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*Original Article*

# Effects of simvastatin and atorvastatin on biochemical and hematological markers in patients with risk of cardiovascular diseases

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**Abstract:** Objective: This study aimed to investigate the effects of simvastatin (SVS) and atorvastatin (AVS) on the biochemical and hematological markers in patients with risk of cardiovascular diseases. Methods: One hundred and fifty outpatients were enrolled from the Department of Cardiology. Patients were treated with AVS or SVS. The lipids and hematological parameters were measured at baseline and after 4-week treatment, and the risk factors of cardiovascular diseases were recorded. Results: After 4-week treatment, the lipids significantly changed. However, for hematological parameters, only mean platelet volume (MPV) significantly decreased after statins treatment (SVS: t = 68.748, P = 0.000; AVS: t = 39.472, P = 0.000), and the extent of decline was similar between SVS group and AVS group (t = 1.063, P = 0.289). There were no correlations between MPV and lipids. SVS and AVS had comparable effects on the lipid parameters after 4-week treatment, and there were no significant correlations of ΔMPV with the Δtotal cholesterol, Δhigh density lipoprotein-cholesterol, Δlow density lipoprotein-cholesterol, Δtriglyceride, Δapolipoproteint A1, Δapolipoproteint B and Δlipoproteint (a) after treatments (all P > 0.05). Conclusion: After statins treatment, the lipids significantly change; only MPV significantly decreases among hematological parameters, but it has no relationship with lipids reduction. The synthetic atorvastatin has similar effects to native simvastatin in the management of patients with risk for cardiovascular diseases.

**Keywords:** Statin, blood, mean platelet volume, lipid

## Introduction

Statins are the most commonly used lipid-lowering drugs worldwide. They mainly act on HMG-CoA reductase, a key rate-limiting enzyme for cholesterol synthesis, to block mevalonic acid pathways and reduce cholesterol synthesis in cells. This may increase the low density lipoprotein (LDL) receptor (mainly on hepatocytes) and its activity, accelerate the serum cholesterol removal, and thus block the endogenous cholesterol synthesis in the hepatocytes [1]. However, statins have pleiotropic effects besides its cholesterol-lowering effect [2]. For example, statin treatment may reduce the plasma LDL of patients with cardiovascular disease (CVD), either primary or secondary, and decrease the incidence of cardiovascular complications, resulting in the improvement of quality of life and increase in survival time [3]. Satins may also reduce plasma ox-LDL and thus decrease the risk for stroke [4]. Preoperative application of statin for 1 week is found to reduce the risk for angioplasty-related myocardial infarction by more than 80% [5]. In addition, statins may have positive effect on the platelet activation, vascular endothelial function, inflammation, and coagulation [6, 7].

Dyslipidemia is a risk factor of CVD. Recently, the multinational INTERHEART study showed that apolipoprotein B (apoB) was a stronger predictor of myocardial infarction than low-density lipoprotein cholesterol(LDL-Ch) [8]. Lipoprotein (a) [Lp (a)] has been considered as a cardiovascular risk factor for many years [9]. Many serum lipid parameters besides cholesterol have been used in clinical practice, such as triglyceride (TG), lipoprotein, apolipoprotein A1 (Apo A1), etc. However, whether and how these parame-

ters change after stain treatment are still poorly understood. Hematologic parameters such as mean platelet volume (MPV) [10], red cell distribution width [11], and neutrophil to lymphocyte ratio [12] are associated with the increased risk for CVD. However, whether other parameters of the complete blood count (such as hematocrit, erythrocyte and its related parameters, including mean corpuscular volume [MCV], mean corpuscular hemoglobin [MCH], mean corpuscular hemoglobin concentration [MCHC]) are also associated with the risk for CVD and whether the combination of these parameters with blood lipids can improve the ability to predict the risk For CVD are still unclear.

Simvastatin (SVS), which is a natural compound statin, is a synthetic derivative of fermentation products of Aspergillus terreus [13]. However, atorvastatin (AVS) is a complete synthetic compound statin [14]. Both of them are effective lipid-lowering drugs, which are widely used as therapeutics of hyperlipemia [15, 16]. Some reserchers have compared efficacy, safety, cost and even differences in gender, and found that they have great consistency in all these areas [17-19]. But whether the mechanisms of natural and synthetic statins are the same or not? Thus, in this study, the serum lipids and hematological markers were measured in patients with risk for CVD after statin treatment, and the correlations of lipids with hematological parameters were evaluated, which is to explore whether the mechanisms are the same.

## Materials and methods

### *Patient selection*

One hundred and fifty outpatients were enrolled from the Department of Cardiology. There were 82 males and 69 females, and the mean age was 47.1 ± 7.3 years (range: 35-60 years). All the patients were diagnosed with coronary heart disease, hypertension, hyperlipemia or other CVD, and received statin therapy. Exclusion criteria: 1) all kinds of liver disease, kidney disease, acute infections, thrombophilia, intracranial hemorrhage, active malignancies and hematological diseases; 2) hypersensitivity to statins; 3) current use of oral contraceptives, steroids, heparins, adrenal hormones, oral anticoagulants and immunosuppressants or presence of radiotherapy and chemotherapy; 4) acute coronary syndrome, vasculitis, nonnormocytic anemia, myocardial infarction and cerebrovascular event (< 3 months).

### *Therapeutic regimen*

All the patients did not receive statin therapy before this study. Besides statins, symptomatic treatment was also performed with antihypertensive agents, antidiabetic agents or drugs for ischemic heart disease. Written informed consent was obtained from each patient.

AVS, a completely synthetic compound, was purchased from MSD China (Hangzhou, China), and SVS, a natural compound, was purchased from Jialing Pharmaceutical Company (Beijing, China). Individualized statin therapy was applied according to the manufacturer's instructions and considering the individual disease condition. SVS was administered at four alternative doses: 5 mg/qd (n = 30), 10 mg/qd (n = 33), 15 mg/qd (n = 9), and 20 mg/qd (n = 4); AVS was also given at four doses: 10 mg/qd (n = 29), 20 mg/qd (n = 33), 40 mg/qd (n = 8), and 80 mg/qd (n = 4). Patients were asked to take medicine orally at 8 PM.

### *Blood sampling*

Patients were asked to fast for at least 12 h. According to the order of Vacutainer® (Becton Dickinson Company, USA) Serum Tubes (yellow tube, containing separating gel and coagulant, no preservatives), and $K_2$EDTA anticoagulant tube, venous blood was collected (5.0 ml and 3.0 ml), and serum was collected following centrifugation at 3000 rpm for 15 min within 2 h after sample collection. The serum was stored at -80°C for use if it was not used for detection immediately. $K_2$EDTA anticoagulated blood was used for the detection of hematologic parameters.

### *Laboratory measurements*

Hematological variables, including platelets, MPV, hemoglobin, red blood cells and their related parameters, including mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC) and hematocrit (Hct), were measured by a XE-2100 Auto Hematology Analyzer with the supporting diagnostic reagents (Sysmex, Japan).

**Table 1.** Clinical and demographic characteristics of patients

| Characteristics | SVS (n = 76) | AVS (n = 74) | $\chi^2$/t, P |
|---|---|---|---|
| Age (years) | 48.9 ± 8.1 | 47.6 ± 7.9 | 1.016, 0.311 |
| Gender (male/female) | 39/37 | 40/34 | 0.113, 0.737 |
| Smoking | 27 | 20 | 1.259, 0.262 |
| Drinking | 19 | 21 | 0.219, 0.640 |
| Pre-existing diseases | | | |
| Coronary artery disease | 29 | 25 | 0.311, 0.577 |
| Hypertension | 38 | 36 | 0.027, 0.869 |
| Diabetes mellitus | 21 | 22 | 0.081, 0.776 |
| Hyperlipidaemia | 23 | 25 | 0.214, 0.644 |
| Current medications | | | |
| Pioglitazone | 9 | 6 | 0.581, 0.446 |
| Ca-CB | 23 | 21 | 0.064, 0.800 |
| β-blocker | 30 | 33 | 0.404, 0.525 |
| EPA | 15 | 13 | 0.116, 0.733 |
| Nitrates | 17 | 11 | 1.390, 0.238 |
| Aspirin | 48 | 47 | 0.002, 0.964 |
| Clopidogrel | 8 | 15 | 2.742, 0.098 |
| Insulin | 7 | 11 | 1.135, 0.287 |
| ACEI/ARB | 12 | 9 | 0.430, 0.522 |
| RASB | 34 | 35 | 0.099, 0.753 |

Notes: RASB, Renin-angiotensin system blocker; Ca-CB, calcium channel blockers; ARB, denotes angiotensin II receptor blocker; ACE-I, angiotensin-converting enzyme inhibitor; EPA, eicosapentaenoic acid.

Biochemical parameters, including triacylglycerols (TG), total cholesterol (TCh), low-density lipoprotein cholesterol (LDL-Ch), high-density lipoprotein cholesterol (HDL-Ch), Lp (a), apolipoprotein A1 (ApoA1) and ApoB were measured with a 7600-20 Automatic Analyzer (Hitachi, Japan), and supporting kits were purchased from the Sichuan Maker Biotechnology Co., Ltd. (Sichuan, China).

Besides the parameters measured above, the risk factors of CVD in these patients were also recorded, including age, gender, history of hypertension (confirmed diagnosis of hypertension, use of antihypertensive agents, or blood pressure higher than 140/90 mmHg at more than two measurements), history of diabetes (confirmed diagnosis of diabetes, presence of glucose-lowering therapy with diet control and/or anti-diabetic agents, or fasting blood-glucose higher than 7.0 mmol/L for more than two measurements), smoking (more than 1 year), alcohol consumption (more than 50 ml of white wine of 45 degrees or above per day), and coronary artery disease (> 50% stenosis of epicardial coronary artery). All the patients had more than 2 risk factors of coronary heart disease and LDL-Ch > 3.38 mmol/L (130 mg/dL).

Risk factors and treatment goals were evaluated in patients with primary hypercholesterolaemia according to the 2013 ACC/AHA Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults, Chinese Guidelines on the Prevention and Treatment of Dyslipidemia in Adults, and the China Cholesterol Education Program [20-22].

*Statistical analysis*

Data are expressed as means ± standard deviation (SD). t-test was applied for the comparisons of parameters before and after treatment. Pearson correlation analysis was used to evaluate the correlation of MPV with lipid parameters. Linear regression analysis was employed to assess the relationships of MPV change (ΔMPV) with changes in other lipid parameters. Statistical analysis was performed with SPSS version 19.0. A value of $P < 0.05$ (two-tailed) was considered statistically significant.

## Results

The demographics and clinical characteristics of these patients are listed in **Table 1**. There were no significant differences in the risk factors of CVD and demographics between SVS group and AVS group (P > 0.05).

After 4-week treatment, all the lipid parameters significantly changed (**Table 2**), but significant differences were not observed in them between two groups (**Table 3**). For hematological parameters, the platelets remained unchanged after treatment, while MPV significantly decreased in SVS group (t = 68.748, P = 0.000) and AVS group (t = 9.472, P = 0.000), and the extent of decline was similar in two groups (t = 1.063, P = 0.289) (**Table 3**).

Pearson correlation analysis revealed no significant correlation of MPV with lipid parame-

**Table 2.** Biochemical and hematological parameters in patients receiving statin therapy before and after treatment

| | SVS (n = 76) | | AVS (n = 74) | | t, P§ |
|---|---|---|---|---|---|
| | $\bar{x}$ ± SD | t, P# | $\bar{x}$ ± SD | t, P# | |
| TG (mmol/L) | 2.22 ± 1.08 | 77.870, 0.000 | 2.21 ± 1.13 | 74.34, 0.000 | 0.065, 0.948 |
| | 1.61 ± 0.85 | | 1.58 ± 0.82 | | 0.187, 0.852 |
| TCh (mmol/L) | 6.77 ± 0.97 | 32.292, 0.000 | 6.54 ± 1.17 | 24.683, 0.000 | 1.330, 0.186 |
| | 5.06 ± 0.50 | | 4.94 ± 0.61 | | 1.325, 0.187 |
| HDL-Ch (mmol/L) | 1.01 ± 0.26 | 118.077, 0.000 | 1.04 ± 0.23 | 98.449, 0.000 | 0.712, 0.478 |
| | 0.91 ± 0.22 | | 0.94 ± 0.19 | | 0.713, 0.477 |
| LDL-Ch (mmol/L) | 4.67 ± 0.48 | 18.052, 0.000 | 4.80 ± 0.58 | 22.109, 0.000 | 1.554, 0.122 |
| | 2.58 ± 0.33 | | 2.67 ± 0.39 | | 1.552, 0.123 |
| Lp(a) (mg/L) | 326.8 ± 142.4 | 44.227, 0.000 | 337.6 ± 140.5 | 47.831, 0.000 | 0.551, 0.577 |
| | 295.9 ±144.6 | | 306.9 ± 143.1 | | 0.554, 0.581 |
| ApoA1 (g/L) | 1.12 ± 0.13 | 141.09, 0.000 | 1.14 ± 0.11 | 145.00, 0.00 | 0.778, 0.438 |
| | 1.21 ± 0.12 | | 1.22 ± 0.11 | | 0.771, 0.442 |
| ApoB (g/L) | 0.81 ± 0.11 | 107.58, 0.000 | 0.82 ± 0.10 | 110.95, 0.000 | 0.881, 0.380 |
| | 0.50 ± 0.08 | | 0.51 ± 0.08 | | 0.887, 0.376 |
| RBC (× $10^{12}$/L) | 3.68 ± 0.71 | 0.116, 0.908 | 3.78 ± 0.63 | 0.117, 0.907 | 0.913, 0.362 |
| | 3.64 ± 0.66 | | 3.72 ± 0.58 | | 0.782, 0.436 |
| Hb (g/L) | 122.6 ± 18.1 | 1.898, 0.062 | 124.6 ± 17.8 | 1.976, 0.052 | 0.705, 0.482 |
| | 121.7 ± 19.4 | | 124.2 ± 19.0 | | 0.818, 0.415 |
| Hct (v/v) | 0.342 ± 0.067 | 1.925, 0.058 | 0.352 ± 0.059 | 0.439, 0.662 | 0.913, 0.363 |
| | 0.340 ± 0.063 | | 0.351 ± 0.056 | | 1.113, 0.268 |
| MCV (fl) | 93.1 ± 1.42 | 1.082, 0.283 | 93.1 ± 1.08 | 3.150, 0.002 | 0.289, 0.773 |
| | 93.4 ± 2.72 | | 94.4 ± 3.51 | | 1.877, 0.062 |
| MCH (pg) | 33.7 ± 2.53 | 0.655, 0.515 | 34.2 ± 1.71 | 3.091, 0.003 | 1.518, 0.131 |
| | 33.6 ± 1.92 | | 33.4 ± 1.56 | | 0.797, 0.427 |
| MCHC (g/L) | 362.1 ± 27.3 | 0.962, 0.339 | 356.3 ± 18.4 | 0.714, 0.478 | 1.512, 0.133 |
| | 360.0 ± 23.3 | | 354.0 ± 21.0 | | 1.669, 0.097 |
| Plt (× $10^9$/L) | 184 ± 55 | 0.147, 0.884 | 189 ± 58 | 0.908, 0.365 | 0.549, 0.584 |
| | 181 ± 52 | | 190 ± 61 | | 1.044, 0.298 |
| MPV (fL) | 9.48 ± 0.58 | 68.748, 0.000 | 9.56 ± 0.62 | 39.472, 0.000 | 0.822, 0.412 |
| | 8.83 ± 0.59 | | 8.94 ± 0.75 | | 1.073, 0.285 |

Notes: Up line, before treatment; Down line, after treatment; #before treatment *vs.* after treatment; §SVS *vs.* AVS; TG, triglyceride; TCh, total cholesterol; HDL-Ch, high density lipoprotein-cholesterol; LDL-Ch, low density lipoprotein-cholesterol; Lp(a), lipoproteint(a); ApoA1, apolipoproteint A1; ApoB, apolipoproteint B; RBC, red blood cell; Hb, hemoglobin; Hct, hematocrit; MCV, mean corpuscular volume; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; Plt, platelet; MPV, mean platelet volume.

ters before and after treatment (**Table 4**). Linear regression analysis showed there was no significant correlation of ΔMPV with the change in each lipid parameter (R: multiple correlation coefficient): for SVS group: ΔTG (R = 0.045, P = 0.703), ΔTCh (R = 0.030, P = 0.798), ΔLDL-Ch (R = 0.082, P = 0.483), and ΔHDL-Ch (R = 0.195, P = 0.091); for AVS group: ΔTG (R = 0.010, P = 0.936), ΔTCh (R = 0.155, P = 0.187), ΔLDL-Ch (R = 0.185, P = 0.114), and ΔHDL-Ch (R = 0.029, P = 0.810) (**Table 4**).

## Discussion

HMG-CoA reductase can catalyze the conversion of HMG-CoA to mevalonate, the metabolites of which are crucial for some physiological processes in eukaryotic cells. Statins are HMG-CoA reductase inhibitors and can competitively inhibit endogenous HMG-CoA reductase. Statins have various effects through inhibiting the mevalonate pathway. It has been reported [23] that statins can lower the serum, liver and

**Table 3.** Changes in different parameters after 4-week treatment with statins

| Variables | SVS (n = 76) | AVS (n = 74) | t, P |
|---|---|---|---|
| ΔTG (mmol/L) | 0.62 ± 0.39 | 0.63 ± 0.32 | 0.325, 0.746 |
| ΔTCh (mmol/L) | 1.72 ± 0.46 | 1.61 ± 0.58 | 1.313, 0.191 |
| ΔLDL-Ch (mmol/L) | 2.09 ± 0.19 | 2.12 ± 0.22 | 0.812, 0.418 |
| ΔHDL-Ch (mmol/L) | 0.10 ± 0.07 | 0.10 ± 0.04 | 0.090, 0.929 |
| ΔLp(a) (mg/L) | 32.7 ± 5.4 | 30.6 ± 5.5 | 0.041, 0.967 |
| ΔApoA1 (g/L) | 0.09 ± 0.01 | 0.08 ± 0.01 | 0.790, 0.431 |
| ΔApoB (g/L) | 0.31 ± 0.02 | 0.31 ± 0.02 | 0.854, 0.395 |
| ΔRBC (× $10^{12}$/L) | 0.036 ± 0.078 | 0.058 ± 0.057 | 1.966, 0.051 |
| ΔHct (v/v) | 0.0021 ± 0.0095 | 0.0007 ± 0.0129 | 0.778, 0.438 |
| ΔHb (g/L) | 0.087 ± 3.99 | 0.038 ± 1.64 | 0.986, 0.326 |
| ΔMCV (fl) | 0.34 ± 2.72 | 1.30 ± 3.53 | 1.867, 0.064 |
| ΔMCH (pg) | 0.103 ± 1.521 | 0.301 ± 0.799 | 2.028, 0.044 |
| ΔMCHC (g/L) | 2.09 ± 18.95 | 1.27 ± 15.41 | 0.292, 0.771 |
| ΔPlt (× $10^{9}$/L) | 3.16 ± 2.75 | 1.45 ± 2.90 | 0.025, 0.980 |
| ΔMPV (fL) | 0.66 ± 0.08 | 0.62 ± 0.14 | 1.063, 0.289 |

Notes: Δ, change in a specific parameter after treatment (The results were not considered up or down).

aorta cholesterol contents as well as the VLDL-Ch and LDL-Ch in hyperlipemia patients. In past decades, many large case-control studies have confirmed that statins are effective for the prevention and treatment of CVD [24]. Our findings revealed that, after 4-week statin treatment, the blood lipids as well as MPV significantly changed, while MPV decline was not associated with the change in each lipid parameter AVS treated patients and SVS treated patients (all $P > 0.05$), which indicates that AVS and SVS have similar effects on MPV.

Hyperlipidemia is a risk factor of systemic atherosclerosis [25]. The platelet aggregation and cholesterol-rich lipoproteins have been found in the atherosclerotic plaques, which suggest that such lipoproteins and activated platelets are involved in the pathogenesis of atherosclerosis [26]. Therefore, the blood lipid-related indicators and hematological parameters should be regularly monitored for patients with a risk for atherosclerosis. In the present study, patients with a high risk for CVD, such as hyperlipidemia, hypertension and/or diabetes were recruited, and the effects of statins on the serum lipids and blood cell count were investigated, which may be helpful to guide the clinical therapy of these patients. Our results showed, for patients with a high risk for CVD, the blood lipids (7 parameters used in this study) significantly changed, but reduced after treatment with AVS and SVS, both of which showed similar effects.

For the hematological parameters, only MPV significantly decreased after statins treatment. It is well known that MPV is an indicator of platelet activation and has been widely studied in CVD [27]. The platelets transform from static dish into globular swelling shape after activation, resulting in MPV increase. The adhesion and aggregation of platelets increase significantly after activation. However, the platelets are basically at the rest state in the blood circulation of health subjects. In the prothrombotic state, platelets at rest state may be activated by various factors, which significantly increase the incidence of coronary heart complications and thrombosis. Therefore, reducing platelet activity is very important for the clinical treatment of coronary heart disease and the prevention of cardiovascular events. It is well known that statins have antithrombotic effect. For hyperlipidemia patients, the inhibition of statins on the platelet-dependent thrombosis is not ascribed to its lipid lowering effect, indicating that statins have some biological effects independent of their lipid lowering effects, i.e., anti-platelet aggregation [2]. The present study showed, after treatment with statins, MPV significantly reduced, but ΔMPV was not associated with the changes of serum lipids. This means that statins may affect the platelet function, which is independent of its lipid-lowering effect. Statins have anti-platelet activation effect, and can prevent or delay the occurrence or development of CVD in patients with hypertension, coronary heart disease, hyperlipidemia or diabetes [28].

The deformation of red blood cell (RBC) has been found to be related to ATP release from cells [29]. Membrane cholesterol has been shown to alter the properties of cell membrane such as fluidity and bending stiffness [30], and membrane cholesterol increase has been observed in some CVD. Therefore, one of the

**Table 4.** Correlation between MPV and serum lipids (r/R, p)

| | TG (mmol/L) | TCh (mmol/L) | LDL-Ch (mmol/L) | HDL-Ch (mmol/L) | ApoA1 (g/L) | ApoB (g/L) | Lp(a) (mg/L) |
|---|---|---|---|---|---|---|---|
| $MPV_{SVS}$ (fL) | 0.025, 0.831 | 0.050, 0.665 | 0.023, 0.842 | 0.077, 0.508 | 0.125, 0.062 | 0.203, 0.078 | 0.082, 0.481 |
| | 0.026, 0.823 | 0.049, 0.676 | 0.051, 0.661 | 0.036, 0.756 | 0.214, 0.064 | 0.203, 0.079 | 0.067, 0.566 |
| $MPV_{AVS}$ (fL) | 0.026, 0.826 | 0.173, 0.139 | 0.179, 0.128 | 0.011, 0.924 | 0.013, 0.935 | 0.039, 0.743 | 0.085, 0.471 |
| | 0.031, 0.791 | 0.185, 0.114 | 0.163, 0.166 | 0.006, 0.957 | 0.014, 0.908 | 0.038, 0.750 | 0.086, 0.468 |
| | ΔTG | ΔTCh | ΔLDL-Ch | ΔHDL-Ch | ΔApoA1 | ΔApoB | ΔLp(a) |
| $\Delta MPV_{SVS}$ | 0.045, 0.703 | 0.030, 0.798 | 0.082, 0.483 | 0.195, 0.091 | 0.027, 0.815 | 0.214, 0.073 | 0.046, 0.692 |
| $\Delta MPV_{AVS}$ | 0.010, 0.936 | 0.155, 0.187 | 0.185, 0.114 | 0.029, 0.810 | 0.085, 0.470 | 0.030, 0.797 | 0.061, 0.606 |

Notes: $MPV_{SVS}$, MPV in SVS group; $MPV_{AVS}$, MPV in AVS group. R, multiple correlation coefficient.

mechanisms underlying the antithrombotic effect of statins may be ascribed to the decrease in erythrocyte membrane lipid composition which increases red blood cell deformability, and then decreases RBC aggregation. Our findings revealed that, after statin treatment for one month, MCV discrete degree (SD) became larger, 93.1 ± 1.42 vs. 93.4 ± 2.72 for SVS, 93.1 ± 1.08 vs. 94.4 ± 3.51 for AVS, and there was significant difference between before and after treatment with AVS. It is suggested that statins may affect red blood cell volume, but different statins may possess distinct capabilities.

Although high white blood cell count is a strong and independent predictor of coronary risk in patients with and without coronary heart disease [31], the white blood cells count and its differential count may be affected by many factors, such as inflammation, exercise, drugs and diseases. In the present study, the two items were not included in the hematological parameters. In addition, all the patients were from cardiovascular clinic, the treatment was not delayed, the severity of disease varied among patients, and the dose applied was also different among these patients considering the specific disease condition. Whether statins at different doss may lead to similar change in MPV is needed to be investigated in future studies. However, our study had a small sample size, and results might be biased by random errors. Therefore, further works are required to investigate the correlation of MPV change with statin dose.

## Disclosure of conflict of interest

None.

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