Relationship Between Renal Dysfunction and Severity of Coronary Artery Disease in Japanese Patients – Reply –

Dr Oda gave us important suggestions with respect to the role of dyslipidemia in the so-called cardiorenal syndrome. Dyslipidemia is one of the conventional and well-established risk factors for coronary artery disease (CAD). Among the cholesterol fractions, low-density lipoprotein cholesterol (LDL-C) has been especially targeted by lipid-lowering therapy to prevent CAD, because lowering LDL-C with statins has been found to significantly reduce the relative risk for major vascular events as compared with placebo.¹ High-density

lipoprotein cholesterol (HDL-C) is also important because several studies have found low HDL-C significantly related to the possibility of developing CAD.^{2,3} However, at present there is no direct way medically intervening to change the level of HDL-C.

In the past years, some researchers reported that dyslipidemia was somehow related to the development of renal dysfunction. Schaeffner et al reported that in apparently healthy men, elevated total cholesterol (TC), high non-HDL-C, a high ratio of TC/HDL, and low HDL-C were significantly associated with an increased risk for developing renal dysfunction (creatinine ≥ 1.5 mg/dl) after 14 years.⁴ Using multiple regression analysis, Tozawa et al demonstrated that in the Japanese general population, HDL-C in men and triglycerides in women, but not LDL-C, significantly correlated with deterioration in glomerular filtration rate (GFR) after 3 years.⁵

Table 1. Correlation Between the Number of Stenotic Coronary Arteries and Risk Factors

	Univariate analysis		Multivariate analysis ($r^2=0.1387$)		
	r^2	P value	β	f value	P value
Age	0.0007	0.5173	0.0768	1.6826	0.0928
Sex	0.0130	0.0064	0.1263	2.8077	0.0052
BMI	0.0117	0.0099	0.0035	0.0792	0.9369
Hypertension	0.0024	0.2382	-0.0038	-0.0904	0.9280
Systolic BP	0.0068	0.0515	0.0616	1.1992	0.2310
Diastolic BP	0.0007	0.5234	-0.0108	-0.2147	0.8301
FPG	0.0348	<0.0001	0.1845	4.4345	<0.0001
HDL-C	0.0439	<0.0001	-0.1511	-3.2664	0.0012
LDL-C	0.0247	0.0002	0.1548	3.7164	0.0002
Triglycerides	0.0129	0.0066	0.0229	0.5186	0.6042
Smoking habit	0.0053	0.0831	0.0352	0.8399	0.4013
CKD	0.0266	0.0001	0.1412	3.3780	0.0008

BMI, body mass index; BP, blood pressure; FPG, fasting plasma glucose; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; CKD, chronic kidney disease.

Table 2. Correlation Between the Percent GFR Deterioration During Follow-up and Clinical Parameters

	Univariate analysis		Multivariate analysis ($r^2=0.1576$)		
	r^2	P value	β	f value	P value
Age	0.0031	0.1828	0.0860	1.7574	0.0795
Sex	0.0041	0.1244	-0.0389	-0.8177	0.4139
BMI	0.0001	0.8558	-0.0094	-0.2043	0.8382
Hypertension	0.0001	0.7903	-0.0572	-1.3224	0.1866
Systolic BP	0.0351	<0.0001	0.1459	2.7773	0.0057
Diastolic BP	0.0069	0.0488	0.0205	0.3965	0.6919
FPG	0.0238	0.0002	0.0830	1.8811	0.0605
HDL-C	0.0003	0.6903	0.0028	0.0571	0.9545
LDL-C	0.0098	0.0181	0.0858	1.9515	0.0516
Triglycerides	0.0031	0.1849	0.0532	1.1579	0.2474
Smoking habit	0.0021	0.2736	0.0097	0.2218	0.8246
Baseline GFR	0.0135	0.0053	0.1815	4.0122	0.0001
LVEF	0.0045	0.1092	-0.0359	-0.7897	0.4301
Plasma BNP	0.0468	<0.0001	0.2013	4.1966	<0.0001
No. of stenotic coronary arteries	0.0399	<0.0001	0.1068	2.2292	0.0262
No. of CAG and PCI per patient during follow-up	0.0118	0.0094	0.0483	1.0614	0.2890

GFR, glomerular filtration rate; LVEF, left ventricular ejection fraction; BNP, B-type natriuretic peptide; CAG, coronary angiography; PCI, percutaneous coronary intervention. Other abbreviations see in Table 1.

If we consider the results of those studies, LDL-C, although well established as one of the most important risk factors for CAD, seems to play a lesser role in the development of renal insufficiency. However, recently, at least cross-sectionally, Oda and Kawai reported that in Japanese men, the levels of LDL-C increased significantly in relation to the stage of chronic kidney disease (CKD),⁶ which contradicts the previously reported data.

Based on their findings, Dr Oda pointed out the potential effects of lipid-related factors on our results concerning the relationship between renal dysfunction and severity of CAD in Japanese patients.⁷ In fact, there are many possible mechanisms for the progression of both renal dysfunction and CAD, with dyslipidemia probably being one of them. Dyslipidemia may lead to renal damage through atherosclerosis of the renal arterioles and other mechanisms. On the other hand, dyslipidemia is associated with renal damage through substantial urinary excretion of protein.

We adopted a morbidity rate instead of the numeric data of fasting plasma glucose (FPG), HDL-C, LDL-C or triglycerides to analyze the effect of diabetes mellitus or dyslipidemia on the progression of renal dysfunction, because our patient setting was limited to inpatients suspected of having CAD. Some of them had already started to be treated medically and the numeric data per se may lead us to underestimate their real risks. However, we may be able to add some information by showing those data, as Dr Oda indicated: FPG 123.5 ± 45.1 mg/dl; HDL-C 49.8 ± 13.6 mg/dl; LDL-C 119.3 ± 31.6 mg/dl; triglycerides 143.5 ± 85.7 mg/dl (mean $\pm$ SD). We performed multiple regression analysis using the number of stenotic coronary arteries as a dependent variable and risk factors such as age, sex, body mass index, conventional risk factors, including lipids and CKD, as independent variables. In our results, CKD was still an independent risk factor of coronary artery stenosis (Table 1). Moreover, stepwise multiple regression analysis showed that the number of stenotic coronary arteries was independently and significantly associated with GFR deterioration, even after including the numeric

data instead of the morbidity rate of diabetes mellitus or dyslipidemia (Table 2). FPG and LDL were significantly associated with GFR deterioration if analyzed univariately, although neither was when subjected to multivariate analysis, which may be related to medical intervention for diabetes mellitus or dyslipidemia, or to instability of the effect of each cholesterol fraction on the progression of renal dysfunction.

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