Usefulness of myocardial damage biomarkers in predicting cardiogenic shock in patients undergoing heart valve surgery

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INTRODUCTION

One of the clinical variants of cardiogenic shock is postcardiotomy shock (PCS), which is a possible complication of surgical treatment of valvular heart disease. The use of mechanical circulatory support (MCS) in the early phase of PCS development can improve the physiological condition of a patient in cardiogenic shock. It stabilizes hemodynamics and tissue metabolism, provides the necessary time for myocardial regeneration and thus reduces the risk of developing postoperative multiple organ dysfunction syndrome (MODS) and increases the patient's chances of survival [1–4]. Knowledge of the predictors of postoperative PCS in patients undergoing heart valve surgery is extremely important because it allows for earlier selection of patients at high risk of this complication, selection of the optimal date of qualification for surgical treatment, special supervision of high-risk patients during surgery and in the early postoperative period, as well as implementation of immediate, necessary treatment if the first symptoms of developing postoperative PCS appear. However, there is little information in the available literature about the pathomechanism and predictive factors of postoperative PCS [5, 6]. In recent decades, two very important biomarkers have emerged in various areas of cardiology, particularly in terms of diagnosis, treatment, and prognosis, i.e., high-sensitivity troponin T (hs-TnT) and N-terminal pro B-type natriuretic peptide (NT-proBNP), whose use is now part of daily practice of every cardiologist [7].

Due to the dramatic risks to patients with PCS, limited treatment options, and high postoperative mortality, we aimed to evaluate selected perioperative parameters in predicting postoperative PCS requiring MCS use in the early postoperative period in patients undergoing heart valve surgery.

METHODS

This prospective study was conducted at the National Institute of Cardiology in Warsaw, Poland in the years 2014–2021 on a group of patients with hemodynamically severe, symptomatic valvular heart disease who underwent heart valve surgery. The exclusion criteria from participation in the study were: patients under 18 years of age, lack of consent to participate in the study, porcelain aorta, significant atherosclerotic changes in the carotid arteries identified by ultrasound, autoimmune diseases, chronic inflammatory bowel, and active neoplastic diseases. A blood sample to determine NT-proBNP was taken from each patient one day before surgery and measured using Elecsys 2010 (Roche) electrochemiluminescent immunoassays. The day before (hs-TnT), immediately after the patient arrived at the intensive care unit after surgery (hs-TnT I), and in the morning on the first day after surgery (hs-TnT II); a blood sample for troponin T was collected from each patient. The plasma troponin T was determined using troponin T hs-STAT (Roche). Cardiac surgery was performed through a median sternotomy under general anesthesia. Patients received an initial dose of 15–20 ml/kg of cold-blooded cardioplegia during surgery, followed by booster doses of 5–10 ml/kg every 20 minutes. The primary endpoint of in-hospital follow-up was postoperative cardiogenic shock requiring MCS in the form of an intra-aortic balloon pump (IABP) and/or extracorporeal membrane oxygenation (ECMO). The follow-up period of patients included in the study lasted until discharge from the hospital or until the day of death during the current hospitalization. The

Table 1. Baseline characteristics of the study population (n = 608)

Preoperative characteristics of patients	Values All patients	Values Patients with MCS (n = 21)	Values Patients without MCS (n = 587)	*P*-value
Age, years*	65 (57–71)	63 (52–71)	65 (57–71)	0.58
Male: men, n (%)	350 (57)	9 (42)	341 (58)	0.17
Body mass index, kg/m^2*	27 (24.5–31)	26.7 (21–29)	27 (24.5–31)	0.53
LV ejection fraction, %*	60 (51–65)	60 (45–65)	60 (51–65)	0.8
EuroSCORE II, %*	3.4 (1.4–4)	3.6 (1.5–5.9)	2.5 (1.4–4)	0.03
Atrial fibrillation, n (%)	242 (39)	12 (57)	212 (39)	0.09
Chronic kidney disease (GFR <60 ml/min/1.73 m^2), n (%)	186 (30)	25 (50)	161 (28)	0.15
Coronary artery disease, n (%)	92 (15)	13 (26)	79 (14)	0.46
Previous myocardial infarction, n (%)	46 (7)	5 (10)	41 (7)	0.5
Stroke history, n (%)	33 (5)	5 (10)	28(5)	0.89
Hypertension, n (%)	372 (61)	27 (54)	344 (61)	0.25
Diabetes mellitus, n (%)	96 (15)	11 (22)	85 (15)	0.67
Hemoglobin, g/dl*	13.7 (12.7–14.7)	13 (10.7–13.6)	13.7 (12.7–14.7)	0.07
GFR, ml/min/1.73 m^2	67 (55–82)	60 (53–72)	67 (55–82)	0.06
hs-TnT, ng/l*	12.4 (8–32)	24.3 (16–63)	12.2 (8–30)	0.008
NT-proBNP, pg/ml	928 (317–2104)	3129 (842–4680)	848 (294–1938)	<0.001
CRP, mg/dl	0.2 (0.1–0.6)	0.5 (0.2–0.7)	0.2 (0.1–0.5)	0.02
Aortic cross-clamp time, min*	104 (62–95)	133 (90–150)	96 (62–92	0.22
Cardiopulmonary bypass time, min*	137 (76–140)	204 (108–248)	114 (74–120)	0.01
Postoperative characteristics of patients				
Postoperative major blending, n (%)	50 (8)	7 (33)	43 (8)	0.007
hs-TnT I, ng/l	624 (363–1124)	1649 (845–3100)	599 (361–1052)	<0.001
hs-TnT II, ng/l	683 (393–1501)	2278 (999–3832)	665 (387–1374)	<0.001
Hospital stay after surgery, n (%)	13 (8–18)	21 (6–30)	13 (8–16)	0.01
Main procedures				
AVR, n (%)	307 (50)	4 (19)	303 (51)	0.11
AVP, n (%)	10 (2)	1 (5)	9 (15)	0.25
AVR + MVR, n (%)	56 (10)	2 (10)	54 (10)	0.91
AVR + MVP, n (%)	11 (2)	1 (5)	10 (17)	0.3
AVP + MVP, n (%)	3 (0.5)	0 (0)	3 (1)	0.74
MVP, n (%)	109 (17.5)	5 (23)	104 (17)	0.47
MVR, n (%)	107 (17.5)	6 (28)	101 (18)	0.17
TVR, n (%)	5 (1)	1 (5)	4 (1)	0.11
Concomitant procedure				
CABG, n (%)	92 (15)	2 (10)	80 (14)	0.46

The values are presented as medians (Q1–Q3) and number (%)

Abbreviations: AVR, aortic valve replacement; AVP, aortic valve plasty; CABG, coronary artery bypass graft; CRP, C-reactive protein; GFR, glomerular filtration rate; hs-TnT, high sensitivity troponin T; hs-TnT I, high-sensitivity troponin T measured immediately after surgery; hs-TnT II, high-sensitivity troponin T measured one day after surgery; ICU, intensive care unit; LV, left ventricle; MCS, mechanical circulatory support; MVR, mitral valve replacement; MVP, mitral valve plasty; NT-proBNP, N-terminal pro B-type natriuretic peptide; TVR, tricuspid valve replacement

study protocol was approved by the Bioethics Committee of the National Institute of Cardiology in Warsaw, Poland — study number 2.32/VI/18.

Statistical analysis

Data were presented as median (Q1–Q3) and frequency (%). Intergroup cooperation was performed using the Mann-Whitney U test for quantitative variables and the chi-square test for qualitative variables. Univariable logistic regression analysis was conducted to determine the predictors of primary endpoint. Variables that were statistically significant in the mentioned univariable analysis were taken into account by multivariable logistic regression analysis. The predictive value of NT-proBNP and hs-TnT II for the occurrence of the primary endpoint was estimated using the area under the receiver operating characteristic curve. All statistical calculations were performed using STATISTICA 12 software (StatSoft Polska Sp. z o.o., Kraków, Poland). The significance level was set as $P < 0.05$.

RESULTS AND DISCUSSION

The study evaluated 608 patients undergoing heart valve surgery. The characteristics of the studied patients are presented in Table 1. Postoperative cardiogenic shock requiring MCS occurred in 21 patients (ECMO was used in 15 patients and IABP in 6 patients). MCS was used in 11 patients on postoperative day (day 0), 6 patients on the first postoperative day (day 1), 2 patients on postoperative day 2, and in further 2 patients on postoperative day 3. In univariable analysis, preoperative NT-proBNP level (OR,

1.994; 95% CI, 1.400–2.839; P <0.001), preoperative hemoglobin level (OR, 0.761; 95% CI, 0.590–0.982; P = 0.03), hs-TnT I (OR, 3.855; 95% CI, 2.345–6.338; P <0.001), and hs-TnT II (OR, 3.248; 95% CI, 2.156–4.893; P <0.001) remained predictors of the primary endpoint. In multivariable analysis, preoperative NT-proBNP level (OR, 1.991; 95% CI, 1.333–2.971; P <0.001) and hs-TnT II (OR, 3.279; 95% CI, 2.072–5.191; P <0.001) remained independent predictors of the primary endpoint. The area under the receiver operating characteristic curve for the primary endpoint for NT-proBNP was 0.726 (95% CI, 0.610–0.843) and for hs-TnT II was 0.839 (95% CI, 0.761–0.916). In the follow-up of patients with the primary endpoint, death occurred in 11 patients as a result of progressive MODS (8 with ECMO and 3 patients with IABP). The median hospital stay for patients with postoperative cardiogenic shock who died was 12 (3–30) days. The total mortality in the 30-day follow-up was 3.6%. The co-occurrence of coronary heart disease did not increase the incidence of postoperative shock.

Hemodynamic instability, defined as the need for a prolonged supply of catecholamines from the time of disconnecting the patient from extracorporeal circulation is a common complication observed in postoperative intensive care units in patients treated with cardiac surgery, and in our study, it occurred in as many as 210 patients, which constitutes as much as 33% of the entire study group. Conservative treatment in most patients in this group stabilizes the circulatory system, and the patient's clinical condition allows for a gradual reduction of catecholamines until their complete discontinuation. However, there is a group of patients with postoperative hemodynamic instability who, despite intensive conservative therapy, develop symptoms of cardiogenic shock, an extremely serious complication with a high risk of death. In this group of patients, early implementation of MCS improves perfusion and oxygenation of peripheral tissues and relieves the load on the heart muscle, promoting its regeneration and thus increasing the patient's chance of survival [8, 9]. In our study, PCS occurred in 21 patients, which constituted 3.4% of all patients included in the study, and despite the implementation of MCS in the form of ECMO or IABP, as many as 11 patients died due to the development of MODS. The results of this study showed that the predictors of postoperative cardiogenic shock were preoperative hemoglobin and NT-proBNP levels and troponin T concentration measured immediately and on the first day after the end of surgery. In addition, patients with an increased EuroSCORE II value, higher preoperative C-reactive protein and hs-TnT values as well as prolonged extracorporeal circulation time and major postoperative bleeding were at higher risk of developing the primary endpoint.

In patients with severe valvular heart disease, pressure and/or volume overload of the left ventricular muscle occurs, which in turn causes increased secretion of NT-proBNP by cardiomyocytes [10]. Significantly elevated values of NT-proBNP in the blood serum of patients with hemodynamically significant valvular heart disease may indicate decompensation of the overloaded left ventricle. The results of our study may, therefore, indicate that the decompensated myocardium is particularly sensitive to non-physiological conditions prevailing in the perioperative period. They include the use of extracorporeal circulation or blood loss, which may result in the development of postoperative hemodynamic instability and, in some patients, even PCS. On the other hand, this study indicates that the early postoperative measurements of troponin T, a protein that is a marker describing the degree of myocardial damage, also allow us to identify a group of patients at risk of developing PCS. Taking into account the fact that PCS is a dynamic complication that develops in most cases during the first postoperative day, the results of our study indicate the need for careful monitoring of patients from the moment of completion of cardiac surgery. The group at particular risk of developing PCS are primarily hemodynamically unstable patients, with elevated preoperative NT-proBNP values as well as increased hs-TnT I and hs-TnT II values.

Article information

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REFERENCES

1. McDonagh TA, Metra M, Adamo M. 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: Developed by the Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC) With the special contribution of the Heart Failure Association (HFA) of the ESC. Eur J Heart Fail. 2021; 42(36): 3599–3726, doi: 10.1093/eurheartj/ehab368.
2. Chioncel O, Parissis J, Mebazaa A, et al. Epidemiology, pathophysiology and contemporary management of cardiogenic shock — a position statement from the Heart Failure Association of the European Society of Cardiology. Eur J Heart Fail. 2020; 22(8): 1315–1341, doi: 10.1002/ejhf.1922, indexed in Pubmed: 32469155.
3. Thiele H, Ohman EM, de Waha-Thiele S, et al. Management of cardiogenic shock complicating myocardial infarction: an update 2019. Eur Heart J. 2019; 40(32): 2671–2683, doi: 10.1093/eurheartj/ehz363, indexed in Pubmed: 31274157.
4. Mebazaa A, Combes A, van Diepen S, et al. Management of cardiogenic shock complicating myocardial infarction. Intensive Care Med. 2018; 44(6): 760–773, doi: 10.1007/s00134-018-5214-9, indexed in Pubmed: 29767322.
5. Zymliński R, Biegus J, Sokolski M, et al. Increased blood lactate is prevalent and identifies poor prognosis in patients with acute heart failure without overt peripheral hypoperfusion. Eur J Heart Fail. 2018; 20(6): 1011–1018, doi: 10.1002/ejhf.1156, indexed in Pubmed: 29431284.
6. Duchnowski P. N-Terminal of the Prohormone Brain Natriuretic Peptide Predicts Postoperative Cardiogenic Shock Requiring Extracorporeal Membrane Oxygenation. J Clin Med. 2022; 11(19), doi: 10.3390/jcm11195493, indexed in Pubmed: 36233362.
7. Gardner RS, Ozalp F, Murday AJ, et al. N-terminal pro-brain natriuretic peptide. A new gold standard in predicting mortality in patients with

advanced heart failure. Eur Heart J. 2003; 24(19): 1735–1743, doi: 10.1016/j.ehj.2003.07.005, indexed in Pubmed: 14522568.
8. Desai AS, Jarcho JA. Levosimendan for the Low Cardiac Output Syndrome after Cardiac Surgery. N Engl J Med. 2017; 376(21): 2076–2078, doi: 10.1056/NEJMe1705455, indexed in Pubmed: 28538112.
9. Bowles C, Hiesinger W. Postcardiotomy shock extracorporeal membrane oxygenation: Peripheral or central? JTCVS Open. 2021; 8: 66–69, doi: 10.1016/j.xjon.2021.10.020, indexed in Pubmed: 36004095.
10. Weidemann F, Herrmann S, Störk S, et al. Impact of myocardial fibrosis in patients with symptomatic severe aortic stenosis. Circulation. 2009; 120(7): 577–584, doi: 10.1161/CIRCULATIONAHA.108.847772, indexed in Pubmed: 19652094.