

## Does increased troponin-T in patients undergoing percutaneous transluminal coronary angioplasty have any clinical significance ?

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### Abstrak

Dilakukan penelitian untuk menilai arti klinis peningkatan troponin-T (TnT) setelah angioplasty koroner (PTCA) pada 52 pasien. Setelah PTCA, 35 pasien (67.3%) mengalami peningkatan Tnt. Kecuali seorang penderita yang mengalami gagal jantung, penderita lain tidak mengalami komplikasi. Disimpulkan bahwa PTCA dapat menyebabkan kerusakan ringan miokardium, yang tidak berpengaruh terhadap terjadinya penyulit dini. Penggunaan TnT untuk stratifikasi risiko setelah PTCA masih harus diteliti.

### Abstract

A study was undertaken to evaluate the significance of elevated troponin-T after percutaneous transluminal coronary angioplasty (PTCA) in 52 patients. After PTCA, 35 patients (67.3%) showed elevated TnT. Except in one patient who developed heart failure, the other patients had uneventful clinical course. We conclude that PTCA might induce minor myocardial injury, which is not associated with immediate adverse outcomes. The role of TnT for risk stratification after PTCA should be further refined.

**Keywords:** angioplasty, PTCA, myocardium, cardiac enzymes

Myocardial infarction is an uncommon complication of percutaneous transluminal coronary angioplasty (PTCA) and is usually related to inadvertent total occlusion of a major coronary artery.<sup>1,2</sup> The patients usually present with ischemic pain, ECG changes and creatine kinase (CK) release. Most of these patients require emergency surgery in an attempt to salvage ischemic myocardium.<sup>3,4</sup> One of the most controversial issues is whether PTCA induced "small" myocardial damage or infarctions, diagnosed by enzymatic abnormalities or other markers such as troponin T (TnT) or I, clinically relevant.<sup>5-7</sup> Among interventional cardiologists, the commonly used term "infarctlet" or microinfarction implies a small an insignificant event. However, the importance of these infarctlets after PTCA is both understudied and underappreciated, despite the well established prognostic importance of even small enzymatic infarctions in the setting of unstable angina<sup>8</sup> or after acute myocardial infarction.<sup>9</sup>

In the present study, we evaluated the clinical significance of PTCA induced small myocardial damage as diagnosed by elevations of TnT.

### METHODS

#### Patients

Fifty-two non-consecutive patients were studied, of whom 40 were males and 12 females. Their ages ranged from 35 to 79 years old (mean age  $57 \pm 10.5$  years). All patients underwent single or multivessel PTCA with or without related procedures such as rotational atherectomy and/or stenting. PTCA was performed to treat significant coronary artery stenosis with clinical and/or objective evidence of ischemia. None of the patients had a history of myocardial infarction within one month of the PTCA procedure. PTCA was considered successful if a  $\geq 20\%$  increase in luminal diameter was achieved with a final diameter stenosis of  $< 50\%$  and without the occurrence of death, acute non-Q-wave infarction, or emergency coronary artery bypass surgery.

## PTCA

PTCA was performed under local anesthesia using transfemoral route. All patients were started on aspirin 160 mg/day and ticlopidine 250 to 500 mg/day at least 3 days prior to the procedure. They were also put on oral nitrates and calcium antagonist or beta-blocking drugs provided there were no contraindications. Patients were fully heparinized during angioplasty and at least 24 hours PTCA. Intracoronary nitroglycerine was given liberally during the procedure.

## Determination of CK, CK-MB and troponin T

Blood samples were drawn from an antecubital vein into dry glasses before PTCA, and 4 and 24 hours afterwards. CK activity was determined by DGKC (Deutsche Gesellschaft für Klinische Chemie) method (normal value < 80 U/L). Serum CK-MB activity was assayed using immunoassay method of Wurzburg (normal value < 10 U/L). The TnT immunoassay (ELISA Troponin T) was carried out using Enzymun-Test System ES22 analyzer (Boehringer Mannheim GmbH, Germany). The method is based on a single-step sandwich principle, with streptavidine-coated tubes as the solid phase and two monoclonal antihuman cardiac TnT antibodies. Normal value is < 0.10 µg/l.

## Data analysis

Data were expressed as mean  $\pm$  SD. A *p* value < 0.05 was considered statistically significant. Comparison was made using Student's *t*-test.

## RESULTS

PTCA was successful in all patients. None developed acute Q-wave myocardial infarction. None required emergency coronary artery bypass surgery. All patients survived. One patient developed heart failure, which could be controlled with appropriate medications. All patients were discharged asymptomatic, on average 2 – 3 days after the procedure.

The mean and SD of CK, CK-MB and TnT levels before PTCA, 4 and 24 hours after PTCA were presented in Table 1. Six patients had normal CK, CK-MB and TnT levels before and after PTCA. Thirty-three patients had normal CK and CK-MB levels before and after PTCA, but TnT levels increased after PTCA. Of these 33 patients, 17 had raised TnT levels even

before PTCA. PTCA induced elevations in either CK and/or CK-MB as well as TnT levels in 7 patients. One patient showed elevation of CK-MB after PTCA, but CK and TnT levels remained normal before and after PTCA. Four patients had normal CK and CK-MB levels before and after PTCA, and raised TnT levels at baseline which normalized after PTCA. One patient had elevated CK-MB before PTCA, which declined, to normal afterwards, but TnT levels were high before and after the procedure.

Table 1. Mean (SD) values of CK, CK-MB, and TnT before, 4 and 24 hours after PTCA

Time (hour)	0	4	24
CK	31 (20)	37 (85*)	38 (117*)
CK-MB	4.5 (2.8)	5 (9.5**)	5.5 (12.9**)
TnT	0.08 (0.43)	0.22 (1.36#)	0.17 (2.47#)

Comparison vs. value at hour 0: \* *p* < 0.04; \*\* *p* < 0.02; # *p* < 0.05

## DISCUSSION

Several observational studies have shown that elevated cardiac enzyme is not uncommon after an apparently successful PTCA and these enzyme elevations do not have negative prognostic importance.<sup>5-7</sup> However, recent reports indicated that these infarctlets may not be benign. In the largest series reported to date, Abdelmeguid et al reported on 4664 consecutive patients with successful PTCA or directional coronary atherectomy.<sup>10-11</sup> Clinical follow-up, extending up to 8.5 years, was available in 99.6% of the patients. The primary finding of this study was that elevations of CK of more than twice the upper limit of laboratory normal were associated with decreased survival and event-free survival. This study confirms that a CK value of 2 to 5 times the control value, with abnormal CK-MB levels after PTCA, imparts a worse prognosis than no CK elevation (CK < 2 times control). In a further study comprising 4484 patients, the same investigators found out that even minor elevations of CK (< 2 times the upper limit of laboratory normal) were associated with adverse long-term outcome.<sup>12</sup> They concluded that any degree of necrosis was harmful and that attempting to conclude that a certain amount of necrosis was not significant by setting the threshold at an arbitrary level was simply not accurate. Several potential explanations may be offered. Increased CK or CK-MB reflects small zones of necrosis. Microscopic zones of necrosis or microinfarcts may provide a nidus of ventricular

arrhythmias via a microreentry or a focal mechanism. Furthermore, it may also indicate interruption of collateral blood flow due to microembolization.<sup>13</sup>

It is, however, known that CK and CK-MB are non-specific markers of myocardial damage.<sup>14,15</sup> Moreover experimental studies in baboon model showed that CK and CK-MB release might occur after short periods of coronary occlusion even without myocardial necrosis.<sup>16</sup>

Cardiac specific troponin T (TnT) and troponin I are new biochemical markers which offer substantial advantages with respect to sensitivity and specificity for detection of myocardial cell injury. Assays based on monoclonal antibodies against cardiac troponins, which have hardly cross-reactivity to their skeletal muscle isoforms, allow accurate assessment of cardiac involvement. Accordingly, troponins have become a new gold standard for biochemical detection of myocardial injury. In addition, so called "minor myocardial injury" or microinfarcts such as in unstable angina can be detected, which usually escapes routine measurements of CK and CK-MB. Accumulated data have shown that troponins in patients with acute coronary syndrome are highly predictive of death and myocardial infarction.<sup>8,17-20</sup>

In our study, although the mean CK, CK-MB and TnT levels were higher post-PTCA, the wide standard deviations indicated that this was attributed by marked elevations of those parameters in some patients. In fact, 39 patients (75%) had normal CK and CK-MB levels before and after PTCA. Of these patients, 33 (63.5%) showed elevation of TnT after PTCA. In 17 patients of them TnT level was already elevated before PTCA. This suggested that PTCA might indeed induce minor myocardial damage. The significance of TnT in identifying events after PTCA has not been well defined.<sup>21</sup> All the 33 patients had uneventful clinical course. The above observations suggested that elevated TnT after PTCA is not predictive for early (in-hospital) adverse outcomes.

In our study CK and CK-MB were elevated after PTCA in 8 patients (15.4%), and in one patient it was not accompanied by elevation of TnT. Except for one patient who developed heart failure, the other patients were also discharged without complication.

Four patients had elevated TnT levels before PTCA, which normalized after the procedure, indicating

reperfusion. In these 4 patients, the CK and CK-MB levels were normal before and after PTCA. In another patient TnT levels were high before and after PTCA, but CK-MB level which was raised before the procedure declined to normal after PTCA.

Our study confirms that measurement of TnT level confers additional advantage over CK and CK-MB in the early detection of myocardial injury after PTCA. However, the marker does not seem to portend poor short term prognosis. Further studies are required to further elucidate its clinical significance.

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