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ORIGINAL ARTICLE

Postoperative high-sensitivity troponin T as a predictor of sudden cardiac arrest in patients undergoing cardiac surgery

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Abstract

Background: *The usefulness of high-sensitivity troponin T (hs-TnT) as a predictor of sudden cardiac arrest (SCA) in patients undergoing valve surgery is currently unknown.*
Methods: *A prospective study was conducted on a group of 815 consecutive patients with significant valvular heart disease that underwent elective valve surgery. The primary end-point was postoperative SCA.*
Results: *The postoperative SCA occurred in 26 patients. At multivariate analysis of hs-TnT measured immediately after surgery (hs-TnT I) and age remained independent predictors of the primary end-point.*
Conclusions: *Elevated postoperative hs-TnT was associated with a higher risk of postoperative SCA.* (Cardiol J 2019; 26, 6: 777–781)
Key words: sudden cardiac arrest, high-sensitivity troponin T, valve surgery

Introduction

Postoperative sudden cardiac arrest (SCA) is a complication which significantly increases the risk of hospital death as well as the length of hospital stay. The diagnosis of SCA can be made if the cardiac arrest occurs within an hour of the onset of acute symptoms and has been reversed or not been reversed by ongoing resuscitation. Sudden cardiac arrest usually occurs in the course of cardiac arrhythmias such as ventricular fibrillation, ventricular tachycardia, pulseless electrical activity or asystole. The reasons for sudden arrest are different in younger people than in older people. Young people are dominated by canalopathies and cardiomyopathies. Chronic degenerative diseases such as coronary heart disease, valvular heart disease and heart failure are prevalent in older populations [1–5]. Predictors of SCA include left ventricular ejection fraction (LVEF), programmed ventricular stimulation, QT interval dispersion, late potentials, heart rate variability, microvolt T-wave alternans, baroreflex sensitivity and heart rate turbulence [6, 7]. Among emerging variables that look promising for predicting sudden cardiac death are biochemical indicators such as the B-type natriuretic peptide and N-terminal pro-B-type natriuretic peptide, which have shown encouraging results in preliminary investigations [1].

Troponin T (TnT) is a polypeptide that is part of the striated contractile muscle apparatus. A very important aspect from a diagnostic point of view is the fact that the sequence of troponins of cardiac origin differs from the sequence of skeletal troponins. Thanks to this, after obtaining specific monoclonal antibodies, it became possible to use them in the diagnosis of ischemia and hypoxia of cardiomyocytes [8]. In the available literature, numerous articles describe high sensitivity troponin T (hs-TnT) as a biomarker of predictive importance in various diseases of the cardiovascular system, such as heart failure, coronary artery disease (CAD) and aortic stenosis [9–13]. The usefulness of the hs-TnT as a predictor of perioperative SCA in patients with valve disease undergoing valve surgery is currently unknown.

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Methods

The current prospective study was performed on consecutive patients with hemodynamically significant valve defects (aortic stenosis, aortic regurgitation, mitral stenosis and mitral regurgitation) who underwent elective replacement or repair of the valve. The exclusion criteria were: patients under 18 years of age, a lack of consent to participate in the study, autoimmune diseases, chronic inflammatory bowel, active neoplastic diseases and active infective endocarditis.

Complete blood count was performed with K2-EDTA samples, using a Cobas 6000 electronic counter (Roche, Mannheim, Germany). The day before surgery, immediately after patient arrival at the intensive care clinic after surgery and one day after operation, a blood sample for hs-TnT was collected from each patient. The plasma levels of cardiac TnT (cTnT) concentrations were measured by the troponin T hs-STAT (Roche).

All procedures were performed through a midline sternotomy incision under general anesthesia in a normothermia. All patients were given cold blood cardioplegia at the initial dose of 15–20 mL/kg followed by booster doses of 5–10 mL/kg every 20 min. The primary end-point at intra-hospital follow-up was postoperative SCA defined as cardiac arrest within an hour of the onset of acute symptoms and has been reversed or not reversed by ongoing resuscitation. Patients were followed up for 30 days or until death. The follow-up of discharged patients was conducted through direct observation during hospitalization and clinic visits 30 days after surgery. The study was conducted at the Institute of Cardiology, Warsaw, between 1 January 2014 and 20 September 2018. The protocol was approved by the Institutional Ethics Committee.

Statistical analysis

A statistical analysis was performed using the SAS version 9.2. Data are presented as the mean $\pm$ standard deviation and the frequency (%). Intergroup comparisons were made using the Mann-Whitney U test, the Pearson χ^2 test or Student t-test. The Shapiro-Wilk test of normality was used to test the sample distribution. Logistic regression was used to assess relationships between variables. The following covariates: age, aortic cross-clamp time, cardiopulmonary bypass time, atrial fibrillation, body mass index, chronic obstructive airway disease, CAD, coronary artery bypass grafting (CABG) procedure, creatinine, hs-TnT, hemoglobin, hypertension, left ventricular end-diastolic and end-systolic diameters, LVEF, New York Heart Association classes, peripheral atherosclerosis, pulmonary blood pressure, tricuspid annulus plane systolic excursion, high-sensitivity troponin T measured immediately after surgery (hs-TnT I) and high-sensitivity troponin T measured 1 day after operation (hs-TnT II) were investigated for association with endpoints in univariate analysis. Significant determinants ($p < 0.05$) identified from univariate analysis were subsequently entered into multivariate models. The Spearman rank correlation coefficient was used to search for associations between the postoperative serum hs-TnT level and cardiopulmonary bypass time, aortic cross-clamp time. Predictive value of hs-TnT I was assessed by a comparison of the areas under the receiver operator characteristics of the respective curve. On the basis of the Youden index, a cut-off point was determined that met with the criterion of maximum sensitivity and specificity for perioperative SCA.

Results

The study included 815 patients who underwent heart valve surgery with or without concomitant procedures. The mean age in the study group was 64 ± 13. Sixty-three (7.7%) patients had significantly impaired left ventricular systolic function (LVEF $\leq 35\%$). The mean preoperative hs-TnT level was 35 ± 29 ng/L, hs-TnT I level was 925 ± 802 ng/L and hs-TnT II level was 1321 ± 1103 ng/L. Table 1 shows the characteristics of the patients studied. A postoperative SCA occurred in 26 patients (ventricular fibrillation 11 patients, ventricular tachycardia 6 patients, pulseless electrical activity 3 patients and asystole 6 patients). In all patients with SCA resuscitation was initiated, which resulted in the restoration of hemodynamically stable cardiac rhythm in 18 patients. In 8 (1%) patients, cardiopulmonary resuscitation was ineffective. During further follow-up, in another 8 patients after SCA, death occurred due to gradually increasing multi-organ failure. The statistically significant predictors of postoperative SCA at univariate analysis are presented in Table 2. At multivariate analysis hs-TnT I (odds ratio [OR] 1.304, 95% confidence interval [CI] 1.201–1.409; p = 0.004), and age (OR 1.059; 95% CI 1.013–1.108; p = 0.01) remained independent predictors of the primary end-point. The area under receiver operator characteristic curve for postoperative SCA for hs-TnT I is 0.776 (95% CI 0.702–0.850; Fig. 1). The total mortality in the 30-day follow-up was 4.4%. The main cause of death

**Table 1.** Baseline characteristics of the study population (n = 815).

Parameters	Values
Preoperative characteristics of patients	
Age [year]	64 ± 13
Atrial fibrillation	350 (42%)
Body mass index [kg/m^2]	27 ± 9
Coronary artery disease	115 (14%)
Chronic kidney disease (GFR < 60 mL/min/1.73 m^2)	250 (31%)
COAD	53 (7%)
Creatinine [mg/dL]	0.9 ± 0.5
Hemoglobin [g/dL]	13.6 ± 1.5
LVEF [%]	57 ± 12
Male: men	470 (57%)
NYHA classes	2.5 ± 0.5
Peripheral atherosclerosis	135 (16%)
Hs-TnT [ng/L]	35 ± 29
Intraoperative characteristics of patients	
Aortic cross-clamp time [min]	95 ± 39
Cardiopulmonary bypass time [min]	123 ± 52
Lactates [mmol/L]	1.6 ± 0.5
Ph	7.4 ± 0.1
Postoperative characteristics of patients	
Hs-TnT I [ng/L]	925 ± 802
Hs-TnT II [ng/L]	1321 ± 1103
Creatinine II [mg/dL]	1.4 ± 0.4
Hemoglobin II [g/dL]	10.2 ± 1.5
The day of SCA [days]	2 ± 1.5
Main procedures	
AVR	411 (50%)
AVR + MVR	61 (7.4%)
AVP	30 (3.6%)
MVR	162 (30%)
MVP	151 (18.5%)
Concomitant procedures	
Aortic surgery	166 (20%)
CABG	111 (14%)
TVP	179 (22%)

Values are represented by the mean and a measure of the variation of the internal standard deviation. AVP — aortic valve plasty; AVR — aortic valve replacement; CABG — coronary artery bypass grafting; COAD — chronic obstructive airways disease; Creatinine II — creatinine measured one day after operation; GFR — glomerular filtration rate; Hemoglobin II — hemoglobin measured one day after operation; Hemoglobin — hemoglobin measured one day before operation; Hs-TnT I — high-sensitivity troponin T measured immediately after surgery; Hs-TnT II — high-sensitivity troponin T measured one day after operation; LVEF — left ventricular ejection fraction; MVP — mitral valve plasty; MVR — mitral valve replacement; NYHA — New York Heart Association; SCA — sudden cardiac arrest; TVP — tricuspid valve plasty

Table 2. Analysis of predictive factors for the occurrence of postoperative sudden cardiac arrest.

Variable	Odds ratio	95% CI	P
Age [years]	1.050	1.008–1.095	0.01
LVEF [%]	0.971	0.944–0.998	0.04
NYHA [classes]	2.377	1.173–4.815	0.01
Hs-TnT I [ng/L]	1.211	1.106–1.326	0.001

CI — confidence interval; Hs-TnT I — high-sensitivity troponin T measured immediately after surgery; LVEF — left ventricular ejection fraction; NYHA — New York Heart Association
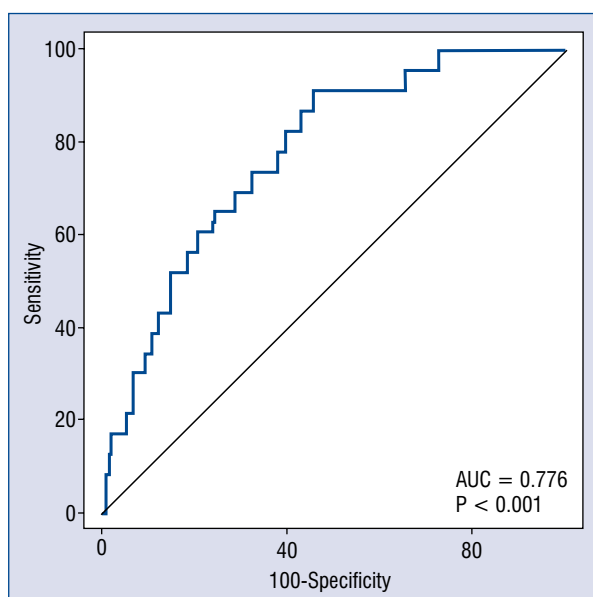
Figure 1. Area under receiver operating characteristic curve of high-sensitivity troponin T measured immediately after surgery for a sudden cardiac arrest following valve replacement/repair surgery.

in the post-operative period was gradually increasing multiple organ dysfunction syndrome. In the subgroup of 115 patients with concomitant CAD, an additional CABG procedure was performed in 111 patients, while in the postoperative period 4 patients experienced SCA. At univariate analysis CAD (p = 0.21) and the additional CABG procedure (p = 0.2) were not predictors of SCA in the early postoperative period. Patients with concomitant CAD did not have significantly higher hs-TnT I levels (p = 0.35) compared with patients without CAD. In the postoperative period 63 patients experienced acute kidney injury (AKI). Patients with postoperative AKI did not have significantly higher hs-TnT I levels (p = 0.36) compared with patients

without AKI, but patients with postoperative AKI had significantly higher hs-TnT II levels (p = 0.02) compared to patients without AKI. A positive correlation was found between the level of hs-TnT II and aortic cross-clamp time (r = 0.35; p = 0.005) as well as between the level of hs-TnT II and cardiopulmonary bypass time (r = 0.47; p = 0.0001), but wasn't found between the level of hs-TnT I and aortic cross-clamp time (p = 0.1) or cardiopulmonary bypass time (p = 0.12). At univariate analysis hs-TnT II (p = 0.09), aortic cross-clamp time (p = 0.13) and cardiopulmonary bypass time (p = 0.11) were not predictors of postoperative SCA. The mean preoperative value of LVEF in the group of patients with SCA was 44% ± 15% and was significantly lower compared to patients with no SCA 58% ± 10% (p = 0.01).

Discussion

Postoperative SCA is a serious complication in patients undergoing heart valve surgery and is associated with very high mortality. The present paper demonstrated the prognostic significance of hs-TnT I in predicting SCA in the early postoperative period in patients undergoing heart valve surgery.

Currently, it is believed that cTnT is the best laboratory parameter in the diagnosis of myocardial injury. Considering the fact that the cytoplasm of cardiomyocytes contains a small amount of free TnT, even small damage to the cell membrane causes their release and the possibility of detection in the blood sample under investigation. Therefore, TnT detected in plasma is a highly specific marker of myocardial injury [14–16]. To date, numerous publications have demonstrated a significant relationship between higher troponin values and worse prognosis in patients with acute myocardial infarction, heart failure or severe aortic valve disease [9–13]. It has also been described that TnT is a predictor of cardiac death in patients with CAD, atrial fibrillation or impaired left ventricular function [17–21]. However, Rahimi et al. [22] did not show a significant correlation between postmortem TnT level and sudden death.

Significant heart valve defects are often result in a volume or pressure overload of the heart cavities. It is worth noting that, a long-lasting additional burden on the myocardium causes progressive degenerative changes of the myocardium, which are accompanied by slow processes of necrosis and fibrosis [23–25]. According to some researchers, increased values of postoperative troponin level are associated with increased permeability of the cell membrane after myocardial reperfusion [26]. However, Opfermann et al. [27] did not find a linear correlation between maximum values of the postoperative TnT and ejection fraction, left ventricular hypertrophy, operating time, cardiopulmonary bypass time, time of cardiac arrest, lowest body temperature, perfusion pressure, cardioplegia volume, reperfusion time, or ventilation time [27]. In the present study, on a group of 815 patients undergoing heart valve surgery only hs-TnT I was an independent predictor postoperative SCA. The presented study did not show a significant correlation between the value of hs-TnT I and the length of aortic clamping time as well as extracorporeal circulation time. Moreover, patients with postoperative SCA were shown to have significantly lower preoperative LVEF compared with patients without SCA. This may suggest that higher values of TnT in the very early postoperative period are associated with the severity of preoperative damage to the myocardium resulting from cardiac valvular disease and increased permeability of hs-TnT across the cell membrane after myocardial reperfusion. Moreover, the higher values of hs-TnT I may indicate a seriously damaged myocardium which is susceptible to the occurrence of life-threatening heart rhythm disturbances that may lead to SCA. It is worth noting that of the 26 patients who experienced SCA, up to 16 patients had a maximum 30-day period before death.

Conclusions

Sudden cardiac arrest occurs in the course of cardiac arrhythmias. Troponin T is a polypeptide that is part of the striated contractile muscle apparatus, moreover it is the best laboratory parameter in the diagnosis of myocardial injury. The results of this study indicate that troponin T measured immediately after surgery is a predictor of SCA in the early postoperative period in patients undergoing heart valve surgery. Further study is needed to clarify the pathomechanisms linking an increased risk of SCA in patients with a higher hs-TnT in the early postoperative period. Enlargement of the number of participants may allow for confirmation of results obtained. The results of this research may be helpful in perioperative strategy for patients undergoing heart valve surgery.

Conflict of interest: None declared

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