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Liver function tests and hyperbilirubinemia in adult patients undergoing open heart surgery

Açık kalp cerrahisi uygulanan erişkin hastalarda karaciğer fonksiyon testleri ve hiperbilirubinemi

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Abstract

Aim: The effects of cardiac surgery and cardiopulmonary bypass on postoperative liver function tests and hyperbilirubinemia in adult patients undergoing open heart surgery were studied, and related literature was reviewed and compared with our results.

Materials and Methods: Between January 2013 and March 2013, forty adult patients who undergone open heart surgery were included in this study. Patients were prospectively evaluated in regard of the alterations in liver function tests, the risk factors that effects these alterations; their effects on morbidity and mortality after cardiopulmonary bypass were evaluated and were compared with recent literature results. Patients' preoperative and postoperative 0, 1, 2, 7 and 14th day liver function tests and bilirubin levels were measured.

Results: Blood total protein, albumin, total cholesterol, ALP levels were fallen remarkably on postoperative day 1, followed with gradual increase ultimately reaching preoperative levels, and these alterations were statistically significant. The total bilirubin, AST, ALT, LDH, GGT, INR levels were elevated in the early postoperative period, and fell to normal levels later on. All increases of the enzymes were statistically significant except ALT. In our study, only 7 patients displayed hyperbilirubinemia. When patients with hyperbilirubinemia were compared with patients who did not have hyperbilirubinemia, preoperative albumin and CK levels were found to be risk factors for hyperbilirubinemia.

Conclusion: By studying the effects of heart and cardiopulmonary bypass surgery on the liver and the probable risk factors, we believe that by detecting the patients with high risk of hepatic failure required measures should be taken preoperatively, perioperative patient care quality improved and any complication can be fixed appropriately. To understand the reasons and prevention of perioperative hepatic failure, we think that the studies should be performed with larger patient groups with longer periods.

Keywords: Liver Function Tests; Hyperbilirubinemia; Open Heart Surgery.

Öz

Amaç: Çalışmamızda açık kalp cerrahisi uygulanan erişkin hastalarda cerrahinin ve kardiyopulmoner bypassın postoperatif karaciğer fonksiyon testlerine ve hiperbilirubinemi gelişimi üzerine etkisi araştırıldı ve bu konuyla ilgili güncel literatür derlenerek sonuçlarımızla karşılaştırıldı.

Gereç ve Yöntemler: Ocak 2013 ve Mart 2013 tarihleri arasında kliniğimizde kardiyopulmoner bypass eşliğinde kalp cerrahisi uygulanan 40 erişkin hasta çalışmaya dahil edildi. Hastalar prospektif olarak kardiyopulmoner bypass sonrası gelişen karaciğer fonksiyon testlerindeki değişiklikler, bunlara etki eden risk faktörleri ve bunların mortalite ve morbiditeye etkisi yönünden değerlendirildi ve sonuçlar güncel literatür sonuçlarıyla karşılaştırıldı. Hastaların preoperatif dönemde ve postoperatif 0, 1, 2, 7 ve 14. günlerde karaciğer fonksiyon testleri ve bilirubin düzeyleri çalışıldı.

Bulgular: Kandaki total protein, albümin, total kolesterol, ALP düzeylerinde postoperatif 1. gün belirgin düşüş izlendi ve daha sonra giderek yükseliş ve preoperatif değerlere kadar artış gözlendi, ve değişiklikler istatistiksel olarak anlamlıydı. Total bilirubin, AST, ALT, LDH, GGT, INR düzeyleri postoperatif erken dönemde yükseldi, sonrasında normal sınırlara geriledi. ALT deki artışlar istatistiksel olarak anlamlı saptanmamışken, diğer enzimlerdeki artışlar istatistiksel olarak anlamlıydı. Çalışmamızdaki hastalardan sadece 7 tanesinde hiperbilirubinemi gelişti. Hiperbilirubinemi gelişen ve gelişmeyen hasta grupları karşılaştırıldığında preoperatif albümin ve CK düzeyleri hiperbilirubinemi açısından risk faktörü olarak saptandı.

Sonuç: Kalp cerrahisi ve kardiyopulmoner bypassın karaciğer üzerine olan etkileri ile birlikte muhtemel risk faktörleri incelenerek karaciğer yetmezliği gelişme riski yüksek olan hastaların operasyon öncesi belirlenerek perioperatif gerekli önlemlerin alınması, operasyon öncesi ve sonrası hasta bakımında kalitenin arttırılması ve ortaya çıkan komplikasyonlarla uygun bir yaklaşımla baş edilmesi gerektiği kanaatindeyiz. Perioperatif karaciğer yetmezliği gelişiminin nedenlerini ve korunma yollarını bulmak için daha geniş hasta katılımı ile yapılacak daha uzun süreli çalışmalara gereksinim olduğunu düşünüyoruz.

Anahtar Kelimeler: Karaciğer Fonksiyon Testleri; Hiperbilirubinemi; Açık Kalp Cerrahisi.

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INTRODUCTION

The dysfunction of organ systems can be observed in patients undergoing open heart surgery due to employment of cardiopulmonary bypass (CPB). Due to a lot of different mechanisms and etiological causes, hepatic damage at the cellular level and hyperbilirubinemia can occur in these patients postoperatively (1). In patients undergoing open heart surgery with implementation of CPB, during postoperative period, hepatocellular damage in changing degrees and hyperbilirubinemia are observed in 80-90% of patients and 25-35% of patients, respectively (2,3). Hypoperfusion of the liver and splanchnic organs, systemic inflammatory response, hemolysis, dilutional anemia secondary CPB have all been implicated in the etiology of dysfunction of the hepatobiliary system (4,5). With improvements in CPB techniques and medications, the effects of open heart surgery on liver and related risk factors can be studied, thus patients with high risk for hepatic failure detected and necessary precautions can be taken. The evaluation of the hepatobiliary system functions preoperatively, detecting patients with borderline hepatobiliary system dysfunction and anticipating the problems that can occur in patients with high risk are important and could have an impact on postoperative results (6). The effects of surgery and CPB on postoperative liver function tests and hyperbilirubinemia in adult patients undergoing open heart surgery were studied and our results were compared with the related recent literature in this present study.

MATERIALS and METHODS

Study Design

Between January 2013 and March 2013, forty consecutive adult patients whom have undergone cardiac surgery with CPB have been included in this prospective study. Patients' preoperative demographic features, accompanying diseases, intraoperative data and postoperative results were all recorded. Patients were evaluated according to their postoperative hepatic functions, hepatocellular damage, incidence and risk factors of hyperbilirubinemia, resulting morbidity and mortality, and our results were compared with recent literature results. Patients with hyperbilirubinemia prior to the operation, dysfunction of the hepatic function tests, chronic renal failure, who were under 18 years of age, operated on an emergency basis and redo cases were excluded from the study. The study protocol was approved by the institutional ethics committee. The informed consent forms were obtained from all of patients before operation.

Anesthesia and surgical technique

Standard anesthesia technique was employed to the patients. As premedication, 0.1 mg/kg of morphine sulphate was given subcutaneously to all patients. The routine monitorization which included electrocardiography (ECG), radial arterial catheterization, pulse oxymeter, foley catheterization and central venous pressure catheterization was employed in all cases. After implementation of pulse oxymeter and ECG, two 16-gauge peripheral venous catheters were placed, and 5-7 ml/kg/h of isotonic saline solution was used in the maintenance of fluid infusion. Radial arterial catheterization was employed for hemodynamic monitorization on preferably non-dominant arm under sedation, and central venous catheter was placed into the right internal juguler vein. Anesthesical induction was performed with the administration of 5 mcg/kg of fentanyl, 2 mg/kg of ketamine and 0.1 mg/kg of vecuronium intravenously. Maintenance of anesthesia was provided by intravenously administrating 3-5 mcg/kg of fentanyl, 0.1 mg/kg of vecuronium, 0.03 mg/kg of midazolam and minimum alveolar concentration (MAC) 0.5-1% of sevoflurane. With the commencement of the operation nitroglycerin infusion was instituted for prophylaxis of ischemia and to prevent volume overload. Non-pulsatile flow, membrane oxygenation, normothermia or mild hypothermia were employed during the operations. The extracorporeal system was primed with 1000 mL ringer lactate solution, 500 mL hydroxyethyl starch (voluven) solution,1 mL/kg sodium bicarbonate, 2 mL/kg mannitol %20, 1 mg/kg prednisolone and 1 gr cefazolin sodium. In all of the patients, 60-80 mmHg of average blood pressure had been aimed with the employment of a minimum of 2.4 L/m^2/min blood flow. Unfractioned heparin was administered in 350 IU/kg dosage and the desired activated clotting time (ACT) was set as over 450 seconds. After ascending aorta had been cross clamped, 10-15 mL/kg of antegrade crystalloid cardioplegia solution was given with application of topical hypothermia and infusion of cardioplegia solution was repeated every 20 minutes. Arterial blood gases were measured periodically and patients' pH were aimed to be kept in the range of 7.35-7.45. Aortic cross clamp was removal after completion of the coronary revascularization, valve replacement or repair, and deairing of the heart. If the heart did not resume beating spontaneously, the cardioversion was applied. CPB was terminated when sufficient hemodynamics was attained and the patient had been warmed to normal temperature. The effect of unfractionated heparin was neutralized with protamine during decannulation.

Obtaining data and their evaluation

Biochemical analysis of the blood samples taken in the 5 days period prior to operation and on postoperative 0, 1, 2, 7 and 14th days was conducted measuring aspartate transaminase (AST), alanine transaminase (ALT), alkaline phosphatase (ALP), lactate dehydrogenase (LDH), gamma glutamyl transferase (GGT), total bilirubin, direct and indirect bilirubin, total protein, albumin, total cholesterol, low density lipoprotein (LDL) cholesterol, high density lipoprotein (HDL) cholesterol, triglyceride, creatine kinase (CK), international normalized ratio (INR), hemoglobin and platelet. Each result obtained on postoperative days 0, 1, 2, 7 and 14 were compared with their respective preoperative values, thus postoperative hepatic functions were assessed. In addition patients whom displayed postoperative hyperbilirubinemia and those who had not were compared for evaluating probable risk factors pertaining onset of hyperbilirubinemia. Total bilirubin exceeding at least once the 1.2 mg/dL border postoperatively was accepted as postoperative hyperbilirubinemia.

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Statistical analysis

All statistical analyses were conducted out using the Statistical Package for Social Sciences (SPSS) package program (version 13.0, SPSS, Chicago, Illinois, USA). For categorical variables, the percentage, frequency and distribution were used as definitive statistics. To delineate whether the constant variables presented normal distribution, they were evaluated with Kolmogorov-Smirnov test. For variables with normal distribution, average ± standard deviation was used for definitive statistics. Independent sampling t-test and one way ANOVA test were used for comparison of two independent groups and comparison of more than two independent groups, respectively. When ANOVA test was significant, the paired comparison of the groups was performed using Tukey multi comparison test. For variables that did not demonstrate normal distribution median (minimum-maximum) values were used for definitive statistics, for comparison of two independent groups Mann-Whitney U test, for comparison of more than two independent groups Kruskal-Wallis tests were employed. When Kruskal-Wallis test results were significant, the paired comparison of the groups was performed with Mann-Whitney U test. Furthermore, the relationships between variables were assessed with Pearson correlation constant. A p value < 0.05 were considered as significant.

RESULTS

The average age of the patients was 61.2±11.3 and 26 (65%) of them were male. Low left ventricular ejection fraction (LVEF <50%) was observed in 13 patients (37.5%) and the overall average LVEF was 52.7±10.7 %. The most observed comorbid conditions were hyperlipidemia in 65% of patients, hypertension in 57.5% of patients and diabetes mellitus in 37.5% of patients. Aortic cross clamp was not placed in only 4 cases, instead beating heart surgery was performed under CPB without aortic cross clamping. Coronary artery bypass grafting (CABG) was performed on 25 (62.5%) and valvular operation on 11 (27.5%) patients along with total CPB support. Eighty percent of patients were operated under normothermic body temperature while rest of the patients were operated with mild hypothermia. Postoperative mortality was observed in only one patient (who underwent aortic and mitral valve replacement and had a low LVEF) and overall mortality rate was 2.5%. The characteristics of the patients included in the study were summarized in Table 1.

Perioperative course of average levels of liver function tests was shown in Table 2. When AST levels of the patients were analyzed; the average AST levels that began to increase on postoperative (PO) day 0, reached their peak levels on PO day 2. AST levels gradually decreased after PO day 2 eventually falling below preoperative levels by PO day 14 (Figure 1). When the AST levels of PO days 0, 1, 2, and 7 were compared with preoperative AST levels, the increase in the postoperative period were statistically significant (p<0.05). When preoperative values compared with PO day 14 values, the difference was not significant (p=0.143). When ALT levels of the patients were analyzed; the average ALT levels started to increase on PO day 0, reaching their peak levels on PO day 7, they tended to decline after PO day 7, finally decreasing to average levels equal to preoperative values (Figure 2). When compared with the preoperative levels, the changes in postoperative ALT values were not statistically significant (p=0.28). When ALP levels of the patients were analyzed; the average ALP levels began falling on PO day 0, with the most decline observed on PO day 1, on following days increased progressively reaching higher levels than preoperative levels on PO day 14 (Figure 3). All the changes in postoperative ALP levels were compared with preoperative levels and were found statistically significant (p<0.05). When LDH levels of the patients were analyzed; the average LDH levels had started increasing on PO day 0, reaching peak levels on PO day 2, and later on gradually decreased (Figure 4). When compared with preoperative LDH levels, the changes in the postoperative LDH levels were found statistically significant (p<0.05). When GGT levels of the patients were analyzed; the average GGT levels showed a minimal increase on postoperative day 0 and reached its highest levels on PO day 7, decreasing after that (Figure 5). When the preoperative values were compared with the values of PO days 0 and 1, the differences were not statistically significant (p values were 0.407 and 0.967, respectively) while they were compared with values of PO days 2, 7 and 14, the difference were found to be statistically significant (p<0.05). When INR levels of the patients were analyzed; the average INR levels started elevating on PO day 0, and after reaching their peak levels tended to gradually decrease on the following days (Figure 6). The differences between PO days 0, 1 and 2 levels with the preoperative values were statistically significant (p<0.05), the difference between levels of INR on days 7 and 14 were not statistically significant (p>0.05). When total bilirubin levels of the patients were analyzed; the average total bilirubin levels began elevating on PO day 0, reaching peak levels on PO day 1, and decreasing on the following days. On PO day 2 levels were below preoperative levels, reaching their lowest levels on PO day 14 (Figure 7). When compared with preoperative total bilirubin levels, only the differences with PO days 7 and 14 were statistically significant (p<0.05), the other PO days were not statistically significant (p>0.05). During postoperative period, hyperbilirubinemia was developed in 7 of 40 patients (17.5%). Patients that developed postoperative hyperbilirubinemia were compared with those had not in terms of the possible risk factors, and preoperative low levels of average albumin and CK were found to be statistically significant in the development of postoperative hyperbilirubinemia (p<0.05). Some parameters of patients in whom postoperative hyperbilirubinemia developed and did not develop are listed in Table 3.

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Table 1. The characteristics of the study population

Average age (years)		61.2±11.3
Male / Female		26 / 14
Operation (no. of patients, %)	Conventional CABG	25 (62.5%)
	Empty beating heart CABG	4 (10%)
	Valvular surgery	11 (27.5%)
Underlying diseases (no. of patients, %)	HT	23 (57.5%)
	DM	13 (32.5%)
	MI	1 (2.5%)
	CVE	0
	PAD	2 (5%)
	HL	25 (62.5%)
	COPD	0
LVEF	> 50%	25 (62.5%)
	< 50%	15 (37.5%)
	Average (%)	52.7
Aortic cross clamping rate		36 / 40
Average aortic cross clamping time (minutes)		61.9
Average CPB time (minutes)		93.2
Average anesthesia time (minutes)		259.8
Average total operation time (minutes)		208.0
Intraoperative temperature (no. of patients, %)	Normothermia	32 (80%)
	Hypothermia	8 (20%)
Average CVP (cmH2O)	Preoperative	12.4
	Postoperative	11.2
Blood transfusion (no. of patients, %)		4 (10%)
Inotrope requirement (no. of patients, %)		16 (40%)
IABP requirement (no. of patients)		0
Mortality (no. of patients, %)		1 (2.5%)

CABG: Coronary artery bypass grafting; COPD: Chronic obstructive pulmonary disease; CPB: Cardiopulmonary bypass; CVE: Cerebrovascular events; CVP: Central venous pressure; DM: Diabetes mellitus; HL: Hyperlipidemia; HT: Hypertension; IABP: Intraaortic balloon pump; LVEF: Left ventricular ejection fraction; MI: Myocardial infarction; PAD: Peripheral arterial disease

Table 2. The levels of liver function tests during perioperative period

	Preop	PO day 0	PO day 1	PO day 2	PO day 7	PO day 14
AST (IU/L)	32.9 (10-164)	39.12 (10-132)	56.55 (21-475)	77.65 (16-772)	40.28 (12-148)	22.22 (9-85)
ALT (IU/L)	21.85 (6-55)	21.7 (6-54)	23.85 (6-78)	26.45 (6-89)	29.57 (6-113)	21.82 (6-82)
ALP(IU/L)	79.05 (45-142)	57.67 (27-115)	55.65 (37-125)	69.6 (30-245)	102.1 (46-256)	111.42 (49-277)
LDH (IU/L)	197.55 (101-246)	293.6 (171-694)	342.27 (192-1271)	373.15 (224-1499)	315.95 (210-1056)	265.35 (122-569)
GGT (IU/L)	32.2 (11-67)	33.52 (11-86)	34.07 (9-98)	43.22 (10-141)	80.77 (14-240)	65.67 (16-203)
INR	1.02 (0.89-1.2)	1.23 (1.08-1.57)	1.15 (0.99-1.42)	1.11 (0.99-1.23)	1.04 (0.92-1.16)	1.05 (0.93-1.17)
Total bilirubin (mg/dL)	0.71 (0.27-1.17)	0.74 (0.46-1.02)	0.86 (0.2-2.38)	0.7 (0.23-2.32)	0.62 (0.23-1.48)	0.56 (0.31-0.81)

ALP: Alkaline phosphatase; ALT: Alanine transaminase; AST: Aspartate transaminase; GGT: Gamma glutamyl transferase; INR: International normalized ratio; LDH: Lactate dehydrogenase; PO: Postoperative ** The levels of liver function tests were given as average and range*

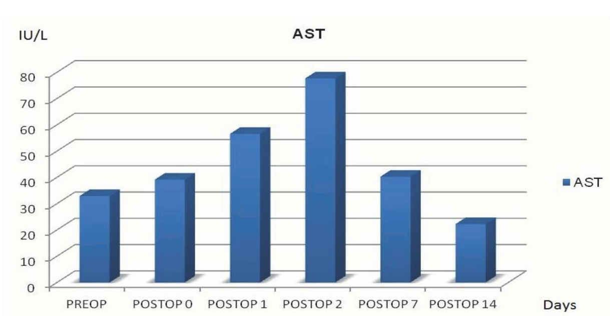

Figure 1. Perioperative course of average AST levels

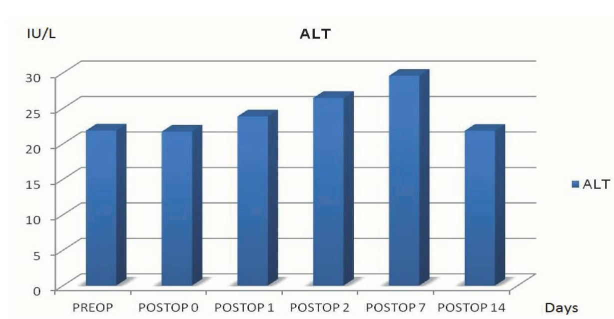

Figure 2. Perioperative course of average ALT levels

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Figure 3. Perioperative course of average ALP levels

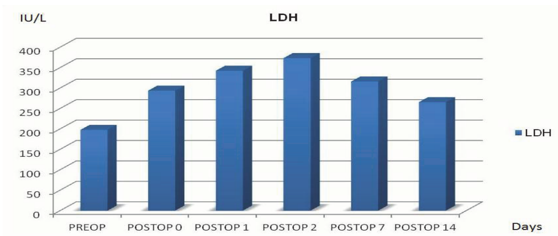

Figure 4. Perioperative course of average LDH levels

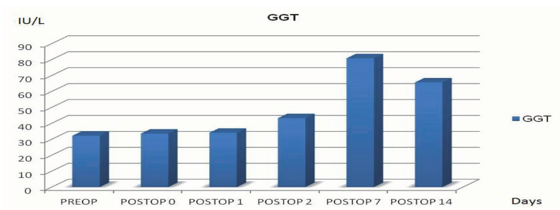

Figure 5. Perioperative course of average GGT levels

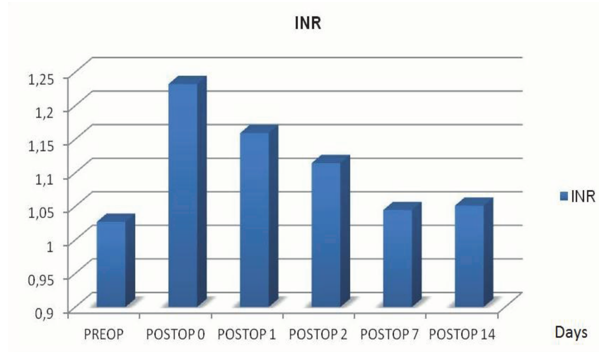

Figure 6. Perioperative course of average INR levels

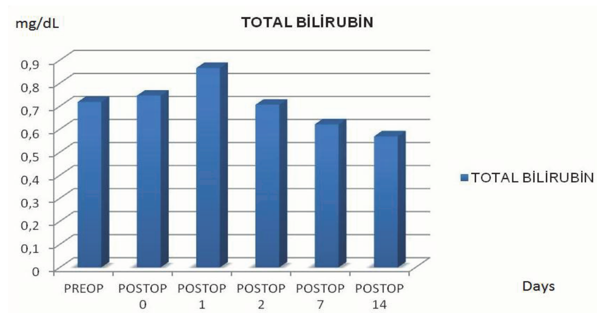

Figure 7. Perioperative course of average total bilirubin levels

Table 3. The parameters of patients in whom postoperative hyperbilirubinemia developed and did not develop

Parameter (average)	Postoperative hyperbilirubinemia (+) n:7]	Postoperative hyperbilirubinemia (-) n:33]	P value
Age (years)	65.8±10.5	60.4±11.4	0.280
Preoperative total protein level (g/dL)	7.02±0.49	7.13±0.46	0.596
Preoperative albumin level (g/dL)	3.68±0.08	4.91±3.19	<0.05
Preoperative AST level (IU/L)	19 (15-24)	22 (11-23)	0.425
Preoperative ALT level (IU/L)	12.5 (11-23)	20 (6-55)	0.092
Preoperative ALP level (IU/L)	73 (60-128)	68.5 (45-142)	0.618
Preoperative LDH level (IU/L)	220.5±25.1	193.5±38.6	0.109
Preoperative GGT level (IU/L)	36 (19-64)	29 (11-67)	0.425
Preoperative CK level (IU/L)	43.5 (23-61)	64.5 (30-1505)	<0.05
Preoperative total bilirubin level (mg/dL)	0.66±0.27	0.73±0.28	0.608
Preoperative CVP (cmH2O)	14.33±2.88	12.03±3.49	0.136
Aortic cross clamping time (minutes)	73.00±32.85	59.73±24.78	0.264

ALP: Alkaline phosphatase; ALT: Alanine transaminase; AST: Aspartate transaminase; CK: Creatine kinase; CVP: Central venous pressure; GGT: Gamma glutamyl transferase; LDH: Lactate dehydrogenase

DISCUSSION

Cardiopulmonary bypass implementation in open heart surgery is known to cause physiological stress and have adverse effects on organ functions and perfusions. Ischemia of the abdominal organs, inflammation and failure, gastrointestinal bleeding and perforation are few of these group of pathologies (1,2,5). Hepatobiliary complications that can be encountered after open heart surgery are basically evaluated into two groups. The first group includes a wide range spectrum between mild increase in hepatic enzymes and acute hepatic failure caused by hepatocellular necrosis, and the second group includes prehepatic, hepatic or posthepatic originating hyperbilirubinemia states (7). For the changes in the splanchnic organs to clinically evident and elicit findings will take at least 24 hours. In another words, in adult patients undergoing open heart surgery, the ischemia of the somatic organs can be recognized after the first 24 hours after the operation when clinical signs appear. Thus, the observance of the perfusion of the splanchnic organs is necessary and crucial. Studies have stressed the importance of the issue, advocating the importance of suspecting early on of postoperative acute hepatic damage facilitating early diagnosis and taking early measures (6-8). Hepatic hypoperfusion, hepatotoxic drugs and viral agents are implicated in development of postoperative hepatocellular damage. Hepatic hypoperfusion leads to necrosis in the centrilober area where oxygenation is the poorest. Hepatic congestion

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due to right heart failure and other etiologies is also considered as important risk factors in hepatocellular damage (9).

Different results have been reported on the hepatic function tests after open heart surgery in the literature. In a study performed by Shahbazi et al. (10); AST, ALT, ALP, direct and indirect bilirubin levels were measured for evaluating postoperative hepatic functions in patients undergoing CABG with CPB. It was found that the statistically significant increases in postoperative AST, ALT, direct and indirect bilirubin levels according to their preoperative levels, but the decrease in postoperative ALP levels was not statistically significant. In the same study, the authors claimed that longer aortic cross clamp time and need for intraaortic balloon pump were related with the postoperative deterioration of the hepatic function tests, and they purported the usage of methods that would shorten CPB and aortic cross clamp times would be beneficial for preserving hepatic function. Akhlagh et al. (11) have studied the changes of hepatic enzymes and bilirubin levels after CABG. They found that there were no significant difference between postoperative AST, ALT, ALP levels and preoperative levels, but it was found a statistically significant increase in postoperative bilirubin levels compared with the preoperative bilirubin levels. Aral et al. (2) have studied the postoperative hepatic function tests of patients after open heart surgery with CPB. In their study, it was studied the postoperative changes of AST and ALT levels, and the authors found that the AST levels made a peak on PO days 1 and 2, prominently falling on PO day 7, ALT levels on PO days 1, 2, 7 were prominently higher than preoperative levels. In another recent study; AST, ALP and total bilirubin levels on postoperative third day were statistically higher than preoperative levels after open heart surgery, while this statistically significant increase was not observed for ALT levels. In consequence of their study, the authors thought that the temporary increases in hepatic enzymes after open heart surgery could be related to decrease of hepatic blood flow, hypoxia and secondary to CPB-associated inflammation (12). Yamada et al. (13) analyzed postoperative hepatic functions in patients undergoing CABG with and without CPB, and they used more sensitive markers such as alcohol dehydrogenase and alpha glutation S transpherase for the evaluation of hepatic damage. The increases of both two parameters were lower in the group that operated on beating heart without CPB compared with the patients operated with CPB, and this difference was statistically significant. In the same study; in patients operated under CPB, the levels of alcohol dehydrogenase and alpha glutation S transpherase increased right after the commencement of CPB, reaching peak levels at the end of surgery, a decline to preoperative levels 12 to 24 hours after cessation of anesthesia, and the authors concluded that CPB induces temporary subclinical hepatocellular damage. In our study; the blood levels of AST, ALT, LDH, GGT, bilirubin and INR increased in early postoperative period and later resumed to normal range. Meanwhile, ALP, albumin, total protein, total cholesterol levels exhibited a prominent decrease on postoperative day 1, followed with gradual increase recovering their preoperative levels. Since AST levels are susceptible to other parameters other than the liver, we regarded the ALT levels as indicator for hepatic damage. In addition to this being a specific indicator for hepatic damage, GGT was included in our study and has not displayed a significant increase.

Though the incidence of hyperbilirubinemia after open heart surgery varies according to the type of surgery, it is observed in 25-35% of patients (3,9,14,15). In our case series, postoperative hyperbilirubinemia was observed with a lower incidence compared with the studies in the literature, and our postoperative hyperbilirubinemia rate was 17.5%. This discrepancy can be explained by the small number of patients in our study, most of our cases being subjected to isolated first-time CABG, and the difference in the definition of hyperbilirubinemia. Postoperative hyperbilirubinemia can be classified into three main groups; as prehepatic, hepatic and posthepatic. In the etiology of prehepatic hyperbilirubinemia; CPB systems, blood transfusions, hemolysis and resorption of hematomas occurring in the postoperative period are implicated. The interesting point here is that postoperative hemorrhagic incidents have a multifactorial etiological effect on the development of hyperbilirubinemia. These are resorption of the hematomas occurring during bleeding and/or later and blood transfusions (7).

In our study population, patients that displayed postoperative hyperbilirubinemia and those who did not were compared for probable risk factors, and as a result, high levels of preoperative CK values and low levels of preoperative albumin values were both associated with the development of postoperative hyperbilirubinemia. Although there is numerous studies on this subject in the literature, similar results have been attained in different studies. Mastoraki et al. (14) have concluded that long CPB and aortic cross clamp times, need for inotropes and intraaortic balloon pump, and quantity of blood transfusions as factors related to development of hyperbilirubinemia after cardiac surgery. An et al. (15) have stated that the risk factors for postoperative hyperbilirubinemia as increase in preoperative bilirubin levels, increase in right atrium pressure, need for transfusion, number of replaced valves. They also believed that there was a relation between prolonged mechanical ventilator need, length of intensive care unit stay, increased mortality and postoperative hyperbilirubinemia. Kraev et al. (3) have shown that hyperbilirubinemia after CPB was related both with early morbidity and mortality, and it was also an independent predictor for long-term mortality. In the study by Nishi et al. (16) the factors related to hyperbilirubinemia after cardiac valve surgery were preoperative hepatic dysfunction, history of congestive heart failure, infective endocarditis, presence of cardiogenic shock and prolonged CPB time, furthermore when the multivariate analysis performed, preoperative hepatic dysfunction and prolonged CPB time were found to be the independent predictors of postoperative hyperbilirubinemia. In another recent study, high preoperative bilirubin levels and prothrombin time, prolonged CPB and aortic cross clamp times, increase in

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blood transfusions, prolonged inotropic support, prolonged mechanical ventilator dependency, prolonged intensive care unit and hospital stay were all implicated as risk factors for postoperative hyperbilirubinemia (17).

In our study, we observed only one mortality and since it would not be statistically significant correlation analysis between postoperative hyperbilirubinemia and mortality was not performed. Patients with high levels of bilirubin prior to the operation were excluded from the study. When the levels of preoperative bilirubin were compared between the groups that displayed postoperative hyperbilirubinemia and those did not the differences were statistically insignificant. In analyzing our patients in regard to the aortic cross clamp times, no statistically significant relation was found among the patients developing hyperbilirubinemia and those did not. Our findings did not correlate with the results in the literature. In a similar way, no statistically significant relation was established between patients developing hyperbilirubinemia and those did not develop hyperbilirubinemia in relation with the amount of blood transfusion, and our this finding did not correlate the findings in the literature. In our opinion, the reason for these situations is our relatively small number of patients.

CONCLUSION

Hepatocellular damage and hyperbilirubinemia can occur in various degrees and due to multitude of causes following open heart surgery. In this present study, patients undergoing open heart surgery were evaluated in regard to postoperative hepatic dysfunction and hyperbilirubinemia. We think that the most notable point of our study is that very frequently measuring of numerous liver function tests after open heart surgery. Furthermore, related articles in the literature are old dated and few. Therefore, we also aimed to review the recent literature and compare with our results. However, our study had several limitations. The major limitations of our study were relatively small number of study population, lacks of both homogeneous patient distribution and long-term follow-up results. Finally, we believe that the effects of cardiac surgery performed with CPB on the hepatobiliary system and the probable risk factors should be investigated, patients posing high risk for developing hepatic failure and hyperbilirubinemia should be predicted preoperatively, necessary precautions should be taken perioperatively, the quality of perioperative patient care should be improved, and the complications should be managed appropriately. For this purpose, further studies with larger patient populations and longer follow-up periods are required.

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