Supplementary Tables to

Apolipoprotein A-IV concentrations and clinical outcomes in a large chronic kidney disease cohort: results from the GCKD study

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Supplementary Table 1: Association of apolipoprotein A-IV with prevalent cardiovascular disease. Data are as in model 2 from Table 3 but additionally adjusted for hs-CRP.

	OR	95% CI	p-value
Calculations per 10 mg/dL increment of apoA-IV concentrations			
	0.83	(0.76-0.91)	$8x10^{-5}$
Calculations per quartile of ApoA-IV concentrations			
Quartile 1	1.00		
Quartile 2	0.84	(0.68-1.03)	0.10
Quartile 3	0.93	(0.76-1.15)	0.51
Quartile 4	0.71	(0.56-0.89)	0.004

OR, Odds ratio; CI, confidence interval

Data are adjusted for age, sex, eGFR, ln-UACR, serum albumin, LDL cholesterol, smoking status, diabetes mellitus, statin use, ln-triglycerides, BMI, systolic and diastolic blood pressure and ln-hs-CRP

Prevalent cardiovascular disease was defined as myocardial infarction, coronary artery bypass grafting, percutaneous transluminal coronary angioplasty, stroke, interventions at the carotid arteries.

Supplementary Table 2: Association of apolipoprotein A-IV with outcomes during the prospective follow-up. Data are as in model 2 from Table 4 but additionally adjusted for hs-CRP.

	For each increase of apoA-IV by 10 mg/dL	
Endpoints	**HR (95% CI)**	**p-value**
All-cause mortality	0.87 (0.78-0.97)	0.009
Non-cardiovascular mortality	0.82 (0.73-0.93)	0.002
3-point-MACE	0.93 (0.83-1.04)	0.21
4-point-MACE	0.94 (0.85-1.03)	0.18
Death and hospitalization due to heart failure	0.91 (0.79-1.04)	0.16

HR, hazard ratio; CI, confidence interval

Data are adjusted for age, sex, eGFR, ln-UACR, serum albumin, LDL cholesterol, smoking status, diabetes mellitus, statin use, ln-triglycerides, BMI, systolic and diastolic blood pressure, cardiovascular disease at baseline and ln-hs-CRP.

3-point-MACE (Major Adverse Cardiovascular Events) was defined as acute myocardial infarction (STEMI and NSTEMI), non-fatal stroke, fatal myocardial infarction, fatal coronary heart disease, sudden cardiac death, death from congestive heart failure and death due to non-hemorrhagic stroke;

4-point-MACE comprised all endpoints included in 3-point-MACE plus fatal peripheral ischemia, amputation due to peripheral vascular disease, surgical or percutaneous revascularization due to peripheral vascular disease

Hospitalization due to heart failure was defined as follows: hospitalization with either evidence of a reduced left ventricular ejection fraction (< 35%) or radiological evidence of pulmonary venous congestion, alveolar edema or presence of bilateral or right-sided pleural effusion with a presumed cardiac cause.

Supplementary Table 3: Association of apolipoprotein A-IV with outcomes during the prospective follow-up in patients free of cardiovascular disease at the time of enrollment (n=3,852 out of 5,141). Data are adjusted for age, sex, eGFR, ln-UACR, serum albumin, LDL cholesterol, smoking status, diabetes mellitus, statin use, ln-triglycerides, BMI, systolic and diastolic blood pressure.

	For each increase of apoA-IV by 10 mg/dL	
Endpoints (n of events)	**HR (95% CI)**	**p-value**
All-cause mortality (n=300)	0.84 (0.73-0.96)	0.009
Non-cardiovascular mortality (n=233)	0.78 (0.66-0.91)	0.002
3-point-MACE (n=235)	0.85 (0.73-0.99)	0.04
4-point-MACE (n=321)	0.88 (0.78-1.01)	0.06
Death and hospitalization due to heart failure (n=159)	0.87 (0.72-1.05)	0.15

HR, hazard ratio; CI, confidence interval

3-point-MACE (Major Adverse Cardiovascular Events) was defined as acute myocardial infarction (STEMI and NSTEMI), non-fatal stroke, fatal myocardial infarction, fatal coronary heart disease, sudden cardiac death, death from congestive heart failure and death due to non-hemorrhagic stroke;

4-point-MACE comprised all endpoints included in 3-point-MACE plus fatal peripheral ischemia, amputation due to peripheral vascular disease, surgical or percutaneous revascularization due to peripheral vascular disease

Hospitalization due to heart failure was defined as follows: hospitalization with either evidence of a reduced left ventricular ejection fraction (< 35%) or radiological evidence of pulmonary venous congestion, alveolar edema or presence of bilateral or right-sided pleural effusion with a presumed cardiac cause.

Supplementary Table 4: Association of apolipoprotein A-IV with outcomes during the prospective follow-up based on subdistribution hazard ratio (SHR) models

		For each increase of apoA-IV by 10 mg/dL	
Adjustment model		**SHR (95% CI)**	**p-value**
Non-cardiovascular mortality (n=433)*			
	Model 1	0.80 (0.71-0.91)	0.0009
	Model 2	0.77 (0.68-0.87)	0.00005
3-point-MACE (n=506) *			
	Model 1	0.91 (0.82-1.01)	0.09
	Model 2	0.91 (0.81-1.02)	0.097
4-point-MACE (n=681) *			
	Model 1	0.92 (0.84-1.01)	0.09
	Model 2	0.91 (0.83-1.00)	0.05
Death and hospitalization due to heart failure (n=346) *			
	Model 1	0.86 (0.74-0.99)	0.03
	Model 2	0.88 (0.76-1.01)	0.06

CI, confidence interval

* Number of events refer to model 1.

Model 1: adjusted for age, sex, eGFR, ln-UACR;

Model 2: as model 1 plus serum albumin, LDL cholesterol, smoking status, diabetes mellitus, statin use, ln-triglycerides, BMI, systolic and diastolic blood pressure and cardiovascular disease at baseline

3-point-MACE (Major Adverse Cardiovascular Events) was defined as acute myocardial infarction (STEMI and NSTEMI), non-fatal stroke, fatal myocardial infarction, fatal coronary heart disease, sudden cardiac death, death from congestive heart failure and death due to non-hemorrhagic stroke;

4-point-MACE comprised all endpoints included in 3-point-MACE plus fatal peripheral ischemia, amputation due to peripheral vascular disease, surgical or percutaneous revascularization due to peripheral vascular disease

Hospitalization due to heart failure was defined as follows: hospitalization with either evidence of a reduced left ventricular ejection fraction (< 35%) or radiological evidence of pulmonary venous congestion, alveolar edema or presence of bilateral or right-sided pleural effusion with a presumed cardiac cause.

Supplementary Table 5: Association of apolipoprotein A-IV with outcomes during the prospective follow-up when data are additionally adjusted for HDL cholesterol concentrations. For better comparison data from model 2 given in Table 4 of the main manuscript are added to this table.

	For each increase of apoA-IV by 10 mg/dL	
Adjustment model	**HR (95% CI)**	**p-value**
All-cause mortality		
Model 2 from Table 4	0.81 (0.73-0.89)	0.00005
Model 2 + HDL cholesterol	0.81 (0.73-0.90)	0.000098
Non-cardiovascular mortality		
Model 2 from Table 4	0.76 (0.68-0.86)	0.00001
Model 2 + HDL cholesterol	0.75 (0.66-0.85)	0.000005
3-point-MACE		
Model 2 from Table 4	0.88 (0.79-0.99)	0.03
Model 2 + HDL cholesterol	0.92 (0.82-1.03)	0.14
4-point-MACE		
Model 2 from Table 4	0.88 (0.80-0.97)	0.01
Model 2 + HDL cholesterol	0.91 (0.83-1.01)	0.07
Death and hospitalization due to heart failure		
Model 2 from Table 4	0.83 (0.72-0.95)	0.006
Model 2 + HDL cholesterol	0.85 (0.74-0.98)	0.02

HR, hazard ratio; CI, confidence interval

Model 2: taken from Table 4 and is adjusted for age, sex, estimated glomerular filtration rate , ln-urine albumin-creatinine ratio, serum albumin, LDL cholesterol, smoking status, diabetes mellitus, statin use, ln-triglycerides, body mass index, systolic and diastolic blood pressure and cardiovascular disease at baseline

Model 2 + HDL cholesterol: additional adjustment for HDL cholesterol

3-point-MACE (Major Adverse Cardiovascular Events) was defined as acute myocardial infarction (STEMI and NSTEMI), non-fatal stroke, fatal myocardial infarction, fatal coronary heart disease, sudden cardiac death, death from congestive heart failure and death due to non-hemorrhagic stroke;

4-point-MACE comprised all endpoints included in 3-point-MACE plus fatal peripheral ischemia, amputation due to peripheral vascular disease, surgical or percutaneous revascularization due to peripheral vascular disease

Hospitalization due to heart failure was defined as follows: hospitalization with either evidence of a reduced left ventricular ejection fraction (< 35%) or radiological evidence of pulmonary venous congestion, alveolar edema or presence of bilateral or right-sided pleural effusion with a presumed cardiac cause.

Supplementary Table 6: Association of apolipoprotein A-IV with outcomes during the prospective follow-up including time-updated covariables for eGFR, UACR, BMI, triglycerides, LDL cholesterol, serum albumin, systolic and diastolic blood pressure and statins from follow-up examinations two, three and four years after baseline.

	For each increase of apoA-IV by 10 mg/dL	
Adjustment model	**HR (95% CI)**	**p-value**
All-cause mortality (n=606) *		
Model 1	0.83 (0.75-0.91)	0.0006
Model 2	0.80 (0.72-0.88)	0.00001
Non-cardiovascular mortality (n=438) *		
Model 1	0.81 (0.72-0.92)	0.001
Model 2	0.77 (0.69-0.87)	0.00003
3-point-MACE (n=510) *		
Model 1	0.89 (0.80-0.99)	0.03
Model 2	0.86 (0.77-0.96)	0.008
4-point-MACE (n=686) *		
Model 1	0.89 (0.81-0.97)	0.01
Model 2	0.86 (0.78-0.94)	0.002
Death and hospitalization due to heart failure (n=350) *		
Model 1	0.76 (0.67-0.87)	0.0002
Model 2	0.75 (0.66-0.86)	0.00004

HR, hazard ratio; CI, confidence interval

* Number of events refer to model 1.

Model 1: adjusted for age, sex, estimated glomerular filtration rate (longitudinal), ln- urine albumin-creatinine ratio (longitudinal);

Model 2: as model 1 plus serum albumin (longitudinal), LDL cholesterol (longitudinal), smoking status, diabetes mellitus, statin use (longitudinal), ln-triglycerides (longitudinal), body mass index (longitudinal), systolic and diastolic blood pressure (longitudinal) and cardiovascular disease at baseline

3-point-MACE (Major Adverse Cardiovascular Events) was defined as acute myocardial infarction (STEMI and NSTEMI), non-fatal stroke, fatal myocardial infarction, fatal coronary heart disease, sudden cardiac death, death from congestive heart failure and death due to non-hemorrhagic stroke;

4-point-MACE comprised all endpoints included in 3-point-MACE plus fatal peripheral ischemia, amputation due to peripheral vascular disease, surgical or percutaneous revascularization due to peripheral vascular disease

Hospitalization due to heart failure was defined as follows: hospitalization with either evidence of a reduced left ventricular ejection fraction (< 35%) or radiological evidence of pulmonary venous congestion, alveolar edema or presence of bilateral or right-sided pleural effusion with a presumed cardiac cause.