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Association between mean corpuscular volume and severity of coronary artery disease in the Northern Chinese population: a cross-sectional study

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Abstract

Objective: This study was performed to explore the relationship between the mean corpuscular volume (MCV) and the severity of coronary artery disease (CAD) in the Northern Chinese population.

Methods: In total, 1326 patients who underwent coronary angiography from July 2015 to February 2017 were retrospectively enrolled in this cross-sectional study. Coronary artery stenosis was evaluated by the Gensini score. Linear regression analysis was performed to investigate the association between the severity of CAD and the MCV.

Results: Patients within the fourth quartile of the Gensini score had a significantly higher MCV than those within the third, second, and first quartiles (94.1 ± 6.7 vs. 93.2 ± 6.4 vs. 92.8 ± 5.1 vs. 92.6 ± 6.2, respectively). After adjustment for potential confounding factors, the multivariate linear regression analysis showed that the MCV was significantly associated with the severity of CAD. Additionally, the red blood cell distribution width (RDW) and red blood cell count were significantly associated with the severity of CAD.

Conclusions: These results suggest that the MCV, RDW, and red blood cell count are correlated with and may serve as biomarkers for the severity of CAD.

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Keywords
Mean corpuscular volume, Gensini score, cross-sectional study, coronary angiography, red blood cell distribution width, coronary artery disease

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Introduction

Coronary artery disease (CAD) is the most common form of heart disease and affects millions of people worldwide.[1] Stenosis of the coronary artery, which may lead to myocardial infarction or sudden cardiac death, reduces blood flow and oxygen to the heart muscle.[2] Many risk factors, including smoking, diabetes, hypertension, and obesity, are associated with CAD.[3–6] Red blood cells (RBCs) deliver oxygen to the whole body via the circulatory system.[7] The mean corpuscular volume (MCV), a measure of the size of RBCs, is closely associated with endothelial dysfunction and cardiovascular events.[8] Additionally, the RBC distribution width (RDW), an important biomarker in patients with pathological conditions, is closely associated with the incidence of CAD.[9,10] However, little is known about the role of routine blood examinations such as measurement of the MCV, RDW, and RBC count in the progression of coronary artery stenosis. We therefore performed a cross-sectional study to explore whether the MCV, RDW, and RBC count are correlated with the severity of CAD in the Northern Chinese population.

Methods

Study population

From July 2015 to February 2017, 1326 in-hospital patients were recruited from the database of Shaanxi Provincial People's Hospital and the First Affiliated Hospital of Xi'an Jiaotong University. All patients had standard clinical indications for cardiac interventional therapy and underwent coronary angiography (CAG) during the hospital stay.[11] The exclusion criteria were (1) missing data from CAG reports and medical records, (2) the presence of haematological disease (including RBC disorders, white blood cell disorders, and platelet disorders) and systemic disease, and (3) pregnancy. All patients provided written informed consent, and their data were anonymised and de-identified before the statistical analysis. The study protocol was approved by the Ethics Committee of Shaanxi Provincial People's Hospital and the First Affiliated Hospital of Xi'an Jiaotong University.

Hypertension was diagnosed as an in-office blood pressure measurement of $>140/90$ mmHg or 24-hour ambulatory blood pressure measurement of $>135/85$ mmHg.[12] Diabetes mellitus was defined as a fasting plasma glucose level of ≥ 7.0 mmol/L (126 mg/dL) or 2-hour post-load plasma glucose level of ≥ 11.0 mmol/L (200 mg/dL).[13] Smoking was defined as currently smoking every day or some days or ever having smoked 100 cigarettes.[14] Dyslipidaemia was defined as a triglyceride level of ≥ 150 mg/dL, low-density lipoprotein level of ≥ 130 mg/dL, high-density lipoprotein level of ≤ 40 mg/dL, or total cholesterol level of ≥ 200 mg/dL.[15]

Biochemical measurements

Routine haematology tests included measurement of the white blood cell count, RBC count, MCV, RDW, haemoglobin level, and haematocrit using ethylenediamine tetraacetic acid tubes. Blood samples were collected from all patients in the morning after a 12-hour fasting period. The MCV, RDW, RBC count, haematocrit, and haemoglobin level were detected by automated haematology analysers. The following formulas were used: MCV = haematocrit/RBC count and RDW = (coefficient of variability of RBCs/mean MCV) $\times$ 100. The MCV was divided into the first tertile (<91.2 fl, n = 442), second tertile (91.2–95.2 fl, n = 442), and third tertile (>95.3 fl, n = 442).

CAG results

All patients underwent CAG using a standard clinical technique through the femoral artery or radial artery approach.[11] The CAG findings were reported and checked by two interventional cardiologists. The severity of CAD was calculated by the Gensini score. In the Gensini scoring system, a score of 0 indicates no abnormality, 1 represents stenosis of $\leq$25%, 2 represents stenosis of 26% to 50%, 4 represents stenosis of 51% to 75%, 16 represents stenosis of 76% to 99%, and 32 represents complete occlusion. The score is then multiplied by different factors according to the functional significance of the coronary artery stenosis. The importance of the segment is scored from 5.0 for the left main trunk to 0.5 for the most distal segments.[16–18] In the present study, the Gensini scores were categorised into the first quartile ($\leq$5 points, n = 340), second quartile (6–20 points, n = 337), third quartile (21–48 points, n = 319), and fourth quartile ($\geq$49 points, n = 330).

Statistical analysis

Descriptive statistics are presented as percentages for categorical variables and as mean $\pm$ standard deviation for continuous variables. The comparisons of continuous variables and categorical variables were based on analysis of variance, Student's t-test, and the chi-square test. Linear regression analysis was conducted to investigate the relationship between the severity of CAD and several variables (age, sex, smoking, diabetes mellitus, hypertension, heart rate, family history of CAD, hyperlipidaemia, systolic blood pressure, diastolic blood pressure, total cholesterol, high-density lipoprotein, low-density lipoprotein, very-low-density lipoprotein, and MCV). Variables with a P value of <0.05 in the univariate models were then included in the multivariate analyses. A P-value of <0.05 was considered statistically significant. All statistical analyses were performed by SPSS version 24.0 (IBM Corp., Armonk, NY, USA).

Results

Patient characteristics

The descriptive characteristics according to the Gensini score quartiles are shown in Table 1. This study included 1326 patients (927 men, 399 women; mean age, 58.5 $\pm$ 10.3 years). Patients in the fourth quartile of the Gensini score were older and comprised a higher proportion of men. The MCV was significantly higher in the fourth quartile of the Gensini score than in the third, second, and first quartiles (94.1 $\pm$ 6.7 vs. 93.2 $\pm$ 6.4 vs. 92.8 $\pm$ 5.1 vs. 92.6 $\pm$ 6.2, respectively; P = 0.010). The RDW was also higher in patients in the fourth quartile of the Gensini score than in the third, second, and first quartiles (45.6 $\pm$ 5.0 vs. 45.1 $\pm$ 4.9 vs. 44.7 $\pm$ 3.5 vs. 44.5 $\pm$ 3.8, respectively; P = 0.007).

Association between Gensini score and MCV

The patients were divided into three groups based on the MCV: <91.2 fl (first grade, n = 442), 91.2 to 95.2 fl (second grade,

Table 1. Descriptive characteristics by Gensini score quartiles.

Characteristics	Total (n = 1326)	Gensini score quartiles: First quartile (n = 340)	Second quartile (n = 337)	Third quartile (n = 319)	Fourth quartile (n = 330)	P value
Age, years	58.5 ± 10.3	55.7 ± 9.5	59.0 ± 9.9	59.6 ± 10.4	60.0 ± 10.8	<0.001
Sex						<0.001
Male	927 (69.9)	187 (55.0)	237 (70.3)	231 (72.4)	272 (82.4)	–
Female	399 (30.1)	153 (45.0)	100 (29.7)	88 (27.6)	58 (17.6)	–
Current smoking	590 (44.5)	117 (34.4)	159 (47.2)	156 (48.9)	158 (47.9)	<0.001
Diabetes mellitus	211 (15.9)	14 (4.1)	46 (13.6)	77 (24.1)	74 (22.4)	<0.001
Hypertension	681 (51.4)	155 (45.6)	171 (50.7)	189 (59.2)	166 (50.3)	0.005
Hyperlipidaemia	154 (11.6)	31 (9.1)	48 (14.2)	39 (12.2)	36 (10.9)	0.203
Family history of CAD	394 (29.7)	105 (30.9)	92 (27.3)	110 (34.5)	87 (26.4)	0.093
Baseline SBP, mmHg	134.8 ± 20.5	134.2 ± 18.8	135.7 ± 18.4	135.1 ± 21.9	134.3 ± 22.8	0.763
Baseline DBP, mmHg	78.1 ± 11.8	77.5 ± 11.0	78.8 ± 11.9	77.9 ± 11.9	78.3 ± 12.4	0.482
Heart rate, bpm	75.5 ± 13.7	74.5 ± 15.2	74.9 ± 12.5	75.6 ± 13.1	75.5 ± 13.7	0.102
RBCs, 10^{12}/L	4.8 ± 4.3	4.9 ± 3.0	4.6 ± 3.2	4.9 ± 3.6	5.0 ± 6.3	0.688
Hb, g/L	134.4 ± 15.9	132.6 ± 15.4	134.5 ± 16.5	135.3 ± 15.9	135.3 ± 15.9	0.101
RDW, fl	45.0 ± 4.4	44.5 ± 3.8	44.7 ± 3.5	45.1 ± 4.9	45.6 ± 5.0	0.007
MCV, fl	93.2 ± 6.2	92.6 ± 6.2	92.8 ± 5.1	93.2 ± 6.4	94.1 ± 6.7	0.010
HCT, %	40.2 ± 4.4	39.8 ± 4.2	40.3 ± 4.5	40.5 ± 4.4	40.4 ± 4.4	0.142
TC, mmol/L	1.8 ± 1.2	1.7 ± 1.1	1.8 ± 1.0	1.7 ± 0.9	1.9 ± 1.7	0.431
HDL, mmol/L	1.1 ± 0.3	1.2 ± 0.3	1.1 ± 0.3	1.1 ± 0.3	1.1 ± 0.3	0.003
LDL, mmol/L	2.7 ± 0.9	2.7 ± 0.8	2.7 ± 0.9	2.6 ± 0.9	2.7 ± 1.0	0.912
VLDL, mmol/L	0.6 ± 0.4	0.6 ± 0.4	0.6 ± 0.4	0.5 ± 0.4	0.6 ± 0.5	0.691

Results are presented as mean ± standard deviation or n (%). The P values represent the difference among the four quartiles.
First quartile, ≤5 points; second quartile, 6–20 points; third quartile, 21–48 points; fourth quartile, ≥49 points.
CAD, coronary artery disease; DBP, diastolic blood pressure; Hb, haemoglobin; HCT, haematocrit; HDL, high-density lipoprotein; LDL, low-density lipoprotein; MCV, mean corpuscular volume; RBCs, red blood cells; RDW, red blood cell distribution width; SBP, systolic blood pressure; TC, total cholesterol; VLDL, very-low-density lipoprotein.

n = 442), and >95.3 fl (third grade, n = 442). Patients with third-grade MCV had higher Gensini scores than those with second- and first-grade MCV (35.6 ± 36.5 vs. 30.5 ± 33.7 vs. 29.6 ± 30.7, respectively; P = 0.019) (Table 2). Additionally, patients with a higher RDW had higher Gensini scores (data not shown).

The univariate linear regression analysis showed that the MCV was positively correlated with an increasing Gensini score (β = 0.575, 95% confidence interval [CI] = 0.281–0.870, P < 0.001). After adjustment for age, sex, smoking, hypertension, diabetes, and heart rate, the MCV was still positively associated with the Gensini score (β = 0.503, 95% CI = 0.205–0.801, P = 0.001). The multivariate linear regression model also showed that the RDW (β = 0.818, 95% CI = 0.360–1.276, P < 0.001) and RBC count (β = 0.438, 95% CI = 0.025–0.852, P = 0.038) were closely associated with the Gensini score (Table 3). No significant correlation was found among the haemoglobin level, haematocrit, and Gensini score. We further investigated the relationship between the MCV or RDW and the Gensini score in

Table 2. Baseline characteristics of MCV categories.

Characteristics	MCV < 91.2 fl (n = 442)	MCV 91.2–95.2 fl (n = 442)	MCV >95.3 fl (n = 442)	P value
Age, years	57.0 ± 10.8	58.9 ± 10.2	59.7 ± 9.7	<0.001
Sex				<0.001
Male	286 (64.7)	295 (66.7)	346 (78.3)	–
Female	156 (35.3)	147 (33.3)	96 (21.7)	–
Current smoking	166 (37.6)	186 (42.1)	238 (53.8)	<0.001
Diabetes mellitus	95 (21.5)	70 (15.8)	46 (10.4)	<0.001
Hypertension	235 (53.2)	240 (54.3)	206 (46.6)	0.047
Hyperlipidaemia	67 (15.2)	43 (9.7)	44 (10.0)	0.017
Family history of CAD	139 (31.4)	139 (31.4)	116 (26.2)	0.148
Baseline SBP, mmHg	135.6 ± 20.4	136.5 ± 20.3	132.4 ± 20.8	0.009
Baseline DBP, mmHg	78.8 ± 11.6	78.8 ± 12.2	76.8 ± 11.4	0.012
Heart rate, bpm	75.9 ± 13.6	75.9 ± 14.4	74.6 ± 13.2	0.243
TC, mmol/L	2.0 ± 1.5	1.7 ± 1.0	1.6 ± 1.0	0.004
HDL, mmol/L	1.1 ± 0.3	1.2 ± 0.3	1.1 ± 0.3	0.389
LDL, mmol/L	2.7 ± 0.9	2.7 ± 0.9	2.5 ± 0.8	0.033
VLDL, mmol/L	0.6 ± 0.5	0.6 ± 0.4	0.5 ± 0.4	0.002
Gensini score	29.6 ± 30.7	30.5 ± 33.7	35.6 ± 36.5	0.019

Results are presented as mean ± standard deviation or n (%). The P values represent the difference among the three groups.
CAD, coronary artery disease; DBP, diastolic blood pressure; HDL, high-density lipoprotein; LDL, low-density lipoprotein; MCV, mean corpuscular volume; SBP, systolic blood pressure; TC, total cholesterol; VLDL, very-low-density lipoprotein.

Table 3. Univariate and multiple linear regression analyses of the Gensini score.

	Univariate models		Multivariate adjusted	
Variable	β (95% CI)	P	β (95% CI)	P
MCV	0.575 (0.281–0.870)	<0.001	0.503 (0.205–0.801)	0.001
RDW	0.889 (0.429–1.349)	<0.001	0.818 (0.360–1.276)	<0.001
RBC count	0.382 (−0.046–0.810)	0.080	0.438 (0.025–0.852)	0.038
Hb	0.076 (−0.038–0.190)	0.191	−0.040 (−0.169–0.088)	0.540
HCT	0.247 (−0.170–0.663)	0.245	−0.158 (−0.616–0.301)	0.500

Univariate models were adjusted for age, sex, smoking, hypertension, diabetes mellitus, heart rate, hyperlipidaemia, family history of coronary artery disease, systolic blood pressure, diastolic blood pressure, total cholesterol, high-density lipoprotein, low-density lipoprotein, and very-low-density lipoprotein.
Variables with a P value of <0.05 in the univariate models were then included in the multivariate analyses (adjusted for age, sex, smoking, hypertension, diabetes mellitus, and heart rate).
CI, confidence interval; Hb, haemoglobin; HCT, haematocrit; MCV, mean corpuscular volume; RBC, red blood cell; RDW, red blood cell distribution width.

a subgroup analysis. The results showed that the association of the MCV or RDW with the Gensini score was more prominent in patients with a smoking habit (Supplemental Table 1).

Discussion

The coronary artery, a blood vessel located in the heart, is a main part of the circulatory system and provides the heart with oxygen and nutrients. Coronary artery stenosis occurs secondary to atherosclerosis in the epicardial coronary arteries. Measurement of the Gensini score is a quick and easy way to evaluate the severity of CAD in clinical practice.[19] This scoring system involves the summation of each lesion score and has been found to be a predictor of the cardiovascular outcome.[19] We therefore used the Gensini score to further explore the relationship between the MCV and the severity of CAD in the present cross-sectional study and found that the MCV was positively correlated with the Gensini score.

RBCs, which are produced in the bone marrow, are the most common cell type in the blood.[20] The most important function of RBCs is to deliver oxygen to organs and tissues. The MCV is the mean volume of an RBC, while the RDW is proportionate to the standard deviation of the MCV. The MCV and RDW have been found to be associated with CAD, heart failure, diabetes, stroke, and venous thromboembolism.[21,22] However, the association between the MCV or RDW and the severity of CAD has long remained unknown.

In the present study, we investigated the role of the MCV and RDW in the severity of CAD. A previous study showed that the RDW was correlated with the Gensini score.[23] The RDW was also found to be an independent predictor of CAD and the severity of coronary stenosis.[24] In the present study, we found that patients in the Northern Chinese population with a higher MCV and RDW had higher Gensini scores. Moreover, a linear regression analysis was further performed to test the association between the severity of CAD and the MCV. After adjustment for age, sex, smoking, hypertension, diabetes, and heart rate, the MCV and RDW were significantly associated with the severity of CAD.

Several reports have discussed mechanisms that might explain the association between the MCV or RDW and the severity of CVD. The RDW is closely associated with coronary atherosclerosis and is a marker of inflammatory processes.[23] In addition, chronic inflammation is one of the main driving forces of atherosclerotic plaque progression.[25] Chronic inflammation can also lead to an increase in the MCV and RDW. Furthermore, Solak et al.[8] showed that the MCV was inversely correlated with flow-mediated dilatation, indicating that the MCV is associated with endothelial function. Therefore, an elevated MCV and RDW may reflect the severity of atherosclerosis. The specific mechanisms underlying these associations require further exploration.

The current study has several limitations. First, the patients were recruited from the Northwest region of China; therefore, the results may not be extended to all ethnicities. Second, the study was retrospective, making it difficult to conclude that a causal relationship exists between the MCV or RDW and the severity of CAD. A multi-centre study with a long observation period is needed to verify our findings.

Conclusion

The present study showed that an elevated MCV, RDW, and RBC count were significantly associated with more severe coronary artery stenosis. The MCV, RDW, and RBC count were thus associated with the severity of CAD.

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Declaration of conflicting interest

The authors declare that there is no conflict of interest.

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Supplemental material

Supplemental material for this article is available online.

References

1. Ross R. The pathogenesis of atherosclerosis: a perspective for the 1990s. *Nature* 1993; 362: 801–809.
2. Paradis JM, Fried J, Nazif T, et al. Aortic stenosis and coronary artery disease: what do we know? What don't we know? A comprehensive review of the literature with proposed treatment algorithms. *Eur Heart J* 2014; 35: 2069–2082.
3. Montalescot G, Sechtem U, Achenbach S, et al. 2013 ESC guidelines on the management of stable coronary artery disease: the Task Force on the management of stable coronary artery disease of the European Society of Cardiology. *Eur Heart J* 2013; 34: 2949–3003.
4. Keil U. Coronary artery disease: the role of lipids, hypertension and smoking. *Basic Res Cardiol* 2000; 95: I52–I58.
5. Naito R and Miyauchi K. Coronary artery disease and type 2 diabetes mellitus. *Int Heart J* 2017; 58: 475–480.
6. Rosendorff C and Writing C. Treatment of hypertension in patients with coronary artery disease. A case-based summary of the 2015 AHA/ACC/ASH scientific statement. *Am J Med* 2016; 129: 372–378.
7. Byrnes JR and Wolberg AS. Red blood cells in thrombosis. *Blood* 2017; 130: 1795–1799.
8. Solak Y, Yilmaz MI, Saglam M, et al. Mean corpuscular volume is associated with endothelial dysfunction and predicts composite cardiovascular events in patients with chronic kidney disease. *Nephrology (Carlton)* 2013; 18: 728–735.
9. Felker GM, Allen LA, Pocock SJ, et al. Red cell distribution width as a novel prognostic marker in heart failure: data from the CHARM Program and the Duke Databank. *J Am Coll Cardiol* 2007; 50: 40–47.
10. Tonelli M, Sacks F, Arnold M, et al. Relation between red blood cell distribution width and cardiovascular event rate in people with coronary disease. *Circulation* 2008; 117: 163–168.
11. Levine GN, Bates ER, Blankenship JC, et al. 2011 ACCF/AHA/SCAI Guideline for percutaneous coronary intervention: a report of the American College of Cardiology Foundation/American Heart Association task force on practice guidelines and the society for cardiovascular angiography and interventions. *Circulation* 2011; 124: e574–e651.
12. Mancia G, Fagard R, Narkiewicz K, et al. 2013 ESH/ESC Guidelines for the management of arterial hypertension: the Task Force for the management of arterial hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). *J Hypertens* 2013; 31: 1281–1357.
13. Vijan S. Type 2 diabetes. *Ann Intern Med* 2010; 152: ITC31-15; quiz ITC316.
14. Hou X, Qiu J, Chen P, et al. Cigarette smoking is associated with a lower prevalence of newly diagnosed diabetes screened by OGTT than non-smoking in Chinese men with normal weight. *PLoS One* 2016; 11: e0149234.
15. Joint Committee for Developing Chinese guidelines on Prevention and Treatment of Dyslipidemia in Adults. [Chinese guidelines on prevention and treatment of dyslipidemia in adults]. *Zhonghua Xin Xue Guan Bing Za Zhi* 2007; 35: 390–419.
16. Wang GN, Sun K, Hu DL, et al. Serum cystatin C levels are associated with coronary artery disease and its severity. *Clin Biochem* 2014; 47: 176–181.

17. Yongsakulchai P, Settasatian C, Settasatian N, et al. Association of combined genetic variations in PPARgamma, PGC-1alpha, and LXRalpha with coronary artery disease and severity in Thai population. *Atherosclerosis* 2016; 248: 140–148.
18. Ndrepepa G, Tada T, Fusaro M, et al. Association of coronary atherosclerotic burden with clinical presentation and prognosis in patients with stable and unstable coronary artery disease. *Clin Res Cardiol* 2012; 101: 1003–1011.
19. Sinning C, Lillpopp L, Appelbaum S, et al. Angiographic score assessment improves cardiovascular risk prediction: the clinical value of SYNTAX and Gensini application. *Clin Res Cardiol* 2013; 102: 495–503.
20. Kleinbongard P, Schulz R, Rassaf T, et al. Red blood cells express a functional endothelial nitric oxide synthase. *Blood* 2006; 107: 2943–2951.
21. Huang YL, Hu ZD, Liu SJ, et al. Prognostic value of red blood cell distribution width for patients with heart failure: a systematic review and meta-analysis of cohort studies. *PLoS One* 2014; 9: e104861.
22. Xanthopoulos A, Giamouzis G, Melidonis A, et al. Red blood cell distribution width as a prognostic marker in patients with heart failure and diabetes mellitus. *Cardiovasc Diabetol* 2017; 16: 81.
23. Akboga MK, Canpolat U, Sahinarslan A, et al. Association of serum total bilirubin level with severity of coronary atherosclerosis is linked to systemic inflammation. *Atherosclerosis* 2015; 240: 110–114.
24. Nagula P, Karumuri S, Otikunta AN, et al. Correlation of red blood cell distribution width with the severity of coronary artery disease-A single center study. *Indian Heart J* 2017; 69: 757–761.
25. Nilsson J, Gonçalves I and Edsfeldt A. Chronic inflammation and atherosclerosis. In: Nilsson P, Olsen M and Laurent S (eds) *Early vascular aging*. 1st ed. Cambridge, MA: Academic Press, 2015, pp.157–167.