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The relationship between levels of von Willebrand factor and mean platelet volume in subjects with isolated impaired fasting glucose

Authors' Contribution:

- A** Study Design
- B** Data Collection
- C** Statistical Analysis
- D** Data Interpretation
- E** Manuscript Preparation
- F** Literature Search
- G** Funds Collection

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Summary

Background:

To understand the heterogeneity of platelets, we investigated the correlation between von Willebrand factor (vWf) and mean platelet volume (MPV) in subjects with isolated impaired fasting glucose (IFG).

Material/Methods:

We selected 48 subjects with isolated IFG and 48 normoglycemic control subjects matched for age, sex, and body mass index. We measured levels of vWf and MPV in all subjects.

Results:

The levels of vWf and MPV were significantly higher in the isolated IFG group than the control group ($p < 0.05$). Also, vWf level was positively correlated with MPV level in subjects in the isolated IFG group ($r = 0.452$, $p = 0.001$).

Conclusions:

Our results suggest that vWf seems to be profoundly related to platelet volume in subjects with isolated IFG.

key words:

von Willebrand factor • endothelial dysfunction • mean platelet volume • impaired fasting glucose

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BACKGROUND

Endothelial dysfunction (ED), which is characterized by an imbalance between relaxing and contracting factors, procoagulant and anticoagulant substances, and between pro-inflammatory mediators, may play a particularly significant role in the pathogenesis of atherosclerosis [1]. Under physiological conditions, the vascular endothelium produces many substances that are closely involved in hemostasis, fibrinolysis, growth factor synthesis, and the regulation of vessel tone and permeability. One of these substances is von Willebrand factor (vWf), which is synthesized by and stored in endothelial cells. vWf is a multimeric glycoprotein, and it is essential for platelet aggregation and adhesion [2]. Numerous clinical and experimental reports suggest that a high vWf level reflects endothelial damage or ED. vWf levels have been proposed as an indicator of ED [3–5].

Mean platelet volume (MPV), which is routinely determined by complete blood count analyzers, is a parameter reflecting the platelet size. Large platelets are more thrombogenic and active than normal sized platelets since they have a higher content of granules [6]. MPV, a determinant of platelet activation, is a newly emerging risk factor for atherothrombosis [7]. Elevated MPV levels have been identified as an independent risk factor for myocardial infarction in patients with coronary heart disease [8] and for death or recurrent vascular events after myocardial infarction [9]. Moreover, increased platelet size has been reported in patients with vascular risk factors such as diabetes mellitus [10,11], and in patients with acute ischemic stroke [12], essential hypertension [13], obesity [14].

There have been few studies of the relationship between vWf and MPV [15,16]. To the best of our knowledge, there

has been no study on the relationship between levels of vWf and MPV in subjects with isolated IFG. Therefore, we investigated the relationship between von vWf and MPV in subjects with isolated IFG.

MATERIAL AND METHODS

Patients

This study was performed in the population of our previous study (48 subjects with isolated IFG and 48 normoglycemic healthy controls matched for age, sex, and body mass index, who attended our outpatient clinic) [17]. We performed a retrospective analysis of the data of our previous study to determine if there is a relationship between levels of vWf and MPV levels.

Measurement of vWf

Plasma vWf levels were measured quantitatively by STA-LIATEST [(Diagnostica Stago (France)]. All of the sample measurements were performed in the same run.

Measurement of MPV

We measured MPV in blood samples collected in tubes containing citrate (1:4 v/v) in order to avoid the platelet swelling induced by EDTA [18]; samples were analyzed within 1 hour. A Cell-Dyn 3500 (Abbot) was used for all blood counts.

Statistical analysis

SPSS 10.0 for Windows was used for the statistical analysis. For $\alpha=0.05$ (between each group) and power =80%, a sample

Table 1. The main characteristics and laboratory results of study groups.

Parameter	Impaired fasting glucose group	Control group	P values
N (men/women)	48 (33/15)	48 (29/19)	NS
Age (y)	48.89±7.94	45.79±8.91	NS
Body mass index (kg/m ²)	23.76±1.40	23.59±1.72	NS
Systolic blood pressure (mmHg)	122.81±16.32	123.56±15.46	NS
Diastolic blood pressure (mmHg)	74.18±9.16	73.47±10.07	NS
Fasting glucose (mg/dl)	107.29±5.27	87.87±6.86	0.001
Alanin amino transferase (U/l)	27.14±6.83	26.38±5.92	NS
Creatinine (mg/dl)	1.0±0.3	0.9±0.2	NS
Total cholesterol (mg/dl)	181.18±21.21	186.64±19.35	NS
LDL-cholesterol (mg/dl)	103.18±23.05	109.12±21.75	NS
HDL-cholesterol (mg/dl)	52.60±13.22	57.41±13.39	NS
Trygliceride (mg/dl)	120.75±44.10	109.62±41.46	NS
Von Willebrand faktor (%)	111.08±52.78	74.08±48.47	0.001
Mean platelet volume (fl)	8.49±0.83	7.99±0.57	0.002
Platelet counts (×10 ⁹ /l)	249.7±68.9	253.1±66.3	NS

NS – not significant.

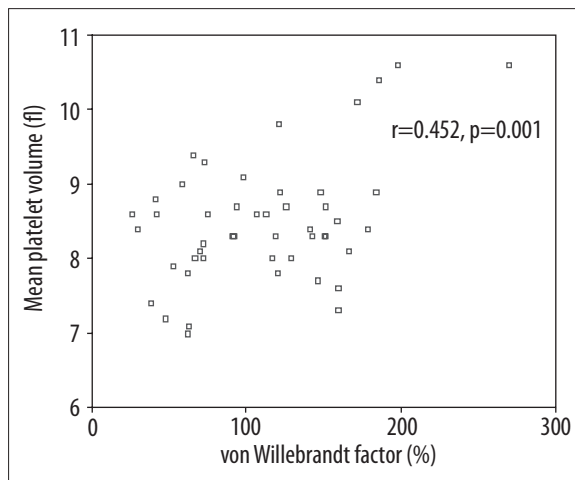


Figure 1. Relationship between vWf and mean platelet volume in isolated IFG group.

size of >36 subjects per group was needed to detect an actual difference. Two-group comparisons (IFG *vs.* control) were performed with independent *t*-tests. Correlation between levels of vWf and MPV were assessed using Pearson's correlation analysis. Data were expressed as the mean \pm SD. A value of $p < 0.05$ was considered as statistically significant.

RESULTS

The main characteristics and laboratory results of the study population are reported in Table 1. The level of vWf was significantly higher in the IFG group than in the normoglycemic control group ($111.08 \pm 52.78\%$ *vs.* $74.08 \pm 48.47\%$, $p = 0.001$). MPV was significantly higher in the isolated IFG group than in the control group (8.49 ± 0.83 *vs.* 7.99 ± 0.57 , $p = 0.002$). vWf level was positively correlated with MPV level in the IFG group ($r = 0.452$, $p = 0.001$) (Figure 1).

DISCUSSION

The present study demonstrated that there was significant correlation between vWf and MPV in subjects with isolated IFG. These results demonstrate that there was a relationship between endothelial dysfunction and platelet activation in subjects with isolated IFG. This finding has not been reported previously. Endothelial dysfunction may be triggering the same mechanisms, and stimulate the production of large platelets in the bone marrow. On the other hand, hyperglycemia activates coagulation by raising concentrations of procoagulant factors such as vWF [19]. There have been few studies of the relationship between vWf and MPV. Ihara et al reported positive correlation between vWf and MPV in patients with ischemic heart disease and in patients with aortic aneurysm [15,16]. However, with the current data it is not possible to say whether high vWf levels are the cause of large platelet volume. Future cohort studies will be helpful in providing an answer.

Multiple mechanisms are involved in platelet activation of patients with diabetes mellitus, which can be categorized as follows: 1) hyperglycemia, 2) insulin deficiency and resistance, 3) associated metabolic conditions, and 4) other cellular abnormalities, and there may be similar mechanisms

for IFG [20]. Several mechanisms have been proposed to contribute to the increased platelet activity caused by hyperglycemia, including the following: 1) non-enzymatic glycation of platelet membrane proteins that decrease membrane fluidity, which may increase platelet adhesion [21,22]; 2) osmotic effect of glucose that activates platelet GP IIb/IIIa and P-selectin expression [23]; 3) activation of protein kinase C, a mediator of platelet activation [24], and 4) glycation of circulating low-density lipoproteins (LDL), which increases intracellular calcium concentration and nitric oxide (NO) production [25].

The present study has some limitations. First, the study population was rather small, thus large-scale studies would be helpful in order to make further comments on the relation between MPV and vWf. Second, unfortunately, we could not perform the measurement of other ED and platelet activation markers. The third limitation is that our analyses were based on a single baseline determination that may not reflect the patients' status over long periods.

CONCLUSIONS

In conclusion, our results suggest that VWF seems to be related to platelet volume in subjects with isolated IFG.

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