

RESEARCH

Platelet parameters in Chinese older adults with metabolic syndrome

Xue-Jiao Yang^{1,*}, Le-Yang Zhang^{2,*}, Qing-Hua Ma³, Hong-Peng Sun¹, Yong Xu¹, Xing Chen⁴ and Chen-Wei Pan¹¹School of Public Health, Medical College of Soochow University, Suzhou, China²Medical College of Soochow University, Suzhou, China³The 3rd People's Hospital of Xiangcheng District, Suzhou, China⁴Department of Children Health Care, Affiliated Suzhou Hospital of Nanjing Medical University, Suzhou, ChinaCorrespondence should be addressed to X Chen or C-W Pan: cx1708@126.com or pcwonly@gmail.com

*(X-J Yang and L-Y Zhang contributed equally to this work)

Abstract

Purpose: We aimed to examine the associations of platelet parameters with the presence of metabolic syndrome in community-dwelling older Chinese adults.

Methods: Study sample was from the Weitang Geriatric Diseases Study, which included 4338 individuals aged 60 years or above. The mean age of the participants was 68 years. Metabolic syndrome was defined based on the Adult Treatment Panel III criteria. Platelet parameters were assessed using an automated hematology analyzer. Multiple logistic regression models were fitted to examine relationships between the platelet parameters and the presence of metabolic syndrome after adjusting for potential confounders.

Results: The adjusted odds ratio (95% CI) of metabolic syndrome for the highest quartile of platelet parameters (platelet count, mean platelet volume, plateletcrit, platelet distribution width, platelet larger cell ratio) when compared to the lowest quartile were 1.32 (1.06, 1.64), 1.00 (0.81, 1.24), 1.37 (1.10, 1.71), 1.45 (1.14, 1.83), 1.11 (0.89, 1.39), respectively. Hypertension and diabetes modified the relationship between platelet distribution width and metabolic syndrome with the associations being significant in hypertensive and non-diabetic groups. The levels of platelet distribution width increased with the risk of metabolic syndrome in men but not in women.

Conclusion: The levels of platelet count, plateletcrit and platelet distribution width increased in older adults with metabolic syndrome, suggesting that these parameters may be useful biomarkers for further risk appraisal of metabolic syndrome in aged population.

Key Words

- ▶ metabolic syndrome
- ▶ platelet parameter
- ▶ platelet count
- ▶ older adults
- ▶ sex differences

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Introduction

Metabolic syndrome (MetS) affects about one-fourth of the global adult population. The prevalence of MetS has been increasing rapidly in the mainland of China over the past few decades (1), reaching 33.9% (31.0% in men and 36.8% in women) in 2010 (2). MetS refers to a cluster of metabolic risk factors that promote atherosclerotic cardiovascular disease and type 2 diabetes mellitus (3). Patients are not diagnosed with MetS until they manifest multiple symptoms related to obesity, dyslipidemia, hyperglycemia, and/or hypertension (3). However, any

combinations of these conditions take heavy tolls on an individual's long-term health. Therefore, strategies are needed for prevention and early detection of this condition.

Platelet parameters may be promising biomarkers for predicting early signs of metabolic abnormalities. The pathophysiology of MetS includes inflammation, insulin resistance, oxidative stress and endothelial dysfunction and triggers platelet hyperactivity (4). Common platelet parameters that reflect platelet reactivity include platelet

count (PC), platelet distribution width (PDW), mean platelet volume (MPV), plateletcrit (PCT) and platelet larger cell ratio (P-LCR). Among them, MPV was relatively more widely investigated in epidemiological studies and was reported to be positively associated with cardiovascular events and type 2 diabetes mellitus, but its associations with MetS was inconsistent in meta-analyses (5, 6). Other platelet parameters are also commonly available in clinical routines and there was limited evidence supporting their roles in developing MetS. Future investigations, especially on aged population, examining the associations between a broad spectrum of platelet parameters and MetS would contribute to identifying reliable blood biomarkers for screening and early detection of MetS.

Based on a large sample of community-dwelling Chinese adults aged 60 years or older, the present study aimed to examine the association of five major platelet parameters (PC, PDW, MPV, PCT, and P-LCR) with MetS. The findings might have crucial implications in developing a cheap and easy-to-operate way for MetS screening in the communities.

Methods

Study population

The Weitang Geriatric Diseases Study is a community-based study conducted in Weitang town located in Suzhou of China from August 2014 to January 2015. The detailed study protocol and some other findings have been reported in previous reports (7, 8, 9, 10, 11). In brief, invitation letters were sent to 6030 residents aged 60 years or older in the Weitang town based on official records. Older adults were excluded if he or she had migrated from the residing address, lived in the town less than 6 months, or had died. As a result, 5613 adults were considered 'eligible' to participate. Among them, 4611 attended the clinical examination and 4579 had complete data including blood samples. In addition, 241 participants with a medical history of diseases which could potentially influence the distributions of platelet parameters (e.g. liver, blood, inflammation, tumor) were excluded from the current analyses. Ultimately, 4338 healthy participants were included.

The Weitang Geriatrics Study complied with the Helsinki Declaration and was approved by the Institutional Review Board of the Soochow University. All participants involved in this study have signed informed consent.

Assessment and definition of metabolic syndrome components

Anthropometric measurements are performed by trained medical staff following standardized procedures. Body height in centimeters and weight in kilograms were measured without shoes using a wall-mounted measuring stadiometer and a digital scale. BMI was calculated using weight in kilograms divided by height in meters squared (kg/m^2). Blood pressure (BP) was measured at least three times with a minimum 5-min interval by well-trained nurses using a digital automatic blood pressure monitor. Measurements were taken under the following conditions: participants had been seated for at least 5 min after questionnaire completion, refrained from smoking and at least 30 min after blood sampling. The average of the last two readings was used in the analysis. Venous blood samples were taken after fasting for 12 h. Blood high-density lipoprotein cholesterol (HDL-C), triglycerides, and glucose levels were measured using a chemistry analyzer (Roche cobas c 501).

According to the modified Adult Treatment Panel III (ATP III) guidelines (12), MetS was diagnosed when a participant had three or more of the following conditions: (1) BMI $\geq 25 \text{ kg}/\text{m}^2$; (2) systolic blood pressure (SBP) $\geq 130 \text{ mmHg}$ or diastolic blood pressure (DBP) $\geq 85 \text{ mmHg}$ or history of antihypertensive medication; (3) blood triglycerides $\geq 150 \text{ mg}/\text{dL}$ ($1.7 \text{ mmol}/\text{L}$); (4) HDL-C of lower than $40 \text{ mg}/\text{dL}$ (men) and $50 \text{ mg}/\text{dL}$ (women); and (5) fasting plasma glucose $\geq 7.0 \text{ mmol}/\text{L}$ or have been diagnosed with diabetes mellitus (13).

Assessment of platelet parameters

Five types of platelet parameters were measured in this study including platelet count (PC), mean platelet volume (MPV), platelet distribution width (PDW), plateletcrit (PCT) and large platelet ratio (P-LCR) by professional physicians in a contracted clinical laboratory. We collected the blood samples in ethylenediamine tetra acetic acid (EDTA) tube and processed them within 4 h. The results of measurement were recorded based on public unit of measurement. For platelet parameters, normal reference ranges were as follows: PC, $150\text{--}450 \times 10^9/\text{L}$; MPV, $6.7\text{--}9.6 \text{ fL}$; PCT, $0.15\text{--}0.31\%$ for women and $0.14\text{--}0.28\%$ for men (14); PDW, $15.0\text{--}17.6\%$ (15) and P-LCR, $21.3\text{--}51.2\%$ for men and $21.1\text{--}51.4\%$ for women (16).

Assessment of covariates

Socio-demographic data, medical history, smoking status, alcohol consumption and tea consumption were obtained through a standardized questionnaire carried out by trained interviewers. Education attainment from low to high is divided into five levels: no formal education, primary school, middle school, high school and university or above. Smoking status was classified into ‘never’, ‘current’ and ‘former smoker’, while alcohol and tea consumption was divided into ‘drinkers’ and ‘non-drinkers’.

Statistical analysis

All statistical analyses were performed using commercial software IBM SPSS version 25.0 (Spss Inc). Descriptive analyses included mean and s.d. for continuous variables and frequency for categorical and ordinal variables. The differences in platelet parameters between older adults with and without MetS were compared using the Student’s *t*-test. Participants were divided into four quartiles by the level of platelet parameters. Multiple logistic regression models were fitted to examine relationships between the quartiles of platelet parameters and the presence of MetS after adjusting for sex, age, smoking status and alcohol drinking status as covariates. Adjusted odds ratios (ORs) and corresponding 95% CIs were used to assess the strength of the platelet-MetS relationship. We also assessed the association of MetS components with platelet parameters in multivariable models.

Since hypertension and diabetes mellitus are the major causes of MetS, we further conducted a stratified analysis of the population with these two conditions. The relationships between platelet parameters and MetS and its components in different disease status were analyzed. We also investigated the potential interaction between gender and platelet parameters, and the results of the gender stratification analysis are shown in a forest plot. In all analyses, two-sided *P* values <0.05 were considered as the level of statistical significance.

Results

In this analysis, 820 out of 4338 (18.9%) individuals were found to be affected by MetS based on the ATP III criteria. Platelet parameters of the study population by metabolic syndrome status are displayed in Table 1. Subjects with MetS had significantly higher levels of PC (167±48.5), PDW (16.1±1.06) and PCT (0.16±0.04) compared to those without (PC: 161±50.3, PDW: 16.0±1.14, PCT: 0.16±0.04, *P*<0.05 for all). However, levels of MPV and P-LCR were not different between the two groups. When stratified by gender, higher levels of PDW was observed (*P*<0.01) in men with MetS. In women, levels of PC and PCT were significantly higher in subjects with MetS compared to those without.

Table 2 shows the associations between platelet parameters and MetS after adjusting for potential confounders. We found that participants with MetS tended to have higher levels of PDW, PC and PCT.

Table 1 Platelet parameters of the study population by metabolic syndrome status.

Platelet parameters	n	Metabolic syndrome		P value
		Absent	Present	
All persons	n = 4338	n = 3518	n = 820	
Platelet count, mean (s.d.), 10 ⁹ /L	162 (50.1)	161 (50.3)	167 (48.5)	<0.01
Mean platelet volume, mean (s.d.), fL	9.84 (1.29)	9.84 (1.29)	9.84 (1.30)	0.94
Platelet crit, mean (s.d.), %	0.16 (0.04)	0.16 (0.04)	0.16 (0.04)	<0.01
Platelet distribution width, mean (s.d.), %	16.1 (1.13)	16.0 (1.14)	16.1 (1.06)	<0.05
Large platelet ratio, mean (s.d.), %	35.7 (10.7)	35.6 (10.6)	36.0 (10.7)	0.35
Men	n = 2117	n = 1832	n = 285	
Platelet count, mean (s.d.), 10 ⁹ /L	159 (50.2)	159 (50.6)	160 (47.5)	0.77
Mean platelet volume, mean (s.d.), fL	9.78 (1.29)	9.78 (1.29)	9.79 (1.32)	0.83
Platelet crit, mean (s.d.), %	0.15 (0.04)	0.15 (0.04)	0.15 (0.04)	0.61
Platelet distribution width, mean (s.d.), %	16.1 (1.17)	16.0 (1.20)	16.3 (0.94)	<0.01
Large platelet ratio, mean (s.d.), %	35.0 (10.5)	34.9 (10.5)	35.7 (10.8)	0.21
Women	n = 2221	n = 1686	n = 535	
Platelet count, mean (s.d.), 10 ⁹ /L	166 (49.6)	165 (49.9)	171 (48.6)	<0.05
Mean platelet volume, mean (s.d.), fL	9.91 (1.29)	9.92 (1.29)	9.87 (1.30)	0.40
Platelet crit, mean (s.d.), %	0.16 (0.04)	0.16 (0.04)	0.16 (0.04)	<0.01
Platelet distribution width, mean (s.d.), %	16.0 (1.09)	16.0 (1.08)	16.1 (1.12)	0.41
Large platelet ratio, mean (s.d.), %	36.4 (10.8)	36.4 (10.8)	36.2 (10.7)	0.62

Table 2 Relationships of platelet parameters to the prevalence of metabolic syndrome.

	Unadjusted model		Multiple adjusted model ^a	
	OR (95% CI)	P value	OR (95% CI)	P value
Platelet count, 10 ⁹ /L	1.002 (1.001, 1.004)	<0.01	1.001 (1.000, 1.003)	0.05
Q1 (<129)	Reference		Reference	
Q2 (130–160)	1.21 (0.97, 1.51)	0.09	1.22 (0.97, 1.52)	0.09
Q3 (161–191)	1.12 (0.90, 1.40)	0.33	1.05 (0.84, 1.32)	0.66
Q4 (>192)	1.45 (1.17, 1.80)	<0.01	1.32 (1.06, 1.64)	<0.05
Mean platelet volume, fL	1.00 (0.94, 1.06)	0.94	0.99 (0.93, 1.05)	0.61
Q1 (<8.9)	Reference		Reference	
Q2 (9.0–9.7)	0.98 (0.79, 1.21)	0.84	0.97 (0.78, 1.20)	0.76
Q3 (9.8–10.6)	0.91 (0.73, 1.13)	0.40	0.87 (0.70, 1.09)	0.22
Q4 (>10.7)	1.04 (0.84, 1.29)	0.72	1.00 (0.81, 1.24)	0.99
Platelet crit, %	1.38 (1.15, 1.66)	<0.01	1.24 (1.03, 1.49)	<0.05
Q1 (<0.130)	Reference		Reference	
Q2 (0.131–0.154)	1.19 (0.95, 1.49)	0.12	1.14 (0.91, 1.43)	0.26
Q3 (0.155–0.180)	1.26 (1.01, 1.57)	<0.05	1.15 (0.92, 1.44)	0.22
Q4 (>0.181)	1.58 (1.28, 1.97)	<0.01	1.37 (1.10, 1.71)	<0.01
Platelet distribution width, %	1.09 (1.02, 1.17)	<0.05	1.11 (1.03, 1.19)	<0.01
Q1 (<15.8)	Reference		Reference	
Q2 (15.9–16.1)	1.31 (1.05, 1.64)	<0.05	1.32 (1.06, 1.66)	<0.05
Q3 (16.2–16.5)	1.59 (1.28, 1.96)	<0.01	1.65 (1.33, 2.05)	<0.01
Q4 (>16.5)	1.36 (1.08, 1.72)	<0.01	1.45 (1.14, 1.83)	<0.01
Platelet larger cell ratio, %	1.003 (0.996, 1.011)	0.35	1.00 (0.99, 1.01)	0.70
Q1 (<27.9)	Reference		Reference	
Q2 (28.0–34.7)	1.08 (0.87, 1.34)	0.51	1.07 (0.86, 1.34)	0.54
Q3 (34.8–42.0)	1.16 (0.94, 1.44)	0.17	1.12 (0.90, 1.40)	0.30
Q4 (>42.0)	1.17 (0.94, 1.45)	0.16	1.11 (0.89, 1.39)	0.34

^aAdjusted for gender, age, smoking status (never, current and former smoker), and alcohol drinking status (drinkers and non-drinkers).

For example, the OR of MetS for the highest vs lowest quartile of PDW, PC and PCT were 1.45 (95% CI:1.14–1.83), 1.32 (95% CI:1.06–1.64) and 1.37 (95% CI:1.10–1.71) in multiple-adjusted models, respectively (all *P*<0.05). No significant associations were observed between levels of MPV/P-LCR and the presence of MetS.

We also assessed the association of MetS components with platelet parameters (Table 3). Results indicated that the increased PC and PCT level was significantly correlated with three MetS factors (*P*<0.05 for all) and that the level

of PDW was correlated with the high blood triglycerides (OR:1.13, 95% CI: (1.05, 1.21)).

We further examined the relationship between platelet parameters and MetS in subgroup analyses stratified by the presence of diabetes or hypertension and gender (Tables 4 and 5). We found that the presence of hypertension or diabetes modified the relationship between PDW and MetS. Among individuals with hypertension, levels of PDW showed a positive association with MetS (*P*<0.01), while this associations were not observed in

Table 3 Odds ratios (ORs) and 95% CIs for the association between platelet parameters and each criterion of metabolic syndrome.

	Overweight/obesity	Elevated BP	Elevated TG	Reduced HDL-C	Elevated FPG
	OR ^a (95% CI)	OR ^a (95% CI)	OR ^a (95% CI)	OR ^a (95% CI)	OR ^a (95% CI)
Platelet count, 10 ⁹ /L	1.001 (1.000, 1.003) <i>P</i> = 0.13	1.004 (1.002, 1.005) <i>P</i> < 0.01	1.002 (1.001, 1.004) <i>P</i> < 0.01	1.002 (1.000, 1.003) <i>P</i> < 0.05	0.999 (0.997, 1.001) <i>P</i> = 0.52
Mean platelet volume, fL	1.01 (0.96, 1.08) <i>P</i> = 0.66	1.00 (0.94, 1.07) <i>P</i> = 0.96	0.97 (0.92, 1.03) <i>P</i> = 0.36	0.92 (0.87, 0.98) <i>P</i> < 0.01	1.04 (0.96, 1.12) <i>P</i> = 0.32
Platelet crit, %	1.25 (1.03, 1.50) <i>P</i> < 0.05	1.75 (1.39, 2.20) <i>P</i> < 0.01	1.32 (1.11, 1.58) <i>P</i> < 0.01	1.12 (0.94, 1.34) <i>P</i> = 0.22	0.84 (0.61, 1.16) <i>P</i> = 0.28
Platelet distribution width, %	1.03 (0.96, 1.10) <i>P</i> = 0.48	1.01 (0.94, 1.09) <i>P</i> = 0.77	1.13 (1.05, 1.21) <i>P</i> < 0.01	1.05 (0.98, 1.12) <i>P</i> = 0.20	1.05 (0.95, 1.15) <i>P</i> = 0.34
Platelet larger cell ratio, %	1.004 (0.996, 1.011) <i>P</i> = 0.32	1.00 (0.99, 1.01) <i>P</i> = 0.96	1.00 (0.99, 1.01) <i>P</i> = 0.36	0.992 (0.985, 0.999) <i>P</i> < 0.05	1.01 (1.00, 1.02) <i>P</i> = 0.12

^aAdjusted for gender, age, smoking status (never, current and former smoker), and alcohol drinking status (drinkers and non-drinkers). BP, blood pressure; FPG, fasting plasma glucose; HDL-C, high-density lipoprotein cholesterol; TG, triglycerides.

Table 4 Associations of platelet parameters with metabolic syndrome by diabetes.

PC, 10 ⁹ /L	P		MPV, fL	P		PCT, %	P		PDW, %	P		P-LCR, %	P	
	OR (95% CI)	Value		OR (95% CI)	Value		OR (95% CI)	Value		OR (95% CI)	Value		OR (95% CI)	Value
Diabetes														
All persons	1.009 (1.003, 1.014)	<0.05	All persons	0.87 (0.72, 1.06)	0.16	All persons	1.84 (1.04, 3.25)	<0.05	All persons	0.96 (0.79, 1.06)	0.68	All persons	0.98 (0.96, 1.00)	0.99
Q1 (≤121)	Reference		Q1 (≤8.90)	Reference		Q1 (≤0.13)	Reference		Q1 (≤15.9)	Reference		Q1 (≤28.3)	Reference	
Q2 (121–157)	1.32 (0.68, 2.57)	0.41	Q2 (8.91–9.80)	1.12 (0.57, 2.19)	0.74	Q2 (0.14–0.15)	0.86 (0.44, 1.68)	0.66	Q2 (16.0–16.2)	0.93 (0.48, 1.81)	0.84	Q2 (28.4–35.6)	1.64 (0.83, 3.26)	0.16
Q3 (158–192)	1.65 (0.84, 3.23)	0.15	Q3 (9.81–10.70)	0.48 (0.24, 0.95)	<0.05	Q3 (0.16–0.18)	1.40 (0.71, 2.76)	0.34	Q3 (16.3–16.5)	0.66 (0.34, 1.27)	0.22	Q3 (35.7–43.0)	0.91 (0.46, 1.79)	0.78
Q4 (>192)	1.91 (0.96, 3.82)	0.07	Q4 (>10.70)	1.05 (0.53, 2.08)	0.89	Q4 (>0.18)	1.45 (0.72, 2.91)	0.30	Q4 (>16.5)	0.94 (0.48, 1.85)	0.85	Q4 (>43.0)	0.77 (0.39, 1.50)	0.44
Men	1.004 (0.997, 1.011)	0.28	Men	1.02 (0.78, 1.34)	0.23	Men	1.92 (0.81, 4.57)	0.14	Men	1.17 (0.89, 1.56)	0.26	Men	1.01 (0.98, 1.04)	0.61
Women	1.008 (0.999, 1.012)	0.06	Women	0.74 (0.56, 0.97)	<0.05	Women	1.71 (0.79, 3.69)	0.18	Women	0.71 (0.47, 1.08)	0.11	Women	0.96 (0.92, 0.99)	<0.05
Non-diabetes														
All persons	1.001 (1.000, 1.003)	0.16	All persons	0.99 (0.93, 1.06)	0.83	All persons	1.20 (0.97, 1.48)	0.90	All persons	1.15 (1.05, 1.25)	<0.05	All persons	1.00 (1.00, 1.01)	0.44
Q1 (≤129)	Reference		Q1 (≤8.90)	Reference		Q1 (≤0.13)	Reference		Q1 (≤15.8)	Reference		Q1 (≤27.8)	Reference	
Q2 (130–160)	1.32 (1.03, 1.69)	<0.05	Q2 (8.91–9.70)	0.96 (0.76, 1.22)	0.76	Q2 (0.14–0.15)	1.23 (0.96, 1.60)	0.11	Q2 (15.9–16.1)	1.51 (1.17, 1.94)	<0.01	Q2 (27.9–34.5)	1.10 (0.86, 1.41)	0.46
Q3 (161–191)	1.09 (0.84, 1.40)	0.52	Q3 (9.71–10.6)	0.92 (0.72, 1.18)	0.52	Q3 (0.16–0.18)	1.26 (0.98, 1.62)	0.07	Q3 (16.2–16.5)	1.88 (1.47, 2.40)	<0.01	Q3 (34.6–41.9)	1.13 (0.88, 1.44)	0.33
Q4 (>191)	1.36 (1.06, 1.74)	<0.05	Q4 (>10.6)	0.98 (0.77, 1.25)	0.87	Q4 (>0.18)	1.38 (1.08, 1.78)	<0.05	Q4 (>16.5)	1.58 (1.21, 2.06)	<0.01	Q4 (>41.9)	1.13 (0.88, 1.44)	0.33
Men	0.999 (0.996, 1.002)	0.56	Men	1.00 (0.90, 1.12)	0.98	Men	0.86 (0.59, 1.26)	0.43	Men	1.25 (1.09, 1.45)	<0.01	Men	1.01 (0.99, 1.02)	0.30
Women	1.002 (1.000, 1.004)	<0.05	Women	0.99 (0.91, 1.08)	0.81	Women	1.42 (1.09, 1.84)	<0.01	Women	1.09 (0.98, 1.21)	0.12	Women	1.00 (0.99, 1.01)	0.81

Adjusted for gender, age, smoking status (never, current and former smoker), and alcohol drinking status (drinkers and non-drinkers).

Table 5 Associations of platelet parameters with metabolic syndrome by hypertension.

PC, 10 ⁹ /L	P		MPV, fL	P		PCT, %	P		PDW, %	P		P-LCR, %	P	
	OR (95% CI)	Value		OR (95% CI)	Value		OR (95% CI)	Value		OR (95% CI)	Value		OR (95% CI)	Value
Hypertension														
All persons	1.001 (0.998, 1.002)	0.71	All persons	0.97 (0.90, 1.04)	0.37	All persons	1.04 (0.82, 1.30)	0.77	All persons	1.12 (1.02, 1.22)	<0.05	All persons	1.00 (0.99, 1.01)	0.81
Q1 (≤131)	Reference		Q1 (≤8.90)	Reference		Q1 (≤0.13)	Reference		Q1 (≤15.9)	Reference		Q1 (≤28.1)	Reference	
Q2 (132–163)	1.19 (0.91, 1.57)	0.21	Q2 (8.91–9.70)	0.86 (0.65, 1.13)	0.27	Q2 (0.14–0.16)	1.17 (0.89, 1.54)	0.27	Q2 (16.0–16.1)	1.54 (1.16, 2.04)	<0.01	Q2 (28.2–35.2)	1.08 (0.82, 1.42)	0.58
Q3 (164–195)	1.07 (0.81, 1.40)	0.65	Q3 (9.71–10.70)	0.812 (0.62, 1.06)	0.12	Q3 (0.17–0.18)	1.04 (0.79, 1.38)	0.78	Q3 (16.2–16.5)	1.91 (1.45, 2.52)	<0.01	Q3 (35.3–42.4)	1.04 (0.79, 1.37)	0.77
Q4 (>195)	1.13 (0.86, 1.49)	0.39	Q4 (>10.70)	0.90 (0.69, 1.18)	0.45	Q4 (>0.18)	1.10 (0.84, 1.45)	0.48	Q4 (>16.5)	1.52 (1.13, 2.04)	<0.01	Q4 (>42.4)	1.06 (0.81, 1.40)	0.67
Men	0.999 (0.996, 1.002)	0.44	Men	1.03 (0.92, 1.06)	0.57	Men	0.89 (0.60, 1.32)	0.56	Men	1.22 (1.05, 1.41)	<0.01	Men	1.01 (1.00, 1.03)	0.13
Women	1.001 (0.999, 1.004)	0.25	Women	0.93 (0.84, 1.02)	0.11	Women	1.15 (0.86, 1.35)	0.36	Women	1.05 (0.93, 1.17)	0.43	Women	1.00 (0.98, 1.01)	0.36
Non-hypertension														
All persons	1.002 (0.999, 1.004)	0.27	All persons	0.99 (0.89, 1.04)	0.86	All persons	1.23 (0.86, 1.76)	0.25	All persons	1.06 (0.93, 1.21)	0.38	All persons	1.00 (0.99, 1.01)	0.91
Q1 (≤126)	Reference		Q1 (≤8.90)	Reference		Q1 (≤0.13)	Reference		Q1 (≤15.8)	Reference		Q1 (≤27.6)	Reference	
Q2 (127–156)	1.14 (0.77, 1.70)	0.51	Q2 (8.91–9.60)	1.37 (0.94, 2.01)	0.11	Q2 (0.14–0.15)	0.87 (0.58, 1.31)	0.51	Q2 (15.9–16.1)	0.98 (0.66, 1.47)	0.93	Q2 (27.7–34.0)	1.15 (0.77, 1.70)	0.49
Q3 (157–187)	1.03 (0.70, 1.54)	0.87	Q3 (9.61–10.50)	0.95 (0.64, 1.43)	0.82	Q3 (0.16–0.18)	0.94 (0.63, 1.39)	0.75	Q3 (16.2–16.5)	1.35 (0.93, 1.96)	0.11	Q3 (34.1–41.6)	1.05 (0.71, 1.56)	0.81
Q4 (>187)	1.25 (0.85, 1.84)	0.26	Q4 (>10.50)	1.14 (0.77, 1.68)	0.52	Q4 (>0.18)	1.21 (0.83, 1.77)	0.33	Q4 (>16.5)	1.29 (0.86, 1.94)	0.23	Q4 (>41.6)	1.19 (0.81, 1.76)	0.38
Men	0.999 (0.994, 1.001)	0.74	Men	0.94 (0.77, 1.14)	0.50	Men	0.77 (0.40, 1.49)	0.44	Men	1.20 (0.94, 1.53)	0.15	Men	1.00 (0.98, 1.02)	0.91
Women	1.003 (0.999, 1.006)	0.14	Women	1.02 (0.89, 1.06)	0.78	Women	1.50 (0.98, 2.31)	0.06	Women	1.00 (0.85, 1.17)	0.99	Women	1.00 (0.98, 1.02)	0.75

Adjusted for gender, age, smoking status (never, current and former smoker), and alcohol drinking status (drinkers and non-drinkers).



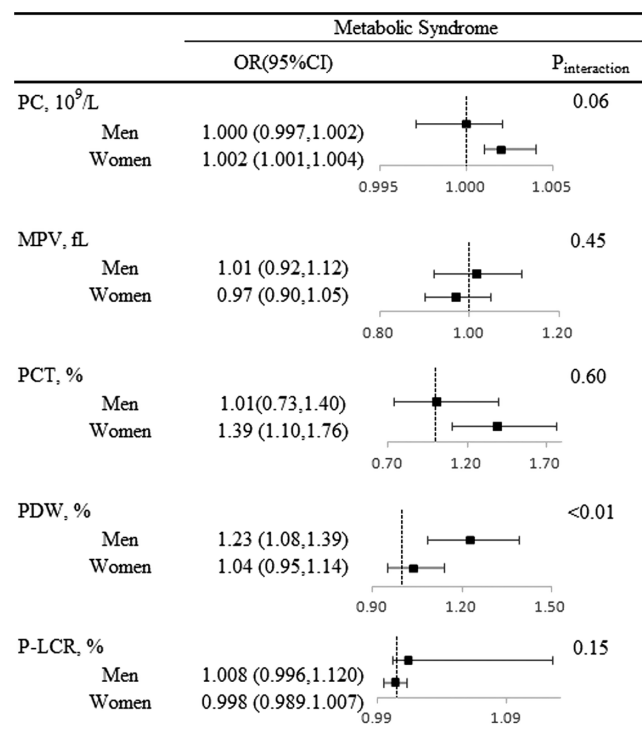


Figure 1 Subgroup analyses of the association between platelet parameters and MetS. Interactions between platelet parameters and sex on the MetS were tested by the likelihood ratio test with adjustment for the same variables as multiple model in Table 2 in addition to sex. Odds ratio and 95% CIs were showed by forest plot.

non-hypertensive ones. In the stratified analysis of diabetes, however, this relationship was only significant in men without diabetes. Meanwhile, the relationships between PC/PCT and MetS were always significant in diabetic participants. In addition, significant interaction effect of gender on the relationship between levels of PDW and MetS were observed (*P* value for interaction <0.01).

In subsequent analyses stratified by gender (Fig. 1), the levels of PDW increased with the risk of MetS in men but not in women.

Table 6 shows that high BP and high triglycerides were accompanied by increased levels of PC and PCT in non-diabetes participants. Meanwhile, as shown in Table 7, PC and PCT levels were associated with high triglycerides in patients with hypertension.

Discussion

In the present study, we found that some platelet parameters such as PC, PCT and PDW were significantly associated with MetS in a large sample of community-dwelling older adults. In general, older individuals with MetS tended to have higher PC, PCT and PDW levels compared with those without. Moreover, gender and the presence of hypertension and diabetes modified the association between PDW and MetS. These findings added new knowledge on role of platelets in the pathogenesis of MetS and may help to develop early diagnostic strategies for MetS-related complications.

To the best of our knowledge, this is the first study assessing the relationship of platelet parameters with MetS in older adults. PDW represents the morphologic changes and the activity of platelets (17). Therefore, elevated PDW indicates the presence of larger, younger and more active platelets in peripheral blood (6, 18, 19). The biological mechanisms underlying observed associations between MetS and PDW are not fully elucidated, but some possibilities have been suggested. Insulin resistance plays an important role in the development of MetS and type 2 diabetes mellitus. Vascular dysfunction caused by insulin resistance may lead to a decrease in prostacyclin and nitric

Table 6 Associations of platelet parameters with components of metabolic syndrome by diabetes.

	Elevated BP		Elevated BMI		Elevated TG		Reduced HDL-C	
	OR (95% CI)	<i>P</i> value	OR (95% CI)	<i>P</i> value	OR (95% CI)	<i>P</i> value	OR (95% CI)	<i>P</i> value
Diabetes								
PC, 10 ⁹ /L	1.00 (0.99, 1.01)	0.56	1.00 (1.00, 1.01)	0.45	1.01 (1.00, 1.01)	<0.05	1.00 (1.00, 1.01)	0.74
MPV, fL	1.07 (0.74, 1.54)	0.73	1.00 (0.82, 1.22)	0.99	0.84 (0.69, 1.03)	0.10	0.93 (0.76, 1.14)	0.49
PCT, %	1.97 (0.65, 6.00)	0.23	1.36 (0.76, 2.43)	0.31	1.63 (0.93, 2.87)	0.09	1.04 (0.59, 1.83)	0.90
PDW, %	1.27 (0.67, 1.97)	0.08	1.19 (0.66, 2.16)	0.56	1.09 (0.88, 1.35)	0.55	0.90 (0.73, 1.11)	0.32
P-LCR, %	1.01 (0.97, 1.06)	0.58	1.00 (0.89, 1.03)	0.88	0.98 (0.96, 1.01)	0.19	0.99 (0.96, 1.01)	0.29
Non-diabetes								
PC, 10 ⁹ /L	1.004 (1.002, 1.006)	<0.05	1.000 (0.999, 1.003)	0.23	1.002 (1.000, 1.003)	<0.05	1.002 (1.000, 1.003)	<0.05
MPV, fL	1.00 (0.93, 1.07)	0.94	1.02 (0.96, 1.08)	0.59	0.99 (0.93, 1.05)	0.61	0.92 (0.86, 0.98)	<0.01
PCT, %	1.77 (1.40, 2.24)	<0.05	1.22 (1.00, 1.49)	0.05	1.29 (1.07, 1.55)	<0.01	1.13 (0.93, 1.21)	0.21
PDW, %	1.00 (0.93, 1.08)	0.92	1.02 (0.95, 1.10)	0.61	1.13 (1.05, 1.22)	<0.01	1.07 (0.99, 1.15)	0.09
P-LCR, %	1.00 (1.00, 1.01)	0.82	1.00 (1.00, 1.01)	0.29	1.01 (1.00, 1.01)	0.19	0.99 (0.99, 1.10)	<0.05

Adjusted for gender, age, smoking status (never, current and former smoker), and alcohol drinking status (drinkers and non-drinkers). BP blood pressure, TG triglycerides, HDL-C high-density lipoprotein cholesterol.

Table 7 Associations of platelet parameters with components of metabolic syndrome by hypertension.

	Elevated FPG		Elevated BMI		Elevated TG		Reduced HDL-C	
	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value
Hypertension								
PC, 10 ⁹ /L	0.998 (0.996, 1.001)	0.21	1.000 (0.998, 1.002)	0.95	1.002 (1.000, 1.004)	<0.05	1.002 (1.000, 1.004)	<0.05
MPV, fL	1.03 (0.94, 1.12)	0.60	1.03 (0.95, 1.11)	0.47	0.93 (0.87, 1.01)	0.07	0.90 (0.83, 0.97)	<0.01
PCT, %	1.14 (0.10, 2.73)	0.20	0.96 (0.18, 21.01)	0.58	1.25 (1.01, 1.56)	<0.05	1.11 (0.89, 1.40)	0.35
PDW, %	1.06 (0.95, 1.19)	0.27	1.03 (0.94, 1.12)	0.55	1.09 (1.00, 1.19)	0.05	1.03 (0.94, 1.12)	0.55
P-LCR, %	1.01 (1.00, 1.02)	0.70	1.01 (1.00, 1.02)	0.20	1.00 (0.99, 1.01)	0.08	0.99 (0.98, 1.00)	<0.05
Non-hypertension								
PC, 10 ⁹ /L	0.999 (0.995, 1.003)	0.70	1.002 (0.998, 1.004)	0.18	1.000 (0.998, 1.003)	0.54	1.001 (0.998, 1.003)	0.66
MPV, fL	1.04 (0.90, 1.27)	0.60	0.97 (0.88, 1.08)	0.61	1.02 (0.93, 1.13)	0.63	1.95 (0.87, 1.04)	0.25
PCT, %	0.96 (0.58, 1.60)	0.87	1.28 (0.92, 1.78)	0.15	1.16 (0.85, 1.59)	0.35	0.96 (0.71, 1.30)	0.79
PDW, %	0.98 (0.83, 1.15)	0.80	1.00 (0.89, 1.12)	0.99	1.19 (1.05, 1.36)	<0.01	1.07 (0.96, 1.19)	0.25
P-LCR, %	1.01 (0.99, 1.03)	0.44	1.00 (0.99, 1.01)	0.96	1.01 (1.00, 1.02)	0.14	1.00 (0.98, 1.01)	0.37

Adjusted for gender, age, smoking status (never, current and former smoker), and alcohol drinking status (drinkers and non-drinkers). FPG, fasting plasma glucose; HDL-C, high-density lipoprotein cholesterol; TG, triglycerides.

oxide production by the vascular endothelium, resulting in promoting increased platelet activity (20). Furthermore, a plethora of studies have indicated that platelet activation is associated with the development of atherosclerosis and thrombosis, which is a result of MetS components such as hypertension, obesity, and inflammation. People with atherosclerosis and thrombosis exhibit greater platelet activation, which promotes increased peripheral platelet consumption, resulting in platelets produced by the bone marrow being larger and more active.

We also found that levels of PC/PCT were higher in older adults with MetS than those without. In accordance with results of Table 3, both PC and PCT were associated with three components of MetS. First, it is suggested that metabolic disorders are often accompanied by low-grade inflammation (21), characterized by increased secretion of a variety of adipokines and cytokines such as adiponectin, interleukin 6 (IL-6), and tumor necrosis factor- α (TNF- α), leading to changes in levels of PC (22). Meanwhile, the value of PCT is derived from PC and MPV with increased PC levels being associated with higher PCT levels. Secondly, physical activity showed a significant and inverse dose-response relationship with levels of PC (23). PC can also be influenced by nutritional status, which is closely related to metabolic function. Martin *et al.* (24) demonstrated that the animals on the high-cholesterol diet had significantly higher levels of PC than the control group, which indicates that a high-cholesterol diet produces might change platelet production. The development of MetS is highly dependent of physical activity, nutrition, lifestyle, and family genetics and these risk factors for MetS may, at least partially, explain the relationship between PC/PCT and MetS. This also explains the increased levels of PC and PCT in people

who have both high BP and high triglycerides. Our study suggested that the presence of hypertension modified the association between increased PDW levels in people who had both hypertension and MetS. High blood pressure might cause endothelial dysfunction and vascular damage, which promotes platelet activation and adhesion (25). According to previous studies, PDW is a more specific marker of platelet activation than MPV (26). Furthermore, hypertension is a major risk factor for cardiovascular disease (CVD) (27) and PDW associated with or predicting cardiovascular disorders (28).

Our study showed that the association of PC/PCT with MetS was gender specific and was significant in women rather than men. This finding was consistent with some previous studies (29, 30). We provided some explanations for the gender difference in the PC/PCT-MetS associations. First, women tend to have higher body fat rates than men with similar BMI. Pro-inflammatory cytokines are released by perivascular white adipose tissue, which may increase the numbers of platelets and lead to chronic low-grade inflammation (31). Second, there are differences in lifestyles between men and women. Chinese men are significantly more likely to smoke and drink alcohol than women. Cigarette smoking has been shown to increase platelet count and platelet aggregation (32, 33), while alcohol consumption can lead to abnormalities in platelet function (34, 35). Third, higher testosterone levels might be associated with a reduced risk of MetS in men and an elevated risk in women (36). Thus, one may hypothesize that gender-specific sex hormones may explain some of this phenomenon. Our study had a relatively large sample size so that the study power was sufficient to detect the association between platelet parameters and MetS as well as some possible interaction effects. However, some

limitations exist in the current study. First, the causal relationship could not be identified because of the nature of the cross-sectional design. It is also likely that MetS may result in a higher level of platelet parameters. In addition, although some confounding factors have been adjusted, other potential confounding effects (such as long-term medication) may still exist and may distort the findings.

In conclusion, our study provided preliminary evidence on the association between platelet parameters including PC, PCT and PDW and MetS in older Chinese adults. Higher PC/PCT levels tended to increase the risk of MetS in women and increased PDW levels in hypertensive patients was associated with MetS. Longitudinal cohort studies are warranted to confirm the findings and evaluate the power and ability of platelet parameters in predicting MetS and its associated complications.

Declaration of interest

The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

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Ethical approval

This study was conducted complying with the tenets of the Helsinki Declaration and with the approval of the Institutional Review Board of Soochow University.

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