Prognostic value of the „estimated albumin excretion rate“ to predict renal events in chronic kidney disease

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Background / Hypothesis

- Albuminuria predicts progression of chronic kidney disease (CKD), cardiovascular morbidity and mortality.
- 2013 Kidney Disease: Improving global outcomes (KDIGO) guidelines recommend estimating albuminuria from spot urine samples by using the urine albumin-creatinine ratio (ACR).
- Creatinine excretion substantially varies inter-individually, as it strongly associates with muscle mass and metabolism.
- ACR particularly underestimates albuminuria in young and male individuals.
- Several equations were recently introduced which estimate individual creatinine excretion rate (CER) based on individual's sex, ethnicity and age, and multiplying CER with ACR yields an estimated albumin excretion rate (eAER).
- In cross-sectional analyses, 24 h albuminuria stronger associates with eAER than with ACR.

Hypothesis: In longitudinal studies eAER better predicts CKD progression than ACR.

Methods

- 444 CKD patients (stage G2 – G4) were recruited from 2008 – 2012.
- Urine albumin and creatinine were measured from morning spot urine, and ACR and $eAER_{Ellam}$ were calculated.
- For both ACR and eAER, each patient was classified into an albuminuria category, defined by KDIGO as A1 (< 30 mg/g), A2 (30 – 300 mg/g), A3 (> 300 mg/g).
- The renal endpoint was pre-defined as need for renal replacement therapy (RRT) or halving of eGFR within three years after recruitment.

Results

- By January 2015, 357 participants had information on three years outcome.
- The use of eAER reclassified 22 participants in a more advanced albuminuria category, 3 in a less advanced albuminuria category, 332 remained in the same albuminuria category.
- 33 participants reached the predefined renal endpoint.

	total cohort (n=357)	no event (n=324)	event (n=33)	p value
age [years]	65.2 ± 12.4	65.2 ± 12.5	65.2 ± 11.1	0.99
gender (female)	141 (39.4 %)	128 (42.4 %)	13 (39.4 %)	0.673
diabetes (yes)	140 (39.1 %)	111 (36.8 %)	29 (87.9 %)	0.038
systolic BP [mmHg]	154 ± 24	153 ± 24	161 ± 28	0.155
diastolic BP [mmHg]	87 ± 13	87 ± 13	86 ± 14	0.614
BMI [kg/m²]	30 ± 5	30 ± 5	30 ± 5	0.354
total cholersterol [mg/dl]	194 ± 43	194 ± 42	190 ± 51	0.667
LDL-cholesterol [mg/dl]	117 ± 36	117 ± 35	117 ± 38	0.971
albuminuria [mg/mg]	37 [8; 202]	29 [7; 137]	370 [99; 1958]	0.003
eAER [mg/d]	41 [10; 263]	37 [9; 188]	472 [156; 2698]	0.003
eGFR [ml/min/1,73 m²; CKD-EPI $_{creat-cys}$]	45 ± 18	46 ± 17	24 ± 10	< 0.001

Table 1: Baseline characteristics of the total cohort and of patients stratified by subsequent renal events.
BP: Blood pressure; BMI: body mass index; LDL-cholesterol: low-density lipoprotein cholesterol; eAER: estimated albuminuria excretion rate, eGFR: estimated glomerular filtration rate.

Results

- Among 33 participants with renal events, one patient was reclassified in a more advanced albuminuria category, one participant in a less advanced albuminuria category and 31 participants remained in the same albuminuria category, resulting in a Net Reclassification Index (NRI) $_{event}$ of 0 %.
- Among 324 participants who did not suffer a renal event, eAER reclassified 21 in a more advanced albuminuria category, two in a less advanced albuminuria category, and 301 remained in the same albuminuria category. This leads to a NRI $_{non-event}$ of -5.9 %.

no event (n = 324)	reclassification towards a less advanced albuminuria category	2
	no reclassification	301
	reclassification towards a more advanced albuminuria category	21
event (n = 33)	reclassification towards a less advanced albuminuria category	1
	no reclassification	31
	reclassification towards a more advanced albuminuria category	1

Table 2: Reclassification from urine albumin-creatinine ratio (ACR) based to estimated albumin-creatinine ratio based albuminuria categories. NRI $_{event}$ = 0 %; NRI $_{non-event}$ = -5.9 %.

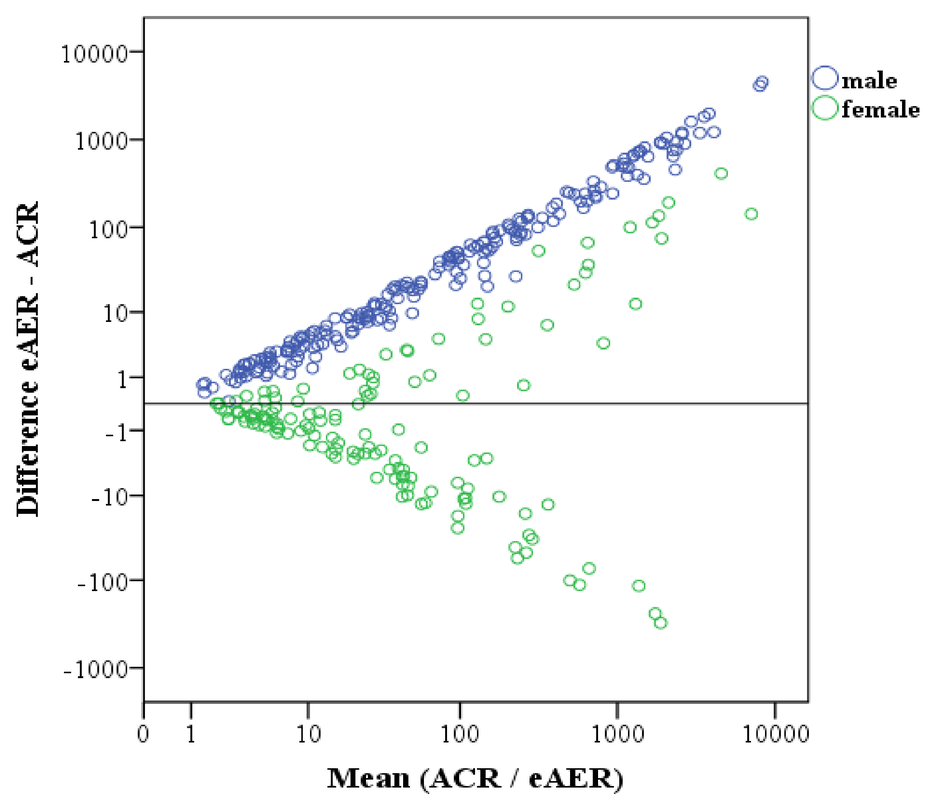

Figure 1: Bland-Altman-Diagram: in many female participants, eAER yields lower estimates of albuminuria than ACR; in all male participants, eAER yields higher estimates of albuminuria than ACR.

Conclusion

- Substituting eAER for ACR re-classifies one out of 16 CKD patients to a more advanced KDIGO albuminuria category.
- Up-classification to more advanced albuminuria affects both patients who subsequently suffer renal events, as well as patients who do not suffer renal events.
- Data on cardiovascular outcome are presented separately (L. Bauer, FP 251).

Take HOMe message / Glossary

- The use of eAER for stratifying CKD patients into albuminuria categories fails to improve renal outcome prediction; however, it improves cardiovascular outcome prediction (L. Bauer, FP 251).

ACR: urine albumin (mg/l) / urine creatinine (mg/l)

eAER(mg/d): ACR (mg/mg) * $eCER_{Ellam}$(mg/d)

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

1413.9 + (23.2 x age) – (0.3 x age²) in black males

1148.6 + (15.6 x age) – (0.3 x age²) in black females

1307.3 + (23.1 x age) – (0.3 x age²) in nonblack males

1051.3 + (5.3 x age) – (0.1 x age²) in nonblack females