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Troponin_I as a predictor of outcome in pediatric postoperative cardiac surgeries

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***Abstract*---**Background: Troponin-I (TN-I) levels are elevated following pediatric cardiac surgery with speculation that particular patterns may have prognostic significance. There is lack of procedure-specific data regarding postoperative TN-I levels in infants undergoing cardiac surgery. Aim and objectives: the aim of the study was to assess the usefulness of routine monitoring of cardiac troponin I concentrations within 24 hours of surgery (cTn-I<24h) in neonates and infants undergoing cardiopulmonary bypass surgery. Also, correlate troponin I with postoperative mortality and morbidity in patients between one day and 15 years old who underwent cardiac surgery for congenital heart disease. Subjects and methods: This was a prospective randomized study in the period from April 2019 to November 2021, was conducted on 103 pediatric patients from Pediatric cardiac intensive care units in Abu El-Rish children's Hospital and Al-Nas hospital aging from one day old to 15 years old and had cardiopulmonary bypass surgery. Blood samples for troponin levels were taken from all patients in ICU on admission and 24 hours after

operation. Results: Troponin level on admission (ng/ml), Troponin level after 24Hrs (ng/ml) and Inotropic score in first day showed significant increase in above median group when compared to below median group (p>0.001, <0.001, 0.013) respectively while other parameters didn't show significant difference between two groups (p>0.05). Conclusion: In conclusion, the cTnI level on postoperative day 1 is an independent predictor of the duration of the inotropic use and ICU stay. We are certain that an assessment of the cTnI level on postoperative day 1 is one of the most useful options to assess impaired cardiac conditions and to predict the postoperative course after the CHD operation.

***Keywords*---**troponin-I (TN-I), cardiac surgery, predictor, outcome, cardiopulmonary bypass surgery.

Introduction

It is well known that myocardial injury secondary to surgery or CPB affects cardiac functions, therefore increase morbidity and mortality. Pediatric open-heart surgery is a special operation that has different success rates depending on the quality of technique. Intraoperative myocardial tissue injury affects a postoperative cardiac function which is directly related with morbidity and mortality (1). Several studies have shown that cardiac troponin I levels are safe can be used as an indicator of myocardial damage both in pediatric and adult cardiac surgery. Increased troponin I levels have been associated with postoperative complications like delayed extubation time, necessity of higher inotropic support, and mortality (2).

Any type of cardiac injury, including a myocardial infarction, pericarditis advanced heart failure, inflammatory process, toxic agents, or trauma can result in the release of the cTnI into the blood. Also, pre-operative and postoperative elevations of the cTnI are usually considered predictors of the mortality and morbidity not only in adults but also in infants and children (3). Moreover, a significant volume and pressure overload can cause myocardial injury and a cTnI elevation (4). Cardiac surgery for congenital heart disease (CHD) is associated with the postoperative morbidity and mortality, especially in neonates and infants. Severe cardiac damage and necrosis after cardiac surgery may result in a longer ICU stay and may cause death. However, little is known about the relationship between the cTnI and duration of the catecholamine use, ICU stay, and other clinical parameters including the urine volume and lactate level (5). In the present study, we aimed to assess whether the cTnI is an independent prognostic marker after a CHD operation. In this study, we will aim to evaluate the effects of troponin I on postoperative mortality and morbidity in patients who underwent cardiac surgery for congenital heart diseases.

Patients and Methods

This was a prospective randomized study in the period from April 2019 to November 2021 that was conducted on 103 pediatric patients in pediatric cardiac

intensive care unit in Abu El-Rish children's Hospital and Al-Nas hospital who underwent surgery for congenital heart disease on cardiopulmonary bypass whose age ranged from one day to 15 years old . Blood samples for troponin levels were taken from all patients at ICU on admission and 24 hours after operation. All patients underwent the same anesthesia protocol for sedation.

A written consent was obtained from all guardians prior to the enrollment of their children in the study. Study protocol was approved by Institutional Research Board (IRB), faculty of medicine, Cairo University.

Exclusion criteria

Pediatric patients with neuromuscular disorder, developmental and behavioral problems, demyelinating disease, cerebral palsy, inborn errors of metabolism, liver injury and kidney injury.

Methodology

1. Clinical evaluation: History taking with special emphasis laid on the age at onset, duration and therapeutic history in addition to full clinical and general examination were done to assess any abnormality in hemodynamic status after operation.
2. Vasoactive inotropic score (VIS): This score is an objective tool used to quantify the need for cardiovascular support in children after surgery (1). Vasoactive inotropic score (VIS) = Wernovsky Inotropic score (Referrence) [dopamine (mic/kg/min) + dobutamine (mic/kg/min) + 100×adrenaline (mic/kg/min)] + 10 X Milrinone dose (µg/kg/min) + 10,000 × Vasopressin dose (U/kg/min) + 100× Norepinephrine dose (µg/kg/min).
3. Duration of mechanical ventilation
4. Duration of ICU stay
5. Lactate levels measurement on admissionand after 24h from ICU admission.
6. Troponin (cTn-I) measurement on admission and after 24h from ICU admission

Statistical analysis

The collected data was revised, coded and tabulated using Statistical package for Social Science (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp). Chi-Square test was used to examine the relationship between two qualitative variables. Fisher's exact test was used to examine the relationship between two qualitative variables

Results

As regard troponin level on admission to ICU median troponin level was 32 ng/ml ranging from 4 to 172ng/ml. Table (3) Troponin and lactate level show significant decrease after 24 hours when compared to its level on admission (p=0.001). Perfusion, heart rate, average blood pressure and urine output showed significant difference between admission and after 24 hours. Troponin level on admission

(ng/ml), Troponin level after 24Hrs (ng/ml) and Inotropic score in first day showed significant increase in above median group when compared to below median group (p>0.001, <0.001, 0.013) respectively while other parameters didn't show significant difference between two groups (p>0.05). Table (4) Bleeding, Collapsing needs CPR, Any Morbidity and Mortality didn't show any significant difference between Q1, Q2-3 and Q4 (P>0.05). Table (5) Troponin level area under curve is excellent with best detected cut off point is ≥27.9 yielding sensitivity of 100% , specificity 43.75% in detection of mortality after ICU admission following surgery. Table (6)

Table (1): Personal and clinical data of the studied population

		Total N=103	
Age, years		1 (0.06-11)	
Body weight (kg)	<5	25	24.3%
	[5-10]	43	41.7%
	[10-20]	28	27.2%
	>20	7	6.8%
Type of CHD	cyanotic	54	52.4%
	Acyanotic	49	47.6%

Data expressed by median (Aladrén, Garre, Valderas-Martínez, Piquero-Casals, & Granger) or n (%) as appropriate

Table (2): Outcome of patients (Complications and Mortality)

		Total N=103	
		N	%
Bleeding	Absent	73	70.9%
	Present	30	29.1%
Collapsing needs CPR	Absent	91	88.3%
	Present	12	11.7%
Mortality	No	96	93.2%
	Yes	7	6.8%

Table (3): The validity of the Troponin level on admission (ng/ml) with area under the ROC curve (AUC) to detect mortality after ICU admission following surgery

Cut-off	Sensitivity 95% CI	Specificity 95% CI	PPV 95% CI	NPV 95% CI	AUC 95% CI	P-value
>27.9 (ng/ml)	100 59.0 - 100.0	43.75 33.6 - 54.3	11.5 9.8 - 13.4	100	0.725 0.629 - 0.809	0.007

The 95%CI: 95% confidence interval, Positive predictive value (PPV) and negative predictive value (NPV), Area under the ROC curve (AUC).

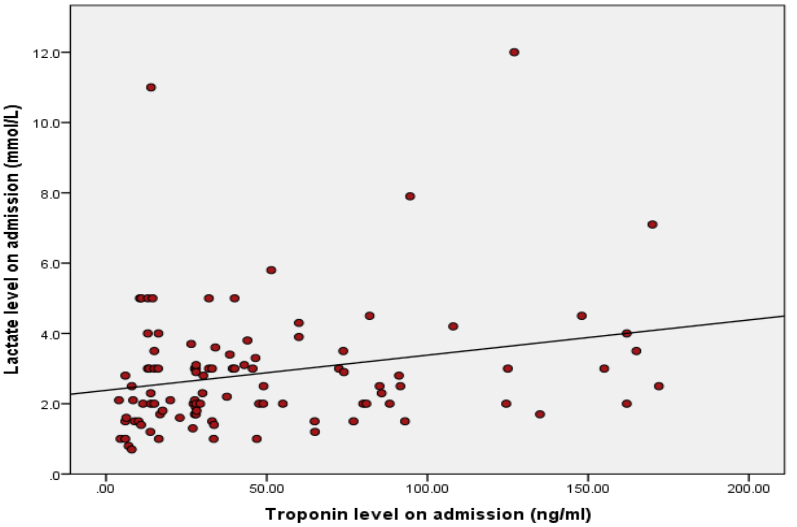

Figure (1): Correlations between Troponin level on admission (ng/ml) and Lactate level on admission (mmol/L) in the studied population

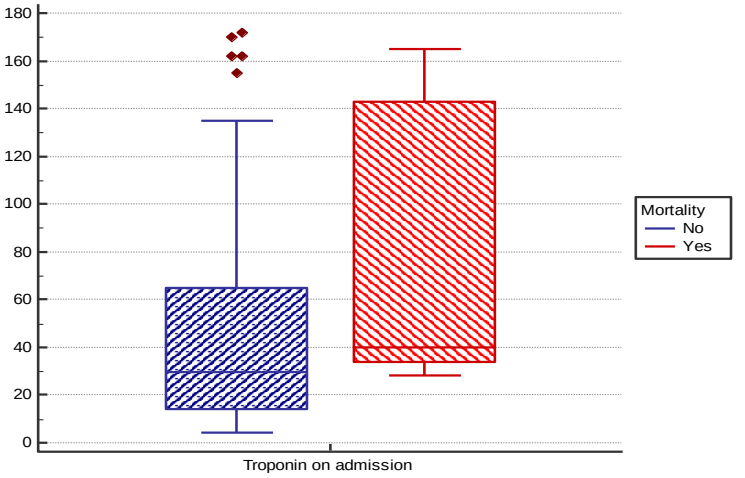

Figure (2): Box-plot diagram represents the range of Troponin level (ng/ml) on admission as regard mortality; the upper & lower line in each box represents the 75th & 25th percentile respectively while the line through each box indicates the median. Whiskers represent the range between the minimum and maximum values

Discussion

Systemic inflammatory response is generated as a result of tissue edema that leads to organ failure. Other complications of CPB include coagulation disorders, embolisms, electrolyte imbalances, and acute respiratory distress syndrome. Troponin is a complex of three regulatory proteins: C, I, and T; it is released during the takedown of cardiomyocytes and plays and important role in the contraction of cardiac muscles (6).

The present study was conducted on one hundred three pediatric patients, aging from one day old to 15 years old, of both sexes, having congenital heart disease and undergoing cardiopulmonary bypass surgery. The most common surgery done was tetralogy of Fallot (TOF) repair (23.3%) followed by VSD closure (11.7%) and Arterial switch operation (ASO) (9.7%), & as regard patient outcome 29.1% had bleeding, 11.7% had cardiopulmonary events that needed cardiopulmonary resuscitation (CPR) and mortality occurred in 6.8% of cases.

Ahmed, El-minshawy group, (7) demonstrated that of 100 patients, VSD-closure was the commonest procedure (34%), followed by TOF-correction (19%). According to the studied complications, chest infection was the commonest (10%) followed by heart failure (8%), wound infection & pulmonary hypertension (7% each), and Mortality accounted for 7%. In the present study troponin and lactate levels were found to show significant decrease after 24 hours when compared to its level on admission ($p=0.001$). Also agrees Checchia et al., (8) who found that the mean ± SD troponin I measurements of survivors was lower than non-survivors, although this failed to reach statistical significance (0.4 ± 0.6 vs 14.3 ± 18.8 ng/mL, P = NS). Bottio et al., (9) also reported that troponin I measurements of survivors was significantly lower than non-survivors ($p=0.05$).

In the present study subjects were stratified according to median level of troponin on admission into two groups 1st group below Median (32 ng/mL) and 2nd group above Median (32 ng/mL). Heart rate in 1st day showed significant difference between the two groups ($p<0.001$). Other parameters didn't show any significant difference between two groups ($p> 0.05$). Troponin level on admission (ng/ml), Troponin level after 24Hrs (ng/ml) and Inotropic score in first day showed significant increase in above median group when compared to below median group ($p>0.001$, <0.001, 0.013) respectively.

This agrees the result of Bottio et al., (9) who found that Tn-I was higher than 35 ng/ml in 19 patients (27%; median age 2.76 months), while it was lower in the remaining 51 patients, within the range of 20—34 ng/ml in 19, between 10 and 19 ng/ml in 20, and 1—9 ng/ml in 10; only two patients (0.3%) had a postoperative Tn-I value lower than 1 ng/ml. Among those with a Tn-I >35 ng/ml (high-risk group, 19 patients), 9 deaths (47%) were observed. Mean value of Tn-I observed in these patients who died was 163 _186 ng/ml {median Tn-I was 91 ng/ml; range 55—548 ng/ml}. Among survivors (10 patients), Tn-I mean value was 73 _ 37 ng/ml {median value 67 ng/ml; range 35—150 ng/ml} ($p = 0.16$). Among those with a Tn-I <35 ng/ml (low-risk group), 4 died (4/52: 7.7%). Median Tn-I was 22 ng/ml (range between 15 and 32 ng/ml) (9).

Carmona et al., (10) reported that Peak cTnI concentrations post-operative correlated with peak NT-proBNP levels which might suggest that states of cardiovascular decompensation may lead to myocardial ischemia, cell necrosis and ultimately death. Accordingly, there is evidence that mitochondrial ultrastructure and function are abnormal in heart failure, resulting in low myocardial energy production via oxidative phosphorylation. In the ASD group, no significant correlation coefficients were noted between postoperative cTnI elevation and outcome parameters at any time ($p> 0.05$) (11).

In the present study age, (in years) showed significant negative correlation with troponin level after 24Hrs (ng/ml), length of stay in ICU (days),ventilation duration, inotropic score in the first day and inotropic score in second day showed significant positive correlation with Troponin level after 24Hrs (ng/ml). This agrees Imura et al., (12) who found that the peak TnI level correlated with the total TnI release ($r = 0.83$, $p = 0.0001$). Peak TnI correlated with the durations of inotropic support ($r = 0.54$, $p = 0.001$), ventilation ($r = 0.51$, $p = 0.01$), and ICU stay ($r = 0.50$, $p = 0.01$). The duration of CPB, aortic cross clamping, and circulatory arrest did not correlate with the peak or total TnI release ($p > 0.05$).

Kojima et al., (5) found that in the multivariable regression analysis including that for the cTnI level on postoperative day 1, urine volume 24 h after the ICU stay, lactate level 24 h after the ICU stay, and aortic cross clamp time, which might affect a longer catecholamine use and longer ICU stay, the cTnI on postoperative day 1 was an independent predictor of the catecholamine use ($p = 0.002$) and ICU stay ($p = 0.003$). AK et al., (13) also found that the cut-off point of 24th hour troponin level for prediction of morbidity and mortality was 15 with a sensitivity of 58.82%; specificity of 67.69%; positive predictive value of 48.78%; and negative predictive value of 75.86%. Area under ROC curve was 65.5% with 5.9% standard deviation. The cases without any morbidity and/or mortality had significantly lower 24th hour troponin levels than those who suffered morbidity and/or mortality ($p= 0.012$; $p< 0.05$). Regarding the mortality rates, there was no statistically significant difference between preoperative, postoperative, 1st, and 24th hour's troponin levels ($p> 0.05$). However, postoperative 48th hour Troponin levels were significantly higher in deceased patients than the survivors ($p< 0.023$; $p< 0.05$).

In the present study area under the ROC curve (AUC) to detect mortality after ICU admission following surgery was 0.725, at cut off value (> 27.9 ng/ml) the sensitivity was 100%, specificity was 43.75, PPV 11.5%, NPV 100%, $p=0.007$. Dent et al., (11) demonstrated that there was overlap and variability of cTnI concentrations within and between the different procedure groups. This reflects differences in patient-to patient surgical technique, and individual differences in patient responses to myocardial trauma and myocardial protection. Thus, although some difference in cTnI concentrations could be attributed to the generally longer CPB and aortic cross-clamp times for TOF versus VSD versus ASD repairs, cTnI also appears to reflect the difficulty of postoperative recovery of an individual patient with a VSD or TOF.

Conclusion

In conclusion, the cTnI level on postoperative day 1 is an independent predictor of the duration of the inotropic use and ICU stay. We are certain that an assessment of the cTnI level on postoperative day 1 is one of the most useful options to assess impaired cardiac conditions and to predict the postoperative course after the CHD operation.

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