

Effects of Early Alirocumab Plus Statin Therapy on Lipid Control and Vascular Endothelial Function After PCI in Patients With Coronary Artery Disease

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Abstract

Objective

To compare the effects of early treatment with alirocumab injection (brand name: Praluent) plus statin therapy versus statin monotherapy on lipid control, vascular function, and short-term laboratory safety at 8 weeks after percutaneous coronary intervention (PCI) in patients with coronary artery disease.

Methods

This single-center observational cohort study included 62 patients with coronary artery disease who underwent PCI. Based on the post-PCI lipid-lowering regimen, 22 patients received alirocumab plus statin therapy and 40 received a regimen without a PCSK9 inhibitor; follow-up was scheduled at 8 weeks. Lipid profiles and inflammatory and laboratory safety measures were compared between baseline and follow-up. Paired vascular ultrasonography was available in 22 patients (9 in the combination group and 13 in the comparison group), in whom brachial artery flow-mediated dilation (FMD), quantitative intima-media thickness (QIMT), and local carotid stiffness indices were evaluated.

Results

At 8 weeks, total cholesterol and LDL-C had decreased from baseline in both groups (all $P < 0.001$). The reductions in total cholesterol, LDL-C, and ApoB were greater in the combination group than in the comparison group, with between-group P values for change of < 0.001 , 0.001 , and 0.017 , respectively. In the vascular subgroup, between-group differences were observed for changes in FMD, compliance coefficient, right QIMT, stiffness coefficient beta, and local PWV ($P = 0.013$, $P = 0.008$, $P = 0.018$, $P = 0.012$, and $P = 0.038$, respectively). ALT and AST decreased from baseline in the combination group ($P = 0.030$ and $P = 0.002$, respectively), while between-group differences in changes in creatinine and CK were not statistically significant ($P = 0.373$ and $P = 0.335$, respectively).

Conclusion

Compared with statin monotherapy, early alirocumab plus statin therapy after PCI achieved greater reductions in LDL-C, total cholesterol, and ApoB and was associated with favorable changes in FMD and selected measures of arterial elasticity. No consistent adverse changes in hepatic or renal function or muscle enzyme levels associated with alirocumab plus statin therapy were observed within 8 weeks.

Introduction

Patients with coronary artery disease remain at high risk of atherosclerotic cardiovascular events after PCI. LDL-C is the primary treatment target in secondary prevention. Chinese, European, and US guidelines emphasize the early initiation and intensification of lipid-lowering therapy according to individual risk and the timely addition of nonstatin agents based on baseline LDL-C and the anticipated magnitude of reduction [1–7]. However, real-world

studies, including SANTORINI, have shown that most patients at high or very high risk do not achieve their risk-based targets [8].

Proprotein convertase subtilisin/kexin type 9 (PCSK9) promotes the degradation of hepatic LDL receptors. By blocking the interaction between PCSK9 and the LDL receptor, alirocumab produces further reductions in LDL-C when added to statin therapy [9]. ODYSSEY OUTCOMES and subsequent analyses showed that adding alirocumab in patients with recent acute coronary syndrome reduced ischemic cardiovascular events and that reductions in LDL-C and lipoprotein(a) were associated with lower risk [10–13]. FOURIER and its subgroup analysis of patients with prior PCI provided complementary evidence of reductions in cardiovascular events and repeat revascularization [14, 15]. PACMAN-AMI provided imaging evidence that alirocumab promotes coronary plaque regression and stabilization [16]. Studies conducted during hospitalization or the peri-PCI period showed that early initiation of PCSK9 inhibition rapidly lowers LDL-C [17–19], while HUYGENS provided additional imaging evidence that evolocumab improves plaque phenotype [20].

Whether PCSK9 inhibition improves vascular endothelial function beyond its potent lipid-lowering effect remains controversial. FMD reflects endothelium-dependent vasodilation, whereas the compliance coefficient, stiffness coefficients, and PWV reflect arterial elasticity and stiffness [9]. Small observational studies have reported improvements in FMD and selected measures of arterial stiffness after treatment with PCSK9 inhibitors [21, 22]. However, a prespecified PACMAN-AMI substudy found no additional improvement in FMD at 52 weeks when alirocumab was added to high-intensity statin therapy [23]. Recent systematic reviews have likewise reported inconsistent overall effects, and background statin therapy itself may improve FMD [24, 25]. A study conducted in China reported greater improvement in FMD after six weeks of PCSK9 inhibitor plus statin treatment than with statin treatment alone in patients with ACS [26]. Short-term evidence in Chinese patients after PCI that jointly assesses endothelial function and arterial stiffness following early alirocumab initiation remains limited.

Accordingly, this study compared the effects of early alirocumab plus statin therapy versus statin monotherapy on lipid control and vascular function at 8 weeks after PCI and evaluated inflammatory markers and short-term laboratory safety.

1 Patients and Methods

1.1 Study Design and Population

The STROBE guidelines were followed for this cross-sectional study. This single-center observational cohort included 62 patients with coronary artery disease who underwent PCI at Shanghai Sixth People's Hospital between March 26, 2021, and June 10, 2025. Patients were classified according to documented PCSK9 inhibitor exposure after PCI: 22 received alirocumab plus background lipid-lowering therapy and 40 did not receive a PCSK9 inhibitor. Follow-up assessments were scheduled at 8 weeks.

This study has been approved by the Ethics Committee of Shanghai Sixth People's Hospital (Approval No.2019-KY-042(K)). This observational study involving human participants was in accordance with the ethical standards of the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Written informed consent was obtained from all participants prior to inclusion in the study. The original informed consent (or the IRB) allows for secondary analysis without additional consent. The study data were anonymous. There was no research fee involved in the study, and our subjects were unpaid. There was no identification of individual

participants/users in any images of the manuscript or supplementary material. Clinical trial number: not applicable.

1.2 Inclusion and Exclusion Criteria

Participants were eligible if they met all of the following criteria: 1. A first diagnosis of atherosclerotic cardiovascular disease requiring PCI, corresponding to very-high cardiovascular risk; 2. age 18–75 years; 3. willingness to follow a therapeutic lifestyle-change diet; 4. voluntary participation with written informed consent; 5. no participation in another clinical study within the preceding 3 months; and 6. statin exposure for less than 2 weeks before enrollment. Exclusion criteria: Patients meeting any of the following criteria were excluded: 1. A history of cardiovascular surgery or other major surgery before admission, or cerebral hemorrhage and its complications; 2. a contraindication or hypersensitivity to a PCSK9 inhibitor; 3. concomitant rheumatic heart disease, cardiomyopathy, congenital heart disease, or psychiatric disease; 4. hypotension or shock; 5. New York Heart Association class III–IV heart failure; 6. alanine aminotransferase or aspartate aminotransferase greater than 1.5 times the upper limit of normal, serum creatinine above the upper limit of normal, poorly controlled diabetes defined as glycated hemoglobin greater than 7.0%, or a history of hypothyroidism; 7. statin treatment for more than 2 weeks before presentation; or 8. refusal to provide written informed consent.

1.3 Treatment

Post-PCI treatment was determined by routine clinical care. According to the investigator-initiated protocol, the combination group received subcutaneous alirocumab 75 or 150 mg every 2 weeks together with conventional lipid-lowering therapy, whereas the comparison group did not receive a PCSK9 inhibitor. Vascular ultrasonography was performed in a subset at baseline and 8 weeks. Concomitant antiplatelet agents, cholesterol absorption inhibitors, renin-angiotensin-aldosterone system inhibitors, beta-blockers, and other cardiovascular medications are summarized in Table 1.

1.4 Outcomes

The primary outcome was the change in LDL-C and the brachial artery FMD from baseline to 8 weeks. Secondary lipid outcomes included total cholesterol, triglycerides, HDL-C, Lp(a), ApoA-I, and ApoB. Inflammatory and laboratory safety measures included C-reactive protein, hemoglobin, ALT, AST, gamma-GT, lactate dehydrogenase, urea, creatinine, uric acid, cardiac troponin, pro-BNP, creatine kinase, and fasting blood glucose. Other vascular outcomes included left and right QIMT, distensibility coefficient (DC), compliance coefficient (CC), stiffness coefficients alpha and beta, and local carotid PWV. FMD was interpreted as an index of endothelium-dependent vasodilation, while QIMT and QAS-derived indices characterized local carotid structure and mechanical properties.

1.5 Vascular Ultrasonography

Brachial artery FMD was assessed after at least 8 hours of fasting, at least 12 hours without caffeine or nicotine, and 10 minutes of quiet supine rest in a temperature-controlled room (22–24°C). A 10-MHz linear probe (UNEXEF38G; Omron Healthcare, Kyoto, Japan) was positioned longitudinally over the right brachial artery 2–10 cm above the antecubital crease. The right arm was mildly abducted with the palm supinated, a pneumatic cuff was placed on the forearm approximately 2–3 cm distal to the antecubital fossa, and three-lead electrocardiography was monitored. The Doppler angle was maintained at 55°, and baseline diameter was

recorded before cuff inflation to 200–250 mm Hg for 5 minutes. After rapid deflation, automated wall tracking recorded the peak relative increase in arterial diameter during reactive hyperemia, expressed as FMD (%) .

Local carotid structure and stiffness were assessed with an Esaote MyLab Class C ultrasound system and LA523 linear transducer (5–13 MHz; Esaote, Genoa, Italy) using radiofrequency-based QIMT and QAS modules. With the participant supine, a longitudinal common carotid artery view was obtained with the ultrasound beam perpendicular to the vessel walls, avoiding plaque-bearing segments. A 15-mm region of interest was placed 1 cm distal to the carotid bulb. The software averaged six cardiac cycles to derive QIMT and the QAS indices DC (kPa^{-1}), CC (mm^2/kPa), stiffness coefficients alpha and beta (dimensionless), and local PWV (m/s). Measurements were accepted when the within-region SD criterion was ≤ 15 , as specified in the source protocol, and all examinations were performed by the same sonographer with more than 10 years of vascular ultrasound experience.

1.6 Statistical Analysis

For database management and statistical analysis, we used SPSS (version 27.0; IBM Corp). Departure from normality was tested using the Shapiro-Wilk statistic. Parameters of a normal distribution are described with mean (SD). Parameters of a non-normal distribution are described as the median and quartile. Counted distributions are described as absolute values. For parameters with a non-normal distribution, the Mann-Whitney U test was used to compare between 2 groups. For parameters with a normal distribution, the Student t test was used to compare between 2 groups. To compare counted parameters between groups, the chi-square test was used. The Wilcoxon signed-rank test was used to compare the treatment outcomes of patients within the same group before and after the treatment. A P value < 0.05 was considered statistically significant.

2 Results

2.1 Baseline Characteristics and Concomitant Medications

A total of 62 patients were included, comprising 22 in the alirocumab group and 40 in the comparison group without a PCSK9 inhibitor. The groups did not differ significantly in age, sex, smoking, alcohol consumption, history of hypertension, diabetes, hyperlipidemia, stroke, renal insufficiency, or the proportion with ACS. The use of cholesterol absorption inhibitors was lower in the alirocumab group than in the comparison group (22.7% and 50.0%, respectively; $P = 0.036$), whereas the use of ARBs, ACE inhibitors, or ARNIs was higher (68.2% and 37.5%, respectively; $P = 0.021$). Statin use was not recorded in two patients in the alirocumab group; the proportions with documented statin use were 90.9% and 100%, respectively ($P = 0.235$; Table 1).

Table 1
Baseline Characteristics and Concomitant Medications in the Two Groups

Variable	Alirocumab group n = 22	Comparison group n = 40	Statistic	P value
Sex (female/male)	5/17	12/28	$\chi^2=0.377$	0.571
Age (years)	62.23 ± 13.29	66.05 ± 11.50	t = 1.187	0.240
Smoking (yes/no)	6/16	16/24	$\chi^2=1.004$	0.409
Alcohol consumption (yes/no)	2/20	7/33	$\chi^2=0.273$	0.621
Hypertension (yes/no)	16/6	23/17	$\chi^2=1.410$	0.235
Diabetes (yes/no)	8/14	11/29	$\chi^2=0.525$	0.469
Hyperlipidemia (yes/no)	4/18	5/35	$\chi^2=0.053$	0.817
Hyperuricemia (yes/no)	2/20	2/38	$\chi^2=0.008$	0.931
Stroke (yes/no)	1/21	1/39	Fisher	1.000
Renal insufficiency (yes/no)	1/21	3/37	Fisher	1.000
ACS (yes/no)	7/15	10/30	$\chi^2=0.332$	0.565
Antiplatelet therapy (yes/no)	22/0	40/0	—	—
Cholesterol absorption inhibitor (yes/no)	5/17	20/20	$\chi^2=4.387$	0.036
Statin (yes/no)	20/2	40/0	$\chi^2=1.410$	0.235
Vasodilator (yes/no)	0/22	4/36	$\chi^2=0.987$	0.321
PPI (yes/no)	8/14	23/17	$\chi^2=2.536$	0.111
CCB (yes/no)	8/14	9/31	$\chi^2=1.371$	0.242
ARB/ACEI/ARNI (yes/no)	15/7	15/25	$\chi^2=5.350$	0.021
Beta-blocker (yes/no)	12/10	23/17	$\chi^2=0.050$	0.822
Diuretic (yes/no)	1/21	5/35	$\chi^2=0.319$	0.572
Aldosterone antagonist (yes/no)	0/22	1/39	Fisher	1.000
Note: Categorical variables are presented as counts; age is presented as mean ± standard deviation. ACS, acute coronary syndrome; PPI, proton pump inhibitor; CCB, calcium channel blocker; ARB, angiotensin II receptor blocker; ACEI, angiotensin-converting enzyme inhibitor; ARNI, angiotensin receptor-neprilysin inhibitor.				

2.2 Changes in Lipid Levels

At 8 weeks, total cholesterol and LDL-C had decreased from baseline in both groups (all $P < 0.001$). In the alirocumab group, LDL-C decreased from 3.285 (2.375, 4.270) mmol/L to 1.120 (0.680, 1.933) mmol/L; in the comparison group, it decreased from 2.590 (1.732, 3.275) mmol/L to 1.435 (1.205, 1.955) mmol/L. The reduction in LDL-C was greater in the alirocumab group than in the comparison group ($P = 0.001$), as were the

reductions in total cholesterol and ApoB ($P < 0.001$ and $P = 0.017$, respectively). Between-group differences in the changes in TG, HDL-C, Lp(a), and ApoA-I were not statistically significant.

Table 2
Lipid Measures Before and After Treatment in the Two Groups

Variable	Comparison group, baseline	Comparison group, week 8	Within-group P	Alirocumab group, baseline	Alirocumab group, week 8	Within-group P	Between-group P for change
TC (mmol/L)	4.255 (3.195, 5.260)	3.155 (2.790, 3.675)	< 0.001	5.135 (4.188, 6.582)	2.750 (2.215, 3.720)	< 0.001	< 0.001
TG (mmol/L)	1.205 (0.803, 2.140)	1.100 (0.797, 1.715)	0.226	1.510 (1.087, 2.283)	1.140 (0.947, 1.755)	0.024	0.242
HDL-C (mmol/L)	1.085 (0.870, 1.228)	1.165 (0.870, 1.458)	0.024	1.045 (0.853, 1.268)	1.010 (0.927, 1.255)	0.273	0.522
LDL-C (mmol/L)	2.590 (1.732, 3.275)	1.435 (1.205, 1.955)	< 0.001	3.285 (2.375, 4.270)	1.120 (0.680, 1.933)	< 0.001	0.001
Lp(a)	18.15 (7.725, 28.50)	16.30 (8.175, 33.82)	0.199	29.75 (13.35, 53.13)	20.40 (5.925, 48.92)	0.709	0.317
ApoA-I	1.270 (1.152, 1.377)	1.370 (1.125, 1.490)	0.014	1.205 (1.110, 1.353)	1.310 (1.195, 1.500)	0.071	0.638
ApoB	0.850 (0.635, 0.968)	0.560 (0.470, 0.660)	< 0.001	1.010 (0.805, 1.272)	0.540 (0.340, 0.650)	< 0.001	0.017
Note: Data are presented as median (P25, P75). TC, total cholesterol; TG, triglycerides; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; Lp(a), lipoprotein(a); ApoA-I, apolipoprotein A-I; ApoB, apolipoprotein B.							

2.3 Inflammatory Markers and Hepatic and Renal Function

CRP decreased from baseline in both groups, with within-group P values of 0.004 in the comparison group and 0.048 in the alirocumab group; however, the between-group difference in change was not statistically significant ($P = 0.747$). ALT and AST decreased after treatment in the alirocumab group, whereas ALT increased in the comparison group; the between-group P values for the changes in ALT and AST were 0.001 and 0.032, respectively. Creatinine increased to varying degrees in both groups, but the between-group difference in change was not statistically significant ($P = 0.373$). Between-group differences in the changes in gamma-GT, lactate dehydrogenase, urea, uric acid, cardiac troponin, pro-BNP, creatine kinase, and fasting blood glucose were not statistically significant.

Table 3
Inflammatory and Laboratory Safety Measures Before and After Treatment in the Two Groups

Variable	Comparison group, baseline	Comparison group, week 8	Within-group P	Alirocumab group, baseline	Alirocumab group, week 8	Within-group P	Between-group P for change
CRP	1.885 (0.500, 6.598)	0.500 (0.500, 2.060)	0.004	1.215 (0.500, 7.633)	0.500 (0.500, 1.340)	0.048	0.747
Hb	136.5 (126.0, 150.3)	141.0 (123.0, 150.0)	0.669	142.0 (128.5, 159.0)	138.5 (127.5, 150.5)	0.039	0.056
ALT	25.0 (19.0, 35.5)	30.0 (21.25, 48.5)	0.027	28.0 (16.75, 56.0)	22.0 (16.75, 30.0)	0.030	0.001
AST	29.5 (25.0, 37.25)	26.0 (22.0, 32.0)	0.069	31.0 (24.0, 81.75)	22.0 (17.0, 29.0)	0.002	0.032
γ-GT	29.0 (19.0, 41.75)	28.0 (18.5, 42.0)	0.919	22.0 (16.0, 34.0)	19.5 (15.75, 26.5)	0.265	0.323
LDH	199.5 (172.0, 221.8)	187.0 (168.0, 207.0)	0.059	190.0 (150.8, 277.3)	175.0 (153.8, 213.0)	0.091	0.558
Urea	6.40 (5.45, 7.70)	6.30 (5.225, 7.55)	0.074	5.80 (5.35, 6.575)	6.45 (5.475, 7.95)	0.578	0.126
Creatinine	81.25 (61.75, 89.75)	91.80 (68.50, 104.3)	< 0.001	79.50 (66.0, 91.5)	84.05 (79.3, 95.93)	0.050	0.373
Uric acid	361.0 (285.3, 427.3)	330.5 (279.3, 408.5)	0.615	351.5 (289.5, 476.0)	333.5 (298.8, 421.5)	0.338	0.643
Cardiac troponin	0.0545 (0.005, 1.006)	0.006 (0.004, 0.0132)	< 0.001	0.238 (0.005, 12.74)	0.013 (0.005, 0.0425)	0.208	0.585
pro-BNP	128.0 (57.8, 331.0)	111.0 (68.15, 277.5)	0.953	182.5 (54.77, 620.0)	120.0 (40.2, 881.3)	0.961	0.759
CK	92.5 (62.75, 209.5)	78.0 (52.25, 117.0)	0.021	83.5 (57.75, 304.8)	60.0 (55.0, 91.75)	0.011	0.335
Fasting blood glucose	5.13 (4.84, 6.28)	5.465 (5.065, 6.067)	0.190	5.435 (4.96, 7.055)	5.510 (5.078, 6.388)	0.658	0.527
Note: Data are presented as median (P25, P75). CRP, C-reactive protein; Hb, hemoglobin; ALT, alanine aminotransferase; AST, aspartate aminotransferase; gamma-GT, gamma-glutamyl transferase; LDH, lactate dehydrogenase; pro-BNP, pro-B-type natriuretic peptide; CK, creatine kinase.							

2.4 Vascular Endothelial Function and Arterial Stiffness

In the subgroup with paired vascular ultrasonography, FMD in the combination group increased from 5.6% (3.9%, 6.95%) to 6.95% (3.85%, 8.40%), with a within-group P value of 0.058. The change in FMD was not statistically significant in the statin monotherapy group (P = 0.239), whereas the between-group P value for the change was 0.013. In the combination group, the compliance coefficient increased, while right QIMT and stiffness coefficient beta decreased; the corresponding between-group P values for the changes were 0.008, 0.018, and 0.012, respectively, and the directions of change were consistent with improved vascular function. A between-group difference was also observed in the change in PWV (P = 0.038), whereas the changes in left QIMT, distensibility coefficient, and stiffness coefficient alpha did not differ significantly between groups.

Table 4
Vascular Function Measures Before and After Treatment in the Two Groups

Variable	Comparison group, baseline	Comparison group, week 8	Within-group P	Alirocumab group, baseline	Alirocumab group, week 8	Within-group P	Between-group P for change
FMD (%)	5.5 (3.9, 7.3)	6.3 (4.2, 7.6)	0.239	5.6 (3.9, 6.95)	6.95 (3.85, 8.40)	0.058	0.013
Left QIMT	715 (711, 834)	716 (711, 854.5)	0.739	712 (580.5, 832)	672.5 (504, 809.5)	0.072	0.097
Distensibility coefficient (DC)	0.01 (0.01, 0.02)	0.02 (0.01, 0.02)	0.317	0.02 (0.015, 0.020)	0.02 (0.0175, 0.340)	0.317	0.738
Compliance coefficient (CC)	0.55 (0.53, 0.78)	0.57 (0.52, 0.77)	0.177	0.590 (0.545, 0.665)	0.605 (0.5775, 1.485)	0.031	0.008
Right QIMT	732 (661.5, 855.5)	732 (661.5, 855.5)	0.705	723 (580.5, 832)	683.5 (494.75, 807)	0.028	0.018
Stiffness coefficient alpha	6.3 (5.7, 6.5)	6.3 (5.7, 6.5)	0.888	6.180 (6.015, 6.295)	6.11 (5.97, 6.32)	0.128	0.103
Stiffness coefficient beta	12.9 (12.0, 13.0)	12.9 (12.0, 13.0)	0.629	11.95 (11.73, 12.87)	11.79 (10.2525, 12.7375)	0.030	0.012
PWV	9.4 (9.0, 9.7)	9.2 (9.0, 9.7)	0.684	9.120 (8.715, 9.635)	9.135 (8.7825, 9.8275)	0.027	0.038
Note: Data are presented as median (P25, P75). FMD, flow-mediated dilation; QIMT, quantitative intima-media thickness; DC, distensibility coefficient; CC, compliance coefficient; PWV, pulse wave velocity.							

3 Discussion

This study showed that early alirocumab plus statin therapy after PCI produced greater reductions in LDL-C, total cholesterol, and ApoB than statin monotherapy. In the vascular ultrasonography subgroup, FMD, compliance coefficient, right QIMT, and stiffness coefficient beta changed favorably in the combination group, with statistically significant between-group differences in these changes.

The lipid findings with combination therapy are consistent with the pharmacologic mechanism of alirocumab. Statins inhibit cholesterol synthesis and upregulate LDL receptors, but they may also increase PCSK9 expression. Alirocumab blocks PCSK9-mediated LDL receptor degradation, making the two mechanisms complementary [9]. Although baseline LDL-C was higher in the combination group, median LDL-C at 8 weeks was lower than in the statin monotherapy group, indicating a more potent early lipid-lowering effect. ODYSSEY OUTCOMES and its subsequent analyses demonstrated that alirocumab added to intensive statin therapy reduced the risk of recurrent ischemic events in patients with recent ACS and supported an association between greater LDL-C reduction and lower risk [10–13]. PACMAN-AMI provided imaging evidence that alirocumab improves coronary plaque burden and phenotype [16]. EPIC-STEMI, EVOPACS, and EVACS showed that PCSK9 inhibitors administered during hospitalization or the peri-PCI period can rapidly lower LDL-C [17–19], while HUYGENS provided complementary evidence that evolocumab improves plaque phenotype [20]. The short follow-up in the present study precluded assessment of clinical events or plaque outcomes, but the direction of the 8-week lipid changes was consistent with this body of evidence.

FMD reflects endothelium-dependent vasodilation. In this study, FMD increased in the combination group, and the between-group difference in change was statistically significant. This finding is consistent with improvements in FMD or microvascular measures reported in previous small observational studies [21, 22]. In contrast, the randomized PACMAN-AMI substudy found no additional improvement in FMD at 52 weeks when alirocumab was added to high-intensity rosuvastatin therapy [23], and related systematic reviews have also reached inconsistent overall conclusions [24, 25]. More recent primary studies reported changes in selected endothelial measures after PCSK9 inhibition in high-risk cardiovascular and acute coronary syndrome populations [26, 27]. The present study indicates that, early after PCI, favorable changes in FMD and selected measures of arterial elasticity occurred in parallel with alirocumab plus statin therapy.

Several primary studies suggest biologically plausible vascular effects, but none establishes the mechanism in this cohort. PCSK9 inhibitor initiation was associated with higher circulating endothelial progenitor-cell counts and function in a 26-patient prospective study [28]. Early alirocumab after acute myocardial infarction was also associated with lower TNF-alpha and a higher L-arginine/asymmetric dimethylarginine ratio in a retrospective cohort [29]. Because the present study did not measure these pathways or model mediation by LDL-C change, the FMD finding can only be described as an exploratory association.

The PWV result requires separate interpretation. A 6-month real-world study in 30 patients with heterozygous familial hypercholesterolemia reported lower PWV after adding a PCSK9 inhibitor [30], but its population and treatment duration differ substantially from the present PCI cohort. In the present cohort, local carotid PWV changed only slightly over 8 weeks and did not parallel the more favorable changes in FMD and selected elasticity indices. This discordance may reflect differences in vascular physiology: FMD can respond relatively rapidly to endothelium-dependent vasodilation, whereas local PWV reflects arterial-wall material properties, vascular tone, and distending pressure. The short interval after PCI may have been insufficient for consistent arterial-wall remodeling, while changes in blood pressure and concomitant vasoactive treatment could alter local PWV independently of endothelial recovery. In addition, QAS-derived local carotid PWV is not interchangeable with regional carotid-femoral PWV [31], and repeatability differs across methods and devices [32]. Large multicenter data further indicate that blood pressure and metabolic factors are important determinants of radiofrequency ultrasound-derived carotid stiffness and PWV [33]. Together, these factors may explain why the

PWV pattern was less coherent than the FMD and selected elasticity findings, and the present data do not establish a treatment-related improvement in arterial stiffness.

During the 8-week follow-up, the combination group showed no consistent adverse changes in hepatic or renal function or muscle enzyme levels relative to the statin monotherapy group. ALT and AST decreased from baseline in the combination group, with statistically significant between-group differences in the changes, whereas the between-group differences in the changes in creatinine and CK were not statistically significant. These findings support the short-term laboratory safety of alirocumab plus statin therapy in this cohort.

This study has several limitations. The nonrandomized single-center design is vulnerable to confounding by indication, particularly given the baseline LDL-C and concomitant-medication imbalances. Only 22 patients had paired vascular measurements, including 9 alirocumab-treated patients, and the reason for missing vascular follow-up was not documented. Multiple correlated vascular outcomes were tested without multiplicity correction, making false-positive nominal P values plausible. The very small 8-week changes in QIMT and stiffness indices may also reflect measurement variability rather than structural remodeling. Finally, the exposure records do not fully specify statin intensity, alirocumab dosing and adherence, and the short follow-up precludes conclusions about clinical events or long-term safety. Larger prospective studies with prespecified vascular endpoints, standardized hemodynamic conditions, and adjusted analyses are needed.

4 Conclusion

In this single-center observational cohort, early alirocumab plus statin therapy after PCI in patients with coronary artery disease achieved greater reductions in LDL-C, total cholesterol, and ApoB. Combination therapy was associated with favorable changes in FMD, compliance coefficient, right QIMT, and stiffness coefficient beta, and laboratory measures at 8 weeks showed no consistent adverse changes in hepatic or renal function or muscle enzyme levels. These findings support intensive lipid control with early alirocumab plus statin therapy after PCI and suggest potential clinical value for improving vascular endothelial function.

Declarations

Conflicts of Interest

All authors have read and approved the final manuscript. They declare no conflicts of interest. Additionally, the manuscript has not been published previously.

Author Contribution

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Data Availability

The data set supporting the conclusions of this article is included within the article. Please contact the corresponding author directly if necessary.

References

1. Joint Committee on the Chinese Guidelines for Lipid Management. Chinese guidelines for lipid management 2023. *Chin Circ J*. 2023;38(3):237–71.
2. Byrne RA, Rossello X, Coughlan JJ, et al. 2023 ESC Guidelines for the management of acute coronary syndromes. *Eur Heart J*. 2023;44(38):3720–826. 10.1093/eurheartj/ehad191.
3. Mach F, Koskinas KC, van Roeters JE, et al. 2025 Focused Update of the 2019 ESC/EAS Guidelines for the management of dyslipidaemias. *Eur Heart J*. 2025;46(42):4359–78. 10.1093/eurheartj/ehaf190.
4. Lloyd-Jones DM, Morris PB, Ballantyne CM, et al. 2022 ACC Expert Consensus Decision Pathway on the role of nonstatin therapies for LDL-cholesterol lowering in the management of atherosclerotic cardiovascular disease risk. *J Am Coll Cardiol*. 2022;80(14):1366–418. 10.1016/j.jacc.2022.07.006.
5. Aversa M, Banach M, Bruckert E, et al. Practical guidance for combination lipid-modifying therapy in high- and very-high-risk patients: a statement from a European Atherosclerosis Society Task Force. *Atherosclerosis*. 2021;325:99–109. 10.1016/j.atherosclerosis.2021.03.039.
6. Krychtiuk KA, Ahrens I, Drexel H, et al. Acute LDL-C reduction post ACS: strike early and strike strong: from evidence to clinical practice. *Eur Heart J Acute Cardiovasc Care*. 2022;11(12):939–49. 10.1093/ehjacc/zuac123.
7. Arnold N, Koenig W. Lipid lowering drugs in acute coronary syndromes. *Curr Atheroscler Rep*. 2023;25(12):939–46. 10.1007/s11883-023-01163-6.
8. Ray KK, Aguiar C, Arca M, et al. Use of combination therapy is associated with improved LDL cholesterol management: 1-year follow-up results from the European observational SANTORINI study. *Eur J Prev Cardiol*. 2024;31(15):1792–803. 10.1093/eurjpc/zwae199.
9. Xu S, Ilyas I, Little PJ, et al. Endothelial dysfunction in atherosclerotic cardiovascular diseases and beyond: from mechanism to pharmacotherapies. *Pharmacol Rev*. 2021;73(3):924–67. 10.1124/pharmrev.120.000096.
10. Schwartz GG, Steg PG, Szarek M, et al. Alirocumab and cardiovascular outcomes after acute coronary syndrome. *N Engl J Med*. 2018;379(22):2097–107. 10.1056/NEJMoa1801174.

11. Schwartz GG, Steg PG, Bhatt DL, et al. Clinical efficacy and safety of alirocumab after acute coronary syndrome according to achieved level of low-density lipoprotein cholesterol. *Circulation*. 2021;143(11):1109–22. 10.1161/CIRCULATIONAHA.120.049447.
12. Schwartz GG, Szarek M, Bittner VA, et al. Transiently achieved very low LDL-cholesterol levels by statin and alirocumab after acute coronary syndrome are associated with cardiovascular risk reduction. *Eur Heart J*. 2023;44(16):1408–17. 10.1093/eurheartj/ehad144.
13. Szarek M, Bittner VA, Aylward P, et al. Lipoprotein(a) lowering by alirocumab reduces the total burden of cardiovascular events independent of low-density lipoprotein cholesterol lowering. *Eur Heart J*. 2020;41(44):4245–55. 10.1093/eurheartj/ehaa649.
14. Sabatine MS, Giugliano RP, Keech AC, et al. Evolocumab and clinical outcomes in patients with cardiovascular disease. *N Engl J Med*. 2017;376(18):1713–22. 10.1056/NEJMoA1615664.
15. Furtado RHM, Fagundes AA Jr, Oyama K, et al. Effect of evolocumab in patients with prior percutaneous coronary intervention. *Circ Cardiovasc Interv*. 2022;15(3):e011382. 10.1161/CIRCINTERVENTIONS.121.011382.
16. Räber L, Ueki Y, Otsuka T, et al. Effect of alirocumab added to high-intensity statin therapy on coronary atherosclerosis in patients with acute myocardial infarction: the PACMAN-AMI randomized clinical trial. *JAMA*. 2022;327(18):1771–81. 10.1001/jama.2022.5218.
17. Mehta SR, Pare G, Lonn EM, et al. Effects of routine early treatment with PCSK9 inhibitors in patients undergoing primary percutaneous coronary intervention for ST-segment elevation myocardial infarction: a randomised, double-blind, sham-controlled trial. *EuroIntervention*. 2022;18(11):e888–96. 10.4244/EIJ-D-22-00735.
18. Koskinas KC, Windecker S, Pedrazzini G, et al. Evolocumab for early reduction of LDL cholesterol levels in patients with acute coronary syndromes. *J Am Coll Cardiol*. 2019;74(20):2452–62. 10.1016/j.jacc.2019.08.010.
19. Leucker TM, Blaha MJ, Jones SR, et al. Effect of evolocumab on atherogenic lipoproteins during the peri- and early post-infarction period: a placebo-controlled, randomized trial. *Circulation*. 2020;142(4):419–21. 10.1161/CIRCULATIONAHA.120.046320.
20. Nicholls SJ, Kataoka Y, Nissen SE, et al. Effect of evolocumab on coronary plaque phenotype and burden in statin-treated patients following myocardial infarction. *JACC Cardiovasc Imaging*. 2022;15(7):1308–21. 10.1016/j.jcmg.2022.03.002.
21. Schremmer J, Busch L, Baasen S, et al. Chronic PCSK9 inhibitor therapy leads to sustained improvements in endothelial function, arterial stiffness, and microvascular function. *Microvasc Res*. 2023;148:104513. 10.1016/j.mvr.2023.104513.
22. Di Minno A, Gentile M, Iannuzzo G, et al. Endothelial function improvement in patients with familial hypercholesterolemia receiving PCSK9 inhibitors on top of maximally tolerated lipid-lowering therapy. *Thromb Res*. 2020;194:229–36. 10.1016/j.thromres.2020.07.049.
23. Rexhaj E, Bär S, Soria R, et al. Effects of alirocumab on endothelial function and coronary atherosclerosis in myocardial infarction: a PACMAN-AMI randomized clinical trial substudy. *Atherosclerosis*. 2024;392:117504. 10.1016/j.atherosclerosis.2024.117504.
24. Arabi SM, Chambari M, Bahrami LS, et al. Statin therapy and flow-mediated dilation: a systematic review and dose-response meta-analysis using the GRADE of data from randomized controlled trials. *Curr Vasc*

- Pharmacol. 2024;20(2):90–100. 10.2174/0115734021280797240212091416.
25. Antza C, Anyfanti P, Savva C, et al. Potential beneficial effect of treatment with PCSK9 inhibitors on vascular endothelial dysfunction: a systematic review and meta-analysis. *Expert Rev Clin Pharmacol*. 2026;19(5):491–8. 10.1080/17512433.2026.2667341.
 26. Xu L, Wang Y, Wang Y, et al. Early use of PCSK9 inhibitors in the prognosis of patients with acute coronary syndrome by protecting vascular endothelial function. *Pharmacology*. 2025;110(1):1–14. 10.1159/000540083.
 27. Kannenkeril D, Bosch A, Kolwelter J, et al. PCSK-9-inhibitor therapy improves endothelial function in high-risk patients with cardiovascular disease. *Clin Res Cardiol*. 2026;115(2):220–31. 10.1007/s00392-024-02556-6.
 28. Itzhaki Ben Zadok O, Mager A, Leshem-Lev D, Lev E, Kornowski R, Eisen A. The effect of proprotein convertase subtilisin kexin type 9 inhibitors on circulating endothelial progenitor cells in patients with cardiovascular disease. *Cardiovasc Drugs Ther*. 2022;36(1):85–92. 10.1007/s10557-020-07119-1.
 29. Shimizu T, Morishita T, Uzui H, et al. Anti-inflammatory effects of proprotein convertase subtilisin/kexin 9 inhibitor therapy in the early phase of acute myocardial infarction. *Heart Vessels*. 2025;40(4):312–9. 10.1007/s00380-024-02473-8.
 30. Scicali R, Mandraffino G, Scuruchi M, et al. Effects of lipid lowering therapy optimization by PCSK9 inhibitors on circulating CD34 + cells and pulse wave velocity in familial hypercholesterolemia subjects without atherosclerotic cardiovascular disease: real-world data from two lipid units. *Biomedicines*. 2022;10(7):1715. 10.3390/biomedicines10071715.
 31. Simova I, Katova T, Santoro C, Galderisi M. Comparison between regional and local pulse-wave velocity data. *Echocardiography*. 2016;33(1):77–81. 10.1111/echo.12985.
 32. Grillo A, Parati G, Rovina M, et al. Short-term repeatability of noninvasive aortic pulse wave velocity assessment: comparison between methods and devices. *Am J Hypertens*. 2018;31(1):80–8. 10.1093/ajh/hpx140.
 33. Xing C, Xie X, Wu Y, et al. Reference values of carotid intima-media thickness and arterial stiffness in Chinese adults based on ultrasound radio frequency signal: a nationwide, multicenter study. *Chin Med J (Engl)*. 2024;137(15):1802–10. 10.1097/CM9.0000000000003156.