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Original Article

The potency of intraoperative execution on immediate postoperative outcome in patients with chronic hepatitis C viral infection undergoing mitral valve replacement

Ahmed Saber[1], Waleed Adel[1], Khalid Ragab[2], Sherif Nasr[3]

[1]Department of Cardiothoracic Surgery, Cairo University, Cairo, Egypt

[2]Department of Cardiothoracic Surgery, Beni Suef University, Beni Suef, Egypt

[3]Department of Cardiothoracic Surgery, El-Fayoum University, El-Fayoum, Egypt

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Abstract

Background: Prior studies on chronic hepatitis C viral (HCV) infection patients in cardiac surgery were generalized focusing on cirrhotic patients, not on milder forms. Thus, recommendations, surgical indications, and maneuvers were not conclusive. This work aims at illustrating the impact of intraoperative performance of mitral valve replacement (MVR) on the immediate postoperative outcome parameters, recovery, and survival to deduce beneficial recommendations to improve the operative and postoperative results of this high-risk group of patients.

Methods: This study included 144 chronic HCV infection patients presenting with rheumatic mitral valve disease necessitating MVR between April 2012 and March 2019. Group (I) included 108 patients with <45 minutes ischemic time and group (II) included 36 patients with >45 minutes ischemia.

Results: Group (I) who was subjected to statistically significant lower ischemic time showed statistically significant operative and immediate postoperative outcome parameters: total cardiopulmonary bypass (CPB) time, total operative time, smooth weaning off bypass, intraoperative hemodynamic parameters, duration of mechanical ventilation, duration of inotropic support medications in intensive care unit (ICU), postoperative platelets transfusion, postoperative values of transaminases, alkaline phosphatase, total bilirubin and creatinine, incidence of postoperative acute renal failure, time needed to reach target INR, total ICU stay, and total duration of hospital admission. The overall postoperative mortality was 6 (4.16%); 3 (2.77%) deaths in group (I) and 3 (8.33%) deaths in group (II) (p>0.05) and the overall hospital complication rate was 32.41% and 38.88% for group (I) and (II) respectively (p>0.05).

Conclusions: Efficient intraoperative performance: meticulous quite fast surgical maneuver, proper oxygenation, CPB flow rate, and pressure maintenance, metabolic acidosis and glucose level control, and fresh blood transfusion post-CPB have a great positive impact on the immediate postoperative outcome on this high-risk cohort.

Keywords: hepatitis C, mitral valve, rheumatic diseases, surgery

Address for Correspondence: Ahmed Saber, Department of Cardiothoracic Surgery, Cairo University, Cairo, Egypt.
E-mail: ahmedsaber78@yahoo.com

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Introduction

Rheumatic heart disease (RHD) represents a serious problem affecting health in poor countries [1-4]. There are 33 million people around the world affected by RHD [5]. However, this is underestimated due to lack of diagnosing RHD [6], and the scarcity of needed studies in the affected regions. Egypt is one of the high-risk affected areas but, unfortunately, no accurate data on the prevalence of RHD is available using the World Heart Federation (WHF) criteria used currently although the survey that shows the overall prevalence of 31 cases per 1000 children [7]. Mitral valve replacement (MVR) remains the favorable definitive treatment for rheumatic mitral valve disease (MVD) causing mitral stenosis and/or regurgitation in developing countries [8,9]. It is even preferable to trials of mitral valve repair because of the rheumatic mitral valve affection causing severe annular calcification, valvular fibrosis and thickening, commissural fusion, subvalvular chordal thickening, fusion and/or rupture, and progressive cardiomyopathy [10].

The seventh leading cause of mortality globally is viral hepatitis [11]. Hepatitis C virus (HCV) alone shares with 50%. It is a major etiological factor of liver fibrosis, cirrhosis, and tumor [12,13]. About 180 million people, that is almost doubled in the past two decades, are affected by HCV around the world representing 3% of its population. HCV infection is highly prevalent in Egypt. Antibody prevalence studies done by the Egypt Demographic and Health Surveys (EDHS) shows higher levels than global ones. They were done among population aged 15–59 years and showed prevalence of 14.7% in 2009 [14] and 10.0% in 2015 [12,13,15,16]. Proper preoperative assessment became mandatory for the increasing number of surgical candidate patients having HCV (due to recent lines of viral hepatitis management) because they are at high risk of perioperative mortality as an effect of the surgery and anesthetic agents on the liver [17,18]. Cardiovascular operations, particularly, have much higher-risk of adverse events in this subset of patients necessitating proper operative and postoperative management [19].

This work is initiated to illustrate the impact of intraoperative performance of MVR in this cohort of patients on the immediate postoperative outcome parameters, recovery, and survival in favor to deduce whatever recommendations and precautions could be of benefit to improve the operative and postoperative results of this high-risk group of patients.

Methods

Study design

This retrospective observational non-randomized study included 144 documented chronic HCV infection patients presenting with rheumatic MVD necessitating mitral valve surgery with a decision made for MVR. Written informed consent of each and every patient was obtained preoperatively. All surgeries were carried out in Egypt (conducted in the operating theatre of the Department of Cardiothoracic Surgery, Faculty of Medicine, Cairo University and other open-heart surgery centers) using standard open-heart surgical procedures. Data of the study was collected for the operated-upon patients in the period between April 2012 and March 2019. In concordance with the purpose of the study, the study population was divided into two groups based on the ischemic (cross clamp) time needed to conduct the procedure where group (I) included 108 patients with less than 45 minutes ischemic time and group (II) included 36 patients with more than 45 minutes ischemia. The data of the study population was collected from the cardiothoracic section computer database supplemented by a review of hospital records. All the data was studied and thoroughly evaluated in the preoperative, intraoperative, and immediate postoperative periods.

Inclusion and exclusion criteria

The included chronic HCV patients were those having rheumatic MVD that required MVR surgery. The excluded patients were those with echocardiographic evidence of rheumatic MVD requiring repair attempt, patients with associated tricuspid valve disease requiring concomitant repair or replacement, patients with concomitant aortic valve surgery, patients with concomitant ischemic heart disease (IHD) requiring coronary artery bypass grafting (CABG) surgery, and re-do MVR cases. Patients with liver diseases other than HCV infection, hepatocellular carcinoma, acute fulminant hepatitis, MELD (Model for End-stage Liver Disease) score more than 20 were also excluded. Extremes of age (less than 18 or more than 70 years) were not involved in the study.

Management protocol

Preoperatively

Assessed preoperative variables were age, sex, smoking, hypertension, diabetes mellitus, chronic obstructive pulmonary disease (COPD), atrial fibrillation (AF), chronic renal disease (defined as a creatinine clearance of less than 30 ml/min), previous cerebrovascular accidents (CVA), peripheral vascular disease (defined as the presence of lower limb arterial disease stage I or II according to Leriche and Fontaine classification or a history of vascular surgery), rheumatic fever history, HCV infection history and MELD score, routine preoperative laboratory investigations (complete blood count (CBC), liver and renal function tests, coagulation profile, serum electrolytes (sodium and potassium), fasting blood glucose (FBG)), resting 12-lead electrocardiogram (ECG), plain chest X-ray, cardiac catheterization, and preoperative baseline transthoracic echocardiography (TTE). Risk assessment was done by calculation of EuroSCORE II (European System for Cardiac Operative Risk Evaluation) and MELD score.

Intraoperatively

The analyzed operative variables included intraoperative mortality, aortic cross-clamping (ischemic) time, cardiopulmonary bypass (CPB) time, blood glucose level (during and after CPB), metabolic acidosis, hemodynamics, the difficulty of weaning off CPB, inotropic support demand, and blood transfusion. At the operating room, all patients were pre-medicated by intravenous 0.1 mg/kg midazolam. They were monitored with arterial catheter connected to a pressure transducer for invasive arterial blood pressure monitoring, nasopharyngeal temperature probe, central venous catheter inserted in the internal jugular vein, pulse oximetry, ECG, capnography, urinary catheter, and frequent arterial blood gases (ABGs) measurements for pH, electrolytes, and glucose every 15 minutes. Diabetic patients were subjected to intra-operative tight (strict) glycemic control using intravenous insulin infusion (prepared by mixing 100 units of insulin with 50 ml 0.9% normal saline) aiming to keep blood glucose measures at 110-150 mg/dl. General anesthesia was induced with 3–5 mg/kg thiopental, 2–10 mg/kg fentanyl, and 0.1 mg/kg pancuronium. Manual ventilation was followed by endotracheal intubation using proper-sized cuffed endotracheal tube. Maintaining general anesthesia was done with isoflurane and additional doses of propofol infusion, 1–2 micro.gm/kg fentanyl, and 0.01 mg/kg pancuronium. Prior to major vessels cannulation, an initial dose of heparin (300–400 IU/kg) was administered to get activated clotting time (ACT) higher than 400 s. Extra doses of heparin were given on the need to maintain ACT higher than 400 s during CPB time. Protamine chloride was used to reverse heparin at a 1:1 ratio of the initial loading dose at the end of CPB. Operative technique was always the same for all the study population. All the patients were routinely scrubbed and draped exposing the chest. After standard median sternotomy, pericardiotomy, and suspension of the pericardial edges, the ascending aorta was cannulated followed by bicaval cannulation for venous drainage with application of tapes around the superior (SVC) and inferior (IVC) vena cava (to be snared if un-intentionally the right atrium was opened to guard against air embolism). A two-way cannula was inserted in the aortic root for venting. After institution of CPB, cooling started to achieve systemic core body temperature of 28-30°C. The ascending aorta is then cross-clamped and myocardial protection was achieved by intermittent antegrade infusion of cold crystalloid cardioplegia initially for 45 minutes then every 30 minutes for the subsequent doses. The priming volume was always 800–1000 mL. The pump flow was between 2.0 and 2.8 L/min/m^2 and the target mean arterial pressure was at 60-80 mmHg. Typically for all patients, left atriotomy was done, manual left atrial retractor was applied, through visualization of the gross patho-anatomy of the mitral valve apparatus to confirm the preoperative TTE description and dealing with it, e.g. removal of calcified deposits and left atrial (LA) thrombus removal. All the patients were submitted for isolated MVR using metallic bileaflet prostheses sized 27-29 (St. Jude) after resection of the anterior mitral leaflet (AML) and preservation of the posterior mitral leaflet (PML) using 2/0 pledgeted ethibond sutures. After completion of the procedure and closure of left atriotomy with 4/0 prolene and insertion of LA vent, the aorta was declamped after de-airing maneuvers and the patient was completely re-warmed to 37°C and all electrolytes and acid-base imbalances adjusted and properly corrected. The patient was then weaned off CPB. Protamine was then administered, followed by decannulation, meticulous hemostasis, placement of epicardial pacemaker wires and closure over wide-pore 32-36F retrosternal and may be pleural drains (if either pleura was opened). All monitoring lines and hemodynamic support were maintained during the transfer of the patient to the intensive care unit (ICU). All the patients were transferred mechanically ventilated.

Postoperatively

All patients were followed-up during ICU stay for hemodynamic status, duration of mechanical ventilation, total blood loss, blood products (packed red blood cells, platelets, and fresh frozen plasma) transfusion, blood glucose level, the need and duration of inotropic support, daily laboratory investigations, and total ICU stay. All patients were followed-up during postoperative hospital stay for postoperative mortality, morbidity, and adverse complications (cerebrovascular accidents, pulmonary embolism, low cardiac output syndrome, rhythmic complications, hemorrhagic complications, respiratory complications, acute renal failure, deep and superficial sternotomy wound infections), time taken to reach the target INR, total duration of hospital stay, and routine postoperative TTE. The overall hospital complication rate was estimated upon the number of patients with at least one hospital complication. CVA was defined as a new stroke or a transient ischemic attack (TIA) for at least 24 hours. Low cardiac output syndrome was defined as the need for the use of two catecholamines beyond 10 microgram/kg/min dose. Perioperative mortality was defined as any death occurring during the 30 days postoperatively. Rhythmic complications were defined by the presence of a supraventricular, nodal or ventricular rhythm disorder. Hemorrhagic complications were defined by re-operation to control bleeding or to relieve cardiac tamponade. Respiratory complications were defined by the development of pneumonia, pulmonary atelectasis, and respiratory failure (prolonged ventilation more than 48 hours postoperatively, re-intubation or tracheostomy). Acute renal failure was defined as a rise in the creatinine level (absolute ≥0.3 mg/dl, percentage ≥50%) needing treatment or dialysis. Deep sternotomy wound infections were defined as a surgical infection occurring within 30 days, extending beyond the deep tissue plane with bacteriological samples of positive infected tissues or purulent discharge. Packed red blood cells were administered according to the Society of Thoracic Surgeons score guidelines [20], and fresh frozen plasma and platelets were administered only when necessary (if the platelet count is less than $70\times10^3/mm^3$) [19].

Table 1. Patients' preoperative characteristics

	Group (I) (n= 108)	**Group (II) (n= 36)**	***p*-value**	**Significance**
Age (years)	35.24 ± 6.87	35.66 ± 6.43	>0.05	NS
Male/Female	50/58 (46.29/53.70%)	14/22 (38.88/61.11%)	>0.05	NS
Positive RF history	90 (83.33%)	28 (77.77%)	>0.05	NS
Smoking	28 (25.92%)	8 (22.22%)	>0.05	NS
HTN	12 (11.11%)	6 (16.66%)	>0.05	NS
Chronic renal disease	10 (9.25%)	4 (11.11%)	>0.05	NS
Diabetes mellitus (DM)	6 (5.55%)	4 (11.11%)	>0.05	NS
COPD	8 (7.41%)	2 (5.55%)	>0.05	NS
AF	40 (37.03%)	14 (38.88%)	>0.05	NS
Mean C/T ratio	0.69 ± 0.01	0.65 ± 0.03	>0.05	NS
LVEDD (cm)	5.71 ± 0.5	5.69 ± 0.7	>0.05	NS
LVESD (cm)	4.39 ± 0.7	4.35 ± 0.7	>0.05	NS
LA (cm)	4.10 ± 0.3	4.05 ± 0.6	>0.05	NS
EF (%)	60.7 ± 4.1	60.3 ± 3.5	>0.05	NS
Hemoglobin (gm/dl)	11.5 ± 1.6	11.4 ± 1.3	>0.05	NS
Platelet count ($x10^3/mm^3$)	160.5 ± 77.7	159.5 ± 61.9	>0.05	NS
Total bilirubin (mg/dl)	1.46 ± 0.45	1.47 ± 0.38	>0.05	NS
ALT (IU/l)	55.41 ± 24.92	56.11 ± 22.53	>0.05	NS
AST (IU/l)	53.18 ± 28.32	55.17 ± 29.24	>0.05	NS
AST/ALT ratio	0.93 ± 0.22	0.94 ± 0.21	>0.05	NS
Alkaline phosphatase (IU/l)	78.63 ± 38.12	78.88 ± 32.43	>0.05	NS
Albumin (gm/dl)	3.38 ± 0.30	3.34 ± 0.28	>0.05	NS
Creatinine (mg/dl)	1.56 ± 0.19	1.51 ± 0.25	>0.05	NS
Urea (mg/dl)	36.30 ± 19.80	37.44 ± 17.91	>0.05	NS
Prothrombin conc. (%)	85.57 ± 7.70	84.94 ± 7.92	>0.05	NS
PTT (sec)	32.65 ± 5.41	32.55 ± 5.33	>0.05	NS
INR	1.16 ± 0.05	1.17 ± 0.05	>0.05	NS
Na^+ (mmol/l)	138.8 ± 4.4	138.2 ± 4.6	>0.05	NS
K^+ (mmol/l)	4.2 ± 0.6	4.4 ± 0.5	>0.05	NS
FBG	127.8 ± 31.1	123.3 ± 19.1	>0.05	NS
MELD score	13.35 ± 1.68	13.39 ± 1.59	>0.05	NS
EuroSCORE II	1.29 ± 0.71	1.31 ± 0.50	>0.05	NS

RF: Rheumatoid factor, HTN: Hypertension, COPD: Chronic obstructive pulmonary disease, AF: Atrial fibrillation, LVEDD: Left Ventricular End-Diastolic Diameter, LVESD: Left Ventricular End-Systolic Diameter, LA: Left atrium, EF: Ejection fraction, ALT: Alanine transaminase, AST: Aspartate transaminase, PTT: Partial thromboplastin time, INR: International normalized ratio, FBG: Fasting blood glucose, MELD: Model for end-stage liver disease

Statistical analysis

All patients' data were tabulated and processed using SPSS V13.0 (SPSS Inc., Chicago, IL) for Windows 2007. Quantitative variables were expressed using mean and standard deviation and were compared using the t-student test. Qualitative variables were compared using the Chi-square test or Fischer's exact test when appropriate. Correlation between parameters was performed using Spearman's rank correlation coefficient. In all tests, the p-value was considered significant when p<0.05, highly significant when p<0.01, and extremely significant when p<0.001.

Results

In the period between April 2012 and March 2019, 144 documented chronic HCV infection patients were operated upon for their diagnosis of rheumatic MVD necessitating mitral valve surgery with a decision made for MVR. The study population was divided into two groups based on the ischemic (cross clamp) time needed to conduct the procedure where group (I) included 108 patients with less than 45 minutes ischemic time and group (II) included 36 patients with more than 45 minutes ischemia. The preoperative, operative, and postoperative data of both groups were thoroughly studied and compared.

Preoperative data

The study populations were 64 (44.44%) men and 80 (55.55%) women whose ages ranged from 21 to 52 years with a median age of 36.7 years. Further analysis of the preoperative patients' characteristics of both groups is summarized in Table 1.

Operative data

All patients of both groups were submitted for MVR. No intraoperative mortality occurred. Group (I) showed statistically significant differences regarding total ischemic (cross clamp) time, total CPB time, total operative time, and smooth weaning off bypass. Hemodynamic parameters (mean arterial blood pressure and mean central venous pressure) showed statistically significant differences among both groups. Table 2 illustrates the analyzed operative data.

Table 2. Intraoperative data

	Group (I) (n= 108)	Group (II) (n= 36)	*p*-value	Significance
Total operation time (min)	185.21 ± 3.56	240.11 ± 6.52	<0.05	Significant
Total CPB time (min)	61.71 ± 5.53	102.32 ± 3.73	<0.05	Significant
Total cross clamp time (min)	40.61 ± 3.32	74.11 ± 5.41	<0.05	Significant
Smooth weaning off CPB	95 (87.96%)	25 (69.44%)	<0.05	Significant
Blood glucose (during CPB) (mg/dl)	190.5 ± 21.8	198.6 ± 36.1	>0.05	NS
Blood glucose (after CPB) (mg/dl)	136.5 ± 21.8	138.6 ± 36.1	>0.05	NS
Metabolic acidosis	20 (18.51%)	8 (22.22%)	>0.05	NS
ABP (before CPB) (mmHg)	95.85 ± 17.81	95.61 ± 15.17	>0.05	NS
ABP (after CPB) (mmHg)	83.93 ± 18.31	81.42 ± 12.51	>0.05	NS
ABP (before shift to ICU) (mmHg)	91.05 ± 13.39	83.55 ± 11.29	<0.05	Significant
CVP (before CPB) (cmH_2O)	13.32 ± 3.06	13.35 ± 2.61	>0.05	NS
CVP (after CPB) (cmH_2O)	13.66 ± 4.11	13.97 ± 5.32	>0.05	NS
CVP (before shift to ICU) (cmH_2O)	13.95 ± 2.10	14.2 2 ± 3.81	<0.05	Significant
Blood transfusion (ml)	517.5 ± 411.1	531.1 ± 415.2	>0.05	NS

CPB: Cardiopulmonary bypass, APB: Arterial blood pressure, CVP: Central venous pressure, ICU: Intensive care unit

Postoperative data

All the patients were discharged to the ICU mechanically ventilated and discharged to a regular room after stabilization. Overall postoperative mortality was 6 (4.16%); 3 (2.77%) deaths in group (I) and 3 (8.33%) deaths in group (II) (p>0.05). Group (I) showed statistically significant differences as regards duration of mechanical ventilation, duration of inotropic support medications needed to normalize hemodynamics, platelets transfusion, values of ALT, AST, alkaline phosphatase, total bilirubin and creatinine, incidence of acute renal failure, time needed to reach target INR for MVR, total ICU stay, and total duration of hospital admission. Postoperative data are shown in Table 3.

Table 3. Postoperative data

	Group (I) (n= 108)	Group (II) (n= 36)	*p*-value	Significance
Mechanical ventilation duration (hrs)	7.12 ± 1.31	30.4 ± 4.31	<0.01	Highly significant
Inotropic support (hrs)	22.9 ± 1.35	42.2 ± 4.89	<0.05	Significant
Total blood loss (ml)	547.5 ± 411.1	631.7 ± 515.2	>0.05	NS
Reoperation for bleeding	8 (7.41%)	3 (8.33%)	>0.05	NS
Platelets transfusion	28 (25.92%)	15 (41.66%)	<0.05	Significant
APB (mmHg)	99.73 ± 25.11	96.45 ± 28.32	>0.05	NS
CVP (cmH_2O)	10.75 ± 2.21	11.85 ± 2.11	>0.05	NS
Total bilirubin (mg/dl)	1.03 ± 0.23	1.78 ± 1.63	<0.05	Significant
ALT (mmol/l)	78.23 ± 54.33	119.5 ± 75.21	<0.05	Significant
AST (mmol/l)	64.98 ± 64.12	108.3 ± 67.91	<0.05	Significant
Alkaline phosphatase (IU/l)	100.2 ± 15.07	138.4 ± 13.09	<0.05	Significant
Albumin (gm/dl)	3.01 ± 0.20	3.04 ± 0.18	>0.05	NS
Creatinine (mg/dl)	1.64 ± 0.82	1.92 ± 0.97	<0.05	Significant
Urea (mg/dl)	39.24 ± 9.12	45.01 ± 24.31	>0.05	NS
Blood glucose level (mg/dl)	130.7 ± 29.2	130.5 ± 31.8	>0.05	NS
Platelet count ($x10^3/mm^3$)	151.2 ± 68.4	150.3 ± 42.7	>0.05	NS
Respiratory complications	5 (4.63%)	5 (13.88%)	>0.05	NS
AF	45 (41.66%)	17 (47.22%)	>0.05	NS
Nodal rhythm	2 (1.85%)	1 (2.77%)	>0.05	NS
ARF	7 (6.48%)	8 (22.22%)	<0.05	Significant
Low COP syndrome	1 (0.93%)	1 (2.77%)	>0.05	NS
Stroke	0 (0.00%)	1 (2.77%)	>0.05	NS
Total ICU stay (days)	2.52 ± 1.41	5.17 ± 3.34	<0.05	Significant
Deep wound infection	1 (0.93%)	1 (2.77%)	>0.05	NS
Superficial wound infection	6 (5.55%)	5 (13.88%)	>0.05	NS
Time to reach target INR (days)	4.12 ±1.13	9.87 ± 1.50	<0.05	Significant
Total hospital stay (days)	8.47 ± 1.25	21.24 ± 1.13	<0.05	Significant
Postoperative mortality	3 (2.77%)	3 (8.33%)	>0.05	NS
Overall hospital complications	35 (32.41%)	14 (38.88%)	>0.05	NS

APB: Arterial blood pressure, CVP: Central venous pressure, ALT: Alanine transaminase, AST: Aspartate transaminase, AF: Atrial fibrillation, ARF: Acute renal failure, COP: Cardiac output syndrome, ICU: Intensive care unit, INR: International normalized ratio

Discussion

A higher percentage of patients with hepatic dysfunction is met in the cardiac surgery operating theater for different types of cardiac pathology due to increased incidence of liver disease and more survival owing to better management and newer lines of treatment [21].

During surgery, liver cell necrosis is usually prevented by some hepatic compensatory mechanisms. The liver reduces its oxygen need and/or increases its extraction from the bloodstream. Thus, liver ischemia may not occur due to reduced total blood flow coming to it [22,23]. In cardiac surgeries using CPB, these mechanisms are reported namely: low hepatic venous oxygen saturation (ShvO2) and increased hepatosplanchnic oxygen extraction both during and after bypass [24].

Because the liver cells are usually protected against short periods of ischemia, like those met during CPB, hepatic dysfunction does not result after it [25]. However, patients with preoperative hepatic disease are at high risk of postoperative hepatic dysfunction with prompt morbidity and possible mortality [26].

To estimate the hepatic function degree, it is necessary to evaluate the results of the different liver function tests because it has multiple functions and the results of every single test do not reveal the same degree of its dysfunction. Thus, there is no single test alone properly evaluating the liver function [26]. One of the currently used scores is the MELD score. It is the currently used standard tool for liver transplantation for organ allocation [27], and also for risk estimation of patients with hepatic dysfunction [28]. It was first used to predict survival in a small number of patients undergoing transjugular intrahepatic portosystemic shunt procedures [29]. It is worthy to note that current cardiac risk scores such as EuroSCORE II and the Society of Thoracic Surgeons score do not include hepatic dysfunction despite its importance with respect to postoperative complications [30]. These scores and the Child–Turcotte–Pugh (CTP) classification are used to predict post-cardiac surgery morbidity and mortality in cirrhotic patients [31].

In this retrospective observational non-randomized study, 144 documented chronic HCV infection patients were included presenting with clinically and echocardiographically diagnosed severe rheumatic MVD and had undergone MVR surgery. According to the total ischemic (cross clamp) time needed to perform the surgical procedure, they were classified into two groups; group (I) involved 108 patients who had less than 45 minutes (mean 40.61±3.32 minutes) corresponding to a single dose cardioplegic cardiac arrest and group (II) involved 36 patients who had more than 45 minutes (mean 74.11±5.41 minutes) corresponding to more than one dose of cardioplegia ($p<0.05$).

On examining the cardiac surgery risk on patients with liver disease, most studies focused on cirrhotic patients and less is reported about milder degrees of hepatic dysfunction. Moreover, intraoperative performance and execution of a specific cardiac procedure e.g. MVR and its impact on the operative and postoperative outcome was scarcely addressed [32,33].

The preoperative profile and demographic characteristics of the study population were homogenous showing no statistically significant differences between the two groups. 55.55% were females and 44.44% were males with a median age of 36.7 years (range 21-52 years) representing a younger study population than other studies [17,19,28]. In agreement with others [28-30], no association between age and postoperative morbidity and mortality was found. This is in contrast to Amal et al [17], Morisaki et al [19] who studied 42 cirrhotic patients who underwent cardiovascular operations and found that age was significantly associated with hospital morbidity in multivariate analysis, and Teh et al [28] who examined abdominal, orthopedic, and cardiovascular surgery in 772 cirrhotic patients, and their results showed that age contributes to postoperative mortality risk and demonstrated that an age more than 70 years added 3 MELD points to the mortality rate. Their results may be attributed to increasing cardiopulmonary comorbidity associated with increasing age. We believe that age associated with other co-morbidities may be used as predictors of morbidity and/or mortality. However, in general, patients aged less than 18 years or more than 75 years are at higher risk of mortality [17].

The MELD score is now a standard test for evaluating hepatic dysfunction [34]. It is a simple and objective test. It consists of three laboratory results: INR, total bilirubin, and creatinine. It is preferred to CTP classification which uses subjective indicators, such as ascites and encephalopathy and it involves renal function examination which is not present in the CTP classification. So, for cardiovascular surgery patients with hepatic dysfunction, MELD score is considered a more suitable scoring system. Both MELD and CTP scores have been used in multiple cohorts of patients with different degrees of hepatic dysfunction [35]. The CTP score ranges between 5 and 15 and has only three classes (classes A, B, and C). The MELD score ranges more widely (between 6 and 40). Thus, the MELD score provides a more accurate estimation of morbidity whereas the CTP score provides only information about which group the patient can belong to (low-risk, intermediate risk, or high-risk group). The CTP score does not predict the mortality risk definitely. However, Filsoufi et al [36] in their study on 27 patients with cirrhosis who underwent cardiac surgery reported that the CTP classification was a better predictor of hospital death than the MELD score. We believe that the reason of this conflicting result may be attributed to the relatively small sample size taken by Filsoufi et al. Our study analyzed the preoperative INR, serum creatinine and total serum bilirubin, which represent the three components of the MELD score, between the two groups showing no statistically significant differences between them. The mean MELD score was 13.35±1.68 for the group (I) and 13.39±1.59 for the group (II) ($p>0.05$) that is associated with a probable 6% mortality [34]. This is higher than what was mentioned by Amal et al [17] who reported a mean score of 10.12±2.7 and that their results implied that MELD score may affect hospital morbidity based on univariate analysis and it is an independent risk factor for morbidity based on multivariate analysis. Their results indicated that the best cutoff value for MELD score was found to be 12, with an optimal sensitivity of 69% and a specificity of 96%, and they stated that a MELD score exceeding 12 may, therefore, be a reliable predictive value for morbidity in patients with liver dysfunction undergoing cardiovascular operations. This association that was not found in our studied groups who showed almost similar preoperative MELD score and different postoperative outcome explained by the different intraoperative parameters that affected the postoperative results. Our results may come matched with those reported by Hsieh et al [30] who studied 105 elective cardiac surgery patients with documented chronic viral hepatitis.

The EuroSCORE II is nowadays the best scoring system assessing quantitatively the surgical risk factors and providing good estimates of postoperative cardiac surgery outcomes [35,37]. Surprisingly, it does not include in its components any parameter concerning hepatic dysfunction although there are many studies expressing the impact of hepatic dysfunction on cardiac performance [31,33]. In our study, the mean EuroSCORE II was low (1.29±0.71 and 1.31±0.50 ($p>0.05$) for group (I) and (II) respectively) and the overall hospital complication rate was (32.41% and 38.88% for group (I) and (II) respectively); results denoting that EuroSCORE II is not a sensitive tool for risk assessment in hepatic patients undergoing cardiac surgery with the use of CPB. One recent study [17] that showed a lower mean EuroSCORE II value (1.12±0.56) and even higher postoperative morbidity and mortality (43% of their patients experienced significant morbidity or mortality postoperatively) agrees with our deduction.

In the present study, it was found that group (I) patients who were subjected to statistically significant lower ischemic (cross clamp) time showed statistically significant operative and immediate postoperative outcome parameters. This group showed statistically significant total CPB time, total operative time, smooth weaning off bypass, intraoperative hemodynamic parameters (mean arterial blood pressure and mean central venous pressure), duration of mechanical ventilation, duration of inotropic support medications needed to normalize hemodynamics in ICU, postoperative platelets transfusion, postoperative values of ALT, AST, alkaline phosphatase, total bilirubin and creatinine, incidence of postoperative acute renal failure, time needed to reach target INR for MVR, total ICU stay, and total duration of postoperative hospital admission. These results express the importance of intraoperative execution which is not only related to surgical performance that represents the most important item but also the overall work of proper oxygenation, CPB flow rate and pressure maintenance, metabolic acidosis and glucose level control and of great importance, fresh blood transfusion post-CPB intraoperatively.

The overall postoperative mortality was 6 (4.16%); 3 (2.77%) deaths in group (I) and 3 (8.33%) deaths in group (II) ($p>0.05$). Deaths in group (I) were one due to low cardiac output and ventricular failure due to intractable persistent metabolic acidosis unresponsive to frequent correction, one due to persistent postoperative nodal rhythm and hemodynamic instability at day 9 postoperatively, and the last one was due to fulminating deep sternotomy wound infection, sepsis, and death at day 28 postoperatively. These victims (the first and the second ones) endorsed our attention of the importance of use of intraoperative transoesophageal echocardiography (TEE) even in cases of MVR and not only in mitral valve repair surgeries; to document particularly biventricular function as addressing the circumflex artery during the valve suturing cannot be excluded although no ischemic changes appeared on routinely daily done ECG in ICU. The other deaths occurred in the group (II) were; one due to low cardiac output syndrome, one due to bronchopneumonia, and one due to cerebral stroke. We believe that the first and second deaths are related to the prolonged operative setting impacting on prolonged mechanical ventilation and overall ICU stay. However, the death due to stroke was due to unpleasant air embolism, again, related to operative prolongation.

In the present study, the postoperative complications were related to the impact of intraoperative performance of the procedure in this subset of patients with hepatic dysfunction and the vulnerability of their livers to withstand prolonged durations of anesthesia, operative ischemia and CPB, a matter that addresses our conclusion of the better intraoperative execution parameters, the better the postoperative outcome. That was evident by the immediate postoperative statistically significant differences between the two groups. However, neither the operative nor the postoperative mortality showed a significant difference, and even the overall hospital complication rate was comparable between the two groups. Other studies showed comparable postoperative results to ours where Arif et al [38] and Thielmann et al [31] in their separate studies showed that renal complications were the postoperative complications. Another report by Sugimura et al [39] showed that hepatic complications were the main postoperative complications. The studies reported by Amal et al [17] and Hsieh et al [30] showed that cardiac complications were the main postoperative complications and the same result was obtained by Lopez-Delgado et al [40]. However, it is noted that the postoperative complication rate was very high in all these studies. Moreover, the incidence of complications increases with minimal degrees of hepatic dysfunctions, as demonstrated by Amal et al [17], Hsieh et al [30], and Bizouarn et al [41]. Complications like severe hepatic dysfunction, massive transfusions, and septicemia might result in elevated liver enzymes, higher renal functions, and coagulation profile in the postoperative period [17].

In agreement with our study results, Amal et al [17] demonstrated that prolongation of the aortic cross-clamping and CPB times were strongly related to hospital morbidity and death, which was confirmed by other researchers. They showed that only MELD score, cross-clamp time, and CPB time were independent risk factors for morbidity. However, they demonstrated that preoperative factors associated with hospital morbidity or mortality include age, MELD score, platelet count, serum creatinine, and total serum bilirubin.

Several studies showed that there is a strong association between thrombocytopenia and fibrosis in chronic viral hepatitis patients [42]. Filsoufi et al [36] showed that preoperative thrombocytopenia is associated with operative death in cirrhotic patients undergoing cardiac operations. They demonstrated the inverse relationship between the preoperative platelet count and the severity of cirrhosis according to CTP class. Morisaki et al [19] in their study showed that a good cutoff value for predicting postoperative morbidity was a platelet count of less than 9.6×10^4/µl and indicates the presence of advanced liver fibrosis or cirrhosis while Amal et al [17] demonstrated 15.0×10^4/µl and this cutoff value did not indicate advanced liver fibrosis or cirrhosis. However, other studies reported no difference in platelet count between the groups [39]. In the current study, preoperative platelet count was comparable to other studies with no differences between the two studied groups ($16.05\pm7.77\times10^4$/µl and $15.95\pm6.19\times10^4$/µl for group (I) and (II) respectively), but group (II) showed statistically significant difference as regards postoperative need for platelet transfusion (41.66% compared to 25.92% in group (I)) which again confirms that prolonged operative time and CPB time deplete platelets more. The reason for this conflicting result is that most of these studies contained in their groups patients with documented liver cirrhosis, and thus there were no statistical differences between groups; an example is demonstrated in the study by Lin et al [32], who investigated 55 patients with liver cirrhosis and compared between patients with mild cirrhosis (child A) and advanced cirrhosis (child B and child C), and in both groups platelet count was found to be low and ranged from 9.4 to 19.9×10⁴/µl and 8.2 to 14.7×10⁴/µl, respectively, which makes it difficult to find a significant difference between groups.

In agreement with other studies, patients with hepatic dysfunction usually have significant postoperative bleeding because of preoperative thrombocytopenia, platelet dysfunction, and low levels of coagulation factors. In the present study, we had 7.41% and 8.33% of the group (I) and (II) respectively (p>0.05) needed re-exploration for bleeding. Amal et al [17] reported that morbidity group showed significant bleeding from chest tubes with six patients needing re-exploration (6.6%), and blood products requirements were higher in the same group. An et al [33] reported that 25% of patients required re-opening to control bleeding while Murashita et al [43] reported the sum of 33% of their patients. These results confirmed the bleeding tendency in liver disease patients after open heart surgery, which was almost demonstrated by several studies [28,30-33].

Limitations

Although this study was carried out on a relatively large number of patients, it is not free from limitations. It is a retrospective observational non-randomized study. It deals with patients having chronic HCV infection (no other hepatitis viruses like HBV or other liver disease etiologies were involved). The cohort of patients was in the stage of compensated hepatic dysfunction (cirrhotic decompensated cases were not included). The study implies the results of primary (first-go) MVR (redo-MVR, mitral valve repair, other cardiac valves surgery, and IHD cases were not included). Age extremes (<17 years and >75 years) were not involved in the study.

Conclusion and Recommendations

This study represents a stepwise approach for dealing with patients with hepatic dysfunction due to chronic HCV infection representing severe rheumatic MVD requiring MVR surgery. Proper and efficient intraoperative performance in terms of meticulous and quite fast surgical maneuver, proper oxygenation, CPB flow rate and pressure maintenance, metabolic acidosis and glucose level control and of great importance, fresh blood transfusion post-CPB have a great positive impact on the immediate postoperative outcome on this high-risk cohort. We strongly recommend intraoperative TEE use in all cases of mitral valve surgery. These results address a question about the feasibility of minimally invasive and endoscopic approaches for mitral valve surgery in this subset of patients. Proper surgical decision-making is mandatory in chronic HCV patients with high MELD score, low platelet count, and high serum transaminases, creatinine, and bilirubin. It is advisable to add hepatic dysfunction to the risk scoring systems.

Conflict of interest

The authors declare no conflict of interest.

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