Creatinine Clearance (CrCl) as a Measure of Kidney Function

Measures and Methods

Samples from years 2009 to 2012 in the National Health and Nutrition Examination Survey (NHANES) dataset was used; and all analyses were weighted by the 4-year sample weights accounting for the survey design (1). To avoid a glomerular filtration rate (GFR) estimating method that includes age as a factor and to allow comparison between people of different body sizes, we used the creatinine clearance (CrCl) adjusted for body surface area as follows: A, W and H are used to denote age (in years), weight (in kgs) and the height (in cms) of a subject. Let S_{cr} be the serum creatinine concentration (mg/dL), and U_{cr} and U_{rate} be the urine creatinine concentration (mg/dL) and the urine flow rate (mL/min). A body-surface-area-corrected creatinine clearance (in ml/min per 1.73 m^2) is defined as $CrCl = U_{cr} / S_{cr} \times U_{rate} \times 1.73/(0.007184 \times W^{0.425} \times H^{0.725})$.

Subjects with outlying values of CrCl, defined as CrCl greater than 228.3 mL/min determined using the box-plot rule, were excluded (N = 407) from the analysis. All remaining subjects (N = 11,318) were divided into 8 age groups: 12 to 19, 20 to 29, 30 to 39, 40 to 49, 50 to 59, 60 to 69, 70 to 79 and > 80 years of age, and the average of CrCl was calculated for each age group. Because exact ages greater than 80 were not recorded in the NHANES, regression analyses were performed using the subjects with age 12 to 79 (N = 10,755). Age-group average and the regression results were also obtained on a subsample excluding those with diabetes and/or hypertension (N = 6,985/6,895 with/without those older than 80 years). Under the concept that hypertrophic adaptation of remaining nephrons would mask reduced renal function until nephron reserve had been exhausted thereby causing an acceleration of decrease in the curve, a quadratic regression equation was fitted to the data. The fitted regression curve was project till it reached 5 ml/min per 1.73 m^2 (assumed to be end stage), to get the half-life of a native kidney.

Mean CrCl (mL/min per 1.73 m^2) by Age Groups

Averages of CrCl (mL/min per 1.73 m^2) for each age group are plotted in Figure 1 for all subjects (left panel) and only the subjects without diabetes or hypertension (right panel). Both panels exhibit a similar pattern such that the difference between adjacent bars becomes larger as age increases.

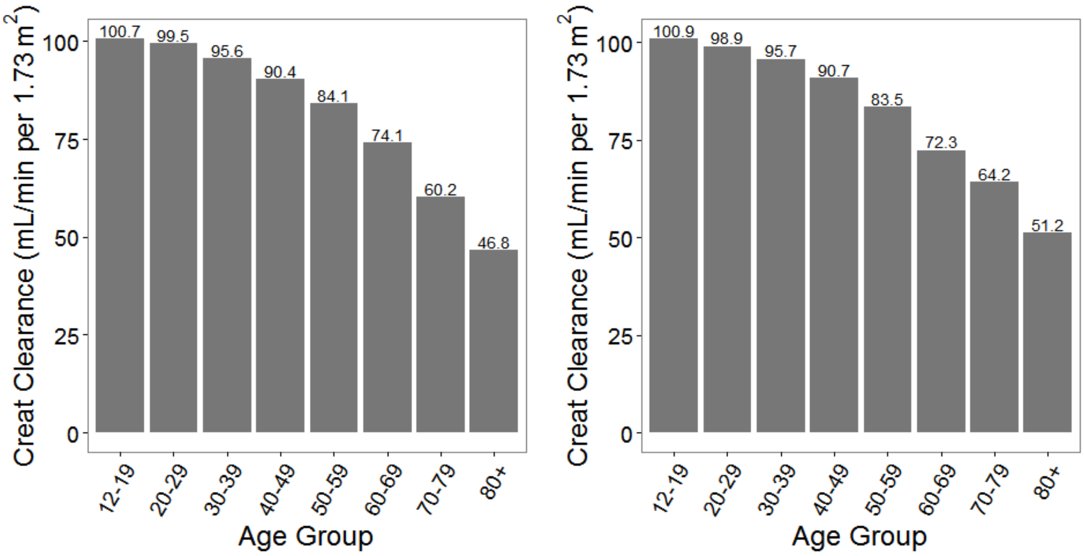

Figure 1. Average creatinine clearance for each age group. Left panel: all subjects; Right panel: only subjects without diabetes or hypertension.

Regression Analyses of CrCl on Age

We fitted quadratic regression of CrCl on age: $CrCl = \beta_0 + \beta_1 Age + \beta_2 Age^2$. In the regression, age was centered at the overall average age (42.2 years) so that the coefficients were more interpretable. The parameter β_2 measures the extent to which the decrease of CrCl is accelerating.

1. Curve fitting for all subjects.

Table 1 lists the estimated regression coefficients from the quadratic regression. The decrease of $CrCl_c$ is 0.607 mL/min/1.73 m^2 per year around the average age, and it will be 0.721 mL/min/1.73 m^2 per year ten years later and 0.836 mL/min/1.73 m^2 per year 20 years later and so on.

	Estimate	Std. Error	p value
β_0	92.3	0.586	<0.001
β_1	-0.607	0.0234	<0.001
β_2	-0.0115	0.0013	<0.001

Table 1. Regression coefficient estimates for all subjects. Corresponding standard errors and p values are also given.

The fitted curve gives a projected average half-life at CrCl of 5 mL/min/1.73 m^2 (presumed to be ESKD) for all subjects of 107 (95% confidence interval ranges from 103 years to 113 years). The fitted curve is plotted in Figure 2 along with the average CrCl values for each age group.

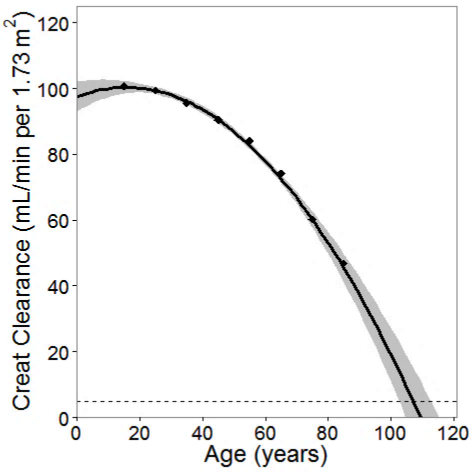

Figure 2. Fitted quadratic equation to the curve of CrCl vs. age. The dashed line indicates CrCl of 5 mL/min/1.73 m^2. The dots are the average CrCl for each age group centered at 15, 25, 35, 45, 55, 65, 75 and 85 years. The solid line is the regression fitted curve. Shaded area

stands for the 95% confidence interval.

2. Curve fitting for only the subjects without diabetes or hypertension.

Table 2 lists the estimated regression coefficients from the quadratic regression. The decrease of CrCl is 0.602 mL/min/1.73 m^2 per year around the average age, and it will be 0.700 mL/min/1.73 m^2 per year ten years later and 0.800 mL/min/1.73 m^2 per year 20 years later and so on, all of which are slightly slower than the overall sample.

	Estimate	Std. Error	p value
β_0	91.7	0.758	<0.001
β_1	-0.602	0.0351	<0.001
β_2	-0.0099	0.0020	<0.001

Table 2. Regression coefficient estimates for all subjects. Corresponding standard errors and p values are also given.

The fitted curve gives a projected average half-life at CrCl of 5 mL/min/1.73 m^2 (presumed to be ESKD) of 110 (95% confidence interval ranges from 102 years to 123 years) for the subjects without diabetes or hypertension. The fitted curve is plotted in Figure 3 along with the by-group average CrCl values.

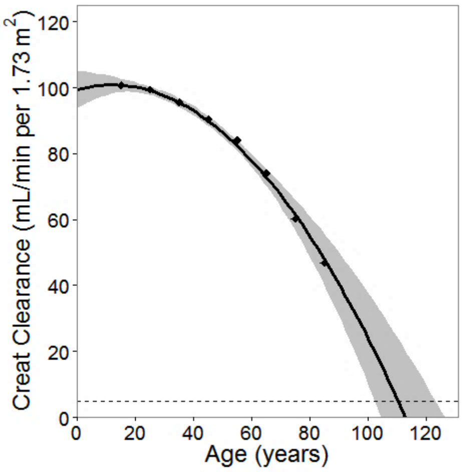

Figure 3. Fitted quadratic equation to the curve of CrCl vs. age. The dashed line indicates CrCl of 5 mL/min/1.73 m^2. The dots are the average CrCl for each age group centered at 15, 25, 35, 45, 55, 65, 75 and 85 years. The solid line is the regression fitted curve. Shaded area stands for the 95% confidence interval.

References

(1) Johnson, Clifford L., et al. "National health and nutrition examination survey: analytic guidelines, 1999-2010." *Vital and health statistics. Series 2, Data evaluation and methods research* 161 (2013): 1-24.