The prognostic value of „estimated albumin excretion rate“ (eAER) versus urine albumin/creatinine ratio (ACR) for predicting adverse cardiovascular outcome among patients with chronic kidney disease G 2 – G 4

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Background / Hypotheses

- 24 h measured albumin excretion is used as gold standard for quantifying albuminuria but it is considered to be too cumbersome for clinical practice.
- ➢ KDIGO guidelines recommend using the albumin-creatinine ratio (ACR) in spot urine samples.
- However, ACR underestimates 24 h albumin excretion in muscular individuals.
- Equations were recently developed that adjust ACR for muscle mass surrogates (sex, age, ethnicity) and yield an “estimated albumin excretion rate” (eAER).
- The prognostic implication of substituting eAER for ACR is unknown hitherto.

Methods / Results

- The CARE FOR HOMe study is an ongoing prospective cohort study which recruited 444 patients with CKD G 2 – G 4 between 2008 and 2012.
- ACR was quantified from a morning spot urine sample.
- eAER was calculated according to the Ellam equation (Box).
- Patients were classified in KDIGO albuminuria categories:

  A1 (< 30 mg), A2 (30 – 300 mg), or A3 (> 300 mg).
- 379 patients had complete three year follow-up for cardiovascular events (pre-defined as acute myocardial infarction, stroke, amputation above the ankles, any surgical or interventional coronary/cerebrovascular or peripheral-arterial revascularization, or death of any causes).
- NRI_{events} and $NRI_{non\text{-}events}$ were calculated for the reclassification to different albuminuria categories by eAER *versus* ACR.

	Total cohort	CVE event	No CVE event	p
Age (years)	66 ± 12	71 ± 9	64 ± 13	< 0.001
Gender (female)	148 (39 %)	25 (31 %)	123 (41 %)	0.075
Body mass index (kg/m²)	30 ± 5	30 ± 5	30 ± 5	0.362
Diabetes mellitus (yes)	148 (39 %)	43 (52 %)	105 (35 %)	0.007
Systolic blood pressure (mmHg)	154 ± 24	154 ± 24	153 ± 26	0.889
Diastolic blood pressure (mmHg)	87 ± 13	81 ± 13	88 ± 12	< 0.001
Smoking (yes)	35 (9 %)	9 (11 %)	26 (9 %)	0.522
Prevalent CVD (yes)	122 (32 %)	55 (67 %)	67 (23 %)	< 0.001
LDL-Cholesterol (mg/dl)	117 ± 36	107 ± 33	120 ± 36	0.005
Cholesterol (mg/dl)	193 ± 43	178 ± 39	197 ± 43	< 0.001
Phosphorus (mg/dl)	3.4 ± 0.7	3.5 ± 0.7	3.4 ± 0.7	0.075
Albuminuria (mg/g)	40 (8 –193)	66 (22 – 316)	32 (7 – 152)	0.298
CRP (mg/l)	2.8 (1.2 –5.4)	4.0 (1.8 – 9.2)	2.6 (1.1 – 4.8)	0.061

Table 1: Baseline characteristics of CARE FOR HOMe participants. Indicated are mean ± standard deviation, or patient numbers (percentages). Because of skewed distribution, albuminuria and CRP are given as median (interquartile range).

- 82 patients suffered a cardiovascular event during the three year follow-up time
- 12 out of these 82 patients were re-classified to a higher AU category, and only one patient to a lower AU category.
- ➢ NRI_{event} 13,4% (CI 95%: 5.2 to 21.6)
- 297 patients had no CVE during FU
- 13 out of these 297 patients were reclassified to a higher, and two patient to a lower AU category.
- ➢ $NRI_{no\ event}$ -3,7% (CI 95%: -8.2 to -1.2)

Results

Ellam Equation for Estimated Creatinine Excretion Rate

$eCER_{Ellam}$ (mg/d) =

Male/black:	1413.9	+ (23.2 x age)	– (0.3 x age²)
Female/black:	1148.6	+ (15.6 x age)	– (0.3 x age²)
Male/nonblack:	1307.3	+ (23.1 x age)	– (0.3 x age²)
Female/nonblack:	1051.3	+ (5.3 x age)	– (0.1 x age²)

Estimated albumin excretion rate (mg/d) = ACR (mg/mg) * $eCER_{Ellam}$ (mg/d)

Box: Ellam equations for eCER and eAER

		Events			No events		
		eAER			eAER		
		A1	A2	A3	A1	A2	A3
ACR	A1	21 (26%)	9 (11%)	0	141 (48%)	6 (2%)	0
	A2	0	27 (33%)	3 (4%)	2 (1%)	87 (30%)	7 (2%)
	A3	0	1 (1%)	21 (26%)	0	0	54 (18%)
		NRI_{event} = 13.4% (5.2 to 21.6)			$NRI_{noevent}$ = -3.7% (-8.2 to -1.2)		

Table 2: Reclassification matrices for CARE FOR HOMe participants with and without CVE (patients reclassified to a more advanced AU category are given in red, and patients reclassified to a less advanced AU category in yellow colour). 95% confidence intervals are shown in parentheses.

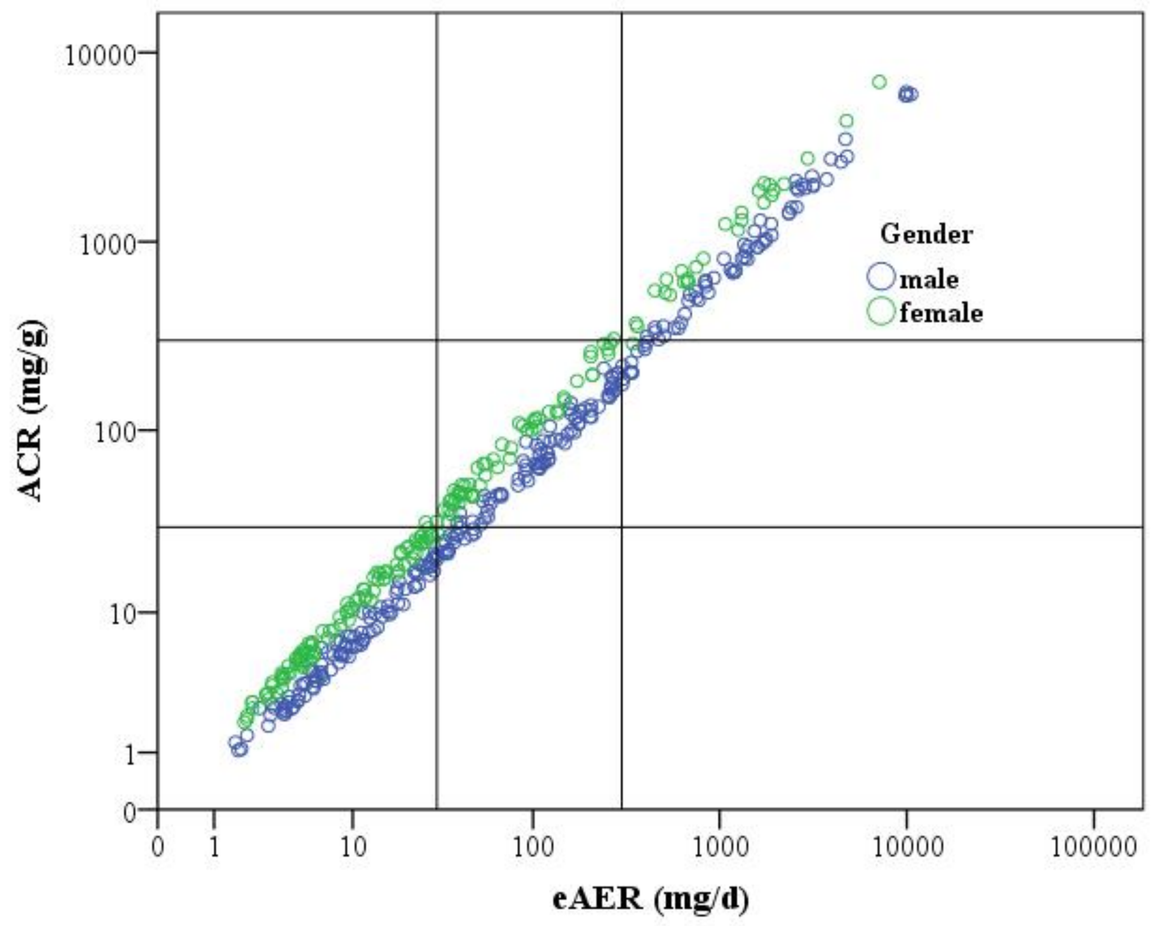

Figure 1: Correlation between the albumin-creatinine ratio (ACR) and the estimated albumin excretion rate (eAER) in CARE FOR HOMe study participants.

Discussion

Our findings underlines that eAER outperforms ACR as a predictor of CVE among patients with CKD G 2 – G 4.

We propose the substitution of eAER for ACR in clinical nephrology.