Loss of Kidney Function in Older Adults: Common but Limited. The Framingham Heart Study

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Introduction

- Current guidelines suggest that creatinine-based estimates of glomerular filtration rate (GFR) may help to identify individuals at risk of advanced kidney disease.
- The objective of this study was to evaluate the utility of creatinine-based estimates for longitudinal evaluation of kidney function in older community dwelling adults.

Methods

- We used the limited-access Framingham Heart Study data set to study participants at the 14th and 15th biennial examinations.
- Four-variable MDRD Study to calculate GFR. Associations of calibrated creatinine levels from NHANES III were used to standardize creatinine levels between examinations.
- Generalized linear models were used to evaluate associations of change of GFR between examinations.
- The observed population mean and standard deviation and the correlation between measurements were used to estimate the regression-to-the-mean effect associated with two measurements, when a threshold eGFR of 60 mL/min/1.73 m^2 was used to identify 'cases'.

Results

- The mean (standard deviation) GFR values at the 14th and 15th biennial examinations were 74.5 (21.7) and 73.3 (22.5), respectively.
- Changes in GFR and initial GFR were related, suggesting that regression to the mean occurred between examinations (R^2 0.37, β -0.78 [95% confidence interval -0.81,-0.74], P < 0.0001).
- When an initial GFR of 60 was used as a threshold, GFR decreased from 83.5 (82.8, 84.2) to 75.5 (74.5, 76.5) in those with initial GFR ≥ 60 and increased from 49.6 (48.3, 50.8) to 65.4 (63.7,67.2) (P < 0.0001) in those with GFR < 60.
- The regression-to-the mean effect for a threshold GFR < 60 was +22.0 mL/min/1.73 m^2 and 8 measurements would have been needed to reduce this effect to < 5 mL/min/1.73 m^2.

Table 1

Baseline Characteristics at 14th Biennial Examination

Mean GFR ml/min	74.5
GFR < 60 ml/min	26.2%
Albuminuria	4.2%
Age > 66	48.3%
Female	58.5%
BMI ≥ 30 kg/m^2	15.5%
Current smoker	29.3%
Diabetes	6.6%
Hypertension	53.0%
Cholesterol ≥ 194 mg/dl	82.1%
W.H.O. Anemia	0.9%

Table 2

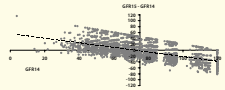
Changes in GFR between the 14th and 15th examinations

	Unadjusted	Adjusted[a]
All	-2.1 (SD 27.7)	
GFR < 60	P < 0.0001	P < 0.0001
No	-8.0 (-9.2,-6.8)	-8.4 (-9.6,-7.2)
Yes	15.9 (15.8,17.9)	17.8 (15.7,20.0)
Albuminuria	P = 0.1071	P = 0.0162
No	-1.9 (-3.0,-0.7)	-1.8 (-2.8,-0.7)
Yes	-6.7 (-12.4,-0.9)	-8.6 (-14.0,-3.1)
Age	P = 0.7103	P = 0.0030
≤ 66	-2.2 (-3.7,-0.8)	-0.5 (-1.9,0.9)
> 66	-1.8 (-3.5,-0.2)	-3.9 (-5.5,-2.3)
Gender	P = 0.0155	P < 0.0001
Male	-0.4 (-2.1,1.3)	0.8 (-0.9,2.4)
Female	-3.2 (-4.6,-1.8)	-4.0 (-5.4,-2.6)
BMI (kg/m^2)	P = 0.7058	P = 0.6652
< 30	-2.1 (-3.4,-0.9	-2.1 (-3.2,-1.0)
≥ 30	-1.6 (-4.3,1.2)	-1.5 (-4.1,1.1)
Current smoker	P = 0.1145	P = 0.1023
No	-2.6 (-3.9,-1.3)	-2.6 (-3.8,-1.4)
Yes	-0.7 (-2.7,1.4)	-0.6 (-2.6,1.3)
Diabetes	P = 0.0234	P = 0.0085
No	-1.7 (-2.9,-0.6)	-1.7 (-2.7,-0.6)
Yes	-7.0 (-11.4,-2.6)	-7.4 (-11.6,-3.3)
Hypertension	P = 0.0429	P = 0.0310
No	-0.9 (-2.5,0.7)	-0.8 (-2.3,0.7)
Yes	-3.2 (-4.7,-1.6)	-3.2 (-4.6,-1.7)
High Cholesterol	P = 0.0185	P = 0.0496
No	0.8 (-1.8,3.5)	0.3 (-2.2,2.8)
Yes	-2.7 (-3.9,-1.5)	-2.5 (-3.6,-1.4)
W.H.O. Anemia	P = 0.4653	P = 0.3736
No	-2.1 (-3.2,-1.0)	-1.9 (-3.0,-0.9)
Yes	0.4 (-6.3,7.1)	-4.9 (-11.3,1.5)

a. Adjusted for all the variables shown in the first column

Figure 1

Scatter plot of change in GFR between examinations against GFR at examination 14 (R=0.37, P < 0.0001).



The regression line intersected the X axis at 72. 2 mL/min/1.73 m^2. Thus, GFR estimates typically declined with initial GFR above this value and typically increased with lower GFR values. This plot suggests prominent regression to the mean effects. When the population mean and standard deviation 75.1 of 21.7 at the 14th examination and the correlation co-efficient between GFR values at the 14th and 15th examinations (0.21) were considered, a threshold GFR value < 60 was associated with an estimate for regression to the mean of + 22.0mL/min/1.73 m^2. In other words, on the basis of regression to the mean, alone, GFR would be expected to increase by 22.0 mL/min/1.73 m^2 at the next examination, among individuals with values < 60 mL/min/1.76 m^2 at the previous examination; 8 measurements would have been required to reduce the regression-to-the-mean effect to less than 5 mL/min/1.73 m^2.

Conclusions

- Regression-to-the mean effects may limit the utility of creatinine-based estimates of GFR for identifying subjects at risk of progression to end-stage renal disease.

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