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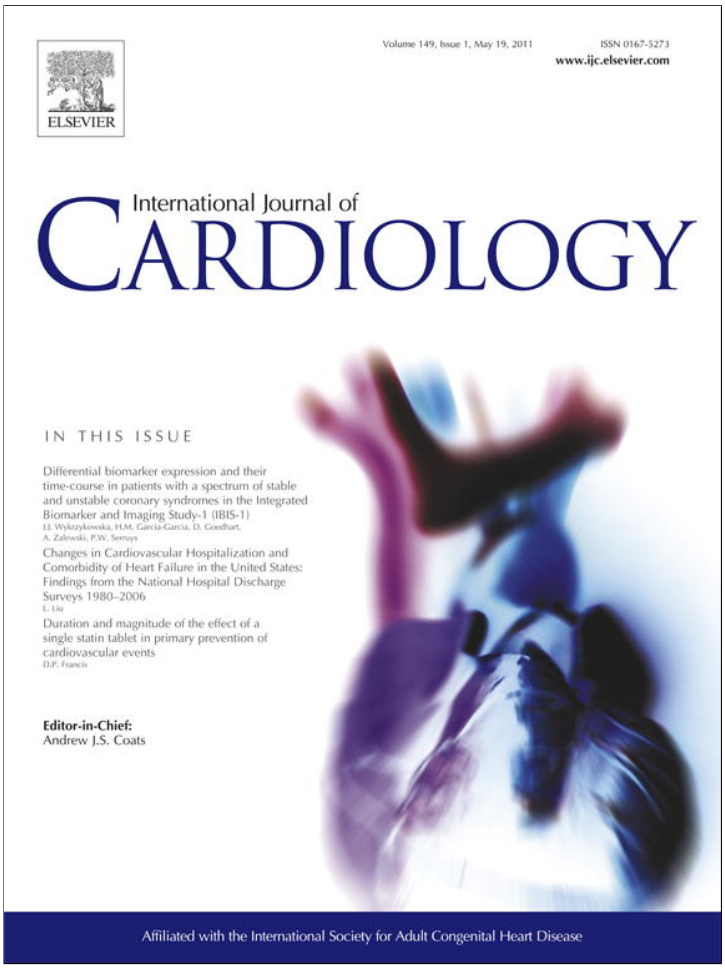

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Lower frequency of non-target lesion intervention in post-successful percutaneous coronary intervention patients with an LDL to HDL cholesterol ratio below 1.5

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ARTICLE INFO

Article history:
Received 24 January 2011
Accepted 29 January 2011
Available online 1 March 2011

Keywords:
Non-target lesion intervention
LDL to HDL cholesterol ratio
Low HDL

Although drug-eluting stent (DES) drastically reduces angiographic restenosis, Chacko et al. reported that the incidences of myocardial infarction involving non-target vessel territory and non-target vessel revascularization did not differ between patients with DES and bare metal stent implantation [1]. Park et al. reported that several clinical factors such as the number of significantly stenosed coronary arteries, and a poor lipid profile were important predictors of non-culprit coronary lesion progression [2]. This finding indicated that the improvement of the lipid profile is one of the important points for preventing adverse events associated with a non-target vessel. Nicholls et al. reported that a regression of coronary plaque volume as analyzed by intravascular ultrasound (IVUS) was observed in patients with L/H ratios below 1.5[3].The percent change in the total atheroma volume was not correlated with LDL-C, but was significantly correlated with the L/H ratio [4]. The results suggested that the L/H ratio may be a more effective surrogate marker than LDL-C alone. We aimed to investigate the abilities of several clinical factors, including the L/H ratio, to predict predicting non-target vessel revascularization.

Seven hundred ninety-six consecutive patients with successful PCI and follow-up catheterization about 6–9 months after PCI were enrolled and assessed for eligibility from March 2003 to March 2009.

The patients were divided into two groups, a severe L/H ratio-controlled group (L/H ratio<1.5) and an uncontrolled group (L/H ratio>1.5), and if patients with L/H ratios<1.5 had a lower incidence of non-target vessel PCI, we investigated whether statins affected these results. Non-target vessel PCI was defined as clinically driven PCI of a previously untreated vessel segment. PCI was performed in the following cases: 1) when the percent diameter stenosis (%DS) of the lesion was more than 50% on coronary angiography and chest pain or myocardial ischemia was documented in the corresponding vessel area as diagnosed by a non-invasive method and 2) when the %DS of lesion was more than 75% with ischemic symptoms or positive coronary atherosclerosis progression without ischemic symptoms.

LDL-C was basically calculated using the Friedewald equation and the direct measurement of LDL-C was accepted when the triglyceride value was more than 400 mg/dl. Patients who had LDL-C>100 mg/dl or who were receiving lipid-lowering medication were defined as having dyslipidemia. Lipid-lowering medication was prescribed as follows: 1) if the baseline LDL-C is more than 100 mg/dl, statins are started and 2) if LDL-C is more than 100 mg/dl during treatment, the LDL-C-lowering therapy is intensified [5].

The patient characteristics, medication and biochemical biomarkers in are shown in Table 1.There were no significant differences in patient characteristics and the use of statin, nitroglycerin or nicorandil between the two groups. However, patients with an L/H ratio below 1.5 were prescribed calcium channel blockers (CCB) more often and beta-blocker less often. There were significantly lower LDL-C and higher HDL-C levels at the date of PCI and at follow-up. On the other

Table 1
Patient characteristics, medications, and biochemical biomarkers.

	L/H<1.5 ($n=97$)	L/H≧1.5 ($n=699$)	p value
Patient characteristics			
Follow-up period, days	183±47	199±116	0.66
Gender male, *n* (%)	72 (74%)	544 (78%)	0.41
Age, years	66±10	66±10	0.69
Prior MI, *n* (%)	24 (25%)	195 (30%)	0.50
ACS, *n* (%)	29 (30%)	257(37%)	0.12
Current smoker, *n* (%)	32 (33%)	243 (35%)	0.67
Dyslipidemia, *n* (%)	75 (77%)	534 (77%)	0.90
DM, *n* (%)	51 (55%)	330 (49%)	0.22
CAD family history, *n* (%)	0 (0%)	5 (6%)	0.59
Renal failure, *n* (%)	5 (5%)	18 (3%)	0.20
BMI, kg/m^2	24±4	24±3	0.28
Medications			
Statin, *n* (%)	67 (74%)	454 (68%)	0.31
ARB, *n* (%)	60 (67%)	450 (67%)	0.93
CCB, *n* (%)	53 (55%)	291 (42%)	0.015
ACEI, *n* (%)	11 (12%)	78 (12%)	0.95
Beta blocker, *n* (%)	3 (3%)	80 (11%)	0.01
Diuretics, *n* (%)	15 (15%)	147 (21%)	0.20
Nitrol, *n* (%)	37 (38%)	264 (38%)	0.94
Nicorandil, *n* (%)	31 (32%)	216 (31%)	0.83
Biochemical biomarkers			
At PCI			
T-Cho, mg/dL	159±26	189±37	<0.0001
LDL-Cho, mg/dL	72±20	118±31	<0.0001
HDL-Cho, mg/dL	60±13	44±11	<0.0001
L/H	1.2±0.2	2.9±1.0	<0.0001
TG, mg/dL	133±104	134±74	0.09
At follow-up			
T-Cho, mg/dL	167±30	178±32	0.02
LDL-Cho, mg/dL	82±23	102±29	<0.0001
HDL-Cho, mg/dL	61±15	48±13	<0.0001
L/H	1.4±0.5	2.3±0.9	<0.0001
TG, mg/dL	124±67	147±122	0.04

MI: myocardial infarction; BMI: body mass index; ACS: acue coronary syndrome; DM: diabetes mellitus; CAD: coronary artery disease; BMI: body mass index; ARB: angiotensin II receptor blockers; ACEI: angiotensin converting enzyme inhibitor; CCB: calcium channel blocker; T-Cho: Total cholesterol; LDL-C: low-density lipoprotein cholesterol; HDL-C: high-density lipoprotein cholesterol; L/H ratio: LDL-C/ HDL-C ratio; TG: triglyceride.

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Table 2
Long term clinical event.

	L/H<1.5 (n=97)	L/H≧1.5 (n=699)	p value
Death, n (%)	0 (0%)	3 (0.4%)	1.0
MI, n (%)	0 (0%)	15 (2%)	0.24
TLR PCI, n (%)	18 (19%)	109 (16%)	0.46
NTV PCI, n (%)	4 (4%)	77 (11%)	0.04

MI: myocardial infarction; TLR: target lesion revascularization;
PCI: percutaneous coronary intervention; and NTV: non-target lesion vessel.

hand, in patients with L/H ratios >1.5 at follow-up, LDL-C was decreased to nearly 100 mg/dl and HDL-C was increased about 10% and remained over 40 mg/dl.

There were no statistically significant differences in the long-term clinical outcomes in death, myocardial infarction or TLR (Table 2). Patients with L/H ratios<1.5 group had a significantly lower incidence of non-target vessel PCI than those with L/H ratios>1.5 group. (4% vs. 11%, $p=0.04$).

Kaplan–Meier curves for the absence of non-target vessel PCI are shown in Fig. 1a–d. Significant differences were seen between L/H ratios<1.5 and >1.5 ($p=0.04$) and between HDL-C<40 and >40 ($p=0.0002$), but not between LDL-C<70 and >70 ($p=0.65$) or between LDL-C<100 and >100 ($p=0.45$). These univariate analyses revealed that L/H ratio<1.5 and HDL-C<40 appeared to contribute to an absence of non-target vessel PCI.

The multivariate analysis revealed that L/H ratio group (cutoff 1.5) was the only factor that significantly contributed to clinical adverse events in non-target vessel PCI (Table 3).

Although the lowering of LDL-C has well-established benefits in the prevention of CAD [6,7], a low level of HDL-C remains a cardiovascular risk factor despite statin therapy [8]. In the TNT trial, even with the intensive lowering of LDL-C below 70 mg/dl, HDL-C levels predicted major cardiovascular events [9]. Low HDL-C levels were an independent risk factor for CAD in the Framingham Heart study [10].

Based on our results, it is likely that plaque regression occurs only when the L/H ratio is maintained below 1.5. The lowering of LDL levels is undoubtedly useful, patients with lower HDL-C levels had a higher incidence of non-target vessel PCI, and therapy to maintain the L/H ratio<1.5 was useful in patients with CAD.

Although an L/H ratio<1.5 at the initial PCI period predicted a lower incidence of subsequent non-target vessel PCI, an L/H ratio<1.5 at follow-up did not have a similar predictive power. The present results suggested that maintaining LDL-C below 100 mg/dl, by itself, was insufficient for preventing non-target vessel PCI, and cardiologists should consider both HDL-C levels and an L/H ratio of less than 1.5.

We concluded that an L/H ratio <1.5 after PCI was important for reducing non-target vessel revascularization in patients with coronary artery disease, and contributed to an improved quality of life in these patients.

The authors of this manuscript have certified that they comply with the Principles of Ethical Publishing in the International Journal of Cardiology [11].

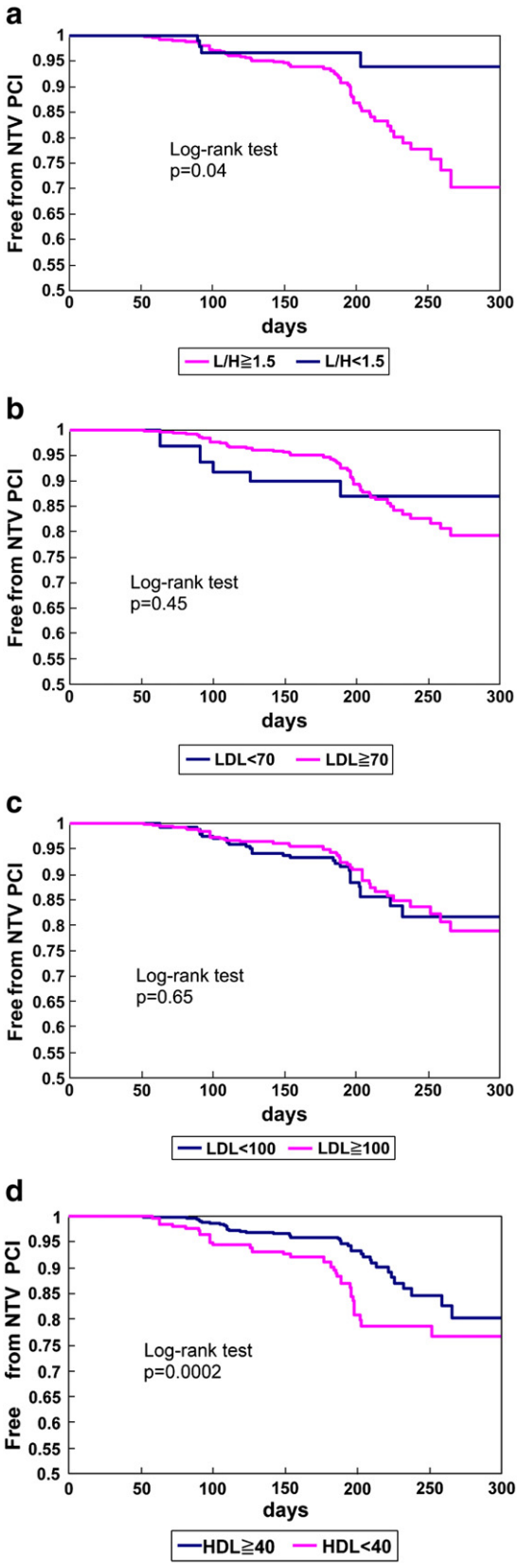

Fig. 1. a–d Relationship between the absence of non-target vessel PCI and the lipid profile. Kaplan–Meier curves for the absence of non-target vessel PCI: a) L/H ratio<1.5 and >1.5, b) LDL-C<70 and >70, c) LDL-C<100 and >100 and d) HDL-C<40 and >40.

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Table 3
Multivariable analysis.

	Odds ratio	95% confidence interval		p value
Age	0.99	0.97	1.0	0.38
Gender (male)	1.2	0.66	2.19	0.56
CCB	0.85	0.52	1.34	0.50
Beta-BL	0.59	0.25	1.41	0.23
L/H (≧1.5)	2.93	1.05	8.24	0.04
LDL (<100)	1.35	0.81	2.24	0.25
HDL (<40)	1.52	0.94	2.47	0.09

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doi:10.1016/j.ijcard.2011.01.088

Clinical course of patients with chronic systolic heart failure due to the association of Chagas disease and systemic arterial hypertension

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ARTICLE INFO

Article history:
Received 20 January 2011
Accepted 29 January 2011
Available online 22 February 2011

Keywords:
Chagas disease
American trypanosomiasis
Heart failure
Systemic arterial hypertension
Carvedilol
Metoprolol

Chronic systolic heart failure (CHF) may affect about 8% of patients with Chagas disease (ChD) and concomitant systemic arterial hypertension (SAH) [1]. Despite this high frequency of coexistence, the impact of SAH in patients with CHF secondary to ChD is unknown at the present time. In this study, we compare the clinical course of patients with CHF secondary to ChD with that of patients with CHF associated with ChD and SAH (ChD–SAH).

All patients routinely and prospectively followed at the Cardiomyopathy Outpatient Service of our Institution from January, 2000 to December, 2008 with the diagnosis of CHF secondary to ChD with or without SAH were considered for the study. Criteria for inclusion in the ChD group were as follows: 1) positive serology for ChD; 2) a left ventricular ejection fraction less than or equal to 55% as established by the Teicholz method on Doppler-echocardiography or <50% on radionuclide ventriculography.

Criteria for inclusion in the ChD–SAH group were the above items 1 and 2 plus one of the following; 3) systolic blood pressure >140 mm Hg or diastolic blood pressure >90 mm Hg at presentation; 4) a documented medical history of SAH or patients confirmation of previous treatment for SAH on admission at the Outpatient Cardiomyopathy Service in the case systemic arterial pressure was normal at presentation, but with patients receiving antihypertensive therapy [2].

Table 1
Baseline characteristics of the study population.

	Chagas ($n=246$)	Chagas–SAH ($n=107$)	Overall ($n=353$)
Age (years)	55 ± 14*	63 ± 11	52 ± 15
NYHA Class III/IV	78 (32%)	34 (32%)	112 (32%)
Inotropic support	68 (28%)*	22 (21%)	90 (25%)
ACEI/ARB	229 (93%)	98 (92%)	327 (93%)
Beta-Blockers	128 (52%)	69 (64%)**	197 (56%)
Furosemide	194 (79%)	82 (77%)	276 (78%)
Spironolactone	165 (67%)	66 (62%)	231 (65%)
Amiodarone	97 (39%)***	28 (26%)	125 (35%)
Digoxin	176 (71%)****	55 (51%)	231 (65%)
SBP (mm Hg)	107.6 ± 16.3	127.9 ± 21.7***	113.8 ± 20.3
DBP (mm Hg)	70.6 ± 11.1	80.3 ± 14.1***	73.6 ± 12.9
Na (mEq/L)	140.8 ± 5.5	141.9 ± 4.5	141.2 ± 5.2
K (mEq/L)	4.4 ± 0.6	4.5 ± 0.5	4.4 ± 0.6
LAFB	99 (40%)	33 (31%)	132 (37%)
LVDD (mm)	64.5 ± 8.9	61.3 ± 9.1	63.5 ± 9.1
LVSD (mm)	53.6 ± 10.5	49.3 ± 9.7	52.3 ± 10.4
RVD (mm)	25.1 ± 7.4	23.5 ± 6.6	24.6 ± 7.2
LVEF (%)	35.2 ± 12.9*****	37.9 ± 9	36.1 ± 11.9

NYHA = New York Heart Association Class; ACEI = Angiotensin Converting Enzyme Inhibitor; ARB = Angiotensin Receptor Block; SBP = Systolic Blood Pressure; DBP = Diastolic Blood Pressure; LAFB = Left Anterior Fascicular Block; LDDD = Left Ventricular Diastolic Diameter; LVSD = Left Ventricular Systolic Diameter; RVD = Right Ventricular Diameter; LVEF = Left Ventricular Ejection Fraction; *$p=0.008$; **$p=0.036$;***$p=0.02$; ****$p<0.005$; *****$p=0.001$ by Mann–Whitney test.

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