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ORIGINAL ARTICLE

The usefulness of selected biomarkers in aortic regurgitation

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Abstract

Background: *The aim of the study was to investigate the prognostic value of selected biomarkers in patients with aortic regurgitation undergoing valve surgery.*

Methods: *A prospective study was conducted on a group of consecutive patients with hemodynamically significant aortic regurgitation that underwent elective aortic valve surgery. The primary endpoint was 30-day mortality and any major adverse event within 30 days.*

Results: *The study group included 205 consecutive patients who underwent replacement or repair of the aortic valve. The primary endpoint occurred in 72 patients. At multivariate analysis red cell distribution width (RDW; $p = 0.03$) and high-sensitivity troponin T (hs-TnT; $p = 0.02$) remained independent predictors of the major complications including death.*

Conclusions: *Elevated preoperative RDW and hs-TnT were associated with a poorer outcome following aortic valve surgery.* (Cardiol J 2019; 26, 5: 477–482)

Key words: aortic regurgitation, biomarkers, EuroSCORE II, risk stratification, high-sensitivity troponin T

Introduction

Troponin T (TnT) is a protein forming part of the contractile apparatus of striated muscle. Moreover TnT is a recognized biomarker of myocardial injury [1]. In the available literature, several studies have reported that elevated high-sensitivity TnT (hs-TnT) is associated with poor outcomes in patients with stable coronary heart disease, acute myocardial infarction (MI), heart failure (HF), dilated cardiomyopathy, atrial fibrillation or significant aortic stenosis [2–9].

Another biomarker, red cell distribution width (RDW), is a measure of the differentiation of the size of red blood cells (anisocytosis). Until now, the RDW parameter has been used mainly as a hematological auxiliary marker indicating an increased destruction of erythrocytes or erythrocytes production dysfunction related to a deficiency of folic acid, vitamin B12, iron or ongoing inflammation. Recently, numerous publications have demonstrated the usefulness of RDW also as a prognostic factor for various cardiovascular diseases, such as coronary artery disease, chronic HF, perioperative stroke, idiopathic pulmonary hypertension and severe aortic stenosis [10–14]. The usefulness of hs-TnT and RDW in patients with severe symptomatic aortic regurgitation undergoing valve surgery in a 30-day follow-up are not established. As there is a need to complement the tools to determine the risk in patients with aortic regurgitation eligible for valve surgery it was sought to observe the usefulness of these biomarkers in this group of patients.

Methods

This was a prospective study of consecutive patients with hemodynamically significant aortic regurgitation (vena contracta > 6 mm, effective regurgitant orifice area > 30 mm^2 or pressure

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half-time < 200 ms) and without significant atherosclerotic changes in the coronary arteries that were qualified to cardiac surgery and subsequently underwent elective replacement or repair of the aortic valve. The exclusion criteria were: a lack of consent to participate in the study, significant atherosclerotic changes in the coronary arteries identified by angiography, patients under 18 years of age, autoimmune diseases, chronic inflammatory bowel, active neoplastic diseases and active infective endocarditis. Patients who were eligible for surgery but subsequently refused the procedure, or did not undergo surgery for logistic or other reasons were not included in the study. The following data were collected: age, gender, body mass index (BMI), comorbidities (coronary artery disease, MI, hypertension, chronic obstructive pulmonary disease, stroke, diabetes), the results of echocardiography findings and the assessment of the coronary arteries. The risk of surgery using EuroSCORE II was calculated for each patient. The day before surgery a blood sample for biomarkers was collected from each patient. Complete blood count was performed with K2-EDTA samples, using a Cobas 6000 electronic counter (Roche, Mannheim, Germany). The plasma levels of cardiac TnT (cTnT) concentrations were measured with the Troponin T hs-STAT (Roche). All procedures were performed through a midline sternotomy incision under general anaesthesia 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 was death from all causes as well as: hemodynamic instability (defined as the need for a supply of catecholamines more than 48 h after completing the cardiopulmonary bypass surgery or the need to resupply), perioperative MI (defined as the development of new Q waves in two or more leads on an electrocardiogram, or alterations of myocardial contractility that did not previously exist in echocardiography), stroke (evidence of a new neurological deficit or a transient ischemic attack, confirmed by an imaging test), perioperative renal failure (requiring renal replacement therapy), prolonged mechanical ventilation (either mechanical ventilatory support lasting longer than 24 h, or the need for reintubation) and the occurrence of multiple-organ failure (the dysfunction of two or more organs — based on laboratory parameters and/or the need to use organ replacement therapy). In all patients the follow up was conducted through direct observation during hospitalization, telephone interviews, or clinic visits for 30 days after surgery. The study was conducted at the Institute of Cardiology, Warsaw, Poland. The protocol was approved by The Institutional Ethics Committee.

Statistical analysis

A statistical analysis was performed using SAS version 9.2. Data are presented as the mean ± standard deviation and the frequency (%). Intergroup comparisons were made using the Mann-Whitney U test, the Pearson's χ^2 test or Student t-test. Logistic regression was used to assess relationships between variables. The following preoperative covariates: age, atrial fibrillation, BMI, chronic kidney disease, chronic obstructive airway disease, coronary artery disease, creatinine, high-sensitivity C-reactive protein (hs-CRP), hs-TnT, hematocrit, hemoglobin, hypertension, left ventricular end-diastolic diameter (LVEDD), left ventricular end-systolic diameter (LVESD), left ventricular ejection fraction (LVEF), mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, mean corpuscular volume, New York Heart Association (NYHA) classes, N-terminal pro-hormone of B-type natriuretic peptide (NT-proBNP), peripheral atherosclerosis, platelets, pulmonary blood pressure, red blood cell count, RDW, stroke history, tricuspid annulus plane systolic excursion and white blood cell count were investigated for association with the endpoints in univariate analysis. Significant determinants ($p < 0.05$) identified from univariate analysis were subsequently entered into multivariate models. Receiver operating characteristic (ROC) curves were plotted for the EuroSCORE II alone and for the model combined of EuroSCORE II, hs-TnT and RDW for 30-day survival following aortic regurgitation surgery. The additional predictive value of RDW and hs-TnT was assessed by a comparison of the areas under the ROC of the respective curves.

Results

The study included 205 patients who underwent aortic valve surgery with or without concomitant procedures. In 97 patients a mechanical aortic valve prosthesis was implanted, and in 77 a biological valve. The mean age in the study group was 58.7 ± 7.7. Seven (3.4%) of the patients in the study had a previous MI, but currently none of the patients had significant atherosclerotic changes in the coronary arteries. Sixteen (8%) patients had significantly impaired left ventricular systolic function (LVEF ≤ 35%). The mean plasma preoperative hs-TnT level was

20.7 ± 13.9 ng/L. Patients in NYHA class II, III and IV had a significantly higher levels of hs-TnT compared to patients in NYHA class I. Baseline characteristics of the patients are presented in Table 1.

Six patients died during the follow-up period as a result of gradually increasing multi-organ failure (2 patients with LVEF ≤ 35%, 3 patients with LVEF 36–50%, 1 patient with LVEF > 50%). The actual mortality was 2.9% vs. the mortality 3.5% predicted by the EuroSCORE II model. The primary end-point occurred in 72 patients: perioperative renal failure in 11 patients, prolonged mechanical ventilation in 21 patients, stroke in 7 patients and catecholamine infusion for over 48 h in 57 patients. Multi-organ failure was observed in 17 patients. Myocardial infarction occurred in 6 patients. In the postoperative period, 4 patients developed pneumonia. In addition, 6 patients experienced sternal wound infections. Statistically significant predictors of major complications including death at univariate analysis are presented in Table 2. At multivariate analysis RDW (odds ratio [OR] 1.526; 95% confidence interval [CI] 1.011–2.331; p = 0.03) and hs-TnT (OR 1.384; 95% CI 1.082–1.686; p = 0.02) remained independent predictors of the primary endpoint. A positive correlation was found between the level of hs-TnT and LVEF (r = –0.37; p = 0.001), moreover between RDW and CRP (r = 0.42; p = 0.0007). Patients with concomitant chronic kidney disease hadn't significantly higher preoperative hs-TnT levels (p = 0.36) compared with patients without chronic kidney disease. The optimal cut-of points for primary end-point were calculated at the hs-TnT level of 27.5 ng/L and the RDW 14.2%. RDW, hs-TnT and combined with EuroSCORE II was a better predictor of 30-day major complications including death in patients with aortic regurgitation undergoing valve surgery (area under receiver operator characteristic curve [AUROC] = 0.802; 95% CI 0.716–0.886) compared with EuroSCORE II alone (AUROC = 0.699; 95% CI 0.601–0.797).

Figure 1 shows the areas under receiver operator characteristic curves of EuroSCORE II and the combined model RDW + hs-TnT + EuroSCORE II for 30-day major complications.

Discussion

The present paper demonstrated the prognostic significance of hs-TnT and RDW in predicting major complications including death in patients with severe symptomatic aortic regurgitation

Table 1. Baseline characteristics of the study population (n = 205).

Parameters	Values
Preoperative characteristics of patients	
Age [years]	58.7 ± 7.7
Male: men	154 (75%)
Previous myocardial infarction	7 (3.4%)
Stroke in history	5 (2.4%)
Atrial fibrillation	62 (30%)
Peripheral atherosclerosis	4 (1.9%)
Diabetes mellitus	22 (11%)
Hypertension	115 (56%)
Current smoker	37 (18%)
Hyperlipidemia	56 (27%)
Body mass index [kg/m^2]	26.8 ± 3.9
Chronic obstructive airways disease	4 (1.9%)
Chronic kidney disease (GFR < 60 mL/min/1.73 m^2)	48 (23.4%)
LVEF > 50%	149 (73%)
LVEF 50–36%	40 (19%)
LVEF ≤ 35%	16 (8%)
LVEDD [mm]	65 ± 13
LVESD [mm]	46 ± 12
Pulmonary BP [mmHg]	39.1 ± 15.6
NYHA I class	6 (3%)
NYHA II class	112 (55%)
NYHA III class	82 (40%)
NYHA IV class	5 (2%)
EuroSCORE II [%]	3.5 ± 3.1
Hemoglobin [g/dL]	14.1 ± 1.6
RDW [%]	13.8 ± 0.4
Plateletes [1000/µL]	193 ± 51
Hs-TnT [ng/L]	20.7 ± 13.9
Hs-TnT I [ng/L]	7.3 ± 3
Hs-TnT II [ng/L]	18.4 ± 9
Hs-TnT III [ng/L]	22.2 ± 11
Hs-TnT IV [ng/L]	26.1 ± 12
NT-proBNP [pg/mL]	1922 ± 1017
GFR [mL/min/1.73 m^2]	69.7 ± 17.7
Aortic regurgitation severe	205 (100%)
Aortic stenosis mild	26 (13%)
Aortic stenosis moderate	20 (10%)
Aortic stenosis severe	0 (0%)
Postoperative characteristics of patients	
Aortic cross-clamp time [min]	93 ± 36
Cardiopulmonary bypass time [min]	122 ± 53
Time at the ICU [days]	6.4 ± 4.5
Time in the hospital [days]	14.7 ± 5.7

→

Table 1 (cont.). Baseline characteristics of the study population.

Parameters	Values
Drainage after 12 h [mL]	552 ± 240
Drainage after 24 h [mL]	780 ± 365
Number of RBC units transfused	4.5 ± 3
RDW I	13.8 ± 0.4
RDW II	14.0 ± 0.5
Main procedures	
AVR	153 (74.6%)
AVP	28 (13.6%)
AVR + supracoronary ascending aortic replacement	11 (5.4%)
Bentall procedure	10 (4.9%)
David procedure	3 (1.5%)

Values are represented by number (percentage) or mean ± and a measure of the variation of the internal standard deviation. AVR — aortic valve replacement; AVP — aortic valve plasty; BP — blood pressure; GFR — glomerular filtration rate; Hs-TnT — high-sensitivity troponin T; Hs-TnT I, II, III, IV — high-sensitivity troponin T in NYHA class I, II, III, IV, respectively; ICU — intensive care unit; LVEF — left ventricular ejection fraction; LVEDD — left ventricular end-diastolic diameter; LVESD — left ventricular end-systolic diameter; NT-proBNP — N-terminal pro-hormone of B-type natriuretic peptide, NYHA — New York Heart Association; RDW — red cell distribution width (preoperative); RDW I — red cell distribution width measured immediately after surgery; RDW II — red cell distribution width measured one day after surgery

Table 2. Univariate analysis of predictive factors for the occurrence of the primary endpoint.

Variable	Odds ratio	95% CI	P
Age [years]	1.028	1.006–1.051	0.01
NT-proBNP [pg/mL]	1.023	1.011–1.034	0.006
Hs-TnT [ng/L]	1.095	1.033–1.134	0.004
LVEF [%]	0.959	0.935–0.983	0.001
LVEDD [mm]	1.264	1.124–1.421	0.008
Hemoglobin [g/dL]	0.663	0.543–0.811	0.006
RDW [%]	1.699	1.281–2.253	0.002

CI — confidence interval; Hs-TnT — high sensitivity troponin T; LVEDD — left ventricular end-diastolic diameter; LVEF — left ventricular ejection fraction; NT-proBNP — N-terminal pro-hormone of B-type natriuretic peptide; RDW — red cell distribution width

undergoing aortic valve surgery in postoperative 30-day follow-up.

Troponin T is a polypeptide that is part of the striated contractile muscle apparatus. The TnT function in all types of striated muscles is the same. As one of the three proteins included in the troponin complex, it performs key functions in the process of muscle contraction. 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 muscle troponins. Thanks to this, after obtaining specific monoclonal antibodies, it became possible to use them in the diagnosis of ischemic heart disease. Currently, it is believed that cTnT is the best laboratory parameter in the early diagnosis of acute MI. Considering the fact that cytoplasm of cardiomyocytes contains a small amount of free troponins TnT and TnI, even small damage to the cell membrane (e.g. in the initial phase of myocardial ischemia) causes their release and the ability to be detected in the blood sample under study [15, 16]. High sensitivity tests, which have been available for several years, are able to detect very low levels of troponin T present in the blood with high reliability [17]. Significant heart valve defects are often the result of pressure or volume overload of the heart cavities. Hypertrophy and remodeling of the myocardium is a response to increasing overload. This mechanism initially restores and maintains the tension of the left ventricular wall. However, long-lasting additional burden on the myocardium causes progressive degenerative changes of the myocardium, which are accompanied by slow processes of necrosis and fibrosis, which may be a reason for the presence of TnT in the blood [18–20].

The predictive power of the preoperative TnT for death in 30-days follow-up in a group of 224 patients with surgically treated severe aortic stenosis was previously demonstrated [9]. Moreover, in a small group of 60 patients with severe aortic valve stenosis undergoing aortic surgery, preoperative TnT was an important predictor of serious post-operative complications in long-term follow-up [21]. Also, in a study of a group of 24 patients undergoing mitral valve replacement surgery, elevated values of postoperative TnT significantly correlated with the length of postoperative hospital stay [22]. On the other hand, Piekarska et al. [23] didn't show a significant correlation between postoperative TnT level and the results of surgical treatment of patients with severe aortic stenosis. It has also not been shown that the preoperative troponin improved the result of the Society of Thoracic Surgeons score in patients undergoing aortic valve replacement [24].

Red cell distribution width is a simple, cheap and widely available parameter, determined in each patient during the standard blood test. So far, the predictive capacity of the RDW in the area of patients with valvular heart disease has been described in a few publications [10–14]. The predictive value of the RDW for serious complications and death in patients with severe aortic stenosis has previously been described, and the occurrence

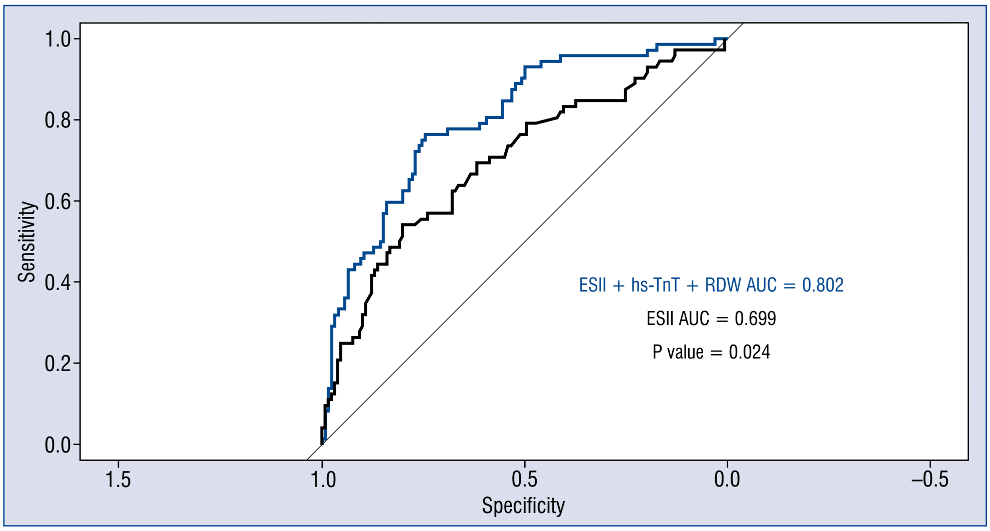

Figure 1. Areas under receiver operator characteristic curves of EuroSCORE II (ESII) and combined model EuroSCORE II + high sensitivity troponin T (hs-TnT) + red cell distribution width (RDW) for 30-day major complications including death following aortic valve surgery; AUC — area under curve.

of perioperative stroke of the central nervous system in the group of patients undergoing heart valve surgery [12, 14]. In turn, two studies on groups of 250 and 175 patients with severe aortic valve stenosis who underwent transcatheter aortic valve implantation showed a significant correlation between elevated RDW values and the occurrence of an increased risk of death and serious complications in long-term observation [25, 26]. So far, the relationship between value of RDW and worse results in numerous clinical observations hasn't been fully understood and explained. In the literature the hypotheses available combine higher RDW values with the occurrence of inflammation and treat them as a marker of oxidative stress. This hypothesis can be confirmed by a significant correlation between the CRP value, determined by the high sensitivity method, with the RDW parameter ($r = 0.42$; $p = 0.0007$) as demonstrated in the presented study.

The results of the presented study indicate the usefulness of two laboratory parameters commonly used in clinical practice in a group of patients with significant aortic valve regurgitation undergoing valve surgery. Hs-TnT, which indicates damage to the myocardium and RDW, which according to some authors indicate the physiological reserve of humans, may be important in making therapeutic decisions in patients with aortic regurgitation. It is worth noting that multi-organ failure which occurred in 17 patients in the early post-operative period was the cause of all 6 deaths.

Conclusions

It was a single-center study with a limited number of patients. Enlargement of the group of participants may allow confirmation of the results obtained and to develop a risk calculator using selected biomarkers. Further studies are needed regarding the suitability of other biomarkers as predictors of complications in patients with aortic regurgitation undergoing cardiac surgery. The results of the presented studies may be helpful in the perioperative risk stratification in patients with aortic regurgitation. It is worth noting that hs-TnT levels in combination with RDW and EuroSCORE II were better predictors of postoperative major complications including death compared to EuroSCORE II alone.

Conflict of interest: None declared

References

1. Grąbczewska Z, Dębski R, Góralczyk K, et al. Associations between selected angiographic parameters and the number of CD34+ cells and plasma levels of vascular endothelial growth factor and angiogenin in patients with ST-segment elevation myocardial infarction. Pol Arch Med Wewn. 2015; 125(3): 132–140, indexed in Pubmed: 25643927.
2. Reichlin T, Schindler C, Drexler B, et al. One-hour rule-out and rule-in of acute myocardial infarction using high-sensitivity cardiac troponin T. Arch Intern Med. 2012; 172(16): 1211–1218, doi: 10.1001/archinternmed.2012.3698, indexed in Pubmed: 22892889.

3. Koide K, Yoshikawa T, Nagatomo Y, et al. Elevated troponin T on discharge predicts poor outcome of decompensated heart failure. Heart Vessels. 2010; 25(3): 217–222, doi: 10.1007/s00380-009-1194-6, indexed in Pubmed: 20512449.
4. Gualandro DM, Puelacher C, Mueller C. High-sensitivity cardiac troponin in acute conditions. Curr Opin Crit Care. 2014; 20(5): 472–477, doi: 10.1097/MCC.0000000000000132, indexed in Pubmed: 25159476.
5. Kawahara C, Tsutamoto T, Nishiyama K, et al. Prognostic role of high-sensitivity cardiac troponin T in patients with nonischemic dilated cardiomyopathy. Circ J. 2011; 75(3): 656–661, indexed in Pubmed: 21178288.
6. Parissis JT, Papadakis J, Kadoglou NPE, et al. Prognostic value of high sensitivity troponin T in patients with acutely decompensated heart failure and non-detectable conventional troponin T levels. Int J Cardiol. 2013; 168(4): 3609–3612, doi: 10.1016/j.ijcard.2013.05.056, indexed in Pubmed: 23711451.
7. Rybicka J, Dobrowolski P, Lipczyńska M, et al. High sensitivity troponin T in adult congenital heart disease. Int J Cardiol. 2015; 195: 7–14, doi: 10.1016/j.ijcard.2015.05.077, indexed in Pubmed: 26011405.
8. Petäjä L, Røsjø H, Mildh L, et al. Predictive value of high-sensitivity troponin T in addition to EuroSCORE II in cardiac surgery. Interact Cardiovasc Thorac Surg. 2016; 23(1): 133–141, doi: 10.1093/icvts/ivw060, indexed in Pubmed: 26984965.
9. Duchnowski P, Hryniewiecki T, Zatorska K, et al. High-sensitivity troponin T as a prognostic marker in patients undergoing aortic valve replacement. Pol Arch Intern Med. 2017; 127(9): 628–630, indexed in Pubmed: 28984283.
10. Tonelli M, Sacks F, Arnold M, et al. Relation between red blood cell distribution width and cardiovascular event rate in people with coronary disease. Circulation. 2008; 117: 163–168.
11. Hampole CV, Mehrotra AK, Thenappan T, et al. Usefulness of red cell distribution width as a prognostic marker in pulmonary hypertension. Am J Cardiol. 2009; 6: 868–872.
12. Duchnowski P, Hryniewiecki T, Kusmierczyk M, et al. Red cell distribution width is a prognostic marker of perioperative stroke in patients undergoing cardiac valve surgery. Interact Cardiovasc Thorac Surg. 2017; 25(6): 925–929, doi: 10.1093/icvts/ivx216, indexed in Pubmed: 29049563.
13. Allen LA, Felker GM, Mehra MR, et al. Validation and potential mechanisms of red cell distribution width as a prognostic marker in heart failure. J Card Fail. 2010; 3: 230–238.
14. Duchnowski P, Szymański P, Orłowska-Baranowska E, et al. Raised red cell distribution width as a prognostic marker in aortic valve replacement surgery. Kardiol Pol. 2016; 74: 547–552.
15. Reichlin T, Schindler C, Drexler B, et al. One-hour rule-out and rule-in of acute myocardial infarction using high-sensitivity cardiac troponin T. Arch Intern Med. 2012; 172(16): 1211–1218, doi: 10.1001/archinternmed.2012.3698, indexed in Pubmed: 22892889.
16. European patent 394816 and US patent 6376206 by Roche Diagnostic GmbH. Specific antibodies to Troponin T, their production and use in a reagent for the determination of myocardial necrosis.
17. Apple FS, Ler R, Murakami MM. Determination of 19 cardiac troponin I and T assay 99th percentile values from a common presumably healthy population. Clin Chem. 2012; 58(11): 1574––1581, doi: 10.1373/clinchem.2012.192716, indexed in Pubmed: 22983113.
18. Lindman BR, Breyley JG, Schilling JD, et al. Prognostic utility of novel biomarkers of cardiovascular stress in patients with aortic stenosis undergoing valve replacement. Heart. 2015; 101(17): 1382–1388, doi: 10.1136/heartjnl-2015-307742, indexed in Pubmed: 26037104.
19. Hein S, Arnon E, Kostin S, et al. Progression from compensated hypertrophy to failure in the pressure-overloaded human heart: structural deterioration and compensatory mechanisms. Circulation. 2003; 107(7): 984–991, indexed in Pubmed: 12600911.
20. 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.
21. Saito T, Hojo Y, Hirose M, et al. High-sensitivity troponin T is a prognostic marker for patients with aortic stenosis after valve replacement surgery. J Cardiol. 2013; 61(5): 342–347, doi: 10.1016/j.jjcc.2013.01.005, indexed in Pubmed: 23473763.
22. Oshima K, Kunimoto F, Takahashi T, et al. Postoperative cardiac troponin I (cTnI) level and its prognostic value for patients undergoing mitral valve surgery. Int Heart J. 2010; 51(3): 166–169, indexed in Pubmed: 20558905.
23. Piekarska ML, Szurlej B, Latusek T, et al. Postoperative serum troponin T concentration in patients undergoing aortic valve replacement does not predict early postoperative outcome. Kardiol Pol. 2013; 71(12): 1237–1244, doi: 10.5603/KP.a2013.0147, indexed in Pubmed: 23799619.
24. Lindman BR, Breyley JG, Schilling JD, et al. Prognostic utility of novel biomarkers of cardiovascular stress in patients with aortic stenosis undergoing valve replacement. Heart. 2015; 101(17): 1382–1388, doi: 10.1136/heartjnl-2015-307742, indexed in Pubmed: 26037104.
25. Magri CJ, Chieffo A, Latib A, et al. Red blood cell distribution width predicts one-year mortality following transcatheter aortic valve implantation. Int J Cardiol. 2014; 172(2): 456–457, doi: 10.1016/j.ijcard.2013.12.216, indexed in Pubmed: 24529824.
26. Aung N, Dworakowski R, Byrne J, et al. Progressive rise in red cell distribution width is associated with poor outcome after transcatheter aortic valve implantation. Heart. 2013; 99: 1261–1266.