

Albuminuria or creatinine-based eGFR, a survival-based classification system: NHANES III

Robert Foley, MB, MSc, Changchun Wang, MS, Allan Collins, MD, FACP

United States Renal Data System, Minneapolis Medical Research Foundation, University of Minnesota Twin Cities

Introduction

- Low GFR and high urinary ACR levels are common in US adults and are associated with adverse health outcomes.
- The utility of screening GFR and ACR levels is unknown.
- Ideally, the threshold values chosen to define normal/abnormal would be a good discriminator of death or survival: "normals" would have high survival rates and "abnormals" would have high mortality rates.
- Expressed differently, the threshold value would have a combination of high specificity, high sensitivity and a high C-statistic in binary logistic models with death or survival as outcome.
- In addition, to be useful from a public health perspective, GFR and ACR thresholds should add prognostic discrimination beyond that obtained with other typical screening tests, such as blood pressure, LDL, HDL and glucose levels.

Methods

- NHANES III was a probability-based sample of the US civilian population (1988-1994). As classic cardiovascular risk factors were considered, subjects ≥ 20 years with fasting blood tests were included (n = 6,165).
- The CKD-EPI formula was used to estimate GFR from serum creatinine.
- Vital status was ascertained through December 31, 2000. To identify GFR and ACR levels maximally discriminating between survival and death, C-statistics were computed with logistic regression for each whole-number thresholds between 30 and 120 for GFR and between 1 and 100 for ACR. As the discriminatory power of many variables might reflect correlations with other variables, most notably age, we constructed classification and regression trees (CART) for death/survival that also considered age and classic risk factors.
- NHANES-recommended weights were used to generate national parameter estimates.

Results

- The characteristics of US adults (1988-1994) are shown in Table 1.
- Mean GFR and median ACR levels were 99.4 and 5.7, respectively.
- Table 2 shows odds ratios and C-statistics for death/survival. As continuous variables, GFR and ACR levels were the 2nd and 4th greatest discriminators for death/survival.
- For the overall population, the threshold GFR and ACR values with the best discrimination for death/survival were 95 mL/min/1.73 m² and 8 mg/g, respectively (Figure 1).
- With CART, age >58 was the 1st discriminator of death/survival and systolic blood pressure >119 was the sole discriminator of death/survival for age ≤ 58 . For age >58, ACR >12 was the greatest discriminator. For age >58 with ACR ≤ 12 , GFR ≤ 63 was the best discriminator, while for age >58 with ACR >12, GFR ≤ 66 was the best discriminator.

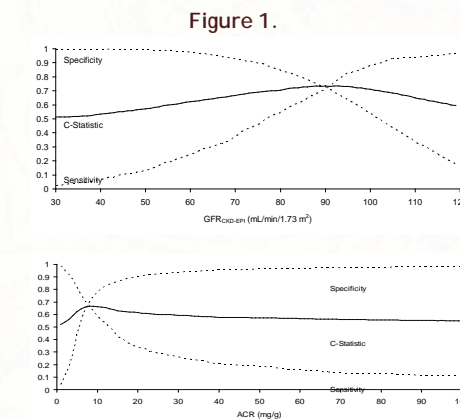
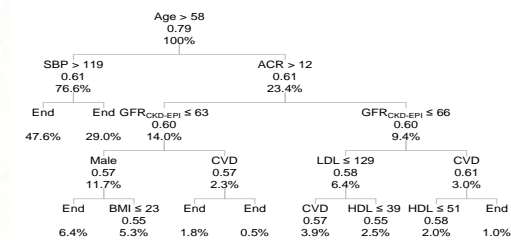
Table 1. US Adult Population (1988-1994)

GFR	99.4 (SE 0.7)
ACR, median (IQR)	5.7 (3.7, 9.8)
Age	44.9 (0.6)
Female, %	53.2 (0.9)
Race, %	
White	78.3 (1.4)
African American	9.4 (0.6)
Hispanic	5.0 (0.4)
Other	7.4 (1.05)
Hypertension, %	23.6 (0.9)
Diabetes, %	4.2 (0.3)
CVD, %	5.4 (0.5)
Current smoker, %	27.1 (1.0)
Systolic BP	121.9 (0.5)
Diastolic BP	73.8 (0.2)
BMI	26.6 (0.2)
LDL	127.9 (0.9)
HDL	50.4 (0.4)
Glucose	98.0 (0.8)

Table 2. Mortality: C-statistics and Odds Ratios

	C-Statistic	Odds Ratio (95% CI)
Age	0.87	1.10 (1.09, 1.11)
GFR	0.80	0.95 (0.94, 0.95)
Systolic BP	0.74	1.05 (1.05, 1.06)
Log ACR	0.71	1.91 (1.70, 2.14)
Glucose	0.63	1.01 (1.01, 1.01)
LDL	0.55	1.01 (1.01, 1.01)
Diastolic BP	0.51	1.01 (1.00, 1.03)
HDL	0.49	1.00 (0.99, 1.01)
BMI	0.47	1.01 (0.99, 1.03)

Figure 2



Conclusions

- GFR and ACR thresholds demonstrate prognostic discrimination close to optimal age thresholds, and with the exception of systolic blood pressure, higher than those of commonly-advocated public health screening measures.
- ACR and GFR carry prognostic discrimination in older adults.
- Optimum ACR thresholds are substantially less than 30 mg/g.