El Boustany and coworkers.

Plasma copeptin and chronic kidney disease risk in 3 European cohorts from the general population

SUPPLEMENTAL MATERIAL

Supplemental Acknowledgements

The DESIR Study Group. INSERM U1018: B. Balkau, P. Ducimetière, E. Eschwège; INSERM U367: F. Alhenc-Gelas; CHU D'Angers: Y Gallois, A. Girault; Centre de Recherche des Cordeliers, INSERM U1138, Bichat Hospital: F. Fumeron, M. Marre, R Roussel; CHU de Rennes: F. Bonnet; CNRS UMR8090, Lille: A. Fonnebond, S. Cauchi, P. Froguel; Centres d'Examens de Santé: Alençon, Angers, Blois, Caen, Chateauroux, Chartres, Cholet, Le Mans, Orléans, Tours; Institute de Recherche Médecine Générale: J. Cogneau; General practitioners of the region; Institute inter-Regional pour la Santé: C. Born, E. Caces, M. Cailleau, O Lantieri, J.G. Moreau, F. Rakotozafy, J. Tichet, S. Vol.

Supplemental Table 1: Characteristics of participants at baseline by CKD status during follow-up.

	CKD stage 3 (eGFR<60 ml/min/1.73 m^2)			KDIGO *"Certain drop in eGFR"*		
	progressors	**non-progressors**	**p**	**progressors**	**non-progressors**	**p**
n	1124	11909		1233	12364	
Age (years)	59 ± 7	49 ± 10	<0.0001	55 ± 10	50 ± 11	<0.0001
Sex: men	486 (43.2%)	5667 (47.6%)	0.005	544 (44.1%)	5771 (46.7%)	0.09
BMI (Kg/m^2)	26.1 ± 4.0	25.3 ± 3.9	<0.0001	26.0 ± 4.3	25.4 ± 3.9	<0.0001
SBP (mmHg)	142 ± 21	130 ± 18	<0.0001	139 ± 22	131 ± 18	<0.0001
DBP (mmHg)	84 ± 10	78 ± 11	<0.0001	82 ± 11	78 ± 11	<0.0001
Antihypertensive treatment	283 (25.2%)	1149 (9.6%)	<0.0001	275 (22.3%)	1326 (10.7%)	<0.0001
Use of ACE-I or ARBs	88 (7.8%)	349 (2.9%)	<0.0001	88 (7.1%)	400 (3.2%)	<0.0001
Use of diuretics	83 (7.4%)	296 (2.5%)	<0.0001	83 (6.7%)	358 (2.9%)	<0.0001
eGFR ($mL/min/1.73m^2$)	74 ± 9.9	92 ± 15	<0.0001	86 ± 17	88 ± 16	<0.0001
ACR (µg/mg creatinine)	9.3 (14.3)	6.8 (6.6)	<0.0001	9.3 (14.2)	6.8 (6.7)	<0.0001
FPG (mmol/L)	5.20 ± 1.33	5.03 ± 1.00	<0.0001	5.27 ± 1.55	5.03 ± 0.96	<0.0001
Glycaemic status: NFG/IFG/DM (%)	90.8 / 4.5 / 4.6	93.4 / 4.1 / 2.6	0.0002	89.5 / 4.8 / 5.8	93.4 / 4.2 / 2.5	<0.0001
Current smoker	282 (25.1%)	3415 (28.7%)	0.01	334 (27.1%)	3462 (28.0%)	0.50
Total cholesterol (mmol/L)	6.09 ± 1.05	5.71 ± 1.07	<0.0001	5.91 ± 1.14	5.76 ± 1.08	<0.0001
LDL cholesterol (mmol/L)	4.08 ± 0.95	3.73 ± 0.95	<0.0001	3.93 ± 1.03	3.78 ± 0.96	0.0004

HDL cholesterol (mmol/L)	1.43 ± 0.42	1.46 ± 0.42	0.03	1.41± 0.42	1.46 ± 0.42	<0.0001
Triglycerides (mmol/L)	1.40 ± 0.88	1.28 ± 0.97	<0.0001	1.37 ± 0.90	1.29 ± 0.96	<0.0001
Plasma copeptin (pmol/L)						
Men	7.23 (6.23)	5.68 (4.83)	<0.0001	6.97 (5.57)	5.76 (4.98)	<0.0001
Women	4.05 (3.40)	3.41 (2.81)	<0.0001	3.87 (3.30)	3.46 (2.87)	<0.0001

Data from pooled cohorts, expressed as mean ± SD or percent (number), except ACR and plasma copeptin expressed as median (interquartile range). Statistics for quantitative parameters are ANOVA with log-transformed data or Wilcoxon (rank sums) test (eGFR and ACR) and for qualitative variables, Pearson's chi-squared test. ACR: albumin to creatinine ratio assessed only in DESIR and PREVEND cohorts. FPG: fasting plasma glucose, NFG: normal fasting glucose, IFG: impaired fasting glucose, DM: diabetes mellitus. SBP, DBP: systolic and diastolic blood pressure, ACE-I: Angiotensin converting enzyme Inhibitors, ARBs: Angiotensin receptor blockers. eGFR was calculated using the CKD-EPI creatinine equation. Progression towards CKD defined as eGFR below 60 ml/min/1.73 m^2 (CKD stage 3) in at least one of the follow-up visits (non-progression defined as eGFR equal or above this value at all visits) or by the KDIGO criterion *"Certain drop in eGFR"*.

Supplemental Table 2. Incidence of eGFR outcomes during follow-up by tertiles of baseline plasma copeptin - Data from individual cohorts

	CKD stage 3 (eGFR<60 ml/min/1.73m^2)		KDIGO *"Certain drop in eGFR"*	
	HR (95% CI)	**p**	**OR (95% CI)**	**p**
DESIR				
T3 vs. T1	1.36 (1.02-1.83)	0.03	1.52 (1.14-2.04)	0.004
T3 vs. T2	1.06 (0.79-1.41)	0.69	0.93 (0.71-1.21)	0.59
T2 vs. T1	1.29 (0.97-1.73)	0.07	1.64 (1.24-2.18)	0.0005
Log_e[copeptin]	1.30 (1.06-1.60)	0.01	1.32 (1.07-1.63)	0.008
MDCS-CC				
T3 vs. T1	1.57 (1.27-1.94)	<0.0001	1.48 (1.16-1.91)	0.002
T3 vs. T2	1.25 (1.02-1.52)	0.03	1.14 (0.90-1.44)	0.28
T2 vs. T1	1.26 (1.01-1.57)	0.04	1.30 (1.01-1.68)	0.04
Log_e[copeptin]	1.23 (1.11-1.38)	<0.0001	1.32 (1.13-1.56)	0.0006
PREVEND				
T3 vs. T1	1.42 (1.08-1.89)	0.01	1.62 (1.25-2.10)	0.0003
T3 vs. T2	1.58 (2.22-1.07)	0.0006	1.45 (1.13-1.85)	0.003
T2 vs. T1	0.90 (0.67-1.22)	0.49	1.12 (0.85-1.47)	0.44
Log_e[copeptin]	1.30 (1.08-1.56)	0.006	1.36 (1.15-1.61)	0.0003

Copeptin tertiles are cohort and sex-specific. Cox regression analyses and logistic regression analyses performed separately in individual cohorts. Hazard ratio (HR) and Odds ratio (OR) with 95% confidence interval (CI) for tertiles of plasma copeptin and for 1 unit of log_e[copeptin], adjusted for sex, age and eGFR at baseline, plus duration of follow-up for KDIGO "Certain drop in eGFR" outcome.

Supplemental Table 3: Incidence of eGFR outcomes (CKD-EPI cystatin C equation) during follow-up in the PREVEND cohort by tertiles of plasma copeptin at baseline

	CKD stage 3 (eGFR<60 ml/min/1.73m^2)		**KDIGO *"Certain drop in eGFR"***		**Rapid kidney function decline**	
Sex-specific tertiles	**No**	**Yes**	**No**	**Yes**	**No**	**Yes**
T1	1787 (93.1)	133 (6.9)	1766 (90.1)	195 (9.9)	1866 (94.5)	108 (5.5)
T2	1745 (90.4)	185 (9.6)	1778 (89.3)	214 (10.7)	1904 (94.5)	111 (5.5)
T3	1574 (84.4)	226 (12.6)	1667 (86.2)	268 (13.9)	2549 (85.8)	159 (8.2)
	HR (95% CI)	***P***	**OR (95% CI)**	**p**	**OR (95% CI)**	**p**
T3 vs. T1	1.35 (1.09-1.68)	0.006	1.29 (1.05-1.60)	0.02	1.57 (1.21-2.26)	0.0009
T3 vs. T2	1.20 (0.98-1.45)	0.07	1.29 (1.05-1.58)	0.01	1.39 (1.07-1.81)	0.01
T2 vs. T1	1.13 (0.90-1.42)	0.28	1.00 (0.81-1.25)	0.97	1.13 (0.85-1.50)	0.40
Log_e[copeptin]	1.16 (1.01-1.33)	0.04	1.19 (1.04-1.37)	0.01	1.27 (1.07-1.52)	0.007

Data are n (%). Copeptin tertiles are cohort and sex-specific. Hazard ratio (HR) and Odds ratio (OR) with 95% confidence interval (CI) for sex-specific tertiles of plasma copeptin and for 1 unit of log_e[copeptin], adjusted for sex, age and eGFR at baseline, plus duration of follow-up (for KDIGO "Certain drop in eGFR" and rapid kidney function decline criteria only).

Supplemental Table 4: Incidence of eGFR outcomes during follow-up in men by tertiles of plasma copeptin at baseline

	CKD stage 3 (eGFR<60 ml/min/1.73m^2)		KDIGO *"Certain drop in eGFR"*		Rapid kidney function decline	
Sex-specific tertiles	**No**	**Yes**	**No**	**Yes**	**No**	**Yes**
T1	1985 (94.2)	121 (5.8)	1994 (93.5)	139 (6.5)	2066 (96.9)	67 (3.1)
T2	1894 (92.2)	160 (7.8)	1914 (91.0)	190 (9.0)	2031 (96.5)	73 (3.5)
T3	1787 (89.7)	205 (10.3)	1862 (89.6)	215 (10.4)	1970 (94.9)	107 (5.2)
	HR (95% CI)	***P***	**OR (95% CI)**	***P***	**OR (95% CI)**	**p**
T3 vs. T1	1.54 (1.14-1.94)	0.0001	1.64 (1.30-2.06)	<0.0001	1.70 (1.23-2.37)	0.008
T3 vs. T2	1.30 (1.06-1.60)	0.01	1.15 (0.93-1.43)	0.19	1.43 (1.04-1.96)	0.03
T2 vs. T1	1.19 (0.94-1.51)	0.15	1.42 (1.13-1.80)	0.003	1.20 (0.84-1.70)	0.31
Log_e[copeptin]	1.39 (1.20-1.62)	<0.0001	1.35 (1.16-1.56)	<0.0001	1.37 (1.10-1.71)	0.005

Data are n (%). Copeptin tertiles are cohort and sex-specific. Cox regression analysis and logistic regression analyses performed in pooled cohorts. Hazard ratio (HR) and Odds ratio (OR) with 95% confidence interval (CI) for sex-specific tertiles of plasma copeptin and for 1 unit of log_e[copeptin], adjusted for cohort membership, sex, age and eGFR at baseline, plus duration of follow-up (for KDIGO "Certain drop in eGFR" and rapid kidney function decline criteria only). eGFR was calculated using the CKD-EPI creatinine equation.

Supplemental Table 5: Incidence of eGFR outcomes during follow-up in women by tertiles of plasma copeptin at baseline

	CKD stage 3 (eGFR<60 ml/min/1.73m^2)		**KDIGO *"Certain drop in eGFR"***		**Rapid kidney function decline**	
Sex-specific tertiles	**No**	**Yes**	**No**	**Yes**	**No**	**Yes**
T1	2146 (92.3)	179 (7.7)	2254 (92.5)	184 (7.5)	2357 (96.7)	81 (3.3)
T2	2104 (91.2)	204 (8.8)	2204 (90.3)	237 (9.7)	2326 (95.3)	115 (4.7)
T3	1993 (88.7)	255 (11.3)	2136 (88.9)	268 (11.2)	2267 (94.3)	137 (5.7)
	HR (95% CI)	***P***	**OR (95% CI)**	***P***	**OR (95% CI)**	**p**
T3 vs. T1	1.46 (1.21-1.78)	<0.0001	1.60 (1.31-1.96)	<0.0001	1.82 (1.36-2.46)	<0.0001
T3 vs. T2	1.27 (1.06-1.53)	0.01	1.20 (0.99-1.44)	0.06	1.12 (0.85-1.47)	0.42
T2 vs. T1	1.15 (0.94-1.41)	0.18	1.34 (1.09-1.65)	0.005	1.63 (1.21-2.21)	0.001
Log_e[copeptin]	1.33 (1.17-1.51)	<0.0001	1.45 (1.27-1.65)	<0.0001	1.48 (1.22-1.80)	<0.0001

Data are n (%). Copeptin tertiles are cohort and sex-specific. Cox regression analysis and logistic regression analyses performed in pooled cohorts. Hazard ratio (HR) and Odds ratio (OR) with 95% confidence interval (CI) for sex-specific tertiles of plasma copeptin and for 1 unit of log_e[copeptin], adjusted for cohort membership, sex, age and eGFR at baseline, plus duration of follow-up (for KDIGO "Certain drop in eGFR" and rapid kidney function decline criteria only). eGFR was calculated using the CKD-EPI creatinine equation.