ORIGINAL ARTICLE

Single sST2 protein measurement predicts adverse outcomes at 1-year follow-up in patients with chronic heart failure

Sebastian Sobczak[1], Karolina Wojtczak-Soska[1], Tomasz Ciurus[1], Agata Sakowicz[2], Tadeusz Pietrucha[2], Małgorzata Lelonek[1]

1 Department of Cardiology, Medical University of Lodz, Łódź, Poland
2 Department of Medical Biotechnology, Medical University of Lodz, Łódź, Poland

KEY WORDS

chronic heart failure, prognosis, sST2, systolic dysfunction

ABSTRACT

INTRODUCTION sST2 protein is a new biomarker. Its prognostic value in chronic heart failure (CHF) is still unclear.

OBJECTIVES The aim of the study was to evaluate the value of sST2 protein in patients with CHF during 1-year follow-up after hospitalization for prediction of adverse events: cardiovascular death, rehospitalization, an increase in diuretic doses, and/or worsening of the New York Heart Association functional class, defined as the composite endpoint.

PATIENTS AND METHODS The study involved 145 consecutive patients (mean age, 62.16 ±11.25 y; men, 82.76%) with left ventricular (LV) ejection fraction of 30% or less and symptomatic CHF. We analyzed clinical and biochemical data along with the serum concentrations of N-terminal pro-B-type natriuretic peptide (NT-proBNP) and sST2. The optimal cut-off points for significant predictors of the composite endpoint were determined using receiver operating characteristic curves.

RESULTS Patients with elevated levels of sST2 and NT-proBNP had more than a 4-fold higher risk of composite endpoint (odds ratio [OR], 4.033; 95%CI, 1.540–10.559) compared with patients in whom both biomarkers were below the cut-off points. The C-statistic for predicting the composite endpoint was improved when both biomarkers were incorporated into the model (C-statistic, 0.692; $P = 0.0001$) compared with an individual analysis for NT-proBNP (C-statistic, 0.606; $P = 0.009$) and sST2 (C-statistic, 0.613; $P = 0.003$). Moreover, after the addition of sST2 to NT-proBNP, the continuous net reclassification improvement index (OR, 0.256; 95% CI, 0.090–0.401; $P = 0.007$) and the integrated discrimination improvement index (OR, 0.104; 95% CI 0.011–0.221; $P = 0.007$) significantly improved.

CONCLUSIONS A single measurement of sST2 levels on admission in patients with poor LV systolic function and stable CHF is useful in short-term risk stratification and, in combination with NT-proBNP, it could be more useful in identifying patients with unfavorable course of CHF.

Correspondence to:
Prof. Małgorzata Lelonek, MD, PhD, Klinika Kardiologii, Uniwersytet Medyczny w Łodzi, ul. Sterlinga 1/3, 91-425 Łódź, Poland, phone: +48-42-636-44-71, fax: +48-42-636-44-71, e-mail: mlelonek@poczta.fm
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INTRODUCTION The interleukin-33/ST2 system is described as a novel cardioprotective pathway in the pathogenesis of heart failure (HF). ST2 is a member of the Toll-like/interleukin 1-receptor family with 2 isoforms: soluble ST2 (sST2) and transmembrane ST2 (ST2L). Interleukin (IL)-33 acts by ST2L and produces the cardioprotective effects; in particular, it protects against hypertrophy, fibrosis, and cardiomyocyte apoptosis.[1,2] It has been reported that sST2 isoform could act as a "decoy receptor" by binding interleukin 33 and eliminating its effect. Damage to stromal cells leads to the production of IL-33 by fibroblasts, smooth muscle cells, epithelial cells, endothelial cells, and IL-33/ST2L signaling system leads to the synthesis of inflammatory cytokines. sST2 is produced by stromal cells in the lungs, heart, kidneys, and small intestines as a result of inflammatory cytokine stimulation (IL-1α, IL-1β, IL-6, and tumor necrosis factor α);

therefore, sST2 is considered as an inflammatory biomarker.[3] However, sST2 is not a specific marker for cardiac diseases, and hence it is not a diagnostic biomarker, but it has been established that sST2 is a valuable prognostic biomarker in myocardial infarction and acute HF.[4,5]

There are only a few studies that investigated the prognostic value of sST2 in chronic HF (CHF). Furthermore, a recent study has shown that sST2 was superior to another new biomarker, galectin 3, in the risk stratification in patients with CHF.[6] Nowadays, it is necessary to identify patients at high risk of unfavorable course of CHF that is defined as unplanned readmission to the hospital for decompensated HF or cardiovascular death, which occurs at the highest rate early after hospitalization.[7] Despite advances in HF therapy, mortality from CHF remains a considerable challenge in Poland and other European countries.[8] Unfortunately, there are still no optimal diagnostic tools to identify patients at high risk of HF worsening in short-term follow-up after discharge from the hospital. Moreover, CHF remains a serious public health problem, which is increasingly prevalent in both sexes owing to population aging.[9,10]

The aim of our study was to assess the value of sST2 in patients with stable CHF and poor left ventricular (LV) systolic function during 1-year follow-up for prediction of cardiovascular death, hospitalization for HF exacerbation, an increase in diuretic doses, and/or worsening of the New York Heart Association (NYHA) functional class, defined as the composite endpoint.

PATIENTS AND METHODS

This prospective study included 145 consecutive patients (mean age, 62.16 ±11.25 y; men, 82.76%) with LV ejection fraction (LVEF) of 30% or less and CHF, who were hospitalized to determine the etiology of HF. All patients were clinically stable for at least 4 weeks (NYHA functional class, II–III). Subjects with acute HF, acute coronary syndrome, autoimmune diseases, and other inflammatory states were excluded.

At baseline, detailed demographic and clinical data (age, sex, body mass index, and comorbidities) were collected and 12-lead electrocardiogram was performed. On admission, the following laboratory parameters were measured: hemoglobin, white blood cells, neutrophils, platelets, sodium, creatinine, estimated glomerular filtration rate, blood urea nitrogen, glucose, total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, triglycerides, high-sensitivity C-reactive protein, high-sensitivity troponin T (hsTnT), and N-terminal pro-B-type natriuretic peptide (NT-proBNP). Moreover, all patients underwent a complete echocardiographic examination and the following parameters were assessed: LV end-diastolic diameter, LV end-systolic diameter (LVESD), LV end-diastolic volume and LV end-systolic volume (LVESV). The LVEF was measured at 4- and 2-chamber apical views by the Simpson method. All examinations were performed by experienced echocardiographers.

To determine the etiology of HF (ischemic vs. nonischemic), coronary angiography was performed according to the European Society of Cardiology recommendations.

On enrollment to the study, blood samples for sST2 measurement were obtained by venipuncture and collected to the EDTA vacuum tubes. Immediately after collection, the samples were centrifuged and the plasma was separated to a new tube and then frozen at –76°C. sST2 concentrations were measured using sandwich monoclonal enzyme-linked immunosorbent assay kits (Medical and Biological Laboratories, no. 7638, Woburn, Massachusetts, United States). The longest period of plasma storage at –76°C was 12 months. All samples were assessed in triplicate. The limit of detection (sensitivity) was 0.032 ng/ml and the upper limit of the reference range was 4 ng/ml. All measurements were conducted in the Department of Medical Biotechnology at Medical University of Lodz, Poland.

All patients received optimal drug treatment with such agents as angiotensin-converting enzyme inhibitors/angiotensin receptor blockers, β-blockers, and mineralocorticoid receptor antagonists, according to the European Society of Cardiology recommendations. We defined the composite endpoint of the study as cardiovascular death, hospitalization for HF exacerbation, an increase in diuretic doses, and/or worsening of the NYHA functional class. All patients received a phone call and were intervied by a cardiologist 12 months after hospitalization. The cause of death was established during the interview on the basis of medical records or, if the patient died, on the basis of death protocols, if available, or an interview with a family member if the patient died outside the hospital.

The study conformed to the principles of the Declaration of Helsinki and was approved by the Bioethics Committee of the Medical University in Lodz. All subjects provided written informed consent to participate in the study.

Statistical analysis

Categorical variables were reported as the number of observations (N) and the corresponding percentage (%) and analyzed with the χ^2 test or χ^2 test with Yates' correction. Normality of quantitative variables was tested using the Shapiro–Wilk test for normality. Because of the lack of normality for most variables, they were presented as medians with interquartile range. Differences between groups were analyzed using the Mann–Whitney test.

For quantitative variables that were significantly associated with the presence of the composite endpoint, receiver operating characteristic (ROC) curves were drawn and optimal decision thresholds were found using the Youden index. Sensitivity, specificity, positive predictive value, and

TABLE 1 Baseline characteristics of total cohort and comparison between patients with or without composite endpoint

Variables		Total cohort, n = 145	Composite endpoint (–), n = 62 (42.76%)	Composite endpoint (+), n = 83 (57.24%)	*P* value
age, y		63 (57–69)	64 (56–73)	62 (57–68)	0.4
men, n (%)		120 (82.76)	51 (82.26)	69 (83.13)	0.9
BMI, kg/m^2		26.3 (23.7–28.7)	26.45 (23.2–28.3)	26.15 (23.95–9.85)	0.7
SBP, mmHg		120 (110–130)	120 (110–125)	115 (110–130)	0.9
DBP, mmHg		70 (70–80)	70 (70–80)	70 (70–90)	0.3
NYHA class		3 (3–3)	3 (3–3)	3 (3–3)	0.45
heart rate, bpm		80 (70–85)	70 (67–80)	81.5 (70–90)	0.01
QRS duration, ms		120 (100–140)	118 (100–140)	120 (100–140)	0.2
QTc duration, ms		410 (380–460)	405 (360–447)	410 (380–466)	0.2
LVESD, cm		6 (5.4–6.7)	5.75 (5.1–6.2)	6.1 (5.7–7)	0.01
LVEDD, cm		7 (6.3–7.6)	6.8 (6.2–7.3)	7.1 (6.6–7.6)	0.06
LVESV, ml		165.5 (127–211)	153 (116–193)	175 (135–228)	0.05
LVEDV, ml		218 (176–266)	203 (161–250)	230 (184–294)	0.09
LVEF, %		24 (19–28)	25 (20–28)	24 (19–27)	0.17
number of affected coronary arteries		1 (0–2)	1 (0–2)	1 (0–2)	0.25
etiology of HF, n (%)	ischemic	83 (57.24)	34 (54.84)	49 (59.04)	0.7
	nonischemic	62 (42.76)	28 (45.16)	34 (40.96)	
sST2, ng/ml		0.515 (0.286–1.42)	0.377 (0.274–1)	0.670 (0.306–1.740)	0.04
NT-proBNP, pg/ml		2510 (1334–4846)	1934 (925.9–3624)	2932 (1486–5777)	0.03
hsTnT, mg/dl		6 (0.34–30)	1.68 (0.25–19.9)	15 (0.42–31)	0.13
TC, mmol/l		4.2 (3.6–5.3)	4.2 (3.7–4.8)	4.2 (3.4–5.4)	0.5
LDL cholesterol, mmol/l		2.4 (1.9–3.2)	2.2 (1.9–2.8)	2.57 (1.8–3.3)	0.16
HDL cholesterol, mmol/l		1.25 (0.94–1.53)	1.27(1.06–1.57)	1.24 (0.92–1.50)	0.7
TG, mmol/l		1.21 (0.93–1.67)	1.22 (0.95–1.65)	1.14 (0.88–1.72)	0.7
glucose, mmol/l		5.9 (5.3–6.8)	5.8 (5.3–6.3)	5.9 (5.3–6.9)	0.5
BUN, mg/dl		7.2 (5.6–9.4)	7 (6–8.3)	7.3 (5.2–10.7)	0.6
creatinine, µmol/l		88 (75–102)	87 (72–95)	88 (78–115)	0.08
bilirubin, µmol/l		14 (9.5–20)	13 (9.1–19)	16 (11–22)	0.2
hs-CRP, mg/l		3.9 (1.5–10)	3.55 (0.9–7.5)	3.95 (1.8–11.4)	0.1
eGFR, ml/min/1.73 m^2		74 (55–103)	79 (59–106)	70 (54–98)	0.3
WBC, 10^3/µl		7.6 (6.6–8.85)	7.5 (6.3–8.9)	7.75 (6.8–8.75)	0.5
hemoglobin, g/dl		14.30 (13.27–15.48)	14.35 (13.31–15.10)	14.15 (13.20–15.57)	0.6
neutrophils, %		64.2 (59–72)	61.4 (55.8–69.6)	66.2 (60.9–73.8)	0.03
CRT/ICD, n (%)		40 (27.6)	15 (24.2)	25 (30.1)	0.8

Data are presented as medians with interquartile range or the number of observations (n) and the corresponding percentage (%).

Variables are shown as medians with upper and lower quartiles.

Abbreviations: BMI – body mass index, BUN – blood urea nitrogen, DBP – diastolic blood pressure, eGFR – estimated glomerular filtration rate, HDL – high-density lipoprotein, HF – heart failure, hs-CRP – high-sensitivity C-reactive protein, CRT – cardiac resynchronization therapy, hsTnT – high-sensitivity troponin T, ICD – implantable cardioverter defibrillator, LVEDD – left ventricular end-diastolic diameter, LVEDV – left ventricular end-diastolic volume, LVEF – left ventricular ejection fraction, LVESD – left ventricular end-systolic diameter, LVESV – left ventricular end-systolic volume, NT-proBNP – N-terminal pro-B-type natriuretic peptide, NYHA – New York Heart Association, SBP – systolic blood pressure, sST2 – soluble ST2, TC – total cholesterol, TG – triglycerides, WBC – white blood cells

negative predictive value were calculated. Odds ratios (ORs) with 95% confidence intervals (CIs) were also presented.

A univariate Cox regression analysis was used to assess the association between the composite endpoint and each significant continuous variable dichotomized according to optimal cut-off points. Backward stepwise elimination was used in the multivariate Cox regression model to identify the independent predictors of the composite endpoint. The multivariate analysis included all variables with a *P* value of less than 0.1 except LVESD (excluded from the model because of its correlation with NT-proBNP and LVESV).

The results were presented as hazard ratios (HRs) with 95% CI. To compare differences in survival between the optimal sST2 and NT-proBNP cut-off point groups, the Kaplan–Meier analysis was performed.

TABLE 2 Receiver operating characteristic (ROC) curve analyses of significant variables for predicting the composite endpoint

Variables	Cut-off point	AUC (95% CI)	*P* value	Sensitivity, %	Specificity, %	PPV, %	NPV, %	OR (95% CI)	*P* value (OR)
sST2, ng/ml	≥0.296	0.61 (0.51–0.71)	0.04	80.72	39	65	59	2.68 (1.27–5.63)	0.001
NT-proBNP, pg/ml	≥2664	0.62 (0.52–0.72)	0.03	57.3	66	71.7	51	2.61 (1.25–5.44)	0.01
heart rate, bpm	≥81.5	0.62 (0.53–0.72)	0.01	50.0	75.9	74.5	52	3.14 (1.52–6.50)	0.002
LVESD, cm	≥5.65	0.64 (0.54–0.75)	0.01	78.7	50	72.8	58	3.69 (1.67–8.12)	0.001
LVESV, ml	≥185.5	0.6 (0.5–0.7)	0.05	46.7	72	72	47	2.32 (1.08–4.97)	0.03
neutrophils,%	≥61.5	0.6 (0.51–0.71)	0.03	72.1	52.7	68.7	59.9	2.89 (1.4–5.95)	0.003

Abbreviations: AUC – area under the curve, CI – confidence interval, NPV – negative predictive value, OR – odds ratio, PPV – positive predictive value, others – see **TABLE 1**

TABLE 3 Univariate and stepwise multivariate Cox proportional hazards analysis for the prediction of the composite endpoint at 1 year

Variables	Univariate analysis		Multivariate analysis	
	HR (95%CI)	*P* value	HR (95% CI)	*P* value
sST2 ≥0.296, ng/ml	2.645 (1.292–5.417)	0.008	3.77 (1.55–9.18)	0.003
NT-proBNP ≥2664, pg/ml	2.087 (1.184–3.679)	0.011	2.043(1.088–3.837)	0.026
heart rate ≥81.5, bpm	2.553 (1.484–4.394)	0.001	2.720 (1.436–5.149)	0.002
LVESD ≥5.65, cm	2.193 (1.147–4.191)	0.018	–[a]	–[a]
LVESV ≥185.5, ml	1.617 (0.929–2.816)	0.089	2.319 (1.207–4.457)	0.012
neutrophils ≥61.5, %	2.103 (1.147–3.855)	0.016	2.587 (1.277–5.241)	0.008

a variable not included into the model because of its correlation with NT-proBNP and LVESV

Abbreviations: HR – hazard ratio, others – see **TABLES 1** and **2**

To evaluate the utility of biomarkers for predicting the presence of the composite endpoint and to assess the potential improvement in risk prediction, C-statistic, continuous net reclassification improvement (NRI) index, and integrated discrimination improvement (IDI) index were used. To assess correlations between sST2 and other quantitative variables, Spearman correlation coefficients were used. The correlations between sST2 and qualitative variables (sex, etiology of HF) were analyzed using the Mann–Whitney test (nonnormally distributed data).

A *P* value of less than 0.05 was considered statistically significant. Statistical calculations were performed using STATISTICA 10 PL (StatSoft Inc., United States), SPSS v. 20 (SPSS Inc., United States), and R-project v. 3.0.2 (R Core Team, The R Foundation for Statistical Computing, Vienna, Austria).

RESULTS The baseline characteristics of the total cohort and comparison between patients with or without the composite endpoint are listed in **TABLE 1**. During 1-year follow-up, 83 patients (57.24%) achieved the composite endpoint: cardiovascular death (26 patients), hospitalization for HF exacerbation (41 patients), need for increased diuretic doses (18 patients), and worsening of the New York Heart Association (NYHA) functional class (30 patients). The total number of events exceeds 83 because some patients had more than 1 component of the composite endpoint. The cut-off points of significant variables for predicting the composite endpoint at 1-year follow-up were determined using the ROC curves. The results are shown in **TABLE 2**.

Proportional hazard Cox regressions were performed to determine associations between the composite endpoint and studied variables. In a multivariate analysis, both NT-proBNP and sST2 remained significant predictors of the composite endpoint together with heart rate, neutrophils, and LVESV. The results are shown in **TABLE 3**. To estimate the significance of combined assessment of NT-proBNP and sST2, the total cohort was divided into 4 groups based on sST2 and NT-proBNP cut-off points. Only patients with elevated serum levels of both biomarkers had a significantly increased risk of the composite endpoint compared with the subgroup with sST2 and NT-proBNP levels below the cut-off points (odds ratio [OR], 4.033; 95% CI, 1.540–10.559; $P = 0.005$; **FIGURE 1**). C-statistic for predicting the composite endpoint was markedly improved when both biomarkers were incorporated into the model (C-statistic, 0.692; $P = 0.0001$) compared with an individual analysis for NT-proBNP (C-statistic, 0.606; $P = 0.009$) and sST2 (C-statistic, 0.613; $P = 0.003$). Moreover, the continuous NRI index significantly improved after ST2 had been added to NT-proBNP (OR, 0.256; 95% CI, 0.090–0.401; $P = 0.007$) as well as the IDI index (OR, 0.104; 95% CI, 0.011–0.221; $P = 0.007$). sST2 levels were positively correlated with hsTnT, glucose, creatinine, white blood cells, and QTc duration. There were no other correlations of sST2 levels with sex ($P = 0.5$) and etiology of HF ($P = 0.5$), as shown in **TABLE 4**.

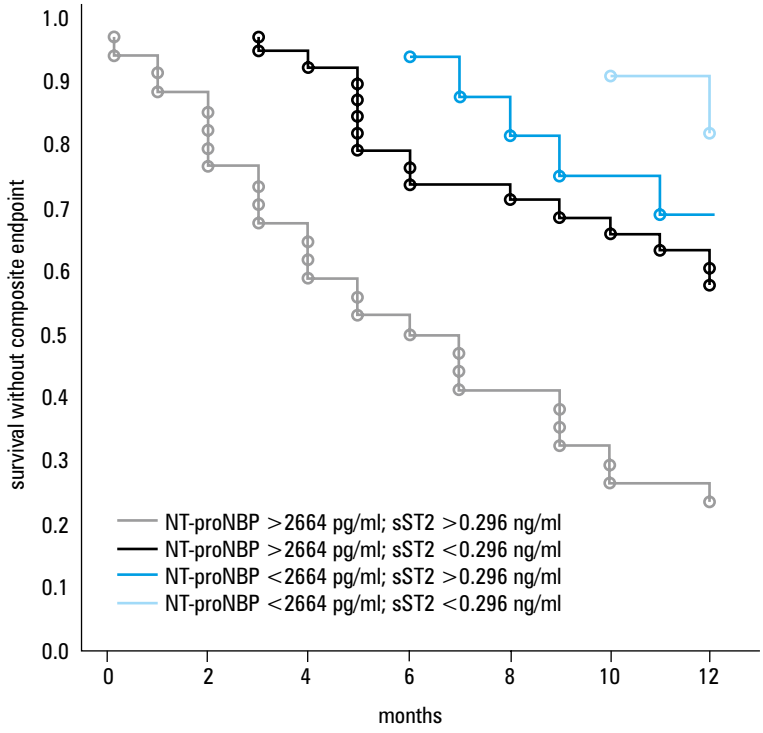

FIGURE 1 Kaplan–Meier survival curves according to NT-proBNP and sST2 levels (above or below the cut-off points)
Abbreviations: see **TABLE 1** and **TABLE 2**

TABLE 4 Spearman rank order correlations between sST2 and other variables

Variables	*R*	*P* value	Variables	*R*	*P* value
age	–0.0289	0.7	hsTnT	0.2726	0.02
BMI	0.0698	0.4	TC	–0.0808	0.4
DBP	0.0294	0.7	LDL cholesterol	–0.0534	0.6
SBP	0.0861	0.3	HDL cholesterol	–0.1500	0.1
NYHA class	0.0258	0.7	TG	0.0807	0.4
heart rate	0.0450	0.6	glucose	0.2471	0.004
QRS duration	0.0852	0.3	BUN	0.0753	0.4
QTc duration	0.1894	0.02	creatinine	0.1793	0.04
LVESD	0.1244	0.2	bilirubin	–0.0566	0.6
LVEDD	–0.0633	0.5	hs-CRP	0.0971	0.3
LVESV	0.0225	0.8	eGFR	–0.1597	0.08
LVEDV	–0.0235	0.8	WBC	0.1931	0.02
EF	–0.1174	0.2	hemoglobin	–0.0198	0.8
number of affected coronary arteries	0.0334	0.7	neutrophils	0.0736	0.4
NT-proBNP	0.0319	0.7			

Abbreviations: see **TABLE 1**

DISCUSSION Our study showed that patients suffering from stable CHF and poor LV systolic function (≤30%) with elevated sST2 and NT-proBNP levels at presentation had a considerably higher risk of unfavorable course of HF at 1-year follow-up compared with patients with normal levels. The probability of survival without composite endpoint at 1-year follow-up was reduced from 68.75% to 23.53% when sST2 and NT-proBNP levels were both above the cut-off points. We established that the serum sST2 concentration on admission was an independent predictor of a severe course of HF at 1-year follow-up after discharge. Patients with elevated levels of sST2 (≥0.296 ng/ml) had more than a 3-fold higher risk of reaching the composite endpoint compared with patients with sST2 levels below the cut-off point (P = 0.003). The second independent predictor of the composite endpoint, serum NT-proBNP concentration of 2664 pg/ml and higher, was associated with a 2-fold higher risk of reaching the composite endpoint compared with patients with the levels below the cut-off point (P = 0.026).

Unlike in other centers, we analyzed the associations of sST2 levels not only with mortality but also with adverse cardiac events, including hospitalization for HF exacerbation, an increase in diuretic doses, and/or worsening of the NYHA functional class. To the best of our knowledge, this has been the first study to investigate the relation between sST2 levels and widely defined adverse course of HF in high-risk population with CHF with markedly impaired LV systolic function.

Our study also showed a heart rate of 81.5 bpm or higher, neutrophils of 61.5% and higher, and LVESV of 185.5 ml and higher to be independent predictors of the composite endpoint. Increased heart rate is a recognized predictor of mortality in patients with CHF[11] as well as an increase in neutrophils.[12] LVESV and other LV volumetric parameters are important for clinical prognosis in HF as variables related to LVEF.

Biomarkers are widely used for identifying patients at high risk of adverse outcomes, for diagnosis, or for monitoring therapy of cardiovascular diseases including HF.[13,14] It has been established that multiple biomarker measurements significantly improve risk stratification of adverse events in HF.[15] sST2, a member of the interleukin 1-receptor family, released in response to mechanical strain of the LV wall, is emerging as a valuable predictive factor in cardiovascular diseases. However, there are still only a few studies about sST2 in patients with stable CHF. Pascual-Figal et al.[16] confirmed that sST2 levels (cut-off point, 0.15 ng/ml) are predictive of sudden cardiac death in patients with stable CHF and LV systolic dysfunction (LVEF ≤45%) at 1-year follow-up.The higher cut-off point obtained in our study (0.296 ng/ml) was presumably the result of poorer LV systolic function in the study population. Ky et al.[17] conducted an analysis of 1141 outpatients with systolic CHF (LVEF = 32.2% ±17%) and showed that higher sST2 levels on enrollment were associated with a significantly increased risk of all-cause death or cardiac transplantation after a median follow-up of 2.8 years. On the other hand, it is suggested that serial measurements of sST2 levels can provide prognostic information in patients with stable CHF[18] or with acutely destabilized HF.[19] However, in our study, we measured sST2 levels only at presentation and proved associations with the unfavorable course of HF independently of NT-proBNP levels.

Our results are consistent with previous reports that demonstrated an independent relationship of sST2 and NT-proBNP levels with adverse cardiac events. In a study of 891 ambulatory patients with HF (median LVEF, 34%; interquartile range, 26%–43%), Bayes-Genis et al.[20] revealed independent prognostic value of NT-proBNP and sST2 in predicting death. The cut-off points of NT-proBNP levels for predicting adverse cardiac events (2664 pg/ml) estimated in our study are higher than those described in the previous studies: 2000 pg/ml,[16] 1829 pg/ml,[20] and 1720 pg/ml.[21] We hypothesize that a higher NT-proBNP cut-off point in the studied cohort was the result of poorer LV systolic function (median LVEF, 24%) than in the other studies (LVEF, 29%–34%).[15,20,21]

Of note, biomarkers are independent of other variables. It has been established that serum concentrations of NT-proBNP depend on several clinical factors such as age, sex, LV hypertrophy, tachycardia, myocardial ischemia, renal dysfunction, liver cirrhosis, metabolic risk factors, or infection.[22,23] In contrast to NT-proBNP, sST2 is emerging as a valuable biomarker in CHF, independent of traditional clinical prognostic factors.[18,24] Our results are consistent with previous reports in that we revealed weak correlations between sST2 levels and hsTnT, glucose, creatinine, and white blood cell count or QTc duration. Furthermore, in a study of 17 healthy subjects, Wu et al.[25] showed lower biological variation of sST2 than of NT-proBNP. They postulated that repeated measurements of sST2 levels may be useful for therapy monitoring.

Our study has several limitations including the inclusion only of NYHA functional classes II and III and a relatively small number of patients. We mainly studied men in a single center, so caution should be taken in extrapolating the results to broader populations, including women. In some studies assessing sST2 concentrations, a high-sensitivity sandwich monoclonal immunoassay was used. We performed measurements using sandwich monoclonal enzyme-linked immunosorbent assay kits so the cut-off points should not be compared.

In summary, we revealed that a single measurement of sST2 on admission in patients with poor LV systolic function and symptomatic stable CHF is useful in short-term risk stratification. Moreover, in this group of patients, the assessment of both sST2 and NT-proBNP could be used to better identify patients at high risk of unfavorable course of HF.

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ARTYKUŁ ORYGINALNY

Pojedynczy pomiar stężenia białka sST2 prognozuje niekorzystne zdarzenia sercowe w rocznej obserwacji u chorych z przewlekłą niewydolnością serca

Sebastian Sobczak[1], Karolina Wojtczak-Soska[1], Tomasz Ciurus[1], Agata Sakowicz[2], Tadeusz Pietrucha[2], Małgorzata Lelonek[1]

1 Klinika Kardiologii, Uniwersytet Medyczny w Łodzi, Łódź
2 Zakład Biotechnologii Medycznej, Uniwersytet Medyczny w Łodzi, Łódź

SŁOWA KLUCZOWE

dysfunkcja skurczowa, przewlekła niewydolność serca, rokowanie, sST2

STRESZCZENIE

WPROWADZENIE Białko sST2 jest nowym biomarkerem. Nadal niejasne jest jego znaczenie w krótkoterminowej ocenie w przewlekłej niewydolności serca (PNS).

CELE Celem badania była ocena zdolności prognostycznej białka sST2 do przewidywania niekorzystnych zdarzeń w rocznej obserwacji pacjentów z PNS po hospitalizacji – zgonu z przyczyn sercowo-naczyniowych, rehospitalizacji, konieczności zwiększenia dawek leków moczopędnych i/lub pogorszenia klasy czynnościowej wg NYHA, które łącznie stanowiły złożony punkt końcowy.

PACJENCI I METODY Badaniem objęto 145 kolejnych pacjentów (średni wiek 62,16 ±11,25 lata, 82,76% mężczyzn) z frakcją wyrzutową lewej komory ≤30% i objawową PNS. Analizowano kliniczne i biochemiczne dane wraz ze stężeniem N-końcowego propeptydu natriuretycznego typu B (NT-proBNP) i sST2 w surowicy. Optymalne punkty odcięcia dla istotnych zmiennych do prognozowania złożonego punktu końcowego wyznaczono przy użyciu krzywych ROC.

WYNIKI U pacjentów z podwyższonymi stężeniami sST2 i NT-proBNP ryzyko wystąpienia złożonego punktu końcowego było ponad 4-krotnie wyższe (OR = 4,033; 95%CI 1,540–10,559) w porównaniu z pacjentami ze stężeniami obu biomarkerów poniżej punktów odcięcia. Wartość C-statystyki dla prognozowania złożonego punku końcowego wzrosła, gdy oba biomarkery zostały włączone do modelu (C-statystyka = 0,692; p = 0,0001) w porównaniu do każdego oddzielnie: NT-proBNP (C-statystyka = 0,606; p = 0,009) oraz sST2 (C-statystyka = 0,613; p = 0,003). Ponadto po dołączeniu sST2 do NT-proBNP wartość ciągłego wskaźnika NRI (*net reclassification improvement*; OR = 0,256; 95% CI 0,090–0,401; p = 0,007) oraz IDI (*integrated discrimination improvement*; OR = 0,104; 95% CI 0,011–0,221; p = 0,007) istotnie wzrosła.

WNIOSKI Pojedynczy pomiar stężenia sST2 przy przyjęciu do szpitala u pacjentów ze znacznie upośledzoną funkcją skurczową lewej komory i stabilną PNS jest użyteczny w krótkoterminowej ocenie ryzyka, a w połączeniu z NT-proBNP mógłby lepiej identyfikować populację o niekorzystnym przebiegu PNS.

Adres do korespondencji:
prof. dr hab. n. med. Małgorzata Lelonek, Klinika Kardiologii, Uniwersytet Medyczny w Łodzi, ul. Sterlinga 1/3, 91-425 Łódź, tel.: 42-636-44-71, fax: 42-636-44-71, e-mail: mlelonek@poczta.fm

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