第41回　MSGR

Effect of Two Intensive Statin Regimens on Progression of Coronary Diseae

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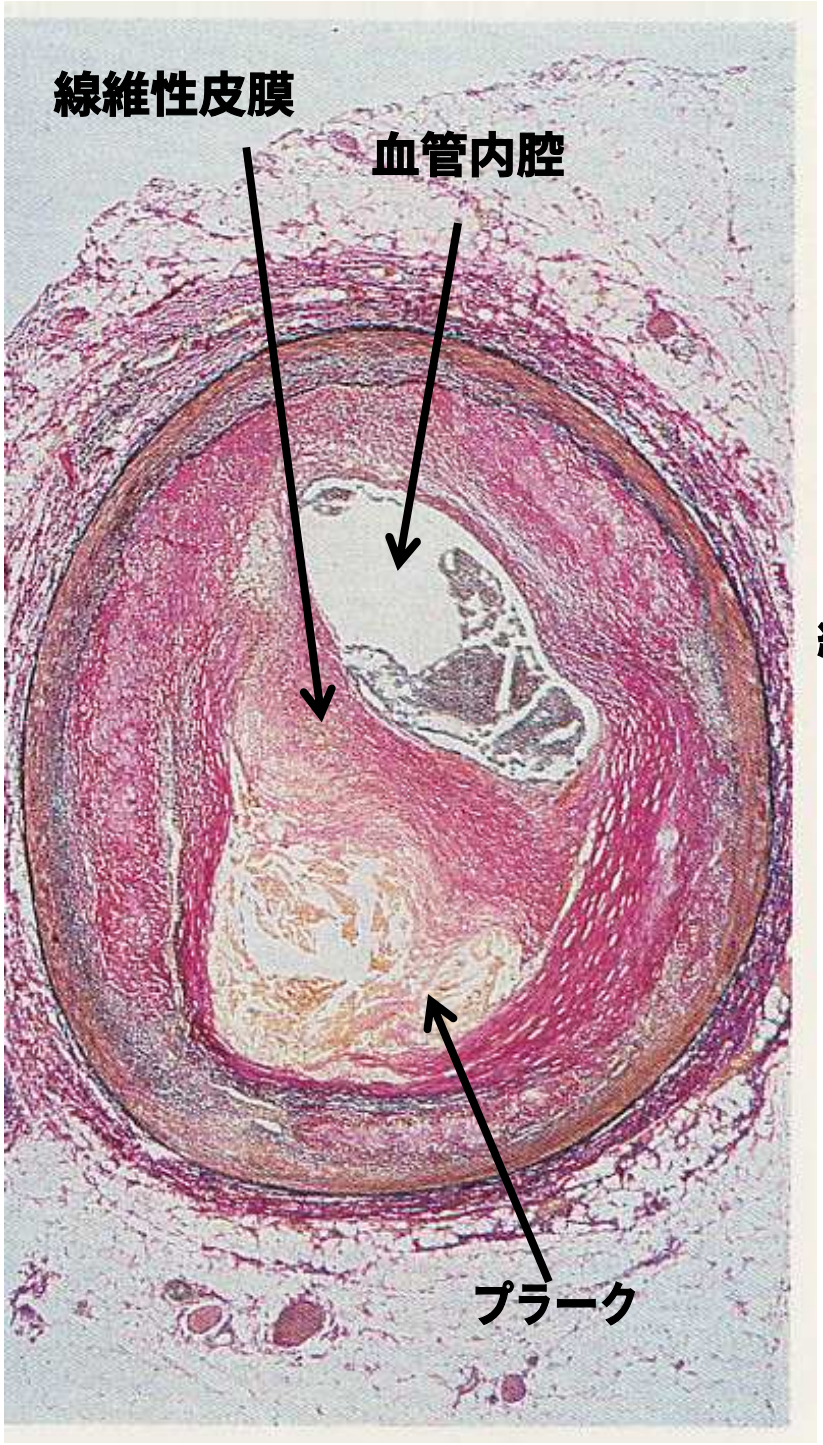
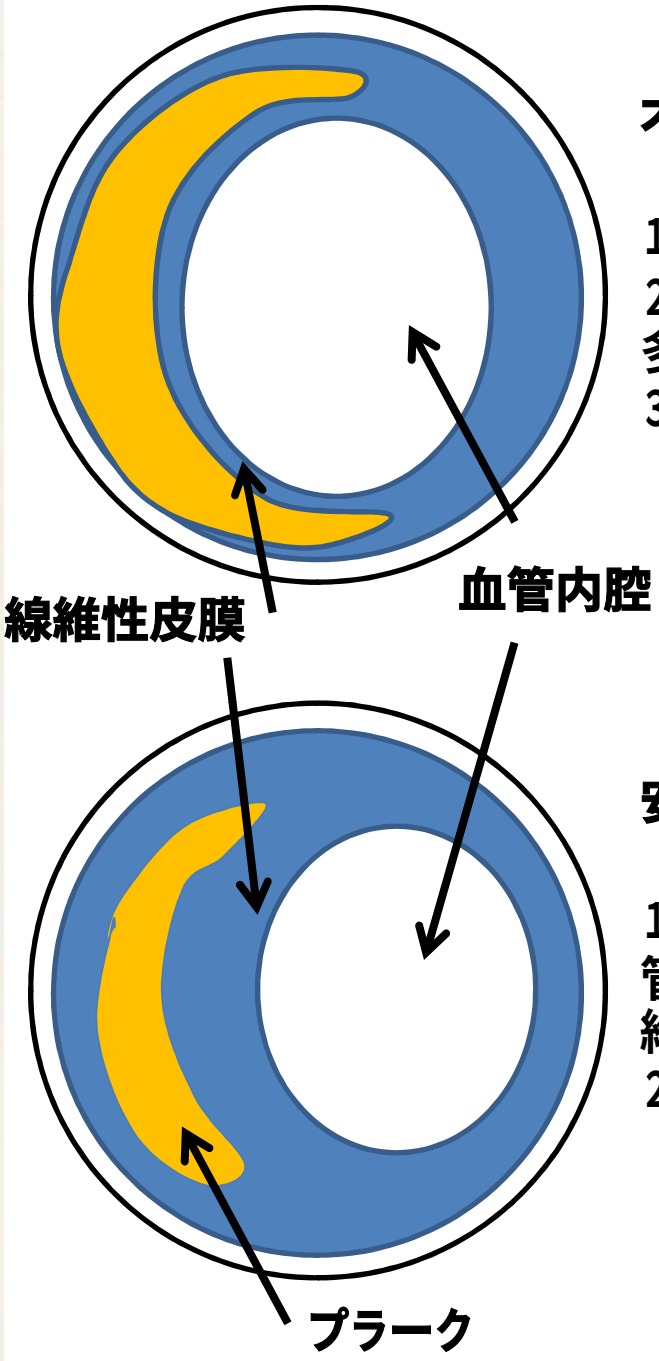




不安定プラーク

1) 脂質コアが大きい
2) マクロファージ浸潤多い
3) 線維性皮膜が薄い

安定プラーク

1) コラーゲン増生、血管平滑筋増生にて線維性皮膜が厚い
2) 脂質コアが小さい

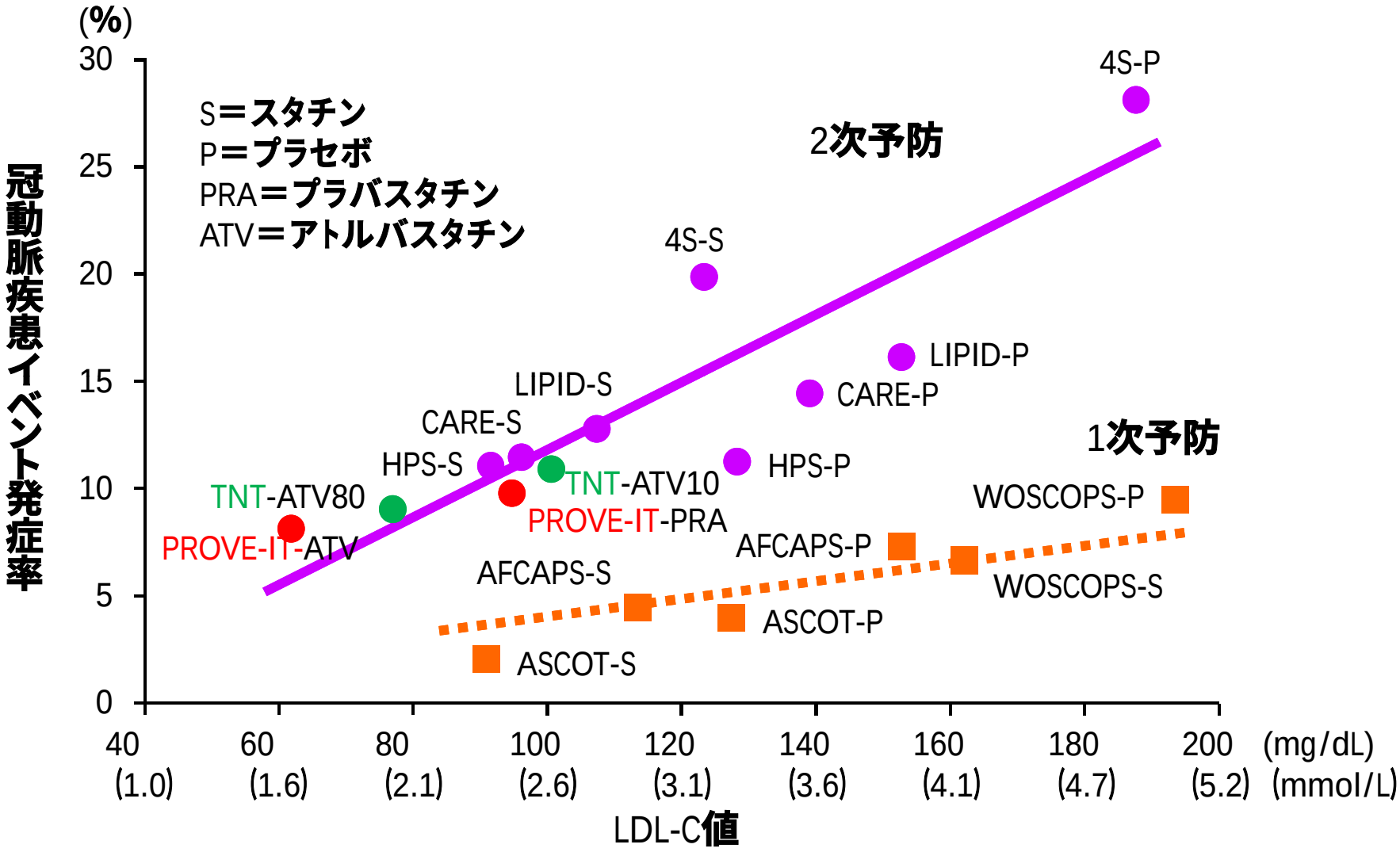
動脈硬化

危険因子：

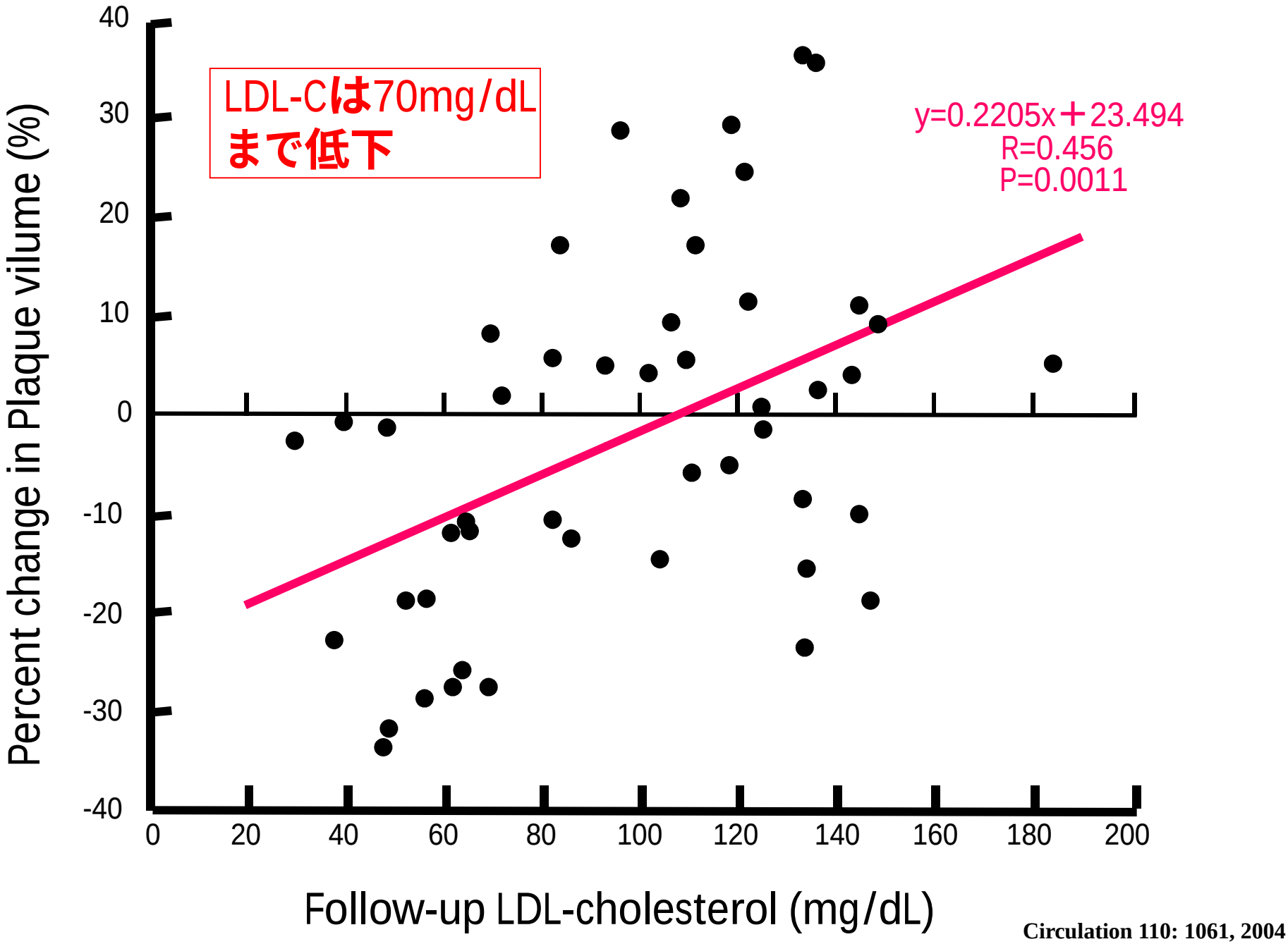
脂質代謝異常：high LDL , low HDL, high TG, non-HDL, Lp(a), RLP
糖尿病：HbA1c**の増加、インスリン感受性低下**
高血圧
喫煙
肥満
炎症マーカー： high CRP
高ホモシスチン血症
慢性腎不全
加齢
男性

動脈硬化が基盤となって血栓ができる： Atherothrombosis

スタチン大規模臨床試験における LDL-C低下率と冠動脈疾患イベント発症率



〔Rosensen RS.: Exp Opin Emerg Drugs 2004; 9(2): 269-279.**一部改変**〕
〔La Rosa JC. et al.: N Engl J Med 2005; 352: 1425-1435.〕



Circulation 110: 1061, 2004

背景

- スタチンが血中LDL-Chol濃度を低下させることで、冠動脈粥状硬化の進展を遅らせ、心血管イベントを減らすことは周知の事実

- 2種類の強力なスタチン療法の比較？
- 病変の退縮は？
- 安全性･副作用は？

N Engl J Med 2011;365:2078-87

・18〜75歳
・冠動脈1本以上に狭窄があり、対象血管の狭窄は50%以下
・直近4週にスタチン投与を受けていない→LDL<100mg/dl
受けている　→LDL<80mg/dl
以上を満たす1578人を
atorvastatin(リピトール)40mg/day群
rosvastatin(クレストール)20mg/day群
に割り付け、2週間投与

終了時にLDL<116mg/dlかつTG<500mg/dlを満たす1385人を
atorvastatin　80mg/day群(n=691)
rosvastatin　40mg/day群(n=694)
に割り付け、104週間投与
1039人(75%)が評価対象に
→atorvastatin群(n=519)
→rosvastatin群(n=520)

以上2群に対し再び血管内エコーを施行
ベースラインと比較した

Table 1. Baseline Characteristics of Patients in the Intention-to-Treat Population.*

Characteristic	Atorvastatin (N=519)	Rosuvastatin (N=520)
Age — yr	57.9±8.5	57.4±8.6
Male sex — no. (%)	386 (74.4)	379 (72.9)
White race — no. (%)†	500 (96.3)	496 (95.4)
Body-mass index‡	29.2±5.5	28.9±5.0
Diabetes — no. (%)	87 (16.8)	72 (13.8)
Hypertension — no. (%)	367 (70.7)	364 (70.0)
Current smoking — no. (%)	157 (30.3)	179 (34.4)
Previous MI — no. (%)	137 (26.4)	117 (22.5)
Previous PCI — no. (%)	112 (21.6)	131 (25.2)
Prior statin use — no. (%)§	319 (61.5)	303 (58.3)
Concomitant medications — no. (%)		
Antiplatelet agent	508 (97.9)	507 (97.5)
Beta-blocker	317 (61.1)	315 (60.6)
ACE inhibitor	231 (44.5)	226 (43.5)
Angiotensin-receptor blocker	82 (15.8)	87 (16.7)

Table 2. Biochemical Values and Blood Pressure at Baseline and during Treatment in the Intention-to-Treat Population.*

Variable	At Baseline			During Treatment†		
	Atorvastatin (N=519)	Rosuvastatin (N=520)	P Value	Atorvastatin (N=519)	Rosuvastatin (N=520)	P Value
Cholesterol						
Total (mg/dl)	193.5±34.2	193.9±34.1	0.86	144.1±1.2	139.4±1.2	<0.006
LDL (mg/dl)	119.9±28.9	120.0±27.3	0.94	70.2±1.0	62.6±1.0	<0.001
HDL (mg/dl)	44.7±10.7	45.3±11.8	0.41	48.6±0.5	50.4±0.5	0.01
Non-HDL (mg/dl)	148.8±33.1	148.6±33.0	0.91	95.4±1.1	88.9±1.2	<0.001
LDL:HDL	2.8±0.9	2.8±0.9	0.81	1.5±0.1	1.3±0.1	<0.001
Triglycerides (mg/dl)						
Median	130	128	0.55	110	120	0.02
Interquartile range	97–177	91–181		87–150	91–159	
Apolipoprotein						
B (mg/dl)	104.9±21.7	105.4±21.2	0.68	75.1±0.9	72.5±0.9	0.03
A-I (mg/dl)	126.2±23.3	128.0±25.2	0.23	137.7±1.0	146.8±1.0	<0.001
B:A-I	0.9±0.2	0.9±0.3	0.72	0.6±0.1	0.5±0.1	<0.001
C-reactive protein (mg/liter)‡						
Median	1.5	1.7	0.29	1.0	1.1	0.05
Interquartile range	0.8–3.3	0.8–3.8		0.5–2.0	0.5–2.4	
Glucose (mg/dl)‡						
Median	97	97	0.74	99	97	0.49
Interquartile range	90–110	88–108		92–112	90–110	
Glycated hemoglobin (%)‡§	6.2±0.8	6.2±1.1	0.45	6.3±0.1	6.3±0.1	0.82
Blood pressure (mm Hg)						
Systolic	130.6±18.4	130.2±18.1	0.72	131.2±0.7	129.7±0.7	0.16
Diastolic	77.2±11.3	76.6±10.7	0.39	77.8±0.4	77.0±0.4	0.18

Table 3. Primary and Secondary End Points, as Evaluated on Intravascular Ultrasonography.*

End Point	Atorvastatin (N=519)	Rosuvastatin (N=520)	P Value
At baseline			
PAV — %			
Mean	36.0±8.3	36.7±8.2	0.33
Median (95% CI)	36.2 (30.6 to 41.4)	36.2 (31.4 to 42.0)	
TAV — mm^3			
Mean	144.2±63.8	144.1±60.8	0.99
Median (95% CI)	136.6 (95.8 to 182.9)	133.4 (95.9 to 180.1)	
At 104 weeks			
PAV — %			
Mean	34.9±8.1	35.4±8.2	0.64
Median (95% CI)	34.9 (29.6 to 40.3)	34.8 (29.5 to 40.2)	
TAV — mm^3			
Mean	138.5±63.2	135.7±57.7	0.67
Median (95% CI)	127.6 (91.0 to 176.1)	124.9 (93.4 to 167.7)	
Median change from baseline			
PAV — % (95% CI)	−0.99 (−1.19 to −0.63)	−1.22 (−1.52 to −0.90)	0.17†
TAV — mm^3 (95% CI)	−4.42 (−5.98 to −3.26)	−6.39 (−7.52 to −5.12)	0.01†
Disease regression — % of patients			
Based on change in PAV	63.2	68.5	0.07
Based on change in TAV	64.7	71.3	0.02

* Plus–minus values are means ±SD. CI denotes confidence interval, PAV percent atheroma volume, and TAV total atheroma volume.

† The P value for the between-group comparison of the change from baseline was calculated with the use of analysis of covariance, with the rate of change in PAV or in TAV as the independent variable and the rank of the corresponding baseline value as a covariate and treatment group as a factor.

PAV =**アテローム容積率**

TAV =**総アテローム容積**

Table 4. Clinical and Biochemical Adverse Events and Reasons for Discontinuation of Treatment.

Event	Atorvastatin (N=689)	Rosuvastatin (N=691)
Cardiovascular event — no. (%)		
Death from cardiovascular causes	2 (0.3)	2 (0.3)
Nonfatal myocardial infarction	11 (1.6)	11 (1.6)
Nonfatal stroke	2 (0.3)	3 (0.4)
Hospitalization for unstable angina	13 (1.9)	16 (2.3)
Arterial revascularization	41 (6.0)	42 (6.1)
First major adverse cardiovascular event	49 (7.1)	52 (7.5)
Abnormal laboratory value — no./total no. (%)*		
Aspartate aminotransferase >3× ULN	11/668 (1.6)	3/668 (0.4)
Alanine aminotransferase >3× ULN	14/668 (2.1)	5/668 (0.7)
Creatine kinase		
>5× ULN	5/668 (0.7)	2/668 (0.3)
>5× ULN on two consecutive visits	0/654 (0)	0/668 (0)
>10× ULN	4/668 (0.6)	1/668 (0.1)
New proteinuria†	11/654 (1.7)	25/652 (3.8)
Creatinine >ULN	20/668 (3.0)	22/668 (3.3)
Discontinuation of treatment — no. (%)		
Total	142 (20.6)	145 (21.0)
Reason for discontinuation		
Preference of patient	53 (7.7)	54 (7.8)
Adverse event	48 (7.0)	45 (6.5)
Loss to follow-up	9 (1.3)	20 (2.9)
Noncompliance	16 (2.3)	13 (1.9)
Other	16 (2.3)	13 (1.9)

* Laboratory data were missing for 44 patients. ULN denotes upper limit of the normal range.

† New proteinuria was defined as 2+ or greater protein on urinalysis during the follow-up period in patients with a negative finding or trace protein at baseline.

結論

- LDL-Chol低下、HDL-Chol上昇作用はともに
  atorvastatin ＜ rosuvastatin であった
- plaqueの退縮については有意差はなかった
- 最大容量のstatin療法による有害事象はほとんど認められなかった
- 約1/3の患者はplaqueの退縮を認めなかった

当院での２０１０年1月１日以降の急性心筋梗塞患者の脂質管理

2010/1/1-2012/1/25　までの期間で当院に急性心筋梗塞にて入院した患者120 人。院内死亡、慢性腎不全 (cre > 3.0 mg/dl)を除いた110 人

男/女：75/35 人、age　68±13 year-old　(male 67 yo, female 70 yo)

	Total	male	female	age < 51(n=11)
T-chol	192	192	194	232
TG	107	111	99	151
HDL	52	51	54	57
LDL	121	121	120	146

当院での２０１０年1月１日以降の急性心筋梗塞患者の脂質管理

81%の患者にスタチンが使用されていた
crestol 2.5 mg(４０人)、crestol 5mg (８　人)
lipitol (１５人)、livalo (１９人)、mevalotin 10 mg (２人)、その他 (４人)
８人でzetia 10 mg 併用

退院時、６カ月後、共に LDL < 100 mg/dlにcontrolされていた。

	入院時 (n=110)	退院時(n=89)	６カ月後(n=83)
T-chol	197	156	161
TG	111	135	135
HDL	52	43	53
LDL	125	90	87