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Analysis of Troponin I to determine myocardial injury following diagnostic cardiac catheterization.

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Abstract

An increased level of serum cardiac troponin I is a specific biomarker for myocardial injury. The objective of this study was to evaluate the changes in cardiac troponin I levels to determine myocardial injury following diagnostic cardiac catheterization. A prospective cohort study was carried out between July 1 2006 and March 31 2012 among patients who underwent diagnostic cardiac catheterization in a tertiary hospital. Blood samples were collected at baseline and at 6- and 12- hours of the procedure to measure any changes in cardiac troponin I levels. A total of 264 adult patients; consisting of 157 males and 107 females, who underwent diagnostic cardiac catheterization were chosen for the study. Out of them 42 (16%) had a positive family history of coronary artery disease (CAD). Before the procedure, the mean cardiac troponin I level was 0.059 ± 0.030 ng/mL. However, the mean cardiac troponin I level after 6 hours of catheterization was 0.062 ± 0.041 ng/mL (P = 0.189) and was 0.063 ± 0.026 ng/mL (P = 0.099) after 12 hours. Average cardiac troponin I levels at 6- and 12- hours following diagnostic cardiac catheterization did not differ according to patients' demographic or clinical characteristics (P >0.05). No in-cathlab complications and major adverse cardiac events were observed after one-month. There were no significant changes in cardiac troponin I levels before or at 6- and 12-hours after diagnostic cardiac catheterization. This study, therefore, suggests that diagnostic cardiac catheterization does not appear to be associated with substantial subclinical myocardial injury.

Keywords: Troponin-I; catheterization; myocardial injury; diagnosis

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Introduction

Cardiac troponin I is a sensitive and specific marker for detecting myocardial damage. This biomarker is normally not found in the circulation. Injured cardiac muscles release troponin from the contractile proteins into the blood stream and thus an increased level of serum cardiac troponin I may suggest myocardial injury [1-3]. Elevated serum cardiac troponin I levels have been reported to occur in 5% to 40% of patients undergoing percutaneous coronary intervention [4-6]. Two recent meta-analyses indicates that cardiac troponin I or cardiac troponin T elevation after elective percutaneous coronary intervention is indicative of an increase in long-term all-cause mortality as well as the composite adverse events of all-cause mortality and acute coronary syndromes [7-8].

Although the safety of diagnostic cardiac catheterization has been demonstrated in several large cohort studies which showed very rare clinical complications following the procedure [9-12], very few studies have investigated for any evidence of subclinical myocardial injury resulting from the procedure. In a pediatric population, Kannankeril et al. documented elevations in serum cardiac troponin I levels occurring in 79% of cases immediately after the procedure, and in 86% of them six hours post-diagnostic cardiac catheterization [13]. However, these elevations in serum cardiac troponin I have not yet been shown to be predictive of future adverse cardiac events [14]. The objective of this study was to determine the occurrence of myocardial injury due to diagnostic cardiac catheterization procedure in adults by evaluating the elevation in serum cardiac troponin I levels.

Materials and Methods

Subjects

Using a cohort study design, we prospectively studied patients presenting to our hospital between July 1 2006 and March 31 2012; who underwent diagnostic cardiac catheterization. Patients whose pre-procedure serum cardiac troponin I levels were >0.15 ng/mL indicative of myocardial infarction, as well as pregnant or lactating mothers were excluded from the study. The study fully complied with the Declaration of Helsinki and the study protocol was approved by the hospital institutional review board. All patients gave a written informed consent to participate in the study.

Blood sample collection and serum cardiac troponin I measurement

Before the patients underwent diagnostic cardiac catheterization, blood samples were collected for the baseline profile. Patients with normal serum cardiac troponin I levels were further screened for their medical history, family history and any allergies, if present. Blood was sampled for serum cardiac troponin I into tubes with anticoagulant immediately before, and at 6- and 12- hours after the procedure. The samples were centrifuged at 3,000 rpm for 10 minutes, serum was separated and freezed at -70°C, batch thawed and analyzed using the paramagnetic-particle, chemiluminescent immunoenzymatic assay (Beckman, Coulter Inc., California). Using this assay, serum cardiac troponin I levels in the sample can be accurately measured within the reportable range of the lower limit of detection and the highest calibrated value (0.03 to 50 ng/ml). The upper limit of the 95% non-parametric range for a presumably healthy population is below the mean minimum detectable concentration of the assay (0.03 ng/ml), and the diagnostic cut-off value (as specified by the manufacturer) for myocardial damage based on receiver-operating characteristic (ROC) plots is ≥0.1ng/ml [14]. Therefore, any value equal to or higher than 0.1 ng/ml indicates evidence of myocardial damage.

Study endpoints and patient follow-up

A follow-up study was done at 30 ± 5 days after the procedure to report any in-cathlab complications and major adverse cardiac events. The study endpoint was taken as the occurrence of any major adverse cardiac events (MACE) at 30- days follow up. MACE is defined as cardiac death or Q wave myocardial infarction (MI/). Q-wave MI was diagnosed using clinical symptoms, new significant (> 1 mm depth) Q waves in at least two contiguous ECG leads, and a creatine kinase-MB concentration 99th centile of our own laboratories' reference control value. Follow-up involved regular clinical review until the study endpoint was reached.

Statistical analysis

Data analyses were performed with SPSS 17.0 for Windows (Chicago, IL, USA). Continuous variables were summarized as mean (SD). Categorical variables were expressed as frequencies and percentages. We used paired Student's t - test, to compare the means of pre- and post-procedural serum cardiac troponin I levels. A P value of <0.05 was considered significant.

Results

Patient characteristics

The patient cohort was comprised of 264 patients; 157 males and 107 females, aged ≥ 18 years; who underwent diagnostic cardiac catheterization. Of these patients, 42 (16%) had a positive family history of coronary artery disease and 10 (4%) had a past history of coronary artery disease. The demographic and clinical characteristics of the patients are as shown in Table 1. Overall, 98 (37%) were hypertensive, 37 (14%) had type II diabetes mellitus, 74 (28%) uses tobacco and 32 (12%) uses alcohol. Also, among the enrolled patients, 77 (29%) patients were overweight and 63 (24%) patients were obese [Table 1].

Table 1. *Demographic and clinical characteristics of the patients*

Variable	n (%)
Age (years)	
18 – 40	88 (33)
41 – 64	134 (51)
≥ 65	42 (16)
Gender	
Male	157 (59)
Female	107 (41)
Body Mass Index (kg/m2)	
<18	8 (3)
18 – 24.9	116 (44)
25 – 29.9	77 (29)
≥30	63 (24)
BP status	
Normotensive	166 (63)
Hypertensive	98 (37)
Diabetes Mellitus	
Yes	37 (14)
No	227 (86)
Tobacco use	
Yes	74 (28)
No	190 (72)
Mean Heart rate (bpm)	75.2 ± 10.28
Mean LVEF (%)	43.63 ± 12.83

LVEF = left ventricular ejection fraction; SD = standard deviation

Table 2. *Mean cTnI levels at baseline, 6h and 12h after diagnostic cardiac catheterization*

TEST	Mean ± S.D.	P (paired t test)
cTnI (0 hrs) (ng/ml)	0.059 ± 0.030	-
cTnI (6 hrs) (ng/ml)	0.062 ± 0.041	0.189
cTnI (12 hrs) (ng/ml)	0.063 ± 0.026	0.099

cTnI = cardiac troponin; SD = standard deviation

Table 3*. Comparison of serum cardiac troponin I levels at baseline and at 6-hours after the procedure according to patients' characteristics*

Variable	Mean ± S.D. at baseline (ng/ml)	Mean ± S.D. at 6-hours (ng/ml)	P- value
Age (years)			0.20
18 – 40	0.057 ± 0.026	0.061 ± 0.034	
41 – 64	0.061 ± 0.015	0.063 ± 0.033	
≥ 65	0.059 ± 0.021	0.060 ± 0.016	
Gender			0.32
Male	0.59 ± 0.032	0.061± 0.011	
Female	0.61 ± 0.041	0.62 ± 0.021	
Body Mass Index (kg/m2)			0.18
<18	0.063 ± 0.015	0.069 ± 0.017	
18 – 24.9	0.061 ± 0.031	0.066 ± 0.031	
25 – 29.9	0.057 ± 0.023	0.063 ± 0.034	
≥30	0.059 ± 0.021	0.063 ± 0.026	
Blood Pressure			0.43
Normotensive	0.059 ± 0.022	0.061 ± 0.045	
Hypertensive	0.060 ± 0.026	0.062 ± 0.038	
Diabetes Mellitus			0.72
Yes	0.059 ± 0.026	0.063 ± 0.021	
No	0.060 ± 0.032	0.061 ± 0.041	
Tobacco use			0.21
Yes	0.059 ± 0.047	0.065 ± 0.040	
No	0.059 ± 0.029	0.061 ± 0.035	

Table 4. *Comparison of serum cardiac troponin I levels at baseline and at 12-hours after the procedure according to patients' characteristics*

Variable	Mean ± S.D. at baseline (ng/ml)	Mean ± S.D. at 6-hours (ng/ml)	P- value
Age (years)			0.08
18 – 40	0.060 ± 0.030	0.063 ± 0.021	
41 – 64	0.059 ± 0.021	0.068 ± 0.011	
≥ 65	0.061 ± 0.021	0.064 ± 0.031	
Gender			0.27
Male	0.060 ± 0.027	0.066 ± 0.022	
Female	0.058 ± 0.033	0.063 ± 0.034	
Body Mass Index (kg/m2)			0.16
<18	0.058 ± 0.029	0.060 ± 0.020	
18 – 24.9	0.060 ± 0.021	0.063 ± 0.035	
25 – 29.9	0.059 ± 0.037	0.061 ± 0.027	
≥30	0.059 ± 0.041	0.064 ± 0.031	
BP status			0.34
Normotensive	0.059 ± 0.036	0.063 ± 0.033	
Hypertensive	0.060 ± 0.029	0.065 ± 0.032	
Diabetes Mellitus			0.61
Yes	0.066 ± 0.012	0.065 ± 0.019	
No	0.062 ± 0.021	0.063 ± 0.023	
Tobacco use			0.31
Yes	0.068 ± 0.035	0.069 ± 0.031	

No	0.060 ± 0.010	0.062 ± 0.012

Cardiac troponin I level

The mean serum cardiac troponin I levels of the patients, at different time intervals, are shown in Table 2. Its variations with patients' demographic and clinical characteristics are shown in Tables 3 & 4. Before the procedure, the mean serum cardiac troponin I level was 0.059 ± 0.030 ng/mL. The mean serum cardiac troponin I level after 6 hours of catheterization was 0.062 ± 0.041 ng/mL (P = 0.189) and after 12 hours was 0.063 ± 0.026 ng/mL (P = 0.099) indicating that there was a minor statistically insignificant increase in the mean serum cardiac troponin I levels at 6 and 12 hours after diagnostic cardiac catheterization. Mean serum cardiac troponin I levels at 6- and 12- hours post diagnostic catheterization did not differ according to patients demographic or clinical characteristics (P >0.05). Overall, at 6- and 12-hours post catheterization only 2 (1%) asymptomatic patients had serum cardiac troponin I levels of 0.12ng/ml and 0.14ng/ml indicative of some myocardial injury. Furthermore, none of the patients studied reported any major adverse cardiac event during one-month follow-up and there were no in-cathlab complications reported.

Discussion

Diagnostic cardiac catheterization is an invasive procedure that is prone to complications, including death. Our primary aim was to establish the possibility of myocardial injury due to diagnostic cardiac catheterization. We collected complete data prospectively to avoid the bias associated with retrospective studies, particularly where data are collected from subsidiary source records such as theatre logbooks. Over the last two decades, there have been improvements in catheterization technique and technology that have reduced the morbidity and mortality associated with routine diagnostic coronary angiography, which according to published records is between 0.05% and 0.2% [8-12]. Severe and progressive myocardial ischemia starting during or shortly after percutaneous coronary intervention is an important cause of morbidity and mortality requiring emergency surgery [8-10]. Early recognition of ischemia post-catheterization and immediate surgery has been shown to improve survival rate [10].

In this study, there was no significant elevation of serum cardiac troponin I level following diagnostic cardiac catheterization, indicating no significant myocardial injury. Only 1% of the patients who were asymptomatic showed evidence of myocardial injury after diagnostic cardiac catheterization. However, there was no incidence of in-cathlab complications and after one month of follow-up none of the patients in this series showed any major adverse cardiac event. Serum cardiac troponin I elevations in this study was lower compared with a study in children which showed substantial elevations in serum cardiac troponin I following diagnostic cardiac catheterization [13-15]

The potential clinical benefit of this study is in highlighting the need for a cut-off value for the initiation of close monitoring for possible procedure-related complications where myocardial injury is suspected [13-14]. In such cases, the clinical relevance of high levels of serum cardiac troponin I found in the patients may be difficult to interpret unless a good knowledge of the expected procedure–related elevation after an uneventful procedure is known [13]. Therefore, establishing a reference range of "expected"/normal elevation would allow levels of serum cardiac troponin I to be used as a valid diagnostic tool to detect "unexpected/sub-clinical" myocardial injury following diagnostic/therapeutic cardiac catheterization.

Conclusion

The result of this study extends our understanding of the potential uses of post-diagnostic catheterization elevations in cardiac biomarkers. Unlike what was observed in children, we found that there was no marked substantial myocardial damage from the procedure in adults [13-14]. Although the findings of this preliminary study are limited by small sample size, these results need to be confirmed on a larger scale, and with more diagnostic cases, for more validity, reliability and clinical applicability. Moreover, clinical and demographic predictors of myocardial injury evidenced by elevations in serum cardiac troponin I need to be better characterized.

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