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The Relationship between Serum Levels of Cardiac Enzymes and Junctional Ectopic Tachycardia (JET) after Cardiac Surgery of Congenital Heart Disease

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Abstract

Background

In this study, we aimed to survey the relationship between serum levels of cardiac enzymes and junctional ectopic tachycardia (JET) after corrective surgery of congenital heart disease (CHD).

Materials and Methods: In this cohort study, 140 children with CHD who were hospitalized in intensive care unit of Shahid Modarres hospital in Tehran, Iran, were divided into case group (the JET group including 37 patients), and control group including 103 patients. These two groups were compared based on the previous studies and collected data.

Results: Based on the analysis of the area under the Receiver Operating Characteristic curve, the Creatine Kinase Myocardial Band (CK-MB) level assessment can predict the occurrence of JET after the surgery (area under the curve is 0.849, 95% confidence interval is 0.786- 0.911), and the best cut-off point for it is 95.5 to predict the occurrence of JET. So, CK-MB will diagnose the occurrence of JET with 97.3% sensitivity and 67% specificity. In the same analysis, the troponin level assessment can predict the occurrence of JET after the surgery (area under the curve is 0.877, 95% confidence interval is 0.821- 0.933). Accordingly, the best cut-off point for the troponin is 45 to predict the occurrence of junctional ectopic tachycardia which will diagnose it with 97.3% sensitivity, and 72.8% specificity.

Conclusion

There is a positive correlation between the occurrence of JET after corrective surgery of CHD and an increase in the level of CK-MB and troponin enzymes. So that the level of CK-MB above 95.5 and the level of troponin above 45 might predict the occurrence of JET in these patients with high accuracy.

Key Words: Children, Cardiac surgery, Congenital heart disease, JET.

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1- INTRODUCTION

Junctional ectopic tachycardia or His-bundle tachycardia is a narrow complex tachycardia. It is called congenital JET because it occurs as a primary idiopathic arrhythmia in childhood, but it often develops after corrective surgery of congenital heart disease and is an important cause of mortality and morbidity after these surgeries (1). Tachycardia and the lack of ventriculoatrial synchrony cause severe hemodynamic instability (2). This kind of tachycardia often originates from the junctional zone beside the atrioventricular node, whereby an ectopic focus causes an automatic tachycardia with the rate of 170- 260 beats per minute (3).

The total incidence of JET is 2-11.2 percent which often occurs immediately or in the first day after corrective surgery of congenital heart disease as mentioned (4, 5). Its estimated mortality rate is 3- 13.5 percent (5, 6). In very rare cases, the occurrence of junctional ectopic tachycardia has been documented up to 50 days after surgery (7). The diagnosis of the junctional ectopic tachycardia is difficult and some therapeutic drugs for tachycardia may cause junctional ectopic tachycardia or worsen it, so it is better to avoid administering them to the patients (8).

The main etiology of junctional ectopic tachycardia is undetermined and its predictive factors are under study. Paying attention to these factors can help us to prevent its occurrence and to offer preventive approaches for this form of tachycardia (9). Of course, these items are not available yet. Although the main pathophysiologic etiology of junctional ectopic tachycardia is unknown, the surgical interventions near the atrioventricular node or proximal to the electrical conduction system of the heart (in the closing area of the Ventricular Septal Defect for example) are known as the main etiology (8). The direct heart manipulation during the surgery, for example, can injury its myocardium and increase its irritability (10). In addition, heart biopsy from the mentioned area showed the hemorrhagic veins near the atrioventricular node (11). So, the surgeon can minimize the occurrence of junctional ectopic tachycardia by decreasing the tractions of the myocardium and manipulation on it (8). The risk factors of the junctional ectopic tachycardia may occur prior to, during and after the surgery. The patient's age and performing the surgery near the atrioventricular node are the pre-surgery risk factors. Younger patients with less weight are more prone to having junctional ectopic tachycardia; because the traction of the smaller hearts and occurrence of manipulation on them is more common (12, 13).

In addition, the systolic and diastolic functions of the heart slightly decrease in the first hours after the surgery because of the myocardial edema and cardiac output will be more dependent on heart rate. Ventricles do not have enough time to be completely filled during the tachycardia that, may negatively affect the cardiac output. There is some evidence which shows that the junctional ectopic tachycardia often occurs in children with periods of heart failure before the reconstructive surgery (5).

Cardiopulmonary bypass and the aortic cross-clamp which are commonly used in the corrective surgery decrease the myocardial perfusion and may lead to myocardial damage. So, the aortic cross-clamp time is an important factor to predict the occurrence of junctional ectopic tachycardia (4, 5). In addition, it is shown that increasing the cardiopulmonary bypass time more than 90 minutes increases the chance of junctional ectopic tachycardia (8). Difficult cardiac surgeries such as redo surgery, because of more manipulations and longer cardiopulmonary bypass time, are more likely to lead to junctional ectopic tachycardia (14).

So, according to the relationship between myocardial damage and the risk of junctional ectopic tachycardia, it seems that evaluation of cardiac enzymes such as Creatine Kinase Myocardial Band (CK-MB), and troponin can be an important predictive factor for occurrence of junctional ectopic tachycardia (15). Positive inotropic drugs usage, anemia, and electrolyte imbalances are the post-surgery risk factors for JET. In the warming period and often during the surgery, doing cardiopulmonary bypass and prescribing inotropic drugs such as dobutamine and epinephrine are necessary for increasing the myocardial contractility. But chronotropic and arrhythmogenic positive effects are some of the important complications of these drugs. These effects are more evident in the immature myocardium of younger children and during the cardiac failure because of the decrement of cardiac output and the increment of myocardial oxygen consumption (5). In addition to positive inotropic drugs, hyperthermia and anemia can increase the heart rate and may cause more incidence of junctional ectopic tachycardia (7). Despite the acute electrolyte imbalances in the case of arrhythmia, hypomagnesemia is also related to the occurrence of junctional ectopic tachycardia (13). So, magnesium and other electrolytes should be monitored during and after the reconstructive surgery. Twelve-lead electrocardiography (12-lead Electrocardiogram) is the most important and the only way to diagnose the junctional ectopic tachycardia (16). Due to retrograde atrial activity, P waves will reverse. P intervals depend on the precise position of the ectopic focus. So that, if the ectopic focus is in the top of the atrioventricular node, P waves will occur prior to QRS (ventricular wave) complex, if the ectopic focus is in line with the center of the atrioventricular node, P wave will disappear in the QRS complex, and finally, if the ectopic focus is under the AV node or proximal to bundle of His, the P wave appears simultaneously with the ST segment or the T wave (17). When myocardial injury occurs, enzymes from myocardium are released approximately 2 hours later. After 12 hours, the enzymes will increase, and perhaps for several hours. By 12 hours, the creatine kinase-MB will begin to decrease and by 24 hours the sensitivity of the troponins remains high whereas the CK-MB sensitivity diminishes (18, 19). In this study, six hours after the patients had entered intensive care unit ward, serum level of specific cardiac enzyme (CK-MB, Troponin I) was checked. As mentioned, the occurrence of myocardial damage due to different manipulations during the surgery can be a cause for junctional ectopic tachycardia. In addition, myocardial damages increase the level of cardiac enzymes such as CK-MB and troponin. So, it seems that the occurrence of junctional ectopic tachycardia is related to an increase in the level of these enzymes. In this study, the relationship between serum levels of cardiac enzymes and junctional ectopic tachycardia after reconstructive surgery of congenital heart defects will be surveyed.

2- MATERIALS AND METHODS

2-1. Subjects and methods

In this cohort prospective study, 140 children with congenital heart defects who were hospitalized in intensive care unit after open heart surgery of Shahid Modarres hospital in Tehran, Iran, during one year (2016) were studied. Patients were divided into case (the junctional ectopic tachycardia group including 37 patients), and control groups (control group including 103 patients).

2-2. Measuring tool

These two groups were compared based on the previous studies and collected data. The variables such as age, sex, weight,

type of congenital heart disease, pump time, intensive care unit conditions, laboratory data, specific cardiac enzymes and other variables were compared in two groups. The necessary information was collected through the patients' history via hospital records and patient reports. Information about the time of surgery was taken from the heart surgeon's report. Blood samples were taken six hours after entering the intensive care unit and then quickly sent from intensive care unit to the hospital laboratory and examined there.

2-3. Inclusion and exclusion criteria

Inclusion criterion for children was having congenital heart disease and undergoing open heart surgery with pump, with age less than 18 years old. Exclusion criterion was patients who died less than 6 hours after entering the intensive care unit.

2-4. Data analysis

The results for quantitative and qualitative variables were expressed as mean, standard deviation and percentage. Statistical significance was defined as $P<0.5$. T-test and Chi-square test were used to compare quantitative and qualitative variables. Data were analyzed by SPSS software version 23.0.

3- RESULTS

A total number of 140 patients who had corrective congenital heart disease surgery were surveyed in this study. The prevalence of junctional ectopic tachycardia in our patients was 26.4%. They were divided into control group including 103 patients (73.6%), and case group, which comprised 37 (26.4%) that have junctional ectopic tachycardia. The number of male and female patients in the junctional ectopic tachycardia group was 27 (73%), and 10 (27%), respectively and these numbers in the control group were 51 (49.5%) for male and 52 (50.5%) for female. So, the junctional ectopic tachycardia group had a higher proportion of males than the control group (P= 0.027). The average age of participants in case and control group was 2.47± 3.06 years and 3.82± 4.85 years, respectively, which is lower in the case group (P= 0.049). In terms of underlying cardiac abnormalities, the prevalence of cyanotic and acyanotic cardiac disorders was 23 (62.2%), and 14 (37.8%) in the junctional ectopic tachycardia group and 35 (34%), and 68 (66%) in control group, respectively. So, the prevalence of cyanotic disorders was higher in the junctional ectopic tachycardia group (P=0.004). The most common cyanotic and acyanotic congenital heart diseases were tetralogy of Fallot (TOF), and Ventricular Septal Defect (VSD).

The average time of pumping in case and control group was 107.19± 44.78 and 83.60± 30.04 minutes, respectively which was longer in the case group (P= 0.006). Also, the average of inotrope score in case and control group was 408.65± 50.24 and 94.83± 31.56, respectively which was higher in the case group (P= 0.001). The incidence of junctional ectopic tachycardia was higher in the patients who entered the intensive care unit with open sternum than patients with closed chest (P= 0.012), and it was also higher in intubated patients in intensive care unit than extubated ones (P= 0.015). In addition, the average time of intubation was longer in the junctional ectopic tachycardia group (P= 0.001).

The frequency of peritoneal dialysis was higher in the case group than the control (P<0.001). The average hospitalization time in intensive care unit was 4.85± 2.31 days and 3.19± 0.89 days in case and control group, respectively which was longer in the case group (P<0.001). The mortality rate in junctional ectopic tachycardia group and control group was 8 (21.6%), and 6 (5.8%), which was higher in the case group (P= 0.01). Different demographic data and laboratory values and markers in the two groups and their ratios are presented in **Tables 1 and 2**.

Table-1: Demographic data of the case and control groups.

Variables	Case Group	Control Group	P- value
Gender (male)	27 (73%)	51 (49.5%)	0.027
Age (year)	2.47±3.06	3.82±4.58	0.049
Weight (Kg)	11.20±7.61	15.28±14.11	0.031
BMI (kg/m^2)	14.68±1.79	15.24±2.95	0.181
Cyanotic Heart Disease	23 (62.2)	35 (34%)	0.004
Pump Time (minute)	107.19±44.78	83.60±30.04	0.006
Inotrope Score	408.65±50.24	94.83±31.56	0.001
Temperature (C)	36.95±0.27	36.97±0.23	0.678
Open Sternum	6 (16.2%)	4 (3.9%)	0.012
Peritoneal Dialysis	10 (27%)	4 (3.9%)	>0.001
Extubated at the time of ICU entry	1 (2.7%)	20 (19.4%)	0.015
Intubation time (hour)	61.41±49.78	19.23±22.08	0.001
ICU Duration (day)	4.85±2.31	3.19±0.89	>0.001
Mortality	8 (21.6%)	6 (5.8%)	0.001

BMI; Body Mass Index; ICU: Intensive Care Unit.

Table-2: Laboratory data of the case and control group.

Variables	Case Group	Control Group	P- value
PH	7.35±0.08	7.36±0.07	0.617
PCO_2 (mmHg)	38.85±7.42	37.93±6.15	0.503
PO_2 (mmHg)	149.67±75.96	163.04±81.62	0.371
O_2 Sat (%)	97.46±2.65	97.47±5.05	0.994
HCO_3 (mmol/L)	20.70±2.55	21.54±2.36	0.084
Lactate	5.03±1.14	2.88±1.44	0.001
WBC ($x10^3$/ml)	12.67±3.80	13.64±2.96	0.118
Hemoglobin (mg/dl)	12.07±1.36	11.76±1.56	0.282
Platelet ($x10^3$/ml)	196.35±77.61	201.41±95.92	0.774
Calcium (mg/dl)	9.43±0.85	9.17±0.71	0.101
Mg (mg/dl)	2.38±0.31	2.46±0.35	0.169
Na (meq/l)	144.97±4.88	143.41±4.59	0.095
K (meq/l)	3.84±0.47	4.38±3.77	0.173
BUN (mg/dl)	32.41±10.05	30.26±8.20	0.249
Creatinine (mg/dl)	0.62±0.11	0.63±0.14	0.675
Glucose (mg/dl)	185.94±55.30	178.50±50.17	0.475
CK-MB (U/L)	190.41±94.14	91.66±94.70	<0.001
Troponin (ng/ml)	106.59±53.40	34.55±48.84	<0.001

U: Unit, HCO3: Bicarbonate; Mg: Magnesium; Na: Sodium; K: Potassium; CK-MB: Creatine Kinase Myocardial Band.

The average serum level of CK-MB after the surgery was 190.41± 94.14, and 91.66± 94.70 in case and control groups, respectively which was higher in the junctional ectopic tachycardia group (P< 0.001). Similarly, the average serum level of troponin after the surgery was 106.59± 53.40 and 34.55± 48.84 in case and control groups, respectively which was higher in the junctional ectopic tachycardia group (P<0.001). Based on the analysis of the area under the Receiver Operating Characteristic (ROC) curve, the CK-MB level assessment can predict the occurrence of junctional ectopic tachycardia after the surgery (area under the curve is 0.849, 95% confidence interval is 0.786- 0.911), and the best cut-off point for it is 95.5 to predict the occurrence of junctional ectopic tachycardia. So, CK-MB can diagnose the occurrence of junctional ectopic

tachycardia with 97.3% sensitivity and 67% specificity. In the same analysis, the troponin level assessment can predict the occurrence of junctional ectopic tachycardia after the surgery (area under the curve is 0.877, 95% confidence interval (95% CI) is 0.821- 0.933). Accordingly, the best cut-off point for the troponin is 45 to predict the occurrence of junctional ectopic tachycardia which can be will diagnosed with 97.3% sensitivity, and 72.8% specificity. The ROC curve for JET prediction based on the CK-MB and troponin serum level is shown in **Figures 1 and 2**.

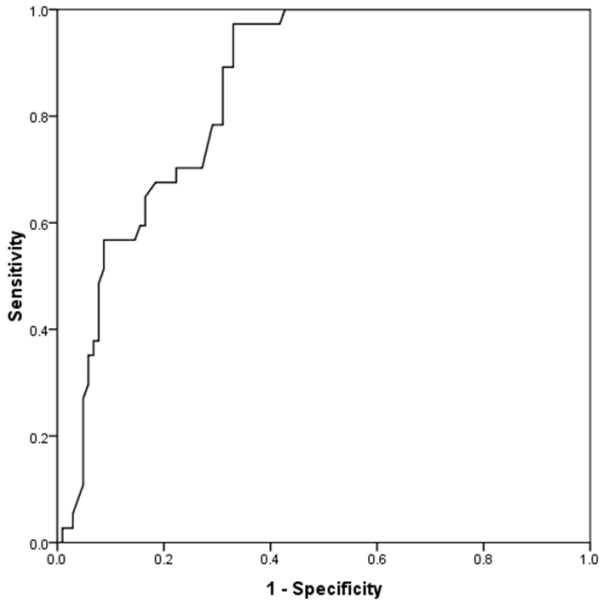

Fig.1: The area under the ROC curve for JET prediction based on the CK-MB serum level.

ROC: Receiver Operating Characteristic; CK-MB: Creatine Kinase Myocardial Band; JET: junctional ectopic tachycardia.

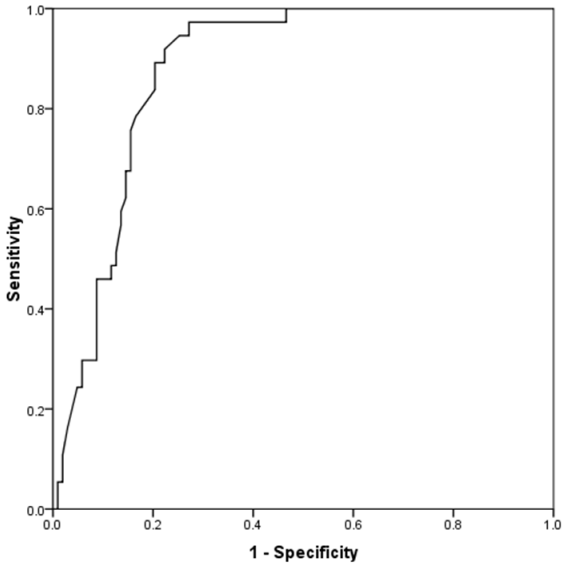

Fig.2: The area under the ROC curve for JET prediction based on the Troponin serum level.

ROC: Receiver Operating Characteristic; CK-MB: Creatine Kinase Myocardial Band; JET: junctional ectopic tachycardia.

4- DISCUSSION

Doing any diagnostic or treatment intervention or occurrence of a traction or manipulation on the myocardium may lead to its damage, which will increase the secretion of specific heart enzymes such as creatine kinase-MB and troponin. So, it is predictable that a correlation between the increase in the secretion of these enzymes and the occurrence of some arrhythmias like junctional ectopic tachycardia exist. This is according to the effects of physical interventions on myocardium in sinoatrial and atrioventricular origin tachycardia.

Pfammatter et al., in their study in 2002 monitored all the patients who underwent corrective congenital heart disease surgery and evaluated their tachycardia for 24 hours after the surgery. The prevalence of primary arrhythmias, especially JET is 30% of atrial septal defect (ASD) patients, 35% of tetralogy of Fallot (TOF) patients, and 47% of atrioventricular canal defect (AVSD) patients and the patients with arrhythmia were younger. In all three mentioned groups, there was a meaningful relationship between the occurrence of JET and the longer time of cardiopulmonary bypass and aortic cross-clamp. Also, there was a positive correlation between the JET occurrence and an increase in troponin level in serum (20).

In 2011, Mildh et al., monitored 1001 children with open heart surgery for 5 years. The occurrence of junctional ectopic tachycardia was confirmed in 5% of patients. After the surgery, these patients experienced longer cardiopulmonary bypass time (138 vs 119 minutes), higher body temperature (38 vs 37.4 ◦c), and a higher level of troponin (3.7 vs 2.1 µg) compared to other children. The most common heart defect in children with JET was the ventricular septal defect (VSD) which was observed in 64.7% of patients. The mortality rate in patients with junctional ectopic tachycardia and without it was 8% and 5%, respectively (21). Andreasen et al., in their study in 2008 monitored 89 patients with junctional ectopic tachycardia and 178 patients without it after the reconstructive heart surgery under cardiopulmonary bypass and the total incidence of junctional ectopic tachycardia was 10.2%. In this study, cardiopulmonary bypass time over 90 minutes, the need for more inotropes, and a higher level of CK-MB after the surgery (the probability ratio was 3.1) were related to more chance for the junctional ectopic tachycardia occurrence. The mortality rate in intensive care unit was higher in the patients with junctional ectopic tachycardia than the control group (13.5% vs. 1.7%). In addition, the duration of admission to cardiac intensive care unit, in the junctional ectopic tachycardia group was three times more than the control group (7 vs. 2 days) (22).

In this study, significant increases in CK-MB and troponin enzymes were observed in children with junctional ectopic tachycardia after corrective surgery of congenital heart defects. In other words, it is possible to predict the occurrence of junctional ectopic tachycardia from an increment in the level of these enzymes with high sensitivity and specificity. Actually, we showed that the risk of junctional ectopic tachycardia in children with increased levels of cardiac enzymes is more than children without the increment and according to the high mortality and morbidity rate due to postoperative junctional ectopic tachycardia, it is clinically important. Few studies have been performed similar to our study about the relationship between the level of cardiac enzymes and the occurrence of junctional ectopic tachycardia, but all of them confirmed this meaningful correlation. In the study of Pfammatter et al., there was a positive correlation between the occurrence of junctional ectopic tachycardia and an increase in the

serum level of troponin after the surgery (20). Also, Mildh et al., showed that the patients with junctional ectopic tachycardia have higher levels of troponin after the surgery than other children (21). In the study of Andreasen et al., the higher level of Ck-MB after the surgery (the probability ratio was 3.1) was related to greater risk of junctional ectopic tachycardia (22). So, our findings are consistent with other similar studies. The most important finding of this study was determining the best cut-off points for both enzymes which can predict and diagnose the occurrence of junctional ectopic tachycardia. So that it was 95.5 for the prediction of CK-MB and 45 for the prediction of troponin. In other words, it is predictable that if the levels of these enzymes in patients are greater than mentioned values, they will have junctional ectopic tachycardia with high precision and reliability. So, evaluation and monitoring of mentioned cardiac enzymes are crucial in high -risk patients. The limitation of this study may be the number of low surgical cases and the lack of multicenter study.

5- CONCLUSION

According to the mentioned sentences, it can be concluded that there is a positive correlation between the occurrence of JET after corrective surgery of congenital heart disease and an increase in the level of CK-MB and troponin enzymes. So that the level of CK-MB above 95.5 and the level of troponin above 45 with a high accuracy might predict the occurrence of JET in these patients. However, more studies are needed, especially considering the type of underlying cardiac defects or the type of surgical intervention performed on patients.

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7- CONFLICT OF INTEREST

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