Evaluation of Platelet Volume Indices in Adults with Hyperlipidemia and Correlation with Lipid Ratio

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Abstract

Purposes
Platelet volume indices (PVIs) includes the mean platelet volume (MPV), platelet distribution width (PDW), and platelet large cell ratio (P-LCR). Larger platelets tend to be metabolically and enzymatically more active compared to smaller platelets and secrete more prothrombotic factors. The low-density lipoprotein (LDL) / high-density lipoprotein (HDL) ratio is a more powerful coronary risk predictor than either LDL or HDL alone. This study invesgated PVIs in adults with hyperlipidemia and the correlation between PVIs and the LDL/HDL ratio.

Methods
The study enrolled adults aged ≥18 years who visited the outpatient division of a regional teaching hospital in central Taiwan from January 9 to March 31, 2015. Subjects were tested for serum lipids and platelet counts and were divided into hyperlipidemic and normolipidemic group according to the Dyslipidemia Classifications suggested by the Health Promotion Administration and Taiwan Society of Lipids & Atherosclerosis in 2003. Of the 85 adults eventually included, 35 were in the hyperlipidemic group and 50 in the normolipidemic group.

Results
The mean values for MPV (9.94±0.71), PDW (10.99±1.48) and P-LCR (24.29±5.65) in the study group were significantly higher compared to those in the control group (MPV = 8.97 ± 0.42, PDW= 9.19 ± 0.83, P-LCR= 16.39 ± 3.24; p< 0.05). MPV (r=0.285, p=0.008), PDW (r=0.396, p=0.001) and P-LCR (r=0.269, p=0.013) all showed significant positive correlations with LDL/HDL.

Conclusions
Adults with hyperlipidemia had significantly higher MPV, PDW, and P-LCR values compared to normolipidemic adults. There was a significant correlation between the LDL/HDL ratio and PVIs. Platelets of adults with hyperlipidemia may become more aggregable and reactive owing to increased PVIs. The increased risk of atherosclerosis in adults with hyperlipidemia may be a result of high PVIs. These indices may be used for early, cost-effective and rapid identification of coronary risk factors in adults with hyperlipidemia.

Keywords: Platelet volume, Platelet indices, Hyperlipidemia, Lipid ratios
Introduction

Hyperlipidemia is a major risk factor for coronary heart disease, myocardial infarction and stroke [1]. Many studies have concluded that hyperlipidemia is associated with diabetes mellitus, coronary heart disease, obesity, and hypertension [2,3,4,5]. In spite of this, it is often overlooked because of its being totally asymptomatic most of the times. Automated hematology analyzers in most clinical laboratories have made the platelet count (PC) and the platelet volume indices (PVIs), including mean platelet volume (MPV), platelet distribution width (PDW), and platelet large cell ratio (P-LCR), routinely available at no additional cost. Larger platelets tend to be metabolically and enzymatically more active compared to smaller platelets, and secrete more prothrombotic factors [6]. Platelet volume reflects platelet reactivity [7] and has been suggested as an independent risk factor for ischemic events in cardiovascular disease [8]. Some studies have shown a consistent association of increased MPV with various types of diseases like coronary artery disease, myocardial infarction, cerebral infarction and diabetes mellitus [9,10,11,12]. Given these close associations, hyperlipidemia could be indicated by changes in platelet size. The current study aimed to evaluate PVIs in adults with hyperlipidemia, and to explore the associations of PVIs with coronary risk. It was suggested that the lipid ratios such as total cholesterol (Tchol)/high density lipoprotein (HDL) ratio or low density lipoprotein (LDL)/HDL ratio could be more effective coronary risk predictors than a single serum lipid value (e.g., Tchol, HDL, or LDL) [13]. We investigated PVIs in adults with hyperlipidemia and the correlation between PVIs and the LDL/HDL ratio to study the relationship between PVI levels and the increased risk of atherosclerosis in a hyperlipidemic cohort.

Methods

This retrospective study included adults aged \( \geq 18 \) years who visited the outpatient division of a regional teaching hospital in central Taiwan from January 9 to March 31, 2015. Subjects were tested for serum lipids levels and platelet counts, and were divided into hyperlipidemic and normolipidemic groups according to the Dyslipidemia Classifications suggested by the Health Promotion Administration and Taiwan Society of Lipids & Atherosclerosis in 2003 (Table 1) [14]. We set strict exclusion criteria, men with a hemoglobin level below 12 mg/dL, and women with a hemoglobin level below 11 mg/dL were excluded because of possible nutritional anemias resulting in reactive thrombocytosis and thus influencing PVI levels. Subjects with a history of coronary artery disease were also excluded. Patients with glycated hemoglobin (HbA1c) > 6.5%, erythrocyte sedimentation rate (ESR) > 10, and those who were taking lipid-lowering agent (e.g., statins) or antiplatelet drugs such as aspirin or clopidogrel, which might affect lipid levels or PVIs were all excluded. Of the 85 adults finally included, 35 were in the hyperlipidemic group and 50 were in the normolipidemic group. We compared PVI values of hyperlipidemic adults with normolipidemic adults, and determined correlations between PVIs and the LDL/HDL ratio. Platelet parameters, including PVI (e.g. MPV, PDW, and P-LCR) and PC, were analyzed using an automatic blood counter (Sysmex XN-1000™ Hematology Analyzer, Santung instruments Co., LTD). Venous blood samples, were collected in hemogram tubes with dipotassium EDTA

Table 1 The Dyslipidemia Classifications Suggested by Health Promotion Administration and Taiwan Society of Lipids & Atherosclerosis in 2003

<table>
<thead>
<tr>
<th>Classifications</th>
<th>Blood Lipid Levels (mg/dl)</th>
</tr>
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<tbody>
<tr>
<td>Hypercholesterolemia</td>
<td>Total cholesterol (TC) ( \geq 200 )</td>
</tr>
<tr>
<td>Mixed hyperlipidemia</td>
<td>Total cholesterol (TC) ( \geq 200 ) and Triglyceride (TG) ( \geq 200 )</td>
</tr>
<tr>
<td>Hypertriglyceridemia</td>
<td>Triglyceride (TG) ( \geq 200 ) plus:</td>
</tr>
<tr>
<td></td>
<td>(1) TC/ High-density lipoprotein (HDL) ( \geq 5 ), or</td>
</tr>
<tr>
<td></td>
<td>(2) HDL(&lt;40)</td>
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</tbody>
</table>
and biochemistry tubes, and tested within 1 hour of collection to minimize variations caused by sample aging. Samples were stored at room temperature. The lipid profile was measured using a chemistry analyzer (Hitachi 7180 chemistry analyzer, Medicare Products INC). Statistical evaluation was performed using the SPSS statistics package program version 12 (for Windows) using independent t-tests, and Pearson correlation tests (with the r value as the coefficient). Data were expressed as mean ± standard deviation. A P value <0.05 was considered statistically significant. Pearson's Chi-squared test was performed to examine nominal variables in this study (e.g. the difference in sex distributions between the two groups) to acquire a p value, p<0.05 was considered statistically significant.

**Results**

A total of 85 subjects were enrolled in the present study. Out of 50 patients with hyperlipidemia, 24 were men and 26 were women. The patients were aged between 31 and 69 years, with a mean age of 51.08 years in the hyperlipidemic group and 46.00 years in the normolipidemic group and normolipidemic groups. There were no significant differences in sex (p=0.127) and age (p=0.99) between the hyperlipidemic and normolipidemic groups (Table 2). The PC observed

![Figure 1 Mean platelet volume indices of Study group and Control group: (A).MPV&PDW; (B).P-LCR](image)

**Table 2 Demographic characteristics of study participants**

<table>
<thead>
<tr>
<th>Factors</th>
<th>Hyperlipidemia (n:50)</th>
<th>Normolipidemia (n:35)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (n)</td>
<td>24(M)/26(F)</td>
<td>11(M)/24(F)</td>
<td>0.127*</td>
</tr>
<tr>
<td>Age (years)</td>
<td>51.1±12.4</td>
<td>46.0±15.7</td>
<td>0.990</td>
</tr>
<tr>
<td>Tchol (mg/dl)</td>
<td>218.7±27.8</td>
<td>170.2±20.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>TG (mg/dl)</td>
<td>126.5±67.1</td>
<td>85.1±37.8</td>
<td>0.001</td>
</tr>
<tr>
<td>HDL (mg/dl)</td>
<td>61.5±20.8</td>
<td>60.0±10.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LDL (mg/dl)</td>
<td>140.8±28.6</td>
<td>98.4±21.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Tchol/HDL</td>
<td>3.9±1.1</td>
<td>2.9±0.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LDL/HDL</td>
<td>2.5±0.9</td>
<td>1.7±0.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PC (10^9/uL)</td>
<td>236.9±70.8</td>
<td>263.3±47.2</td>
<td>0.058</td>
</tr>
<tr>
<td>MPV (fl)</td>
<td>9.9±0.7</td>
<td>9.0±0.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PDW (fl)</td>
<td>11.0±1.5</td>
<td>9.1±0.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>P-LCR (%)</td>
<td>24.3±5.7</td>
<td>16.4±3.2</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Note: a. The difference of gender distributions in 2 groups is a nominal variable, Pearson's chi-squared test was applied to obtain p=0.127>0.05, therefore gender distributions in 2 groups were statistically no significant differences.
was not significantly different between the two groups (p=0.058). The mean values for MPV, PDW, and P-LCR in the hyperlipidemic group (9.94 ± 0.71, 10.99 ± 1.48, 24.29 ± 5.65, respectively) were significantly higher compared to those in the normolipidemic group (MPV = 8.97 ± 0.42; PDW = 9.19 ± 0.83, P-LCR = 16.39 ± 3.24) as shown in Figure 1. In the independent t-test, a p-value < 0.001 indicated that there was a significant difference between hyperlipidemic and normolipidemic groups with respect to MPV, PDW and P-LCR. A p-value >0.05 for PC indicated that there was no significant difference between the hyperlipidemic and normolipidemic groups. All three studied PVIs were subsequently confirmed to be significantly higher in the hyperlipidemic adults compared to the normolipidemic adults. Moreover, MPV (r=0.285, p=0.008), PDW (r=0.396, p=0.001), and P-LCR (r=0.269, p=0.013) platelet volume indices all showed significant positive correlations with LDL/HDL (Figure 2).

**Conclusions**

Hyperlipidemia is often asymptomatic, and therefore tends to be ignored. However, it might be the source of a large number of complications, including life-threatening thromboembolic disorders. Platelets are well-known to be associated with such thromboembolic risks and various platelet volume indices have been widely studied in these conditions. In the current study, we set strict criteria to exclude factors that might affect PVIs and the lipid profile. Some previous studies have shown that platelet count and size might be sex- and age-dependent [15,16]. For this reason, we have conducted this study with no statistically significant difference between age and sex in the hyperlipidemic and normolipidemic groups to avoid any such bias in our results. We found that the hyperlipidemic group had significantly higher MPV, PDW, and P-LCR values compared to normolipidemic group. It has been widely acknowledged that larger platelets are biologically more active and have greater prothrombotic potential, thereby representing an important risk factor for cardiovascular disease [17]. Our data indicated that the hyperlipidemic group had significantly higher MPV, PDW, and P-LCR.
compared to the normolipidemic group. This finding is consistent with the results of previous studies [18,19,20]. Vagdatli et al found that PDW is a specific marker of platelet activation, since it does not increase during simple platelet swelling [21]. In our study, hyperlipidemic adults had significantly higher MPV, PDW, and P-LCR than the normolipidemic adults and there was also a significant correlation between PVI and the LDL/HDL ratio. The platelets of adults with hyperlipidemia may become more aggregable and reactive owing to increased PVIs. The increased risk of atherosclerosis in adults with hyperlipidemia may be a result of high PVIs. These indices may be used for early, cost-effective, and rapid identification of coronary risk factors in adults with hyperlipidemia.

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References

14. 丁予安、何橈通、宋育民 等: 高血脂防治手冊－國人血脂異常診療及預防指引。臺北市：衛生福利部國民健康署。2003。
18. Coban E, Afacan B: The effect of rosvuvastatin treatment on the mean platelet volume in patients with uncontrolled primary dyslipidemia with


血小板體積參數於高血脂成人的評估
以及與血脂比值的相關性

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摘要

目的
血小板體積參數包括平均血小板體積、血小板分佈寬度與大型血小板比例。血小板在代謝上與氧化反應密切相關，當血小板體積大小較大時，其易具有活化與產生較多的血栓因子。而低密度脂蛋白 / 高密度脂蛋白比值已證明比起單獨使用低密度或高密度脂蛋白來預測冠心病風險是更有力的預測因子。本研究調查高血脂成人的血小板體積參數及其與低密度脂蛋白 / 高密度脂蛋白比值之間的相關性。

方法
本研究收納 18 歲以上，於 2015 年 1 月 9 日至 3 月 31 日間曾到台灣中部某教學醫院門診看診，並同時檢驗脂質與血小板數的民衆，依 2003 年國民健康署與中華民國血栓與黏稠凝塊學會制定之「中華民國血栓異常分類之建議」而被區分為高血脂與非高血脂成人。最終納入 85 位受試者，高血脂組 35 位，而非高血脂組 50 位。

結果
在高血脂組血小板參數的平均值：平均血小板體積為 9.94±0.71；血小板分佈寬度為 10.99±1.48；大型血小板比例為 24.29±5.65，皆顯著高於控制組（平均血小板體積 8.97±0.42；血小板分佈寬度為 9.19±0.83；大型血小板比例 16.39±3.24，p<0.05）。而平均血小板體積（r=0.285, p=0.008）；血小板分佈寬度（r=0.396, p=0.001）；與大型血小板比例（r=0.269, p=0.013）亦顯示與 LDL/HDL 為顯著正相關。

結論
高血脂相較於非高血脂組成人明顯有較高數值的平均血小板體積、血小板分佈寬度與大型血小板比例，而且這些血小板參數與低密度脂蛋白 / 高密度脂蛋白比值之間也呈現顯著相關性。高血脂成人的血小板因有較高數值的血小板參數而可能顯得較為凝集與活化。高血脂成人罹患粥樣動脈硬化的風險可能就是高數值血小板體積參數的結果。這些血小板參數亦能作爲高血脂族群心血管風險的早期、經濟與快速的識別標記。

關鍵詞：血小板體積、血小板參數、高血脂、血脂比值

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