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Plasma P-selectin level is associated with severity of coronary heart disease in Chinese Han population

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Abstract

Objective: This study aimed to evaluate the association between plasma P-selectin levels and the severity of coronary heart disease (CHD) in a Chinese Han population.

Methods: We enrolled 219 patients with CHD and 168 healthy individuals without CHD as a control group. Coronary stenosis was evaluated based on the number of diseased coronary arteries and the Gensini scoring system. P-selectin levels were quantified by enzyme-linked immunosorbent assay and the association between CHD and plasma P-selectin level was analyzed.

Results: P-selectin levels were significantly higher in CHD patients compared with controls. Levels were highest in patients with three-vessel disease and lowest in those with one-vessel disease, with significant differences among the groups. P-selectin levels were also highest in the high-score and lowest in the low-score group according to Gensini score, with significant differences among the groups. P-selectin level was significantly positively correlated with Gensini score and C-reactive protein level. Elevated P-selectin was identified as an independent risk factor for CHD.

Conclusion: P-selectin levels were increased in Chinese Han patients with CHD. P-selectin level is an independent risk factor for CHD and may serve as a biomarker reflecting the severity of CHD in the Chinese Han population.

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Introduction

Coronary heart disease (CHD) is a common cardiovascular disease caused by atherosclerosis, resulting in myocardial ischemia, hypoxia, and even necrosis. Rapid developments in social economics and changes in people's lifestyles and environments mean that cardiovascular disease has become a leading cause of disability and death in China. The incidence of CHD is increasing.[1] Invasive coronary angiography is currently the gold standard for diagnosing CHD; however, this is expensive and associated with risks to the patient. Novel non-invasive biomarkers are therefore needed for diagnosing and/or stratifying CHD.[2]

CHD involves a cascade of coronary atherosclerotic events, including lipid and fibrous matrix deposition on the walls of the coronary arteries to form atherosclerotic plaques,[3,4] and recruitment and adhesion of circulating leukocytes to the vascular endothelium.[3,5] Accumulating evidence indicates that inflammation and platelet activation participate in the occurrence and development of thrombus formation and atherosclerosis.[6,7] P-selectin is a granule membrane protein belonging to the lectin family, which is released from the α-granules of platelets. P-selectin plays a key role in the rolling and tethering of platelets on the surface of activated endothelial cells[8] and is therefore an important marker for endothelial dysfunction and platelet activation. Accumulating evidence indicates that peripheral blood P-selectin levels are significantly increased in patients with cardiovascular diseases.[9,10]

However the association between plasma P-selectin level and the severity of CHD in the Chinese Han population remains unclear. In this study, we measured plasma P-selectin levels in Chinese Han patients with CHD and analyzed their association with the severity of CHD. These results will further our understanding of the role of P-selectin in CHD in the Chinese Han population.

Subjects and methods

Study subjects

Chinese Han subjects who underwent coronary angiography because of suspected CHD at the People's Hospital of Funing from 2016 to 2018 were enrolled in this study. All individuals provided written informed consent and the study was approved by the Ethics Committee and Institutional Review Board of the People's Hospital of Funing. Patients were diagnosed with CHD according to clinical symptoms, electrocardiogram changes, coronary angiograms, and laboratory markers, and patients without confirmed CHD served as the control group.

Patients with severe valvular heart disease, pulmonary heart disease, severe hepatic or renal dysfunction, autoimmune diseases, pulmonary embolism, acute infection, cerebrovascular disease, malignant tumor, or mental illness were excluded.

Baseline data

Baseline characteristics were recorded including age, sex, body mass index (BMI), history of diabetes mellitus, history of smoking, history of hypertension, ejection fraction (EF), platelets, triglycerides (TG), total cholesterol (TC), low-density

lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), lipoprotein a (LP(a)), apolipoprotein B (APO-B), and C-reactive protein (CRP). The above laboratory parameters were measured using an automatic analyzer 7600 series (Hitachi Medical Corporation, Tokyo, Japan) in the clinical laboratory of the People's Hospital of Funing.

Evaluation of coronary lesion severity

The severity of the coronary lesions was evaluated based on the number of diseased coronary arteries and the Gensini scoring system. CHD patients were then divided into groups according to the number of major coronary arteries with stenosis >50% (one, two, or three).[6] CHD patients were also divided into groups according to coronary stenosis determined by Gensiniscore (low <20, middle 20–40, and high >40).[6,11]

Detection of plasma P-selectin levels

Elbow venous blood was drawn from all subjects in the early morning after hospitalization. Plasma P-selectin concentration was determined using a P-selectin enzyme-linked immunosorbent assay kit (Abcam, Cambridge, MA, USA) according to the manufacturer's instructions.

Statistical analysis

All the data were analyzed using SPSS Statistics for Windows, Version 21.0 (IBM Corp., Armonk, NY, USA). Continuous data were expressed as mean ± standard deviation and compared by independent t-tests or one-way analysis of variance (ANOVA). Qualitative data were expressed as composition ratio and compared by χ^2 tests. Correlations between P-selectin levels and clinicopathological factors were analyzed by Spearman's or Pearson's correlation analysis. Independent risk factors for

Gensini score were evaluated by multinomial logistic regression analysis and independent risk factors for CHD were evaluated by binary logistic regression analysis. Statistical significance was set at $P < 0.05$.

Results

Patient characteristics

This study included 387 patients who underwent coronary angiography because of suspected CHD, of whom 219 were diagnosed with CHD. The remaining 168 patients without CHD served as the control group. The baseline clinical features of the CHD and control groups are shown in Table 1. TC, TG, CRP, and P-selectin levels were all significantly higher in the CHD compared with the control group (all $P < 0.05$) while HDL-C and EF were both significantly lower (both $P < 0.05$). The incidences of other conventional risk factors for CHD including hypertension, diabetes mellitus, and smoking were also significantly higher in the CHD group (all $P < 0.05$). There were no significant differences in age, sex, platelets, LDL-C, LP(a), and APO-B between the CHD patients and controls.

Comparison of P-selectin and CRP levels according to number of vessels involved

P-selectin and CRP levels were significantly increased in patients with one-, two-, and three-vessel disease compared with the control group ($P < 0.01$). We further compared P-selectin and CRP levels among the one-, two-, and three-vessel disease groups and showed that both levels were highest in the three-vessel group and lowest in the one-vessel group. P-selectin and CRP levels were significantly different among the four groups, ($P < 0.01$), apart from no significant difference in CRP levels between

Table 1. Baseline data and P-selectin levels in patients with coronary heart disease and controls.

	CHD group (n = 219)	Control group (n = 168)	t or χ^2	P Value
Age (years)	59.83 ± 7.65	60.38 ± 6.40	0.751	0.453
Sex (male, %)	131 (59.82)	85 (50.59)	3.279	0.070
Mean BMI (kg/m^2)	27.87 ± 5.41	25.57 ± 3.78	−4.693	<0.01
Hypertension n (%)	143 (65.30)	68 (40.48)	23.621	<0.01
Diabetes, n (%)	66 (30.14)	21 (12.50)	16.970	<0.01
Smoking, n (%)	90 (41.10)	33 (19.64)	20.181	<0.01
EF (%)	57.76 ± 6.16	59.11 ± 6.65	2.063	0.040
Platelets (×10^9/L)	186.96 ± 21.16	186.24 ± 21.01	0.336	0.737
TC (mmol/L)	5.02 ± 1.05	4.40 ± 0.76	−6.533	<0.01
TG (mmol/L)	1.50 ± 0.59	1.03 ± 0.37	−9.118	<0.01
LDL-C (mmol/L)	2.86 ± 0.72	2.79 ± 0.74	−0.946	0.345
HDL-C (mmol/L)	1.20 ± 0.43	1.37 ± 0.32	4.210	<0.01
LP (a) (mmol/L)	180.86 ± 68.44	182.11 ± 68.14	0.179	0.858
APO-B (mmol/L)	0.84 ± 0.14	0.82 ± 0.13	−0.984	0.326
CRP (mmol/L)	5.01 ± 1.79	1.86 ± 0.88	−20.932	<0.01
P-selectin (ng/mL)	27.59 ± 5.94	16.39 ± 3.03	−22.311	<0.01

CHD, coronary heart disease; BMI, body mass index; EF, ejection fraction; TC, total cholesterol; TG, triglycerides; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; LP (a), lipoprotein a; APO-B, apolipoprotein B; CRP, C-reactive protein.

Table 2. Comparisons of P-selectin and C-reactive protein levels in patients with coronary heart disease involving different numbers of vessels.

Group	n	CRP (mmol/L)	P-selectin (ng/mL)
Control	168	1.86 ± 0.88	16.39 ± 3.03
One-vessel	66	4.59 ± 1.54*	22.65 ± 4.08*
Two-vessel	75	4.89 ± 1.70*	27.34 ± 4.74*,#
Three-vessel	78	5.48 ± 1.99*,#,@	32.02 ± 4.84*,#,@
F value		155.566	316.444
P value		<0.01	<0.01

*P<0.05 vs control group; #P<0.05 vs one-vessel group; @P<0.05 vs two-vessel group. CRP, C-reactive protein.

the one-vessel and two-vessel groups. The results are shown in Table 2.

Comparison of P-selectin and CRP levels according to Gensini score

P-selectin and CRP levels were significantly higher in patients with low, middle, and high Gensini scores compared with the control group (P < 0.01). P-selectin and CRP levels were further analyzed among the low-, middle-, and high-score groups, and P-selectin levels were highest in the high-score group and lowest in the low-score group (P < 0.01). CRP levels were significantly different between the high- and low-score groups (P < 0.01). The results are shown in Table 3.

Table 3. Comparisons of P-selectin and C-reactive protein levels in patients according to Gensini score.

Group	n	CRP (mmol/L)	P-selectin (ng/mL)
Control	168	1.86 ± 0.88	16.39 ± 3.03
Low score	59	4.48 ± 1.50*	22.09 ± 3.64*
Middle score	45	5.00 ± 1.73*	26.17 ± 5.04*,#
High score	115	5.29 ± 1.91*,#	30.97 ± 4.79*,#,@
F value		153.902	316.444
P value		0.000	0.000

*$P < 0.05$ vs control group; #$P < 0.05$ vs low-score group; @$P < 0.05$ vs middle-score group. CRP, C-reactive protein.

Correlation between P-selectin level and other CHD risk factors

Spearman's correlation analysis revealed that the P-selectin level was positively correlated with CRP ($r = 0.149$, $P = 0.028$) (Figure 1a) but not with BMI, TG, TC, HDL-C, smoking, hypertension, or diabetes mellitus.

Relationship between P-selectin level and the extent of coronary lesions in the CHD group

Pearson's correlation analysis revealed that P-selectin level was positively correlated with Gensini score ($r = 0.491$, $P < 0.01$) (Figure 1b). This association was further evaluated by multinomial logistic regression analysis with BMI, TG, TC, HDL-C, CRP, P-selectin, smoking, hypertension, and diabetes mellitus substituted into the regression equation. However, P-selectin level was identified as the only independent risk factor for Gensini score (odds ratio = 0.603, 95% confidence interval: 0441–0.824, $P = 0.002$).

Evaluation of independent risk factors for CHD

The independent risk factors for CHD were analyzed by binary logistic regression analysis with BMI, TG, TC, HDL-C, CRP,
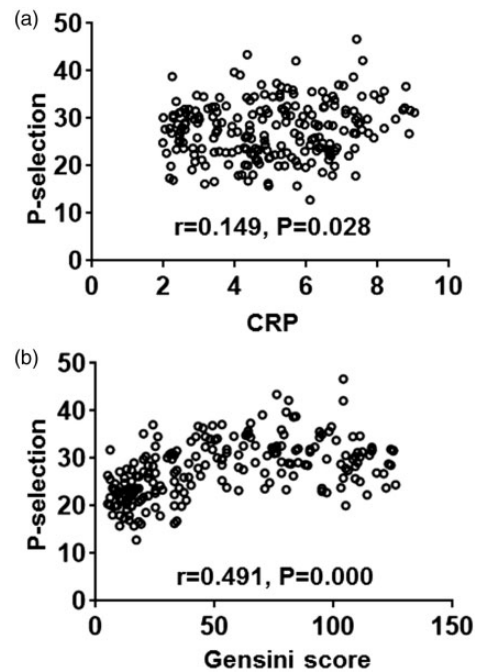

Figure 1. (a) Spearman's correlation analysis revealed that P-selectin level was positively correlated with C-reactive protein ($r = 0.149$, $P = 0.028$). (b) Pearson's correlation analysis revealed that P-selectin level was positively correlated with Gensini score ($r = 0.491$, $P < 0.01$). CRP, C-reactive protein.

P-selectin, smoking, hypertension, and diabetes mellitus substituted into the regression equation. TC, TG, CRP, P-selectin, and smoking were identified as independent

Table 4. Independent risk factors for coronary heart disease evaluated by binary logistic regression analysis

	B	SE	P	OR	95%CI	
					Lower limit	Upper limit
TC	2.027	0.911	0.026	7.593	1.273	45.296
TG	3.144	1.250	0.012	23.190	2.001	268.683
CRP	3.621	1.002	<0.01	37.362	5.246	266.093
P-selectin	1.115	0.287	<0.01	3.051	1.739	5.354
Smoking	5.606	1.810	0.002	0.004	0.000	0.128

TC, total cholesterol; TG, triglycerides; CRP, C-reactive protein; SE, standard error; OR, odds ratio; CI, confidence interval

risk factors for CHD. The results are shown in Table 4.

Discussion

This study aimed to explore the association between plasma P-selectin levels and the severity of CHD in a Chinese Han population. Plasma P-selectin levels were significantly higher in patients with CHD compared with a control group without CHD, with the highest levels in patients with three-vessel disease and the lowest in patients with one-vessel disease. Plasma P-selectin level was also positively correlated with Gensini score and CRP level. Elevated P-selectin and CRP levels were independent risk factors for the presence of CHD.

Platelet activation and tethering play a key role in CHD. P-selectin is the most specific marker known to reflect platelet activation and plays a key role in the rolling and tethering of platelets on the surface of activated endothelial cells.[8] P-selectin is thus an important marker of endothelial dysfunction and platelet activation. Accumulating evidence indicates that peripheral blood P-selectin levels are significantly increased in patients with cardiovascular diseases.[9,10] The current study also showed that P-selectin levels were increased in patients with CHD, in accordance with

previous studies.[3] P-selectin level was positively correlated with the severity of CHD, with increasing levels in line with increasing number of lesioned vessels and increasing Gensini score. P-selectin level was the only independent risk factor for Gensini score and was an independent risk factor for CHD according to multivariate stepwise regression analysis.

Accumulating evidence indicates that inflammation and platelet activation participate in the occurrence and development of thrombus formation and atherosclerosis.[6,7] Inflammation is linked to atherosclerosis. CRP is associated with an acute-phase response and is a nonspecific marker for inflammation.[6] In this study, CRP levels were significantly higher in CHD patients compared with controls, in accordance with previous studies.[6,12,13] CRP level was positively correlated with the severity of CHD, being higher in patients with a high compared with a low Gensini score and higher in patients with three-vessel disease compared with those with one- or two-vessel disease. CRP level was identified as an independent risk factor for CHD by multivariate stepwise regression analysis. Furthermore, CRP is associated with an acute-phase response and is a nonspecific marker for inflammation. P-selectin level was positively correlated with CRP level in CHD patients, indicating that P-selectin

may contribute to CHD mediated by systemic inflammation. Platelets play a key role in the inflammatory response.[14–16] However, the role of P-selectin in systemic inflammation requires further investigation.

We also evaluated other traditional risk factors and showed that BMI, TC, and TG were all increased and HDL-C was decreased in patients with CHD compared with controls. The incidences of hypertension, diabetes mellitus, and smoking were also significantly higher in patients with CHD. These results were in accordance with previous studies.[17–19]

This study had some limitations. Notably, the sample size was small and the specific mechanism of P-selectin action was not investigated. Further studies are therefore needed to address these issues.

In conclusion, plasma P-selectin levels were increased in Chinese Han patients with CHD. Plasma P-selectin level is an independent risk factor for CHD and may serve as a biomarker reflecting the severity of CHD in the Chinese Han population.

Declaration of conflicting interest

Funding

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