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Acute Hepatic Injury Following Cardiac Surgery: Retrospective Observational Study

Kardiyak Cerrahi Sonrası Akut Karaciğer Hasarı: Retrospektif Gözlemsel Çalışma

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ABSTRACT

Objective: Cardiopulmonary bypass (CPB) and cardiac surgery can have multiple systemic effects on the patient. This retrospective study aims to investigate the effect of this change on liver enzymes.

Methods: Demographic data, comorbidities, preoperative and postoperative laboratory data, intraoperative cross-clamp and CPB duration, blood and blood product transfusions, and fluid balance of 390 patients who underwent on-pump coronary artery bypass grafting (CABG) were retrospectively reviewed. Patients with a twofold or greater increase in postoperative alanine transaminase were considered to have an acute hepatic injury (Group AHI). Multivariate logistic regression was performed to find independent predictors for AHI.

Results: Body mass index, hyperlipidemia, and diabetic patients were significantly higher in group AHI (p<0.05). Similarly, fresh frozen plasma (FFP) transfusion, platelet transfusion, and the need for insulin, dopamine, and adrenaline were observed to be higher in the AHI group in the intraoperative period (p<0.05).Cardiopulmonary bypass time was longer and total urine volume was less in Group AHI (p<0.05). The need for intraaortic balloon pump (IABP) and/or extracorporeal membrane oxygenation (ECMO) on weaning from the CPB pump was seen in more patients in Group AHI (p=0.021). According to the results of multivariate logistic regression analysis, it was determined that the risk of AHI is 2.27 (1.144-4.543, 95% CI, p=0.019) times higher in hyperlipidemic patients, 2.84 (1.077-7.494, 95% CI, p=0.35) times higher in patients who need intraoperative 3-4 units of FFP, and 4.37 (1.107-17.264, 95% CI, p=0.035) times higher in patients who need IABP and/or ECMO after CPB.

Conclusion: There is a strong relationship between AHI after cardiac surgery and hyperplidemia, FFP transfusion, and the need for IABP and/or ECMO.

Keywords: Acute hepatic injury, cardiac surgery, cardiopulmonary bypass

ÖZ

Amaç: Kardiyopulmoner bypass (KPB) ve kardiyak cerrahi, vücut organları üzerinde çok sayıda sistemik etkiye sahip olabilir. Bu retrospektif çalışmanın amacı bu değişikliğin karaciğer enzimleri üzerindeki etkisini araştırmaktır.

Yöntem: On-pump koroner arter bypass greftleme (KABG) uygulanan 390 hastanın demografik verileri, komorbiditeler, preoperatif ve postoperatif laboratuvar verileri, intraoperatif kross klemp ve KPB süreleri, kan ve kan ürünü transfüzyonları, sıvı balansı, retrospektif olarak tarandı. Postoperatif alanin transaminaz değerine göre iki kat ve daha fazla artış görülmesi akut hepatik hasar (Grup AHI) olarak kabul edildi. Akut hepatik hasar bağımsız prediktörlerinin bulunması için çok değişkenli lojistik regresyon yapıldı.

Bulgular: Grup AHI'de vücut kitle indeksi ve hiperlipidemi ile diabetes mellitusu olan hasta oranı anlamlı olarak yüksekti (p<0,05). Benzer şekilde intraoperatif dönemde taze donmuş plazma (TDP), trombosit transfüzyonu ve insülin, dopamin ve adrenalin ihtiyacı AHI grubunda daha yüksek bulundu (p<0,05). Grup AHI'da KPB süresi daha uzun ve toplam idrar hacmi daha azdı (p<0,05). Kardiyopulmoner bypass pompasından ayırmada intraaortik balon pompası (İABP) ve/veya ekstrakorporeal membran oksijenasyonu (ECMO) ihtiyacı Grup AHI'de daha fazla hastada görüldü (p=0,021). Çok değişkenli lojistik regresyon analiz sonuçlarına göre, hiperlipidemisi olan hastalarda 2,27 (1,144-4,543, %95 CI, p=0,019), intraoperatif 3-4 ünite TDP ihtiyacı olan hastalarda 2,84 (1,077-7,494, %95 CI, p=0,035) ve KPB çıkışı İABP ve/veya ECMO ihtiyacı olan hastalarda 4,37 (1,107-17,264, %95 CI, p=0,035) kat fazla AHI görülme riski vardı.

Sonuç: Hiperplidemi, TDP transfüzyonu ve İABP ve/veya ECMO ihtiyacı ile kardiyak cerrahi sonrası AHI arasında sağlam bir ilişki vardır.

Anahtar sözcükler: Akut karaciğer hasarı, kardiyak cerrahi, kardiyopulmoner bypass

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INTRODUCTION

During cardiac surgery, the cardiopulmonary bypass (CPB) machine has various impacts on the body, including the liver. Organ blood flows are provided by non-pulsatile flow and relatively low pressures. Moreover, anesthetics, antibiotics, and anticoagulant drugs are frequently administered during cardiac surgery, which can affect liver functionality and potentially contribute to acute hepatic injury (AHI). This effect on the liver might be exacerbated in people with underlying liver disease or risk factors. Occurrence of hepatic injury following cardiac surgery is considered an uncommon postoperative complication that has been limitedly mentioned in the literature (1). The incidence of hepatic failure after cardiac surgery is 4%, however, as many as 10% of patients undergoing CPB experience some degree of liver damage (1,2). This temporary and mild elevation in liver function tests is frequently observed after cardiac surgery, and studies focusing on the mechanism of this hepatic injury are needed.

The primary pathophysiological mechanisms underlying liver damage during cardiac surgery involve liver ischemia-reperfusion resulting from CPB, systemic inflammatory response syndrome due to acute inflammation, and oxidative stress (3,4). The release of catecholamines at the outset of CPB leads to a reduction of hepatic perfusion by 20% and hepatic arterial flow by as much as 45% (5). While the hepatic artery contributes 20-25% of the blood supply to the liver, the portal system furnishes 75-80%. This combination of dual oxygen delivery and the liver's near 95% oxygen extraction rate make the liver relatively resistant to necrosis due to hypoperfusion. Nonetheless, a marked decrease in perfusion or severe hypoxemia may override protective mechanisms and result in hypoxic hepatic injury (6). An additional causative factor is indirectly related to bacterial translocation and endotoxemia arising from damage to the intestinal mucosal barrier (7,8). Medications administered during the intraoperative and postoperative periods also contribute to liver damage (9). Patient-specific risk factors for hepatic injury include advanced age, right heart failure, moderate to severe tricuspid regurgitation, pulmonary hypertension (pulmonary artery systolic pressure >45 mmHg), New York Heart Association class II to IV, and low ejection fraction (10). Furthermore, compromised postoperative cardiac function, excessive demand for blood transfusion, arrhythmia, renal dysfunction, requirement for ventilation surpassing 24 hours, and the necessity for re-operation may also lead to hepatic damage (11).

Risk factors such as age and duration of CPB are inherent variables that can contribute to liver damage. Conversely, factors such as drug toxicity and blood transfusion are modifiable and can be optimized. As a result, identifying these risk factors based on the patient demographics specific to each medical facility has the potential to enhance the quality of anesthesia management during both the intraoperative and postoperative phases, consequently leading to improved patient outcomes and survival rates.

Consequently, in this study, we comprehensively investigated a multitude of factors encompassing patient characteristics, surgical variables, and procedural aspects. These factors are believed to exert an influence on AHI subsequent to cardiac surgery. To achieve this, we constructed a multivariate model with the aim of identifying predictive indicators for the occurrence of AHI.

MATERIAL and METHODS

This retrospective observational cross-sectional study was conducted in adherence to the principles of the Helsinki Declaration and received approval from the local clinical research ethics committee (E1-23-3536. 26.04.2023). The study involved a review of patients who underwent isolated on-pump coronary artery bypass grafting (CABG) surgery within the timeframe of January 2021 to March 2021. Data were retrospectively extracted from electronic medical records, as well as from anesthesia and intensive care observation documents. Exclusion criteria included preoperative liver disease, abnormal liver enzyme levels, or lack of information pertaining to transaminase levels. Additionally, patients requiring preoperative inotropic medications, intraaortic balloon pump (IABP) or extracorporeal membrane oxygenation (ECMO) support, individuals diagnosed with autoimmune hepatitis or infective hepatitis, and cases involving emergency surgeries were excluded from the study. A total of 390 patients, meeting the established inclusion criteria from an initial pool of 427 adult patients, were subjected to comprehensive statistical analysis. The need for informed consent was waived for this retrospective study.

A consistent surgical technique was employed for all patients. Induction of anesthesia in both groups involved the administration of midazolam, propofol, fentanyl, and rocuronium. Patients management during the anesthesia maintenance phase was also standardized. General anesthesia was sustained using either 2% propofol/remifentanil or sevoflurane/remifentanil, maintaining a bispectral index within the range of 35-45. Following anesthesia induction, the procedure commenced with a median sternotomy, subsequently progressing to standard aortic and atrial cannulation. Cardiopulmonary bypass was established through the utilization of membrane oxygenation, non-pulsatile perfusion, and moderate systemic hypothermia. Myocardial protection was achieved by means of cold hyperkalemic crystalloid cardioplegia, in conjunction with topical cooling utilizing ice water and cold saline solution. Cardioplegia was administered retrograde and ante-

grade to all patients. The majority of cases involved CABG employing the left internal mammary artery and saphenous veins. Erythrocyte concentrate transfusion was initiated when the hemoglobin (Hb) level fell below 7.5 g dL^{-1}. In the postoperative period within the open heart surgery intensive care unit (ICU), blood transfusion was initiated if the Hb level dropped to 8 g dL^{-1} or less. Furthermore, the administration of fresh frozen plasma (FFP), platelets or cryoprecipitate was undertaken in instances of active bleeding (exceeding 200 mL h^{-1} over 3 consecutive hours) and coagulation abnormalities (platelet count less than $80x10^3$, prothrombin time or activated partial thromboplastin time > 1.5- times the normal value, and significant hypofibrinogenemia below 100 mg dL^{-1}).

Demographic data (age, gender, body mass index), along with any existing comorbidities, ejection fraction values, anesthesia methodology, inotropic/vasopressor requirements, blood and blood product transfusion, total intravenous fluid administration, urine output measurements, CPB durations, and cross-clamp (CC) times of the patients were recorded. Laboratory data encompassing Hemoglobin A1c, fasting blood glucose levels, serum creatinine (sCr), estimated glomerular filtration rate (eGFR), aspartate transaminase (AST), alanine transaminase (ALT), alkaline phosphatase (ALP), lactate dehydrogenase (LDH), γ-glutamyltransferase (GGT), direct bilirubin, white blood cells (WBC), Hb, thrombocyte count, and lactate levels were scrutinized both before and after the surgery.

A hallmark indication of hepatocellular damage is the elevation of ALT and AST, which occurs due to the release of hepatocytes into circulation owing to cell membrane dysfunction. The increase in levels of liver enzymes (AST and/or ALT) is categorized into borderline, mild, moderate, severe, and massive grades according to the evaluation guidelines for abnormal liver enzymes set fourth by the American College of Gastroenterology (ACG) (12). Aspartate transaminase, however, is less specific due to its presence in other tissues such as skeletal muscles, heart muscles, kidneys, and the brain. Consequently, patients exhibiting a two-fold or greater rise in the first postoperative ALT value (classified as mild or higher grade as per the ACG guideline) were classified as AHI and were assigned to Group AHI. Group Non-AHI (non- acute hepatic injury) consisted of patients who displayed normal or less than two-fold (borderline high) increase in postoperative ALT. Postoperative outcome parameters encompassed extubation duration, inotropic drug requirements, necessity for ECMO or IABP, utilization of renal replacement therapy (RRT), length of stay in the hospital and ICU, as well as 30-day mortality rates.

Statistical Analysis

International Business Machines Statistical Package for the Social Sciences (SPSS) 26.0 software was used for all data analysis. The Kolmogorov-Smirnov test was used to determine the normality of the data distribution. Continuous variables were expressed as mean ± standard deviation for normal distributed data and as the median-interquartile range (IQR, 25^{th} to 75^{th} percentiles) for non-normally distributed data. Categorical variables were presented in numbers (n) and percentages (%). Continuous variables were compared using t-tests or the Mann-Whitney U test for independent samples. Categorical variables were compared using chi-square tests. A p-value of <0.05 was considered statistically significant for all analyses. A univariate logistic regression analysis was used to identify potential risk factors for AHI, and the multivariate model only included variables that were significant in the univariate analysis. A Hosmer-Lemeshow test was used to test the model fit. A logistic regression analysis was used to calculate the correlation coefficients for the relationships between variables that showed collinearity with each other and revealed the odds ratios and %95 confidence intervals. The number of cases between the specified dates determined the sample size and posthoc power analysis was performed on the number of existing patients. A post-hoc power analysis was performed with G* Power 3.1.9.7 statistical package program for the independent risk factors for AHI. At a 0.05 margin of type I error, the power of the independent risk factor with the lowest OR (Hyperlipidemia, OR:2.279) was 0.85 in the given sample size.

RESULTS

Out of the 390 patients who underwent on-pump CABG during the specified 3-month period, mild ALT elevation was observed in 82 (21%) patients, moderate elevation in 35 (8.9%) patients, severe elevation in 4 (1%) patients, and massive elevation in 2 (0.5%) patients, according to the ACG classification, in the first postoperative laboratory results. Demographic data, comorbidities, intraoperative details, and postoperative complications are provided in Table I.

Body mass index, hyperlipidemia, and diabetic patients were significantly more prevalent in group AHI (p<0.001, p=0.041, and p=0.045, respectively). Similarly, Group AHI exhibited higher incidences of FFP transfusion (p=0.027), platelet concentrates transfusion (p=0.016), and the need for insulin (p=0.043), dopamine (p=0.047), and adrenaline (p=0.001) during the intraoperative period. Cardiopulmonary bypass duration (107.05 ± 22.3 and 117.51 ± 21.1 min) (p<0.001) was prolonged and total urine output (950 mL and 700 mL) (p=0.037) was lower in Group AHI. Group AHI showed a higher occurrence of low cardiac output and requirement for IABP and/or ECMO upon weaning off the CPB pump (p=0.021). Upon comparing preoperative and postoperative laboratory data, postoperative ALT, AST, LDH, and lactate values were found to be higher in Group AHI (Table II).

Tablo I: Demographic Data, Comorbidities, Intraoperative and Postoperative Variables

	Group Non-AHI (n=107)	Group AHI (n=283)	p
	Mean ± SD or Median (IQR) or n (%)		
Age (year)	62 (55-69)	61 (54-68)	0.487
Gender (M)	229 (80.9)	93 (86.9)	0.164
BMI (kg m^{-2})	27.50 (27.0-28.6)	30 (29.3-30)	**<0.001**
LVEF	54.94 ± 5.6	53.83 ± 5.1	0.076
HT	126 (44.5)	43 (40.2)	0.441
DM	86 (30.4)	44 (41.1)	**0.045**
COPD	31 (11.0)	11 (10.3)	0.848
HPL	48 (17.0)	28 (26.2)	**0.041**
CKD	19 (6.7)	6 (5.6)	0.691
Stroke/TIA	15 (5.3)	5 (4.7)	0.802
Hypothyroidism	13 (4.6)	10 (9.3)	0.075
Intraoperative period			
Sevoflurane/propofol maintenance	140/143 (49.5/50.5)	65/42 (60.7/39.3)	**0.047**
CC time (min)	71.18 ± 16.6	73.70 ± 16.1	0.181
CPB time (min)	107.05 ± 22.3	117.51 ± 21.1	**<0.001**
Operation time (min)	317.05 ± 66.8	322.67 ± 62.8	0.452
pRBC transfusion None	194 (68.6)	74 (69.2)	0.320
1-3 Units	85 (30.0)	29 (27.1)	
4+ Units	4 (1.4)	4 (3.7)	
FFP transfusion None	239 (84.5)	82 (76.6)	**0.027**
1-2 Units	31 (11.0)	12 (11.2)	
3-5 Units	13 (4.6)	13 (12.1)	
PC transfusion None	275 (97.2)	98 (91.6)	**0.016**
1 Units	8 (2.8)	9 (8.4)	
Intraoperative insulin use	55 (19.4)	31 (29.0)	**0.043**
Intraoperative dopamine use	79 (27.9)	41 (38.3)	**0.047**
Intraoperative dobutamine use	43 (15.2)	15 (14.0)	0.771
Intraoperative norepinephrine use	16 (5.7)	6 (5.6)	0.986
Intraoperative adrenaline use	7 (2.5)	11 (10.3)	**0.00**1
Total intravenous fluid (mL)	1800 (1400-2200)	1500 (1500-2000)	0.566
Urine output (mL)	950 (500-1500)	700 (500-1200)	**0.037**
IABP and/or ECMO	9 (3.1)	12 (11.5)	**0.021**
Postoperative period			
Atrial Fibrillation	18 (6.4)	8 (7.5)	0.693
Renal Replacement Therapy	8 (5.2)	2 (3.8)	0.702
Extubation time >8h	37 (23.9)	14 (26.9)	0.659
Length of ICU stay (hours)	24 (20-30)	24 (22-32)	0.100
Length of hospital stay (days)	9 (7-12)	10 (8-12)	0.320
Mortality 30-day	6 (2.1)	4 (3.7)	0.367

Non-AHI: Non-acute hepatic injury, **AHI**: Acute hepatic injury, **IQR**: Interquartile range, **M**: Male, **BMI**: Body mass index, **LVEF**: Left ventricular ejection fraction, **HT**: Hypertension, **DM**: Diabetes mellitus, **COPD**: Chronic obstructive pulmonary disease, **HPL**: Hyperlipidemia, **CKD**: Chronic kidney disease, **TIA**: Transient ischemic attack, **CC**: Cross-clamp, **CPB**: Cardiopulmonary bypass, **pRBC**: packed red blood cells, **FFP**: Fresh frozen plasma, **PC**: Platelet concentrate, **IABP**: Intraaortic balloon pump, **ECMO**: Extracorporeal membrane oxygenation, **ICU**: Intensive care unit.

Tablo II: Preoperative and Postoperative Laboratory Data

	Preoperative Period			Postoperative Period		
	Group Non-AHI (n=283)	Group AHI (n=107)		Group Non-AHI (n=283)	Group AHI (n=107)	
	Median (IQR)	Median (IQR)	p	Median (IQR)	Median (IQR)	p
Hemoglobin A1c (%)	7.56 (6.7-7.5)	7.56 (6.3-7.8)	0.618	-	-	-
Blood glucose (mg dL^{-1})	116 (92-154)	118.5 (96-153)	0.551	159 (142-185)	170 (150-199)	0.003
Serum creatinine (mg dL^{-1})	0.91 (0.78-1.05)	0.90 (0.81-1.02)	0.854	0.94 (0.78-1.20)	0.97 (0.85-1.13)	0.523
eGFR (mL min^{-1} 1.73 m^{-2})	86 (72-97)	91 (74-96)	0.228	81 (63-97)	82 (68-93)	0.593
ALT (IU L^{-1})	26 (21-33)	27 (20-39)	0.294	23 (17-30)	58 (49-79)	**<0.001**
AST (IU L^{-1})	23 (19-28)	26 (19-34)	0.197	46 (39-60)	84 (64-126)	**<0.001**
Albumin (g L^{-1})	43 (40-45)	43 (40-45)	0.617	32 (29-34)	32 (30-34)	0.823
ALP (IU L^{-1})	77 (67-95)	87 (68-105)	0.053	76 (55-106)	66 (55-83)	0.053
GGT (IU L^{-1})	27 (19-41)	30 (20-49)	0.292	27 (19-46)	28 (19-49)	0.729
LDH (IU L^{-1})	195 (170-249)	201,5 (214-289)	0.629	336 (268-400)	400 (298-568)	**<0.001**
Direct bilirubin (µmol L^{-1})	0.18 (0.1-0.2)	0.17 (0.1-1.2)	0.802	0.2 (0.2-0.3)	0.3 (0.2-0.4)	0.131
White Blood Cells (giga L^{-1})	8.05 (6.9-9.5)	8.28 (6.7-9.7)	0.361	11.4 (9.53-13.76)	11.77 (9.77-13.67)	0.488
Hemoglobin (g dL^{-1})	13.7 (12.4-14.8)	14.1 (12.9-14.7)	0.335	9.4 (8.9-10.1)	9.6 (9.0-10.3)	0.065
Platelet (10^3 μL^{-1})	257 (205-311)	251 (214-289)	0.477	210 (173-252)	211 (177-265)	0.590
Lactate (mmol L^{-1})	1.2 (0.97-1.58)	1.2 (0.98-1.43)	0.548	2.7 (2.17-3.21)	3.2 (2.36-3.60)	**0.003**

Non-AHI: Non-acute hepatic injury, **AHI**: Acute hepatic injury, **IQR**: Interquartile range, **eGFR**: Estimated glomerular filtration rate, **ALT**: Alanine Aminotransferase, **AST**: Aspartate aminotransferase, **ALP**: Alkaline phosphatase, **GGT**: γ-glutamyltransferase, **LDH**: Lactate dehydrogenase.

A predictive model was constructed for multivariate regression analysis based on the factors identified as potential risk factors for AHI in univariate logistic regression analysis (Table III). Multivariate logistic regression analysis results indicated that the risk of AHI is 2.27 times higher (1.144-4.543, 95% CI, p=0.019) in patients with hyperlipidemia, 2.84 times higher (1.077-7.494, 95% CI, p=0.035) in patients requiring 3-4 Units of FFP intraoperatively, and 4.37 times higher (1.107-17.264, 95% CI, p=0.035) in patients needing IABP and/or ECMO after CPB.

DISCUSSION

Within this study, several independent risk factors associated with AHI in adult patients undergoing CPB surgery were identified. These risk factors include preoperative hyperlipidemia, intraoperative transfusion of ≥3 units of FFP transfusion, as well as the utilization of IABP and/or ECMO.

Cardiovascular diseases stemming from dyslipidemia are recognized as the foremost global cause of mortality (13). The impact of dyslipidemias extends to complications within the endocrine, central nervous, hepatic, and renal systems (14). The liver, as a pivotal organ, undertakes a fundamental role in lipid, lipoprotein, and apolipoprotein metabolism. Typically, the liver synthesizes and subsequently releases the majority of endogenous lipids and lipoproteins into the bloodstream. Furthermore, the liver predominantly catabolizes plasma lipoproteins uphold the equilibrium of lipid and lipoprotein metabolism within the organism (15). Liver dysfunction has been evidenced to disrupt in vivo lipid metabolism and modify the profile of plasma lipids and lipoproteins (16). The liver plays an important role in lipid metabolism by producing, storing, and transporting lipid metabolites. Consequently, deviations in lipid levels can lead to changes in liver metabolism and induce damage to liver tissue (17). Due to the close relationship of dyslipidemia with lipid metabolism, it is thought that the liver is highly affected by this condition. Hyperlipidemia is a known risk factor for fatty infiltration of the liver, a condition that can progress to liver damage and even failure (18). The prevalence of both dyslipidemia and liver enzyme abnormalities is notably higher among hypertensive and diabetic cohorts compared to healthy control group (19). This suggests that diabetes and hypertension are major contributors to both dyslipidemia and hepatic dysfunctions. Underlying these pathologies is a common thread of pro-inflammatory processes. When we evaluate persistent inflammation, hypertension, diabetes, fatty liver, and lipid profile disorders from this perspective, it can be thought that these are interconnected cascades, including genetic and environmental factors. All of these etiopathologies are also at the root of atherosclerosis and cardiovascular diseases. In patients undergoing cardiac surgery with the current hyperlipid-

Tablo III: Univariate and Multivariate Logistic Regresyon Analysis

	Univariate Logistic Regression			Multivariate Logistic Regression		
	p	OR	95% CI	p	OR	95% CI
BMI (kg m^{-2})	<0.001	1.158	1.075-1.247			
Hyperlipidemia	0.042	1.735	1.020-2.952	**0.019**	2.279	1.144-4.543
Diabetes Mellitus	0.046	1.600	1.009-2.537			
Cardiopulmonary bypass time (min)	<0.001	1.022	1.011-1.033			
Fresh frozen plasma, None	0.035			0.057		
1-2 Unit	0.740	1.128	0.554-2.299	0.446	0.646	0.210-1.987
3-4 Unit	0.010	2.915	1.298-6.543	**0.035**	2.841	1.077-7.494
PC transfusion 1 Unit	0.021	3.157	1.185-8.410			
Sevoflurane use	0.047	1.581	1.005-2.486			
Intraoperative insulin use	0.044	1.691	1.014-2.819			
Intraoperative dopamine use	0.048	1.604	1.004-2.562			
Intraoperative adrenaline use	0.002	4.518	1.703-11.986			
IABP and/or ECMO	0.030	3.913	1.142-13.413	**0.035**	4.372	1.107-17.264
Postoperative lactate (mmol L^{-1})	0.026	1.204	1.023-1.418			
Constant				0.031	11.240	

OR: Odds ratio, **CI**: Confidence interval, **BMI**: Body mass index, **PC**: Platelet concentrate, **IABP**: Intra-aortic balloon pump, **ECMO**: Extracorporeal membrane oxygenation.

emic condition, the expected hemodynamic fluctuations due to the nature of the surgery will easily lead to liver damage on this sensitive ground and therefore to increases in liver enzymes. The importance of approaching hyperlipidemic patients more carefully in preoperative evaluation and exercising care in perioperative liver perfusion can be considered an important result of this study.

Evidence from cardiac surgery studies has clearly shown that blood products transfusions correlate with increased morbidity and mortality rates, and these adverse effects increase in a dose-dependent manner (20). In our study, the administration of ≥3 Units of FFP during the intraoperative period emerged as a contributory factor to the elevation of acute hepatic injury. Indications for FFP transfusion are very limited and it is known that inappropriate plasma transfusion is frequently resorted for managing and preventing bleeding during the perioperative period (21). Fresh frozen plasma is indicated coagulopathy and may life saving in that cases, however it has some bioactive substances such as histamine, eosinophil cationic protein, protein X, myeloperoxidase and plasminogen activator inhibitor which are stimulate the immune response and inflammatory processes (22). Lung injury that develops with immunological mechanisms related to FFP is well known. Similarly, this endothelial damage, neutrophil and complement system activation are thought to trigger kidney damage (23). Patients are already under the influence of strong systemic inflammation in CPB and cardiac surgery. When these patients are transfused with FFP, it is predictable to cause more immune responses and related organ dysfunctions (24). Since each unit of transfusion causes exposure to the immunological systems of different donors, adverse effects on organ function will increase with increasing doses. In our study, ≥3 Units of FFP transfusion was determined as the critical threshold. This result once again emphasizes the degree of care required in perioperative evidence-based FFP use.

This study, revealed that among the independent risk factors contributing to the emergence of AHI in adult patients undergoing CPB surgery, utilization of IABP and/or ECMO was identified as significant. Low cardiac output syndrome requiring mechanical circulatory support is one of the major complications after open heart surgery and may result in multiorgan hypoperfusion. It has a prevalence of 5.7% to 30% in patients undergoing coronary artery bypass grafting (25,26). It is not surprising that splanchnic ischemia during intervention and in the postoperative period is an important factor in postoperative liver dysfunction.

The implementation of IABP and/or ECMO following CPB surgery carries inherent risks as well. Incorrect cannula placement or subsequent displacements may lead to hypoperfusion in the visceral organs and lower extremities, potentially resulting in ischemia (27). In addition to diastolic malperfusion, plaque emboli caused by the mechanical effects of the balloon on intraluminal atherosclerotic plaque may also be associated with abdominal ischemia (28). Optimal preload

must be provided for these devices to function properly. In the presence of insufficient volume, they may not function properly. Moreover, given the need for heparinization, careful consideration is necessary to manage bleeding and thrombosis risk. Additionally, due to their operational principles, these devices could potentially damage blood elements, potentially causing hemolysis and platelet dysfunction (29). These processes can cause microemboli and bleeding foci in the microcirculation. Therefore, they may cause deterioration in organ perfusion. Although the exact cause of IABP/ECMO-mediated liver damage in our study could not be determined, the multifactorial causes probably came together to produce this result. To preempt complications that may develop with these devices, care should be taken with a multidisciplinary approach as much as possible. In this way the benefits may outweigh the risks.

Most studies in the literature have focused on methods of protecting organs from the negative effects of CPB. Most of these studies skip the assessment of liver function and focus on organs such as the heart, lungs, and kidneys (30). It has been shown that approximately 10% of patients undergoing high-risk cardiac surgery with CPB experience liver damage, which directly affects morbidity and mortality (3). This study, which is about this potentially mortal and rarely mentioned complication, makes a valuable contribution to the literature.

Our study has some limitations such as it is retrospective and single-center study. The fact that the liver functions in the following days were not evaluated. In addition, laboratory parameters for liver dysfunction were not analyzed except for ALT values specific for hepatocellular necrosis. In cardiac surgery, parameters such as INR and LDH are also affected by factors other than liver damage. Bilirubin was not evaluated due to missing data in many patients.

In conclusion, efforts to eliminate the above-mentioned risk factors to prevent hepatic damage after cardiac surgery may reduce the occurrence of this potentially fatal complication.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

AUTHOR CONTRIBUTIONS

Conception or design of the work: AA, ZAD, ENZ
Data collection: AA, ENZ
Data analysis and interpretation: AA
Drafting the article: AA, ANZ, ZAD
Critical revision of the article: ZAD
The author (AA, ENZ, ZAD) reviewed the results and approved the final version of the manuscript.

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