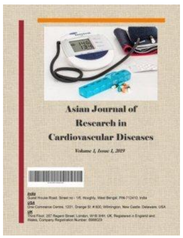

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Sensitivity and Specificity of Cardiac Troponin I and duration of Cardiopulmonary Bypasses in Predicting Arrhythmia

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Aim: The sensitivity and specificity of cardiac troponin I (cTnI) and cardiopulmonary bypasses (CPB) in predicting arrhythmia remain unclear. This study aimed to investigate the association of CPB duration and cTnI with the type of arrhythmias.
Study Design: It is a retrospective observational study.
Place and Duration of Study: The study took place in New Children Hospital in Cairo, Egypt between May 2018-December, 2019.
Methods: The study included a total of thirty-three patients who underwent open-heart surgery. 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. The accuracy was calculated using sensitivity and specificity. The area under the ROC curve (95% CI) and p-value were calculated.
Results: Out of thirty-three patients undergoing open-heart surgery, 58.1% were male and were 12 months or more (71%). A statistically significant correlation between arrhythmia, cTnI, and CPB

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was observed ($p < 0.05$). cTnI predicted high-level sensitivity for arrhythmias, hospital stay, and ICU stay, while low specificity was reported for cTnI as compared to CPB.
Conclusion: The higher level of cTnI was correlated with the underlying burden of arrhythmias. A novel high-sensitivity cTnI assay can protectively recognize patients at low risk of arrhythmias.

Keywords: Arrhythmia; cardiac troponin I; cardiopulmonary bypass; sensitivity; specificity.

1. INTRODUCTION

The prediction of cardiac surgery via perioperative cardiac ischemia results in arrhythmia and postoperative myocardial dysfunction with or without cardiopulmonary bypass (CPB) [1]. Overall, cardiac arrhythmias were prevalent in 5.3% of the general public and considered as a vital source of mortality and morbidity in cardiovascular diseases. Likewise, cardiac arrhythmia is prevalent in 40% of the patients visiting cardiology clinics [2]. Heart diseases leading to circulatory failure are a substantial cause of mortality and morbidity in infants. In the early stages of heart failure in the newborn, diagnosis becomes complex due to non-specific clinical symptoms [3]. The diagnostic methods are usually not sufficient 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 cardiac insufficiency risk and heart muscle damage in neonates [4].

In the myocardium, cardiac troponins are protein elements of the troponin-tropomyosin complex. The appearance of troponins in serum is a sensitive and specific marker of myocardium damage since they do not occur in extracellular space [5]. Troponins occur in blood in 2 to 4 hours after insult, are elevated in approximately 12 hours and then remain progressed for 7 to 10 days. The sensitivity of both cTnI and cTnT is the clinically almost equal in the diagnosis of myocardial damage [6]. They vary in intracellular compartments, molecular weight, and biological half-life. There are further variations in the standardization and obtainability of commercial troponin kits [7]. Approximate values of obtained results are usually incomparable; however, similarities exist for diagnostic features of specific methods.

Cardiac troponins are biochemical markers of myocardial injury with undisputable significance in diagnostic evaluation in adults [8,9]. On the contrary, their role in diagnostics has not been completely explored yet in neonates. In addition, cardiac troponins have not been utilized routinely in neonates due to inadequate data confirming their clinical utility [10]. Studies conducted in other groups showed the benefits of troponins in clinical conditions that lead to cardiomyocytes injury, which include cardiac inflammatory diseases. Literature showed 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 cardiotoxicity [11-13].

Troponin measurements will help 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.

2. MATERIALS AND METHODS

2.1 Design, Setting and Patients

This retrospective observational study was conducted in the New Children Hospital of Cairo University, Egypt from May 2018 to December 2019. A total of thirty-three patients who underwent open-heart surgery 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.

2.2 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.

2.3 Data Analysis

The data was collected and analyzed using SPSS version 15. Data were statistically explained in terms of mean and standard deviation, frequencies and percentages, where 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.

3. RESULTS AND DISCUSSION

3.1 Baseline Data

A total of thirty-three patients underwent open-heart surgery, and 12 had arrhythmias. In 50% of cases, it was junction ectopic tachycardia with 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).

3.2 Arrythmia-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 shown a statistically significant difference between both groups with respect to Doputamineduration, Doputaminedose mg/kg, Creatinine, and I.C.Ustay.

3.3 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.

Fig. 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 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%)

Table 2. Results of the different postoperative outcomes in accordance with the cutoff points of troponin-I values

	Group A cTn-Ilessthan25	Group B cTn-Imorethan25	p value
NO.	10	21	
Age(months)	16(18.6)	14(17.7)	0.471
Acc(minutes)	45(47)	50(51)	0.576
Cbp(minutes)	60(57.5)	70(74.2)	0.056
FS%	34.5(34.3)	33(32)	0.053
Doputaminedose mg/kg	20.5(18.5)	31.5(44.78)	0.043
Doputamineduration	23(26.8)	37.5(56.5)	0.020
Adrenalinedose mg/kg	0.240(0.183)	0.236(0.370)	0.553
Adrenalineduration	40.00(33.33)	47.50(48.70)	0.310
Milrinonedose mg/kg	0	1.800(2.911)	
Milrinoneduration	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.Ustay	3.00(3.60)	6.00(5.84)	0.003
Hospitalstay	6.00(5.40)	6.00(7.37)	0.083

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

This retrospective observational study has evaluated the sensitivity and specificity 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 value (NPV) was low at 90.1% and 98%, respectively, which was below the performance to be accepted in the practice [14]. According to Chapman et al15, 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 cTnI, the findings have shown 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 >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 CAD population using ROC curve analysis [15,16]. Assessing serum cardiac troponin concentrations may majorly enable in making effective decisions

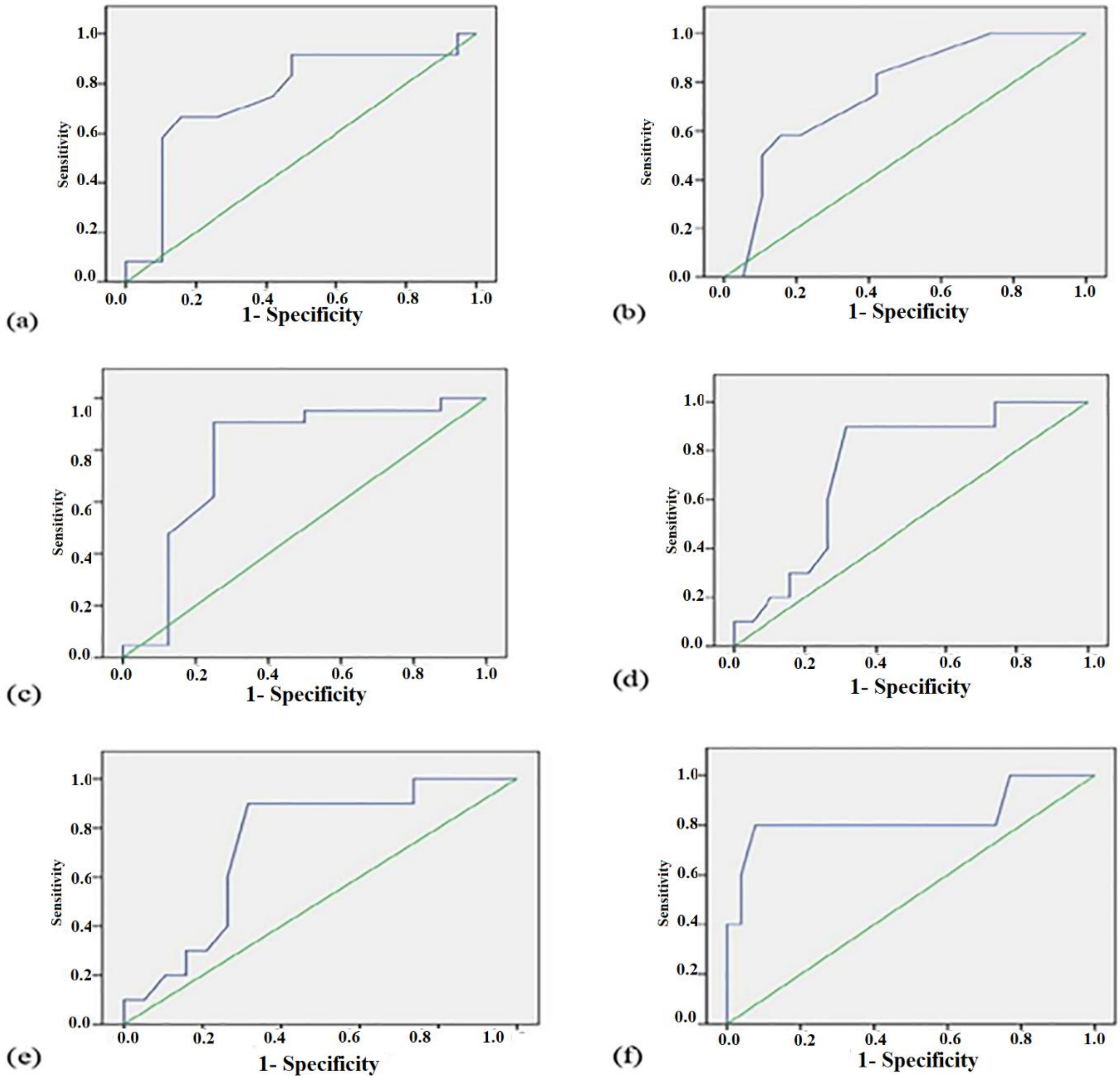

Fig. 1. ROC Curve for cTnI in predicting arrhythmias; (b) ROC Curve for CPB in predicting arrhythmias; (c) ROC Curve for cTnI in predicting ICU stay > 3 days; (d) ROC Curve for cTnI in predicting hospital; stay > 6 days; (e) ROC Curve for troponin in predicting mortality

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 newborns. 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 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 each hospital so that a negative test can be interpreted by an attending physician [24].

4. 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 relationship between CPB and cTnI with arrhythmias as this was a prospective and 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.

5. 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 subjects. 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.

DISCLAIMER

The products used for this research are commonly and predominantly use products in our area of research and country. There is no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by the personal efforts of the authors.

CONSENT

All authors declare that ‘written informed consent was obtained from the patient (or other approved parties) for publication of this case report and accompanying images.

ETHICAL APPROVAL

All authors hereby declare that all experiments have been examined and approved by the appropriate ethics committee and have therefore been performed following the ethical standards laid down in the 1964 Declaration of Helsinki.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Zhou H-m, Ling X-y, Ni Y-j, Wu C, Zhu Z-p. Pre-cardiopulmonary bypass administration of dexmedetomidine decreases cardiac troponin I level following cardiac surgery with sevoflurane postconditioning. J. Int Medi Res. 2019;47:3623-35. DOI: https://doi.org/10.1177/0300060519856750
2. McCarthy CP, Yousuf O, Alonso A, Selvin E, Calkins H, McEvoy JW. High-sensitivity troponin as a biomarker in heart rhythm disease. J Am Coll Cardiol 2017;119:1407-13.

DOI:https://doi.org/10.1016/j.amjcard.2017.01.032

3. Tarkowska A, Furmaga-Jabłońska W. The evaluation of diagnostic role of cardiac troponin T (cTnT) in newborns with heart defects. The Scien World J. 2012;2012. DOI: https://doi.org/10.1100/2012/682538
4. Suthar D, Dodd DA, Godown J. Identifying non-invasive tools to distinguish acute myocarditis from dilated cardiomyopathy in children. Paedia cardio. 2018;39:1134-8.
5. Price S, Bodys A, Celińska A, Rawiak A, Pietrzak R, Małek ŁA, et al. The value of chosen diagnostic tools in evaluating myocarditis in children and adolescents. Pediatria Polska-Polish J. Paedia. 2018; 93:389-95. DOI:https://doi.org/10.5114/polp.2018.78899
6. Cheung YF, Li VW, Lai CT, Shin VY, Keung W, Cheuk DK, et al. Circulating high-sensitivity troponin T and microRNAs as markers of myocardial damage during childhood leukaemia treatment. Pedia Res. 2020;1-8.
7. Abrar S, Ansari MJ, Mittal M, Kushwaha KP. Predictors of mortality in paediatric myocarditis. Journal of clinical and diagnostic research: JCDR. 2016;10:SC12. DOI: 10.7860/JCDR/2016/19856.7967
8. Seliger SL, Hong SN, Christenson RH, Kronmal R, Daniels LB, Lima JA, et al. High-sensitive cardiac troponin T as an early biochemical signature for clinical and subclinical heart failure: MESA (Multi-Ethnic Study of Atherosclerosis). Circulation. 2017;135:1494-505. DOI: https://doi.org/10.1161/CIRCULATIONAHA.116.025505
9. Nakamura H, Niwano S, Fukaya H, Murakami M, Kishihara J, Satoh A, et al. Cardiac troponin T as a predictor of cardiac death in patients with left ventricular dysfunction. J. arrhythmia. 2017;33: 463-8. DOI:https://doi.org/10.1016/j.joa.2017.07.004
10. Crespo-Leiro MG, Metra M, Lund LH, Milicic D, Costanzo MR, Filippatos G, et al. Advanced heart failure: A position statement of the Heart Failure Association of the European Society of Cardiology. Eur. J. heart failure. 2018;20:1505-35. DOI: https://doi.org/10.1002/ejhf.1236
11. Utamayasa IK, Rahman MA, Hidayat T, Prihaningtyas RA. A Preliminary Study: Troponin T and Reg3 in Children with Left-to-Right Shunt Congenital Heart Disease with Heart Failure. IJPHRD. 2020;11:2431-5.
12. Suthar D, Dodd DA, Godown J. Identifying non-invasive tools to distinguish acute myocarditis from dilated cardiomyopathy in children. Pedia cardio. 2018;39:1134-8.
13. Neves AL, Henriques-Coelho T, Leite-Moreira A, Areias JC. Cardiac injury biomarkers in paediatric age: Are we there yet? Heart failure rev. 2016;21:771-81.
14. Than M, Herbert M, Flaws D, Cullen L, Hess E, Hollander JE, et al. What is an acceptable risk of major adverse cardiac event in chest pain patients soon after discharge from the Emergency Department?: A clinical survey. Int J Cardiol. 2013;166:752-4. DOI: https://doi.org/10.1016/j.ijcard.2012.09.171
15. Chapman AR, Fujisawa T, Lee KK, Andrews JP, Anand A, Sandeman D, et al. Novel high-sensitivity cardiac troponin I assay in patients with suspected acute coronary syndrome. Heart. 2019;105: 616-22. DOI: http://dx.doi.org/10.1136/heartjnl-2018-314093
16. Samman Tahhan A, Sandesara P, Hayek SS, Hammadah M, Alkhoder A, Kelli HM, et al. High-Sensitivity Troponin I Levels and Coronary Artery Disease Severity, Progression, and Long-Term Outcomes. J Am Heart Assoc. 2018;7:007914. DOI: https://doi.org/10.1161/JAHA.117.007914
17. Joseph S, Kumar S, Lakshmi S. Cardiac troponin-T as a marker of myocardial dysfunction in term neonates with perinatal asphyxia. IJP. 2018;85:877-84.
18. Zhou L, Xiang X, Wang L, Chen X, Zhu J, Xia H. N-terminal Pro-B-type natriuretic peptide as a biomarker of bronchopulmonary dysplasia or death in preterm infants: a retrospective cohort analysis. Front in pedia. 2019;7:166. DOI: https://doi.org/10.3389/fped.2019.00166
19. Su JA, Kumar SR, Mahmoud H, Bowdish ME, Toubat O, Wood JC, et al. Postoperative serum troponin trends in infants undergoing cardiac surgery. In Seminars in thoracic and cardiovascular surgery 2019;31:244-251.

DOI:https://doi.org/10.1053/j.semtcvs.2018.08.010

20. Momeni M, Poncelet A, Rubay J, Matta A, Veevaete L, Detaille T, et al. Does postoperative cardiac troponin-I have any prognostic value in predicting midterm mortality after congenital cardiac surgery? J. Cardiothorac. Vasc. 2017; 31:122-7.
DOI: https://doi.org/10.1053/j.jvca.2016.02.018
21. Ford I, Shah AS, Zhang R, McAllister DA, Strachan FE, Caslake M, et al. High-sensitivity cardiac troponin, statin therapy, and risk of coronary heart disease. JACC CardioOncol. 2016;68: 2719-28.
DOI: https://doi.org/10.1016/j.jacc.2016.10.020
22. Eggers KM, Venge P, Lindahl B, Lind L. Cardiac troponin I levels measured with a high-sensitive assay increase over time and are strong predictors of mortality in an elderly population. JACC CardioOncol. 2013;61:1906-13.
DOI:https://doi.org/10.1016/j.jacc.2012.12.048
23. Baro R, Haseeb S, Ordoñez S, Costabel JP. High-sensitivity cardiac troponin T as a predictor of acute Total occlusion in patients with non-ST-segment elevation acute coronary syndrome. Clin Cardio. 2019;42:222-6.
DOI: 10.1002/clc.23128
24. Martin AK, Malhotra AK, Sullivan BL, Ramakrishna H. Troponin elevations in patients with chronic cardiovascular disease: An analysis of current evidence and significance. Ann Card Anaesth. 2016;19:321.
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