

Supplemental methods

Friesinger score

Friesinger score was used as a measure for the severity of CAD (1). Lesion sizes are quantified in three regions (left anterior descending artery [LAD], left circumflex artery [LCX] and right coronary artery [RCA] of the coronary circulation. The lesion sizes in these three regions are graded from 0 to 5 (0 – no disease; 1 – lesions < 50 % area stenosis; 2 – single lesion >50 % but < 90 %; 3 – multiple lesions >50 % but <90 %; 4 – 90 % lesion area; 5 – 100 %). The Friesinger score is then calculated as the sum of most severe lesion grade for each of three regions. The maximum Friesinger score is 15.

Supplemental data

Supplemental Table 1: Cox regression analyses for all-cause mortality and cardiovascular mortality according to eGFR calculated by using CKD-EPI creatinine-cystatin C equation (eGFR ≥ 90 ml/min, 60–89 ml/min, < 60 ml/min) in the LURIC study

All-cause mortality			
Model	eGFR (ml/min)	HR (95% CI)	P
Crude	≥ 90	1	...
	60–89	2.0 (1.7–2.3)	<0.001
	<60	4.9 (4.1–5.9)	<0.001
Adjusted 1	≥ 90	1	...
	60–89	1.3 (1.1–1.5)	0.007
	<60	2.4 (1.9–3.0)	<0.001
Adjusted 2	≥ 90	1	...
	60–89	1.3 (1.1–1.5)	0.010
	<60	2.3 (1.8–2.8)	<0.001
Cardiovascular mortality			
Model	eGFR	HR (95% CI)	P
Crude	≥ 90	1	...
	60–89	2.1 (1.7–2.6)	<0.001
	<60	5.7 (4.5–7.2)	<0.001
Adjusted 1	≥ 90	1	...
	60–89	1.4 (1.1–1.7)	0.004
	<60	2.9 (2.3–3.8)	<0.001
Adjusted 2	≥ 90	1	...
	60–89	1.4 (1.1–1.7)	0.008
	<60	2.7 (2.1–3.5)	<0.001

eGFR=estimated glomerular filtration rate. HR=Hazard ratio. 95% CI=95% confidence interval.

Adjustment 1) Adjustment for age and sex

Adjustment 2) Adjustment for age, sex, glycated hemoglobin, body mass index, mean systolic blood pressure, lipid lowering therapy, acute coronary syndrome

Supplemental Table 2: Baseline characteristics according to categories of HDL-C in the LURIC study

	HDL-C ≤25 mg/dl Category 1	HDL-C 26-33 mg/dl Category 2	HDL-C 34-41 mg/dl Category 3	HDL-C 42-49 mg/dl Category 4	HDL-C ≥50 mg/dl Category 5	P*
All-cause mortality (%)	37.5	35.0	29.0	27.2	23.2	<0.001
Cardiovascular mortality (%)	25.4	22.7	18.3	16.2	13.5	<0.001
Age (years)	60.8 (12.0)	62.3 (10.8)	62.3 (10.3)	63.6 (10.1)	63.9 (10.6)	<0.001
Sex (% male)	88.1	80.8	73.1	58.9	47.4	<0.001
BMI (kg/m²)	28.3 (4.3)	28.0 (4.1)	27.8 (4.0)	27.0 (3.9)	26.0 (3.9)	<0.001
Systolic blood pressure (mmHg)	136.0 (24.8)	140.0 (23.8)	142.0 (23.4)	142.2 (22.9)	143.3 (23.6)	<0.001
Diastolic blood pressure (mmHg)	77.9 (11.9)	80.2 (11.6)	81.7 (11.3)	81.6 (11.2)	81.4 (11.2)	<0.001
Total cholesterol (mg/dl)	175.5 (43.9)	182.6 (39.3)	193.0 (37.6)	200.0 (35.0)	206.9 (36.3)	<0.001
Triglycerides (mg/dl)	240.8 (119.0)	203.6 (106.0)	171.9 (88.3)	144.6 (70.7)	123.7 (64.9)	<0.001
HDL cholesterol (mg/dl)	22.2 (3.2)	30.0 (2.3)	37.3 (2.3)	45.1 (2.2)	57.6 (7.6)	<0.001
LDL cholesterol (mg/dl)	99.1 (35.8)	108.6 (34.2)	118.7 (32.5)	124.1 (32.7)	125.2 (33.5)	<0.001
Glycated hemoglobin (%)	6.6 (1.6)	6.5 (1.4)	6.3 (1.3)	6.2 (1.0)	6.0 (0.9)	<0.001
Creatinine (mg/dl)	1.1 (0.2)	1.0 (0.2)	1.0 (0.2)	0.9 (0.2)	0.9 (0.2)	<0.001
Cystatin C (mg/l)	1.2 (0.6)	1.0 (0.4)	1.0 (0.4)	0.9 (0.3)	0.9 (0.2)	<0.001
eGFR (ml/min)	78.5 (23.1)	79.5 (21.2)	83.1 (20.0)	83.1 (22.8)	82.6 (19.0)	<0.001
hsCRP (mg/l)	8.2 (8.0)	5.0 (5.0)	3.5 (6.2)	2.2 (5.4)	1.9 (8.5)	<0.001
IL-6 (ng/l)	8.6 (9.1)	6.2 (6.9)	5.0 (5.5)	4.2 (5.1)	4.1 (5.2)	<0.001
sICAM-1 (mg/l)	293.8 (117.4)	272.8 (115.2)	259.0 (101.6)	241.1 (71.7)	232.3 (61.1)	<0.001
Coronary artery disease (%)	88.8	85.9	78.6	72.3	64.0	<0.001

Friesinger score	6.9 (3.9)	6.2 (6.0)	5.5 (3.8)	4.8 (3.9)	3.8 (3.6)	<0.001
Acute coronary syndrome (%)	48.3	37.8	31.7	23.0	20.5	<0.001
Statin use (%)	56.1	53.2	48.4	40.9	35.6	<0.001
Lipid lowering therapy[§] (%)	57.6	55.0	49.8	42.3	38.0	<0.001
Diabetes (%)	52.8	47.4	40.4	35.8	24.4	<0.001
Smoking (%)	78.1	71.1	66.5	55.3	50.2	<0.001
Hypertension (%)	69.9	73.4	73.4	72.9	71.5	0.762

Values are presented as mean (SD), median (IQR) or number (%). BMI=body mass index. HDL=high-density lipoprotein. LDL=low-density lipoprotein. hsCRP=high-sensitivity C-reactive protein. eGFR=estimated glomerular filtration rate calculated by using CKD-EPI creatinine-cystatin C equation

* comparison between patients with eGFR ≥ 90 ml/min, eGFR 60-89 and eGFR < 60 ml/min. p < 0.05 was considered significant.

[§] comprising usage of statins, niacin, fibrates and selective cholesterol absorption inhibitors

Supplemental Table 3: Cox-Regression for all-cause and cardiovascular mortality in the LURIC study according to categories of HDL-C serum levels (HDL-C; C1: ≤25 mg/dl, C2: 26-33 mg/dl, C3: 34-41 mg/dl, C4: 42-49 mg/dl, C5: ≥50 mg/dl) and lipid-lowering therapy. First category was used as reference.

All-cause mortality					
Model	eGFR (ml/min)	HDL category	No Lipid-lowering therapy (51.4 %)		Lipid-lowering therapy (48.6 %)
			HR (95% CI)	P	
Adjusted *	≥90	C1	1	...	1
		C2	0.43 (0.20-0.95)	0.037	0.83 (0.40-1.74)
		C3	0.48 (0.23-1.01)	0.053	0.97 (0.47-2.02)
		C4	0.32 (0.14-0.75)	0.009	0.86 (0.37-1.99)
		C5	0.38 (0.15-0.92)	0.032	0.52 (0.18-1.52)
	60-90	C1	1	...	1
		C2	1.31 (0.77-2.23)	0.312	0.62 (0.40-0.95)
		C3	1.20 (0.71-2.03)	0.502	0.51 (0.33-0.80)
		C4	1.18 (0.67-2.10)	0.565	0.70 (0.43-1.15)
		C5	0.92 (0.48-1.73)	0.783	0.52 (0.30-0.92)
	<60	C1	1	...	1
		C2	0.91 (0.53-1.54)	0.713	2.32 (1.17-4.62)
		C3	0.89 (0.50-1.54)	0.708	1.37 (0.66-2.85)
		C4	0.92 (0.47-1.80)	0.810	1.30 (0.56-3.05)
		C5	0.96 (0.48-1.90)	0.903	1.31 (0.51-3.37)
Cardiovascular mortality					
Adjusted *	≥90	C1	1	...	1
		C2	0.27 (0.11-0.68)	0.005	0.71 (0.29-1.75)
		C3	0.40 (0.18-0.92)	0.031	0.87 (0.35-2.14)
		C4	0.20 (0.07-0.56)	0.002	0.68 (0.23-2.04)
		C5	0.17 (0.05-0.54)	0.003	0.50 (0.13-1.99)
	60-90	C1	1	...	1
		C2	1.09 (0.58-2.03)	0.793	0.74 (0.42-1.30)
		C3	1.00 (0.53-1.86)	0.991	0.66 (0.37-1.18)
		C4	0.86 (0.42-1.71)	0.647	0.82 (0.43-1.58)
		C5			0.552

	C5	0.72 (0.31-1.68)	0.447	0.83 (0.41-1.67)	0.597
<60	C1	1	...	1	...
	C2	0.91 (0.49-1.67)	0.750	4.10 (1.44-11.68)	0.008
	C3	0.74 (0.37-1.49)	0.398	2.24 (0.75-6.69)	0.149
	C4	0.86 (0.39-1.89)	0.712	3.11 (0.97-10.04)	0.057
	C5	0.72 (0.31-1.68)	0.447	1.43 (0.35-5.85)	0.620

eGFR=estimated glomerular filtration rate. HR=Hazard ratio. 95% CI=95% confidence interval.

* Adjustment for age, sex, glycated hemoglobin, systolic blood pressure, body mass index, acute coronary syndrome, Friesinger score, lipid-lowering therapy, smoking status and hsCRP.

Supplemental Table 4: Baseline characteristics of CKD patients of the validation cohort

	Overall (n=246)	HDL-C ≤49 mg/dl (n=124)	HDL-C ≥50 mg/dl (n=122)	P*
All-cause mortality (%)	84 (34.1)	44 (35.5)	40 (32.8)	0.688
Age	62.7 (14.2)	62.7 (14.5)	62.8 (14.0)	0.988
Sex (% male)	43.9	33.9	54.1	0.002
BMI (kg/m²)	27.7 (5.6)	28.4 (6.2)	27.0 (4.9)	0.044
Systolic blood pressure (mmHg)	157.5 (30.1)	156.9 (30.6)	158.1 (30.6)	0.758
Diastolic blood pressure (mmHg)	89.2 (20.3)	89.1 (23.1)	89.3 (17.0)	0.949
Total cholesterol (mg/dl)	192.6 (50.1)	176.8 (44.8)	209.0 (52.0)	<0.001
Triglycerides (mg/dl)	186.7 (115.6)	176.8 (44.8)	157.1 (74.9)	<0.001
HDL cholesterol (mg/dl)	52.1 (16.5)	40.4 (6.4)	64.0 (15.0)	<0.001
LDL cholesterol (mg/dl)	111.4 (42.2)	102.5 (35.4)	120.4 (46.6)	0.001
Glycated hemoglobin (%)	6.1 (1.0)	6.3 (1.1)	6.0 (0.8)	0.010
Creatinine (mg/dl)	2.7 (2.0)	2.9 (2.2)	2.4 (1.9)	0.120
eGFR (ml/min)[#]	24.2 (23.6)	20.8 (21.5)	27.6 (25.2)	0.023
hsCRP (mg/L)	4.6 (4.3)	5.3 (5.2)	3.3 (3.4)	0.017
Coronary artery disease (%)	23.6	32.3	14.8	0.002
Statin use (%)	29.4	30.9	27.9	0.674
Lipid lowering therapy[§] (%)	31.4	33.3	29.5	0.582
Diabetes (%)	34.1	45.2	23.0	<0.001
Smoking (%)	10.5	11.4	9.8	0.795
Hypertension (%)	96.3	97.5	95.0	0.499

Values are presented as mean (SD), median (IQR) or number (%). BMI=body mass index. HDL=high-density lipoprotein. LDL=low-density lipoprotein. hsCRP=high-sensitivity C-reactive protein.

* comparison between patients with HDL-C ≤ 49 mg/dl and HDL-C ≥ 50 ml/min. p < 0.05 was considered significant.

[§] comprising usage of statins, niacin, fibrates and selective cholesterol absorption inhibitors

for patients on dialysis, a GFR of 5 ml/min was assumed

Supplemental Table 5: Cox regression analyses for all-cause mortality and cardiovascular mortality according to tertiles of apolipoprotein A-I (tertile T1 \leq 118 mg/dl, tertile T2 119-138 mg/dl, tertile T3 $>$ 138 mg/dl) in the LURIC study

All-cause mortality

Model	eGFR (ml/min)	Tertile of Apolipoprotein A-I	HR (95% CI)	P
Crude	≥ 90	T1	1	...
		T2	0.93 (0.67-1.29)	0.657
		T3	0.82 (0.59-1.15)	0.250
	60-89	T1	1	...
		T2	0.71 (0.58-0.87)	0.001
		T3	0.61 (0.59-0.75)	<0.001
	<60	T1	1	...
		T2	1.05 (0.79-1.40)	0.739
		T3	0.77 (0.58-1.03)	0.080
Adjusted 1	≥ 90	T1	1	...
		T2	0.83 (0.60-1.14)	0.248
		T3	0.71 (0.50-1.01)	0.053
	60-89	T1	1	...
		T2	0.71 (0.58-0.87)	0.001
		T3	0.64 (0.51-0.80)	<0.001
	<60	T1	1	...
		T2	1.04 (0.78-1.39)	0.794
		T3	0.84 (0.62-1.14)	0.263
Adjusted 2	≥ 90	T1	1	...
		T2	0.86 (0.55-1.36)	0.269
		T3	0.68 (0.46-1.00)	0.050
	60-89	T1	1	...
		T2	0.76 (0.61-0.95)	0.015
		T3	0.73 (0.57-0.93)	0.012
	<60	T1	1	...
		T2	1.06 (0.78-1.43)	0.713
		T3	0.87 (0.62-1.21)	0.471

Cardiovascular mortality

Crude	≥ 90	T1	1	...
		T2	0.93 (0.67-1.29)	0.657
		T3	0.82 (0.59-1.15)	0.250
Adjusted 1	60-89	T1	1	...
		T2	0.71 (0.58-0.87)	0.001
		T3	0.61 (0.49-0.75)	<0.001
	<60	T1	1	...
		T2	1.05 (0.79-1.40)	0.739
		T3	0.77 (0.59-1.03)	0.080
	≥ 90	T1	1	...
		T2	0.83 (0.60-1.14)	0.248
		T3	0.71 (0.50-1.01)	0.053
	60-89	T1	1	...
		T2	0.71 (0.58-0.87)	0.001
		T3	0.64 (0.51-0.80)	<0.001

	<60	T1	1	...
		T2	1.04 (0.78-1.39)	0.793
		T3	0.84 (0.62-1.14)	0.263
Adjusted 2	≥90	T1	1	...
		T2	0.67 (0.43-1.05)	0.078
		T3	0.56 (0.34-0.92)	0.023
	60–89	T1	1	...
		T2	0.76 (0.57-0.99)	0.049
		T3	0.74 (0.55-1.03)	0.060
	<60	T1	1	...
		T2	1.09 (0.76-1.56)	0.646
		T3	0.82 (0.54-1.25)	0.367

eGFR=estimated glomerular filtration rate. HR=Hazard ratio. 95% CI=95% confidence interval.

Adjustment 1) Adjustment for age and sex

Adjustment 2) Adjustment for age, sex, glycated hemoglobin, systolic blood pressure, body mass index, acute coronary syndrome, lipid-lowering therapy, Friesinger score, **smoking status and hsCRP**.

Supplemental Table 6: Cox-Regression for all-cause and cardiovascular mortality in the LURIC study using HDL-C and eGFR as continuous variables as well as their interaction term

Model	Variable	All cause		Cardiovascular	
		HR (95% CI)	P	HR (95% CI)	P
Crude	HDL-C	0.83 (0.78-0.89)	<0.001	0.79 (0.72-0.91)	<0.001
	HDL-C	0.92 (0.88-0.97)	<0.001	0.90 (0.85-0.95)	<0.001
	eGFR	0.73 (0.71-0.76)	<0.001	0.73 (0.70-0.75)	<0.001
	HDL-C	1.79 (1.12-2.86)	<0.001	2.01 (1.13-3.59)	0.017
Adjusted 1	eGFR	1.29 (0.87-1.91)	0.207	1.44 (0.89-2.33)	0.142
	HDL-C x eGFR	0.69 (0.54-0.89)	0.005	0.64 (0.40-0.88)	0.005
	HDL-C	1.58 (0.91-2.73)	0.104	1.87 (0.96-3.65)	0.066
Adjusted 2	eGFR	1.25 (0.79-1.99)	0.344	1.45 (0.82-2.55)	0.203
	HDL-C x eGFR	0.74 (0.54-1.00)	0.051	0.67 (0.50-0.96)	0.030
	HDL-C	1.97 (0.93-4.65)	0.061	2.06 (1.17-5.09)	0.035
	eGFR	1.28 (0.56-2.30)	0.251	1.63 (0.65-2.27)	0.142
	HDL-C x eGFR	0.69 (0.35-0.97)	0.042	0.57 (0.13-0.84)	0.024

eGFR=estimated glomerular filtration rate. HR=Hazard ratio. 95% CI=95% confidence interval.

Adjustment 1) Adjustment for age and sex

Adjustment 2) Adjustment for age, sex, glycated hemoglobin, systolic blood pressure, body mass index, acute coronary syndrome, Friesinger score, lipid-lowering therapy, **smoking status and hsCRP**.

Supplemental Table 7: Association of estimated glomerular filtration rate (eGFR) and inflammatory markers with HDL-cholesterol serum concentrations in the LURIC study

	HDL (mg/dl)*	Mean Difference %¶	P¶
eGFR (ml/min)			
>90	40.4 (39.5-41.3)		
60–89	39.4 (38.8-40.0)	-2.6	0.006
≤60	37.3 (36.1-38.5)	-7.8	<0.001
hsCRP (mg/L)			
<3	41.4 (40.6-42.2)		
3–10	38.8 (38.1-39.6)	-6.1	<0.001
≥10	36.1 (35.1-37.0)	-12.8	<0.001
sICAM-1 (mg/L)			
<203.7	40.8 (39.1-42.5)		
203.7–239.7	39.7 (38.4-41.0)	-2.7	0.999
239.7–289.1	38.5 (37.3-39.6)	-5.7	0.153
≥289.2	36.3 (35.1-37.5)	-11.0	<0.001
IL-6 (ng/L)			
<1.8	41.6 (40.6-42.6)		
1.8–3.2	40.0 (39.0-41.0)	-3.8	0.157
3.2–6.1	39.2 (38.3-40.1)	-5.7	0.004
≥6.1	36.7 (35.9-37.7)	-11.5	<0.001

eGFR=estimated glomerular filtration rate, hsCRP=high-sensitivity CRP, sICAM-1=soluble intercellular adhesion molecule-1, IL-6=interleukin-6

* Estimated marginal means and 95 % confidence intervals as calculated in a general linear model, adjusted for age, sex, lipid-lowering therapy, acute coronary syndrome, body mass index, mean arterial blood pressure, glycated hemoglobin, Friesinger score, smoking status and hsCRP (where appropriate).

¶ For the comparison with the first category of each variable

Supplemental Table 8: Cox-regression for all-cause and cardiovascular mortality according to tertiles of hsCRP (tertile 1: ≤ 3.0 mg/l, tertile 2: 4.0-10.0 mg/l, tertile 3: > 10 mg/l), IL-6 (tertile 1: ≤ 215.9 ng/l, tertile 2: 215.9-270.2 ng/l, tertile 3: > 270.2 ng/l) and sICAM-1 (tertile 1: 2.2 mg/l, tertile 2: 2.2-4.8 mg/l, tertile 3: > 4.8 mg/l) in the LURIC study

Model	eGFR (ml/min)	Tertile	hsCRP		IL-6		sICAM-1	
			HR (95% CI)	P	HR (95% CI)	P	HR (95% CI)	P
All-cause mortality								
Crude	≥ 90	1	1	...	1	...	1	...
		2	1.27 (0.91-1.76)	0.164	1.80 (1.29-2.51)	0.001	1.53 (1.00-1.83)	0.050
		3	1.55 (1.11-2.16)	0.009	2.03 (1.43-2.88)	<0.001	3.15 (2.12-4.68)	<0.001
	60-90	1	1	...	1	...	1	...
		2	1.33 (1.06-1.67)	0.015	1.27 (1.00-1.62)	0.046	1.26 (0.96-1.64)	0.096
		3	1.75 (1.41-2.19)	<0.001	2.13 (1.72-2.66)	<0.001	1.43 (1.09-1.88)	0.011
	<60	1	1	...	1	...	1	...
		2	0.89 (0.61-1.29)	0.525	1.10 (0.75-1.63)	0.623	1.12 (0.68-1.83)	0.659
		3	1.39 (0.99-1.94)	0.059	1.38 (0.97-1.95)	0.070	1.26 (0.79-1.99)	0.330
Adjusted*	≥ 90	1	1	...	1	...	1	...
		2	1.26 (0.90-1.77)	0.178	1.71 (1.21-2.40)	0.002	1.37 (0.89-2.12)	0.153
		3	1.64 (1.15-2.33)	0.006	1.91 (1.33-2.74)	<0.001	2.80 (1.85-4.24)	<0.001
	60-90	1	1	...	1	...	1	...
		2	1.25 (0.99-1.57)	0.063	1.18 (0.93-1.50)	0.180	1.20 (0.92-1.58)	0.181
		3	1.60 (1.27-2.03)	<0.001	1.79 (1.42-2.26)	<0.001	1.27 (0.96-1.69)	0.095
	<60	1	1	...	1	...	1	...
		2	0.94 (0.64-1.38)	0.737	1.01 (0.68-1.49)	0.981	1.12 (0.68-1.85)	0.649
		3	1.54 (1.07-2.21)	0.019	1.30 (0.91-1.86)	0.154	1.24 (0.78-1.99)	0.360

Cardiovascular Mortality							
Crude	≥90	1	1	...	1	...	1
		2	0.91 (0.58-1.42)	0.667	1.72 (1.10-2.68)	0.017	1.71 (0.99-2.95)
		3	1.41 (0.93-2.14)	0.104	2.14 (1.36-3.37)	0.001	2.39 (1.42-4.04)
	60-90	1	1	...	1	...	1
		2	1.18 (0.88-1.59)	0.258	1.26 (0.93-1.72)	0.134	1.18 (0.84-1.65)
		3	1.79 (1.35-2.35)	<0.001	2.24 (1.69-2.98)	<0.001	1.03 (0.72-1.48)
	<60	1	1	...	1	...	1
		2	1.07 (0.66-1.74)	0.791	1.09 (0.69-1.73)	0.708	1.09 (0.62-1.92)
		3	1.79 (1.15-2.78)	0.010	1.24 (0.82-1.87)	0.312	1.17 (0.69-1.98)
Adjusted*	≥90	1	1	...	1	...	1
		2	0.90 (0.57-1.42)	0.643	1.63 (1.04-2.57)	0.034	1.54 (0.88-2.71)
		3	1.53 (0.98-2.40)	0.062	2.07 (1.29-3.31)	0.002	2.79 (1.60-4.84)
	60-90	1	1	...	1	...	1
		2	1.10 (0.81-1.48)	0.540	1.16 (0.85-1.57)	0.355	1.23 (0.88-1.74)
		3	1.67 (1.24-2.24)	0.001	1.93 (1.44-2.59)	<0.001	1.11 (0.77-1.60)
	<60	1	1	...	1	...	1
		2	1.16 (0.70-1.91)	0.572	1.02 (0.64-1.63)	0.926	1.13 (0.63-2.00)
		3	2.01 (1.26-3.21)	0.004	1.16 (0.75-1.77)	0.511	1.29 (0.74-2.23)

eGFR=estimated glomerular filtration rate. HR=Hazard ratio. 95% CI=95% confidence interval. hsCRP, high-sensitivity C reactive protein. IL-6, interleukin-6. sICAM-1, soluble intercellular adhesion molecule-1.

* Adjusted for age, sex, glycated hemoglobin, systolic blood pressure, body mass index, acute coronary syndrome, lipid-lowering therapy, Friesinger score and smoking status.

Supplemental references

1. Friesinger, GC, Page, EE & Ross, RS: Prognostic significance of coronary arteriography. *Trans Assoc Am Physicians*, 83: 78-92, 1970.