Original article

Plaque stabilization by intensive LDL-cholesterol lowering therapy with atorvastatin is delayed in type 2 diabetic patients with coronary artery disease—Serial angioscopic and intravascular ultrasound analysis

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A B S T R A C T

Background: Diabetes mellitus (DM) is a major risk factor for cardiovascular events. The study purpose was to compare DM and non-DM (nDM) patients in terms of statin-induced change of plaque characteristics using intravascular ultrasound (IVUS) and coronary angioscopy.

Methods: Patients with coronary artery disease and hypercholesterolemia who were enrolled to the TWINS were selected and classified into two groups: DM group and nDM group. Eleven DM patients and 28 nDM patients were studied.

Results: Low-density lipoprotein cholesterol levels decreased significantly to a similar extent at weeks 28 and 80 from baseline in DM and nDM (p < 0.001). The mean angioscopic color grades of yellow plaques in DM and nDM were similar at baseline and significantly decreased at week 80 from baseline in both groups, however, the mean change of angioscopic color grade from baseline in DM were not significantly decreased and the mean angioscopic color was significantly higher than that in nDM (1.34 vs. 1.00, p < 0.05) at week 28. IVUS showed plaque volume reduction in both groups (p < 0.01) except at week 80 in DM group, which was not statistically significant different compared to the baseline.

Conclusion: In DM patients, plaque volume regression by atorvastatin was shown to be attenuated, and its color improvement was significantly delayed. However, the yellowness became comparable between DM and nDM groups at week 80. These results indicate that patients with DM should be treated by intensive lipid-lowering therapy with atorvastatin for at least 80 weeks to stabilize vulnerable plaque.

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Introduction

Our previous study (TWINS: evaluation with simultaneous angioscopic and intravascular ultrasound study) indicated by serial observations using intravascular ultrasound (IVUS) and angioscopy that intensive lipid-lowering therapy with atorvastatin might reduce cardiac events via reduction of plaque vulnerability [1]. The study demonstrated that low-density lipoprotein-cholesterol (LDL-C) lowering below 100 mg/dL by statin was associated with early improvement in yellow color in vulnerable yellow plaques, possibly indicating plaque stabilization, and with subsequent
Diabetes mellitus (DM) is a high risk factor for coronary atherosclerosis and increases the incidence of cardiovascular events. Moreover, the UK Prospective Diabetes Study reported that intensive blood glucose control with sulfonylurea or insulin attenuates the progression of microangiopathy, but not macroangiopathy [2]. It has also been reported that LDL-C level is a major risk factor for CAD in DM patients [3]. In addition to the blood glucose level, both hyperinsulinemia and enhanced inflammatory reaction have important roles in future cardiovascular events in patients with DM [4]. The presence of DM is considered to be an equivalent risk factor of cardiovascular outcome, compared to the existence of past history of significant CAD [5]. Furthermore, DM patients have high likelihood of in-stent restenosis [6,7].

The anti-atherosclerotic efficacy of statins has been proved in many studies assessed by using IVUS as well as coronary angiography [8–13].

Various multicenter studies have revealed that intensive lowering of LDL-C level by statin administration reduces plaque volume in patients with stable CAD or acute coronary syndrome [14–16].

Some previous studies have revealed that color grade of plaque can be reduced by statins [17–24]. Among them, the TWINS we previously performed was a multicenter trial that used both IVUS and angiography to assess the effect of atorvastatin on the plaque volume as well as plaque stability. The study demonstrated early attenuation of angioscopic yellow color in plaques receiving atorvastatin (10–20 mg/day), followed by subsequent plaque volume regression which was relatively delayed compared to the color change. The purpose of this sub-analysis of the TWINS was to elucidate whether diabetes mellitus influences the degrees of stabilization and volume regression of yellow plaques in patients recruited in the TWINS.

Methods

Study protocol and population

The detailed methods have been described in the main paper of the TWINS [1]. Briefly, enrolled patients with CAD complicated by hypercholesterolemia with a fasting LDL-C level $\geq 120$ mg/dL received a daily dose of oral atorvastatin 10–20 mg/day for 80 weeks. Immediately after coronary angiography, coronary yellow plaques of interest were selected and evaluated with coronary angiography and IVUS at weeks 0 (baseline), 28, and 80. The patients with one or more yellow plaques over or equal to grade 2 were enrolled.

Among 57 patients enrolled in the TWINS, 38 patients were followed to 28 weeks and 31 patients were followed to 80 weeks. The results of the angiography and IVUS images observed simultaneously at these three time points for all plaques were reported previously. In this sub-study, DM was diagnosed by the attending physicians, and the patients were divided into 2 groups: DM group and non DM group (nDM). We further compared and analyzed these two groups by using the data of both angiography and IVUS images at these three evaluation time points of baseline and weeks 28 and 80. This protocol was approved by the Institutional Review Board of Osaka Police Hospital and Nihon University Itabashi Hospital. All participants provided written informed consent before participation.

Intravascular imagings (angiography and IVUS)

Angioscopic examination

Immediately after coronary angiography, baseline angioscopic images were obtained with a Fiber Imaging System FT-201 (FiberTech Co Ltd, Tokyo, Japan), using a previously described technique [7]. From these images, yellow color lesions (the color grade was 2 or more) located in major coronary arteries were selected for the main angioscopic examination. The color grade of the enrolled plaque was determined by the attending operator in the catheterization laboratory of the participating hospital, and then reconfirmed by the central committee of the TWINS [1]. The positions of the plaques were confirmed with fluoroscopy by determining the location of the fiberscope tip, and plaque maps were prepared. Images were recorded on a digital videotape and graded using a 6-point scale: 0, not yellow at all; 1, pale yellow; 2, yellow; 3, deep yellow; 4, bright yellow; and 5, ruptured plaque. At weeks 28 and 80, the same positions as at baseline were observed with angiography in reference to the positions of side branches used as landmarks. Average of all color grades at baseline, weeks 28, and 80 in each patient were calculated.

IVUS image acquisition

IVUS was performed with a 2.6F 40-MHz Atlantis Pro IVUS catheter (Boston Scientific Corporation, Natick, MA, USA). The IVUS probe was advanced to a side branch located distal to the target lesion, and images were obtained during automatic pullback at a rate of 0.5 mm/s and recorded on s-VHS videotape. Based on the plaque map, the IVUS volumetric analyses of the target lesions were conducted using a 20-mm segment (IVUS analysis segment) at lesion sites as the unit of analysis. The boundary of the lumen and external elastic membrane (EEM) was traced semi-automatically on digitized cross-sections of the IVUS analysis segment every 0.1 mm (Netra IVUS, Ver.2.04, Sclimage, Inc., Los Angeles, CA, USA). At the baseline examination, the IVUS analysis segment was determined to include a yellow colored position detected by angiography, based on the plaque map and the position of a side branch. At the examinations performed in weeks 28 and 80, the IVUS analysis segment was set using a side branch as a landmark to ensure that at the 3 time points the same position was imaged by IVUS. Averages of plaque volume, vessel volume, and lumen volume of all plaques at baseline, weeks 28, and 80 in each patient were calculated.

Statistical analysis

Numerical data were presented as the mean ± standard deviation (SD). Hemoglobin (Hb) A1c was indicated by National Glycohemoglobin Standardization Program equivalent value (Japan Diabetes Society value + 0.4%). According to whether data were numerical or categorical, unpaired t-test or Fisher’s exact test was employed for the comparison of baseline characteristics. The paired t-test was employed for intergroup comparison of plaque, vessel, and lumen volumes. Wilcoxon signed ranks test was employed for intergroup comparison of the color grade. For intergroup comparison, unpaired t-test was employed for IVUS measurement and Wilcoxon ranks test was for the color grade. In all tests, $p < 0.05$ (2-sided) was considered significant. Bonferroni’s adjustment was applied in case of multiple comparison, $p < 0.025$ (2-sided) was considered significant. All statistical analyses were performed with the SAS statistical software package version 9.1 (SAS Institute Inc., Cary, NC, USA).

Results

Patient characteristics

Baseline characteristics of patients in both DM and nDM groups are shown in Table 1. A total of 11 DM patients and 28 nDM patients were studied. There were no significant differences between the two groups with regard to gender, body mass index, and coronary risk factors except for type of dyslipidemia and the level of HbA1c.

Changes in serum lipids and high-sensitivity C-reactive peptide (hs-CRP) are shown in Table 2. LDL-C levels in the nDM group were
Table 1
Baseline characteristics.

<table>
<thead>
<tr>
<th></th>
<th>nDM (n = 28)</th>
<th>DM (n = 11)</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>58.9 ± 8.7</td>
<td>59.7 ± 7.4</td>
<td>0.781</td>
</tr>
<tr>
<td>Gender (male/female)</td>
<td>20/8 (71.4)</td>
<td>9/2 (81.8)</td>
<td>0.693</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>23.9 ± 2.3</td>
<td>25.8 ± 4.2</td>
<td>0.085</td>
</tr>
<tr>
<td>Type of dyslipidemia</td>
<td>IlA</td>
<td>16 (57.1)</td>
<td>1 (9.1)</td>
</tr>
<tr>
<td></td>
<td>IlB</td>
<td>6 (21.4)</td>
<td>4 (36.4)</td>
</tr>
<tr>
<td></td>
<td>Others</td>
<td>6 (21.4)</td>
<td>6 (54.5)</td>
</tr>
<tr>
<td>Heart disease (not variant angina)</td>
<td>26 (92.9)</td>
<td>10 (90.9)</td>
<td>1.000</td>
</tr>
<tr>
<td>Hypertension</td>
<td>16 (57.1)</td>
<td>7 (63.6)</td>
<td>1.000</td>
</tr>
<tr>
<td>Statin pre-treatment</td>
<td>2 (7.1)</td>
<td>2 (18.2)</td>
<td>0.562</td>
</tr>
<tr>
<td>Current smoker</td>
<td>4 (14.3)</td>
<td>1 (9.1)</td>
<td>0.765</td>
</tr>
<tr>
<td>Concomitant drugs</td>
<td>Aspirin</td>
<td>27 (96.4)</td>
<td>11 (100)</td>
</tr>
<tr>
<td></td>
<td>Antiplatelet agents (except aspirin)</td>
<td>23 (82.1)</td>
<td>9 (81.8)</td>
</tr>
<tr>
<td></td>
<td>ACEI</td>
<td>13 (46.4)</td>
<td>2 (18.2)</td>
</tr>
<tr>
<td></td>
<td>ARB</td>
<td>6 (21.4)</td>
<td>4 (36.4)</td>
</tr>
<tr>
<td></td>
<td>Beta-blockers</td>
<td>7 (25.0)</td>
<td>3 (27.3)</td>
</tr>
</tbody>
</table>

Aspirin
Anti-diabetes therapy

None
28 (100)
6 (54.5)

Diet
5 (45.6)

BG + TZD
1 (3.6)

BG + SU
1 (3.6)

Insulin
3 (27.3)

HbA1c
5.2 ± 0.4
6.4 ± 1.2
<0.001

Data are the number (%) or mean ± SD. Unpaired t-test or Fisher’s exact test were employed for the tests between groups.

Beta-blockers include alpha/beta-blockers; ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker; nDM, non-diabetes mellitus; DM, diabetes mellitus; BG, biguanide; TZD, thiazolidinedione; SU, sulfonylurea.

Table 2
Changes in serum lipids and hs-CRP.

<table>
<thead>
<tr>
<th></th>
<th>Baseline (n)</th>
<th>p-Value (nDM vs DM)</th>
<th>Week 28 (n)</th>
<th>p-Value (vs baseline)</th>
<th>Week 80 (n)</th>
<th>p-Value (vs baseline)</th>
<th>p-Value (nDM vs DM)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LDL-C (mg/dL)</td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>nDM</td>
<td>152.2 ± 26.1 [28]</td>
<td>0.002†</td>
<td>85.1 ± 18.5 [28]</td>
<td>&lt;0.001†</td>
<td>92.0 ± 11.7 [23]</td>
<td>&lt;0.001†</td>
<td>0.018†</td>
</tr>
<tr>
<td>DM</td>
<td>123.8 ± 13.9 [11]</td>
<td>0.118</td>
<td>74.9 ± 16.1 [11]</td>
<td>&lt;0.001†</td>
<td>78.2 ± 20.6 [11]</td>
<td>&lt;0.001†</td>
<td></td>
</tr>
<tr>
<td>TC (mg/dL)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>nDM</td>
<td>215.6 ± 29.6 [28]</td>
<td>0.008†</td>
<td>148.9 ± 23.7 [28]</td>
<td>&lt;0.001†</td>
<td>153.3 ± 20.4 [23]</td>
<td>&lt;0.001†</td>
<td>0.112</td>
</tr>
<tr>
<td>DM</td>
<td>188.5 ± 18.3 [11]</td>
<td>0.139</td>
<td>136.9 ± 17.8 [11]</td>
<td>&lt;0.001†</td>
<td>139.8 ± 26.7 [11]</td>
<td>&lt;0.001†</td>
<td></td>
</tr>
<tr>
<td>HDL-C (mg/dL)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>nDM</td>
<td>40.5 ± 9.4 [28]</td>
<td>0.698</td>
<td>47.1 ± 8.1 [28]</td>
<td>&lt;0.001†</td>
<td>45.9 ± 9.9 [23]</td>
<td>0.001†</td>
<td>0.415</td>
</tr>
<tr>
<td>TG (mg/dL)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>nDM</td>
<td>118.5 ± 64.2 [28]</td>
<td>0.260</td>
<td>109.5 ± 51.2 [28]</td>
<td>0.474</td>
<td>113.0 ± 66.3 [23]</td>
<td>0.357</td>
<td>0.305</td>
</tr>
<tr>
<td>DM</td>
<td>146.0 ± 76.3 [11]</td>
<td>0.746</td>
<td>115.0 ± 36.8 [11]</td>
<td>0.195</td>
<td>142.9 ± 100.0 [11]</td>
<td>0.938</td>
<td></td>
</tr>
<tr>
<td>hsCRP (mg/dL)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>nDM</td>
<td>0.14 ± 0.18 [28]</td>
<td>0.289</td>
<td>0.16 ± 0.32 [28]</td>
<td>0.288</td>
<td>0.06 ± 0.10 [23]</td>
<td>0.001</td>
<td>0.027</td>
</tr>
<tr>
<td>DM</td>
<td>0.07 ± 0.03 [11]</td>
<td>0.148</td>
<td>0.06 ± 0.09 [11]</td>
<td>[9.94 ± 118.0]</td>
<td>0.22 ± 0.34 [11]</td>
<td>0.309</td>
<td></td>
</tr>
</tbody>
</table>

Values are the mean ± SD. Paired t-test is employed for values vs. baseline except for hsCRP.

LDL-C, high-density lipoprotein cholesterol; TC, total cholesterol; TG, triglycerides; nDM, non-diabetes mellitus; DM, diabetes mellitus.

† p < 0.025 is significant with Bonferroni adjustment: Wilcoxon signed ranks test is employed for hsCRP.
† p < 0.05 is significant: tests for between group comparisons used unpaired t-test for lipid parameters and Wilcoxon signed ranks test for hsCRP.

Angioscopic analysis

Angioscopic findings are shown in Fig. 1. The color grade of the plaque did not have a statistical difference at baseline between the two groups. At week 28 the color grade of plaque was significantly improved in the nDM group, but not in the DM group. In addition, the color grade of the DM group was significantly higher than that in the nDM group at week 28. However, this significant difference in the color grade disappeared at week 80. Finally, there was no significant difference in the color grade between both groups at week 80.

IVUS analysis

IVUS findings are shown in Table 3. Plaque volume decreased significantly at week 28 in both groups and at week 80 in the nDM group (p < 0.001, respectively), compared to the baseline. There was no significant difference in change in plaque volume between both
groups during weeks 28 and 80. In addition, there was no significant difference of change in EEM and luminal volume between both groups at every follow-up examination.

Discussion

The present study revealed that both stabilizing and regressive effects of atorvastatin for 80 weeks in patient with CAD was different between the DM and the nDM patients. The color grade observed by angioscopy is reported to be correlated with plaque stability and a lower yellow (whitish) color is associated with more stable plaque [25–27].

Therefore, it is suggested from the present study that the stabilization effect of plaque by statin might be attenuated in DM patients compared to nDM patients. The main findings of the TWINS showed non-parallel characteristics in the effects of statin on plaque stabilization and its volume regression. This sub-study suggested that some specific mechanisms of plaque stabilization were selectively inhibited in patients with DM. Less regressive effect in plaque volume by atorvastatin in DM patients observed in this study supports two previous studies [28,29]. Interestingly, this inhibitory effect in DM patients for plaque volume regression was observed in a different period compared to plaque color change in this study.

Several mechanisms for the inhibitory phenomenon in DM patients should be considered. A previous study using angioscopy showed that unstable plaque is detected more frequently in patients with DM than without DM [30]. In addition, the color grade of plaque, and the incidence of thrombus is higher in patients with DM [25]. However, in the present study, significant thrombus formation could not be seen in both groups, probably because patients enrolled were associated with stable CAD, but not with acute coronary syndrome. Furthermore, the angioscopic color grade as well as total volume of the plaque was not significantly different at baseline between both groups. This might be because yellow plaques were enrolled under certain criteria of yellowness without knowing baseline clinical profiles, so it was not surprising that plaques of both groups had similar color grades. Despite comparable plaque characteristics at baseline, the reason why there were significant differences of stabilizing effect as well as volume regressive effect between DM and nDM in the follow-up period might be as follows. (a) The same intensity of plaque yellowness does not necessarily represent the same vulnerability. The same color grade might represent the equivalent thickness of fibrous cap [31], but may not correspond to the equivalent content of lipid-core. Actually IVUS analysis showed that plaque volume in DM tended to be larger than that in nDM at the baseline in this study. Larger plaque volume might reflect in part plaque vulnerability. (b) It might be possible that even with the same plaque color and the same plaque volume, the enrolled plaques in patients with DM might have unique tissue characteristics at baseline, such as inflammatory cell accumulations, or neo-vessels within plaque, or endothelial dysfunction.

There was significant decrease in hs-CRP at 80 weeks in nDM compared to the baseline. The level of hs-CRP in the DM group was significantly higher than in the nDM group.

These findings suggested that DM patients might have plaques with an advanced degree of inflammation, which might have delayed the stabilization of plaque by statin, although

Table 3
Changes in external elastic membrane volume, luminal volume, and plaque volume.

<table>
<thead>
<tr>
<th></th>
<th>Baseline (n)</th>
<th>p-Value (nDM vs DM)</th>
<th>Week 28 (n) [% change]</th>
<th>p-Value (vs baseline)</th>
<th>p-Value (nDM vs DM)</th>
<th>Week 80 (n) [% change]</th>
<th>p-Value (vs baseline)</th>
<th>p-Value (nDM vs DM)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plaque volume (mm³)</td>
<td>nDM: 136.25 ± 30.21 (25)</td>
<td>0.110</td>
<td>126.64 ± 32.19 (25) [-7.40 ± 8.92%]</td>
<td>&lt;0.001̂</td>
<td>0.305</td>
<td>110.63 ± 30.12 (21) [-19.26 ± 14.44%]</td>
<td>&lt;0.001̂</td>
<td>0.074</td>
</tr>
<tr>
<td></td>
<td>DM: 156.72 ± 37.63 (9)</td>
<td>0.05̂</td>
<td>140.69 ± 41.15 (9) [-10.24 ± 7.89%]</td>
<td></td>
<td></td>
<td>139.50 ± 49.46 (7) [-12.95 ± 11.31%]</td>
<td></td>
<td>0.060</td>
</tr>
<tr>
<td>EEM volume (mm³)</td>
<td>nDM: 345.18 ± 72.95 (25)</td>
<td>0.869</td>
<td>325.68 ± 69.37 (25) [-5.44 ± 7.20%]</td>
<td>0.001̂</td>
<td>0.914</td>
<td>316.59 ± 72.53 (21) [-6.48 ± 7.19%]</td>
<td>&lt;0.001̂</td>
<td>0.943</td>
</tr>
<tr>
<td></td>
<td>DM: 349.82 ± 67.95 (9)</td>
<td>0.003̂</td>
<td>328.59 ± 66.82 (9) [-5.67 ± 4.60%]</td>
<td></td>
<td></td>
<td>314.61 ± 84.00 (7) [-10.88 ± 6.59%]</td>
<td></td>
<td>0.005̂</td>
</tr>
<tr>
<td>Lumen volume (mm³)</td>
<td>nDM: 208.93 ± 69.30 (25)</td>
<td>0.534</td>
<td>199.05 ± 56.10 (25) [-2.34 ± 12.60%]</td>
<td>0.105</td>
<td>0.601</td>
<td>206.37 ± 61.11 (21) [3.34 ± 9.60%]</td>
<td>0.381</td>
<td>0.242</td>
</tr>
<tr>
<td></td>
<td>DM: 193.11 ± 48.83 (9)</td>
<td>0.143</td>
<td>187.90 ± 48.67 (9) [-2.70 ± 6.09%]</td>
<td></td>
<td></td>
<td>175.11 ± 55.34 (7) [-9.18 ± 10.62%]</td>
<td></td>
<td>0.042</td>
</tr>
</tbody>
</table>

Values are the mean ± SD. Paired t-test was employed for values vs. baseline except for hsCRP.

nDM, non-diabetes mellitus; DM, diabetes mellitus; EEM, external elastic membrane; hs-CRP, high sensitivity C-reactive protein.

* p < 0.025 is significant with Bonferroni adjustment: Wilcoxon signed ranks test was employed for hsCRP.
the stabilizing effect caught up with the nDM group at week 80. It was documented using virtual histology-IVUS that the plaque composition of the coronary arteries in patients with DM was remarkably different from a patient without DM [32]. The fibro-fatty fraction could be observed more frequently in DM compared to that in nDM. They also demonstrated that calcified area within plaque was larger in DM patients than that in the nDM group. A study using integrated backscatter-IVUS showed that the group with DM had significantly larger lipid cores and thinner intimal hyperplasia [33]. These differences may reflect the difference in regressive response to statin.

An attenuated effect of statin on plaque volume reduction in DM patients was reported by IVUS in a previous study. A sub-analysis of the JAPAN-ACS study demonstrated that in DM patients with acute coronary syndrome plaque volume did not regress as much as in nDM patients, although the decrease in LDL-C level at the follow-up period was comparable between the DM and nDM groups [26]. Interesting results from the study were that there was a significant correlation between LDL-C level and the degree of plaque volume change in the DM patients but not in the nDM patients. It was speculated that there were two types of plaque regression mechanism by statins in patients with acute coronary syndrome. One is a LDL-C-dependent mechanism, which may be predominant in the DM patients, and another is a LDL-C non-dependent mechanism which may be predominant in the nDM patients. It was suggested that the presence of DM might be an inhibitory factor for the LDL-C non-dependent mechanism.

In the DM group, LDL-C decreased to less than 80 mg/dL as well as in the nDM group. However, the stabilization of yellow plaque was significantly delayed, although the degree of yellow grade of plaques in DM patients decreased to about the same as the nDM patients. Therefore, intensive lipid-lowering therapy should be performed at least over 80 weeks. Whether the LDL-C level around 80 mg/dL is sufficient could not be determined by these data. It might be possible that the lower LDL-C level less than 80 mg/dL might have enhanced stabilization of plaque in DM patients. To prove this speculation, some prospective randomized study would be necessary.

Clinical implications

The present study suggested that in DM patients with stable CAD the plaque stabilizing effect of statins was shown to be attenuated and delayed especially during the first 28 weeks, but that the effect became comparable to nDM patients during the next 1 year. Therefore, statins should be administered in DM patients for a sufficiently long time. Our data also gave insight into the mechanism of plaque regression by statins.

Study limitation

Since we used multiple imaging devices for single patients, the number of patients enrolled in this study is limited, so a larger-scale prospective investigation should be conducted in the future. Because a control group was not included, the natural history of plaques without intervention is unknown. Both IVUS and angiography are invasive methods, making frequent data acquisition impossible for ethical reasons. Thus, the effect of statins before week 28 or after week 80 is unknown.

Conclusion

The plaque volume regression by atorvastatin was shown to be similar in DM and nDM patients, however, the plaque color improvement, in other words, plaque stabilizing effect tended to be delayed in the DM group. These results indicate that patients with DM should be treated by intensive lipid-lowering therapy with atorvastatin for at least 80 weeks to stabilize vulnerable plaque compared with patients without DM.

Acknowledgments

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References


