit (%)				40.3		35.0-43.3				40.9		35.6-43.4				37.0		34.1-40.0	**0.056**†
Platelet count (×10³/mm³)			256±82		103-591				257±83		103-591				249±81		119-376		0.684*
International normalized ratio				1.03		0.96-1.10				1.02		0.96-1.10				1.05		0.97-1.14	0.224†
Alanine aminotransferase				17		12-24				18		12-25				13		7-19	**0.019**†
Creatinine (mg/dL)				0.93		0.76-1.10				0.92		0.76-1.10				1.00		0.82-1.12	0.288†
Glomerular filtration rate (mL/min)			95±40		10-229				98±40		10-229				73±31		12-125		**0.008***
Calcium (mg/dL)			9.1±0.5		7.7-10.5				9.2±0.4		7.7-10.5				8.7±0.5		7.8-9.8		**<0.001***
Potassium (mg/dL)			4.3±0.4		3.3-5.8				4.3±0.4		3.3-5.8				4.4±0.6		3.5-5.7		0.525*
Serum iron			73±32		13-174				73±32		13-174				73±25		33-104		0.958*
Ferritin				108		59-191				108		58-191				108		68-204	0.628†
Iron binding capacity				225		184-288				228		189-304				187		160-206	**0.003**†
Transferrin saturation				25.2		17.6-34.0				25.0		17.5-33.5				30.7		17.6-39.6	0.229†
Folic acid				7.9		5.1-10.0				7.9		5.2-10.1				7.4		4.0-9.2	0.162†
Vitamin B12				367		262-532				369		264-554				357		254-478	0.602†
Left ventricular ejection fraction (%)			53±9		25-70				53±9		25-70				50±10		25-65		0.164*
Anemia	67	34.7					57	32.9					10	50.0					0.129**
Thrombocytopenia	11	5.7					8	4.6					3	15.0					0.092**
Hypofibrinogenemia	66	34.2					57	32.9					9	45.0					0.282**
History of balloon angioplasty	26	13.5					25	14.5					1	5.0					0.212**
<2 weeks	7	26.9					7	28.0					0	0					
2-4 weeks	6	23.1					6	24.0					0	0					
>4 weeks	13	50.0					12	48.0					1	100					
History of coronary stents	40	20.7					35	20.2					5	25.0					0.618**
<3 months	16	40.0					15	42.9					1	20.0					
3-6 months	4	10.0					3	8.6					1	20.0					
>6 months	20	50.0					17	48.6					3	60.0					
Bleeding risk																			**0.006****
Low	108	56.0					102	59.0					6	30.0					
Intermediate	77	39.9					66	38.2					11	55.0					
High	8	4.1					5	2.9					3	15.0					
Preoperative measures																			
Thrombosis risk																			0.481**
Low	19	9.8					18	10.4					1	5.0					
Intermediate	4	2.1					3	1.7					1	5.0					
High	170	88.1					152	87.9					18	90.0					
EuroSCORE II				1.30		0.87-2.90				1.21		0.83-2.55				2.75		1.30-6.56	**0.002**†
CHA_2DS_2-VASc score (of 23 patients)				2		2-4				2		2-3				4		3-Nd	0.090†
Shock	1	0.5					0	0					1	5.0					0.104**
Preoperative medication																			
Anticoagulant bridge	16	8.3					15	8.7					1	5.0					0.487**
Antithrombotic bridge	16	8.3					15	8.7					1	5.0					0.487**
Antifibrinolytic	132	68.4					123	71.1					9	45.0					**0.017****
Intravenous iron supplementation	67	34.7					57	32.9					10	50.0					0.129**

Table 1
Continued

	Total						Survivors group						Nonsurvivors group						
	n	%	Mean±SD	Median	Min-Max	IQR	n	%	Mean±SD	Median	Min-Max	IQR	n	%	Mean±SD	Median	Min-Max	IQR	*p*
Surgical procedure																			
Operation type																			0.375**
Coronary artery bypass graft surgery	122	63.2					112	64.7					10	50.0					
Valvular surgery	26	13.5					23	13.3					3	15.0					
Combined surgery	45	23.3					38	22.0					7	35.0					
Redo operation	3	1.6					3	1.7					0	0					0.719**
Operation timing																			**0.005****
Emergent	11	5.7					7	4.0					4	20.0					
Early	23	11.9					19	11.0					4	20.0					
Elective	159	82.4					147	85.0					12	60.0					
Off-pump procedure	9	4.7					9	5.2					0	0					0.365**
Minimal invasive extra-corporeal circulation	35/184	19.0					31/164	18.9					4/20	20.0					0.553**
Cardiopulmonary bypass time (min)			124±48		28-365				120±43		28-255				156±72		61-365		**0.002***
Aortic cross-clamp duration (min)			83±32		20-179				83±33		20-179				87±30		42-178		0.603*
Lowest body temperature (°C)			30.4±1.6		26.0-35.0				30.5±1.6		26.0-35.0				29.7±2.1		26.0-32.0		**0.044***
Postoperative complications																			
Arrhythmia	60	31.1					46	36.6					14	70.0					**<0.001****
Atrial fibrillation	47	24.4					39	22.5					12	60.0					
Ventricular fibrillation	12	6.2					5	2.9					7	35.0					
Ventricular tachycardia	7	3.6					3	1.7					4	20.0					
Atrioventricular block	5	2.6					1	0.6					4	20.0					
Low cardiac output state	53	27.5					40	23.1					13	65.0					**<0.001****
Intra-aortic balloon pump	19	9.8					8	4.6					8	40.0					**<0.001****
Myocardial infarction	5	2.6					2	1.2					3	15.0					**0.008****
Reexploration	7	3.6					2	1.2					5	25.0					**<0.001****
Late tamponade	4	2.1					3	1.7					1	5.0					0.357**
Erythrocyte replacement (units)				2		1-4				2		0-3				7		3-11	**<0.001**†
Acute renal failure	69	35.8					56	32.3					13	65.0					**<0.001****
Respiratory complications																			**0.002****
Pneumonia	19	9.8					12	6.9					7	35.0					
Pulmonary edema	18	9.3					14	8.1					4	20.0					
Adult respiratory distress syndrome	13	6.7					10	5.8					3	15.0					
Atelectasis	9	4.7					9	5.2					0	0					
TRALI	4	2.1					3	1.7					1	5.0					
Pulmonary thromboembolism	2	1.0					0	0					2	10.0					
Others	9	4.7					6	3.5					3	15.0					

Table 1
Continued

	Total						Survivors group						Nonsurvivors group						
	n	%	Mean±SD	Median	Min-Max	IQR	n	%	Mean±SD	Median	Min-Max	IQR	n	%	Mean±SD	Median	Min-Max	IQR	*p*
Surgical procedure																			
Surgical site infections	13	6.8					12	7.0					1	5.0					0.238**
Superficial	2	1.0					2	1.2					0	0					0.803**
Mediastinitis																			
Gastrointestinal system complications	4	2.1					2	1.2					2	10.0					0.054**
Serebrovascular event	5	2.6					0	0					5	25.0					<0.001**
Disseminated intravascular coagulation	11	5.7					5	2.9					6	30.0					<0.001**
Survival measures																			
Intensive care unit stay (days)				3		2-4				3		2-4				4		1-13	0.166†
Mechanical ventilation duration (h)				9		6-14				9		6-13				18		13-82	**<0.001†**
Hospital stay (days)				7		6-11				7		6-10				6		1-18	0.504†
In-hospital mortality	18	9.3					-	-					-	-					
30-day mortality	20	10.4					-	-					-	-					

SD: Standard deviation; IQR: Interquartile range; EuroSCORE: The European System for Cardiac Operative Risk Evaluation; VAS: Visual Analog Scale; TRALI: Transfusion-related acute lung injury; * Independent samples t test; ** Chi-squared test; † Mann-Whitney U test; Nd: Not defined.

associated with mortality. In this study, it was found that common comorbidities, such as hyperlipidemia, hypertension, chronic kidney disease, and diabetes mellitus, did not have a significant impact on mortality. Although there was no significant difference in the distribution of NYHA functional classes, there was a significant difference in the Canadian Cardiovascular Society Angina Grade. With respect to medication, there were no significant differences observed in the use of acetylsalicylic acid, P2Y12 inhibitors, low-molecular-weight heparin, direct oral anticoagulants, or warfarin between survivors and nonsurvivors.

Nonsurvivors had lower hemoglobin levels, and there was a significant difference in iron binding capacity between the two groups. The presence of WHO-defined anemia was not different between survivors and nonsurvivors, which may be related to sex-related cut-offs. Nonsurvivors had lower alanine aminotransferase levels and reduced glomerular filtration rates.

Periprocedural data

Although specific cardiovascular risk scores, such as EuroSCORE (European System for Cardiac Operative Risk Evaluation) II, showed a significant divergence indicating a higher predicted risk in nonsurvivors, other clinical and procedural history factors, such as a history of balloon angioplasty or coronary stents, did not show a statistical difference in distribution between survivors and nonsurvivors. When considering bleeding and thrombotic risks, a significantly higher proportion of nonsurvivors were classified into higher bleeding risk categories.

No significant differences were found in the types of surgery performed or in the rates of reoperation between survivors and nonsurvivors when analyzing surgical procedures. However, the timing of surgery emerged as a significant factor. Emergent and early surgery had a higher percentage of nonsurvivors compared to elective surgery. In terms of the technical aspects of surgery, nonsurvivors had a significantly longer CPB time. However, there were no significant differences between the groups in terms of the duration of aortic cross-clamping or the use of off-pump or minimally invasive extracorporeal circulation.

When analyzing postoperative complications, it was found that nonsurvivors experienced significantly more arrhythmias, including atrial fibrillation,

ventricular fibrillation, ventricular tachycardia, and atrioventricular block. Nonsurvivors also had higher rates of low cardiac output, requiring intra-aortic balloon pump support. Nonsurvivors had significantly higher rates of myocardial infarction and reexploration for bleeding or tamponade. The difference in RBC transfusion between survivors and nonsurvivors highlights the impact of anemia and the need for blood transfusions on mortality. The median RBC transfusion in the survivors and nonsurvivors groups was 2 and 7 units, respectively (p<0.001). Additionally, nonsurvivors experienced significantly more acute renal failure and respiratory complications, such as pneumonia, pulmonary edema, and adult respiratory distress syndrome.

Survival analysis

The survival analysis showed no significant difference in the median length of stay in the intensive care unit (ICU) between survivors and nonsurvivors. However, the duration of mechanical ventilation was significantly longer in nonsurvivors. It is worth noting that the median length of hospital stay did not differ significantly between the survivors and nonsurvivors groups. The rates of in-hospital and 30-day mortality provide a direct measure of short-term outcomes after cardiovascular surgery, with rates of 9.3% and 10.4%, respectively. The multivariate analysis revealed that CPB time (hazard ratio=1.019, 95% confidence interval [CI]: 1.006-1.033, p=0.004) and the development of newly onset acute renal failure (hazard ratio=36.8, 95% CI: 4.7-284.9, p=0.001) were two independent risk factors for 30-day mortality.

Main endpoints

When comparing anemic patients who received IVIR to those without anemia, significant differences were observed in the NYHA functional class (p=0.001) and the prevalence of congestive heart failure. Anemic patients had higher NYHA classes and a higher prevalence of congestive heart failure (37.3% in anemic patients *vs.* 15.9% in nonanemic patients, p=0.001). Furthermore, it was discovered that anemic patients have a higher preoperative bleeding risk score (p=0.001). The difference in EuroSCORE II scores between anemic and nonanemic patients (median score: 1.79 *vs.* 1.15; p=0.003) emphasizes the higher risk profile of anemic patients. It is worth noting that there was a slightly higher incidence of emergent cases in nonanemic patients (%7.1 *vs.* %3.0 p=0.040). There were no significant differences in the duration of CPB and aortic cross-clamp, ICU length of stay, hospital length of stay, in-hospital mortality, and 30-day mortality between the anemic and nonanemic groups.

DISCUSSION

Several studies have demonstrated that patients with anemia experience worse outcomes after cardiovascular surgery.[11-16] This phenomenon may be due not only to characteristics inherent to anemia itself but also to the fact that anemia is often associated with other comorbidities, suggesting that it may reflect the underlying frailty of the patient.[17] In a meta-analysis that included 35 studies with a total of 159,025 patients, preoperative anemia was associated with an increased risk of death (odds ratio=2.5, 95% CI: 2.2-2.9, p<0.001).[18] Meta-regression analysis revealed that lower hemoglobin levels and studies with a lower proportion of male patients were associated with an increased risk of mortality. Additionally, preoperative anemia was linked to longer hospital stays and an increase in postoperative complications.

Given the significant role of anemia as a factor, the importance of its correction and management prior to surgery has often been studied. Several publications discuss managing anemic patients before surgery, particularly with regard to IVIR therapy. Cladellas et al.[7] conducted a study to assess the effects of treating anemia with recombinant human erythropoietin and iron prior to cardiac surgery on postoperative outcomes and RBC transfusion needs. The study compared a group of 75 patients who received recombinant human erythropoietin at a dose of 500 IU/kg/day for four weeks and a fifth dose 48 h prior to surgery, along with IV iron sucrose supplementation, with an observation group of 59 untreated patients. After adjusting for confounding variables, the study found that the combined therapy was independently associated with reduced postoperative morbidity and in-hospital mortality. Specifically, the intervention reduced postoperative renal failure, decreased the rate of RBC transfusion from 93% in the observation cohort to 67%, and shortened hospital stays.

In their study, Spahn et al.[8] investigated the impact of immediate preoperative combination treatment on reducing perioperative RBC transfusions and improving outcomes in patients with anemia or isolated iron deficiency who were scheduled for elective cardiac surgery. The study involved 505 patients

who were randomly assigned to receive either a placebo or a combination treatment comprising IV ferric carboxymaltose, subcutaneous erythropoietin alpha, vitamin B12, and oral folic acid on the day before surgery. The primary outcome was the number of RBC transfusions during the first seven days after surgery. The combination treatment led to a significant reduction in the median number of RBC transfusions required during the first seven days. Similar reductions were observed on the postoperative Day 90. Additionally, patients in the treatment group exhibited higher hemoglobin concentrations, reticulocyte counts, and reticulocyte hemoglobin content during the first seven days.

Another study by Evans et al.[19] aimed to evaluate the effectiveness of preoperative IV iron administration in anemic patients undergoing cardiac surgery. Out of the 447 patients analyzed, 75 (17%) were anemic and received IV iron treatment, while 72 (16%) were anemic but did not receive any treatment. The aim of the treatment was to achieve a hemoglobin level of ≥130 g/L on the day of surgery. The anemic patients who were successfully treated showed a mean increase in hemoglobin of 17 g/L and received significantly fewer blood transfusions than the untreated anemic patients. The study concluded that anemic patients who were successfully treated required less blood perioperatively. More than half of these patients did not require any transfusion at all.

Klein et al.[20] conducted a prospective multicenter study to investigate the feasibility and effectiveness of introducing a preoperative IV iron service as a national initiative in cardiac surgery. The primary feasibility outcome was to determine if the clinics could be established, while the primary effectiveness outcome was the change in hemoglobin concentration between intervention and surgery. The study found that out of 11 hospitals, seven successfully established iron clinics and recruited 228 patients. Patients with anemia who received IV iron showed a significant increase in hemoglobin concentration from baseline to preoperative, with a mean increase of 8.4 g/L ($p<0.001$). However, despite the increase in hemoglobin, the study was unable to demonstrate an effect on transfusion rates or patient outcomes, possibly due to the small sample size.

Another study by Kong et al.[21] aimed to determine an effective treatment for preoperative anemia associated with iron deficiency in elective cardiac surgery patients. The study was a single-center, open-label, randomized trial involving 156 participants. It compared the effectiveness of IV ferric derisomaltose and subcutaneous darbepoetin (intervention group) to oral ferrous sulfate (control group) in patients with low preoperative hemoglobin levels and iron deficiency. The study's main results indicate that the intervention group had significantly lower odds of requiring RBC transfusion compared to the control group. Additionally, there was a significant increase in hemoglobin levels from randomization to surgery in the intervention group.

Shokri and Ali[22] assessed the impact of preoperative IV iron infusion on hemoglobin levels, blood transfusion needs, and the occurrence of postoperative adverse events in patients undergoing coronary artery bypass grafting. The randomized study enrolled 80 patients aged 52 to 67 years who were assigned to receive either IV ferric carboxymaltose (iron group) or saline (placebo group) seven days before surgery. The study revealed that iron therapy was linked to a lower incidence of anemia four weeks after discharge, significantly higher Hb levels preoperatively, postoperatively, and four weeks after discharge, and shorter hospital and ICU stays. Additionally, iron therapy led to a decreased requirement for packed RBCs after the operation. The study concluded that the treatment is associated with higher postoperative hemoglobin levels, shorter hospital and ICU stays, and reduced perioperative RBC transfusion requirements.

Jafari et al.[23] conducted a study to assess the effectiveness of IV iron sucrose and erythropoietin in reducing transfusion requirements for patients with preoperative iron deficiency anemia undergoing on-pump coronary artery bypass grafting surgery. The study was an open-label, randomized clinical trial that enrolled 114 patients who were divided into two groups: intervention (iron plus erythropoietin) and control. The intervention group received a 200 mg IV dose of iron sucrose and a 100 IU/kg bolus of erythropoietin one to two days prior to surgery. The results showed a significant reduction in the number of RBC units transfused per patient in the intervention group compared to the control group. Additionally, the intervention group exhibited a noteworthy rise in ferritin levels on the seventh postoperative day and experienced shorter stays in both the ICU and hospital. No adverse events were reported in either group.

After evaluating all presented studies, it is observed that administering IVIR to anemic patients before cardiovascular surgery results in positive outcomes for the examined endpoints. However, some publications report contrary results. A recent meta-analysis on the impact of anemia on outcomes after cardiac surgery also conducted a secondary analysis of seven studies involving 1,012 patients and found that short-term preoperative treatments for anemia did not significantly reduce mortality.[18] Similarly, Quarterman et al.[24] presented a retrospective observational review from January 2017 to December 2019. The study evaluated the effectiveness of preoperative IV iron in treating patients with iron deficiency anemia scheduled for elective cardiac surgery. Among the 190 patients who received IV iron, there was a median increase in hemoglobin of 8.0 g/L. However, patients who received IV iron had a significantly higher incidence of transfusion (60%) compared to the nonanemic cohort (22%). Additionally, the treated group had significantly higher rates of new need for renal replacement therapy and stroke, but there was no significant difference in in-hospital mortality.

The present study indicates that patients with anemia who received IVIR prior to cardiovascular surgery had perioperative outcomes comparable to those of nonanemic patients. This includes similar lengths of ICU and hospital stays, as well as in-hospital and 30-day mortality rates. This is consistent with most published literature. These findings suggest that IVIR is a viable strategy to improve the surgical readiness of anemic patients and to bring their outcomes in line with those of their nonanemic counterparts. However, the precise mechanisms by which IV iron influences surgical outcomes, particularly through potential effects on cellular functions, remain to be fully understood.

It is important to note that this study has several limitations. These limitations include its retrospective and observational nature, patient selection based on specific criteria, lack of comparative data with nonsupplemented anemic patients, and exclusion of nonanemic patients who were indicated for iron supplementation. Due to its observational nature, this study cannot establish a cause-and-effect relationship regarding the mechanism of action of iron supplementation.

In conclusion, perioperative outcomes for anemic patients who received IVIR did not differ from patients without anemia. Nonetheless, nonsurvivors had lower preoperative hemoglobin levels, suggesting that more severe anemia may be associated with poorer outcomes. The findings suggest that short-term IVIR may positively impact immediate surgical outcomes, although it is important to consider that many factors influence the complex process of cardiovascular surgery. In addition to correcting hemoglobin levels, further investigation is needed to determine the potential impact of IVIR on cellular function and overall patient recovery and outcomes.

Ethics Committee Approval: The study protocol was approved by the Izmir Bakırçay University Ethics Committee (date: 21.02.2024, no: 210224/1467). The study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guideline. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Patient Consent for Publication: A written informed consent was obtained from each patient.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

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