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ORIGINAL ARTICLE

Correlation of Cardiopulmonary Bypasses and Cardiac Troponin I in Predicting Post-Op Arrhythmia

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ABSTRACT

Aim: The correlation of cardiopulmonary bypasses (CPB) and cardiac troponin I (cTnI) in predicting arrhythmia remain unclear. Aim of this study to investigate the correlation of cardiopulmonary bypasses duration and cardiac troponin I with the type of arrhythmias.

Methods: This is a retrospective observational study took place in our hospital between May 2020-December 2021.The study included a total of thirty-three patients who underwent open-heart surgery. Patients between the age of 2 months and 14 years of both genders with the diagnosis of ventricular septal defect (VSD), atrioventricular defect (AVSD) and tetralogy of Fallot (TOF) were included in this study. Patients with preoperative a history of major intraoperative events and high-level of cardiac troponin I were excluded from the study. The accuracy was calculated using sensitivity and specificity. The area under the ROC curve (95% CI) and p-value were also calculated.

Results: Out of thirty-three patients undergoing open-heart surgery, 58.1% were male and were one year of age or more (71%). A statistically significant correlation among arrhythmia, cardiac troponin I and cardiopulmonary bypasses was observed ($p < 0.05$). Cardiac troponin I predicted high-level sensitivity for arrhythmias, hospital stay, and intensive care unit stay, while low specificity was reported for cardiac troponin I compared to cardiopulmonary bypasses.

Conclusion: The higher level of cardiac troponin I was correlated with the underlying burden of arrhythmias. A novel high-sensitivity cardiac troponin I assay can protectively recognize patients at low risk of arrhythmias.

Keywords: Arrhythmia, Cardiac troponin I, Cardiopulmonary bypass, Sensitivity, Specificity

INTRODUCTION

Patients with perioperative myocardial ischemia after cardiac surgery with or without cardiopulmonary bypass (CPB) results in cardiac arrhythmia and postoperative myocardial dysfunction [1]. Overall, cardiac arrhythmias were prevalent in 5.3% of the general population and are considered a vital source of mortality and morbidity in cardiovascular diseases. Similarly cardiac arrhythmia is prevalent in 40% of the patients presenting to cardiology clinics [2]. Heart diseases leading to circulatory failure are a substantial cause of mortality and morbidity. In the early stages of heart failure in the young patients diagnosis becomes more complex due to non-specific clinical symptoms [3]. The diagnostic methods are often inadequate or cannot be utilized because of high technical requirements or their invasive nature, indicating cardiac damage in many cases. It is essential to explore non-invasive markers that would facilitate a wider diagnosis of the risk of heart failure and myocardial damage in young patients [4].

In the myocardium, cardiac troponins are protein elements of the troponin-tropomyosin complex. The look of troponins in serum is a sensitive and specific marker of myocardium damage since they no longer appear in extracellular space [5]. Troponins arise in blood in two to four hours after insult, are elevated in approximately 12 hours and then remain progressed for seven to ten days. The sensitivity of both cTnI and cardiac troponin T is almost equal in the clinical diagnosis of myocardial damage [6]. They vary in intracellular compartments, molecular weight, and biological half-life. In addition they have variations in the standardization and obtainability of commercial troponin kits [7]. Approximate values of acquired results are usually incomparable; however, similarities exist for diagnostic features of specific methods.

Cardiac troponins are biochemical markers of myocardial damage with undisputable significance in diagnostic evaluation in adults [8,9]. On the contrary, their role in diagnostics has now no longer been completely explored yet in young patients. In addition, cardiac troponins have not been utilized routinely in neonates due to inadequate data confirming their clinical utility [10]. Studies carried out in other groups confirmed the benefits of troponins in clinical conditions that lead to cardiomyocytes damage, which consists of cardiac inflammatory diseases. Literature confirmed the presence of cardiac troponins in the form of heart arrhythmias, perioperative myocardial injury in patients operated for congenital heart diseases, acute myocarditis, cardiac transplantation, and drug-induced cardio toxicity [11-13].

Troponin measurements will assist in identifying patients at high risk for arrhythmic events as the parameters of cardiac troponins predict to enhance the risk beyond single measurements after a preliminary cardiovascular event. To this end, this study identifies the possible use of cardiac troponin I and cardiopulmonary bypasses in predicting patients with arrhythmia. Furthermore, this study determines sensitivity and specificity related to prognostic outcomes in arrhythmia patients.

MATERIAL AND METHODS

This retrospective observational study was carried out in our Hospital from May 2020 to December 2021. A total of thirty-three patients who underwent open-heart surgical procedures were included in this study. Patients between the age of 2 months and 12 years of both gender with the diagnosis of tetralogy of Fallot, ventricular septal defect, and atrioventricular defect were included in the study. Patients with preoperative high- level of cTnI and a history of major intraoperative events were excluded from the study. Patients fulfilling inclusion criteria also provided informed consent at enrollment.

Data Collection: Blood samples were preoperatively collected for cTnI as the baseline with routine preoperative laboratory results. Due to preoperative high-level measurement, two patients were excluded with severe heart failure. These patients died before the operation in PICU. Cardiopulmonary bypass bump was used to measure cTnI level four hours after disconnection. A one-step enzyme immunoassay was used to determine cTnI based on the Sandwich principle diagnosed by the dimension system.

Data Analysis: The data was collected and analyzed using SPSS version 15. Data have been statistically explained in terms of mean and standard deviation, frequencies and percentages, where ever required. Sensitivity and specificity were used to represent the accuracy. The area under the ROC curve (95% CI) and p-value were calculated. The statistically significant value was considered

at a p- value of 0.05. The collected data were examined to show the relationship between the occurrence of arrhythmias and both cTnI and CPB for getting a cut-off value of 25.2 ng/dl and 62 minutes respectively.

RESULTS

A total of thirty-three patients underwent open-heart surgery and out of them 12 had arrhythmias. In 50% of arrhythmia cases, it was junction ectopic tachycardia . The ratio of male (58.1%) and female (41.9%). The majorities of the patients were 12 months or more (71%) and had no occurrence of arrhythmia (61.3%). Junction ectopic tachycardia (JET) was the most prevalent type of arrhythmia reported in children (50%) (Table 1)

Table 1: Baseline Characteristics

Characteristics		N (%)
Gender		
	Female	13 (41.9%)
	Male	18 (58.1%)
Age		
	<12 months	9 (29%)
	12 months or more	22 (71%)
Incidence of Arrhythmia		
	Yes	12 (38.7%)
	No	19 (61.3%)
Arrhythmia Type		
	Heart block	1 (8.3%)
	Junction ectopic tachycardia	6 (50%)
	Ventricular tachycardia	1 (8.3%)
	Right bundle branch block (RBBB)	3 (25%)
	Pulseless electrical activity (PEA)	1 (8.3%)

Arrhythmia-centered analysis: Results of the different postoperative outcomes are presented in accordance with the cutoff points of Troponin-I values (Table 2). The findings have proven a statistically significant difference between both groups with respect to Dobutamine duration, Dobutamine dose mg/kg, Creatinine and I.C.U stay.

Table 2: Results of the Different postoperative outcomes in accordance With the Cutoff Points of Troponin-I Values

	Group A cTn-I less than 25	Group B cTn-I more than 25	p value
NO.	10	21	
Age (months)	16(18.6)	14(17.7)	0.471
Acc (minutes)	45(47)	50(51)	0.576
CPB (minutes)	60(57.5)	70(74.2)	0.056
FS%	34.5(34.3)	33(32)	0.053
Dopamine dose mg/kg	20.5(18.5)	31.5(44.78)	0.043
Dobutamine duration	23(26.8)	37.5(56.5)	0.020
Adrenaline dose mg/kg	0.240(0.183)	0.236(0.370)	0.553
Adrenaline duration	40.00(33.33)	47.50(48.70)	0.310
Milrinone dose mg/kg	0	1.800(2.911)	
Milrinone duration	0	42.00(74.29)	
MV>12h	2	8	0.234
Creatinine	0.40(0.40)	0.60(0.65)	0.002
A.S.T	47.50(47.20)	55.00(74.79)	0.136
A.L.T	53.00(55.80)	55.00(64.32)	0.963
I.C.U stay	3.00(3.60)	6.00(5.84)	0.003
Hospital stay	6.00(5.40)	6.00(7.37)	0.083

ROC Curves and Prognostic Markers: ROC curve analysis is used in this study for obtaining the cut-off points for predicting the incidence of arrhythmia. Table 3 shows ROC curve analysis for cTnI in predicting postoperative factors. Arrhythmia and hospital stay were negatively predicted by cTnI in 61.2% of patients, respectively. cTnI positively predicted hospital stage >6 days in 67.8% of patients.

Figure 1 shows ROC curves for all post-operative factors discussed above based on the cut-off points. The sensitivity and specificity for arrhythmias, ICU stay, and hospital stay predicted by cTnI was 91.7% vs. 47.4%, 83.3% vs. 42.1%, 95.2% vs. 50%, 90% vs. 31.6%, and 80% vs.10%, respectively.

Table 3: ROC Curve analysis for cTnI in predicting arrhythmias, ICU stay > 3 days, hospital stay > 6 days

	N	%
Arrhythmia		
Positive	12	38.8
Negative	19	61.2
ICU stay		
Positive	21	67.8
Negative	8	25.8
Missing	2	6.45
Hospital Stay		
Positive	10	32.2
Negative	19	61.2
Missing	2	6.45

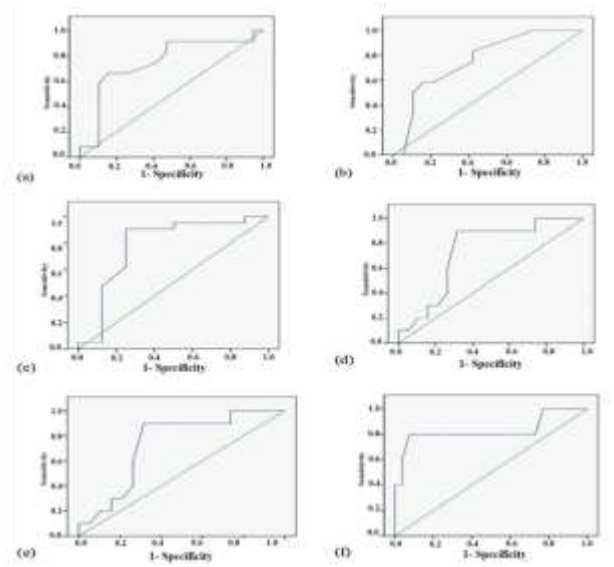

Fig 1: ROC Curve for cTnI in predicting arrhythmias; (b) ROC Curve for CPB in predicting arrhythmias; (c) ROC Curve for cTnI in predicting ICU stay > 3 days; (d) ROC Curve for cTnI in predicting hospital; stay > 6 days; (e) ROC Curve for troponin in predicting mortality.

DISCUSSION

This retrospective observational study has evaluated the correlation of CPB and cTnI levels in predicting arrhythmias. The study has used ROC curve analysis for predicting the incidence of arrhythmia based on the lowest cut-off point. The study has found a higher ROC curve of cTnI level as compared to CPB time. Therefore, there was a statistically significant prediction of arrhythmia through cTnI level as compared to CPB time. In a previous clinical trial, the sensitivity and negative predictive valve (NPV) turned low at 90.1% and 98%, respectively, which was below the performance to be accepted in the practice [14]. According to Chapman et al [15], the development of this pathway was observed when higher diagnostic thresholds were used for modern troponin assays. Therefore, new modalities were needed to fulfill the precision provided by high-sensitivity troponin assays.

Concerning cardiac troponin I (cTnI), the findings have proven a cutoff point at 25 ng/dL in both low (<25 ng/dl) and high (>25 ng/dl) risk cohorts. A total of 10 patients were predicted with a cTnI level <25 ng/dL as compared to 21 patients with a cTnI level of >25 ng/dL. The cut-off point of CPB was adjusted at 62 minutes for a low (< 62 minutes) and high (> 62 minutes) risk cohort. CPB was predicted in 12 patients in the CPB group (<62 minutes) as compared to 19 patients in the CPB group (>62 minutes). A previous study has found 5.2 pg/ml as an optimum cut-off point in a coronary artery disease population using ROC curve analysis [15,16]. Assessing serum cardiac troponin concentrations may

majorly enable in making effective decisions when combined with outcomes of echocardiography [17]. The available literature indicated that cardiac troponins may further serve as a beneficial complement in the assessment of perinatal asphyxia and respiratory distress syndrome in young patients. cTnT serum concentrations were associated with echocardiographic measurements in preterm newborns in their 12th hour of life [18].

A propensity to higher cTnI values was also discussed in previous papers [19, 20]. On the contrary, no statistical analysis has been performed because of the small number of patients and the wide spectrum of surgical interventions. No statistical significance was reported between cTnI in children below 1 year of age as compared with older children. The underlying cause of increased cardiac cTnI levels remained unidentified due to lack of high-throughput assay standardization, greater difference, and confounding factors among different studies regardless of the high sensitivity and specificity [21-23]. Therefore, the particular pathway mechanism remains unidentified. This dilemma should be addressed immediately by identifying the reason for these increased levels and predefined methods. In this study, the highest average cTnI level was selected as the primary outcome variable rather than the cTnI level for avoiding confounding factors at a single time.

The importance of presenting both Net present value (NPV) and sensitivity was demonstrated in this study for assessing the diagnostic accuracy of preliminary modalities for predicting arrhythmias. The prevalence of the targeted disease was directly associated with the NPV specifically population under consideration, which represents a probability of negative test outcome. It becomes essential for establishing the NPV for every health facility in order that a negative test can be interpreted by an attending physician [24].

Strengths and Limitations: Despite the small sample size, this retrospective observational study has important strengths including post-operative factors such as incidence of arrhythmias, type of arrhythmias, examination of the interaction of cTnI and CPB levels with arrhythmias. The selection of patients for cTnI and CPB may have instigated bias as only patients with symptoms were underwent CPB. This may allow future studies to select a cohort with a large size with further comorbidities and advanced arrhythmias. In particular, the accurate overall incidence of arrhythmias progression was overestimated. Nonetheless, the majority of the subjects with CPB had no significant arrhythmias. This study has established the correlation between CPB and cTnI with arrhythmias as this was a observational study. This study has generated questions that should be addressed with large prospective studies, considering its potential selection bias and lack of evidence on CAD and arrhythmias.

CONCLUSION

In conclusion, a highly statistically significant correlation was found between the cTnI levels and arrhythmias, whereas no statistically significant correlation was found between CPB and arrhythmias occurrence. The peak value of cTnI was higher than 25 ng/dl in 21 patients. The cut-off point was adjusted at 25 ng/dl to define a low and a high-risk group of cTnI values. This study has provided further support for the likely important role of cTnI as a surrogate marker of the progression, presence, and findings in arrhythmias. Additional investigation is required with more aggressive treatment to reduce cTnI levels.

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