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Associations between inflammatory markers and myocardial injury in patients treated with pitavastatin: A retrospective clinical study

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Abstract: **Background**: Inflammation drives atherosclerosis and myocardial injury; pitavastatin's effect on related markers lacks research. **Objectives**: For the purpose of ascertaining the link between inflammatory marker levels and myocardial injury indices in patients undergoing pitavastatin treatment. **Methods**: A retrospective study screened 105 pitavastatin-treated patients at the Affiliated Hospital of Guizhou Medical University (January 2022–December 2024). After exclusion criteria application, 100 patients were recruited and stratified into the myocardial injury group (n=32) and non-myocardial injury group (n=68). The primary outcome measures included inflammatory markers, high-sensitivity C-reactive protein (hs-CRP), interleukin-6 (IL-6), tumor necrosis factor-α (TNF-α), monocyte chemoattractant protein-1 (MCP-1) and fibrinogen (FIB). The secondary outcome measures included lipid profiles such as total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C) and the incidence of major adverse cardiovascular events (MACE); as well as myocardial injury indices: cardiac troponin I (cTnI), creatine kinase-MB (CK-MB), lactate dehydrogenase (LDH) and myoglobin (Mb). Spearman's correlation analysis was executed to assess the correlation between baseline inflammatory markers and myocardial injury indices. Logistic regression analysis was adopted to pinpoint independent risk factors for myocardial injury. **Results**: Logistic regression analysis indicated that the baseline characteristics of the two groups were well matched (all $P>0.05$). Hs-CRP, IL-6, TNF-α, MCP-1, FIB, cTnI, CK-MB, LDH, Mb, TC and LDL-C in the myocardial injury group were higher than those in the non-myocardial injury group (all $P<0.05$). The incidence of MACE in the myocardial injury group was higher than that in the non-myocardial injury group ($P=0.002$). Spearman's correlation analysis revealed that hs-CRP, IL-6, TNF-α, MCP-1 and FIB suggested positive correlation with cTnI, CK-MB, LDH and Mb (all $P<0.001$). Logistic regression analysis suggested that elevated hs-CRP, IL-6 and TNF-α levels are independent risk factors for myocardial injury in patients receiving pitavastatin treatment. **Conclusion**: In pitavastatin-treated patients, inflammatory markers correlate with myocardial injury; monitoring hs-CRP, IL-6, TNF-α improves prognosis.

Keywords: Correlation; Inflammatory markers; Myocardial injury; Pitavastatin

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INTRODUCTION

Deaths attributed to cardiovascular diseases (CVDs) account for over 30% of the global total annual deaths. Among these, atherosclerosis (AS) and its consequent acute cardiovascular events, such as myocardial injury and myocardial infarction, represent the core etiological factors of mortality (Libby, 2021). With the accelerating aging process of China's population and changes in residents' lifestyles, the incidence and prevalence of AS-related CVDs have been on a continuous upward trend, evolving into a major public health concern in China (Fu *et al.*, 2024, Xue *et al.*, 2023). Therefore, exploring the pathogenesis of AS and identifying effective early warning and intervention targets hold significant clinical value and social implications.

AS is not a simple lipid-deposition disease but a complex pathophysiological process initiated by vascular endothelial dysfunction, accompanied by chronic inflammatory responses, immune cell infiltration and the formation and rupture of lipid plaques (Kong *et al.*, 2022). A large body of research has confirmed that inflammatory response serves as the core pathological mechanism throughout the occurrence, progression and plaque rupture stages of AS (Fan and Watanabe, 2022). Following vascular endothelial injury, endothelial cells express a variety of adhesion molecules, recruiting immune cells such as monocytes and macrophages to migrate toward the vascular intima. These cells transform into foam cells after phagocytosing lipids and simultaneously release substantial amounts of inflammatory factors, thereby forming a local inflammatory microenvironment (Ibanez *et al.*, 2021). Sustained elevation of inflammatory factors further exacerbates endothelial damage, promotes smooth muscle cell proliferation and collagen fiber synthesis, induces plaque instability and ultimately leads to plaque rupture and thrombosis, which in turn triggers severe myocardial

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injury events such as acute myocardial infarction (Wu *et al.*, 2023a). Consequently, inflammatory markers are regarded as crucial biological indicators reflecting the severity of AS and predicting the risk of cardiovascular events.

To date, numerous inflammatory markers associated with AS and myocardial injury have been identified, among which high-sensitivity C-reactive protein (hs-CRP), interleukin-6 (IL-6), tumor necrosis factor-α (TNF-α), monocyte chemoattractant protein-1 (MCP-1) and fibrinogen (FIB) have garnered widespread attention. As a classic acute-phase reactant, elevated hs-CRP levels directly reflect the intensity of inflammatory responses in the body (Attiq *et al.*, 2024, Small *et al.*, 2024). IL-6, a critical pro-inflammatory cytokine, can amplify inflammatory responses by activating downstream signaling pathways, while also participating in the regulation of lipid metabolism disorders and exacerbating the formation and instability of AS plaques (Ridker and Rane, 2021). TNF-α primarily accelerates the progression of AS by inducing endothelial cell damage, promoting inflammatory cell infiltration and apoptosis (Zhao *et al.*, 2023). MCP-1 can specifically chemoattract monocytes to migrate to the vascular intima, making it a critical regulatory factor in the early inflammatory response of AS (Zhang and Dhalla, 2024, Georgakis *et al.*, 2021). FIB is not only an important protein in the coagulation process but also participates in inflammatory responses and plaque formation; elevated FIB levels can increase blood viscosity, promote thrombosis (Zhang *et al.*, 2025).

By inhibiting the key enzyme involved in cholesterol synthesis, statins significantly reduce the levels of total cholesterol (TC) and low-density lipoprotein cholesterol (LDL-C) in the blood, thereby reducing lipid deposition in the vascular intima and exerting an anti-atherosclerotic effect (Onal *et al.*, 2022). In addition, recent studies have found that statins also possess pleiotropic effects independent of their lipid-lowering properties, such as anti-inflammatory, antioxidant and vascular endothelial function-improving effects, which are also important mechanisms underlying their cardiovascular protective effects. As a novel statin, pitavastatin is characterized by significant lipid-lowering efficacy, minimal drug-drug interactions and high safety (Cao *et al.*, 2025). Clinical studies have confirmed that pitavastatin can effectively reduce blood lipid levels in patients and simultaneously lower inflammatory marker levels (Zhou *et al.*, 2021).

Despite the well-established efficacy of statins in clinical treatment, a subset of patients still experience adverse events such as myocardial injury during treatment and the underlying mechanism remains incompletely elucidated. Currently, research on the correlation between changes in inflammatory marker levels and myocardial injury indices in patients during pitavastatin treatment is insufficient (Zhou *et al.*, 2021). Most existing studies focus on the overall impact of statins on inflammatory markers or the correlation between a single inflammatory marker and cardiovascular events. In contrast, there is a paucity of studies systematically exploring the correlation strength between multiple inflammatory markers and myocardial injury indices, specifically in the population receiving pitavastatin treatment (Libby and Soehnlein, 2025). Clarifying the correlation between the two can not only further reveal the pathogenesis of myocardial injury during pitavastatin treatment but also provide a theoretical basis for clinical early warning of myocardial injury risk and optimizing treatment regimens by monitoring inflammatory marker levels.

Based on the aforementioned background, this study adopted a retrospective clinical research approach to collect clinical data of patients receiving pitavastatin treatment. It systematically analyzed the correlation between inflammatory markers and myocardial injury indices and screened for independent risk factors for myocardial injury. A scientific basis is established to support early clinical identification and targeted intervention for the risk of myocardial injury among patients receiving pitavastatin therapy and improvement in their cardiovascular prognosis is thereby facilitated.

MATERIALS AND METHODS

Study design

Fig. 1 presents clinical data of 105 patients with pitavastatin administration at the Affiliated Hospital of Guizhou Medical University from January 2022 to December 2024. After excluding 5 patients in line with the exclusion criteria, 100 eligible patients were recruited. The patients were classified into the myocardial injury group (n=32) and the non-myocardial injury group (n=68) according to the diagnostic criteria for myocardial injury.

Inclusion criteria

(1) Patients who received pitavastatin treatment in the Affiliated Hospital of Guizhou Medical University with a treatment duration of ≥ 6 months(Ridker *et al.*, 2021); (2) Aged 18-80 years, regardless of gender; (3) Complete clinical data.

Exclusion criteria

(1) Patients complicated with severe hepatic or renal dysfunction; (2) Patients with acute infection, autoimmune diseases, malignant tumors, or other severe systemic diseases; (3) Patients who experienced severe trauma, major surgery, or other acute cardiovascular events within the previous 3 months; (4) Patients concurrently taking drugs that may induce myocardial injury, including chemotherapeutic drugs, anthracyclines, tricyclic antidepressants, certain antiarrhythmic agents, high-dose glucocorticoids and nonsteroidal anti-inflammatory drugs with cardiotoxic potential (Zhou *et al.*, 2021).

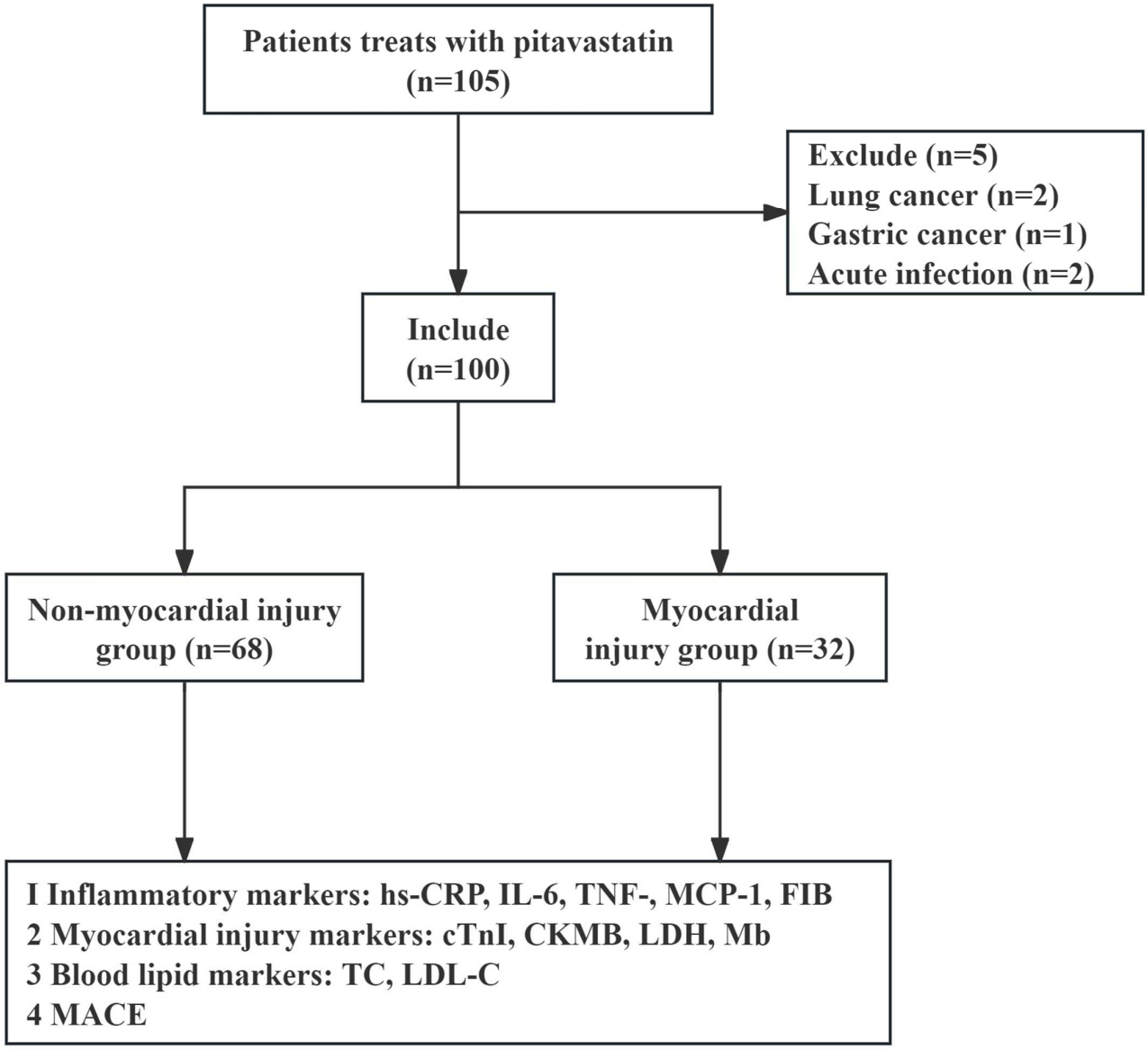

Fig. 1: Study flow diagram.
Note: 105 patients were initially screened in this study, after exclusion, 100 cases were included, with 68 patients in non-myocardial injury group and 32 patients in myocardial injury group. hs-CRP: high-sensitivity C-Reactive Protein; IL-6: Interleukin-6; TNF-α: Tumor Necrosis Factor-α; MCP-1: Monocyte Chemoattractant Protein-1; FIB: Fibrinogen; cTnI: Cardiac Troponin I; CK-MB: Creatine Kinase-MB Isoenzyme; LDH: Lactate Dehydrogenase; Mb: Myoglobin; TC: Total Cholesterol; LDL-C: Low-Density Lipoprotein Cholesterol; MACE: Major Adverse Cardiovascular Events.

Diagnostic criteria for myocardial injury

(1) Cardiac troponin I (cTnI) level exceeding the 99th percentile of the upper limit of the reference range, accompanied by a dynamic upward/downward trend or sustained elevation for ≥ 72 hours; (2) At least 2 of the following indicators exceeding the normal reference range: creatine kinase-MB (CK-MB), lactate dehydrogenase (LDH) and myoglobin (Mb); (3) Exclusion of non-myocardial causes of troponin elevation such as severe liver and kidney dysfunction, rhabdomyolysis and acute infections (Studzinska *et al.*, 2022).

Medication regimen

All patients enrolled in this study received standardized pitavastatin treatment for at least 6 months. According to the medical records of the patients, the specific medication details were as follows:

(1) *Type of medication*: All patients were administered Pitavastatin Calcium Tablets (Manufacturer: Zhejiang Jingxin Pharmaceutical Co., Ltd.; Place of origin: Shaoxing City, Zhejiang Province; Batch numbers: 20191102, 20200305, 20210608, 20220911).
(2) *Administration regimen*: Oral administration with a

daily dose of 2-4 mg, with 2 mg/d as the basic dose. The administration frequency was once daily, all taken 30 minutes after dinner (Ridker *et al.*, 2021).
(3) *Combined medication*: Patients with combined hypertension were all treated with conventional antihypertensive drugs and patients with combined diabetes were treated with hypoglycemic drugs; no other lipid-lowering drugs were used in combination in all patients.

Data collection
The data extraction was independently completed by 2 trained researchers who filled out standardized data collection forms. After extraction, cross-verification was performed and any discrepancies were reviewed and determined by a third senior clinical physician. Meanwhile, the completeness of the data was screened to ensure the data were true, accurate and traceable.

Observation indicators
All laboratory test indicators were measured before pitavastatin administration and 6 months after the start of administration. Harvest 5 mL of fasting venous blood from enrolled patients in the early morning, followed by centrifuging at 3000 r/min for 10 minutes (L535-1, Hunan Xiangyi Laboratory Instrument Development Co., Ltd., Changsha, China) and serum was separated for testing; major adverse cardiovascular events (MACE) were logged 6 months after the start of treatment, before the diagnosis of myocardial injury was confirmed.

Inflammatory markers
hs-CRP was detected by immunoturbidimetry using an automatic biochemical analyzer (7600, Manufacturer: Hitachi High-Technologies Corporation, Tokyo, Japan); IL-6, TNF-α and MCP-1 were all identified via enzyme-linked immunosorbent assay using a microplate reader (Multiskan FC, Manufacturer: Thermo Fisher Scientific Inc., Massachusetts, USA); FIB was assayed by coagulation method using an automatic coagulation analyzer (Sysmex CA-7000, Manufacturer: Sysmex Corporation, Kobe, Japan). The normal reference ranges were as follows: hs-CRP: 0-3 mg/L; IL-6: 0-7 pg/mL; TNF-α: 0-8.1 pg/mL; MCP-1: <250 pg/mL; FIB: 2.0-4.0 g/L.

Myocardial injury indicators
cTnI was assayed by chemiluminescent immunoassay using an automatic chemiluminescent immunoanalyzer (i2000, Manufacturer: Abbott Laboratories, Inc., Illinois, USA); CK-MB, LDH and Mb were assayed by an automatic biochemical analyzer utilizing the immunosuppression method, rate method and latex-enhanced immunoturbidimetry, respectively. Normal reference ranges: cTnI: 0-0.04 ng/mL; CK-MB: 0-24 U/L; LDH: 100-240 U/L; Mb: 0-85 ng/mL.

Blood lipid indicators
TC and LDL-C were measured using the cholesterol oxidase-peroxidase method with an automated biochemical analyzer. Normal reference ranges: TC: 2.8-5.2 mmol/L; LDL-C: < 3.4 mmol/L.

MACE
Utilizing the hospital's electronic medical record system, the occurrence of acute myocardial infarction, exacerbation of heart failure and cardiac death during the 6-month treatment period was counted. The diagnosis of events was based on the relevant standards of "Internal Medicine" (10th Edition) (Ge *et al.*, 2024).

Sample size calculation
Since this was a retrospective study, no a priori sample size calculation was performed. The final sample size (32 cases in the myocardial injury group and 68 cases in the non-myocardial injury group) was determined by counting the number of patients who met the enrollment criteria and had complete clinical data. Based on previous research (Wu *et al.*, 2023b), Cohen's D was 0.75. Setting the two-tailed test level α to 0.05 and the type II error probability β to 0.05, the required sample sizes for the two groups were calculated to be 29 cases and 59 cases, respectively. The actual sample size of this study met and exceeded the estimated value, confirming that the study achieved adequate statistical power (>95%). To verify the reliability of the results, a post hoc power analysis was performed using G*Power 3.1.9.7. The actual effect size for the primary outcome (change in IL-6 level) was 1.65, yielding 99% power. These findings confirm that the sample size enrolled in this study is statistically stable and adequate.

Statistical analysis
Collate and analyze all data in this study via SPSS 27.0 statistical software. Logistic regression analysis was utilized to adjust for confounding factors in the baseline data. The measurement data were first subjected to a normality test (Kolmogorov-Smirnov test) and a homogeneity of variance test (Levene test). Measurement data that adhered to a normal distribution and homogeneous variance were denoted as mean ± standard deviation (mean±SD) and independent t-test was designated for inter-group comparison and paired t-test was used for intra-group comparison; measurement data that did not conform to a normal distribution were expressed as median (interquartile range) [M (Q1, Q3)] and Mann-Whitney U test was used for inter-group comparison and Wilcoxon rank test was designated for intra-group comparison. Count data were denoted as the number of cases (percentage) [n (%)] and chi-square test was designated for inter-group comparison. Pearson correlation analysis was used to examine correlations between inflammatory markers and myocardial injury indicators when both variables were normally distributed; otherwise, Spearman's rank correlation analysis was used.

Variables with a univariate P < 0.05 were further included in the multivariate Logistic regression model to identify independent risk factors for myocardial injury. All statistical tests were two-tailed and a P-value < 0.05 was considered statistically significant.

RESULTS

Baseline data

No statistically significant intergroup differences were detected with respect to age, gender, body mass index, history of hypertension and diabetes, pitavastatin dosage, combined use of antihypertensive drugs, combined use of hypoglycemic drugs, previous use of other lipid-lowering drugs and previous history of MACE (all $P>0.05$), suggesting that the baseline data were adequately balanced (Table 1).

Inflammatory markers

The results suggested that no statistically significant differences existed in the levels of hs-CRP, IL-6, TNF-α, MCP-1 and FIB between the two groups before treatment (Z=-0.640 to -1.571, all $P>0.05$); after 6 months of treatment, the levels of the aforementioned inflammatory markers in both groups were notably lower than the corresponding measurements obtained prior to treatment ($P<0.05$) and the reduction range of each indicator in the non-myocardial injury group was significantly greater than that in the myocardial injury group, with statistically significant differences between the groups (Z=-3.312 to -8.042, all $P<0.001$). These findings suggest that patients without myocardial injury exhibit a more pronounced inflammatory-inhibitory response to treatment (Table 2).

Myocardial injury indicators

The four myocardial injury markers were compared between the two groups at baseline and at 6 months post-treatment. The results showed that there were no statistically significant differences in the levels of the four myocardial injury markers between the two groups before treatment (Z=-0.292 to -1.434, all $P>0.05$); after 6 months of treatment, cTnI, CK-MB, LDH and Mb levels in the two groups were significantly lower relative to the pre-treatment measurements (all $P<0.05$). The myocardial injury group exhibited significantly higher levels of each myocardial injury marker relative to the non-myocardial injury group (Z=-3.168 to -4.188, all $P<0.05$) (Table 3). These results suggested that after pitavastatin treatment, the downregulation effect of myocardial injury markers is more pronounced in patients without myocardial injury.

Blood lipid indicators

Before treatment, with respect to TC and LDL-C concentrations, no significant differences were noted across the two groups (Z=-0.939, $P=0.348$); after 6 months of treatment, the TC and LDL-C levels in both groups were significantly lower than those before treatment (all $P<0.05$), indicating that this treatment regimen has a definite lipid-lowering effect in both types of patients. The TC and LDL-C levels in the non-myocardial injury group were significantly lower than those in the myocardial injury group (Z values: -3.441 and -3.683, respectively; all $P<0.001$), suggesting that the improvement in blood lipid levels after treatment is superior in patients without myocardial injury (Table 4).

MACE

During the 6-month treatment period, myocardial infarction occurred in both groups. During the 6-month follow-up period of this study, only cases of myocardial infarction were observed and no events of heart failure exacerbation or cardiac death occurred. The incidence of MACE was 7.4% in the non-myocardial injury group and 31.3% in the myocardial injury group. The two groups exhibited a statistically significant difference with respect to the incidence of MACE ($\chi^2=9.746$, $P=0.002$), indicating that patients with myocardial injury have an elevated risk of MACE during treatment than those without myocardial injury (Table 5).

Correlation analysis between inflammatory indicators and myocardial injury

The results of correlation analysis indicated a significant positive correlation between inflammatory markers and myocardial injury markers (all r>0.05, all $P<0.001$). The levels of hs-CRP, IL-6, TNF-α, MCP-1 and FIB increased with the elevation of cTnI, CK-MB, LDH and Mb levels, suggesting that the activation degree of the body's inflammatory response is closely related to the severity of myocardial injury. (Fig. 2)

Independent risk factors for myocardial injury

Upon adjustment for the confounding variables detailed in table 1. The results demonstrated that hs-CRP, IL-6 and TNF-α were confirmed to be independent risk factors associated with the development of myocardial injury. Elevated levels of hs-CRP (B=0.385, $P=0.002$, OR=1.469, 95%CI: 1.156, 1.867), IL-6 (B=0.272, $P=0.003$, OR=1.313, 95%CI: 1.096, 1.573) and TNF-α (B=0.186, $P=0.011$, OR=1.204, 95%CI: 1.043, 1.389) were each significantly correlated with a heightened risk of myocardial injury (Table 6).

DISCUSSION

As a commonly used statin lipid-lowering drug in clinical practice, pitavastatin not only exerts the classic effect of reducing LDL-C but also possesses significant anti-inflammatory properties (Ajoolabady *et al.*, 2024, Fici *et al.*, 2022, Bielikova *et al.*, 2024). However, in the population of patients receiving pitavastatin treatment, the specific correlation between changes in inflammatory marker levels and the risk of myocardial injury remains unclear, lacking targeted clinical evidence support.

Table 1: Baseline clinical data [M (Q1,Q3), n (%)].

Indicators	Non-myocardial injury group (n=68)	Myocardial injury group (n=32)	*P*	OR	95%CI for OR
Age (years)	64.5 (55.25,73)	60 (33.25,86.75)	0.295	0.987	0.964,1.011
Gender (n %)	-	-	0.917	1.046	0.448,2.442
Male	39 (57.4%)	18 (56.3%)	-	-	-
Female	29 (42.6%)	14 (43.8%)	-	-	-
BMI (kg/m^2)	23.3(21.23,25.18)	23.35(22.28,25.18)	0.309	1.11	0.908,1.358
Hypertension (n %)	42 (61.8%)	25 (78.1%)	0.109	0.452	0.171,1.194
Diabetes (n %)	31 (45.6%)	16 (50%)	0.680	0.838	0.361,1.943
Pitavastatin dosage (mg/d)	2.5 (2.0,3.0)	2.5 (2.0,3.38)	0.263	1.521	0.729,3.172
Concomitant use of antihypertensive drugs (n %)	63 (92.6%)	30 (93.8%)	0.840	0.840	0.154,4.582
Concomitant use of hypoglycemic drugs (n %)	59 (86.8%)	28 (87.5%)	0.919	0.937	0.265,3.304
Previous use of other lipid-lowering drugs (n %)	5 (7.4%)	3 (9.4%)	0.729	0.767	0.172,3.429
History of previous MACE (n %)	6 (8.8%)	4 (12.5%)	0.569	0.677	0.177,2.591

Note: OR: Odds Ratio; 95%CI: 95% Confidence Interval; BMI: Body Mass Index; MACE: Major Adverse Cardiovascular Events.

Table 2: Comparison of Inflammatory Markers [M (Q1,Q3)].

Indicators		Non-myocardial injury group (n=68)	Myocardial injury group (n=32)	Z	*P*	Bonferroni (*P*)
hs-CRP (mg/L)	Before treatment	6.9 (6.33,7.58)	6.95 (6.5,7.93)	-0.640	0.522	1.000
	Treatment for 6 months	2.05 (1.5,2.58)*	5.45 (4.9,6.08)*	-8.042	<0.001	<0.001
IL-6 (pg/mL)	Before treatment	42.8 (38.2,44.3)	41.95 (38.68,45.93)	-1.101	0.271	1.000
	Treatment for 6 months	20.6 (16.53,23.78)*	30.45 (26.23,33.05)*	-7.658	<0.001	<0.001
TNF-α (pg/mL)	Before treatment	35.7 (32.2,38)	35.95 (32.68,39.93)	-1.571	0.116	1.000
	Treatment for 6 months	13.95 (10.50,17.65)*	24.45 (20.23,27.05)*	-7.806	<0.001	<0.001
MCP-1 (pg/mL)	Before treatment	305.65 (272.20,327.30)	308.45 (287.40,337.43)	-1.245	0.213	1.000
	Treatment for 6 months	175.75 (141.7,208.45)*	234.45 (190.23,254.55)*	-5.440	<0.001	<0.001
FIB (g/L)	Before treatment	4.26 (3.82,4.43)	4.20 (3.85,4.59)	-1.013	0.311	1.000
	Treatment for 6 months	3.00 (2.55,3.37)*	3.29 (2.85,3.71)*	-3.312	<0.001	<0.001

Note: *P<0.05 vs. Before treatment; hs-CRP: high-sensitivity C-Reactive Protein; IL-6: Interleukin-6; TNF-α: Tumor Necrosis Factor-α; MCP-1: Monocyte Chemoattractant Protein-1; FIB: Fibrinogen.

Table 3: Comparison of myocardial injury Markers [M (Q1,Q3)].

Indicators		Non-myocardial injury group (n=68)	Myocardial injury group (n=32)	Z	*P*	Bonferroni (*P*)
cTnI (ng/mL)	Before treatment	0.11 (0.08,0.13)	0.11 (0.09,0.13)	-0.292	0.770	1.000
	Treatment for 6 months	0.05 (0.03,0.07)*	0.07 (0.05,0.09)*	-4.188	<0.001	<0.001
CK-MB (U/L)	Before treatment	15.7 (12.8,16.9)	14.8 (13.4,17.4)	-0.909	0.363	1.000
	Treatment for 6 months	8.95 (6.5,10.65)*	10.4 (8,12.9)*	-3.178	0.001	0.008
LDH (U/L)	Before treatment	170.5 (149.25,191)	168 (155,190)	-0.906	0.365	1.000
	Treatment for 6 months	134.5 (115,156.5)*	144 (129,176)*	-3.168	0.002	0.016
Mb (ng/mL)	Before treatment	76 (60.84)	77 (65,86)	-1.434	0.151	1.000
	Treatment for 6 months	51 (35,64)*	64 (49,79)*	-3.409	<0.001	<0.001

Note: *P<0.05 vs. Before treatment; cTnI: Cardiac Troponin I; CK-MB: Creatine Kinase-MB Isoenzyme; LDH: Lactate Dehydrogenase; Mb: Myoglobin.

Table 4: Comparison of blood lipid markers [M (Q1,Q3)].

Indicators		Non-myocardial injury group (n=68)	Myocardial injury group (n=32)	Z	*P*	Bonferroni (*P*)
TC (mmol/L)	Before treatment	5.55 (5.02,5.91)	5.51 (5.15,5.91)	-0.939	0.348	1.000
	Treatment for 6 months	4.21 (3.83,4.75)*	4.55 (4.2,4.98)*	-3.441	<0.001	<0.001
LDL-C (mmol/L)	Before treatment	3.55 (3.02,3.91)	3.51 (3.15,3.91)	-0.939	0.348	1.000
	Treatment for 6 months	2.12 (1.74,2.72)*	2.55 (2.2,2.98)*	-3.683	<0.001	<0.001

Note: *P<0.05 vs. Before treatment; TC: Total Cholesterol; LDL-C: Low-Density Lipoprotein Cholesterol.

Table 5: Comparison of MACE [n (%)].

Indicators	Non-myocardial injury group (n=68)	Myocardial injury group (n=32)	χ^2	*P*	Bonferroni (*P*)
MACE (myocardial infarction)	5 (7.4%)	10 (31.3%)	9.746	0.002	0.004

Note: MACE: Major Adverse Cardiovascular Events.

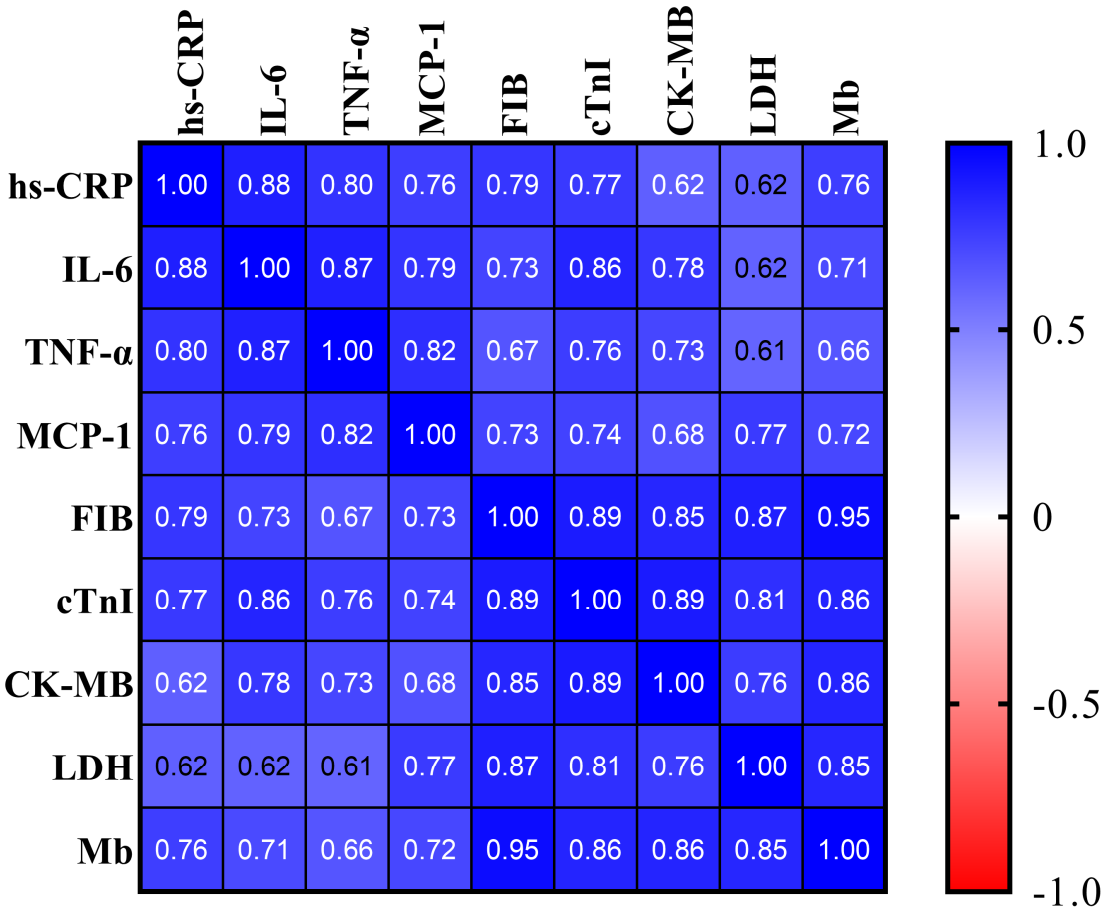

Fig. 2: Correlation analysis between inflammatory markers and myocardial injury markers.
Note: hs-CRP: high-sensitivity C-Reactive Protein; IL-6: Interleukin-6; TNF-α: Tumor Necrosis Factor-α; MCP-1: Monocyte Chemoattractant Protein-1; FIB: Fibrinogen; cTnI: Cardiac Troponin I; CK-MB: Creatine Kinase-MB Isoenzyme; LDH: Lactate Dehydrogenase; Mb: Myoglobin.

Table 6: Analysis of independent risk factors.

Indicators	*B*	*P*	OR	95% for OR
CRP	0.385	0.002	1.469	1.156,1.867
IL-6	0.272	0.003	1.313	1.096,1.573
TNF-α	0.186	0.011	1.204	1.043, 1.389

This also limits the practical effect of optimizing cardiovascular prognosis in patients undergoing pitavastatin treatment through inflammatory marker monitoring in clinical practice. This retrospective analysis demonstrated significant associations between inflammatory biomarkers and myocardial injury. With balanced baseline characteristics, patients in the myocardial injury group presented higher levels of hs-CRP, IL-6, TNF-α, MCP-1 and FIB relative to those in the non-myocardial injury group. Similarly, circulating levels of myocardial injury markers (cTnI, CK-MB, LDH, Mb) and lipid parameters (TC, LDL-C) were elevated in the myocardial injury group, accompanied by an increased incidence of MACE. Correlation analysis revealed that inflammatory markers (hs-CRP, IL-6, TNF-α, MCP-1 and FIB) were positively correlated with myocardial injury indicators including cTnI and CK-MB. Logistic regression analysis indicated that elevated hs-CRP, IL-6 and TNF-α were independently associated with myocardial injury among patients receiving pitavastatin treatment. The present findings provide observational evidence supporting the clinical value of monitoring inflammatory biomarkers to identify patients at higher risk of myocardial injury. Given the retrospective observational design, this study can only confirm statistical associations rather than causal relationships.

The present study observed close correlations between inflammatory markers and myocardial injury in patients administered with pitavastatin and indicated that hs-CRP, IL-6 and TNF-α were independent risk factors for myocardial injury in this patient population. The relevant correlation phenomena are summarized from the perspectives of inflammatory marker characteristics and pitavastatin pharmacological properties, without making deterministic causal inferences. In terms of inflammatory biomarker profiles, hs-CRP is a sensitive indicator reflecting systemic inflammatory status; previous studies have documented its association with vascular inflammation severity, endothelial dysfunction and atherosclerotic plaque progression (Ridker *et al.*, 2023). Consistent with these findings, the significant positive correlation between hs-CRP and myocardial injury markers (cTnI, CK-MB) was observed in the current study, which was concurrent with the abnormal release of myocardial injury biomarkers under coronary perfusion insufficiency (Ridker *et al.*, 2021). As a pivotal pro-inflammatory cytokine, IL-6 is correlated with hepatic hs-CRP synthesis, vascular endothelial dysfunction and vascular inflammatory cell infiltration; additionally, IL-6 level is associated with abnormal myocardial energy metabolism and cardiomyocyte apoptosis in clinical observations (Maaniitty *et al.*, 2024, Pandurangan, 2025). These existing correlational evidences support the independent predictive value of IL-6 for myocardial injury. TNF-α is a potent pro-inflammatory biomarker that correlates with the adhesion and migration of vascular inflammatory cells, atherosclerotic plaque formation and destabilization. Moreover, elevated TNF-α levels are concomitant with impaired cardiomyocyte membrane integrity and increased circulating myocardial injury markers and TNF-α elevation is statistically correlated with higher susceptibility to myocardial injury (Mitsis *et al.*, 2022). In terms of the pharmacological characteristics of pitavastatin, this agent has been documented to have anti-inflammatory and lipid-modulating properties, whereas interindividual variability in therapeutic responses is prevalent. Intense baseline inflammatory status and multiple cardiovascular risk comorbidities are correlated with insufficient inflammatory control during pitavastatin treatment, alongside the concurrent presence of myocardial injury (Iwata *et al.*, 2024). Furthermore, higher TC and LDL-C levels were observed in patients with myocardial injury relative to those without myocardial injury in this cohort. Dyslipidemia is correlated with inflammatory activation and the occurrence of myocardial injury. Collectively, these correlations demonstrate that the association between inflammatory markers and myocardial injury does not exist independently and both inflammatory activation and lipid metabolism abnormalities jointly correlate with cardiovascular prognostic outcomes of patients receiving pitavastatin treatment.

Notably, MCP-1 and FIB were positively correlated with myocardial injury markers, yet they were not identified as independent risk factors, whereas hs-CRP, IL-6 and TNF-α exhibited independent predictive value in this context. Such statistical differences may be associated with varied inflammatory stratification, multicollinearity and differential pathological specificity among these indicators. Statistically, hs-CRP, IL-6 and TNF-α correlated with endothelial dysfunction and myocardial inflammatory injury. MCP-1 and FIB were correlated with monocyte infiltration and secondary hypercoagulability; the two indicators exhibited pronounced multicollinearity with upstream cytokines, which may contribute to the loss of their independent predictive power in regression models. Besides, MCP-1 and FIB were susceptible to non-cardiac influencing factors such as infection, hepatic and renal function status and combined medications, with relatively low cardiac specificity. Pitavastatin has been documented to have lipid-regulating and anti-inflammatory properties and its clinical effects displayed interindividual heterogeneity, which was relatively limited in populations with high baseline inflammatory levels. In addition, higher lipid levels were observed in the myocardial injury group. Dyslipidemia was correlated with exacerbated inflammatory responses and myocardial impairment and both conditions jointly correlated with cardiovascular prognostic outcomes. A study on patients with AS (Chen, 2021) found that the serum level of MCP-1 in the unstable plaque group was significantly elevated relative to that in

the stable plaque group and the healthy control group, confirming that MCP-1 can be used to judge the vulnerability of coronary artery plaques and plaque vulnerability is an important inducement of myocardial injury, which is in agreement with the result of this study that MCP-1 is significantly positively correlated with myocardial injury indicators. A meta-analysis (He *et al.*, 2023) showed that statin treatment can reduce the level of myocardial injury markers by regulating the inflammatory response, which indirectly supports the correlation mechanism between inflammatory markers and myocardial injury in the context of pitavastatin treatment in this study. A study focusing on diabetic cardiomyopathy (Yang *et al.*, 2024, BMJ, 2024) explored the protective effect of the hypoglycemic drug vildagliptin on myocardial inflammatory injury. The study proposed that MCP-1 plays a mediating role in high-glucose-induced myocardial injury, but it did not include the population receiving statin treatment and did not consider the anti-inflammatory effects of lipid-lowering drugs such as pitavastatin, which may explain the failure to observe a significant correlation between MCP-1 and general myocardial injury indicators. This contrasts with the results of this study, which show that MCP-1 is significantly and positively correlated with myocardial injury indicators in patients receiving pitavastatin treatment. The study focused only on hypoglycemic treatment in patients with diabetic cardiomyopathy and was mainly conducted as in vitro cell experiments, so there is a deviation in the assessment of correlation compared with this study.

This study's innovations are predominantly centered on the specific population of patients receiving pitavastatin treatment and targeted at exploring the correlation between inflammatory markers and myocardial injury. As a statin with unique pharmacokinetic characteristics (Tang *et al.*, 2022). The inflammatory state and the risk of myocardial injury in patients treated with pitavastatin may follow special rules. This study fills this research gap and provides targeted evidence for personalized monitoring and management of patients receiving pitavastatin treatment; at the same time, multiple inflammatory markers and myocardial injury indicators are included to comprehensively analyze the correlation between the two. Through multidimensional analysis, the positive correlation between multiple inflammatory markers and myocardial injury indicators is clarified and the core independent risk factors are identified, making the research results more comprehensive and reliable; the analysis, combined with the incidence of MACE, strengthens the clinical significance of the results.

Study Limitations

Despite the meaningful results achieved in this study, there are still some limitations that need to be improved in subsequent studies. First, this study adopted a retrospective observational design, which inevitably introduces selection bias and residual confounding. Second, all enrolled patients received pitavastatin treatment and the absence of an independent non-pitavastatin control group weakened the comparative validity of the research outcomes. In addition, the circular definition of research outcomes may introduce logical bias into the interpretation of results. The single-center enrolled population cannot fully represent the general population receiving pitavastatin, which limits the external generalizability and extrapolation of the research conclusions. This study included only 100 patients, a relatively small sample size that may limit statistical power, especially in the subgroup correlation analysis of inflammatory markers and myocardial injury.

Furthermore, this study merely detected the inflammatory markers and myocardial injury indicators at six months after treatment, without long-term dynamic follow-up monitoring (Dewidar *et al.*, 2025). Thus, the long-term dynamic correlation between indicators and the progression of myocardial injury cannot be clarified. Limited by the completeness of retrospective medical records, this study failed to fully collect and adjust several critical confounding variables, including medication adherence, granular stratification of renal function, baseline acute coronary syndrome status and inflammatory comorbidities. Other unadjusted confounding factors contained pitavastatin dosage, treatment duration, adjustment of therapeutic regimens, smoking history, severity of coronary artery lesions and the application of various cardiovascular drugs. Moreover, this study only confirmed the clinical correlation between inflammatory markers and myocardial injury without exploring the underlying molecular mechanisms. Given the above limitations, potential confounding bias may exist in the current research.

In the future, to further verify the reliability of the conclusions of this study and expand its clinical application value, multicenter, large-sample, prospective and long-term follow-up clinical studies can be carried out to in-depth analyze the correlation between inflammatory markers and myocardial injury in patients receiving pitavastatin treatment with different baseline characteristics and different medication doses; at the same time, combined with basic experimental research, clarify the specific molecular mechanism of myocardial injury mediated by inflammatory markers, so as to provide theoretical support for the development of more effective prevention and treatment strategies for myocardial injury.

CONCLUSION

In patients receiving pitavastatin, inflammatory marker levels are closely associated with indicators of myocardial injury. Future studies are warranted to further corroborate

the reliability of the conclusions herein, preferably through multicenter, large-sample, prospective designs with extended follow-up periods.

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Authors' contributions
Yifan Mao: Conceived and designed the research and analyzed data, drafted and revised the manuscript critically for important intellectual content; Yifan Mao and Wei Zhou: Contributed to the acquisition, analysis and interpretation of data, provided substantial intellectual input during the drafting and revision of the manuscript; Wei Zhou: Participated in the conception and design of the study, played a key role in data interpretation and manuscript preparation. All authors have read and approved the final version of the manuscript.

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Data availability statement
The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

Ethical approval
This study strictly adhered to the Declaration of Helsinki. The protocol was approved by the Ethics Committee of the Affiliated Hospital of Guizhou Medical University [Ethical Approval No.: 2020-(270-01)]. This study was performed in adherence with the RECORD guidelines. See supplementary file for the RECORD checklist.

Conflict of interest
The authors declare no conflict of interest.

Consent to participate
An application for exemption from informed consent was endorsed by the Ethics Committee.

Supplementary data
https://www.pjps.pk/uploads/2026/07/SUP1784797495.pdf

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