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Prognostic value of red blood cell distribution width (RDW) in patients with multi-vessel coronary artery disease.

Wartość prognostyczna współczynnika zmienności rozkładu objętości erytrocytów (RDW) u pacjentów z wielonaczyniową chorobą wieńcową.

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ABSTRACT

Introduction. Coronary artery disease (CAD) is one of the most common cardiovascular problems and a frequent cause of death worldwide. Multi-vessel CAD is an advanced condition in which the lumen of ≥ 3 epicardial arteries becomes narrowed due to atherosclerosis. The red blood cell distribution width (RDW) is a simple parameter of blood count, expressing the anisocytosis of erythrocytes. Higher value of RDW may be related with adverse outcomes in patients with cardiovasculare diseases. We examined the association between RDW and the risk of all-cause mortality and adverse cardiovascular outcomes in patients with multi-vessel CAD.

Material and methods. The study was performed on 112 patients with multi-vessel CAD hospitalised in the Cardiology Department of the Central Clinical Hospital Medical University in Lodz. Demographic, clinical characteristics and 12-months follow-up were performed.

Results. 75% of patients with multi-vessel CAD were men. The average age was 68.2 years and the average BMI was 29.3 kg/m^2. The most common comorbidities were hypercholesterolemia (94%), hypertension (91%), smoking (71%) and diabetes (45%). Most patients presented severe symptoms of angina pectoris in CCS class III (60%) and class IV (10%). The mean RDW was 13.5% (12.8–14.6). In patients with multi-vessel CAD, there was no correlation between RDW and CCS class ($R = 0.05$, $p = 0.6296$), left ventricular ejection fraction ($R = 0.03$, $p= 0.7457$), death rate in 1-year follow-up ($p = 0.1438$) and myocardial infarction ($p = 0.6592$.). Patients who experienced acute or decompensated heart failure (HF) had higher RDW ($p = 0.0420$).

Conclusions. Contrary to the data available in the literature regarding patients with stable CAD, in the group of patients with multi-vessel CAD, no impact of RDW on mortality or myocardial infarction was observed. However, in the analysis higher RDW was demonstrated to be an independent predictor for a new onset of HF or chronic HF decompensation in patients with multi-vessel CAD.

Key words: multivessel coronary artery disease, red blood cell distribution width, heart failure, risk factor

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INTRODUCTION

The red blood cell distribution width (RDW) is a simple parameter, expressing the heterogenity of erythrocytes volumes in the blood sample (known as anisocytosis), and is commonly used in laboratory hematology for diagnosis of anemias. The reference RDW falls within the range 11% to 15%. The value below the reference range has no clinical significance, whereas an increased RDW value means a greater difference in the size of red blood cells (RBCs), due to the escalated or ineffective production of RBCs and exaggerated fragmentation or destruction of RBCs.

The RDW is being considered as a novel inflammatory predictor in various medical conditions including autoimmune diseases, cancer, kidney failure, also in other acute or chronic diseases as well.

Since both RDW and cardiovascular conditions are associated with inflammation, RDW could also be related with cardiovascular diseases. The study by S. Ananthaseshan et al. showed the increased interactions of blood cells with vascular wall in conditions of high RDW. This can also be a source of oxidative stress in the vessel which can initiate endothelial damage and development of atherosclerosis [1].

The studies revealed that higher RDW, even within the reference range, was associated with increased risk of adverse cardiovascular outcomes and death [2].

Cardiovascular diseases are the most common cause of death worldwide (according to WHO > 17.5 million death each year) comparable to cancer and communicable diseases. Multi-vessel coronary artery disease (CAD) is an advanced form of the illness in which the lumen of ≥ 3 epicardial arteries becomes narrowed due to atherosclerosis.

Recent studies suggested that RDW may be a predictive biomarker of morbidity and mortality in cardiovascular diseases. However, there are no studies on the RDW in patients with multivessel CAD.

MATERIAL AND METHODS

Study design and population

The study retrospectively enrolled patients who were diagnosed with multi-vessel coronary artery disease for the first time in coronarography at the Department of Cardiology Central Clinical Hospital Medical University of Lodz in 2017–2018.

Patients with myocardial infarction, severe valve disease, active cancer, were excluded from the study.

The data, such as demographics, comorbidities, laboratory parameters, echocardiography, angiography, was collected from the electronic medical record system of Central Clinical Hospital Medical University of Lodz.

Patients were followed up after 12 months by telephone contact, and asked about multiple adverse endpoints, such as myocardial infarction, new revascularisation, all-cause hospitalization, new onset of acute heart failure or heart failure decompensation and all-cause death.

The study protocol was approved by the Bioethics Committee of the Medical University of Lodz Each participant expressed informed consent during telephone contact.

The aim of this study was to investigate the relation of RDW and aggravation of CAD symptoms. Moreover, it tested the hypothesis that higher RDW was associated with risk of adverse cardiovascular outcomes and all-cause mortality in the population of patients with multi-vessel CAD.

Subjects' demographic and clinical data

Patient characteristics, such as gender, age, and body mass index (BMI), were collected. Clinical information was also obtained from the medical record: left ventricular ejection fraction (EF), Canadian Cardiovascular Society (CCS) class, the history of cigarette smoking, comorbidities as arterial hypertension, hyperlipidaemia, diabetes, chronic kidney disease, and blood tests, such as the hemoglobin concentration (HGB), hematocrit (HCT), white blood cell count (WBC), platelet count (PLT), RDW, low-density lipoproteins (LDL), high-density lipoproteins (HDL), triglycerides (TG) and estimated glomerular filtration rate (eGFR). After 12 months since the diagnosis of multi-vessel CAD, the information of adverse endpoints was gathered through telephone. Three were selected for analysis: all-cause death, myocardial infarction and new onset of acute heart failure or heart failure decompensation.

Data analysis

Statistical analysis was done using Statistica 13.3 (TIBCO Inc.). Categorical data was presented as numbers and as a percentage of the study population. The normal distribution of continuous variables was tested using the Shapiro–Wilk test. In order to describe the central tendency and

dispersion for variables with a normal or near-normal distribution, means and standard deviations were calculated, while for ordinal and continuous variables with a significantly different distribution from normal — the median and interquartile range. To assess the correlation between numerical parameters, the Spearman correlation coefficient was calculated. The relationship between the values of numerical parameters and the occurrence of individual endpoints was tested using the nonparametric Mann–Whitney U test and the Student t–test. P-values less than 0.05 were considered statistically significant.

RESULTS

112 patients were enrolled in the study. The majority of patients with multi-vessel CAD were men (75%) . The average age was 68.2 years and the average BMI was 29.3 kg/m^2. The most common comorbidities were hypercholesterolemia (94%), hypertension (91%), smoking (71%) and diabetes (45%). Most patients presented severe symptoms of angina pectoris in CCS class III (60%) and class IV (10%). The detailed characteristics of the study population are shown in Table 1.

The mean haemoglobin concentration was 13.9 g/dL (1.4), hematocrite: 41,8 % (4.1), RDW: 13.5 % (12.8–14.6) and CRP was 2.7 mg/L (1.3–5.9). The rest of biochemical parameters are presented in Table 2.

The analysis showed that in patients with multi-vessel CAD, there is no correlation between RDW and severity of symptoms according to CCS class (R = 0.05, p = 0.6296) and left ventricular ejection fraction (R = 0.03, p = 0.7457) respectively. There was no correlation between RDW neither with the patient's death (p = 0.1438) nor myocardial infarction (p = 0.6592.). Patients who experienced HF decompensation had, on average, higher RDW, p = 0.0420. The exact data is presented in Table 4 and Figure 1.

DISCUSSION

Several studies have shown the association between RDW and cardiovascular diseases, including CAD. However, no studies have investigated multi-vessel CAD. Therefore, analysis in this report is an original study and provides unique data on this advanced form of CAD.

Due to the data available in the literature RDW were associated with high SYNTAX score indicating the complexity and advancement of coronary lesions in patients with stable CAD [3] as well non-ST-elevation myocardial infarction (NSTEMI), but were not correlated with long-term mortality in patients with NSTEMI [4]. Moreover, RDW is an independent predictor of mortality in patients with stable CAD, higher RDW values correspond to higher comorbidity and higher mortality [5]. In patients with heart failure increased RDW is associated with poor prognosis, independent of clinical risk factors. RDW was also a strong independent predictor of hospitalization

and mortality from HF decompensation [6]. In subjects with no HF history, increased RDW is also related to higher HF risk [7].

Opposite to the data available in the literature regarding patients with stable coronary artery disease or acute coronary syndrome, in the group of patients with multi-vessel CAD no impact of RDW on mortality or myocardial infarction was observed. This may be related to the fact that RDW in cardiovascular patients is associated with a greater degree of coronary artery calcification and, consequently, a greater degree of disease advancement and the risk of ACS and death. Patients with multi-vessel CAD are initially a group of patients with significantly higher risk of adverse vascular events and death, therefore in the study group, RDW did not have a substantial impact on their occurrence.

However, in this study, in patients with multi-vessel CAD, RDW demonstrated to be an independent predictor for heart failure decompensation or new onset of acute heart failure, which is also reflected in the available literature on the relationship between RDW and the occurrence of heart failure in the general population and in the population of patients with ischemic heart failure.

LIMITATIONS

This study was retrospective and involved only one medical centre. During the one-year follow-up, patients were treated in various ways: optimal pharmacotherapy, surgical revascularization (coronary artery bypass graft - CABG) or percutaneous revascularization (percutaneous coronary intervention – PCI). The groups were not sufficient to perform a statistical analysis regarding the impact of RDW on prognosis depending on the method of treatment of multivessel CAD.

CONCLUSIONS

Higher RDW was significantly related to increased risks, and was demonstrated to be an independent predictor, of acute HF or HF decompensation in population of patients with multi-vessel CAD.

STRESZCZENIE

Wstęp. Przewlekła choroba wieńcowa (CAD, *coronary artery disease*) jest jedną z głównych manifestacji chorób sercowo-naczyniowych i częstą przyczyną zgonów na świecie. Wielonaczyniowa postać choroby wieńcowej jest jej zaawansowaną formą, w której dochodzi do zwężenia światła ≥ 3 tętnic nasierdziowych w przebiegu miażdżycy. Współczynnik zmienności rozkładu objętości erytrocytów (RDW, *red blood cell distribution width*) jest prostym parametrem morfologii krwi, wyrażającym stopień anizocytozy. Podwyższony RDW może być związany z niekorzystnymi zdarzeniami u pacjentów z chorobami sercowo-naczyniowymi.

Zbadano związek RDW z ryzykiem śmiertelności z dowolnej przyczyny oraz poważnych zdarzeń sercowo-naczyniowych u chorych z wielonaczyniową CAD.

Materiał i metody. Do badania włączono 112 kolejnych pacjentów z wielonaczyniową CAD, hospitalizowanych w Klinice Kardiologii Centralnego Szpitala Klinicznego Uniwersytetu Medycznego w Łodzi. Analizie poddano dane demograficzne, charakterystykę kliniczną oraz 12-miesięczny okres obserwacji pacjentów.

Wyniki. 75% pacjentów z wielonaczyniową CAD stanowili mężczyźni. Średnia wieku wyniosła 68,2 lata, a średnie BMI 29,3kg/m^2. Najczęstszymi chorobami współistniejącymi były hipercholesterolemia (94%), nadciśnienie tętnicze (91%), nikotynizm (71%), cukrzyca (45%). Większość pacjentów z wielonaczyniową CAD prezentowała nasilone objawy dławicy piersiowej w III (60%) i IV (10%) kl. CCS. Średnia wartość RDW wynosiła 13,5% (12,8–14,6). Wśród pacjentów z wielonaczyniową CAD nie stwierdzono związku RDW z klasą CCS (R = 0,05, p= 0,6296), i frakcją wyrzutową lewej komory (R = 0,03, p= 0,7457), oraz z wystąpieniem śmierci (p = 0,1438) lub zawału mięśnia sercowego w ciągu roku (p = 0,6592.). Pacjenci z rozpoznaniem ostrej niewydolności serca lub zaostrzeniem przewlekłej niewydolności serca prezentowali wyższy RDW (p = 0,0420).

Wnioski. Przeciwnie do danych dostępnych w literaturze, dotyczących ogółu pacjentów z CAD, u chorych w wielonaczyniową postacią CAD nie stwierdzono wpływu RDW na śmiertelność czy wystąpienie zawału serca. Jednak zarejestrowano istotną korelację między wyższym RDW, a wystąpieniem ostrej niewydolności serca lub zaostrzeniem przewlekłej niewydolności serca w tej grupie chorych.

Słowa kluczowe: wielonaczyniowa choroba wieńcowa, współczynnik zmienności rozkładu objętości erytrocytów, niewydolność serca, czynnik ryzyka

ARTICLE INFORMATION

Author contributions. MC — concept author, study design, data collection, analysis and interpretation of results, writing of the publication; JD — concept author, revision of the manuscript, approval of final version of article.

Conflict of interest. The authors declare no conflict of interest.

Ethics statement. The study complied with the Declaration of Helsinki and was approved by the local medical ethics committee.

Data Availability Statement. Source data from the literature describe the relationship between the RDW and cardiovascular diseases. In this study, the authors tried to address the issue of the impact of the RDW on the prognosis of patients with multi-vessel coronary artery disease.

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Table 1. Characteristics of the study group — clinical and demographic data

Gender Women (n, %) Men (n, %)	 28 (25%) 84 (75%)
Age (mean, SD)	68.2 (9,0)
BMI (mean, SD)	29.3 (4,8)
Nicotine addiction (n, %)	79 (71%)
Diabetes mellitus (n, %)	50 (45%)

Hypertension (n, %)	102 (91%)
Hyperlipidaemia (n, %)	105 (94%)
CKD (n, %)	37 (33%)
CCS scale I (n, %) II (n, %) III (n, %) IV (n, %)	 1 (1%) 33 (29%) 67 (60%) 11 (10%)
EF (median, 1st–3rd quartile)	52.5 (42.5–60.0)

% — a percentage of 112 patients; BMI — body mass index; CCS — Canadian Cardiovascular Society angina grade; CKD — chronic kidney disease defined as glomerular filtration rate < 60 mL/min/1.73 m^2; EF – ejection fraction; n — number of patients; SD — standard deviation.

Table 2. Characteristics of a study group — biochemical parameters

HGB [g/dL] (mean, SD)	13.9 (1.4)
HCT (%) (mean, SD)	41.8 (4.1)
RDW (%) (median, 1st–3rd quartile)	13.5 (12.8–14.6)
PLT (*10^3/μL) (mean, SD)	223.2 (62.1)
WBC (*10^3 /μL) (median, 1st–3rd quartile)	7.0 (6.1–8.1)
eGFR (mL/min/1,73 m^2) (1st–3rd quartile)	70.0 (54.5–89.0)
CRP (mg/L (1st–3rd quartile)	2.7 (1.3–5.9)
LDL (mmol/l) (mean, SD)	3.6 (9.4)
HDL (mmol/l) (mean, SD)	1.2 (0.3)
TG (mmol/L) (1st–3rd quartile)	1.4 (1.0–2.1)

eGFR — estimated glomerular filtration rate; HCT — hematocrite; HDL — high-density lipoprotein; Hgb — haemoglobin; LDL — low-density lipoprotein; PLT — platelet count; RBC — red blood cells; RDW — red blood cell distribution width; SD — standard deviation; TG — triglycerides; WBC — white blood cells.

Table 3. Characteristics of a study group — endpoints

Death (n, %)	12 (11%)
Hospitalization (n, %)	39 (35%)
MI (n, %)	9 (8%)
Revascularisation (n, %)	14 (13%)
HF decompensation (n, %)	13 (12%)

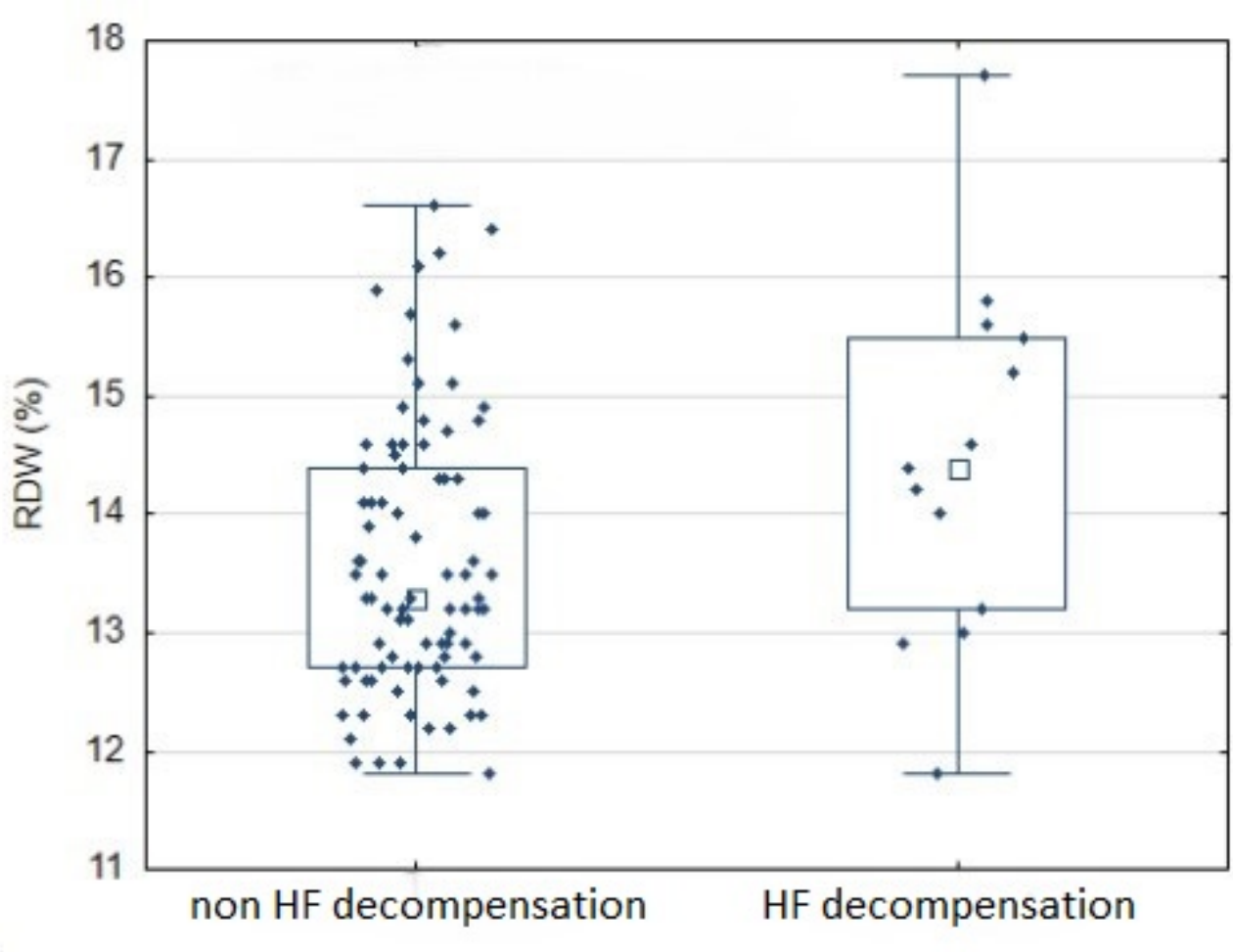
% — a percentage of 112 patients; HF — heart failure; MI — miocardial infarction; n — number of patients.

Table 4. Endpoints in correlation with RDW

	RDW Median (1st–3rd quartile)		
	yes	no	p
Death	14.3 (13.2–14.8)	13.3 (12.7–14.6)	0.1438
MI	13.6 (13.0–14.5)	13.4 (12.7–14.6)	0.6592
HF decompensation	14.4 (13.2–15.5)	13.3 (12.7–14.4)	0.0420

HF — heart failure; MI — miocardial infarction.

Figure 1. Correlation between RDW and new onset of acute heart failure (HF) or heart failure decompensation.


18
17
16
15
14
13
12
11
RDW (%)
non HF decompensation
HF decompensation