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High-density lipoprotein cholesterol levels and cardiovascular outcomes in Japanese patients after percutaneous coronary intervention: A report from the CREDO-Kyoto registry cohort-2

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ABSTRACT

Objective: To determine whether low HDL-C is a risk factor for adverse cardiovascular events in patients with known CAD.
Methods: We evaluated 10,391 patients who underwent PCI from January 2005 to December 2007. In total, 3838 (36.9%) patients had low HDL-C (HDL-C <40 mg/dL in males and <50 mg/dL in females) and 6553 (63.1%) patients had normal HDL-C based on measurements on admission.
Results: The unadjusted 5-year incidence of major adverse cardiac events (MACE: composite of cardiovascular death, myocardial infarction or stroke) was significantly higher in the low HDL-C group than in the normal HDL-C group (17.6% vs. 14.0%, P < 0.0001). However, after adjusting for confounders, low HDL-C was not associated with a higher risk of MACE (adjusted hazard ratio [HR] 1.07, 95% confidence interval (CI) 0.97–1.19; P = 0.19). There was no significant interaction between the effect of low HDL-C on MACE and several subgroup factors including age, sex, clinical presentation of CAD, statins use, serum low-density lipoprotein cholesterol level, and serum triglycerides level.
Conclusion: Low HDL-C, as compared with normal HDL-C, was not associated with higher 5-year risk of MACE in patients who underwent PCI.

1. Introduction

The incidence of coronary events in patients without known coronary artery disease (CAD) appears to be inversely related to serum HDL-cholesterol (HDL-C) concentration, with low levels of HDL-C being associated with increased coronary risks [1,2]. In addition, premature CAD is common in patients with primary or inherited disorders with low serum HDL-C [3–5] and low HDL-C levels are more commonly seen in patients with a first myocardial infarction (MI) than in age-matched controls without CAD [3].

Even among patients with stable CAD treated with statin therapy, lower HDL-C levels are associated with higher risks of cardiovascular events [6]. Moreover, in a post-hoc analysis of 2193 individuals with stable disease, who participated in the COURAGE trial, and were managed on optimal medical therapy, the rate of all-cause death or MI was 33% lower in the highest compared with the lowest HDL-C quartile [7].

Conversely, not all studies have found that HDL-C is predictive of future events in patients with established CAD treated with statin therapy. It is known that intensive statin therapy abolished the inverse association between HDL-C and vascular events in an analysis of the JUPITER (Justification for the Use of Statins in

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Prevention: an Intervention Trial Evaluating Rosuvastatin) trial [8]. A similar lack of an inverse relationship was repeatedly observed in patients receiving intensive statin therapy [7,9].

It is still controversial whether low HDL-C influences cardiovascular outcomes, especially in patients with known CAD receiving current optimized treatments. Therefore, we sought to evaluate this in a large Japanese observational database of patients who underwent first coronary revascularization procedures.

2. Methods

2.1. Study population

The CREDO-Kyoto (Coronary REvascularization Demonstrating Outcome Study in Kyoto) PCI/CABG registry cohort-2 is a physician-initiated non-company sponsored multi-center registry enrolling consecutive patients undergoing first coronary revascularization at 26 centers in Japan between January 2005 and December 2007. The relevant review boards or ethics committees at all 26 participating centers approved the research protocol. Because of retrospective enrollment, written informed consent from the patients was waived; however, we excluded those patients who refused participation in the study when contacted for follow-up.

The study design and patient enrollment of the CREDO-Kyoto PCI/CABG registry cohort-2 were described in detail previously [10]. The current post-hoc subanalysis of the registry intended to evaluate the influence of serum HDL-C levels during the index hospitalization on long-term clinical outcomes in patients who underwent their first PCI. Among 15,939 patients who underwent PCI or coronary artery bypass grafting (CABG) as a first coronary revascularization procedure, 13,144 patients underwent PCI. Excluding 86 patients who refused study participation, 342 patients who died during the index hospitalization, and 2325 patients in whom the level of HDL-C and low-density lipoprotein cholesterol (LDL-C) could not be identified during the index hospitalization, 10,391 patients were included in the present analysis (Fig. 1). To evaluate the impact of serum HDL-C levels on clinical outcomes, patients were divided into two groups according to the level of HDL-C (low HDL-C in males <40 mg/dL and in females <50 mg/dL) at time of admission for the index hospitalization. There were 3838 patients (36.9%) in the low HDL-C group and 6553 patients (63.1%) in the normal HDL-C group.

2.2. Definitions

Definitions of baseline clinical characteristics were as described previously [10]. The primary outcome measure for the current analysis was a composite of MACE (cardiovascular death, MI, or stroke). Secondary outcome measures included the individual components of the composite, all-cause death, target-lesion revascularization (TLR), coronary revascularization other than TLR, and any coronary revascularization.

Death was regarded as being cardiac in origin unless obvious non-cardiac causes could be identified. Vascular death was defined as death related to aortic, cerebral, renal, or peripheral vascular diseases. MI was defined according to the definition in the Arterial Revascularization Therapy Study [11]. Within 1 week of the index procedure, only Q-wave MI was adjudicated as MI. Stroke during follow-up was defined as ischemic or hemorrhagic stroke requiring hospitalization with symptoms lasting >24 h.

The recommended antiplatelet regimen was aspirin (≥81 mg/day) indefinitely and thienopyridine (ticlopidine 200 mg/day or clopidogrel 75 mg/day) for ≥3 months. Duration of thienopyridine administration was left to the discretion of each attending physician. For statins therapy, we did not set indications for using statins, and statin use was left to the discretion of each attending physician. Demographic, angiographic, and procedural data were collected from hospital charts or databases according to prespecified definitions in each participating center by experienced clinical research coordinators in the study management center. Follow-up data were obtained from hospital charts or by contacting patients or referring physicians. Scheduled staged PCI procedures performed during the index hospitalization or within 3

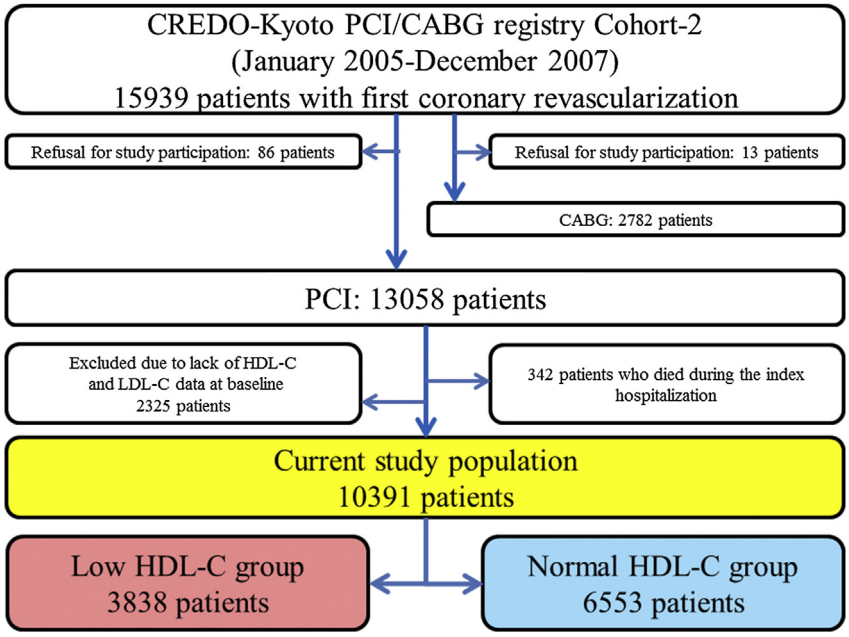


Fig. 1. Study flow chart.

months of the initial procedure were not regarded as follow-up events but were included in the index procedure. Clinical events such as cardiovascular death, MI and stroke were adjudicated from the original source documents by a clinical events committee. Follow-up intervals were calculated from the day of the index PCI procedure. Median follow-up duration was 1870 days (interquartile range [IQR] 1590–2167 days).

2.3. Statistical analysis

Data are presented as numbers and percentages or mean value ± standard deviation or median and IQR. Categorical variables were compared using chi-square test. Continuous variables were compared using Student's *t*-test or Wilcoxon rank sum test based on their distributions. Cumulative incidences of events after the index PCI were estimated using the Kaplan–Meier method, and differences between groups were assessed using the log-rank test. We used Cox proportional hazard models to estimate risk of low HDL-C relative to normal HDL-C for the primary and secondary outcome measures after adjusting for differences in patient characteristics, procedural factors, and medical therapies between groups. Consistent with our previous report, we chose 34 clinically relevant factors (Table 1) as risk-adjusting variables. Continuous variables were dichotomized using clinically meaningful reference values or median values. Centers were included in the model as stratification variables. Effects of low HDL-C relative to normal HDL-C on clinical outcomes were expressed as hazard ratio (HR) and 95% confidence interval (CI). Subgroup analyses were also conducted in accordance with several pre-specified subgroup factors including age (≥75 years and <75 years), sex, clinical presentation of CAD (stable CAD and acute coronary syndrome [ACS]), administration of statins at the time of discharge from the index hospitalization, serum LDL-C level, and serum triglycerides (TG) level. The influences of lipid abnormalities other than low HDL-C on the primary outcome measure were also assessed according to the levels of LDL-C (high LDL-C > 100 mg/dL) and TG (high TG ≥ 150 mg/dL).

All analyses were conducted with the use of JMP 10.0 (SAS Institute Inc, Cary, NC, USA). All the statistical analyses were two-tailed, and P values <0.05 were considered statistically significant.

3. Results

3.1. Baseline characteristics and medications in low HDL-C versus normal HDL-C groups

According to their serum levels of HDL-C, the total population of 10,391 patients was divided into 3838 patients with low HDL-C and 6553 with normal HDL-C. Because of the large number of patients and the observational study design, significant differences were observed in many variables in the baseline characteristics of the low HDL-C and normal HDL-C groups, as shown in Table 1. Compared with patients with normal HDL-C, patients with low HDL-C were older, there more females and these patients had higher rates of higher body mass index (BMI), ACS presentation, diabetes mellitus, current smoking, heart failure, prior MI, prior stroke, renal failure, atrial fibrillation, multivessel CAD, anemia, and liver cirrhosis. TG levels were significantly higher in patients in the low HDL-C group, whereas total cholesterol was significantly higher in patients in the normal HDL-C group. Cilostazol, angiotensin converting enzyme inhibitors/angiotensin receptor blockers, beta blockers, proton-pump inhibitors, and warfarin were used more often in the low HDL-C group, whereas statins and calcium channel blockers were more often used in the normal HDL-C group.

Table 1
Baseline characteristics: low HDL-C vs. normal HDL-C groups.

	Low HDL-C	Normal HDL-C	P value
	N = 3838	N = 6553	
Clinical characteristics			
Age (years)	68.4 ± 11.2	67.6 ± 10.8	<0.001
≥75 years[a]	1237 (32%)	1885 (29%)	<0.001
Male[a]	2409 (63%)	5051 (77%)	<0.001
BMI	24.1 ± 3.6	23.6 ± 3.4	<0.001
<25.0[a]	2465 (64%)	4559 (70%)	<0.001
Acute myocardial infarction[a]	1509 (39%)	2138 (33%)	<0.001
Hypertension[a]	3202 (83%)	5403 (82%)	0.20
Diabetes mellitus[a]	1571 (41%)	2302 (35%)	<0.001
On insulin therapy	331 (8.6%)	432 (6.6%)	<0.001
Current smoking[a]	1297 (34%)	2014 (31%)	<0.001
Heart failure[a]	854 (22%)	992 (15%)	<0.001
Mitral regurgitation grade 3/4[a]	168 (4.4%)	220 (3.4%)	0.009
Ejection fraction (%)	57.6 ± 13.0	59.4 ± 12.6	<0.001
Prior myocardial infarction[a]	461 (12%)	577 (8.8%)	<0.001
Prior stroke[a]	432 (11%)	604 (9.2%)	<0.001
Peripheral vascular disease[a]	293 (7.6%)	450 (6.9%)	0.14
Multivessel disease	2252 (59%)	3447 (53%)	<0.001
Target of proximal LAD[a]	2137 (55%)	3809 (58%)	0.02
Unprotected LMCA disease[a]	166 (4.3%)	220 (3.4%)	0.02
Target of CTO[a]	454 (12%)	746 (11%)	0.49
eGFR < 30, not on dialysis[a]	204 (5.3%)	152 (2.3%)	<0.001
Dialysis[a]	161 (4.2%)	176 (2.7%)	<0.001
Atrial fibrillation[a]	353 (9.2%)	487 (7.4%)	0.002
Anemia (Hb < 11 g/dl)[a]	574 (15%)	534 (8%)	<0.001
Platelets <100 × 10^9/L[a]	70 (1.8%)	70 (1.1%)	0.002
COPD[a]	152 (4.0%)	349 (3.8%)	0.68
Liver cirrhosis[a]	113 (2.9%)	141 (2.2%)	0.01
Malignancy[a]	314 (8.2%)	594 (9.1%)	0.12
Baseline lipid levels			
Total cholesterol (mg/dl)	181 ± 40.4	197 ± 38.7	<0.001
TG (mg/dl)[a]	118 (81–171)	102 (70–145)	<0.001
HDL-C (mg/dl)[a]	36.4 ± 6.3	54.6 ± 11.9	<0.001
LDL-C (mg/dl)[a]	117 ± 35.5	119 ± 34.7	0.01
Baseline medication			
Thienopyridine	3746 (98%)	6410 (98%)	0.48
Aspirin	3797 (99%)	6488 (99%)	0.71
Cilostazol[a]	790 (21%)	1105 (17%)	<0.001
Statin[a]	2027 (53%)	3654 (56%)	0.004
Beta-blocker[a]	1365 (36%)	1963 (30%)	<0.001
ACEI/ARB[a]	2372 (62%)	3845 (59%)	0.002
Calcium-channel blocker[a]	1504 (40%)	2800 (43%)	<0.001
Nitrates[a]	1317 (34%)	2190 (33%)	0.35
Nicorandil[a]	1007 (26%)	1623 (24%)	0.10
Warfarin[a]	352 (9.2%)	492 (7.5%)	0.003
Proton-pump inhibitor[a]	1124 (29%)	1557 (23%)	<0.001
H_2-blocker[a]	1029 (27%)	1716 (26%)	0.49

Values are mean ± SD or median (interquartile range).
ACEI, angiotensin-converting enzyme inhibitors; ARB, angiotensin II receptor blockers; BMI, body mass index; COPD, chronic obstructive pulmonary disease; CTO, chronic total occlusion; eGFR, estimated glomerular filtration rate; Hb, hemoglobin; HDL-C, high-density lipoprotein cholesterol; LAD, left anterior descending artery; LDL-C, low-density lipoprotein cholesterol; LMCA, left main coronary artery; TG, triglycerides.
[a] Potential independent variables selected for multivariate analysis.

3.2. Cardiovascular outcomes: low HDL-C versus normal HDL-C

The cumulative 5-year incidence of MACE was significantly higher in the low HDL-C group than in the normal HDL-C group (17.6% vs. 14.0%, log-rank P < 0.001). However, after adjusting for potential confounders, the excess risk of low HDL-C relative to normal HDL-C for MACE was no longer significant (HR 1.07 [95% CI 0.97–1.19], P = 0.19) (Table 2 and Fig. 2). Adjusted risks of low HDL-C relative to normal HDL-C for the individual components of MACE (all-cause death, cardiovascular death, MI, and stroke) were also not significant (Table 2).

On the other hand, the cumulative 5-year incidence of and adjusted risk of any coronary revascularization was significantly

Table 2
Event rates and risks of low HDL-C relative to normal HDL-C.

	Low HDL-C (N = 3838) no. of patients with event (cumulative 5-year incidence)	Normal HDL-C (N = 6553) no. of patients with event (cumulative 5-year incidence)	Unadjusted HR (95% CI)	P value	Adjusted HR (95% CI)	P value
MACE (cardiovascular death, MI and stroke)	657 (17.6%)	951 (14.0%)	1.29 (1.17–1.43)	<0.001	1.07 (0.97–1.19)	0.19
All-cause death	690 (18.0%)	909 (13.9%)	1.32 (1.19–1.45)	<0.001	1.07 (0.96–1.19)	0.22
Cardiovascular death	333 (8.7%)	415 (6.3%)	1.39 (1.20–1.60)	<0.001	0.99 (0.85–1.16)	0.92
Myocardial infarction	291 (7.6%)	438 (6.7%)	1.15 (0.99–1.33)	0.07	1.19 (0.96–1.31)	0.16
Stroke	250 (6.5%)	364 (5.6%)	1.20 (1.02–1.40)	0.03	1.06 (0.90–1.26)	0.47
TLR	867 (22.6%)	1386 (21.1%)	1.09 (1.00–1.19)	0.04	1.09 (0.99–1.19)	0.07
Coronary revascularization other than TLR	915 (23.8%)	1406 (21.5%)	1.14 (1.05–1.24)	0.002	1.12 (1.03–1.22)	0.01
Any coronary revascularization	1409 (36.7%)	2245 (34.3%)	1.11 (1.03–1.18)	0.003	1.10 (1.02–1.18)	0.009

HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; MACE, major adverse cardiac events (cardiovascular death, myocardial infarction or stroke); TLR, target lesion revascularization.

higher in the low HDL-C group than in the normal HDL-C group (36.7% vs. 34.3%, log-rank P = 0.003, and HR 1.10 [95% CI 1.02–1.18], P = 0.009) (Table 2 and Fig. 3).

3.3. Subgroup analysis

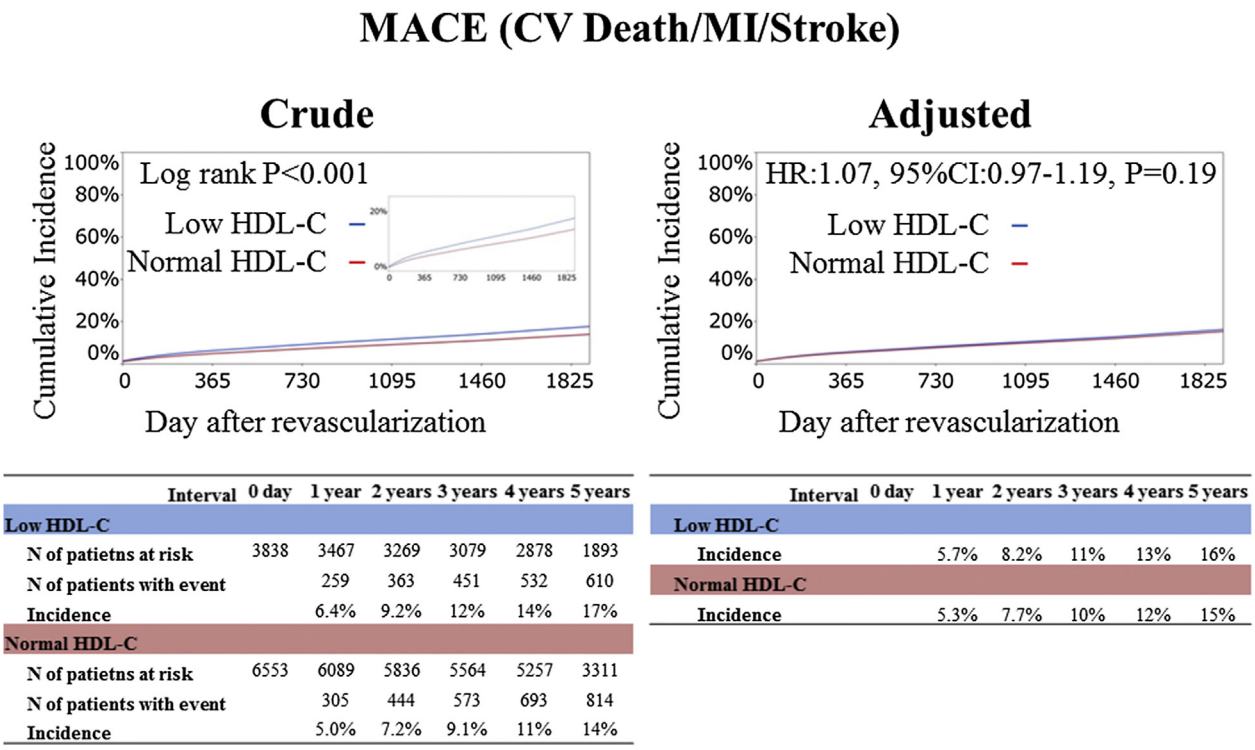
With regard to MACE, there was no significant interaction between the effect of low HDL-C and several subgroup factors including age (≥75 years and <75 years), sex, clinical presentation of CAD (stable CAD and ACS), administration of statins at time of discharge from the index hospitalization, serum LDL-C level, and serum TG level (Supplemental Fig. A). For any coronary revascularization, there was a significant interaction between the effect of low HDL-C and age (Supplemental Fig. B). Low HDL-C was associated with a significantly higher risk of any coronary revascularization in patients <75 years of age, but not in patients ≥75 years of age.

3.4. The relationship between MACE and other lipid parameters

In order to assess the influence of lipid parameters other than HDL-C on MACE, we evaluated the relationship between MACE and LDL-C levels or TG levels (Supplemental Table). In univariate analyses, both high LDL-C levels (>100 mg/dL) and high TG levels (>150 mg/dL) were significantly associated with lower incidences of MACE (14.5% vs. 17.2%, log-rank P < 0.0001, and 13.4% vs. 16.0%, log-rank P = 0.0005, respectively). However, after adjusting for confounders, neither high LDL-C level nor high TG level were associated with an increased risk of MACE (HR 1.03 [95% CI 0.93–1.15] P = 0.49, and HR 1.02 [95% CI 0.91–1.16] P = 0.70, respectively).

4. Discussion

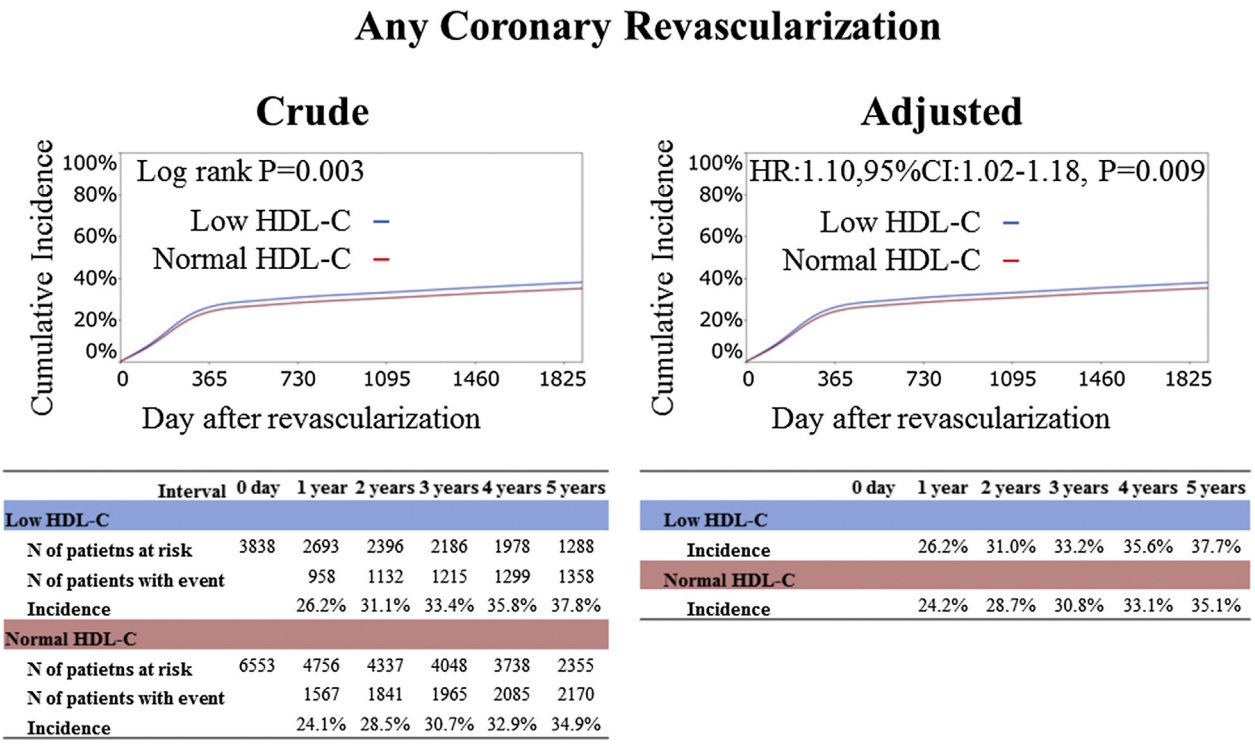
The main finding of this study was that low HDL-C levels, as compared with normal HDL-C levels, were not associated with a



Interval	0 day	1 year	2 years	3 years	4 years	5 years
Low HDL-C						
N of patietns at risk	3838	3467	3269	3079	2878	1893
N of patients with event		259	363	451	532	610
Incidence		6.4%	9.2%	12%	14%	17%
Normal HDL-C						
N of patietns at risk	6553	6089	5836	5564	5257	3311
N of patients with event		305	444	573	693	814
Incidence		5.0%	7.2%	9.1%	11%	14%

Interval	0 day	1 year	2 years	3 years	4 years	5 years
Low HDL-C						
Incidence		5.7%	8.2%	11%	13%	16%
Normal HDL-C						
Incidence		5.3%	7.7%	10%	12%	15%

Fig. 2. Crude and adjusted event curves for the primary outcome measure; low HDL-C versus normal HDL-C: HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; MACE, major adverse cardiac events; MI, myocardial infarction.



Interval	0 day	1 year	2 years	3 years	4 years	5 years
Low HDL-C						
N of patietns at risk	3838	2693	2396	2186	1978	1288
N of patients with event		958	1132	1215	1299	1358
Incidence		26.2%	31.1%	33.4%	35.8%	37.8%
Normal HDL-C						
N of patietns at risk	6553	4756	4337	4048	3738	2355
N of patients with event		1567	1841	1965	2085	2170
Incidence		24.1%	28.5%	30.7%	32.9%	34.9%

	0 day	1 year	2 years	3 years	4 years	5 years
Low HDL-C						
Incidence		26.2%	31.0%	33.2%	35.6%	37.7%
Normal HDL-C						
Incidence		24.2%	28.7%	30.8%	33.1%	35.1%

Fig. 3. Crude and adjusted event curves for any revascularization; low HDL-C versus normal HDL-C.

higher 5-year risk of MACE in patients who underwent PCI. Although the adjusted risk of all coronary revascularization procedures was significantly higher in the low HDL-C group than in the normal HDL-C group, this is secondary outcome and may have been because subjects had a higher incidence of coronary revascularization procedures than that of MACE.

HDL-C is thought to reduce the risk of atherosclerotic cardiovascular diseases. This proposition is based on numerous epidemiologic studies, which have suggested an inverse relationship between HDL-C concentration and the risk of cardiovascular disease [12]. As far as secondary prevention is concerned, many different studies have shown that low levels of HDL-C predict cardiovascular risk [13], are independently associated with acute coronary syndrome in patients hospitalized for chest pain [14], and represent a poor prognosis in patients with acute coronary syndrome [15–17]. Other reports have indicated that the concentration of HDL-C prior to PCI is an independent predictor for restenosis and revascularization of stents [18–20], peri-procedural acute myocardial infarction [21], and 1-year mortality [22]. Similar results have also been shown for the carotid arteries [23].

Conversely, several recent trials including JUPITER [8], PROVE IT-TIMI 22 (Pravastatin or Atorvastatin Evaluation and Infection Therapy-Thrombolysis In Myocardial Infarction 22) [9], and SMART (Second Manifestation of ARTerial disease) [7] have reported an absence of an association between low HDL-C and cardiovascular events in high-risk patients treated with aggressive statin therapy, and our results confirmed these findings in Japanese patients who underwent a first coronary revascularization. The effect of low HDL-C on cardiovascular outcomes might be different according to the presence or absence of lipid-lowering therapy and the intensity of statin therapy. In the SMART study, low HDL-C was still associated with an increased risk of recurrent cardiovascular events among patients who were not receiving lipid-lowering medication or those being treated with a usual dose lipid-lowering medication [7]. Similar observations were reported from the TNT (Treating to New Targets) trial [24], in which HDL-C was associated with cardiovascular events in the atorvastatin 10 mg group, but not in the atorvastatin 80 mg group.

Therefore, a possible hypothesis that can reconcile the results of previous epidemiological studies and those of the recent reports, including ours, is that HDL-C levels may be predictive of MACE, when use or intensity of statin treatment is low, as was observed in subjects in the primary prevention studies, and in those patients in the placebo groups in both JUPITER and SMART trials, or were in the atorvastatin 10 mg group in the TNT study.

While, our subgroup analysis indicated that low HDL-C levels, as compared with normal HDL-C levels, was not associated with a higher 5-year risk of MACE in patients even without statin treatment. In this context, another possible reason why low HDL-C is not a risk factor in patients with known CAD might be the possibility that HDL functionality is already impaired in these patients. It has been shown that HDL functionality in patients with ischemic heart disease is impaired and HDL functionality, but not the plasma levels of HDL-C, seems to be the target to evaluate cardiovascular event risk [25–27]. Mechanistically, the capacity of HDL-C to mediate cholesterol efflux from lipid-laden macrophages has been reported to be impaired after substantial oxidative modification of HDL-C by myeloperoxidase (MPO) [28,29]. It was also shown that the capacity of HDL-C to prevent the proinflammatory effects of LDL-C was impaired in patients with CAD [30], and reduced paraoxonase 1 (PON1) activity was identified as one molecular mechanism leading to the loss of anti-inflammatory effects of HDL-C in patients with stable CAD or an ACS [25]. It has also been demonstrated that MPO, PON1 and HDL form a functional ternary complex and that MPO promotes impairment of PON1 and apoA-I function [31].

Our subgroup analysis also showed that higher LDL-C levels (>100 mg/dL) was not associated with an increased risk of MACE. As shown in our previous study, compared with standard statin therapy, aggressive statin therapy was associated with lower cardiovascular risk and that the risk of cardiovascular events was

comparable, irrespective of achieved LDL-C level, even when LDL-C < 120 mg/dl was achieved in the same study population [32]. Thus, "the lower the better" may not be always applicable, but "make it lower with statins" should always be addressed in secondary prevention, even in relatively low-risk patients, including Japanese patients.

The failure of recent clinical trials to show an effect of raising HDL-C as a therapeutic strategy for the prevention of atherosclerosis may also suggest that low HDL-C is not a risk in known CAD patients. In fact, trials evaluating cholesterol ester transfer protein (CETP) inhibitors such as torcetrapib or dalcetrapib could not demonstrate beneficial results despite large increases in HDL-C levels [33,34]. The Atherothrombosis Intervention in Metabolic Syndrome with Low HDL/High Triglycerides: Impact on Global Health Outcome (AIM-HIGH) trial and Second Heart Protection Study (HPS-2 THRIVE) failed to show beneficial effects of niacin on cardiovascular events in patients treated optimally at low levels of LDL-C [35,36]. However, the failure of these trials of therapies that aimed to raise HDL-C might be due to the possibility that HDL-C levels increased by CETP inhibitors or niacin were not functionally ideal for the treatment of atherosclerosis [37,38].

It has been shown that genetic mechanisms that raise plasma HDL-C do not seem to lower the risk of MI, challenging the concept that raising HDL-C will translate into a reduction in the risk of MI [39]. However, this analysis also does not take HDL-C functionality into account either. It is possible that all kinds of HDL-C, including 'dysfunctional' HDL-C, were elevated in those who have genetic variants that raise HDL-C.

There is plenty of experimental evidence that HDL-C has beneficial effects, including anti-inflammatory and anti-oxidative effects, as well as reverse cholesterol transport [40]. Improving HDL functionality instead of simply increasing HDL-C levels might be much more important. Many HDL-C-based interventions, such as apoA-I-based compounds [41], apoA-I upregulators [42], ABC-transporter up-regulators, including microRNA-mediated therapeutics [43,44], synthetic liver X receptor agonists [45] and lecithin-cholesterol acyltransferase-based therapy [46], are under development and are still holding great promise for the future.

5. Study limitations

There are several important limitations in this study. First, our findings are subject to confounding factors because of the observational retrospective nature of the study. Second, we excluded patients who died during the index hospitalization because this study aimed to evaluate long term outcome of patients who underwent first coronary revascularization procedures. Third, we used only plasma lipid levels measured at start of the study. It is possible that using lipid levels from follow-up data rather than baseline data might have resulted in different outcomes. Fourth, only data about baseline medications were available, which was likely to have changed during follow-up.

6. Conclusion

Low HDL-C levels, as compared with normal HDL-C levels, were not associated with a higher 5-year risk of MACE in patients who underwent PCI.

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Disclosures

Takeshi Kimura serves as an advisory board member for ABBOTT Vascular and Terumo Company. The remaining authors reported no conflicts of interest.

Appendix A. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.atherosclerosis.2015.05.010.

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