# Cardiac troponin I elevation in paediatric cardiac catheterization

## *Çocukluk çağı kalp kateterizasyonunda kardiyak troponin I yükselmesi*

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## ABSTRACT

**Objective:** The aim of this study is to investigate prospectively whether intracardiac catheterization produces myocardial damage in paediatric heart.

**Methods:** The study was performed in all patients undergoing diagnostic cardiac catheterization at our institute. A baseline serum sample was drawn before the procedure. The second serum sample was obtained 4-6 hours after the procedure. Cardiac troponin-I and creatine kinase isoenzyme MB fraction levels were determined quantitatively.

**Results:** Diagnostic cardiac catheterization was performed in 30 patients. There were 17 males and 13 females in the study group. The median age was 12 months (range 1 to 204 months); the median body weight was 8 kilograms (range 2.1 to 45 kilograms). The increase in cardiac troponin I (0.21±0.04 ng/ml to 1.16±1.40 ng/ml, $p<0.05$) and creatine kinase isoenzyme MB (26.68±7.53 U/L to 41.65±22.12 U/L, $p< 0.05$) levels after the procedure was significant.

**Conclusion:** This study shows that serum elevations of cardiac troponin I and creatine kinase isoenzyme MB occur after the most of paediatric diagnostic cardiac catheterization procedures. *(Anadolu Kardiyol Derg 2005; 5: 112-5)*

**Key Words:** Cardiac troponin I, creatine kinase isoenzyme MB, myocardial injury, paediatric cardiac catheterization.

## ÖZET

**Amaç:** Bu çalışmanın amacı çocuklarda uygulanan kalp kateterizasyonunun miyokard hasarına yol açıp açmadığını prospektif olarak araştırmaktır.

**Yöntemler:** Çalışma bölümümüzde teşhis amaçlı kalp kateterizasyonu uygulanan bütün hastalarda yapıldı. İşlemden hemen önce serum örnekleri alındı. İkinci serum örnekleri işlemden sonraki 4-6 saat içinde alındı. Bu serumlarda kardiyak troponin I ve kreatin-kinaz izoenzim-MB kantitatif olarak bakıldı.

**Bulgular:** Teşhis amaçlı kalp kateterizasyonu 30 hastaya uygulandı. Çalışmada 17 erkek ve 13 kız hasta vardı. Ortanca yaşları 12 ay (1 ile 204 ay arasında), ortanca kilo değeri 8 kilogram (2.1 ile 45 kilogram arasında) idi. Kardiyak troponin I (işlem öncesi 0.21±0.04 ng/ml, işlem sonrası 1.16±1.40 ng/ml) ve kreatin kinaz izoenzim-MB ( işlem öncesi 26.68±7.53 U/L, işlem sonrası 41.65±22.12 U/L) düzeylerindeki artışlar istatistiksel olarak anlamlı idi ($p< 0.05$).

**Sonuç:** Bu çalışma ile pediatrik yaş grubunda yapılan teşhis amaçlı kalp kateterizasyonu işlemi sırasında kardiyak troponin I ve kreatin kinaz izoenzim-MB düzeylerinde artış olduğu gösterildi. *(Anadolu Kardiyol Derg 2005; 5: 112-5)*

**Anahtar Kelimeler:** Kardiyak troponin I, kreatin-kinaz izoenzim-MB, miyokard hasarı, pediatrik kalp kateterizasyonu

## Introduction

The degree of myocardial injury associated with paediatric cardiac catheterization is unknown (1, 2). The measurements of creatine kinase and creatine kinase isoenzyme MB (CK-MB) are still used as markers of myocardial damage. However, the release of cardiac troponins into the blood provides the most sensitive and specific biochemical marker of myocardial damage that is currently available (3-5).

Cardiac troponin I (TnI),a sensitive and specific marker for detecting myocardial injury, is a well-established diagnostic tool in adult patients with coronary artery disease (2, 4, 6). In paediatrics, troponin elevation has been demonstrated in patients with congenital and acquired heart disease. The diagnostic utility of cardiac TnI as a marker of myocardial injury after interventional catheterization is evolving. Its elevation after radio-

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frequency ablation has been reported in adults and correlated with procedural variables (1,2,7,8).

The aim of this study is to investigate prospectively whether intracardiac catheterization produces myocardial damage in paediatric heart.

## Material and Methods

**Patients:** The study was performed in all patients undergoing diagnostic cardiac catheterization at our institute from March 1, 2003 to December 31, 2003. The study group consisted of 30 paediatric patients (17 males, 13 females), median age 12 months (range 1 to 204 months), median weight 8 kg (2.1 to 45 kg). Written informed consent was obtained from all patients.

**Procedures:** Cardiac catheterization was done for diagnostic and hemodynamic work-up. The procedures were performed in fasting state after the patient was premedicated with chlorpromazine, diazepam or midazolam. The catheters were introduced after proper femoral venous and/or arterial accesses were established. Iohexol (Omnipaque®) with the iodine concentration of 350 mg I/ml was used as contrast material in all subjects and 1.0-2.0 ml/kg contrast material was injected at a time with the total dose not exceeding 6.0 ml/kg. A balloon catheter or a closed-end catheter with side holes was used for right heart, a pig-tail catheter was preferred for left-sided manipulations. All procedures were successfully completed without any complication. Patients were monitored after the procedure for 24 hours for signs of myocardial injury and dysrhythmia.

**Patient data obtained:** For all patients, the following patient data were obtained: age, gender, weight and diagnosis. The effects of following parameters on cardiac TnI and CK-MB were studied: presence or absence of cyanosis, presence or absence of pulmonary hypertension, patients ≤ 1 year old versus patients > 1 year old, patients receiving treatment for congestive heart failure versus no treatment, number of injections ≤ 4 versus > 4. The mean pulmonary artery pressure above 25 mmHg was identified as pulmonary hypertension.

**Blood samples:** A baseline serum sample was drawn before the procedure. If the baseline level was elevated above the normal range, patients were excluded from the analysis. A second serum sample was obtained 4-6 hours after the procedure. Blood samples were collected from venous sheaths and introduced into tube collectors containing clot activators. Serum samples were centrifuged at 3000 rpm for ten minutes, and the supernatant serum was removed and examined for cardiac TnI and CK-MB. Cardiac TnI and CK-MB levels were determined quantitatively. Cardiac troponin-I concentrations were measured in serum by two-side sandwich immunoassay (detection limit > 0.2 ng/ml ) using direct chemiluminometric technology (The Chiron Diagnostics ACS: 180 Cardiac troponin-I assay). The cut-off value of serum cardiac TnI for myocardial injury was 0.6 ng/ml (5,9). In the same serum samples, the activity of creatine kinase isoenzyme MB was measured by an immunoinhibition assay (Merck), which had an upper reference limit of 35 U/L for CK-MB activity.

**Statistics:** All values are expressed as mean ± SD; median and range values are also provided for data with non-normal distribution. The measurements that changed significantly were explored with the Wilcoxon signed rank test. Mann-Whitney U test was performed while comparing the values of CK-MB and cardiac TnI in subgroups. A "p" value of < 0.05 was considered significant.

## Results

Diagnostic cardiac catheterization was performed in 30 patients. The study included right-sided cardiac catheterization only in 9 patients and left and right heart catheterization in 21

**Table 1. Cardiac troponin I and creatine kinase MB levels in study groups and subgroups**

| | n | cTnI-0 (ng/ml) | CTnI-1 (ng/ml) | P | CKMB-0 (U/L) | CKMB-1 (U/L) | P |
|---|---|---|---|---|---|---|---|
| Total | 30 | 0.21± 0.04 | 1.11 ± 1.4 | 0.002 | 26.68 ± 7.53 | 41.65 ± 22.12 | 0.000 |
| Injection ≤ 4 | 10 | 0.22 ± 0.05 | 1.54 ± 1.86 | 0.018 | 26.73 ± 7.77 | 47.64 ± 32.07 | 0.012 |
| Injection > 4 | 20 | 0.21 ± 0.03 | 0.9 ± 1.1 | 0.000 | 26.65 ± 7.6 | 38.35 ± 14.11 | 0.000 |
| Cyanotic | 11 | 0.21 ± 0.04 | 0.84 ± 0.93 | 0.005 | 29.09 ± 8.34 | 42.0 ± 14.05 | 0.003 |
| Acyanotic | 19 | 0.21 ± 0.04 | 1.27 ± 1.61 | 0.001 | 25.35 ± 6.91 | 41.45 ± 25.85 | 0.003 |
| Medication for CHF | 16 | 0.22 ± 0.05 | 1.49 ± 1.73 | 0.001 | 27.19 ± 6.96 | 47.63 ± 26.59 | 0.001 |
| No medication for CHF | 14 | 0.20 ± 0.01 | 0.68 ± 0.73 | 0.005 | 26.13 ± 8.31 | 35.27 ± 14.36 | 0.001 |
| Pulmonary HT | 17 | 0.22 ± 0.05 | 1.40 ± 1.66 | 0.000 | 27.78 ± 8.14 | 47.11 ± 24.85 | 0.005 |
| No pulmonary HT | 13 | 0.20 ± 0.02 | 0.73 ± 0.89 | 0.008 | 25.15 ± 6.61 | 34.08 ± 15.54 | 0.018 |
| RHC | 9 | 0.20 ± 0.01 | 0.90 ± 0.84 | 0.018 | 28.22 ± 8.04 | 39.00 ± 17.14 | 0.003 |
| LRHC | 21 | 0.22 ± 0.04 | 1.20 ± 1.59 | 0.000 | 26.05 ± 7.41 | 42.73 ± 24.14 | 0.012 |
| Age ≤ 1 year | 16 | 0.22 ± 0.04 | 1.74 ± 1.68† | 0.001 | 27.94 ± 8.04 | 51.37 ± 25.88 | 0.000 |
| Age > 1 year | 14 | 0.20 ± 0.03 | 0.39 ± 0.26 | 0.003 | 25.33 ± 6.97 | 31.27 ± 10.35 | 0.018 |
| Weight ≤ 10 kg | 19 | 0.21 ± 0.04 | 1.58 ± 1.59‡ | 0.000 | 28.68 ± 7.59 | 49.84 ± 23.97 | 0.003 |
| Weight >10 kg | 11 | 0.21 ± 0.03 | 0.30 ± 0.10 | 0.012 | 23.50 ± 6.50 | 28.67 ± 9.73 | 0.012 |

†: subgroup differences are significant p=0.008. ‡: p=0.003
CHF: Congestive heart failure; CKMB-0: Creatine kinase isoenzyme MB levels before the procedures; CKMB-1: Creatine kinase isoenzyme MB levels after the procedures; cTnI-0: Cardiac troponin I levels before the procedures; cTnI-1: Cardiac troponin I levels after the procedures; HT: Hypertension; LRHC: Left and right heart catheterization.; n: number of patients; RHC: Right heart catheterization.

patients. None of these procedures were associated with adverse events potentially responsible for myocardial injury. Patients were monitored after the procedure for 24 hours for signs of myocardial injury and dysrhythmia and no adverse events (hypotension, congestive heart failure and tachycardia) have been detected.

Of the 30 patients, 18 (60%) had serum cardiac TnI levels above 0.6 ng/ml , and 16 (53%) had serum CK- MB levels above 35 U/L. Cardiac TnI levels were 0.21±0.04 ng/ml and 1.16±1.40 ng/ml , before and after the procedures, respectively. Creatine kinase isoenzyme MB levels were 26.68±7.53 U/L and 41.65±22.12 U/L , before and after the procedures, respectively. The cardiac TnI and CK-MB levels taken after the procedures were significantly higher than the values taken before the procedures ($p< 0.05$) (Fig. 1-2).

The study group included the following subgroups: cyanotic (n=11), acyanotic (n= 19), pulmonary hypertension (n= 17), no pulmonary hypertension (n= 13), medication for congestive heart failure (n= 16), no medication for congestive heart failure (n= 14), age ≤ 1 year (n= 16) and >1 year (n= 14), number of injections ≤ 4 (n= 10) and > 4 (n= 20), right heart catheterization (n= 9), left and right heart catheterization (n= 21), body weight ≤ 10 kg (n= 19) and t > 10 kg (n= 11). All the subgroups had elevated cardiac TnI and CK-MB levels after the procedure. These elevations were especially significant in the younger age and the low body weight groups. Cyanosis, more injections, single or double heart catheterization, pulmonary hypertension and medication for congestive heart failure did not have an effect on cardiac TnI and CK-MB levels (Table 1).

## Discussion

Troponins I and T are regulatory proteins that control the calcium-mediated interaction of actin and myosin. The cardiac forms of these proteins are the products of specific genes and therefore have the potential to be unique for the heart. An increase in cardiac TnI circulating levels is highly indicative of myocardium injury (3,4,7-10). Nageh et al. (4) have found cardiac TnI to be more sensitive than cardiac troponin T and CK-MB in detecting variable degrees of myocardial cell injury during and following percutaneous coronary intervention.

Cardiac TnI samples taken between 4 to 24 hours after the procedures give equally reliable prognostic information, with no particular sampling time point being superior to others within that period (1,3,4). In our study, we obtained the blood samples before and 4-6 hours after the procedures.

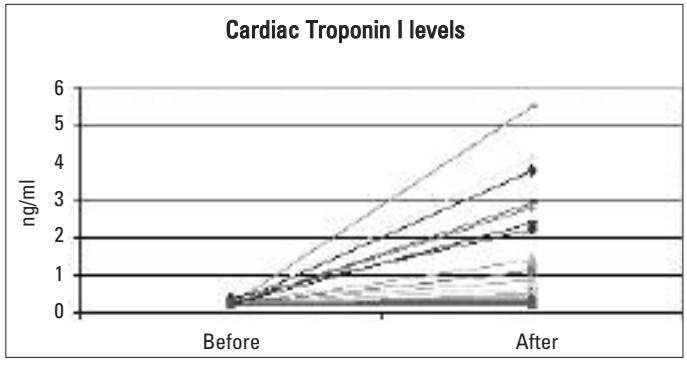
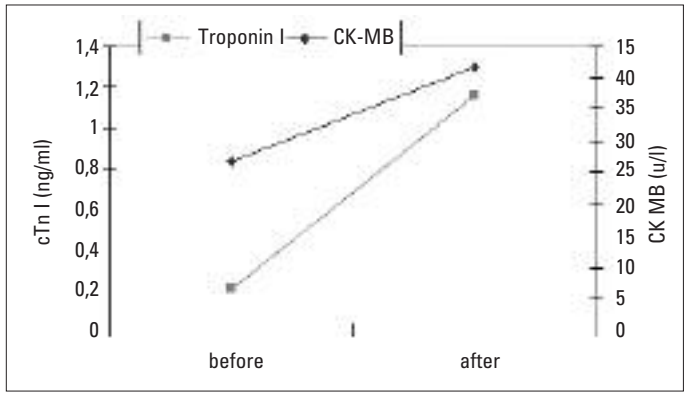



**Figure 1. Cardiac troponin I levels before and after cardiac catheterization in 30 patients**

It is now well established that both cardiac TnI and cardiac troponin T are superior to CK-MB as markers of myocardial injury. Creatine kinase isoenzyme MB' s diagnostic value is limited by its presence in non-cardiac muscular tissue, its variable normal serum concentrations with muscle mass, ethnic origin and its brief elevation during the course of an ischemic cardiac event (4,5,7,9). Unlike a number of studies suggesting different extents of myocardial injury with different interventional strategies (5-8,11), we did not find significant difference between cardiac TnI and CK-MB in detecting variable degrees of myocardial cell injury following paediatric diagnostic cardiac catheterization.

This study is not the first study with cardiac TnI in paediatric patients. In a previous study, Kannankeril et al. (2) showed that diagnostic catheterization did not have an effect on myocardial injury. They claimed that the most of diagnostic procedures did not cause elevation of cardiac TnI above the lower limit of detection, and most interventional procedures were associated with elevation of cardiac TnI, with radio-frequency ablation causing the greatest degree of elevation. However, in our study, we found out that even diagnostic procedures had an impact on myocardial injury. As in our study, Alehan et al. (1) demonstrated that simple diagnostic or therapeutic cardiac catheterization procedures carry the risk of subclinical myocardial damage in paediatric patients, but they studied cardiac troponin T levels as a marker instead of cardiac TnI. They concluded that patients especially at higher risk of myocardial damage after those procedures were younger patients undergoing longer procedures with pulmonary hypertension and compensated heart failure. Myocardial structure is altered in congestive heart failure. Structural abnormalities in variable myocytes are observed in non-ischemic compensated heart failure, including hypertrophied myocardial cells, degeneration of subcellular organelles, lack of contractile materials, and increased cyto-skeletal elements. These morphological changes may be accompanied by an increase in serum cardiac proteins (12-15). In our study, we found out that younger age and lower body weight were the risk factors for myocardial injury. But we revealed no extra risk for pulmonary hypertension and congestive heart failure.

Younger and lower body weight patients had higher cardiac TnI levels. Previous studies have demonstrated that cardiac troponin levels are significantly higher during the first year of life in normal infants than in normal subjects (2,16). The age and we-




cTnI: Cardiac troponin I. CK-MB: Cretine kinase isoenzyme MB

**Figure 2. Cardiac troponin I and creatine kinase isoenzyme MB mean levels before and after cardiac catheterization**

ight dependency of higher cardiac TnI levels can not be postulated in our study group, since these patients had normal basal troponin values. Previous studies have also correlated younger age with higher cardiac TnI levels after paediatric cardiac surgery, particularly marked elevations in children < 12 months of age (2).

Our study has some limitations. Its sample size was relatively small. Although total number of procedures is adequate to establish the differences, there are many subgroups with small number of patients. Additionally we studied only one blood sample for cardiac TnI and CK-MB after the procedures.

## Conclusion

This study shows that serum elevations of cardiac troponin I and creatine kinase isoenzyme MB occur after the most of paediatric diagnostic cardiac catheterization procedures.

The elevation of cardiac troponin I and creatine kinase isoenzyme MB after procedures is inversely correlated with patient`s age and weight. It is apparent that myocardial injury is produced by cardiac catheterization, being even more prominent in a certain group of pediatric patients. These facts favour careful manipulation in young and low body weight patients.

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