Discrepancies in creatinine clearance in centenarians when calculated by two different mathematical formulas

Sir,

It is widely accepted that the glomerular filtration rate (GFR) and the renal blood flow decrease with aging. On the other hand, even after a significant fall in the GFR, the plasma level of creatinine may be normal in elderly patients due to a simultaneous decline in muscle mass. For the estimation of renal function (GFR), the Cockcroft–Gault formula (CG) is routinely used [1]. However, nowadays there are growing doubts about its accuracy, especially in individuals with normal or near normal renal function [2,3]. Recently, Baraekay et al. [4] presented a new formula (CB) for the elderly (CB = 1.2[100/PGr] + 88−age).

We calculated the creatinine clearance according to both formulas mentioned above in 81 centenarian subjects (71 females and 10 males). The mean age of studied subjects was 101.7 ± 1.7 years (range 100–111 years: females, 101.8 ± 1.9 years; males, 101.8 ± 1.0 years). The study is part of the Polish Centenarians Program (co-ordinated by the International Institute of Molecular and Cell Biology in Warsaw), that was developed to assess the environmental and genetic factors associated with aging in Poland. The study was based on a questionnaire, physical examination and hematological blood tests. This study included only four subjects with a small increase in plasma creatinine: one male, 1.57 mg/dl (normal values for males, 0.7–1.5 mg/dl) and three females with plasma creatinine between 2.03 and 2.12 mg/dl (normal values for females, 0.6–1.3 mg/dl). All other studied subjects had plasma creatinine within the normal range.

Among subjects with normal plasma creatinine, when CG was used 13 individuals had a GFR between 10 and 20 ml/min (all of them were females). However, when CB was used there was only one subject who had a GFR between 10 and 20 ml/min. The mean value of CG for these subjects was 17.5 ± 1.2 ml/min and CB was more than double this (37.3 ± 13.6 ml/min; P < 0.0001). The most dramatic difference was found in a subject with a plasma creatinine of 0.54 mg/dl whose CG was 16.1 ml/min and CB was 75.6 ml/min.

The mean GFR according to CG for females was 27.1 ± 10.4 ml/min (range 11.2–54.4 ml/min) whereas when CB was used it was 47.1 ± 17.1 ml/min (range 10.6–89.0 ml/min; P < 0.001). Significant correlation was found between CG and CB for females (r = 0.75; P < 0.0001; regression curve, y = 11.5 + 1.28x). The mean GFR according to CG for males was comparable with the value obtained when CB
was used (CG: 29.3±6.7 ml/min, range 20.7–45.9 ml/min; CB: 32.0±6.3 ml/min, range 18.9–39.1 ml/min). There was no correlation between CG and CB for males but it must be pointed out that the study included only 10 males.

Interestingly, the significant negative correlation was found between the difference of CB and CG (CB – CG) and plasma creatinine ($r = -0.74; P<0.0001$) which showed that for subjects with higher plasma creatinine, results of both calculations were more similar than for the subjects with lower plasma creatinine. When only females with creatinine $>2.00$ mg/dl were included, the results obtained with both formulas were almost the same (CG: 11.5±0.3 ml/min, range 11.2–11.9 ml/min; CB: 11.2±0.4 mg/dl, range 10.5–11.6 ml/min; CB – CG: $-0.30±0.92$ ml/min, range $-1.36–0.29$ ml/min). In males, similarly to females, the significant negative correlation was found between CB – CG and plasma creatinine ($r = -0.70; P<0.05$). CB – CG was statistically significantly higher in females vs males (19.3±11.0 ml/min, range $-1.36–59.5$ ml/min vs 2.6±8.2 ml/min, range $-16.4–13.1$ ml/min).

No impact of gender could be found among subjects with normal plasma creatinine, when CG was used (females, 30.3±6.4 ml/min; males, 28.5±10.0 ml/min). However, according to CB, the mean value for females was statistically significantly higher than in males (48.8±15.5 vs 33.4±4.8 ml/min; $P<0.01$). Also, when plasma creatinine in these groups was compared, the mean value for females was lower vs males (0.85±0.21 vs 1.07±0.11 mg/dl; $P<0.01$). The Cockcroft–Gault study was performed initially among 534 subjects aged 18–92 years and only 4% of them were females. Eventually, they created the calculation according to the results of 249 males. Because of different amounts of fat and muscle mass in women they decided to correct the calculated value by 15% based on the recommendation of other authors [1]. In that study, the 24 h creatinine clearance was used as the reference method.

With the CB formula there is no difference between the calculation for females and males. In the study done by Baracskay et al. [4], 32 out of 41 subjects aged 65–83 years were females, and 4 h iothalamate clearance was used as the standard.

Our results show that the Cockcroft–Gault method gives significantly lower values than results obtained with the Baracskay et al. [4] formula in centenarian females with normal creatinine. In the absence of an accurate reference method we cannot say which method gives reliable results. Until such comparison is made, investigators should be aware of the differences. The formal measurement of GFR in such patients would be needed to confirm the claim that the calculation of GFR according to Baracskay et al. [4] is superior to the Cockcroft–Gault formula.