Plasma lipoprotein profiles change significantly during cardiac catheterization

TAKASHI MIIDA,1* HIDEAKI OTSUKA,2 ATSUSHI TSUCHIYA,2 and MASAHIKO OKADA1

Most patients in acute myocardial infarction (AMI) undergo emergent coronary angiography (CAG). However, when to analyze lipoprotein profiles in AMI is not clear. To determine whether lipoprotein profiles change during catheterization, we measured serum lipid and apolipoprotein concentrations in 65 patients (51 men and 14 women) before and after catheterization. Heparin was injected at 50 units/kg for CAG and 200 units/kg for percutaneous transluminal coronary angioplasty (PTCA). We found that cholesterol and triglyceride decreased by 9.4% (P < 0.001) and 53.1% (P < 0.001), respectively, after catheterization. Apolipoproteins also decreased significantly. Variables decreased two to five times more after PTCA than after CAG. Lipoprotein lipase mass was higher after PTCA (267.8 ± 135.3 μg/L) than after CAG (93.3 ± 48.4 μg/L; P < 0.05). In conclusion, lipoprotein profiles change during catheterization. We recommend avoiding analysis of lipoprotein profiles after emergent CAG in AMI.

Increased total cholesterol (TC) is associated with the increased incidence of coronary heart disease [1–3]. Cholesterol-lowering therapies decreased the incidence of coronary heart disease in primary and secondary prevention trials [4, 5]. LDL is the largest source of plasma cholesterol in most subjects [6], and cholesterol in atherosclerotic lesions derives from LDL [7]. LDL-cholesterol (LDL-C) can be easily estimated without ultracentrifugation by Friedewald formula [8], which requires fasting TC, triglyceride (TG), and HDL-C concentrations. Both TC and HDL-C have little intraday variation [9, 10], while TG increases noticeably in the postprandial state in some patients with coronary artery disease [11]. Although TC and HDL-C concentrations decrease significantly during the course of acute myocardial infarction (AMI) [12–15], some investigators showed that TC concentrations measured within 24 h after AMI are not significantly different from baseline (pre-AMI) concentrations [15, 16]. Therefore, fasting plasma obtained within 24 h after the infarction would be ideal for the determination of LDL-C concentrations in AMI patients.

Now that recanalization therapy for occluded coronary arteries is commonly used [17], most AMI patients undergo emergent coronary angiography (CAG) within the first 6 h of the infarction. Cardiologists may choose intracoronary thrombolysis and (or) angioplasty according to the CAG findings. In such cases, high-dose heparin (50 to 200 units/kg) is usually administered as anticoagulant during the procedures [18]. Heparin is known to release lipase from vascular endothelium, and used to measure plasma lipase activity [19]. In this case, the dose of heparin is lower (10 to 30 units/kg) than that used at cardiac catheterization [18, 19]. However, little is known about the effect of high-dose heparin on plasma lipoprotein profiles. If high-dose heparin changes lipoprotein profiles significantly, lipoprotein analyses must be done before cardiac catheterization. To determine whether lipoprotein profiles change during cardiac catheterization, we examined 65 patients who had CAG or percutaneous transluminal coronary angioplasty (PTCA). We compared serum lipid and apolipoprotein concentrations before and after catheterization. We also determined lipoprotein lipase (LPL) mass in CAG and PTCA groups, because the PTCA requires four times more heparin than CAG.

Materials and Methods

We examined 65 patients (51 men, 14 women, ages 40 to 86 years) who had cardiac catheterization in our institutes. Thirty-eight patients underwent CAG to assess coronary atherosclerosis. Twenty-seven patients had PTCA. Heparin was injected into femoral arteries at a dose of 50 units/kg for CAG and 200 units/kg for PTCA.
All procedures were completed within 1 h in most cases. Before cardiac catheterization, informed consent was obtained from all patients. This protocol was approved by our institutional committee on human research.

**Analytical Methods for Lipoprotein Profiles**

Blood samples were drawn by venipuncture before and after cardiac catheterization. Plasma was immediately separated by low-speed centrifugation. TC and TG concentrations were measured by enzymatic method. HDL-C concentrations were measured enzymatically after the precipitation of VLDL and LDL by phosphotungstic acid/dextran sulfate (HDL2-Daiichi; Daiichi Pure Chemicals). Apolipoprotein (apo) A-I, apo B, and apo E concentrations were determined by turbidity immunoassay. In some patients, LPL mass was measured in postheparin plasma by sandwich enzyme immunoassay [20] with commercially available kits (LPL Elisa Daiichi; Daiichi Pure Chemicals).

**Statistical Analyses**

All values are presented as mean ± SD. Student’s t-test and paired t-test were used for comparisons of data. Linear regression analysis was used to analyze relations between the changes in variables. For all analyses, a value of 0.05 was considered significant.

**Results**

**Lipid and Apolipoprotein Changes During Cardiac Catheterization**

The mean TC and TG concentrations of all patients decreased by 9.4% and 53.1%, respectively, from baseline during cardiac catheterization (Table 1). Apo AI, apo B, and apo E concentrations also decreased significantly. On the contrary, the mean HDL-C concentrations did not change during catheterization.

The decreases in TC and apolipoprotein (AI, B, E) concentrations were two to five times greater in the PTCA group than in the CAG group (Table 2). The dose of heparin used as anticoagulant was four times more in the PTCA group than in the CAG group. LPL mass was three times higher in the PTCA group than in the CAG group (Fig. 1).

For HDL-C, the baseline concentration was the important determinant for the postcatheterization concentration. In those with baseline HDL-C concentrations ≤1.03 mmol/L (40 mg/dL), postcatheterization concentrations increased by 12%. On the other hand, in those with baseline HDL-C >1.03 mmol/L (40 mg/dL), postcatheterization concentrations did not increase. There is a statistical difference in these changes between the two groups (Table 3). However, HDL-C change had no relation to the dose of heparin (Table 2).

### Table 1. Changes in lipid and apolipoprotein concentrations during cardiac catheterization.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Before</th>
<th>After</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lipid change, mmol/L (mg/dL)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TC</td>
<td>4.73 ± 0.93 (183 ± 36)</td>
<td>4.29 ± 1.01 (166 ± 39)*</td>
</tr>
<tr>
<td>TG</td>
<td>1.77 ± 1.46 (157 ± 129)</td>
<td>0.82 ± 0.86 (73 ± 76)*</td>
</tr>
<tr>
<td>HDL-C</td>
<td>1.03 ± 0.28 (40 ± 11)</td>
<td>1.06 ± 0.26 (41 ± 10)</td>
</tr>
<tr>
<td>Apolipoprotein change, mmol/L (mg/dL)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Apo AI</td>
<td>2.77 ± 0.47 (107 ± 18)</td>
<td>2.69 ± 0.57 (104 ± 22)**</td>
</tr>
<tr>
<td>Apo B</td>
<td>2.48 ± 0.62 (96 ± 24)</td>
<td>1.97 ± 0.44 (76 ± 17)*</td>
</tr>
<tr>
<td>Apo E</td>
<td>0.14 ± 0.10 (5.4 ± 3.7)</td>
<td>0.11 ± 0.08 (4.1 ± 3.2)*</td>
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</tbody>
</table>

* *P < 0.001, **P < 0.05 vs before catheterization.

All values are given as means ± SD from 65 patients for lipid concentrations and from 55 patients for apolipoprotein concentrations.

### Table 2. Comparison of changes in lipid and apolipoprotein concentrations during cardiac catheterization between the CAG group and the PTCA group.

<table>
<thead>
<tr>
<th>Variables</th>
<th>CAG</th>
<th>PTCA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lipid change, mmol/L (mg/dL)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TC</td>
<td>−0.26 ± 0.44 (−10 ± 17)</td>
<td>−0.72 ± 0.26 (−28 ± 10)*</td>
</tr>
<tr>
<td>TG</td>
<td>−0.73 ± 0.58 (−65 ± 51)</td>
<td>−1.22 ± 1.19 (−108 ± 105)</td>
</tr>
<tr>
<td>HDL-C</td>
<td>0.05 ± 0.16 (2 ± 6)</td>
<td>−0.13 ± 0.13 (0 ± 5)</td>
</tr>
<tr>
<td>Apolipoprotein change, mmol/L (mg/dL)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Apo AI</td>
<td>0.05 ± 0.21 (2 ± 8)</td>
<td>−0.26 ± 0.21 (−10 ± 8)*</td>
</tr>
<tr>
<td>Apo B</td>
<td>−0.36 ± 0.34 (−14 ± 13)</td>
<td>−0.70 ± 0.28 (−27 ± 11)*</td>
</tr>
<tr>
<td>Apo E</td>
<td>−0.02 ± 0.03 (−0.6 ± 1.3)</td>
<td>−0.06 ± 0.05 (−2.2 ± 1.9)**</td>
</tr>
</tbody>
</table>

* *P < 0.001, **P < 0.01 vs CAG group.

Blood samples were taken before and after catheterization. All values are given as mean ± SD.
emergent CAG. Second, emergent CAG further changes lipoprotein profiles from the baseline status before the onset of AMI. All lipoprotein concentrations except HDL-C decreased significantly during catheterization (Table 1). It takes several weeks for altered lipoprotein profiles after AMI to recover to those at baseline [14, 15].

However, it is practical to analyze lipid profiles before emergent CAG in AMI patients. They are referred to some limited institutes that can do emergent CAG in our area. After completion of rehabilitation, most patients are referred back to the institutes from which they came. Therefore, it is often difficult for us to obtain data on lipid profiles during the chronic phase. In addition, medical staffs need the information on the baseline lipoprotein profiles during hospitalization for an efficient secondary prevention. The proper instruction of diet therapy and life-style modification cannot be done without precise lipoprotein profiles, even by trained dietitians and nurses.

The major changes in lipoprotein profiles during catheterization were caused by the decrease in apo B-containing lipoproteins. Changes in TC were positively correlated with those in TG, apo B, and apo E (Table 4). These results strongly suggest that hydrolyzed VLDL and IDL are removed from the circulation. However, apo B decreased by 21% (Table 1), which was more than we expected. Because the apo B concentration is not so high in VLDL, LDL is also likely to be removed from the circulation.

The mechanism by which lipoprotein profiles change during catheterization is of importance. Heparin showed the dose-dependent effect on lipoprotein concentrations (Table 2) and LPL mass (Fig. 1). These results suggest that heparin releases LPL [19] and promotes the clearance of VLDL, IDL, and possibly LDL during CAG or PTCA. Sehayek et al. demonstrated that lipolysis of human and rat VLDL exposes unreactive endogenous apo E-3 and possibly apo B-100, which promotes efficient and rapid removal of these particles [21]. Other investigators reported that TG-rich lipoprotein remnants that contain LPL are better recognized by hepatic receptors, resulting in preferential removal of such particles [22].

Why the changes in HDL-C during catheterization were dependent on baseline HDL-C concentrations is not clear. Only patients with low baseline HDL-C showed the increase in HDL-C during catheterization (Table 3). Since change in HDL-C was negatively correlated with those in TG, apo B, and apo E (Table 4), HDL is probably produced from TG-rich lipoproteins by lipase. However, there was no dose-dependent effect of heparin on HDL-C changes during catheterization (Table 2). This inconsistency may come from the fact that heparin releases not only LPL but also hepatic lipase [19]. LPL is speculated to supply lipid components to HDL particles during lipolysis of TG-rich lipoproteins [23]. This action seems to increase HDL-C.

On the contrary, hepatic lipase hydrolyzes circulating LDL [24], and reduces its size [25]. Hepatic lipase also promotes the uptake of HDL by the liver [26]. These

### Table 3. Relation between baseline HDL-C concentrations and their changes after catheterization.

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>HDL-C, mmol/L (mg/dL)</th>
<th>Change</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before</td>
<td>After</td>
</tr>
<tr>
<td>Low HDL-C</td>
<td>0.81 ± 0.15</td>
<td>0.90 ± 0.18</td>
</tr>
<tr>
<td>(n = 34)</td>
<td>(31.2 ± 5.9)</td>
<td>(34.9 ± 7.1)*</td>
</tr>
<tr>
<td>Normal HDL-C</td>
<td>1.26 ± 0.15</td>
<td>1.22 ± 0.19</td>
</tr>
<tr>
<td>(n = 31)</td>
<td>(48.8 ± 5.8)</td>
<td>(47.3 ± 7.3)</td>
</tr>
</tbody>
</table>

* P < 0.001 vs HDL-C before catheterization.

According to HDL-C concentrations before catheterization, patients were divided into low HDL-C (≤1.03 mmol/L ≤40 mg/dL) or normal HDL-C (>1.03 mmol/L >40 mg/dL) groups.

Values are given as mean ± SD.

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**Correlations among lipid and apolipoprotein changes during cardiac catheterization**

The change in TC during catheterization was correlated positively with those in all variables except HDL-C (Table 4). The change in TG was correlated positively with those in TC, apo B, and apo E, while negatively with that in HDL-C. Strong positive correlations existed among changes in TG, apo B, and apo E.

**Discussion**

Our results indicate that lipoprotein profiles change markedly during cardiac catheterization. We found that TC and TG concentrations decreased by 9.4% and 53.1%, respectively, from the baseline concentrations (Table 1). Apo AI, apo B, and apo E concentrations also decreased significantly. The decreases in variables were greater in the PTCA group than in the CAG group (Table 2). This inconsistency may come from the fact that heparin releases not only LPL but also hepatic lipase [19]. LPL is speculated to supply lipid components to HDL particles during lipolysis of TG-rich lipoproteins [23]. This action seems to increase HDL-C.

On the contrary, hepatic lipase hydrolyzes circulating LDL [24], and reduces its size [25]. Hepatic lipase also promotes the uptake of HDL by the liver [26]. These...
actions of hepatic lipase seem to decrease HDL-C. Moreover, LPL enhances the transfer of cholesteryl ester mediated by cholesteryl ester transfer protein [27], which may decrease HDL-C. This metabolic complexity makes it difficult to predict changes in HDL-C during catheterization. In conclusion, we have demonstrated that lipoprotein profiles change markedly during cardiac catheterization. We recommend avoiding analysis of lipoprotein profiles after emergent CAG in AMI. We speculate that LPL, released by heparin, may play an important role in changing lipoprotein profiles during catheterization.

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References


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Table 4. Correlations among lipid and apolipoprotein changes during cardiac catheterization.

<table>
<thead>
<tr>
<th></th>
<th>TC</th>
<th>TG</th>
<th>HDL-C</th>
<th>Apo Al</th>
<th>Apo B</th>
<th>Apo E</th>
</tr>
</thead>
<tbody>
<tr>
<td>TC</td>
<td>—</td>
<td>0.335</td>
<td>0.162</td>
<td>0.461</td>
<td>0.590</td>
<td>0.475</td>
</tr>
<tr>
<td>(*)</td>
<td></td>
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<td>(*)</td>
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<tr>
<td>TG</td>
<td></td>
<td>—</td>
<td>−0.347</td>
<td>0.213</td>
<td>0.794</td>
<td>0.665</td>
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<tr>
<td>(**)</td>
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<td>(*)</td>
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<tr>
<td>HDL-C</td>
<td></td>
<td></td>
<td>—</td>
<td>0.325</td>
<td>−0.266</td>
<td>−0.223</td>
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<td>(**)</td>
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<tr>
<td>Apo Al</td>
<td></td>
<td></td>
<td></td>
<td>—</td>
<td>0.228</td>
<td>0.245</td>
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<tr>
<td>Apo B</td>
<td></td>
<td></td>
<td></td>
<td>—</td>
<td>—</td>
<td>0.741</td>
</tr>
<tr>
<td>Apo E</td>
<td></td>
<td></td>
<td></td>
<td>—</td>
<td>—</td>
<td>(****</td>
</tr>
</tbody>
</table>

* P < 0.001, ** P < 0.01, *** P < 0.05.

Blood samples were taken before and after catheterization from 65 patients for lipid concentrations and from 55 patients for apolipoprotein concentrations. Correlations between the changes in variables were examined.
Y, et al. Lipoprotein lipase mass and activity in severe hypertri-

exposes unreactive endogenous apolipoprotein E-3 in human and
rat plasma very low density lipoprotein. J Clin Invest 1991;88:
553–60.

22. Felts JM, Itakura H, Crane RT. The mechanisms of assimilation of
constituents of chylomicrons, very low density lipoproteins and
66:1467–75.

23. Kekki M. Lipoprotein-lipase action determining plasma high den-
sity lipoprotein cholesterol level in adult normolipaemics. Athero-

Kinetic evidence for phosphatidylethanolamine and triacylglycerol
as preferential substrates for hepatic lipase in HDL subfractions:
modulation by changes in the particle surface or in the lipid core.

Distribution of high-density lipoprotein 2 and 3 constituents during
in vitro phospholipid hydrolysis. Eur J Biochem 1987;162:
279–86.

Hepatic lipase promotes the uptake of HDL esterified cholesterol
by the perfused rat liver: a study using reconstituted HDL particles
of defined phospholipid composition. J Lipid Res 1994;35:
373–84.

27. Tall AR, Sammett D, Vita GM, Deckelbaum R, Olivecrona T.
Lipoprotein lipase enhances the cholesteryl ester transfer protein-
mediated transfer of cholesteryl esters from high density lipopro-
teins to very low density lipoproteins. J Biol Chem 1984;259:
9587–94.