ARTYKUL ORYGINALNY / ORIGINAL ARTICLE

Raised red cell distribution width as a prognostic marker in aortic valve replacement surgery

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Abstract

Background and aim: Several studies have reported that elevated red cell distribution width (RDW) is associated with poor outcomes in patients with coronary artery disease, chronic heart failure and aortic stenosis following transcatheter aortic valve replacement. Their prognostic utility in patients undergoing aortic valve replacement (AVR) surgery is unknown.

Methods: We prospectively evaluated the prognostic value of RDW in a group of 191 consecutive patients with severe symptomatic aortic stenosis undergoing AVR. The pre-defined primary endpoint at the 30-day follow-up was composed of: all cause mortality, perioperative myocardial infarction, perioperative renal failure, prolonged mechanical ventilation, stroke, heart failure, successfully resuscitated cardiac arrest, the occurrence of multiple-organ failure, and the need for additional surgery for any reason. The secondary endpoint was total mortality.

Results: The composite endpoint occurred in 54 patients. In univariate analysis RDW (p < 0.0001), haemoglobin level (p = 0.005), haematocrit (p = 0.01), red blood cell count (RBC; p = 0.002), glomerular filtration rate (p = 0.003), New York Heart Association classification (p = 0.02), atrial fibrillation (p = 0.004), and pulmonary blood pressure (p = 0.004) were associated with the occurrence of the composite endpoint. RDW (p = 0.0005), haemoglobin level (p = 0.004), haematocrit (p = 0.004), RBC (p = 0.0009) and mean corpuscular volume (p = 0.01) were associated with an increased risk of death.

In multivariate analysis, RDW (OR 3.274; 95% CI 1.285–8.344; p = 0.0003) and RBC (OR 0.373; 95% CI 0.176–0.787; p = 0.0097) remained independent predictors of the composite endpoint. Receiver operating characteristic analysis determined a cut-off value of RDW for the prediction of the occurrence of the combined endpoint at 14.1%.

Conclusions: Elevated RDW is associated with a worse outcome following AVR, independent of RBC.

Key words: aortic stenosis, valve disease surgery, inflammatory markers, risk assessment, red cell distribution width

INTRODUCTION

Red cell distribution width (RDW) is a parameter that reflects the variability of the size of red blood cells. It is calculated automatically or manually by dividing the standard deviation of red blood cell volume and the volume of red blood cells expressed as a percentage. RDW = (standard deviation of mean corpuscular volume [MCV] ÷ mean MCV) × 100. Until now RDW has been used mainly as an auxiliary marker in haematology indicating the increased destruction or impaired production of red blood cells. Several studies have reported that elevated RDW levels are associated with poor outcomes in patients with such cardiovascular diseases as coronary artery disease, idiopathic pulmonary hypertension, chronic heart failure (HF), and severe aortic stenosis after transcatheter aortic valve implantation [1–5]. Its prognostic utility in patients undergoing aortic valve replacement surgery is unknown. Therefore, we attempted to check the prognostic value of RDW in this group of patients.

METHODS

A prospective study was conducted on a group of 191 consecutive patients with severe symptomatic aortic stenosis (a valve area below 1 cm² and a mean pressure gradient ≥ 40 mm Hg), who were undergoing elective aortic valve replacement surgery.
Statistical analysis
Statistical analysis was performed using SPSS software. Univariate analysis followed by multivariate regression analysis was performed. Data are presented as medians with ranges if continuous, or as frequencies if categorical. Results were considered significant when p was less than 0.05. To assess the predictive ability of the RDW, receiver operating characteristic (ROC) curves analysis was used.

RESULTS
One hundred and ninety-one patients after aortic valve replacement surgery with or without other concomitant procedures were examined. In 124 patients a biological aortic valve prosthesis was implanted, and in 67 a mechanical valve. All procedures were performed through a midline sternotomy incision under general anaesthesia in mild systemic hypothermia (temperature 32–34°C).

Table 1 shows the preoperative characteristics of the patients studied. Ten (5.2%) patients had significantly impaired left ventricular systolic function (ejection fraction < 35%) (Table 1).

In the postoperative period, in the 30-day follow-up, death occurred in 10 patients (the first patient died suddenly — cause of death unknown, the second patient died because of early infective endocarditis, seven patients died as a result of gradually increasing multi-organ failure and the tenth patient died due to post-operative bleeding).

We observed the occurrence of the composite endpoint in 54 patients (perioperative renal failure in six patients, prolonged mechanical ventilation for 21 patients, stroke in 45 patients). Seven patients were successfully resuscitated after cardiac arrest, and the occur-
Raised red cell distribution width as a prognostic marker in aortic valve replacement surgery

The occurrence of multi-organ failure was observed in 16 patients. Re-thoracotomy was performed in 20 patients, myocardial infarction occurred in 11 patients. In univariate analysis RDW (p < 0.0001), haemoglobin level (p = 0.005), haematocrit (p = 0.01), red blood cell count (RBC; p = 0.002), glomerular filtration rate (p = 0.003), New York Heart Association classification (p = 0.02), atrial fibrillation (p = 0.0044), and pulmonary blood pressure (p = 0.004) were associated with the occurrence of the composite endpoint at 30-day follow-up. RDW (p = 0.0005), haemoglobin level (p = 0.004), haematocrit (p = 0.004), RBC (p = 0.0009), and mean corpuscular volume (p = 0.01) were associated with an increased risk of death. In multivariate analysis, RDW (OR 3.274; 95% CI 1.285–8.344; p = 0.0003) and RBC (OR 0.373; 95% CI 0.176–0.787; p = 0.0097) remained independent predictors of the composite endpoint. Tables 2 and 3 show the analysis of the predictors of mortality and the composite endpoint.

The real mortality was 5.2 vs. 2.8 expected mortality calculated using EuroSCORE II.

Receiver operating characteristic analysis determined the cut-off value of RDW for the prediction of the occurrence of the composite endpoint at 14.1% (area under curve = 0.7, p = 0.008). Figure 1 depicts Kaplan-Meier event-free survival curves for composite endpoint according to the cut-off value of red cell distribution width (RDW).

Figure 1. Kaplan–Meier event-free survival curves following aortic valve replacement surgery, for composite endpoint according to the cut-off value of red cell distribution width (RDW)

**DISCUSSION**

To our knowledge, this is the first report showing the prognostic significance of RDW in predicting complications in patients undergoing aortic valve replacement surgery because of severe stenosis at the 30-day follow-up. RDW is a parameter measured during routine complete blood counts. It carries none of the extra costs and risks associated with the performance of additional diagnostics (which are often invasive). Previous studies have indicated higher values of RDW as an applicable parameter in

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<th>Variable</th>
<th>Univariable</th>
<th>Multivariable</th>
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<tr>
<td></td>
<td>Odds ratio</td>
<td>95% CI</td>
</tr>
<tr>
<td>RDW</td>
<td>2.821</td>
<td>1.574–5.056</td>
</tr>
<tr>
<td>Haemoglobin</td>
<td>0.505</td>
<td>0.315–0.810</td>
</tr>
<tr>
<td>Haematocrit</td>
<td>0.786</td>
<td>0.668–0.926</td>
</tr>
<tr>
<td>RBC</td>
<td>0.085</td>
<td>0.020–0.362</td>
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<tr>
<td>MCV</td>
<td>1.219</td>
<td>1.042–1.426</td>
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CI — confidence interval; MCV — mean corpuscular volume; RBC — red blood cell count; RDW — red blood cell distribution width

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<tr>
<th>Variable</th>
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<tr>
<td></td>
<td>Odds ratio</td>
<td>95% CI</td>
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<tr>
<td>RDW</td>
<td>2.540</td>
<td>1.638–3.939</td>
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<tr>
<td>Haemoglobin</td>
<td>0.711</td>
<td>0.561–0.902</td>
</tr>
<tr>
<td>Haematocrit</td>
<td>0.895</td>
<td>0.822–0.975</td>
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<tr>
<td>RBC</td>
<td>0.330</td>
<td>0.162–0.672</td>
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<tr>
<td>Glomerular filtration rate</td>
<td>0.970</td>
<td>0.951–0.990</td>
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<td>NYHA classes</td>
<td>2.077</td>
<td>1.117–3.861</td>
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<td>Atrial fibrillation</td>
<td>2.925</td>
<td>1.398–6.120</td>
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<tr>
<td>Pulmonary blood pressure</td>
<td>1.052</td>
<td>1.016–1.089</td>
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CI — confidence interval; NYHA — New York Heart Association; RBC — red blood cell count; RDW — red blood cell distribution width
reserves are lowered. Some authors suggest that RDW is an indicator of a patient’s physiologic reserve — the ability of cells to defend against the strong stress of hypoxia [25–27]. The reserve is very important in such stressful situations as surgical intervention. It can explain the higher incidence of complications in patients with elevated RDW.

We still do not know whether elevated RDW is an independent cardiovascular risk factor or a marker of inflammatory reaction or oxidative stress. Nevertheless, the role of RDW as a predictor of mortality in different groups of patients has been widely described. RDW has also been included as a key element of the scales based on complete blood counts assessing the risks of mortality and morbidity [28, 29]. Therefore, on the basis of this work, it appears that RDW may be helpful in selecting a group of patients with a higher risk for postoperative complications requiring additional attention in being qualified for surgery.

**Limitations of the study**

This study has some potential limitations. It was a single-centred study that included a limited number of participating patients. Further studies are needed to explain the pathomechanisms linking an increased risk for complications in patients with higher values of the RDW.

**Conclusions**

Without fully understanding the mechanisms linking a higher risk for complications and a tendency towards increased mortality in patients with anisocytosis, it seems to be too early to name RDW as a simple and widely available prognostic predictor in patients undergoing isolated aortic valve replacement surgery. Further investigation is required, and information about RDW’s prognostic value may provide an additional clue for physicians in identifying patients who will not benefit from surgical treatment of aortic stenosis or may be eligible for other types of therapy.

**Conflict of interest:** none declared

**References**


Raised red cell distribution width as a prognostic marker in aortic valve replacement surgery


Podwyższona wartość rozpiętości rozkładu objętości erytrocytów jako marker rokowniczy u pacjentów poddawanych operacji wymiany zastawki aortalnej

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S t r e s z c z e n i e

Wstęp: W dotychczasowych badaniach wykazano, że podwyższone wartości rozkładu objętości erytrocytów (RDW) są związane z gorszym rokowaniem u osób z chorobą wieńcową, niewydolnością serca czy ciężką stenozą aortalną leczoną przecznawcowym wszczepieniem zastawki aortalnej. Znaczenie RDW u pacjentów poddawanych operacji chirurgicznej wymiany zastawki aortalnej jest nieznane.

Cel: Celem niniejszej pracy była ocena wartości prognoicznej RDW u chorych poddawanych operacyjnemu leczeniu ciężkiej stenozie aortalnej.

Metody: Prospektywne badanie przeprowadzono w grupie kolejnych 191 pacjentów z ciężką objawową stenozą aortalną poddawanych operacyjnemu leczeniu wymiany zastawki aortalnej. Na z góry zdefiniowany pierwszorzędowy złożony punkt końcowy w obserwacji 30-dniowej składało się wystąpienie następujących powikłań: zgonu z wszystkich przyczyn, okołozaśmiegowego zawału serca, okołooperacyjnej niewydolności nerek, przedłużonej wentylacji mechanicznej, udaru ośrodkowego układu nerwowego, skutecznie resuscytowanego zatrzymania akcji serca, niewydolności wielonarządowej i konieczności reoperacji z jakiejkolwiek przyczyny. Drugorzędowym punktem końcowym była śmiertelność.

Wyniki: Pierwszorzędowy złożony punkt końcowy w obserwacji 30-dniowej zaobserwowano u 54 pacjentów. W analizie jednoczynnikowej predyktorami wystąpienia pierwszorzędowego punktu końcowego były: RDW (p < 0,0001), hemoglobina (p = 0,005), hematokryt (p = 0,01), liczba erytrocytów (p = 0,002), wskaźnik przesączania kłębuszkowego (p = 0,003), stopień niewydolności serca wg klasyfikacji NYHA (p = 0,02), migotanie przedsiomków (p = 0,0044) i ciśnienie w tętnicy płucnej (p = 0,004). Wartości RDW (p = 0,0005), hemoglobiny (p = 0,004), hematokrytu (p = 0,004), liczba erytrocytów (p = 0,0009) i średnia objętość erytrocytów (p = 0,01) wiązały się ze zwiększonym ryzykiem wystąpienia zgonu. Analiza wieloczynnikowa potwierdziła znaczenie RDW (OR 3.274; 95% Cl 1,285–8,344; p = 0,0003) jako niezależnego predyktora wystąpienia pierwszorzędowego złożonego punktu końcowego. Przy użyciu statystyki krzywej ROC wyznaczono punkt odcięcia RDW dla wystąpienia złożonego punktu końcowego na poziomie 14,1% (pole pod krzywą 0,07; p = 0,008).

Wnioski: Wyższe wartości RDW są związane z gorszym rokowaniem u pacjentów poddawanych operacji wymiany zastawki aortalnej, niezależnie od liczby erytrocytów.

Słowa kluczowe: stenozie aortalnej, operacja zastawki, markery stanu zapalnego, ocena ryzyka, rozpiętość rozkładu objętości erytrocytów

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