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Association of LDL-C with adverse clinical outcomes in Korean patients with chronic kidney disease: Results from KNOW-CKD

Changhyun Lee[1], Tae-Ik Chang[2], Ea Wha Kang[2], Curie Ahn[3], Kook-Hwan Oh[3], Jung Tak Park[4], Tae-Hyun Yoo[4], Shin-Wook Kang[4], Seung Hyeok Han[4]
[1]Department of Internal Medicine, National Health Insurance Service Ilsan Hospital, Korea, Republic of
[2]Department of Internal Medicine-Nephrology, National Health Insurance Service Ilsan Hospital, Korea, Republic of
[3]Department of Internal Medicine-Nephrology, Seoul National University College of Medicine, Korea, Republic of
[4]Department of Internal Medicine-Nephrology, Severance Hospital, Korea, Republic of

Objectives: Lowering low-density lipoprotein cholesterol (LDL-C) level is an important therapeutic strategy in patients with CKD. However, few studies have examined optimal level of LDL-C in these patients.

Methods: We studied the association of LDL-C with adverse clinical outcomes in 1,975 patients from the KoreaN cohort study for Outcome in patients With Chronic Kidney Disease (KNOW-CKD). Patients were classified into four groups according to LDL-C level of <70, 70-99, 100-129, and ≥130 mg/dL. The primary outcome was an extended major cardiovascular events (eMACE), which was defined as non-fatal cardiovascular events, symptomatic arrhythmia, and cardiac death. The secondary endpoints included separate outcomes of composite renal outcome (≥50% decline in eGFR or the onset of end-stage renal disease), non-fatal MACE, and all-cause death.

Results: The mean LDL-C level was 97.2±31.4 mg/dL, and the mean eGFR was 53.3±30.9 ml/min/1.73 m^2. During the mean follow-up of 4.1 years, the primary outcome events occurred in 110 (5.9%) patients with incidence rate of 14.6 per 1,000 person-years. In multivariable Cox analysis after adjustment of confounders, there was a graded association of LDL-C with the primary outcome. The HRs (95% CI) for the corresponding four LDL-C categories were 1.97 (1.06-3.68), 2.60 (1.16-5.82), and 3.30 (1.21-9.00), compared with LDL of <70 mg/dL. In the analyses of secondary outcomes, incidence rates for kidney outcome, non-fatal MACE, and all-cause death were 75.2, 14.2, and 9.5 per 1,000 person-years, respectively. There was a significant association of higher LDL-C level and risk of non-fatal MACE. However, LDL-C level was not associated with adverse kidney outcomes and all-cause mortality.

Conclusions: In Korean CKD patients, LDL-C level was significantly associated with higher risk of MACE.

Table 1. Hazard ratios for the outcomes according to LDL groups.

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	Model 1		Model 2		Model 3		Model 4	
LDL category	HR [95% CI]	*P*	HR [95% CI]	*P*	HR [95% CI]	*P*	HR [95% CI]	*P*
eMACE								
LDL <70	1.00 [Reference]		1.00 [Reference]		1.00 [Reference]		1.00 [Reference]	
LDL 70-99	1.98 [1.07-3.69]	0.03	2.01 [1.08-3.74]	0.03	1.97 [1.06-3.68]	0.03	1.25 [0.46-3.39]	0.66
LDL 100-129	2.71 [1.23-5.97]	0.01	2.72 [1.23-6.00]	0.01	2.60 [1.16-5.82]	0.02	2.74 [0.85-8.87]	0.09
LDL ≥130	3.32 [1.23-8.95]	0.02	3.39 [1.25-9.15]	0.02	3.30 [1.21-9.00]	0.02	3.77 [1.08-13.2]	0.04
Non fatal cardiovascular outcome								
LDL <70	1.00 [Reference]		1.00 [Reference]		1.00 [Reference]		1.00 [Reference]	
LDL 70-99	2.24 [1.18-4.23]	0.01	2.28 [1.20-4.32]	0.01	2.11 [1.11-4.04]	0.02	1.03 [0.30-3.54]	0.96
LDL 100-129	3.24 [1.40-7.49]	0.01	3.27 [1.41-7.58]	0.01	2.73 [1.16-6.44]	0.02	2.79 [0.60-13.0]	0.19
LDL ≥130	5.93 [1.99-17.7]	<0.01	6.10 [2.03-18.3]	<0.01	5.02 [1.65-15.3]	<0.01	1.57 [0.22-11.1]	0.65
Composite renal outcome								
LDL <70	1.00 [Reference]		1.00 [Reference]		1.00 [Reference]		1.00 [Reference]	
LDL 70-99	1.09 [0.84-1.42]	0.52	1.16 [0.90-1.50]	0.25	1.12 [0.86-1.45]	0.41	1.18 [0.83-1.67]	0.36
LDL 100-129	1.05 [0.75-1.48]	0.77	1.35 [0.97-1.88]	0.08	1.28 [0.91-1.80]	0.15	1.07 [0.67-1.72]	0.78
LDL ≥130	1.12 [0.69-1.80]	0.65	1.30 [0.81-2.08]	0.28	1.25 [0.78-2.01]	0.35	1.78 [1.04-3.06]	0.04
All-cause mortality								
LDL <70	1.00 [Reference]		1.00 [Reference]		1.00 [Reference]		1.00 [Reference]	
LDL 70-99	0.96 [0.49-1.88]	0.91	0.98 [0.50-1.91]	0.96	0.98 [0.50-1.94]	0.96	0.88 [0.42-1.82]	0.73
LDL 100-129	0.99 [0.41-2.36]	0.98	1.02 [0.43-2.47]	0.96	1.08 [0.44-2.66]	0.87	1.69 [0.75-3.83]	0.21
LDL ≥130	1.30 [0.41-4.13]	0.66	1.28 [0.40-4.06]	0.67	1.37 [0.42-4.40]	0.60	2.59 [1.07-6.28]	0.04

Note: Model 1 adjusted for age, sex, CAD, DM, coronary calcium score, smoking status, socioeconomic status, educational status, BMI, SBP, laboratory parameters such as serum total cholesterol, hs-CRP, serum albumin, and parathyroid hormone

Model 2 ; adjusted for Model 1 plus renal parameters such as eGFR and uPCR

Model 3 ; adjusted for Model 2 plus medication such as use of statin, fibrate, and RASB

Model 4 ; adjusted for age, sex, CAD, coronary calcium score, smoking status, socioeconomic status, educational status, statin, fibrate, RASB, baseline eGFR, baseline uPCR and time-varing variables at any given visit such as BMI, SBP, serum total cholesterol, hs-CRP, serum albumin, and parathyroid hormone

Abbreviations: BMI, body mass index; CAD, coronary artery disease; CI, confidence interval; eGFR, estimated glomerular filtration rate; HR, hazard ratio; hs-CRP, high-sensitive C-reactive protein; RASB, renin-angiotensin system blockade; SBP, systolic blood pressure; uPCR, urine protein-to-creatinine ratio

Figure1. Cummulative incidence curve

Figure 1. Cumulative incidence curve for (A) primary eMACE outcome and individual secondary outcomes of (B) non-fatal cardiovascular outcome, (C) composite renal outcome, and (D) all-cause mortality according to LDL group.