

# Jaundice and Its Results After Cardiac Surgery

Kalp Cerrahisi Sonrası Görülen Sarılık ve Sonuçları

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#### ABSTRACT

**Objectives:** Jaundice due to hyperbilirubinemia develops in 10–23% of patients in the early period after cardiac surgery. The aim of our study is to examine the risk factors and clinical consequences of hyperbilirubinemia causing jaundice.

**Methods:** In this retrospective study, patients who underwent cardiac surgery in our clinic between February 2015 and March 2021 were evaluated. Patients who underwent routine or emergency surgery, who developed post-operative jaundice, and whose total bilirubin concentration was >3 mg/dL were included in our study. The baseline demographic data, echocardiography data, laboratory data, operative data, and post-operative status were comprehensively collected. The cutoff value of post-operative total bilirubin was calculated according to hospital mortality in receiver operating characteristic analysis.

**Results:**Total bilirubin concentration was found to be >3 mg/dL in 27 patients. Mean total bilirubin (mg/L) was 9.56±6.427 and median total bilirubin score was 9.02 and the maximum bilirubin concentration was reached at 9.52±8.007 post-operative days. In-hospital mortality occurred in 17 (63.0%) patients. The cutoff for post-operative total bilirubin value was calculated as 9.24 by predicting in-hospital mortality (Sensitivity=70.6%, specificity=90%, and likelihood ratio: 7.05).

**Conclusion:** Patients who develop hyperbilirubinemia in the post-operative period of cardiac surgery should be carefully observed for low cardiac output syndrome, sepsis, or acute liver failure. Low-level hyperbilirubinemia is mostly reversible when cardiac output and oxygen delivery are adequate. However, severe persistent hyperbilirubinemia is a condition that needs to be recognized early and precautions should be taken. **Keywords:** Bilirubin, cardiac surgery, jaundice, post-operative

## ÖΖ

**Amaç:** Kalp cerrahisi sonrası erken dönemde hiperbilirubinemiye bağlı sarılık hastaların %10 ila %23'ünde gelişir. Çalışmamızın amacı, sarılığa neden olan hiperbilirubineminin risk faktörlerini ve klinik sonuçlarını incelemektir.

**Yöntem:** Bu retrospektif çalışmada, Şubat 2015-Mart 2021 tarihleri arasında kalp cerrahisi geçiren hastalar değerlendirildi. Acil veya elektif cerrahi uygulanıp postoperatif dönemde sarılık gelişen ve total bilirubin konsantrasyonu >3 mg/dL olan hastalar çalışmamıza dahil edildi. Temel demografik, ekokardiyografik, laboratuvar, ameliyat ve ameliyat sonrası veriler kapsamlı bir şekilde toplandı. ROC analiziyle postoperatif total bilirubin cut-off değeri hastane mortalitesine göre hesaplandı.

**Bulgular:** Toplam bilirubin konsantrasyonu 27 hastada >3 mg/dL olarak bulundu. Hastaların ortalama total bilirubin değeri 9,56±6,427 mg/L, medyan toplam bilirubin değeri 9,02 mg/L olarak bulundu. Hastalar maksimum bilirubin konsantrasyonuna ameliyat sonrası 9,52±8,007 günde ulaştı. Hastanede 17 (%63,0) hastada mortalite görüldü. Hastane içi mortaliteyi öngörmek amacıyla hesaplanan postoperatif total bilirubinin cut-off değeri 9,24 mg/L olarak bulundu (duyarlılık= %70,6, özgüllük= %90, olabilirlik oranı=7,05).

**Sonuç:** Kalp cerrahisi sonrası dönemde hiperbilirubinemi gelişen hastalar düşük kalp debisi sendromu, sepsis veya akut karaciğer yetmezliği açısından dikkatle izlenmelidir. Kalp debisi ve oksijen sunumu yeterli olduğunda düşük seviyeli hiperbilirubinemi çoğunlukla geri dönüşümlüdür. Ancak şiddetli persistan hiperbilirubinemi erkenden fark edilmesi ve önlem alınması gereken bir durumdur.

Anahtar sözcükler: Ameliyat sonrası, bilirubin, kalp ameliyatı, sarılık

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## Introduction

Jaundice due to hyperbilirubinemia develops in 10-23% of patients in the early period after cardiac surgery.<sup>[1,2]</sup> Despite advances in surgical techniques and post-operative patient care, the incidence of hyperbilirubinemia does not appear to have decreased compared to studies 40 years ago.<sup>[3]</sup> Increasing and severe hyperbilirubinemia occurring in the late post-operative days was associated with higher mortality and morbidity than mild hyperbilirubinemia occurring in the 1<sup>st</sup> days.<sup>[4]</sup>

Hyperbilirubinemia is considered by most doctors to be the result of another pathological event.<sup>[5]</sup> Since bilirubin is metabolized and excreted by the liver; hypoxia, low cardiac output, prolonged cardiopulmonary bypass (CPB) time, inotrope use in the perioperative, and early post-operative period of cardiac surgery may cause liver damage.<sup>[6-8]</sup> However, as the previous studies have shown, hyperbilirubinemia can lead to thrombocytopenia and respiratory failure causing apoptosis, inflammation, and oxidative stress.<sup>[9,10]</sup> Therefore, it is essential to treat and prevent hyperbilirubinemia as a separate post-operative problem. The aim of this study is to examine the risk factors and clinical consequences of hyperbilirubinemia causing jaundice.

## Methods

In this retrospective study, patients who underwent cardiac surgery in our clinic between February 2015 and March 2021 were evaluated. Patients who underwent routine or emergency surgery, who developed post-operative jaundice, and whose total bilirubin concentration was >3 mg/dL were included in our study. Our exclusion criteria were patients younger than 18 years of age, patients with known liver disease including positive hepatitis B antigen and anti-HCV antigen, liver transplant patients, patients with biliary tract disease, and patients requiring surgery in the case of sepsis.

The patient files were retrospectively screened. The pre-operative demographic, clinical, perioperative, and post-operative data were evaluated. This study complies with the Helsinki Declaration standards and current ethical guidelines. Hospital ethics committee approval was obtained for the study.

#### Surgical Management

All operations were performed according to the hospital's surgical and anesthesia protocols. Midazolam, fentanyl, and vecuronium were used for anesthesia induction, and inhaled sevoflurane was used for continuation of anesthesia. All operations were performed under CPB and aortic cross clamping. Crystalloid or blood cardioplegia was used with the antegrade technique. Blood transfusion was performed according to institutional protocol.

#### **Post-operative Management**

All patients were transferred to the intensive care unit (ICU) after the operation. Patients inotrope doses and fluid replacement therapy were adjusted according to the hemodynamic data. Depending on the clinical condition of the patients, they were followed up in the ICU for at least 24 h. Patients who met the extubation criteria were weaned off the mechanical ventilator. In all patients, hemogram, serum creatinine, serum glutamic oxaloacetic transaminase, serum glutamic pyruvic transaminase, and international normalized ratio values were examined daily. We also examined bilirubin tests in patients with clinical jaundice.

## Definitions

Hyperbilirubinemia was defined as plasma total bilirubin (TBIL) >3 mg/dL. In our clinic routine, postoperative plasma total bilirubin evaluation is performed only in patients with clinical signs of jaundice. To make a healthy evaluation, we considered the plasma total bilirubin value, at which clinical jaundice began to be seen, as hyperbilirubinemia.

Hourly doses of all vasoactive drugs admitted to the ICU were recorded and vasoactive-inotropic score was calculated. Formula used to calculate vasoactive-inotropic score: (dopamine dose [mcg/kg/min])+(dobutamine dose [mcg/kg/min])+(100×epinephrine dose [mcg/kg/min])+(10×mil-rinone dose [mcg/kg/min])+(10×dose of norepinephrine [mcg/kg/min]). We used the highest calculated vasoactive-inotropic score as data.

#### **Statistical Analysis**

Statistical analyses were performed using the SPSS 23.0 statistical package for Windows. Continuous variables are expressed as mean SD and categorical data as proportions throughout the manuscript. Categorical variables were compared using the  $\chi^2$  test or Fisher's exact test and independent continuous variables were compared by the Mann-Whitney U-test as appropriate. Receiver operating characteristic (ROC) analysis was performed to find the appropriate cutoff value for the post-operative total hyperbilirubinemia value.

## Results

Between February 2015 and March 2021, 5821 patients were operated in our clinic. During this period, total bilirubin level was found to be >3 mg/dL in 38 patients in our clinic, and 11 of these patients were excluded from the study because they met one or more of the exclusion criteria. Twenty-seven patients remained. The prevalence of patients with a total bilirubin level >3 mg/dL was 0.4% **Table 1.** Demographics and clinical characteristics of all patients with hyperbilirubinemia

Patients characteristic	n	%	Mean±SD
Demographic feature			
Age (years)			56.22±16.63
Female	7	25.9	
Male	20	74.1	
Pre-operative clinical feature			
EuroSCORE			6.62±6.362
NYHA status III–IV	18	70.4	
LVEF (%)			47.16±12.85
Pulmonary arterial pressure, mmHg			41.00±19.43
Diabetes mellitus	8	29.6	
Arterial hypertension	17	63	
Atrial fibrillation	6	22.2	
PAD	4	14.8	
COPD	7	25.9	
Previous MI	9	33.3	
Unstable angina	9	33.3	
Renal impairment	9	33.3	
Pre-operative dialysis	2	7.4	
Endocarditis	1	3.7	
Obesity	8	29.6	
Emergency procedure	12	44.4	
Previous cardiac surgery	8	29.6	
Pre-operative intubation	2	7.4	
Pre-operative need for catecholamine support	2	7.4	
Pre-operative laboratory findings			
Total bilirubin (mg/dL)			0.79±0.508
Conjugated bilirubin (mg/dL)			0.31±0.195
INR			1.14±0.147
SGOT (IU/L)			33.92±36.970
SGPT (IU/L)			33.62±30.908
S. creatinine (mg/dL)			1.16±0.417
Hemoglobin (g/L)			12.18±2.379
Leukocytes (109/L)			9.05±4.073
Platelets (109/L)			233.23±91.527

EuroSCORE: The European System for Cardiac Operative Risk Evaluation; NYHA: New York Heart Association; LVEF: Left ventricular ejection fractions; PAD: Peripheral artery occlusion disease; COPD: Chronic obstructive pulmonary disease; MI: Myocardial infarction; INR: International normalized ratio; SGOT: Serum glutamic oxaloacetic transaminase; SGPT: Serum glutamic pruvic transaminase.

Mean age of the 27 patients included in the study was 56.22±16.63. Female population was 7 (25.9%). The mean logistic EuroSCORE (the European System for Cardiac Operative Risk Evaluation) II used in the risk analysis evaluation of patients in cardiac surgery was found to be 6.62±6.362. Eighteen (70.4%) of patients presented with symptoms of congestive heart failure classified as Grades III and IV by the New York Heart Association. Mean pre-operative total bilirubin (mg/dL) value was 0.79±0.508.



**Figure 1.** The distribution of operation types. CABG: Coronary artery bypass graft.

In the pre-operative echocardiography of the patients, the left ventricular ejection fractions were  $47.16\pm12.85$  and pulmonary arterial pressures were found to be  $41.00\pm19.43$  mmHg. Diabetes mellitus was present in 8 (29.6%), arterial hypertension in 17 (63%), atrial fibrillation in 6 (22.2%), peripheral artery occlusion disease in 4 (14.8%), chronic obstructive pulmonary disease in 7 (25.9%), previous myocardial infarction and unstable angina in 9 (33.3%), renal impairment in 9 (33.3%), endocarditis in 1 (3.7%), and obesity in 8 (29.6%) patients. All demographic, clinical, and echocardiographic findings are shown in Table 1.

Aortic surgery (n=8, 29.6%) was found to be the most frequently performed operation type in our cohort. Other operations types were six combined coronary artery bypass graft (CABG) and valve surgery (22.2%), five isolated valve sur gery (18.7%), four isolated CABG (14.8%), three combined valve surgery (11.1%), and one cardiac transplantation (3.7%), respectively. The distribution of operation types is shown in Figure 1. CPB time was 158.41±54.96 min, cross-clamping time was 92.07±39.20 min, and minimal temperature was 28.22±3.25°C on CPB.

Intensive care duration of the patients was 18.67±19.474 days, mechanical ventilation time was 12.44±12.559 days, and inotropic support duration was 8.63±7.249 days. The va-

Post-operative data	n	%	Mean±SD
In-hospital mortality	17	63.0	
ICU stay (days)			18.67±19.474
Intubation time (days)			12.44±12.559
Need for surgical re-exploration	20	74.1	
Infection	9	33.3	
Cerebrovascular event	5	18.5	
Reintubation	12	44.4	
New-onset dialysis	14	51.9	
New-onset atrial fibrillation	17	63.0	
Inotrope requirement			
Vasoactive-inotropic score			35.7±24.974
Norepinephrine (mcg/kg/min)			0.0474±0.0593
Dopamine (mcg/kg/min)			11.89±6.704
Epinephrine (mcg/kg/min)			0.0481±0.073
Time of inotropic support (days)			8.63±7.249
Use of blood/products (package)			
PRBC (package)			14.42±8.865
FFP (package)			12.21±8.121
Thrombocytes (package)			3.95±4.123
Post-operative laboratory findings			
SGOT (IU/L)			920.85±924.705
SGPT (IU/L)			1125.96±1180.710
Creatinine (mg/dL)			2.34±1.218
Total bilirubin (mg/dL)			9.56±6.427
Conjugated bilirubin (mg/dL)			8.36±5.487
Time to maximum bilirubin			9.52±8.007
concentration (days)			

Table 2. Post-operative status of all patients with hyperbilirubinemia

ICU: Intensive care unit; PRBC: Packed red blood cell; FFP: Fresh frozen plasma; SGOT: Serum glutamic oxaloacetic transaminase; SGPT: Serum glutamic pyruvic transaminase.

soactive-inotropic score, which indicates the inotropic need of the patients, was found to be 35.7±24.974. The amount of post-operative transfusion was recorded as a mean of 14.42±8.865 packets for red blood cells, 12.21±8.121 for fresh frozen plasma, and 3.95±4.123 packets for platelets. Need for surgical re-exploration was required in 20 (74.1%) patients due to surgical bleeding or cardiac tamponade. In the abdominal ultrasonography performed in the post-operative period, there was no enlargement of the biliary tract in any of the patients. Other post-operative complications and laboratory parameters are summarized in Table 2.

Mean total bilirubin (mg/L) was 9.56±6.427 and median total bilirubin score was 9.02 and the maximum bilirubin concentration was reached at 9.52±8.007 days. In-hospital mortality occurred in 17 (63.0%) patients. ROC curve analysis was established using the post-operative total bilirubin value to predict the in-hospital mortality. Figure 2 shows that the post-operative total bilirubin value had a significant positive relationship with the in-hospital mortality.



**Figure 2.** Receiver operating characteristic curve analysis to estimate the in-hospital mortality according to the total bilirubin value.

The area under the curve (AUC) was 0.841 p=0.004. The cutoff for post-operative total bilirubin value was calculated as 9.24 by predicting in-hospital mortality (Sensitivity=70.6%, specificity=90%, and likelihood ratio: 7.05).

Two groups were formed according to the calculated cutoff value: Moderate hyperbilirubinemia and high-grade hyperbilirubinemia. There were 15 patients in the moderate hyperbilirubinemia group and 12 patients in the highgrade hyperbilirubinemia group. As shown in Tables 3 and 4, there are no demographic, laboratory, and clinical differences between the two groups in the pre-operative and perioperative periods.

Total bilirubin level was calculated as 5.203±0.648 in the moderate hyperbilirubinemia group and 15.017±1.648 in the high-grade hyperbilirubinemia group. All patients in the high-grade hyperbilirubinemia group and one-third of the patients in the moderate hyperbilirubinemia group died postoperatively. There was no difference between the groups between ICU stay and intubation time (respectively, p=0.373 and p=0.221). Vasoactive inotrope score and duration of inotropic support were significantly higher in the high-grade hyperbilirubinemia group (respectively, p=0.011 and p=0.002). Creatinine was found to be significantly higher in the high-grade hyperbilirubinemia group than in the moderate hyperbilirubinemia group (2.868±0.352 vs. 1.904±0.285, p=0.031). No difference was found between the two groups in terms of new-onset dialysis (p=0.656). Table 5 summarizes other post-operative clinical and laboratory parameters between both groups.

Table 3. Comparison of demographic, pre-operative laboratory, and clinical characteristics of patients with moderate hyperbilirubinemia and high hyperbilirubinemia

Patients characteristic	Moderate hyperbilirubinemia (n=15)			High-grade hyperbilirubinemia (n=12)			р
	n	%	Mean±SD	n	%	Mean±SD	
Demographic feature							
Age (years)			57.875±3.226			58.7±7.169	0.981
Female	5	33.3		2	16.7		0.326
Male	10	66.3		10	83.3		0.326
Pre-operative clinical feature							
EuroSCORE			3.86125±0.757			8.442±2.471	0.262
NYHA status III–IV	11	73.3		8	66.7		0.706
LVEF (%)			53.75±3.75			39.9±4.207	0.077
Pulmonary arterial pressure, mmHg			30.625±3.332			41.7±7.867	0.826
Diabetes mellitus	5	33.3		3	25.0		0.637
Arterial hypertension	8	53.3		9	75.0		0.247
Atrial fibrillation	5	33.3		1	8.3		0.121
PAD	3	20.0		1	8.3		0.396
COPD	4	26.7		3	25.0		0.922
Previous MI	6	40.0		3	25.0		0.411
Renal impairment	4	26.7		5	41.7		0.411
Pre-operative dialysis	1	6.7		1	8.3		0.869
Endocarditis	0	0.0		1	8.3		0.255
Obesity	6	40.0		2	16.7		0.187
Emergency procedure	5	33.3		7	58.3		0.194
Previous cardiac surgery	5	33.3		3	25.0		0.637
Pre-operative intubation	2	13.3		0	0.0		0.189
Pre-operative laboratory findings							
Total bilirubin (mg/dL)			0.786±0.373			0.804±0.658	0.435
Conjugated bilirubin (mg/dL)			0.342±0.223			0.288±0.161	0.602
INR			1.095±0.038			1.198±0.04	0.72
SGOT (IU/L)			21.5±4.494			48.417±13.984	0.157
SGPT (IU/L)			34.357±10.534			32.75±5.272	0.396
S. creatinine (mg/dL)			1.139±0.139			1.195±0.078	0.368
Hemoglobin (g/L)			11.893±0.689			12.533±0.63	0.527
Leukocytes (109/L)			9.625±1.25			8.399±0.956	0.527
Platelets (109/L)			249.786±21.783			213.917±29.485	0.212

EuroSCORE: The European System for Cardiac Operative Risk Evaluation; NYHA: New York Heart Association; LVEF: Left ventricular ejection fractions; PAD: Peripheral artery occlusion disease; COPD: Chronic obstructive pulmonary disease; MI: Myocardial infarction; INR: International normalized ratio; SGOT: Serum glutamic oxaloacetic transaminase; SGPT: Serum glutamic pyruvic transaminase.

## Discussion

Bilirubin, the end-product of heme catabolism, is metabolized by the liver and excreted by intrahepatic and extrahepatic biliary tract.<sup>[11]</sup> The liver receives about 25% of cardiac output through the hepatic artery and portal system. This dual flow of blood and the liver's ability to extract 95% of oxygen from the blood makes the liver relatively resistant to necrosis from hypoperfusion.<sup>[12]</sup> However, significant reduction in cardiac output or severe hypoxemia can override protective mechanisms and cause hypoxic liver injury. <sup>[13]</sup> When the liver is damaged by ischemia, bilirubin uptake and bile secretion are impaired, and hyperbilirubinemia occurs.<sup>[14]</sup> Perioperative and early post-operative hypotension and hypoxia are among the causes of jaundice seen after cardiac surgery.<sup>[15]</sup> It is also known that hemolysis and increased need for transfusion due to prolonged CPB times cause early jaundice and temporary liver damage.<sup>[16]</sup>

Contrary to the low prevalence in our study, there are studies showing that 10-23% of cardiac surgery patients develop jaundice in the early post-operative period.<sup>[1,17]</sup> We attribute this large difference to the fact that studies used different reference ranges for hyperbilirubinemia (TBIL

Operational data	Moderate hyperbilirubinemia (n=15)			High-grade hyperbilirubinemia (n=12)			р
	n	%	Mean±SD	n	%	Mean±SD	
CPB time (min)			149.25±28.162			163.1±15.746	0.486
Cross-clamp time (min)			85.125±17.373			100.9±8.917	0.548
Minimal core temperature (°C)			28.875±0.833			28.3±0.761	0.383
Isolated CABG	3	20.0		1	8.3		0.396
Isolated valve surgery	4	26.7		1	8.3		0.223
Combined CABG and valve surgery	4	26.7		2	16.7		0.535
Aortic surgery	3	20.0		5	41.7		0.221
Combined valve surgery	1	6.7		2	16.7		0.411
Cardiac transplantation	0	0.0		1	8.3		0.255

#### Table 4. Comparison operational data of patients with moderate hyperbilirubinemia and high hyperbilirubinemia

CPB: Cardiopulmonary bypass; CABG: Coronary artery bypass graft.

Table 5. Comparison of post-operative status of patients with moderate hyperbilirubinemia and high hyperbilirubinemia

Post-operative data	Moderate hyperbilirubinemia (n=15)			High-grade hyperbilirubinemia (n=12)			р
	n	%	Mean±SD	n	%	Mean±SD	
In-hospital mortality	5	33.3		12	100.0		<0.001*
ICU stay (days)			13.625±4.226			20.9±5.161	0.373
Intubation time (h)			7.625±2.291			13.20 2.328	0.221
Need for surgical re-exploration	10	66.7		10	83.3	0.326	
Infection	4	26.7		5	41.7	0.411	
Cerebrovascular event	2	13.3		3	25.0	0.438	
Reintubation	5	33.3		7	58.3	0.194	
New-onset dialysis	7	46.7		7	58.3	0.547	
New-onset atrial fibrillation	10	66.7		7	58.3	0.656	
Inotrope requirement							
Vasoactive-inotropic score			17±4.359			52±7.795	0.011*
Time of inotropic support (days)			7.125±2.863			13.3±2.31	0.002*
Use of blood/products (package)							
PRBC (package)			12.63±2.809			15.82±2.879	0.508
FFP (package)			9.25±2.059			14.36±2.744	0.089
Thrombocytes (package)			2.13±1.008			5.27±1.369	0.061
Post-operative laboratory findings							
SGOT (IU/L)			667.643±211.896			1216.25±292.073	0.111
SGPT (IU/L)			1124.429±373.971			1127.75±266.832	0.589
Creatinine (mg/dL)			1.904±0.285			2.868±0.352	0.031*
Total bilirubin (mg/L)			5.203±0.648			15.017±1.648	<0.001*
Conjugated bilirubin (mg/L)			4.238±0.535			13.555±1.06	
Time to maximum bilirubin concentration (days)			9±2.559			10.833±1.691	0.082

\*: P value of less than 0.05 is considered as significant. ICU: Intensive care unit; PRBC: Packed red blood cell; FFP: Fresh frozen plasma; SGOT: Serum glutamic oxaloacetic transaminase; SGPT: Serum glutamic pyruvic transaminase.

>3 mg/dL or TBIL >2 mg/dL) and that we only measured plasma total bilirubin in patients with clinical symptoms of jaundice in the post-operative period.

The population of our study consists of high-risk patients. To be clear, more than half of our patients consisted of high-risk operations such as aortic surgery, combined CABG and valve surgery, and heart transplant surgery. In addition, 29.6% of the patients had previous cardiac surgery and 44.4% were operated in emergency condition, and in our study, it is seen that the CPB duration and cross-clamp duration of the population are higher as mortality risk factors compared to similar studies.<sup>[16,18]</sup> Despite the small number of patients in our study, we achieved striking results. According to the data, we obtained from our study, the mortality rate was 63% in patients diagnosed with hyperbilirubinemia in our clinic. We do not think that this result can be explained only by hyperbilirubinemia. This high mortality rate is both a cause and a consequence of hyperbilirubinemia.

In our study, the total bilirubin cutoff value was calculated as 9.24 mg/gl in the ROC curve analysis to estimate the in-hospital mortality according to the total bilirubin value. According to the calculated cutoff value, two groups were formed as moderate hyperbilirubinemia group and highgrade hyperbilirubinemia group. In studies investigating risk factors for hyperbilirubinemia developing in the early post-operative period in cardiac surgery, the risk factors were generally found to be pre-operative prothrombin time, CPB time, aortic cross-clamp time, and amount of transfused blood. However, when we compare patients with moderate hyperbilirubinemia and patients with highgrade hyperbilirubinemia, as in our study, we see that there is no difference between the two groups in terms of these risk factors. The reason for this may be the pathophysiological differences between the development and deepening of hyperbilirubinemia, as well as the small number of populations in the study. Vasoactive-inotropic score and duration of inotropic support were also higher in the high bilirubin group. This may be due to the inflammatory response and oxidative response caused by hyperbilirubinemia.<sup>[9,19]</sup> Another possible reason for the underlying cause of hyperbilirubinemia may be due to higher doses and variety of inotropes used to treat low cardiac output syndrome.

All patients with a total bilirubin level higher than 9.24 died. We think that this is the most important finding of our study. The study by Farag et al.,<sup>[1]</sup> the maximum total bilirubin value of 25.5 mg/dL was found to be associated with 99% mortality. In our study, the maximum bilirubin value associated with mortality was found to be much lower. But as is known, total bilirubin value is converted to natural logarithm to reduce the effect of extreme laboratory values such as end-stage model of liver disease and albumin-bilirubin scores on the scales. Therefore, in clinical evaluation, the difference between two different results from each study may not be as large as it appears.

This retrospective study includes data from a single-center and small patient population. In our clinic, bilirubin values of blood laboratory evaluations surgery are not routinely performed. The decision to measure bilirubin levels is left to the responsible physicians. Preferably multicentered, prospective studies with larger sample size will give us better results on the matter.

#### Conclusion

Patients who develop hyperbilirubinemia in the post-operative period of cardiac surgery should be carefully observed for low cardiac output syndrome, sepsis, or acute liver failure.

Low-level hyperbilirubinemia is mostly reversible when cardiac output and oxygen delivery are adequate.<sup>[20]</sup> However, severe persistent hyperbilirubinemia is a condition that needs to be recognized early and precautions should be taken. After this study, we routinely started to look up the bilirubin levels of the patients who stayed more than 3 days in the ICU, to prevent any adverse effects.

#### Disclosures

**Ethics Committee Approval:** The study was approved by The İstanbul University of Health Sciences Mehmet Akif Ersoy Thoracic and Cardiovascular Surgery Hospital Clinical Research Ethics Committee (Date: 04/06/2021, No: 2021-48).

**Informed Consent:** Written informed consent was obtained from all patients.

Peer-review: Externally peer-reviewed.

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