Relationship Between Hematocrit Level and Cardiovascular Risk Factors in a Community-Based Population

Yuan-Ze Jin,* Dong-Han Zheng, Zhi-Ying Duan, Ying-Zi Lin, Xue-Ying Zhang, Jing-Ru Wang, Shuo Han, Guo-Feng Wang, and Yi-Jing Zhang

Department of Cardiology, Fourth Affiliated Hospital of China Medical University, Shenyang, P.R. China

Background: This study aimed to determine the relationship between hematocrit (HCT) levels and cardiovascular risk factors in a community-based population of middle-aged adults. **Methods:** From April 2011 to February 2012, a total of 1,884 middle-aged adults were selected from a community-based population in China. Blood and urine samples were collected for routine blood and urine tests, and measurement of plasma glucose and lipid levels. Baseline information including traditional cardiovascular risk factors was obtained by standard questionnaire to analyze. We evaluated the distribution of the HCT values for middle-aged adults with or without cardiovascular risk factors. There were 548 males and 1,336 females in this study. The mean age of all subjects was 54.7 ± 6.7 years. There were 1,209 subjects with risk factors and 675 without risk factors. **Results:** The HCT levels in subjects with

risk factors were higher than those without risk factors ($P = 0.005$). According to a simplified tool for evaluation of the 10-year risk of ischemic cardiovascular diseases (CVDs) in Chinese populations, all subjects were divided into four groups: the ultralow-risk group (1,367, 72.6%), low-risk group (232, 12.3%), intermediate-risk group (201, 10.7%), and high-risk/ultrahigh-risk group (84, 4.4%). Compared with HCT levels in the ultralow-risk group, significant differences were found in the low-risk, intermediate-risk, and high-risk/ultrahigh-risk groups (all $P < 0.05$). **Conclusion:** Our results indicate that elevated HCT levels may be positively associated with cardiovascular risk factors. Thus, the combination of HCT values and cardiovascular risk factors may enable early diagnosis of CVDs. J. Clin. Lab. Anal. 29:289–293, 2015. © 2014 Wiley Periodicals, Inc.

Key words: hematocrit; cardiovascular diseases; risk factors; community-based population; middle-aged adults

INTRODUCTION

Cardiovascular disease (CVD), also identical to circulatory diseases, is a series of diseases closely related to the circulatory system (1,2). CVD represents the leading cause of death and morbidity worldwide. Due to the high mortality rate, severe damage to physical and mental health, long rehabilitation periods, and a high rate of disability, the burden of CVD is a highly significant social issue (3,4). Generally, CVD is recognized as a multifactorial disease induced by complex interactions between environmental and genetic factors (5). Converging evidence indicates that traditional risk factors, such as smoking habit, hypertension, dyslipidemia, and diabetes, occupy an important position in the development and progression of CVD (6–8). Novel markers of cardiovascular risk, such as an altered hemorheologic profile may also influence cardiovascular mortality in these patients (6). An increasing evidence

revealed that abnormalities in blood rheology, including elevations of blood and plasma viscosity, are related to various CVDs (9).

Although the multifactorial mechanisms by which abnormalities of blood viscosity lead to an increased incidence of clinical CVD are not yet fully understood, there are clearly potential mechanisms whereby the elevated blood viscosity abnormalities may cause the disorders of blood circulation, alter microcirculatory

*Correspondence to: Yuan-Zhe Jin, Department of Cardiology, Fourth Affiliated Hospital of China Medical University, Chongshan Road No. 4, Huanggu District, Shenyang 110032, P.R. China. E-mail: cmu4h_jyz@163.com

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perfusion, increase atherogenesis, promote plaque rupture, and thereby contributing to ischemia (10, 11). Clinical studies provided evidence that abnormalities in blood flow properties may worsen microcirculatory blood flow and influence CVD (12–16). More specifically, numerous epidemiologic studies have shown that main factors of blood rheology, including hematocrit (HCT), erythrocyte sedimentation rate, and fibrinogen, are independent risk elements of cardiovascular morbidity and mortality (17, 18). Previous studies demonstrated that the elevated HCT was significantly correlated to the incidence of coronary atherosclerosis, unstable angina, myocardial infarction, etc. (18–20). HCT is strongly beneficial for the flow properties of blood in the microcirculation, and helps to provide a more thorough understanding of the red blood cells variation that plays a role in predicting health conditions, which can be interpreted that HCT may have a corresponding increase when the absolute value of red blood cells is elevating due to various reasons (21). Therefore, we performed a pilot study to determine the relationship between HCT levels and cardiovascular risk factors in a community-based population of middle-aged adults, which may provide a more comprehensive and reasonable conclusion for further diagnostic evaluation of CVD.

MATERIALS AND METHODS

Ethics Statement

The study was approved by the Ethics Committee of the Fourth Affiliated Hospital of China Medical University. Informed consent was obtained in written from all participants using procedures approved by institutional review boards.

Study Design and Subjects

From April 2011 to February 2012, a total of 1,884 middle-aged adults were selected from a community-based population in China. Subjects must meet certain criteria in order to be enrolled in this study: (1) healthy middle-aged adults (age ≥ 30 years); (2) subjects with no recent trauma, surgery, severe diarrhea, vomiting, heavy perspiration, and large area burn; (3) subjects have no history of infectious diseases, malignant tumors, hematopathy, multiple organ dysfunction, and autoimmune diseases. Subjects who could not meet the inclusion criteria would be excluded.

Evaluation of Cardiovascular Risk Factors

Height, weight, waist circumference, blood pressure, blood glucose, and blood lipid were measured. Cardiovascular risk factors included hypertension, diabetes, dys-

lipidemia, smoking, and obesity. We evaluated the risk of CVD in a community-based population according to a simplified tool for evaluation of the 10-year risk of ischemic CVDs in Chinese populations (22). This criteria was designed based on age (0~4), systolic blood pressure ($-2\sim 8$), total cholesterol (0~1), body mass index (0~2), diabetes (0~1), and smoking (0~2). The score ranged from -2 to 18. According to the scores, the 10-year risks of CVD were stratified into five grades: ultralow-risk ($\leq 5\%$), low-risk ($> 5\%$), intermediate-risk ($> 10\%$), high-risk ($> 20\%$), and ultrahigh-risk ($> 40\%$).

A cross-sectional questionnaire survey of cardiovascular risk factors was conducted in all subjects. The following information was collected: demographic characteristics, personal and family history, physical activity, and medication history, etc. Physical examination included anthropometry index, blood pressure, and 12-lead ECG. Blood and urine samples were collected for routine blood and urine tests, and measurement of plasma glucose and lipid levels according to International Committee for Standardization in Hematology. Measurement of HCT levels was performed using the Sysmex XE-2100 automated blood cell analyzer (Sysmex, Kobe, Japan).

Statistical Analysis

Data were presented as mean $\pm$ standard deviation (SD), median with interquartile ranges (IQR), or frequencies. A χ^2 test was used to compare frequencies. One-way analysis of variance (ANOVA) and Student's *t*-test were used for normally distributed variables, whereas the Mann–Whitney's *U*-test was used for non-normal distributed variables. Comparisons between two groups for nominal variables were made by the Fisher's exact test. All tests of statistical significance were two-sided with a *P*-value less than 0.05 considered statistically significant. All statistical analyses were performed using the SPSS 18.0 software (SPSS, Inc., Chicago, IL).

RESULTS

Baseline Characteristics of Subjects

In this study, a total of 1,884 healthy middle-aged adults were involved, including 548 males (29.1%) and 1,336 females (70.9%). The mean age of all subjects was 54.7 ± 6.7 years (range, 35~64 years). There were statistically significant differences in HCT, body mass index, waist circumference, systolic blood pressure, diastolic blood pressure, fasting blood glucose, cholesterol, triglycerides, HDL-C, LDL-C, creatinine, uric acid, and serum sodium between males and females (all *P* < 0.05). The baseline clinical characteristics of all subjects are presented in Table 1.

TABLE 1. Comparison of Baseline Characteristics and Clinical Features Between Males and Females

	Male (<i>n</i> = 548)	Female (<i>n</i> = 1,336)	<i>P</i> -value
Mean age (years)	54.9 ± 7.2	54.6 ± 6.5	0.132
Family history			
Hypertension (%)	205 (37.4)	573 (42.9)	0.028
Coronary heart disease (%)	114 (20.8)	342 (25.6)	0.027
Cerebrovascular disease (%)	136 (24.8)	379 (28.4)	0.116
Diabetes (%)	109 (19.9)	292 (21.9)	0.344
Pulmonary disease (%)	55 (10.0)	161 (12.1)	0.356
Malignant tumor (%)	95 (17.3)	227 (17.0)	0.887
Smoking (%)	261 (47.6)	61 (4.6)	<0.001
BMI (kg/m ²)	25.3 ± 3.2	24.9 ± 3.3	0.027
Waist circumference (cm)	90 (85, 95)	84 (78, 90)	<0.001
SBP (mmHg)	128.6 ± 19.5	125.7 ± 2.5	0.003
DBP (mmHg)	78.7 ± 11.6	75.6 ± 11.6	<0.001
RBC (× 10 ¹²)	5.0 ± 0.4	4.6 ± 0.4	<0.001
Hb (g/l)	145.5 ± 10.7	126.7 ± 10.7	<0.001
HCT	0.44 (0.43, 0.46)	0.40 (0.38, 0.41)	0.009
FPG (mmol/l)	5.23 (4.84, 5.84)	5.04 (4.77, 5.51)	0.006
TC (mmol/l)	5.0 ± 1.0	5.3 ± 1.0	<0.001
TG (mmol/l)	1.44 (0.96, 2.28)	1.27 (0.88, 1.91)	0.02
HDL-C (mmol/l)	1.17 (1.02, 1.37)	1.35 (1.16, 1.55)	<0.001
LDL-C (mmol/l)	2.88 ± 0.74	3.08 ± 0.80	<0.001
Creatinine (umol/l)	88.7 ± 13.5	72.5 ± 13.5	<0.001
Uric acid (umol/l)	343.3 (297.1, 398.2)	263.5 (225.9, 307.2)	<0.001
Albumin (g/l)	44.1 ± 2.6	44.0 ± 2.2	0.383
Na ⁺ (mmol/l)	140.9 ± 2.0	141.3 ± 2.5	0.043
Microalbuminuria (mg/l)	24.6 ± 37.8	20.3 ± 32.6	0.388

CHD, coronary heart disease; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; RBC, red blood cell; Hb, hemoglobin; HCT, hematocrit; FPG, fasting plasma glucose; TC, total cholesterol; TG, triglycerides; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol.

HCT Levels of Subjects With Different Cardiovascular Risk Factors

Table 2 showed HCT levels of subjects with different cardiovascular risk factor. There were 491 (35.8%) subjects with one risk factor, 263 (14.0%) with two risk factors, 455 (24.1%) with more than or equal to three risk factors, and 675 (35.8%) without risk factors. The HCT levels in subjects with risk factors were higher than those without risk factors ($P = 0.005$). There also existed obvious difference in HCT levels between subjects with one risk factor and subjects with two risk factors ($P = 0.007$).

TABLE 2. The HCT Levels of Subjects With Different Cardiovascular Risk Factor

	<i>n</i>	Percentage	HCT levels
Subjects without risk factors	675	35.9%	0.40 (0.38, 0.41)
Subjects with risk factors	1209	64.1%	0.42 (0.40, 0.44)*
1	491	26.1%	0.40 (0.38, 0.42)*
2	263	13.9%	0.41 (0.39, 0.43)*
≥ 3	455	24.1%	0.43 (0.41, 0.45)*

* $P < 0.05$ compared with HCT levels of subjects without risk factors.

Furthermore, we observed significant difference in HCT levels between subjects with two risk factors and subjects with greater than or equal to three risk factors ($P = 0.001$).

HCT Levels of Subjects With Different CVD Risk Grade

The HCT levels of middle-aged adults with different CVD risk grade are summarized in Table 3. There were 1,367 (72.6%) in the ultralow-risk group, 232 (12.3%) in the low-risk group, 201 (10.7%) in the intermediate-risk group, and 84 (4.4%) in the high-risk/ultrahigh-risk

TABLE 3. The HCT Levels of Middle-Aged Adults With Different CVD Risk Grade

Risk grade	<i>N</i>	Percentage	HCT levels
Ultra-low risk	1367	72.6%	0.40 (0.38, 0.42)
Low risk	232	12.3%	0.41 (0.39, 0.43)*
Intermediate risk	201	10.7%	0.42 (0.40, 0.45)*
High-risk/Ultra-high risk	84	4.4%	0.42 (0.40, 0.45)*

* $P < 0.05$ compared with HCT levels of subjects in the ultralow-risk group.

group. Compared with HCT levels in the ultralow-risk group, significant differences were found in the low-risk, intermediate-risk, and high-risk/ultrahigh-risk groups (all $P < 0.05$).

DISCUSSION

The HCT, also known as packed cell volume or erythrocyte volume fraction, is the volume percentage (%) of red blood cells in blood and functions as a major determinant of blood viscosity, blood pressure, venous return, cardiac output, and platelet adhesiveness (23, 24). Abundant epidemiologic studies have shown that HCT level is an important index of blood rheology and an independent risk of cardiovascular morbidity and mortality (6, 25). Skretteberg et al. have demonstrated that HCT levels, as a major determinant of whole blood viscosity, might have a potential adverse role in the risk of CVD (17). Elevated HCT levels might function significantly in increasing Hb levels and promote the increase of blood viscosity; thus dynamically altering the blood rheological parameters, followed by weakening of microvascular perfusion and the acceleration of the thrombus formation. Therefore, it was biologically plausible that HCT might be one of the major pathological mediators of CVD (17). Recently, a growing number of prospective studies have demonstrated that increased levels of HCT may be closely related to cardiovascular risk factors (18, 26–29).

In this study, an independent cross-sectional population study was conducted to explore the relationship between HCT levels and cardiovascular risk factors in a community-based population of 1,884 middle-aged adults. Our results revealed that the HCT levels in subjects with cardiovascular risk factors (hypertension, diabetes, dyslipidemia, smoking, or obesity) were higher than those without risk factors, suggesting that elevated HCT levels were correlated with cardiovascular risk factors. In addition, we also found that subjects with greater than or equal to three risk factors had higher levels of HCT than those with one or two risk factors, indicating that the total number of cardiovascular risk factors was positively associated with the level of HCT. Although the exact mechanism of HCT in the association of cardiovascular risk factors is not clear yet, a potential explanation might be that high HCT levels would alter its function as a major determinant of blood viscosity, whose abnormalities may cause the disorders of blood circulation, alter microcirculatory perfusion, increase atherogenesis, promote plaque rupture, and thereby contributing to ischemia (10). In our study, the results also demonstrated that the HCT levels in the ultralow-risk group were significantly lower than in the low-risk, intermediate-risk, and high-risk/ultrahigh-risk groups, revealing that the HCT levels may be an important determinant of CVD risk grade. Therefore, we speculated

that the combination of HCT levels and cardiovascular risk factors may additionally contribute to the diagnosis of CVD. Paul et al. suggested that HCT levels should be taken into consideration as an important risk predictor in the assessment and management of newly diagnosed hypertensive patients (18). Tamariz et al. confirmed that elevated estimated whole blood viscosity and HCT levels would be cross-sectionally associated with emerging risk factors for insulin resistance and type 2 diabetes mellitus (30). A recent study has showed that continuous cigarette smoking has severe adverse affects on hematological parameters including HCT, and might be associated with a greater risk for developing CVDs (31). Our findings are consistent with previous studies that HCT levels may be associated with cardiovascular risk factors; thereby estimating the combination of HCT levels and cardiovascular risk factors may improve diagnostic accuracy of CVD.

Our study has several limitations that should be acknowledged. The first limitation is that the gender ratio and mean age of subjects in this study were fairly unrepresentative, which may have effects in estimating the relationships between HCT levels and cardiovascular risk factors. On the other hand, this cross-sectional study could not establish the cause-and-effect relationship between HCT levels and cardiovascular risk factors; thereby possibly influencing the reliability of our results (32). Importantly, we failed to confirm the effects of HCT levels on prognosis of CVD patients.

In conclusion, our study indicates that elevated HCT levels may be positively associated with cardiovascular risk factors. Thus, the combination of HCT values and cardiovascular risk factors may enable early diagnosis of CVDs. Due to the limitation of study mentioned above, more detailed studies are needed to confirm our findings.

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CONFLICT OF INTEREST

No competing financial interests exist.

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