ISSN 2307-8960 (online)

World Journal of *Clinical Cases*

World J Clin Cases 2021 February 6; 9(4): 764-998

Published by Baishideng Publishing Group Inc

World Journal of Clinical Cases

Contents

Thrice Monthly Volume 9 Number 4 February 6, 2021

MINIREVIEWS

ORIGINAL ARTICLE

Case Control Study

Retrospective Study

Clinical Trials Study

Observational Study

CASE REPORT

World Journal of Clinical Cases

Thrice Monthly Volume 9 Number 4 February 6, 2021

Contents

World Journal of Clinical Cases

Thrice Monthly Volume 9 Number 4 February 6, 2021

Contents

World Journal of Clinical Cases

Thrice Monthly Volume 9 Number 4 February 6, 2021

Contents

ABOUT COVER

Editorial Board Member of *World Journal of Clinical Cases*, Salim R Surani, MD, MPH, MSHM, FACP, FCCP, FAASM is Chair of Critical Care at Corpus Christi Medical Center, Adjunct Clinical Professor of Medicine, Department of Pulmonary, Critical Care and Sleep Medicine at Texas A&M University, and Program Director of the Pulmonary Fellowship Program at Bay Area Medical Center, Corpus Christi. His training and education involved fellowship in Pulmonary Medicine at Baylor College of Medicine, Master's in Public Health, & Epidemiology from Yale University, and Master's in Health Management from University of Texas, Dallas. Having authored more than 250 peer-reviewed articles and written several books and book chapters. (L-Editor: Filipodia)

AIMS AND SCOPE

The primary aim of *World Journal of Clinical Cases* (*WJCC*, *World J Clin Cases*) is to provide scholars and readers from various fields of clinical medicine with a platform to publish high-quality clinical research articles and communicate their research findings online.

WJCC mainly publishes articles reporting research results and findings obtained in the field of clinical medicine and covering a wide range of topics, including case control studies, retrospective cohort studies, retrospective studies, clinical trials studies, observational studies, prospective studies, randomized controlled trials, randomized clinical trials, systematic reviews, meta-analysis, and case reports.

INDEXING/ABSTRACTING

The *WJCC* is now indexed in Science Citation Index Expanded (also known as SciSearch®), Journal Citation Reports/Science Edition, Scopus, PubMed, and PubMed Central. The 2020 Edition of Journal Citation Reports® cites the 2019 impact factor (IF) for *WJCC* as 1.013; IF without journal self cites: 0.991; Ranking: 120 among 165 journals in medicine, general and internal; and Quartile category: Q3. The *WJCC*'s CiteScore for 2019 is 0.3 and Scopus CiteScore rank 2019: General Medicine is 394/529.

RESPONSIBLE EDITORS FOR THIS ISSUE

NAME OF JOURNAL
World Journal of Clinical Cases

ISSN
ISSN 2307-8960 (online)

LAUNCH DATE
April 16, 2013

FREQUENCY
Thrice Monthly

EDITORS-IN-CHIEF
Dennis A Bloomfield, Sandro Vento, Bao-gan Peng

EDITORIAL BOARD MEMBERS
https://www.wjgnet.com/2307-8960/editorialboard.htm

PUBLICATION DATE
February 6, 2021

INSTRUCTIONS TO AUTHORS
https://www.wjgnet.com/bpg/gerinfo/204

GUIDELINES FOR ETHICS DOCUMENTS
https://www.wjgnet.com/bpg/GerInfo/287

GUIDELINES FOR NON-NATIVE SPEAKERS OF ENGLISH
https://www.wjgnet.com/bpg/gerinfo/240

PUBLICATION ETHICS
https://www.wjgnet.com/bpg/GerInfo/288

PUBLICATION MISCONDUCT
https://www.wjgnet.com/bpg/gerinfo/208

ARTICLE PROCESSING CHARGE
https://www.wjgnet.com/bpg/gerinfo/242

STEPS FOR SUBMITTING MANUSCRIPTS
https://www.wjgnet.com/bpg/GerInfo/239

ONLINE SUBMISSION
https://www.f6publishing.com

World Journal of Clinical Cases

Submit a Manuscript: https://www.f6publishing.com

World J Clin Cases 2021 February 6; 9(4): 812-821

DOI: 10.12998/wjcc.v9.i4.812

ISSN 2307-8960 (online)

ORIGINAL ARTICLE

Observational Study

Effects of different statins application methods on plaques in patients with coronary atherosclerosis

Xia Wu, Xiao-Bo Liu, Ting Liu, Wen Tian, Yu-Jiao Sun

ORCID number: Xia Wu 0000-0001-5991-5641; Xiao-Bo Liu 0000-0001-8678-806X; Ting Liu 0000-0002-0516-6996; Wen Tian 0000-0001-8257-6350; Yu-Jiao Sun 0000-0002-8863-1696.

Author contributions: Wu X participated in the design of the study, acquired the data, performed the statistical analysis, and drafted the manuscript; Liu XB acquired and analysed the data; Liu T and Tian W acquired the data; Sun YJ conceived of the study, participated in its design and coordination, helped to draft the manuscript, and provided critical revision for important intellectual content; all authors approved the final version of the article to be published.

Institutional review board statement: The study was approved by the ethics committee of the First Affiliated Hospital of China Medical University.

Conflict-of-interest statement: All the authors have no conflict of interest related to the manuscript.

STROBE statement: The authors have read the STROBE Statement—checklist of items, and the manuscript was prepared and revised according to the STROBE Statement—checklist of items.

Xia Wu, Xiao-Bo Liu, Wen Tian, Yu-Jiao Sun, Department of Geriatrics, First Affiliated Hospital of China Medical University, Shenyang 110001, Liaoning Province, China

Ting Liu, Department of Radiology, First Affiliated Hospital of China Medical University, Shenyang 110001, Liaoning Province, China

Corresponding author: Yu-Jiao Sun, MD, Chief Doctor, Department of Geriatrics, First Affiliated Hospital of China Medical University, No. 155 Nanjing North Street, Heping Ward, Shenyang 110001, Liaoning Province, China. sunyujiaomy08@sina.cn

Abstract

BACKGROUND

Discontinued application of statins may be related to adverse cardiovascular events. However, it is unclear whether different statins administration methods have effects on coronary artery plaques.

AIM

To evaluate the effects of different statins application methods on plaques in patients with coronary atherosclerosis.

METHODS

A total of 100 patients diagnosed with atherosclerotic plaque by coronary artery computed tomography were continuously selected and divided into three groups according to different statins administration methods (discontinued application group, n = 32; intermittent application group, n = 39; sustained application group, n = 29). The effects of the different statins application methods on coronary atherosclerotic plaque were assessed.

RESULTS

The volume change and rate of change of the most severe plaques were significantly reduced in the sustained application group ($P \leq 0.001$). The volume change of the most severe plaques correlated positively with low-density lipoprotein (LDL-C) levels only in the sustained application group (R = 0.362, P = 0.013). There were no changes in plaques or LDL-C levels in the intermittent and discontinued application groups.

CONCLUSION

Continuous application of statins is effective for controlling plaque progression,

Manuscript source: Unsolicited manuscript

Specialty type: Medicine, research and experimental

Country/Territory of origin: China

Peer-review report's scientific quality classification

Grade A (Excellent): 0
Grade B (Very good): B
Grade C (Good): C
Grade D (Fair): 0
Grade E (Poor): 0

Received: September 28, 2020
Peer-review started: September 28, 2020
First decision: November 3, 2020
Revised: November 23, 2020
Accepted: December 10, 2020
Article in press: December 10, 2020
Published online: February 6, 2021

P-Reviewer: Free J, Jin M
S-Editor: Fan JR
L-Editor: Wang TQ
P-Editor: Liu JH

whereas discontinued or intermittent administration of statins is not conducive to controlling plaques. Only with continuous statins administration can a reduction in LDL-C levels result in plaque volume shrinkage.

Key Words: Coronary atherosclerotic plaque; Statin; Coronary artery computed tomography; Low-density lipoprotein; Plaque volume

Core Tip: In this study, a connection between different ways to take the medicine of statins and changes in coronary atherosclerotic plaques was detected. The sustained application of statins reduced the volume of the most severe atherosclerotic plaques compared with intermittent and discontinued applications, suggesting that sustained application of statins plays an important role in treating atherosclerosis. In contrast, in the discontinued and intermittent application groups, coronary atherosclerotic plaques showed progression. These results suggest that statins are effective for the intervention of atherosclerotic plaques and should be applied consistently and continuously. Intermittent application not only increases the medication cost and patient burden but also may not be effective.

Citation: Wu X, Liu XB, Liu T, Tian W, Sun YJ. Effects of different statins application methods on plaques in patients with coronary atherosclerosis. *World J Clin Cases* 2021; 9(4): 812-821
URL: https://www.wjgnet.com/2307-8960/full/v9/i4/812.htm
DOI: https://dx.doi.org/10.12998/wjcc.v9.i4.812

INTRODUCTION

Administering statins is an important measure for preventing atherosclerotic diseases. Many studies have confirmed that long-term application of statins can reduce cardiovascular events and improve the prognosis of coronary heart disease[1-3]. This effect is mainly related to the abilities of statins to lower cholesterol and stabilize or reverse coronary artery plaque volume (CAPV)[4-7]. A series of intravascular ultrasound studies have also found that lipid-lowering therapy with statins can achieve CAPV reduction[8-11]. However, it is undeniable that in a large number of clinical trials, strict application control was performed for statins, whereas in clinical practice, the application of statins has a very high clinical discontinuation rate[12]. It is believed that the natural withdrawal rate of statins is approximately 30% in the general population[13] and that the discontinuation rate in the first year is as high as 40%-75%[14], regardless of the type of statins[15]. In theory and practice, it is recognized that the cardiovascular benefit of statins depends on their compliance[16]. Overall, discontinued application of statins may be closely related to the occurrence of adverse cardiovascular events[17-19], and adverse events caused by discontinuation are more severe than those in patients who have never taken statins[20]. Although previous studies have found that different ways of administering statins may affect the occurrence of cardiovascular events, it is unclear whether different statins administration methods have effects on coronary artery plaques. Therefore, the main purpose of this study was to analyse the effects of different statins application methods on coronary artery plaques.

MATERIALS AND METHODS

General information

A total of 100 patients in our hospital who were confirmed as having definitive coronary atherosclerotic plaques by 256-row coronary computed tomography angiography (CCTA) were continuously selected from September 2011 to November 2012. These patients were all prescribed statins and did not have definite myocardial ischaemia. The specific type and dose of statins were not limited. Diagnosis of plaques

by CCTA and the inclusion criteria were as follows: Non-calcified and/or mixed plaques with a length of ≥ 5 mm and a degree of luminal stenosis < 50%. All enrolled patients were treated with statins, and the baseline level of low-density lipoprotein (LDL) was not limited. The exclusion criteria were as follows: Known coronary heart disease; heart failure; uncontrollable hypertension; liver and kidney dysfunction; inflammatory or immune disease in the active phase; poor-quality coronary artery images; coronary artery calcification score (CACS) ≥ 400; body weight index ≥ 40 kg/m^2. The study was approved by the ethics committee of the First Affiliated Hospital of China Medical University.

Research methods

Blood biochemical tests, including blood lipids, blood sugar, and liver and kidney function, were performed before the CCTA examination. All patients were followed for 1 year after enrollment on a monthly basis. During the follow-up, the use of medications and major adverse cardiovascular events (MACE) were recorded, including definitive angina, cardiogenic death, non-fatal myocardial infarction, revascularization treatment and stroke, and readmission due to cardiovascular events. At the end of follow-up, blood biochemical tests and CCTA were performed again. The patients were divided into three groups according to the application of statins during the follow-up: Group I (discontinued application of statins, patients who discontinued taking statins during follow-up); Group II (intermittent application of statins, patients who suspended and then re-started statins during the follow-up; the intermittent retake occurred at least twice, and the intermittent retake lasted at least 1 mo); Group III (sustained application of statins, patients who continuously took statins during the follow-up).

Image analysis

All scans were evaluated on computer 3D workstations, and CACS measurements were performed using the integration system proposed by Agatston *et al*[21]. Coronary artery images with artefacts and those which did not allow for assessing the extent of the lesion and the nature of the plaque were excluded from the study. A 16-segment coronary artery tree model was used for analysis[22]. The cross-section perpendicular to the vascular centreline was further reconstructed. On axial, coronal, and/or sagittal images, the cross-section moved 0.3/0.4 mm each time at the site of the plaque with reconstructed blood vessels, and the vascular and lumen area of each cross-section was measured.

The calculation formulas applied in our study are as follows: Plaque volume = total vessel volume - total lumen volume; plaque volume percentage = [(total vessel volume - total lumen volume)/total vessel volume] × 100%; percent change in plaque volume = plaque volume percentage$_{\text{at the end of follow-up}}$ - plaque volume percentage$_{\text{at baseline}}$; most severe plaque volume (5 mm) = blood vessel volume$_{\text{at the most severe lesion (5 mm)}}$ - lumen volume$_{\text{at the most severe lesion (5 mm)}}$; the most severe plaque volume (5 mm) refers to the volume of the 5-mm-long plaque measured at the most severe lesion at baseline, and the calculation of the percentage and percentage change of the most severe plaque volume (5 mm) are the same as that of the plaque volume. The vascular remodelling index of all lesions was recorded.

All plaques were divided into three types according to their compositions: Calcified, non-calcified, and mixed. If the radiation density of the plaque is higher than the lumen density, it is calcified; if the radiation density is higher than the adjacent soft tissue and lower than the lumen, it is non-calcified. Calcified plaque means that the calcified tissue in the plaque exceeds 75% of the area, non-calcified plaque means that the calcified tissue in the plaque is less than 25%, and mixed plaque means that the calcified tissue is between 25% and 75%[23]. In this study, changes in non-calcified and mixed plaques were assessed by volume and in calcified plaques by CACS.

Statistical methods

The enumeration data of the baseline characteristics are expressed as absolute values and percentages; measurement data are expressed as the mean ± SD. Measurement data were compared by analysis of variance, and enumeration data were analysed by the chi-square test. Correlation between the percent change in the most disease (5 mm CAPV) and percent change in LDL-C in the different patterns of statins use was analyzed by liner regression analysis. SPSS 21.0 was used for all statistical analyses. $P < 0.05$ was considered statistically significant.

RESULTS

Basic data

All 100 selected patients completed the follow-up, and there were no significant differences in their baseline characteristics (see Table 1 for details).

Blood lipids and medication applications

At the end of follow-up, the LDL-C and total cholesterol (TC) levels of group III were significantly lower than those of the other two groups ($P < 0.01$). In group III, changes in LDL-C, high-density lipoprotein, and TC levels were significantly higher than those of the other two groups ($P < 0.05$; Table 2). The medication applications during the follow-up of the three groups are shown in Table 3, and there were no significant differences among the groups in types of statins during follow-up.

Coronary atherosclerotic plaque changes

At baseline, there were no significant differences in the number and length of plaques among the three groups, nor were there significant differences in plaque characteristics and number of lesion vessels. And the volume of the most severe plaques among the three groups was similar, but at the end of follow-up, the volume in Group III was significantly smaller than that in the other two groups (10.19 ± 5.66 mm^3 *vs* 10.38 ± 5.81 mm^3 *vs* 6.67 ± 4.99 mm^3, $P = 0.001$). Compared with the other two groups, the volume percentage change of the most severe plaques in Group III was significantly reduced (7.24% ± 4.95% *vs* 6.98% ± 5.18% *vs* -3.48% ± 4.74%, $P < 0.001$). There were no significant differences in plaque changes between Group I and Group II (Table 4).

Correlation between coronary plaque changes and LDL-C changes

Correlation analysis showed that the volume percentage change of the most severe plaques (5 mm) correlated positively with the percentage change of LDL-C only in Group III ($R = 0.362$, $P = 0.013$). There were no such correlations in Group I ($R = 0.270$, $P = 0.058$) or Group II ($R = 0.081$, $P = 0.555$).

Adverse events

There were few occurrences of MACE events among the three groups. No cardiac death or myocardial infarction was observed, and no vascularization treatment occurred. There were three cases of stroke, three cases of angina, and 19 cases of re-hospitalization. Although MACE events were not significantly different among the three groups, Group III exhibited a tendency of improvement.

DISCUSSION

Atherosclerotic disease is a major condition with a high incidence that causes great harm to the population. Applying statins to control cholesterol is one of the most important preventive measures. Studies have found that taking statins caused plaque regression[24,25], but it took at least two years[26]. Nevertheless, discontinuation of statin application is still very common[27] and may be related to adverse cardiovascular events[28-31]. A study even found that discontinuation could cause a worse prognosis than never applying statins[20].

In our study, follow-ups occurred in real clinical practice to observe the effects of different statins application methods on coronary atherosclerotic plaques. Although the application duration of statins was only one year, sustained application reduced the volume of the most severe atherosclerotic plaques compared with intermittent and discontinued applications, suggesting that sustained application of statins plays an important role in treating atherosclerosis. In contrast, coronary atherosclerotic plaques showed progression in the discontinued and intermittent application groups. These results suggest that statins are effective for the intervention of atherosclerotic plaques and should be applied continuously. Intermittent application not only increases the medication cost and patient burden but also may not be effective.

Our study also found that when continuously taking statins, the retraction of coronary atherosclerotic plaques was closely related to a decrease in LDL-C level. This significant correlation only appeared with continuous administration, further showing that the effect of statins in reversing plaque is mainly related to the decrease in LDL-C level. As intermittent or discontinued application of statins makes it difficult to effectively control LDL-C level, plaque progression can still be seen on imaging.

Table 1 Baseline characteristics of the study population

Item	Group I (*n* = 32)	Group II (*n* = 39)	Group III (*n* = 29)	*P* value
Age (yr)	55.56 ± 9.49	55.03 ± 9.35	58.14 ± 9.56	0.38
Male, %	68.8 (22)	46.2 (18)	14.4 (12)	0.07
Body mass index (kg/m^2)	24.66 ± 3.17	25.77 ± 3.49	24.34 ± 2.86	0.15
Smoking, %	40.6 (13)	28.2 (11)	20.7 (6)	0.23
Hypertension, %	50.0 (16)	51.3 (20)	41.4 (12)	0.70
Diabetes, %	21.9 (7)	15.4 (6)	17.2 (5)	0.77
Stroke history, %	3.1 (1)	2.6 (1)	3.4 (1)	0.98
Follow-up period (d)	456.28 ± 27.86	460.08 ± 32.91	460.97 ± 33.61	0.82

Values are expressed as the mean ± SD or % (*n*).

Table 2 Changes in blood lipids

Item	Group I (*n* = 32)	Group II (*n* = 39)	Group III (*n* = 29)	*P* value
LDL-C (mmoL/L)				
Baseline	2.35 ± 0.67	2.88 ± 1.00	3.17 ± 0.98	0.02
Follow-up	2.72 ± 0.57	2.84 ± 0.71	2.12 ± 0.45	< 0.001
Change	0.41 ± 0.40	-0.04 ± 0.51	-1.05 ± 0.75	< 0.001
HDL-C (mmoL/L)				
Baseline	1.16 ± 2.92	1.34 ± 0.99	1.0 ± 0.29	1.37
Follow-up	1.04 ± 0.22	1.33 ± 0.76	1.14 ± 0.22	0.08
Change	-0.12 ± 0.17	-0.01 ± 0.29	0.14 ± 0.19	< 0.001
TC (mmoL/L)				
Baseline	3.89 ± 0.73	4.74 ± 1.05	4.56 ± 1.21	0.04
Follow-up	3.99 ± 0.64	4.64 ± 0.77	4.12 ± 0.83	0.002
Change	0.11 ± 0.22	-0.10 ± 0.59	-0.33 ± 0.58	0.011
TG (mmoL/L)				
Baseline	1.65 ± 0.87	1.09 ± 0.59	1.44 ± 0.95	0.06
Follow-up	1.65 ± 0.53	1.39 ± 0.41	1.36 ± 0.56	0.08
Change	-0.02 ± 0.89	0.05 ± 1.27	-0.03 ± 0.69	0.94

Values are expressed as the mean ± SD. LDL-C: Low density lipoprotein cholesterol; HDL-C: High density lipoprotein cholesterol; TC: Total cholesterol; TG: Triglycerides.

Therefore, continuously using statins to effectively reduce LDL-C level is a very important factor in the prevention and treatment of atherosclerotic lesions. Once discontinued, the nitric oxide level will decrease below baseline[32]. Additionally, endothelial protection disappears and endothelial damage is further exacerbated after discontinuing statin treatment in patients with coronary heart disease[33]. The anti-inflammatory effects of statins were also quickly lost after discontinuation[34]. These effects were not related to LDL-C levels[35]. In our study, LDL-C levels of patients in the intermittent application group also decreased, but there was no reduction in plaque volume. Therefore, the reduction in plaque volume is not only related to reduced LDL-C level but may be also closely associated with the continuous application of statins[36].

Although there were no significant differences in adverse cardiovascular events with the different statins application methods, the incidences in the intermittent and discontinued application groups tended to be higher than that in the sustained

Table 3 Medication application

Item	Group I (*n* = 32)	Group II (*n* = 39)	Group III (*n* = 29)	*P* value
Baseline				
Aspirin	34.3 (11)	23.1 (9)	34.5 (10)	0.48
β-receptor blocker	15.6 (5)	7.7 (3)	20.7 (6)	0.30
ACEI/ARB	15.6 (5)	10.3 (4)	10.3 (3)	0.75
CCB	12.5 (4)	17.9 (7)	24.1 (7)	0.50
Statins	9.4 (3)	7.7 (3)	13.8 (4)	0.70
Glucose-lowering treatment	18.8 (6)	7.7 (3)	17.2 (5)	0.32
Follow-up				
Aspirin	28.1 (9)	20.5 (8)	34.5 (10)	0.43
β-receptor blocker	12.5 (4)	7.7 (3)	20.7 (6)	0.30
ACEI/ARB	18.8 (6)	12.8 (5)	13.8 (4)	0.77
CCB	12.5 (4)	12.8 (5)	17.2 (5)	0.84
Glucose-lowering treatment	18.8 (6)	10.3 (4)	17.2 (5)	0.55
Types of statins during follow-up				0.27
Atorvastatin	46.9 (15)	51.3 (20)	58.6 (17)	
Simvastatin	31.3 (10)	33.3 (13)	27.6 (8)	
Pravastatin	3.1 (1)	0 (0)	3.4 (1)	
Rosuvastatin	15.6 (5)	12.8 (5)	10.3 (3)	
Fluvastatin	3.1 (1)	2.6 (1)	0 (0)	

Values are expressed as % (*n*). ACEI: Angiotensin-converting enzyme inhibitor; ARB: Angiotensin receptor blocker; CCB: Calcium channel blocker.

application group. In general, patients should receive effective statin intervention because early statin treatment has important clinical value. However, in real life, patients often neglect medication because they have no symptoms or discomfort. Clinicians also lack scientific and systematic managements of patients. In actual practice, doctors at different levels need to participate, and advanced instruments for a non-invasive evaluation of atherosclerosis disease should be used[37]. The patients that we observed were close to clinical reality and reflective of statin usage in the real world. Moreover, the population was selected from an outpatient department of a tertiary hospital, yet it was difficult for most of them to continue taking the medication. Overall, the findings suggest that we should strengthen the management of patients and the promotion of patients' health education, disease knowledge, and medication knowledge to improve patients' medication compliance and truly improve clinical prognosis.

Our study has certain limitations: The sample size was small, and the follow-up time was relatively short. There may also be some uncertain confounding factors affecting the results. Despite these limitations, our research reflects the actual clinical situation in the real world and is of great significance for the guidance of clinical practice.

CONCLUSION

The persistent and continuous application of statins to reduce LDL-C level can effectively reverse plaques. The participation and management of the nursing team are also important. Indeed, through careful observation, follow-up, and education, the nursing team can play a better role in the management of such patients who require long-term medication. Nonetheless, the specific mechanism is unclear, and further research is needed.

Table 4 Changes of coronary plaque characteristics

Item	Group I (*n* = 32)	Group II (*n* = 39)	Group III (*n* = 29)	*P* value
Total number of plaques (*n*)[1]	50	56	46	
Number of plaques, per person	1.56 ± 0.62	1.43 ± 0.75	1.52 ± 0.79	0.70
Length (mm), per plaque	10.19 ± 5.12	9.97 ± 4.70	8.84 ± 3.73	0.32
Plaque nature				0.94
Non-calcified	54.0 (27)	57.1 (32)	56.5 (26)	
Mixed	46.0 (23)	42.9 (24)	43.5 (20)	
Lesion number				0.65
Single-vessel	53.1 (17)	64.1 (25)	62.1 (18)	
Double-vessel	31.3 (10)	30.8 (12)	27.6 (8)	
Triple-vessel/left main	15.6 (5)	5.1 (2)	10.3 (3)	
Most severe plaque volume (5 mm), per plaque				
Baseline, mm^3	8.18 ± 5.82	8.34 ± 5.31	8.03 ± 5.48	0.96
Follow-up, mm^3	10.19 ± 5.66	10.38 ± 5.81	6.67 ± 4.99	0.001
Plaque volume change, mm^3	2.01 ± 1.02	2.03 ± 1.35	-1.36 ± 1.94	< 0.001
Plaque volume percentage change, %	7.24 ± 4.95	6.98 ± 5.18	-3.48 ± 4.74	< 0.001
Plaque volume, per plaque				
Baseline, mm^3	14.79 ± 15.11	14.76 ± 11.97	11.28 ± 9.53	0.29
Follow-up, mm^3	17.82 ± 16.75	17.41 ± 13.58	9.58 ± 7.95	0.002
Plaque volume change, mm^3	3.09 ± 2.93	2.64 ± 3.12	-1.79 ± 3.04	< 0.001
Plaque volume percentage change, %	5.38 ± 6.09	5.05 ± 4.82	-2.04 ± 3.68	< 0.001
CACS[2]				
Baseline	41.22 ± 55.04	45.44 ± 31.82	101.00 ± 210.44	0.40
Follow-up	51.72 ± 65.76	56.78 ± 35.18	114.45 ± 229.93	0.44
CACS change	10.5 ± 11.62	11.22 ± 7.07	13.46 ± 20.12	0.86
CACS percentage change, %	89.32 ± 147.81	35.45 ± 21.79	40.65 ± 46.44	0.35
Baseline RI	0.96 ± 0.30	1.00 ± 0.35	0.96 ± 0.35	0.74
Follow-up RI	1.06 ± 0.35	1.12 ± 0.32	0.97 ± 0.32	0.10

Values are expressed as the mean ± SD or % (*n*).
[1]The total number of plaques includes only non-calcified plaques and mixed plaques.
[2]Coronary artery calcification score (CACS) assessment includes 38 patients with CACS in the study population (Group I, *n* = 18; Group II, *n* = 9; Group III, *n* = 11). CACS: Coronary artery calcification score; RI: Remodelling index.

ARTICLE HIGHLIGHTS

Research background

The cardiovascular benefit of statins depends on their compliance, and the cardiovascular events may be related to discontinued application of statins. However, it is unclear whether different administration methods have an effect on coronary artery plaques.

Research motivation

Taking statins can cause plaque regression, but the effects of discontinued and intermittent statins applications on coronary artery plaques are unclear.

Research objectives

To analyse the effects of different statin application methods on plaques in patients

with coronary atherosclerosis.

Research methods

Patients were divided into three groups: Discontinued application of statins, intermittent application of statins, and sustained application of statins groups. The effects of the different statins application methods on coronary atherosclerotic plaques were assessed.

Research results

The results found the volume change and rate of change in the most severe plaques significantly decreased and correlated positively with low density lipoprotein cholesterol (LDL-C) only in the sustained statins application group, but there were no changes in the intermittent and discontinued statins application groups.

Research conclusions

Only with continuous statin administration can a reduction in LDL-C levels result in plaque volume shrinkage, but not discontinued or intermittent administration of statins.

Research perspectives

It is important to strengthen the management of patients and the promotion of patients' health education, disease knowledge, and medication knowledge to improve patients' medication compliance and truly improve clinical prognosis.

REFERENCES

1 *Lancet* 1994; 1383-1389 Randomised trial of cholesterol lowering in 4444 patients with coronary heart disease: the Scandinavian Simvastatin Survival Study (4S) [PMID: 7968073]

2 **Downs JR**, Clearfield M, Weis S, Whitney E, Shapiro DR, Beere PA, Langendorfer A, Stein EA, Kruyer W, Gotto AM Jr. Primary prevention of acute coronary events with lovastatin in men and women with average cholesterol levels: results of AFCAPS/TexCAPS. Air Force/Texas Coronary Atherosclerosis Prevention Study. *JAMA* 1998; **279**: 1615-1622 [PMID: 9613910 DOI: 10.1001/jama.279.20.1615]

3 **Baigent C**, Keech A, Kearney PM, Blackwell L, Buck G, Pollicino C, Kirby A, Sourjina T, Peto R, Collins R, Simes R; Cholesterol Treatment Trialists' (CTT) Collaborators. Efficacy and safety of cholesterol-lowering treatment: prospective meta-analysis of data from 90,056 participants in 14 randomised trials of statins. *Lancet* 2005; **366**: 1267-1278 [PMID: 16214597 DOI: 10.1016/S0140-6736(05)67394-1]

4 **Nissen SE**, Tuzcu EM, Libby P, Thompson PD, Ghali M, Garza D, Berman L, Shi H, Buebendorf E, Topol EJ; CAMELOT Investigators. Effect of antihypertensive agents on cardiovascular events in patients with coronary disease and normal blood pressure: the CAMELOT study: a randomized controlled trial. *JAMA* 2004; **292**: 2217-2225 [PMID: 15536108 DOI: 10.1001/jama.292.18.2217]

5 **Nissen SE**, Tuzcu EM, Schoenhagen P, Crowe T, Sasiela WJ, Tsai J, Orazem J, Magorien RD, O'Shaughnessy C, Ganz P; Reversal of Atherosclerosis with Aggressive Lipid Lowering (REVERSAL) Investigators. Statin therapy, LDL cholesterol, C-reactive protein, and coronary artery disease. *N Engl J Med* 2005; **352**: 29-38 [PMID: 15635110 DOI: 10.1056/NEJMoa042000]

6 **Yamada T**, Azuma A, Sasaki S, Sawada T, Matsubara H; REACH Study Group. Randomized evaluation of atorvastatin in patients with coronary heart disease: a serial intravascular ultrasound study. *Circ J* 2007; **71**: 1845-1850 [PMID: 18037734 DOI: 10.1253/circj.71.1845]

7 **Takashima H**, Ozaki Y, Yasukawa T, Waseda K, Asai K, Wakita Y, Kuroda Y, Kosaka T, Kuhara Y, Ito T. Impact of lipid-lowering therapy with pitavastatin, a new HMG-CoA reductase inhibitor, on regression of coronary atherosclerotic plaque. *Circ J* 2007; **71**: 1678-1684 [PMID: 17965484 DOI: 10.1253/circj.71.1678]

8 **Nissen SE**, Tuzcu EM, Schoenhagen P, Brown BG, Ganz P, Vogel RA, Crowe T, Howard G, Cooper CJ, Brodie B, Grines CL, DeMaria AN; REVERSAL Investigators. Effect of intensive compared with moderate lipid-lowering therapy on progression of coronary atherosclerosis: a randomized controlled trial. *JAMA* 2004; **291**: 1071-1080 [PMID: 14996776 DOI: 10.1001/jama.291.9.1071]

9 **Okazaki S**, Yokoyama T, Miyauchi K, Shimada K, Kurata T, Sato H, Daida H. Early statin treatment in patients with acute coronary syndrome: demonstration of the beneficial effect on atherosclerotic lesions by serial volumetric intravascular ultrasound analysis during half a year after coronary event: the ESTABLISH Study. *Circulation* 2004; **110**: 1061-1068 [PMID: 15326073 DOI: 10.1161/01.CIR.0000140261.58966.A4]

10 **Takayama T**, Hiro T, Yamagishi M, Daida H, Saito S, Yamaguchi T, Matsuzaki M. Rationale and design for a study using intravascular ultrasound to evaluate effects of rosuvastatin on coronary artery atheroma in Japanese subjects: COSMOS study (Coronary Atherosclerosis Study Measuring Effects of Rosuvastatin Using Intravascular Ultrasound in Japanese Subjects). *Circ J* 2007; **71**: 271-275

[PMID: 17251680 DOI: 10.1253/circj.71.271]
11 **Nissen SE**, Nicholls SJ, Sipahi I, Libby P, Raichlen JS, Ballantyne CM, Davignon J, Erbel R, Fruchart JC, Tardif JC, Schoenhagen P, Crowe T, Cain V, Wolski K, Goormastic M, Tuzcu EM; ASTEROID Investigators. Effect of very high-intensity statin therapy on regression of coronary atherosclerosis: the ASTEROID trial. *JAMA* 2006; **295**: 1556-1565 [PMID: 16533939 DOI: 10.1001/jama.295.13.jpc60002]
12 **Simons LA**, Simons J, McManus P, Dudley J. Discontinuation rates for use of statins are high. *BMJ* 2000; **321**: 1084 [PMID: 11053202]
13 **Kamal-Bahl SJ**, Burke T, Watson D, Wentworth C. Discontinuation of lipid modifying drugs among commercially insured United States patients in recent clinical practice. *Am J Cardiol* 2007; **99**: 530-534 [PMID: 17293198 DOI: 10.1016/j.amjcard.2006.08.063]
14 **McGinnis B**, Olson KL, Magid D, Bayliss E, Korner EJ, Brand DW, Steiner JF. Factors related to adherence to statin therapy. *Ann Pharmacother* 2007; **41**: 1805-1811 [PMID: 17925498 DOI: 10.1345/aph.1K209]
15 **Heeschen C**, Hamm CW, Laufs U, Snapinn S, Böhm M, White HD; Platelet Receptor Inhibition in Ischemic Syndrome Management (PRISM) Investigators. Withdrawal of statins increases event rates in patients with acute coronary syndromes. *Circulation* 2002; **105**: 1446-1452 [PMID: 11914253 DOI: 10.1161/01.cir.0000012530.68333.c8]
16 **Rasmussen JN**, Chong A, Alter DA. Relationship between adherence to evidence-based pharmacotherapy and long-term mortality after acute myocardial infarction. *JAMA* 2007; **297**: 177-186 [PMID: 17213401 DOI: 10.1001/jama.297.2.177]
17 **Endres M**, Laufs U. Discontinuation of statin treatment in stroke patients. *Stroke* 2006; **37**: 2640-2643 [PMID: 16946153 DOI: 10.1161/01.STR.0000240690.69406.28]
18 **Stone NJ**. Stopping statins. *Circulation* 2004; **110**: 2280-2282 [PMID: 15492328 DOI: 10.1161/01.CIR.0000145140.06171.3D]
19 **Wei L**, Fahey T, MacDonald TM. Adherence to statin or aspirin or both in patients with established cardiovascular disease: exploring healthy behaviour vs. drug effects and 10-year follow-up of outcome. *Br J Clin Pharmacol* 2008; **66**: 110-116 [PMID: 18492127 DOI: 10.1111/j.1365-2125.2008.03212.x]
20 **Daskalopoulou SS**, Delaney JA, Filion KB, Brophy JM, Mayo NE, Suissa S. Discontinuation of statin therapy following an acute myocardial infarction: a population-based study. *Eur Heart J* 2008; **29**: 2083-2091 [PMID: 18664465 DOI: 10.1093/eurheartj/ehn346]
21 **Agatston AS**, Janowitz WR, Hildner FJ, Zusmer NR, Viamonte M Jr, Detrano R. Quantification of coronary artery calcium using ultrafast computed tomography. *J Am Coll Cardiol* 1990; **15**: 827-832 [PMID: 2407762 DOI: 10.1016/0735-1097(90)90282-t]
22 **Austen WG**, Edwards JE, Frye RL, Gensini GG, Gott VL, Griffith LS, McGoon DC, Murphy ML, Roe BB. A reporting system on patients evaluated for coronary artery disease. Report of the Ad Hoc Committee for Grading of Coronary Artery Disease, Council on Cardiovascular Surgery, American Heart Association. *Circulation* 1975; **51**: 5-40 [PMID: 1116248 DOI: 10.1161/01.cir.51.4.5]
23 **Cheng VY**, Wolak A, Gutstein A, Gransar H, Wong ND, Dey D, Thomson LE, Hayes SW, Friedman JD, Slomka PJ, Berman DS. Low-density lipoprotein and noncalcified coronary plaque composition in patients with newly diagnosed coronary artery disease on computed tomographic angiography. *Am J Cardiol* 2010; **105**: 761-766 [PMID: 20211316 DOI: 10.1016/j.amjcard.2009.11.007]
24 **Koskinas KC**, Windecker S, Räber L. Regression of coronary atherosclerosis: Current evidence and future perspectives. *Trends Cardiovasc Med* 2016; **26**: 150-161 [PMID: 26089122 DOI: 10.1016/j.tcm.2015.05.004]
25 **Park SJ**, Kang SJ, Ahn JM, Chang M, Yun SC, Roh JH, Lee PH, Park HW, Yoon SH, Park DW, Lee SW, Kim YH, Lee CW, Mintz GS, Han KH, Park SW. Effect of Statin Treatment on Modifying Plaque Composition: A Double-Blind, Randomized Study. *J Am Coll Cardiol* 2016; **67**: 1772-1783 [PMID: 27081016 DOI: 10.1016/j.jacc.2016.02.014]
26 **Noyes AM**, Thompson PD. A systematic review of the time course of atherosclerotic plaque regression. *Atherosclerosis* 2014; **234**: 75-84 [PMID: 24632041 DOI: 10.1016/j.atherosclerosis.2014.02.007]
27 **Krüger K**, Leppkes N, Gehrke-Beck S, Herrmann W, Algharably EA, Kreutz R, Heintze C, Filler I. Improving long-term adherence to statin therapy: a qualitative study of GPs' experiences in primary care. *Br J Gen Pract* 2018; **68**: e401-e407 [PMID: 29686133 DOI: 10.3399/bjgp18X696173]
28 **Heeschen C**, Hamm CW, Laufs U, Böhm M, Snapinn S, White HD. Withdrawal of statins in patients with acute coronary syndromes. *Circulation* 2003; **107**: e27 [PMID: 12551886 DOI: 10.1161/01.cir.0000050552.32300.93]
29 **Spencer FA**, Allegrone J, Goldberg RJ, Gore JM, Fox KA, Granger CB, Mehta RH, Brieger D; GRACE Investigators. Association of statin therapy with outcomes of acute coronary syndromes: the GRACE study. *Ann Intern Med* 2004; **140**: 857-866 [PMID: 15172899 DOI: 10.7326/0003-4819-140-11-200406010-00006]
30 **David Spence J**. Advances in Stroke Prevention. *J Transl Int Med* 2018; **6**: 105-114 [PMID: 30425946 DOI: 10.2478/jtim-2018-0024]
31 **Rigatelli G**, Zuin M, Ngo TT, Nguyen HT, Nanjundappa A, Talarico E, Duy LCP, Nguyen T. Intracoronary Cavitation as a Cause of Plaque Rupture and Thrombosis Propagation in Patients with Acute Myocardial Infarction: A Computational Study. *J Transl Int Med* 2019; **7**: 69-75 [PMID: 31380239 DOI: 10.2478/jtim-2019-0014]

32 **Laufs U**, Endres M, Custodis F, Gertz K, Nickenig G, Liao JK, Böhm M. Suppression of endothelial nitric oxide production after withdrawal of statin treatment is mediated by negative feedback regulation of rho GTPase gene transcription. *Circulation* 2000; **102**: 3104-3110 [PMID: 11120702 DOI: 10.1161/01.cir.102.25.3104]

33 **Taneva E**, Borucki K, Wiens L, Makarova R, Schmidt-Lucke C, Luley C, Westphal S. Early effects on endothelial function of atorvastatin 40 mg twice daily and its withdrawal. *Am J Cardiol* 2006; **97**: 1002-1006 [PMID: 16563905 DOI: 10.1016/j.amjcard.2005.10.032]

34 **Lee KT**, Lai WT, Chu CS, Tsai LY, Yen HW, Voon WC, Sheu SH. Effect of withdrawal of statin on C-reactive protein. *Cardiology* 2004; **102**: 166-170 [PMID: 15334028 DOI: 10.1159/000080486]

35 **Tziomalos K**, Athyros VG, Mikhailidis DP. Statin discontinuation: an underestimated risk? *Curr Med Res Opin* 2008; **24**: 3059-3062 [PMID: 18826752 DOI: 10.1185/03007990802469102]

36 **Kolovou G**. The need to improve cardiac care after acute coronary syndrome. *Hellenic J Cardiol* 2019; **60**: 254-255 [PMID: 31901256 DOI: 10.1016/j.hjc.2019.12.002]

37 **Rigatelli G**, Zuin M, Dell'Avvocata F, Nanjundappa A, Daggubati R, Nguyen T. Non-invasive Evaluation of Fluid Dynamic of Aortoiliac Atherosclerotic Disease: Impact of Bifurcation Angle and Different Stent Configurations. *J Transl Int Med* 2018; **6**: 138-145 [PMID: 30425950 DOI: 10.2478/jtim-2018-0020]

Published by **Baishideng Publishing Group Inc**
7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-3991568
E-mail: bpgoffice@wjgnet.com
Help Desk: https://www.f6publishing.com/helpdesk
https://www.wjgnet.com