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Peri-operative Predictors of morbidity and mortality in patients with chronic liver disease undergoing cardiac surgeries

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Abstract

Introduction: The global prevalence of chronic hepatitis C, Hepatitis B, alcoholic-related and non-alcoholic-related fatty hepatitis liver disease has increased. In cardiovascular patients, severe liver failure raises the likelihood of complications including heart, kidney and lung infections and increases the burden of postoperative care. Work aim: to estimate the prevalence of peri-operative morbidity and death in cirrhotic patients and their determinants. Methods: This controlled cross-sectional research evaluated 30 cirrhotic patients who have been undergoing heart chirurgy as controls, as opposed to 30 non-cirrhotic patients. Results: After heart surgery, the mortality rate was 20%, which was much higher than non-cirrhotic post-cardiac surgery 3% (p = 0.04). The association between death rates and ALT, AST and PCR (p = 0.008, 0.01, 0.02 correspondingly) was positive. There has also been a significant negative connection between death rate and AFP level (p=0.01). Conclusion: organ-related dysfunctions are critical for developing post-CS problems and adverse outcomes. ALT, AST, AFP and PCR are important indicators of cirrhotic patient death after heart surgery.

Keywords: Cirrhotic, Cardiac surgery, Liver, Mortality, Egypt.

1. Introduction

The global prevalence of hepatitis C, hepatitis B, alcohol-associated and non-alcoholic linked fatty hepatitis illness is rising. Up to 10% of cirrhosis patients are likely to have non-transplant surgery in the last 2 years [1].

A hepatitis affected patient is most likely especially vulnerable to the hemodynamic alterations associated with surgery [2].

Advanced liver failure in individuals having cardiovascular procedures raises the risk of complications including heart, renal and lung disease. This is linked to the growing post-operational management load [3].

While cardiac surgery increases in presence of end stage liver disease, there are singular cardiac surgery characteristics that predispose cirrhotic patients to problems. Mechanisms contributing to hepatic damage during cardiac operation include hypo-flavoring, ischemic-reperfusion, cardiopulmonary bypass and systemic inflammatory response activation. Contact activation [4].

Cardiac surgery morbidity and mortality in cirrhotic patients are linked to the degree of liver disease. The categorization of Child Turcotte Pugh (CAP) was the conventional standard for the assessment of patients with cirrhosis. We also utilise the End-stage Liver Disease (MELD) Model, a more powerful predictor of liver end-stage mortality [5].

Child–Pugh (CP) class and/or score, created to stratify the risk of Porto systemic shunt surgery in cirrhosis patients and proven to be a reliable forecaster throughout the years for liver function and survival [6].

The End-Stadium Liver Disease (MELD) model, drawn from the International Normalized Ratio (INR), total serum bilirubin, serum creatinine concentration and liver disease aetiology was originally developed to evaluate the short-term prognosis of cirrhosis patients receiving a systemic transjugular Porto intrahepatic shunt. The MELD was then verified as a mortality predictor in individuals suffering from various liver diseases even if the aetiology was not taken into account [7].

The main objectives of operational planning for cirrhosis patients having major cardiac surgery are optimisation of splanchnic infusion, coagulopathic treatment, thermo-regulation, fluid/electrolyte disruption and preventing liver decompensation [8].

2. Aim of Work

1. Assess the prevalence of mortality in cirrhotic cardiac surgery patients.
2. Identify related perioperative morbidity and mortality factors/predictors in cirrhotic patients with heart surgery.

3. Patient and methods

Study design: A cross-sectional, controlled study used to assess of peri-operative morbidity and mortality in cirrhotic patients undergoing cardiac surgeries carried out at cardiothoracic department Hospital &Critical care department of Benha University from October 2020 till April 2021. The study included 30 cirrhotic adult patients undergoing cardiac surgeries with child a & b hepatic cell failure (Group A) and 30 non cirrhotic patients undergoing cardiac surgeries were included as controls (Group B). Patients with child c hepatic cell failure and those had hepatocellular carcinoma were excluded from the study.

Methods: All patients were subjected to complete history taking (age, sex, residency, occupation, smoking, presenting complaint, jaundice, itching, abdominal pain, weight loss, history of previous hepatic encephalopathy, history of previous antiviral treatment, history of previous bilharziasis or antibilharzial treatment and presence of comorbidities, such as diabetes mellitus or hypertension), clinical examination including general and abdomenal examination with special stress on the presence of signs of decompensation as ascites, jaundice, or tremors and chronic obstructive pulmonary disease, hypertension, ischemic heart disease, congestive heart failure, and endocrine disease were considered present if they were listed in the patient's Mayo Clinic medical records and the patient was receiving medical therapy for the condition at the time of operation. Chronic renal failure was defined as a preoperative serum creatinine concentration more than 2 mg/dl, without evidence of recent deterioration in renal function. Each patient was categorized by an anesthesiologist just before surgery into one of five classes in the physical status classification established by the American Society of Anesthesiologists. Laboratory assessment included routine and general evaluation tests as Complete blood count, liver function tests, serum bilirubin, ALT, AST, total proteins and serum albumin, kidney function tests (urea and creatinine), prothrombin time and prothrombin concentration, viral hepatitis markers (HBV surface antigen, HCV antibody), alpha fetoprotein (AFP), quantitative HCV-RNA detection using real-time polymerase chain reaction (PCR) and Serum electrolytes. Radiological assessment included abdominal ultrasonography (US) and abdominal Contrast-enhanced computed tomography (CT) scan. Electrocardiograph (ECG) was done for all patients: Postoperative morbidity was defined as outcome that occurred during the same hospitalization or as long as 30 days after operation.

3.1. Ethical considerations

Approval of Benha Faculty of Medicine's Ethics committee, Benha University, was obtained. An informed written consent was obtained from all patients after clarifying the study's objectives, data confidentiality, and voluntary involvement.

3.2. Statistical analysis

The statistical analysis was conducted using SPSS version 21. Collected data were summarized in terms of mean ± Standard Deviation for quantitative data and frequency and percentage for qualitative data. Chi-square test ($\chi2$) and the Fisher Exact Test (FET) were used to compare proportions as appropriate. The Independent t-test (t) was used to detect difference between parametric quantitative data. Spearman's correlation coefficient (rho) was calculated to assess association relationship between variables where (+) sign indicate positive (direct) correlation & (-) sign indicate negative (inverse) correlation, also values near to 1 indicate strong correlation & values near 0 indicate weak correlation. The adopted level of significance was 0.05 at a 95% level of confidence.

4. Results

4.1. Demographic data

This study was carried out on 60 patients who were divided into two groups ; Group A (cases) included 30 cirrhotic adult patients with child a & b hepatic cell failure undergoing cardiac surgeries and Group B (controls) included 30 non-cirrhotic patients undergoing cardiac surgeries. The mean age of cases was 44.3 ± 13.03. About Two thirds were females [60%]. One third of cases were hypertensive (30%), 23.3% were diabetic and 16.7% were hypertensive and diabetic. The mean age in controls was 45.37 ± 11.14 SD and they included 56.7% males and 43.3% females, 30% of patients were hypertensive and 26.7% were diabetics & 13.3% complained both hypertension and diabetes. Cirrhosis was detected in 100% of patients of Group A while no patients of Group B had cirrhosis. There was no statistical significance difference between cases and control groups regarding mean age, sex or comorbidities P value > 0.05 Table (1).

Regarding Laboratory data, the mean ALT, AST and serum creatinine level in the studied cases were 34.43 ± 27.11, 48.79 ±30.82 and 1.17 ± 0.36 respectively. The mean PCR level was 1293310 ± 1145514. There was highly statistically significant difference between patient of cases and controls regarding ALT, AST, serum creatinine and PCR (p value <0.001) (Table 2).

Table (1) Comparison between the studied groups as regard demographic characteristics, comorbidities & cirrhosis.

Variable	Group A N=30 n (%)	Group B N=30 n (%)	Test	P value
Sex				
Male	12 (40)	17 (56.7)	$\chi2$=0.7	0.8
Female	18 (60)	13 (43.3)		(NS)
Co-morbidity				
No	9 (30)	9 (30)		
HTN	9 (30)	9 (30)	$\chi2$=0.18	0.9

DM	7 (23.3)	8 (26.7)		(NS)
HTN & DM	5 (16.7)	4 (13.3)		
Cirrhosis				
Yes	30 (100)	0 (0)		**<0.001**
No	0 (0)	30 (100)	$\chi2$= 60	**(HS)**
Age (years)	Mean ± SD (Range)	Mean ± SD (Range)	Independent t-test	
	44.3 ± 13.03 (24 - 64)	45.37 ± 11.14 (25 - 62)	t=0.34	0.7 (NS)

Table (2) Comparison between the studied groups as regard non imaging investigations.

Variable	Group A N=30 Mean ± SD (Range)	Group B N=30 Mean ± SD (Range)	Test	P value
Hb (gm/dL)	13.7±1.41 (11.1-16)	14.1±.94 (12.6-16.5)	t=1.2	0.2 (NS)
WBCs (WBCs per microliter)	6.4±1.9 (3.4-9.5)	6.23±1.7 (3.4-9.2)	t=0.36	0.7 (NS)
Platelet (platelets per microliter)	189.38±57.95 (101.6-300.3)	205.49±63.98 (101.8-297.7)	t=1.02	0.3 (NS)
Albumin (g/dL)	4.1±0.58 (3.2-5)	3.96±0.58 (3.2-4.9)	t=0.6	0.5 (NS)
Total bilirubin (mg/dL)	0.73±0.26 (0.31-1.37)	0.88±0.33 (0.33-1.36)	t=1.97	0.054 (NS)
Pt (seconds)	12.23±0.74 (11-13.5)	12.16±0.79 (11-13.5)	t=0.35	0.7 (NS)
INR (ratio)	1.09±0.122 (0.88-1.34)	1.09±0.136 (0.88-1.34)	t=0.23	0.8 (NS)
ALT ((IU/L)	34.43±27.11 (2.6-91.2)	5.76±1.59 (3.1-8.6)	t=5.8	**<0.001 (HS)**
AST (units per liter of serum)	48.79±30.82 (3.2-98.4)	6.69±2.17 (3.2-9.5)	t=7.5	**<0.001 (HS)**
Serum creatinine (mg/dL)	1.17±0.36 (0.29-1.57)	0.85±0.43 (0.31-1.57)	t=3.11	**<0.01 (SS)**
FPG (mg/dl)	97.5±34.42 (51.2-163.7)	100.26±33.7 (53.6-153.7)	t=0.31	0.8 (NS)
AFP (ng/Ml)	4.72±1.82 (2-7.4)	4.92±1.64 (2-7.2)	t=0.45	0.65 (NS)
PCR	1293310±1145514 (109279-5000000)	0	t=6.2	**<0.001 (HS)**

The ECG parameters of the study groups showed significantly lower mean **QT** dispersion (ms) and mean QTc duration (ms) of cases compared with controls (P = 0.005, 0.04 respectively (Table 3).

Table (3) Comparison between the studied groups as regard ECG parameters.

Variable	Group A N=30 Mean ± SD (Range)	Group B N=30 Mean ± SD (Range)	Test	P value
P-wave duration (ms)	94.94±3.36 (90.1 -100.3)	95.45± 2.99 (91.1 – 100.2)	t=0.62	0.5 (NS)
PR duration (ms)	151.46±7.37 (137.3-164.7)	149.8 ± 8.03 (137.5-165.5)	t=0.84	0.4 (NS)
QRS duration (ms)	92.58±8.59 (80.6-105.1)	93.81±6.76 (80.9-106.2)	t=0.62	0.5 (NS)

QT dispersion (ms)	65.4±12.58 (46-91)	75.83±14.93 (49-94)	t=2.9	**0.005 (SS)**
QTc duration (ms)	417.99±5.8 (412-429.2)	420.8±4.67 (413.5-429.6)	t=2.1	**0.04 (SS)**
QTc dispersion (ms)	73.15±15.12 (48.5-95.9)	72.57±15.98 (49.3-98)	t=0.14	0.9 (NS)
JT dispersion (ms)	76.1±10.73 (58-91)	76.9±8.68 (59-90)	t=0.32	0.7 (NS)

The study results showed that after conducting cardiac surgery of cases and controls, higher mortality rate in cases (cirrhotic patients) (20%) compared with Controls (non-cirrhotic patients) (3%) (p = 0.04) (Table 4).

Table (4) Comparison between the studied groups as regard Mortality.

Variable	Group A N=30 n (%)	Group B N=30 n (%)	Test	P value
Mortality				
Yes	6 (20)	1 (3)	FET=4	**0.04**
No	24 (80)	29 (97)		**(SS)**

This study reported significant positive correlation between mortality rate among cirrhotic patients and ALT, AST & PCR levels, where the rate of mortality increased with increased ALT, AST & PCR level. On the other hand, there was significant negative correlation between mortality rate among cases and AFP level, where the rate of mortality increased with decreased AFP level (Table 5).

Table (5) correlation between sociodemographic variables, laboratory investigation and patient's mortality (univariate analysis)

Mortality / Variable	Spearman's Correlation coefficient (rho)	P value
Age (years)	0.22	0.09
Co-morbidity	- 0.005	0.9
Hb (gm/dL)	- 0.22	0.1
WBCs (WBCs per microliter)	0.1	0.4
Platelet (platelets per microliter)	- 0.1	0.4
Albumin (g/dL)	0.09	0. 4
Total bilirubin (mg/dL)	0.06	0.6
Pt (seconds)	0.1	0.4
INR (ratio)	- 0.09	0.4
ALT(IU/L)	0.34	0.008**
AST(units per liter of serum)	0.324	0. 012*
Serum creatinine (mg/dL)	0.009	0.9
FPG (mg/dl)	- 0.4	0.7
AFP(ng/Ml)	- 0.33	0.011*
PCR	0. 29	0.025*

* correlation is significant at the 0.05 level ** correlation is significant at the 0.01 level

5. Discussion

The lack of literature data makes it difficult to identify the reasons for surgery and the treatment of hepatic cirrhosis patients. In clinical practise, it is difficult to differentiate individuals who may benefit from heart surgery from those who are above perioperative risk. It is thus essential to utilise predictive ratings preoperatively to evaluate each patient's unique risks. Although the risk for surgical mortality in cardiac surgery has particular results (e.g. EuroSCORE), liver disease is not incorporated in existing cardiac surgical risk models. Specific values are required in this group to assess operational risk [8].

The objective of this research was to evaluate cardiac surgery prediction and result in patients with chronic liver disorders, identify cardiac surgery variables and reduce long-term ICU complications. In group A, the mean age was 44.3 ± 13.03 SD and consisted of 40.0% men and 60% females, 30%

hypertensive and 23.3% diabetics, while 16.7% had both diabetes and high blood pressure.

In group B the average age was 45,37 ± 11,14 SD with 56,7% men and 43,3% females, 30% with hypertensive patients and 26,7% with diabetics, and 13,3% with hypertension and diabetes. Cirrhosis was found in 100% of Group A patients, whereas there was no cirrhosis in Group B patients. There was no significant difference in mean age, sex or comorbidity between the two groups examined Wert P > 0.05. However, as regards cirrhosis p <0.001, the statistically significant difference between the two groups was substantial. Our findings are confirmed by Ziser et al. (1999) (9) research, in which 338 women and 395 men with a mean age of 59.4 ± 13.1 years were reported (range, 18-87 years). Lin et al., (2014) (10) also showed that 55 liver cirrhosis patients were included. There were 43 males and 12 women of 60 years of average age (range, 19-84).

The number of patients with liver illness needing different operations is rising. However, there are significant variables of risk that occur perioperatively when these patients have anaesthetic surgery. Thus, careful preoperative evaluation and risk stratification is of vital significance for these individuals. Nature and kind of operation also have significant impacts on perioperative morbidity and death [11].

In this research, it was shown that there was a very statistically significant difference in ALT, AST, serum creatinine and PCR (p <0.001) between the two patients in the study groups. No significant difference between the two groups with respect to other non-imaging research p > 0.05. These findings are contrasted with studies in which the average age was 68.7 ± 8.5 years by Morisaki et al., (2010) [12]. Of 10 renal failure patients (level serum creatinine > 1.5 mg/dL), 3 were reliant on dialysis. In addition, Adibi et al. (2012) [13] performed a research in which the median age of participants was 48.7 years, and the standard mean and difference in duration of cirrhosis was 3.7 ± 1.4 years.

Cirrhosis patients with NASH, typically accompanied by metabolic syndromes (including risk factors for cardiovascular disease), have become a major cause of cirrhosis in the industrialised world, increasingly require cardiovascular surgery [14].

The present research revealed statistically significant differences in the p-values of QT dispersion and QTc duration p < 0.05 between the two groups examined. Cirrhosis patients are known to have significant death and morbidity rates after abdominal surgery and the situation in cardiac surgery is similar. In cirrhotic patients, mortality following cardiac intervention is seldom related to heart failure, but rather due to increased infection incidence, gastrointestinal problems and bleeding. Empirically, heart surgery in individuals with advanced cirrhosis is contraindicated [15].

In the present research, the mortality rate in group A was 20% compared with 3% in group B. The statistically significant difference as mortality existed between both groups (p < 0.05.). The connection between the death rate and ALT, AST and PCR levels was significantly positive, with increasing mortality at the level ALT, AST and PCR. On the other hand, a strong negative connection exists between mortality and AFP levels when the mortality rate rises with the AFP level decreasing. No significant connection was shown between death rate and ECG parameters (p>0.05). Our findings were confirmed by a research by An et al. (16), who examined 24 heart cirrhosis patients to assess morbidity, death and outcome factors. Patients were split into three groups based on the categorization of children and via (CPC). They found that 53 percent of Class A patients and 100 percent of Class B and C patients experienced problems after the surgery. The postoperative mortality of Class A, Class B and C cirrhosis patients was 6%, 67%, and 100%, respectively. Increased total serum Bilirubin levels, pre-operative low serum cholinesterase levels and extended cardiopulmonary bypass (CPB) periods have been shown to indicate a poorer result. The clinical results of Murashita et al. [4] were examined and risk factors for death were identified for 12 cirrhotic patients undergoing cardiac surgery. Six patients each with Class A and B cirrhosis had a 50% and 17% mortality and 50 and 100% morbidity correspondingly. There were significantly lower levels of serum cholinesterase (P=0.02) and lower platelet level (P=0.04) for patients suffering from severe morbidities.

An good retrospective study by Filsoufi et al. (17) involving 27 cirrhosis patients after cardiac surgery showed that CPC stratification mortality was 11 percent, 18 percent, and Class A, B, and C 67 percent correspondingly. There was no mortality in patients with "off" revascularization of the pump (n=5). In 22%, 56% and 100% for CPC class A, B and C correspondingly, major postoperative problems occurred. One year's survival in cirrhotic patients was 80%, 45%, 16% correspondingly (P=0.02), and in cirrhotic patients, long-term survival was substantially worse than in the general patient group (P=0.001). Moreover, they concluded that CPC was better a hospital death predictor (P=0.02) than the end-stage liver disease (MELD) score model (P=0.065).

Suman et al. [18] also performed a retrospective research in order to assess risk of cardiac surgery of cirrhosis patients and reported significant combined with Child–Pugh class, Child–Pugh score, and MELD score (P<0.005). Hepatic decompensation occurred 26%, and 16% of patients died. The sensitivity and specificity of a Child–Pugh score of 7 were found to be 86% and 92% for death, respectively with a negative predictive value of 97% and a positive predictive value of 67%.

Lin et al. [19] analysed a series of 18 patients with cirrhosis having cardiac operation and observed a total in-host death rate of 6% with a significant morbidity rate of 39% in CPC-A and 80% in CPC-B and C.

Klemperer et al. retrospectively examined 13 comparable cases [20]. With eight patients in CPC A and five in CPC B, 25% and 100% respectively, significant postoperative problems were identified. There was no death in CPC A while 80% of CPC B patients died. They found that individuals with little clinical signs of cirrhosis may withstand CPB and cardiac surgery, whereas those with worse liver disease should not be given surgery.

Hayashida et al. [21] evaluated perioperative and major organ morbidity death in 18 cardiac cirrhotic surgery patients. They found that CPB-induced clinical mortality in Class A, Class B and C was 0 percent, 50 percent and 100 percent. No fatalities have been reported in CPC B 'off' pump patients. Similarly, 60% of those with Class A cirrhosis and 100% of those with Class B cirrhose and Class C cirrhosis were reported to have significant problems, while only 33% of the Class B patients were reported with CPB. They found that 'off' pump operation may be an alternate treatment approach for advanced cirrhosis patients who need revascularization.

According to Bizouarn et al. [22], a future research evaluated the early and late results following elective heart surgery in 10 CPC A patients and two CPC B patients with cirrhosis. No deaths were recorded in CPC A and 50% in CPC B. However, the complications in both groups remained as high as 50 percent and 100 percent. They found that even after elective heart surgery the incidences of severe complications were high, and the health status remained impaired following surgery due to chronic hepatic dysfunction.

Lee et al., [23] have indicated that low albumin is a risk factor in the amount of cirrhosis to surgical deaths in these patients. The concentration of albumins in non-cardiac and cardiac surgery is a predictor of post-operative mortality and morbidity, reflects nutrition. In this group, additional enteral nutrition is essential to improve the nutritional status.

6. Conclusion

The emergence of dysfunctions associated with the organ is essential for the development of post-CSA problems and outcomes and is strongly linked to preoperative state and surgical damage, The incidence of mortality in cirrhotic patients was high. ALT, AST, AFP, PCR were independent patient death predictors.

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