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ARTYKUŁ ORYGINALNY / *ORIGINAL ARTICLE*

Evaluation of the relationship between renal resistive index and extent and complexity of coronary artery disease in patients with acute coronary syndrome

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Abstract

Background: Despite advances in cardiovascular medicine, acute coronary syndrome (ACS) is still a major cause of morbidity and mortality worldwide. Synergy between percutaneous coronary intervention with TAXUS™ and Cardiac Surgery (SYNTAX) score is used to determine the extent and complexity of coronary artery disease (CAD). Renal resistive index (RRI), a renal Doppler ultrasound parameter, is used to detect renal haemodynamics. Although some risk factors for CAD, including hypertension and diabetes mellitus, were demonstrated to have an association with RRI; a direct relationship between the presence, extent, and complexity of CAD and RRI has not been investigated yet.

Aim: In this study, we evaluated the relationship between RRI and SYNTAX score in patients with ACS.

Methods: This cross-sectional study enrolled 235 patients who were diagnosed with ACS and underwent coronary angiography at our tertiary clinic between February 2016 and August 2016. Regarding clinical presentation, 112 patients were diagnosed with non-ST-segment elevation ACS (NSTE-ACS) and 123 patients were diagnosed with ST-segment elevation ACS (STE-ACS). The patients' demographic, clinical, laboratory, echocardiographic data, SYNTAX scores and measurements of renal Doppler ultrasound parameters, including RRI, renal pulsatility index (RPI) and acceleration time (AT) were recorded.

Results: Among 235 patients, 112 (47.7%) were diagnosed with NSTE-ACS and 123 (52.3%) were diagnosed with STE-ACS. Mean SYNTAX score and RRI of patients with NSTE-ACS and STE-ACS were 15.4 and 0.69, 21.1 and 0.67, respectively. The SYNTAX score was associated with gender, height, plasma uric acid level, left atrial diameter, left ventricular (LV) end-systolic and end-diastolic diameter, RPI, and RRI in patients with NSTE-ACS, as well as with low-density lipoprotein-cholesterol, total cholesterol, ejection fraction, and LV end-systolic diameter in patients with STE-ACS ($p < 0.05$ for each variable). RRI was significantly associated with age, haemoglobin level, left atrial diameter, SYNTAX score, AT, and RPI in patients with NSTE-ACS, as well as with weight, body mass index, interventricular septum thickness at diastole, LV posterior wall thickness at diastole, LV ejection fraction, and RRI in patients with STE-ACS. Multivariate logistic regression analysis demonstrated that LV end-systolic diameter ($\beta = 0.385$, 95% CI 1.065–2.029, $p = 0.019$), RRI ($\beta = 32.230$, 95% CI 5343.15–2.E+24, $p = 0.008$), and RPI ($\beta = -7.439$, 95% CI 0.000–0.231, $p = 0.015$) were independent predictors of moderate to high SYNTAX score in patients with NSTE-ACS.

Conclusions: Non-invasively detected RRI is closely associated with the extent and complexity of CAD in patients with NSTE-ACS. However, there is a need for randomised, controlled studies involving wider populations.

Key words: acute coronary syndrome, coronary artery disease, SYNTAX score, renal resistive index

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INTRODUCTION

Cardiovascular disease is still the largest cause of morbidity and mortality worldwide. The most common cause of coronary artery disease (CAD) is atherosclerosis. Other causes include arthritis, coronary embolism, coronary spasm, coronary artery anomalies, and cocaine use.

Atherosclerosis is a systemic, progressive, chronic, immunoinflammatory, and fibroproliferative disease, which is characterised by lipid accumulation, smooth muscle cell proliferation, and infiltration of macrophages and T lymphocytes that primarily affect the intimal layer of medium-sized elastic arteries [1]. These components are heterogeneously distributed in coronary plaques. Atherosclerosis frequently affects aorta, carotid, coronary, and peripheral arteries and usually begins in early childhood and progresses throughout life. It is characterised by fatty streaks in early childhood and fibrous plaques with more advanced lesions in adulthood. Atherosclerotic plaques, developed over years, lead either to long-term clinically silent obstruction in the coronary arteries or to acute coronary syndrome (ACS) due to an abrupt rupture or erosion of these plaques. Several mechanisms have been proposed regarding the pathogenesis of atherosclerosis. Hypotheses, involving hyperlipidaemia, hypercoagulability, oxidative stress, endothelial dysfunction, inflammation, and infection have been suggested. Nowadays, atherosclerosis is defined as a multifactorial disease, where inflammation plays an essential role [1], not only in the onset and progression of the disease but also in plaque rupture and thrombus formation.

Acute coronary syndrome is characterised by myocardial ischaemia due to a decrease in blood flow or complete obstruction of coronary arteries, and it defines a wide spectrum of clinical manifestations, including unstable angina pectoris, non-ST-segment elevation myocardial infarction (NSTEMI), ST-segment elevation myocardial infarction (STEMI), and sudden cardiac death. The underlying cause of ACS is usually an acute thrombosis of an erosive or ruptured coronary plaque. Symptoms arise when the atheromatous plaque grows and obstructs the coronary artery or when coronary blood flow is blocked by thrombus formation. The degree of occlusion in the coronary artery depends on the content of the plaque, local haemodynamic factors, and coagulation status.

The synergy between percutaneous coronary intervention with TAXUS™ and cardiac surgery (SYNTAX) score is used to assess the extent and complexity of CAD and to determine the optimal treatment by identifying the risk of adverse events following PCI. It is an independent predictor of major adverse cardiac event(s) in patients treated with PCI [2], and a useful indicator for predicting cardiac mortality in patients with NSTEMI [3]. In the SYNTAX scoring system, scores of each coronary lesion are calculated separately, and the total SYNTAX score is obtained by summing all of these scores.

Renal resistive index (RRI) is a simple and commonly used renal Doppler ultrasonography (USG) parameter consisting of a complex interaction between haemodynamic changes. It has been evaluated in many clinical entities, including hypertension (HT) [4], diabetes mellitus (DM) [5], and chronic kidney disease (CKD) [6]. Impaired renal haemodynamics, assessed by increased RRI, were found to be associated with increased renal and cardiovascular risk in patients with essential HT [7]. Despite the relationship with some cardiovascular risk factors, such as HT and DM, the direct association between RRI and the presence, extent, and complexity of CAD has not been investigated yet. In our study, we aimed to evaluate the relationship between RRI and extent and complexity of CAD, assessed by SYNTAX score in patients with ACS.

METHODS

Study design and patient population

A total of 235 consecutive patients (40 female; mean age: 55.4 ± 10.3 years) who were diagnosed with ACS and underwent coronary angiography (CAG) at our hospital between February 2016 and August 2016 were included in this cross-sectional study. Patients were divided into two groups according to ST-segment elevation: non-ST-segment elevation ACS (NSTE-ACS) and ST-segment elevation ACS (STE-ACS). Patients with unstable angina pectoris and NSTEMI were included in the NSTE-ACS group. All patients had a routine 12-derivation electrocardiogram (ECG) and biochemical measurements prior to CAG. All patients underwent transthoracic echocardiography (TTE) performed by a blinded cardiologist, and renal Doppler USG performed by two blinded radiologists. Patients with previous coronary artery bypass grafting, moderate to severe heart valve disease (mitral stenosis, aortic stenosis and aortic insufficiency), history of atrial fibrillation, chronic liver disease, CKD, renal artery stenosis, nephrectomy, malignancy, haemorrhage diathesis, acute/chronic infective or inflammatory disease, and suspected pregnancy were excluded. The study was conducted according to the recommendations set forth by the Declaration of Helsinki on Biomedical Research Involving Human Subjects. The institutional Ethics Committee approved the study protocol and each participant provided written, informed consent.

Identification of cardiovascular risk factors

Cardiovascular risk factors of all patients were questioned. Patients who were previously on oral antidiabetic and/or insulin therapy or those with fasting blood glucose, measured at least twice, ≥ 126 mg/dL were considered diabetic. Patients who were previously on antihypertensive therapy or those with blood pressures, measured at least twice, ≥ 140/90 mm Hg were defined as hypertensive patients. The presence of hyperlipidaemia was considered when a measure of total cholesterol > 200 mg/dL or low-density lipoprotein cholesterol (LDL-C) > 100 mg/dL was obtained or when the patient was previously on lipid-lowering medication in accordance with Adult Treatment Panel III Guidelines [8]. History of CAD in the family was defined as the presence of CAD in first-degree

relatives before the age of 55 years for men and 65 years for women. Patients who were using tobacco products on admission to our hospital and those who had quit smoking within the past month were considered smokers. The height and weight of the patients were measured and body mass indices were calculated using the formula: body mass index (BMI) = weight (kg) / height^2 (m^2). Estimated glomerular filtration rates were calculated using the Chronic Kidney Disease Epidemiology Collaboration equation.

Blood samples and laboratory analysis

Venous blood samples were obtained from all participants on admission, to measure complete blood count, lipid panel, cardiac enzymes, creatinine, and uric acid levels before CAG. Routine blood chemistry and lipid parameters were measured with a standard auto-analyser. Blood counts were measured with a Sysmex K-1000 (Block Scientific, Bohemia, New York, USA) auto-analyser within 5 min of sampling.

Coronary angiographic assessment and calculation of the SYNTAX scores

Coronary angiographies were performed using Siemens (Axiom Sensis XP, Berlin, Germany) and Toshiba (Infinix CSI, Tokyo, Japan) devices at our angiography and catheterisation laboratory. Informed consent was obtained routinely from all of the patients before the procedure. Coronary lesions were evaluated by at least two experienced, blinded interventional cardiologists. Patients with stenosis > 50% in the left main coronary artery and/or > 70% in other coronary arteries were considered as obstructive lesions. A blinded interventional cardiologist calculated the SYNTAX score I of each patient using the online SYNTAX score calculator (http://www.syntaxscore.com).

Measurements of TTE

Transthoracic echocardiographies were performed using an EPIQ 7 device (Philips Healthcare, Andover, MA, USA) by an experienced blinded cardiologist. Examinations were performed with the patient lying in the supine position or in the left decubitus position. Left ventricular end-systolic and end-diastolic diameters (LVESD and LVEDD), left ventricular ejection fraction (LVEF) according to Simpson's method, interventricular septum diastolic thickness (IVSd), left ventricular posterior wall diastolic thickness (PWTd), and left atrial diameter (LAD) were measured from parasternal long axis images in accordance with the recommendations of the American Echocardiography Unit.

Measurement of renal Doppler USG parameters

All patients were examined using a Mindray DC 7 ultrasound device (Medical International Limited, Shenzhen, China) with a 3.5 MHz abdominal probe by two experienced, blinded radiologists. After 6 h of fasting, the patient was evaluated after resting for at least 20 min. Firstly, the USG was performed on the grayscale and then the quantitative Doppler parameters, including kidney size, collection system, and parenchyma echogenicity were obtained. Doppler USG parameters, including peak systolic velocity (PSV), end diastolic velocity (EDV), and acceleration time (AT) of both kidneys, were measured from interlobular arteries with a Doppler angle of 30–600 degrees (Fig. 1). After obtaining the PSV and EDV values they were manually drawn on the spectral waveform device and RRIs were automatically obtained according to the following formula: PSV-EDV/PSV. Renal pulsatility index (RPI) was calculated based on the PSV-EDV/average flow rate formula on the spectral waveform. AT was considered as the time from the onset of the gradient until the end of the first peak. The arithmetic mean values of RRI, RPI, and AT, which were obtained from both kidneys, were recorded.

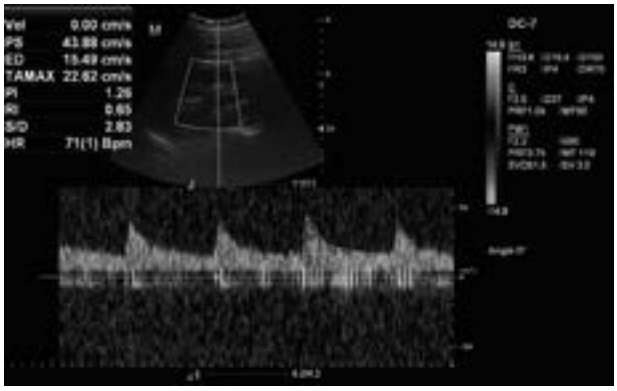

Figure 1. Renal Doppler ultrasonography image demonstrates the measurements of renal Doppler ultrasonography parameters

Statistical analysis

Data analyses were performed using SPSS 22.0 (Chicago, IL, USA) statistical software package. The normal distribution of continuous variables was assessed using the Kolmogorov-Smirnov test. Continuous variables were expressed as mean ± standard deviation and categorical variables were expressed as number and percentage. Comparison of categorical variables between the two groups was performed using the χ^2 test. Comparisons of continuous variables between the two groups were performed using the independent samples T-test. Correlation analysis was performed using the Spearman's rank correlation analysis. All significant parameters ($p < 0.1$) in the univariate analysis were selected for the multivariate model, and multivariate logistic regression analysis was used to determine the independent predictors of moderate to high SYNTAX score. The coefficient of regression and 95% confidence interval (CI) for each independent variable were calculated. A two-tailed p-value of less than 0.05 was considered as significant.

Table 1. Baseline, clinical, laboratory, medical therapy, echocardiographic, angiographic, and renal Doppler USG characteristics of the patients

Variable	NSTE-ACS (n = 112)	STE-ACS (n = 123)	p
Demographic and clinical findings			
Gender, female	22 (19.6%)	18 (14.6%)	0.321
Age [year]	56.4 ± 10.0	54.5 ± 10.5	0.167
Height [cm]	169.9 ± 0.1	170.8 ± 0.1	0.922
Weight [kg]	79.4 ± 14.1	82.0 ± 13.2	0.155
BMI [kg/m^2]	27.4 ± 4.0	28.1 ± 4.2	0.141
Family history	56 (50.0%)	62 (50.4%)	0.926
Diabetes mellitus	46 (41.1%)	24 (19.5%)	**< 0.001**
Hyperlipidaemia	26 (23.2%)	14 (11.4%)	**0.013**
Hypertension	49 (43.8%)	42 (34.1%)	0.100
Smoking status	41 (36.6%)	65 (52.8%)	**0.017**
Laboratory findings			
Haemoglobin level [g/dL]	16.0 ± 16.8	14.7 ± 3.3	**0.003**
Platelets [10^3/uL]	240.6 ± 57.7	260.7 ± 99.6	0.068
HDL-C [mg/dL]	39.7 ± 10.8	37.5 ± 10.1	0.125
LDL-C [mg/dL]	142.3 ± 43.8	136.3 ± 41.3	0.301
Total cholesterol [mg/dL]	206.1 ± 49.6	192.6 ± 43.5	**0.032**
Triglyceride [mg/dL]	204.7 ± 171.9	176.5 ± 108.4	0.507
Creatinine [mg/dL]	0.8 ± 0.2	0.9 ± 0.2	0.092
eGFR [mL/min/1.73 m^2]	95.4 ± 14.3	93.6 ± 16.9	0.408
Uric acid [mg/dL]	5.2 ± 1.2	5.7 ± 3.6	0.439
Troponin I [ng/mL]	0.9 ± 5.3	2.8 ± 8.0	**< 0.001**
Medical therapy			
Antithrombotic:	108 (96.4%)	123 (100%)	**< 0.001**
clopidogrel	85(78.7%)	21(17.0%)	**< 0.001**
prasugrel	2(1.9%)	48(39.0%)	**< 0.001**
ticagrelor	21(19.4%)	54(43.9%)	**< 0.001**
ACE-I/ARB	96 (85.7%)	111 (90.2%)	0.284
Aspirin	112 (100%)	123 (100%)	*
Beta-blockers	106 (94.6%)	114 (92.7%)	0.539
CCB	4 (3.6%)	0 (0.0%)	**0.035**
Statin	103 (92.0%)	119 (96.7%)	0.109
Echocardiographic and angiographic findings			
LVEF [%]	60.3 ± 9.4	51.4 ± 9.7	**< 0.001**
IVSd [mm]	10.8 ± 2.6	11.4 ± 2.5	**0.024**
LAD [mm]	34.2 ± 4.7	33.9 ± 4.6	0.884
LVEDD [mm]	45.2 ± 9.2	46.1 ± 5.9	0.364
PWTd [mm]	11.7 ± 3.1	12.3 ± 2.6	**0.008**
LVESD [mm]	31.3 ± 6.0	32.8 ± 5.6	**0.042**
SYNTAX score	15.4 ± 9.7	21.1 ± 11.9	**< 0.001**
Renal Doppler USG findings			
AT [ms]	33.3 ± 20.7	37.2 ± 17.6	**0.026**
RPI	1.26 ± 0.29	1.23 ± 0.33	0.454
RRI	0.69 ± 0.06	0.67 ± 0.07	**0.032**

Data are presented as the number (%) of patients or mean value ± standard deviation. *P value cannot be calculated because aspirin use is fixed; NSTE-ACS — non–ST-segment elevation acute coronary syndrome; STE-ACS — ST-segment elevation acute coronary syndrome; BMI — body mass index; HDL-C — high-density lipoprotein cholesterol; LDL-C — low-density lipoprotein cholesterol; eGFR — estimated glomerular filtration rate; ACE-I — angiotensin converting enzyme inhibitor; ARB — angiotensin receptor blocker; CCB — calcium channel blocker; LVEF — left ventricular ejection fraction; IVSd — interventricular septum thickness at diastole; LAD — left atrial diameter; LVEDD — left ventricular end-diastolic diameter; PWTd — posterior wall thickness at diastole; LVESD — left ventricular end-systolic diameter; SYNTAX — synergy between PCI with TAXUS™ and cardiac surgery; USG — ultrasonography; AT — acceleration time; RPI — renal pulsatility index; RRI — renal resistive index

RESULTS

A total of 235 patients (40 female; mean age: 55.4 ± 10.3 years) were included in this study. There were 112 patients (22 female; mean age: 56.4 ± 10.0 years) in the NSTE-ACS group and 123 patients (18 female; mean age: 54.5 ± 10.5 years) in the STE-ACS group.

Diabetes mellitus and hyperlipidaemia ratios were significantly higher in the NSTE-ACS group, whereas the smoking ratio was significantly higher in the STE-ACS group. Mean haemoglobin and total cholesterol levels were significantly higher in the NSTE-ACS group, whereas mean troponin I level was significantly higher in the STE-ACS group. In addition, mean LVEF was significantly higher in the NSTE-ACS group, whereas mean values of IVSd, PWTd, and LVESD were significantly higher in the STE-ACS group.

In comparison with the NSTE-ACS group, mean values of SYNTAX score and AT were significantly higher in the STE-ACS group. On the other hand, mean RRI was significantly higher in the NSTE-ACS group. Baseline, clinical, laboratory, medical therapy, echocardiographic, angiographic, and renal Doppler USG characteristics of the patients are shown in Table 1.

Results of correlation analysis of SYNTAX scores

The SYNTAX scores of patients with NSTE-ACS were significantly associated with gender ($p = 0.042$), height ($p = 0.036$), plasma uric acid level ($p = 0.010$), LAD ($p = 0.009$), LVEDD ($p = 0.022$), LVESD ($p = 0.022$), RPI ($p = 0.035$), and RRI ($p = 0.011$) (Fig. 2). On the other hand, the SYNTAX scores of patients with STE-ACS were significantly associated with LDL-C ($p = 0.012$), total cholesterol ($p = 0.003$), LVEF ($p = 0.017$), and LVESD ($p = 0.045$). The results of correlation analysis of SYNTAX scores are shown in Table 2.

Results of correlation analysis of renal resistive indices

Renal resistive indices of patients with NSTE-ACS were significantly associated with age ($p = 0.040$), haemoglobin level ($p = 0.039$), LAD ($p = 0.001$), the SYNTAX score ($p = 0.011$), AT ($p < 0.001$), and RPI ($p < 0.001$). On the other hand, RRIs of patients with STE-ACS were significantly associated with weight ($p = 0.013$), BMI ($p = 0.017$), IVSd ($p = 0.019$), PWTd ($p = 0.020$), LVEF ($p = 0.019$), and RPI ($p < 0.001$). Results of correlation analysis of renal resistive indices are shown in Table 3.

Independent predictors of SYNTAX score

Multivariable logistic regression analysis revealed no independent predictors of moderate to high (> 22) SYNTAX score in patients with STE-ACS. On the other hand, LVESD ($\beta = 0.385$, 95% CI 1.065–2.029, $p = 0.019$), RRI ($\beta = 32.230$, 95% CI 5343.15–2.E+24, $p = 0.008$), and RPI ($\beta = -7.439$, 95% CI 0.000–0.231, $p = 0.015$) were independent predictors of moderate to high SYNTAX score in patients with NSTE-ACS. Independent predictors of SYNTAX score in patients with NSTE-ACS are shown in Table 4.

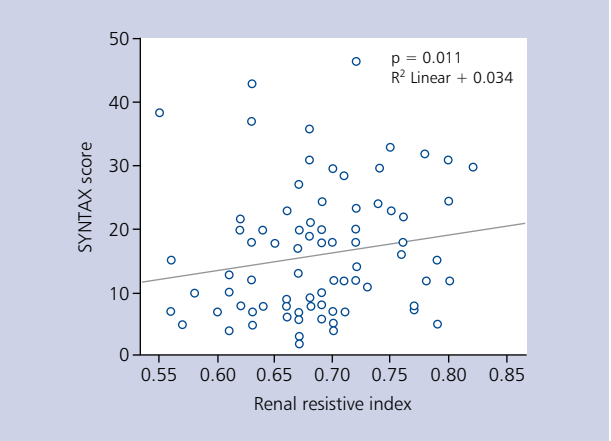

Figure 2. Scatter plot graph demonstrates the relationship between renal resistive index and SYNTAX score in patients with non–ST-segment elevation acute coronary syndrome

DISCUSSION

In our study, RRI and RPI were independent predictors of moderate to high SYNTAX score in patients with NSTE-ACS. The precise mechanisms of the increased SYNTAX score with increasing RRI are uncertain. A histologic study has shown that renal atherosclerosis is the only independent risk factor for increased RRI [9]. Atherosclerosis is a systemic process, and the pathophysiology is almost the same in all vessels involved. On this basis, there can be an association between the extent and complexity of atherosclerotic CAD and RRI. There are no studies in the literature regarding this subject. This relationship was first described in our study, and it was shown that RRI is directly related to clinical atherosclerosis. Although the underlying reason for the lack of correlation between RRI and SYNTAX score in patients with STE-ACS is unknown, the abrupt increase in SYNTAX score due to a complete occlusion of the coronary artery with thrombus formation in these patients may not reflect the chronic atherosclerotic process.

Evaluation of renal haemodynamics is possible by analysing intrarenal arterial waves obtained with Doppler USG. PSV-DSV/PSV-derived RRI is the most widely used measurement of renal Doppler USG [10]. RRI has recently been used for the diagnosis and prognosis of several clinical entities, including detection of renal allograft rejection [11], evaluation of renal arteries in hypertensive patients [4], evaluation of progression in CKD [6], and prediction of renal adverse outcomes in critically ill patients [12]. RRI is actually a result of complex haemodynamic interactions between the kidney and systemic vessels. However, most of these interactions

Table 2. Results of correlation analysis of SYNTAX scores of the patients

Variable	NSTE-ACS (n = 112)		STE-ACS (n = 123)	
	ρ	p	ρ	p
Demographic and clinical findings				
Age [year]	0.060	0.551	0.167	0.067
Gender, female	–0.199	**0.042**	0.139	0.127
Height [cm]	0.210	**0.036**	-0.101	0.268
Weight [kg]	0.185	0.066	-0.091	0.320
BMI [kg/m^2]	0.078	0.441	-0.03	0.740
Diabetes mellitus	0.127	0.208	0.058	0.524
Hyperlipidaemia	–0.091	0.366	0.120	0.190
Hypertension	0.111	0.270	0.122	0.182
Smoking status	–0.075	0.456	0.060	0.516
Laboratory findings				
Haemoglobin level [g/dL]	0.139	0.167	–0.126	0.169
Platelets [10^3/uL]	–0.052	0.610	0.113	0.219
HDL-C [mg/dL]	–0.126	0.223	0.167	0.073
LDL–C [mg/dL]	0.074	0.474	0.231	**0.012**
Total cholesterol [mg/dL]	0.090	0.382	0.267	**0.003**
Triglyceride [mg/dL]	0.020	0.850	0.050	0.592
Creatinine [mg/dL]	0.083	0.410	0.011	0.902
eGFR [mL/min/1.73 m^2]	–0.077	0.448	–0.113	0.217
Uric acid [mg/dL]	0.280	**0.010**	–0.066	0.483
Troponin I [ng/mL]	0.020	0.850	0.114	0.212
Echocardiographic and angiographic findings				
LVEF [%]	–0.158	0.121	–0.217	**0.017**
IVSd [mm]	0.132	0.194	–0.008	0.930
PWTd [mm]	–0.020	0.846	–0.138	0.130
LAD [mm]	0.263	**0.009**	–0.067	0.465
LVEDD [mm]	0.231	**0.022**	0.164	0.070
LVESD [mm]	0.232	**0.022**	0.182	**0.045**
Renal Doppler USG findings				
AT [ms]	0.142	0.150	0.037	0.683
RPI	0.194	**0.035**	0.104	0.126
RRI	0.233	**0.011**	0.034	0.354

NSTE-ACS — non–ST-segment elevation acute coronary syndrome; STE-ACS — ST-segment elevation acute coronary syndrome; ρ — Spearman's rank correlation coefficient; BMI — body mass index; HDL-C — high-density lipoprotein cholesterol; LDL-C — low-density lipoprotein cholesterol; eGFR — estimated glomerular filtration rate; LVEF — left ventricular ejection fraction; IVSd — interventricular septum thickness at diastole; LAD — left atrial diameter; LVEDD — left ventricular end-diastolic diameter; PWTd — posterior wall thickness at diastole; LVESD — left ventricular end-systolic diameter; USG — ultrasonography; AT — acceleration time; RPI — renal pulsatility index; RRI — renal resistive index

are not entirely understood yet [10]. In the 1950s, it was presumed that the name of RRI would merely reflect renal vascular resistance. However, this assumption has gradually declined recently. Indeed, theoretical analyses and artificial experiments have shown that the complex interaction between arterial resistance and compliance can alter the Doppler artery wave pattern [13]. For example, as arterial compliance increases, RRI is more affected by arterial resistance and vice versa [13]. Likewise, impaired renal vascular compliance and increased pulse pressure resulted in a significant increase in RRI [14]. In addition, an inverse relationship between RRI and mean arterial or diastolic blood pressure was reported in the general population [15] and hypertensive patients [16], and RRI was reduced with a higher renal vascular resistance in transplanted kidneys [17]. Actually, these findings reveal that RRI is a product of a complex interaction between renal

Table 3. Results of correlation analysis of renal resistive indices of the patients

Variable	NSTE-ACS (n = 112)	
	ρ	p
Age [year]	0.173	0.040
Haemoglobin level (g/dL]	–0.175	0.039
LAD [mm]	0.318	0.001
SYNTAX score	0.233	0.011
AT [ms]	0.330	< 0.001
RPI	0.695	< 0.001
Variable	**STE-ACS (n = 123)**	
	ρ	p
Weight [kg]	–0.203	0.013
BMI [kg/m^2]	–0.194	0.017
IVSd [mm]	–0.189	0.019
PWTd [mm]	–0.189	0.020
LVEF [%]	0.190	0.019
RPI	0.828	< 0.001

NSTE-ACS — non–ST-segment elevation acute coronary syndrome; ρ — Spearman's rank correlation coefficient; LAD — left atrial diameter; SYNTAX — synergy between PCI with TAXUS™ and cardiac surgery; AT — acceleration time; STE-ACS — ST-segment elevation acute coronary syndrome; BMI — body mass index; IVSd — interventricular septum thickness at diastole; PWTd — posterior wall thickness at diastole; LVEF — left ventricular ejection fraction; RPI — renal pulsatility index

interstitial pressure, peripheral vascular resistance and compliance, and systemic haemodynamics [10].

Arterial compliance is the main determinant of the pulsatile component of blood pressure. During systole, the aortic elastic wall expands and reduces pulsatility, and thus accommodates the sprayed blood from the heart to peripheral organs, including the kidneys, and provides controlled peripheral blood flow. Vascular wall stiffness associated with aging is more prominent in the aorta than in peripheral arteries, therefore a partial microcirculation protection in organs with high flow rates, such as the kidney, is observed [18]. In fact, increased pulsatile stress causes damage in the endothelial and smooth muscle cells of renal arteries [19]. For this reason, the relationship between RRI and central (aortic) pulse pressure or peripheral (brachial) pulse pressure has been investigated in several studies. In all of these studies, a significant and direct correlation between RRI and central or peripheral pulse pressures was demonstrated [15, 20]. Another factor affecting RRI is the amount of renal blood flow. 12–25% of the renal blood flow depends on the volume of the left ventricular blood during systole. Therefore, a reduction in preload may affect RRI. Gender, age, height, and weight are other factors that affect RRI [15, 20].

It has been suggested that RRI, measured in transplanted kidney in renal allograft patients, is significantly related not to the age of the kidney but to the age of the recipient [21]. Thus, extrinsic factors such as the aorta and prerenal vessels have been proposed to have a great effect on renal Doppler indices. In several studies, the relationship between RRI of renal transplanted kidney and cardiovascular disease was investigated and, irrespective of creatinine clearance of the graft, a correlation was determined between RRI and ankle-arm index [22], and carotid-femoral pulse wave velocity [23]. Studies in hypertensive patients have also demonstrated a correlation between RRI and arterial stiffness index [24], RRI and central pulse pressure, and RRI and aortic stiffness [16]. Therefore, RRI should be considered as a specific marker for systemic atherosclerotic vessel injury rather than renal damage.

Previous studies have shown that antihypertensive agents can affect RRI [9, 25]. In our study, there were a number of patients with NSTE-ACS, who were using calcium channel blockers. Leoncini et al. [25] reported that nifedipine did not affect RRI. In our study, we found that the use of calcium

Table 4. Independent predictors of SYNTAX score in patients with non-ST-segment elevation acute coronary syndrome

Variable	β	95% confidence interval		p
		Lower limit	Upper limit	
Gender	1.171	0.065	160.647	0.557
Height [cm]	3.869	0.000	4.6E+9	0.680
Weight [kg]	0.005	0.922	1.096	0.908
Uric acid [mg/dL]	0.467	0.761	3.342	0.217
LAD [mm]	–0.026	0.771	1.231	0.828
LVESD [mm]	0.385	1.065	2.029	**0.019**
LVEDD [mm]	–0.250	0.566	1.071	0.123
Renal resistive index	32.230	5343.15	2.E+24	**0.008**
Renal pulsatility index	–7.439	0.000	0.231	**0.015**

β — beta coefficient; LAD — left atrial diameter; LVESD — left ventricular end-systolic diameter; LVEDD — left ventricular end-diastolic diameter

channel blockers was seen in four patients only, thus its effect can be negligible.

Limitations of the study

Our single-centre study included a certain number of patients. A multicentre study involving more patients could have more significant results and data. In addition, some patients were using drugs at different doses prior to RRI measurement, and the potential effects of these drugs were not assessed in our study.

CONCLUSIONS

Instead of being considered as a specific marker for kidney damage, RRI is a result of the complex interaction between many factors and is closely associated with the angiographic extent and complexity of CAD in patients with NSTE-ACS.

Conflict of interest: *none declared*

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Ocena związku między wskaźnikiem oporu tętnic nerkowych a rozległością i złożonością choroby wieńcowej u pacjentów z ostrym zespołem wieńcowym

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Streszczenie

Wstęp: Mimo postępu w zakresie leczenia chorób sercowo-naczyniowych ostry zespół wieńcowy (ACS) jest nadal główną przyczyną chorób i zgonów na całym świecie. Zbieżność między przezskórną interwencją wieńcową z wszczepieniem stentu uwalniającego tacrolimus TAXUS™ a wskaźnikiem SYNTAX stosuje się do oceny rozległości i złożoności choroby wieńcowej (CAD). Wskaźnik oporu tętnic nerkowych (RRI), parametr określany za pomocą ultrasonografii doplerowskiej, pozwala wykryć istotne hemodynamicznie zwężenia tętnic nerkowych. Chociaż wykazano, że niektóre czynniki ryzyka CAD, w tym nadciśnienie tętnicze i cukrzyca, są powiązane z RRI, bezpośrednia zależność między rozległością i złożonością CAD a wskaźnikiem RRI nie została dotychczas zbadana.

Cel: Celem niniejszej pracy była ocena związku między wskaźnikami RRI i SYNTAX u pacjentów z ACS.

Metody: Do tego przekrojowego badania włączono 235 chorych z rozpoznaniem ACS, u których wykonano koronarografię w ośrodku specjalistycznym autorów w okresie od lutego do sierpnia 2016 r. Na podstawie obrazu klinicznego można wyróżnić dwie grupy chorych: u 112 osób rozpoznano ACS bez uniesienia odcinka ST (NSTE-ACS), a u 123 osób — ACS z uniesieniem odcinka ST (STE-ACS). Odnotowano następujące informacje o uczestnikach: dane demograficzne, parametry kliniczne i laboratoryjne, wyniki badań echokardiograficznych, wskaźnik SYNTAX i parametry uzyskane w badaniu nerek metodą ultrasonografii doplerowskiej, w tym wskaźnik RRI, wskaźnik pulsacyjności (RPI) oraz czas akceleracji (AT).

Wyniki: Spośród 235 uczestników badania u 112 (47,7%) rozpoznano NSTE-ACS, a u 123 (52,3%) — STE-ACS. Średnia wartości wskaźników SYNTAX i RRI u chorych z NSTE-ACS oraz STE-ACS wynosiły odpowiednio 15,4 i 0,69 oraz 21,1 i 0,67. Wskaźnik SYNTAX był związany z płcią, wzrostem, stężeniem kwasu moczowego w osoczu, wymiarem lewego przedsionka, wymiarami końcowoskurczowym i końcoworozkurczowym lewej komory, wskaźnikami RPI i RRI u pacjentów z NSTE-ACS, a także ze stężeniem cholesterolu całkowitego i frakcji LDL, frakcją wyrzutową oraz wymiarem późnoskurczowym lewej komory u chorych ze STE-ACS ($p < 0,05$ dla wszystkich zmiennych). Wskaźnik RRI wiązał się istotnie z wiekiem, stężeniem hemoglobiny, wymiarem lewego przedsionka, wartością wskaźnika SYNTAX, AT i wskaźnikiem RPI u chorych z NSTE-ACS oraz z masą ciała, wskaźnikiem masy ciała, grubością przegrody międzykomorowej w rozkurczu, grubością tylnej ściany lewej komory w rozkurczu, frakcją wyrzutową lewej komory i wskaźnikiem RRI u chorych ze STE-ACS. W wielozmianowej analizie regresji logistycznej wykazano, że wymiar późnoskurczowy lewej komory ($\beta = 0,385$; 95% CI 1,065–2,029; $p = 0,019$),wskaźnik RRI ($\beta = 32,230$; 95% CI 5343,15–2.E+24; $p = 0,008$) i wskaźnik RPI ($\beta = -7,439$; 95% CI 0,000–0,231; $p = 0,015$) były niezależnymi czynnikami predykcyjnymi średniej lub wysokiej wartości wskaźnika SYNTAX u pacjentów z NSTE-ACS.

Wnioski: Wskaźnik RRI w badaniu nieinwazyjnym jest ściśle związany z rozległością i złożonością CAD u chorych z NSTE-ACS. Jednak potrzebne są randomizowane badania z grupą kontrolną obejmujące szerszą populację.

Słowa kluczowe: ostry zespół wieńcowy, choroba wieńcowa, wskaźnik SYNTAX, wskaźnik oporu tętnic nerkowych

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