Relationship between red blood cell distribution width and intermediate-term mortality in elderly patients after percutaneous coronary intervention

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Abstract

Background Large-scale clinical research on the relationship between red blood cell distribution width (RDW) and intermediate-term prognosis in elderly patients with coronary artery disease (CAD) is lacking. Thus, this study investigated the effects of RDW on the intermediate-term mortality of elderly patients who underwent elective percutaneous coronary intervention (PCI).

Methods Data from 1891 patients ≥ 65 years old who underwent elective PCI from July 2009 to September 2011 were collected. Based on the preoperative median RDW (12.3%), the patients were divided into two groups. The low RDW group (RDW < 12.3%) had 899 cases; the high RDW group (RDW ≥ 12.3%) had 992 cases. The all-cause mortality rates of the two groups were compared.

Results Patients in the high RDW group were more likely to be female and accompanied with diabetes, had lower hemoglobin levels. The mean follow-up period was 527 days. During follow-up, 61 patients died (3.2%). The postoperative mortality of the high RDW group was significantly higher than that of the low RDW group (4.3% vs. 2.0%, P = 0.004). After adjusting other factors, multivariate Cox regression analysis revealed that preoperative high RDW was significantly associated with postoperative all-cause mortality (hazard ratio: 2.301, 95% confidence interval: 1.106–4.785, P = 0.026).

Conclusions Increased RDW was an independent predictor of the increased intermediate-term all-cause mortality in elderly CAD patients after elective PCI.

J Geriatr Cardiol 2015; 12: 17–22. doi:10.11909/j.issn.1671-5411.2015.01.013

Keywords: Coronary artery disease; Elderly patients; Percutaneous coronary intervention; Red blood cell distribution width

1 Introduction

Percutaneous coronary intervention (PCI) has been widely used in treating elderly patients with coronary artery disease (CAD); clinical studies have confirmed the safety and efficacy of this treatment towards these patients.[1–5] Given the special systemic conditions of elderly CAD patients, as well as the complexity of CAD, their revascularisation strategies and prognosis differ from those of young patients.[6] Thus, clinicians should perform accurate risk stratification and prognosis assessment in elderly CAD patients to identify the high-risk group.

As an intrinsic parameter in blood tests, red blood cell distribution width (RDW) was initially only used in the diagnosis and differential diagnosis of anemia. In 2007, Felker, et al.[7] firstly discovered that increasing RDW is an independent predictor for the prognosis of heart failure patients, and researchers gradually discovered that RDW is closely associated with the prognosis of cardiovascular diseases. Recent studies showed that increasing RDW is not only a predictor for poor prognosis of heart failure,[7,8] CAD,[9–11] and pulmonary hypertension,[12,13] but it also exhibits a predictive value towards the prognosis of stable CAD patients who have undergone PCI therapy.[14,15] As of this writing, research on the effects of RDW on the prognosis of elderly CAD patients after PCI treatment is lacking. Therefore, this study aimed to clarify the relationship between RDW and intermediate-term all-cause mortality of elderly CAD patients after elective PCI therapy.

2 Methods

2.1 Study group

Among 3574 CAD cases who underwent PCI treatment and had preoperative RDW records in the Beijing Anzhen Hospital from July 2009 to September 2011, 1891 patients aged ≥ 65 years old who underwent elective PCI were selected in this study. Indications for PCI were objective evi-
dence of myocardial ischemia (positive sign on stress test) or ischemic symptoms associated with significant angiographic stenosis (≥ 75% stenosis). Patients who underwent haemodialysis were excluded, and fasting blood specimens were sampled in the morning prior to PCI. The patients’ demographic data, clinical features, laboratory tests, medications, angiographic and procedural information during hospitalisation were recorded.

2.2 Classification of RDW

Based on the preoperative median of RDW (12.3%), the patients were divided into two groups: the high RDW group (RDW ≥ 12.3) and the low RDW group (RDW < 12.3).

2.3 Data source and clinical outcomes

Research-related original data were collected from the hospital’s standard medical records. Laboratory tests and ECG data included records from the time of admission to the time prior to procedure. Data input and follow-up were all completed by cardiologists. Clinic service or telephone follow-up was performed according to a pre-designed questionnaire. The follow-up data were input into a unified form and then encoded into the computer database. The endpoint of this study was the occurrence of all-cause mortality after PCI. The mean follow-up time was 527 days, and the follow-up rate was 92.1%.

2.4 Statistical analysis

Continuous variables were presented as the mean and standard deviation. Inter-group comparison of continuous variables was performed using the Student’s t-test or the Mann-Whitney U-test, whereas categorical variables were analysed using chi-square test or Fisher’s exact test. Kaplan-Meier curves were constructed to compare cumulative survival between the two groups using the log-rank test. Cox regression equation was used to statistically analyse the relevant factors affecting all-cause mortality. Univariate model included the following variables: high RDW, age, gender, hypertension, diabetes, current smoking, family history of CAD, previous stroke, previous myocardial infarction, previous PCI, STEMI, NSTEMI, unstable angina, stable angina, systolic pressure, LVEF, WBC, HCT, Hb, eGFR, total cholesterol, LDL-C, triglyceride, glucose, number of diseased vessels, number of PCI vessels. As covariates for adjustment, those factors were chosen which were found to have a P-value lower than 0.2 in univariate analyses of death. The hazard ratio (HR) and 95% confidence interval (CI) of each relevant factor were calculated. All statistical test were two-tailed, statistical significance was set at P < 0.05. All data were analysed using SPSS 13.0 statistical software.

3 Results

3.1 Baseline characteristics

The baseline clinical characteristics are shown in Table 1.

| Table 1. Baseline characteristics. |
|-----------------------------------|
| RDW < 12.3 (n = 899) | RDW ≥ 12.3 (n = 992) | P value |
|-----------------------|----------------------|---------|
| Age, yrs              | 67.8 ± 5.3           | 68.5 ± 5.4 | 0.644 |
| Female                | 276 (30.7)           | 363 (36.6) | 0.007 |
| BMI, kg/m²             | 25.6 ± 3.2           | 25.4 ± 3.1 | 0.573 |
| Hypertension           | 604 (67.2)           | 681 (68.6) | 0.496 |
| Diabetes               | 210 (23.4)           | 289 (29.1) | 0.004 |
| Current smoking        | 421 (46.8)           | 441 (44.5) | 0.301 |
| Family history of CAD  | 33 (3.7)             | 40 (4.0)   | 0.684 |
| Previous stroke        | 94 (10.5)            | 121 (12.2) | 0.234 |
| Previous myocardial infarction | 159 (17.7)      | 186 (18.8) | 0.550 |
| Previous PCI           | 81 (9.0)             | 104 (10.5) | 0.281 |

Clinical presentation

| STEMI                  | 160 (17.8)           | 170 (17.1) | 0.706 |
| NSTEMI                 | 47 (5.2)             | 47 (4.7)   | 0.624 |
| Unstable angina        | 531 (59.1)           | 586 (59.1) | 0.998 |
| Stable angina          | 161 (17.9)           | 189 (19.1) | 0.523 |
| Systolic pressure, mmHg| 131.6 ± 20.7         | 132.0 ± 20.5 | 0.515 |
| Diastolic pressure, mmHg| 77.3 ± 10.6        | 77.6 ± 10.6 | 0.867 |
| LVEF, %                | 61.5 ± 11.2          | 59.9 ± 11.4 | 0.953 |
| WBC, 10⁹/L             | 7.2 ± 2.2            | 7.2 ± 2.1  | 0.101 |
| HCT, %                 | 38.1 ± 4.1           | 41.2 ± 5.8 | 0.061 |
| Hemoglobin, g/L        | 136.4 ± 15.6         | 132.4 ± 16.6 | <0.001 |
| eGFR, mL·min⁻¹·1.73 m² | 80.4 ± 27.3          | 79.2 ± 23.2 | 0.206 |
| Total cholesterol, mmol/L | 4.62 ± 0.97        | 4.66 ± 1.03 | 0.369 |
| LDL-C, mmol/L          | 2.69 ± 0.80          | 2.68 ± 0.79 | 0.914 |
| Triglyceride, mmol/L   | 1.82 ± 1.17          | 1.82 ± 1.14 | 0.752 |
| Glucose, mmol/L        | 5.93 ± 2.01          | 6.08 ± 2.20 | 0.050 |
| Number of diseased vessels | 332 (36.9)    | 370 (37.3) | 0.868 |
| 1-vessel disease       | 321 (35.7)           | 364 (36.7) | 0.656 |
| 3-vessel disease       | 246 (27.4)           | 258 (26.0) | 0.506 |
| Number of PCI vessels  | 1.5 ± 0.6            | 1.4 ± 0.6  | 0.469 |

Data are presented as mean ± SD or n (%). BMI: body mass index; CAD: coronary artery disease; eGFR: estimated glomerular filtration rate; HCT: haematocrit; LDL-C: Low density lipoprotein cholesterol; LVEF: left ventricular ejection fraction; NSTEMI: non-ST segment elevation myocardial infarction; PCI: percutaneous coronary intervention; RDW: red blood cell distribution width; STEMI: ST segment elevation myocardial infarction; WBC: white blood cells.
The mean age was 68.1 years old and 33.8% of patients were female. The high RDW group was more often accompanied with diabetes, and the proportion of female patients was higher than that of the low RDW group. Patients with high RDW had lower hemoglobin level. No significant difference was found in age, body mass index (BMI), hypertension, current smoking, family history of CAD, previous stroke, previous myocardial infarction, previous PCI, clinical presentation, systolic blood pressure, diastolic blood pressure, LVEF, white blood cells, haematocrit, eGFR, total cholesterol, LDL-C, triglyceride, fasting glucose, number of diseased vessels and number of PCI vessels between the two groups. There were no significant differences in baseline medications between the two groups (Table 2).

Table 2. Baseline medication.

|               | RDW < 12.3 (n = 899) | RDW ≥ 12.3 (n = 992) | P value |
|---------------|----------------------|----------------------|---------|
| DAPT          | 888 (98.8)           | 973 (98.1)           | 0.229   |
| Beta-blocker  | 764 (85.0)           | 870 (87.7)           | 0.085   |
| Statins       | 782 (87.0)           | 838 (84.5)           | 0.120   |
| ACEI/ARB      | 585 (65.1)           | 646 (65.1)           | 0.982   |

Data are presented as n (%). ACEI: angiotensin-converting enzyme inhibitor; ARB: angiotensin receptor blocker; DAPT: dual antiplatelet therapy; RDW: red blood cell distribution width.

3.2 Clinical outcomes

The mean follow-up period was 527 days, and the follow-up rate was 92.1%. During the follow up period, 61 patients died (43 cases in the high RDW group and 18 cases in the low RDW group). The mortality of the high RDW group was significantly higher than that of the low RDW group (4.3% vs. 2.0%, P = 0.004). Results of univariate analyses for all-cause death are shown in Table 3. In multivariate Cox proportional hazards modeling, high RDW was significantly associated with an increased incidence of all-cause death (HR: 2.301, 95%CI: 1.106–4.785, P = 0.026) (Table 4). The cumulative incidence of all-cause death was significantly higher in the high RDW group than in the low RDW group (P = 0.009, Figure 1).

4 Discussion

Two conclusions could be drawn from the results of this study. Firstly, the patients with increased RDW were more often accompanied with diabetes, and the proportion of females was higher, had lower hemoglobin level. Secondly, after adjusting other factors, the increase in RDW was the independent predictor for the elevated mortality of elderly CAD patients after elective PCI, and the postoperative mor-

Table 3. Univariate analysis for all-cause mortality.

|                  | HR     | 95%CI       | P value |
|------------------|--------|-------------|---------|
| High RDW         | 2.052  | 1.182–3.561 | 0.011   |
| Age              | 1.053  | 1.007–1.101 | 0.023   |
| Gender (female)  | 1.468  | 0.884–2.439 | 0.138   |
| Hypertension     | 1.443  | 0.861–2.420 | 0.164   |
| Diabetes         | 1.883  | 1.279–2.772 | 0.001   |
| Previous stroke  | 1.197  | 0.569–2.518 | 0.635   |
| Previous myocardial infarction | 1.200  | 0.650–2.215 | 0.559   |
| Previous PCI     | 0.487  | 0.153–1.556 | 0.225   |
| Current smoking  | 1.069  | 0.869–1.316 | 0.529   |
| Family history of CAD | 1.329  | 0.416–4.250 | 0.631   |
| STEMI            | 1.551  | 1.097–2.193 | 0.013   |
| LVEF             | 0.974  | 0.955–0.995 | 0.014   |
| Hemoglobin       | 0.973  | 0.959–0.988 | <0.001  |
| eGFR (mL·min⁻¹·1.73 m⁻²) | 0.977  | 0.964–0.989 | <0.001  |
| Total Cholesterol| 1.003  | 0.997–1.010 | 0.305   |
| LDL–C            | 1.004  | 0.996–1.012 | 0.341   |
| Triglyceride     | 0.999  | 0.996–1.003 | 0.726   |
| Multivessel disease | 1.709  | 1.235–2.366 | 0.001   |
| Number of PCI vessels | 1.327  | 0.935–1.883 | 0.114   |
| DAPT             | 0.877  | 0.221–6.328 | 0.896   |
| Use of β-blocker | 0.550  | 0.298–1.016 | 0.056   |
| Use of statins   | 0.677  | 0.360–1.272 | 0.225   |
| Use of ACEI/ARB  | 0.898  | 0.485–1.666 | 0.734   |

ACEI: angiotensin converting enzyme inhibitor; ARB: angiotensin receptor blocker; CAD: coronary artery disease; DAPT: dual antiplatelet therapy; eGFR: estimated glomerular filtration rate; LVEF: left ventricular ejection fraction; LDL–C: Low density lipoprotein cholesterol; PCI: percutaneous coronary intervention; RDW: red blood cell distribution width; STEMI: ST segment elevation myocardial infarction.

Figure 1. The Kaplan-Meier curve for cumulative survival. RDW: red blood cell distribution width.
The exact mechanism of the relationship between RDW and prognosis of cardiovascular diseases remains unclear. Data analysis of the America third national health and nutrition examination survey demonstrated that the C-reactive protein (CRP), fibrinogen level and white blood cell count were closely related to increasing RDW. Lippi, et al. discovered the relationship between high RDW and elevated inflammatory markers, which involved the association with the erythrocyte sedimentation rate and CRP, and this contact was independent from other concomitant diseases. When the blood diseases were excluded, this contact was also present. The CRP is an independent risk factor for CAD, and elevated levels of CRP are positively correlated with the incidence of adverse cardiovascular events. CRP as a well-established biomarker of inflammation, has been available and useful for predicting future cardiovascular events in clinical practice. Studies showed that the elevated neutral/lymphocyte ratio, which is a direct indicator of inflammation, is highly correlated with the RDW level; therefore, RDW can be considered an inflammatory factor. As a classic inflammatory cytokine, IL-6 is closely related to the elevation of RDW. IL-6 is a powerful inducer of hepcidin gene transcription; an increase in IL-6 can reduce iron and result in increased RDW.

The predictive roles of RDW in the prognosis of cardiovascular diseases might reflect the predictive roles of inflammation for the same prognosis.

4.1 Study limitations

Some limitation of the present study must be considered. This was a single center, retrospective study. Residual confounding factors possibly affected the results, in addition to the lack of serum iron, folic acid, VitB12 status. Another limitation is that only intermediate-term follow-up results are available. Long-term follow-up is required to further verify the findings. Despite these limitations, the advantages of this study were its large sample size, detailed clinical data and laboratory indicators.

4.2 Conclusions

In conclusion, the present study demonstrated that high RDW is a predictive factor for all-cause mortality in elderly patients after PCI.
CAD patients after elective PCI. RDW had the potential to become a new indicator in prognostic evaluation and risk stratification of the elderly patients with coronary artery disease.

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