

# Kidney function estimated with the different formulas in centenarians

Wieczorowska-Tobis K<sup>1</sup>, Niemir ZI<sup>2</sup>, Guzik P<sup>3</sup>, Mossakowska M<sup>4</sup>

<sup>1</sup> Laboratory for Gerontology and Geriatrics, Department of Pathophysiology, University of Medical Sciences, Poznań, Poland

<sup>2</sup> Department of Nephrology, University of Medical Sciences, Poznań, Poland

<sup>3</sup> Department of Cardiology, University of Medical Sciences, Poznań, Poland

<sup>4</sup> International Institute of Molecular and Cellular Biology, Warsaw, Poland

## Abstract

**Purpose:** There are growing doubts about the accuracy of Cockcroft-Gault formula (CG) used for the estimation of creatinine clearance, especially in elderly. Recently, the authors of the multicenter trial of the Modification of Diet in Renal Diseases (MDRD) have proposed a new equation. Moreover, Baracska et al. (B), proposed the special formula for the estimation of kidney function (KF) in elderly. The aim of our study was to compare the results of KF calculated with these three formulas in centenarians.

**Material and methods:** The study involved 50 centenarian subjects aged 100-111 years (41 females and 9 males) who participated in Polish Centenarians Program. In all of them KF was estimated with the CG, B and MDRD formulas.

**Results:** In the whole population examined, the mean KF according to CG was lower in comparison to both others ( $p < 0.001$  vs both B and MDRD). Also, in females CG results were the lowest ( $p < 0.001$  vs both B and MDRD). In contrast, KF calculated according to CG and B did not differ in males. The results of the MDRD formula significantly exceeded the two others also in males ( $p < 0.001$  vs CG and B). No impact of gender on the obtained results could be found when CG and MDRD were used. However, according to B, the mean values for females were higher ( $p < 0.01$ ).

**Conclusions:** KF calculated with the CG, B and MDRD formulas significantly differed in the centenarians exam-

ined. Thus, further studies, which include a reference standard, are necessary to answer the question which of these mathematical formulas is the most reliable for the calculation of KF in the elderly.

**Key words:** centenarians, kidney function, mathematical formulas.

## Introduction

In elderly, all accepted methods for the estimation of kidney function (KF) are neither precise nor accurate. Since the doses of many drugs should be adjusted for KF, its accurate assessment is crucial in this group of patients [1]. The measurement of creatinine clearance is difficult to carry out due to the increasing with age problem with proper 24 h urine collection [2]. In addition, decline in the muscle mass during the aging may keep creatinine in the normal range even after significant fall in the glomerular filtration rate (GFR) [3].

Thus, mathematical formulas are often used to assess KF in elderly individuals. The most popular one is the Cockcroft-Gault formula [4]. However, due to large body of evidence about its inaccuracy [2,5-7] new equations have been proposed [8,9]. Baracska et al. [8] proposed the special formula for the estimation of KF in elderly. Recently, the authors of the multicenter trial of the Modification of Diet in Renal Diseases (MDRD) created a new one that is recommended as the most accurate estimation of GFR [9].

The aim of our study was to compare the results of KF calculated using these three formulas in centenarians.

## Material and methods

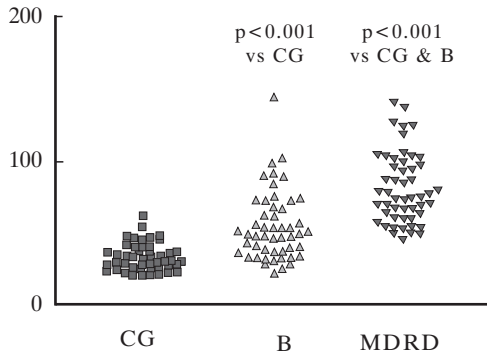
The study is part of the Polish Centenarians Program (coordinated by the International Institute of Molecular and

### ADDRESS FOR CORRESPONDENCE:

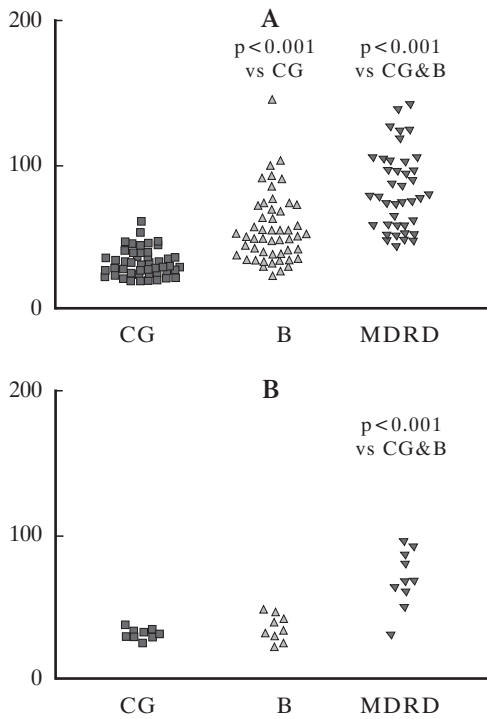
K. Wieczorowska-Tobis M.D.  
Laboratory for Gerontology and Geriatrics  
Department of Pathophysiology  
University of Medical Sciences  
ul. Świącickiego 6  
60-781 Poznań, Poland  
Tel: 061 8659502 Fax: 061 8658879  
e-mail: kwt@tobis.pl

Received 7.05.2004 Accepted 4.06.2004

**Figure 1.** Kidney function estimated with three different formulas (CG – Cockcroft-Gault formula, B – BaracsKay et al. formula, MDRD – The Modified Diet of Renal Diseases formula)



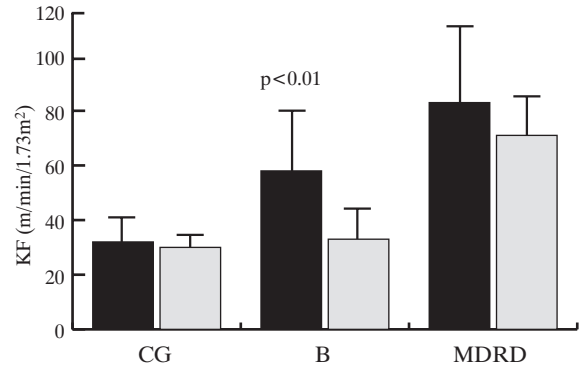
**Figure 2.** Kidney function estimated with three different formulas in females (A) and males (B) (CG – Cockcroft-Gault formula, B – BaracsKay et al. formula, MDRD – The Modified Diet of Renal Diseases formula)



Cell Biology in Warsaw) that was developed to assess the environmental and genetic factors associated with aging in Poland. The details of the study were presented elsewhere [10]. The study was based on a questionnaire and on the analysis of the standard morphological and biochemical parameters, which were performed at the Central Laboratory of the Warsaw Medical Academy (Warsaw, Poland).

The study involved 50 centenarian subjects (41 females and 9 males) aged 100-111 years. The mean age of studied subjects was  $101.7 \pm 2.0$  years. All these individuals had serum creatinine within the normal range.

**Figure 3.** The mean kidney function estimated with three different formulas in females (white bars) and males (gray bars) (CG – Cockcroft-Gault formula, B – BaracsKay et al. formula, MDRD – The Modified Diet of Renal Diseases formula)



In all of them, KF was estimated with three different formulas. The formulas are presented below:

Cockcroft and Gault formula (CG) [4]:

$CG = (140 - \text{age}) / (72 \times PCr(\text{mg/ml}))$ , for females multiplied by 0.85

BaracsKay et al. formula (B) [8]:

$B = \frac{1}{2} [100 / PCr(\text{mg/ml})] + 88 - \text{age}$

MDRD formula [9]:

$MDRD = 186 \times PCr^{-1.154} \times \text{age}^{-0.203}$ , for females multiplied by 0.742.

The obtained results were adjusted for body surface area (BSA), which was calculated in each subject based on the Dubois and Dubois method [11].

**Statistical analysis**

The results are presented as mean  $\pm$  SD. Statistical analysis was performed with t-Student’s test or Kruskal-Wallis one-way ANOVA, as appropriate. A p values less than 0.05 were considered to be significant.

**Results**

The mean KF according to CG was lower than calculated with the two other methods (CG,  $33.4 \pm 9.0$  ml/min/1.73m<sup>2</sup>; B,  $55.5 \pm 23.5$  ml/min/1.73m<sup>2</sup>; B vs CG  $p < 0.001$ ; MDRD,  $83.9 \pm 30.0$  ml/min/1.73m<sup>2</sup>;  $p < 0.001$  vs both CG and B) (Fig. 1). In females, values calculated using the CG formula were lower than obtained with both B and MDRD equations (CG,  $33.6 \pm 9.8$  ml/min/1.73m<sup>2</sup>; B,  $59.5 \pm 23.7$  ml/min/1.73m<sup>2</sup>; B vs CG,  $p < 0.001$ ; MDRD,  $85.9 \pm 31.9$  ml/min/1.73m<sup>2</sup>;  $p < 0.001$  vs CG and B) (Fig. 2A). In males, KF assessed with CG and B was comparable (CG,  $32.0 \pm 3.3$  ml/min/1.73m<sup>2</sup>; B,  $36.3 \pm 8.8$  ml/min/1.73m<sup>2</sup>). However, values obtained with the MDRD formula were higher ( $73.9 \pm 15.2$  ml/min/1.73m<sup>2</sup>;  $p < 0.001$  vs CG and B) (Fig. 2B).

No impact of gender on the obtained results could be found when CG and MDRD were used for the assessment of KF (CG: females,  $33.6 \pm 9.8$  ml/min/1.73m<sup>2</sup>; males,  $32.0 \pm 3.3$  ml/min/1.73m<sup>2</sup>; MDRD: females,  $85.9 \pm 31.9$  ml/min/1.73m<sup>2</sup>;

males,  $73.9 \pm 15.2$  ml/min/1.73m<sup>2</sup>). Though, KF calculated with the B formula was significantly higher in females than in males ( $59.5 \pm 23.7$  ml/min/1.73m<sup>2</sup> and  $36.3 \pm 8.8$  ml/min/1.73m<sup>2</sup>,  $p < 0.01$ ) (Fig. 3).

## Discussion

In the absence of a simple and accurate method for the assessment of KF, to estimate it mathematical formulas are used. With the aim to find the best one, the results obtained with different formulas are often compared. However, as far as we know there is no data about the usage of different formulas in centenarians. We decided to compare the results of KF calculated with the three mostly used formulas in subjects aged 100 years and more.

One has to realize that the CG formula is used for the assessment of creatinine clearance ( $C_{cr}$ ), whereas both B and MDRD equations estimate the GFR [4,8,9]. Due to these differences we decided to define calculated values as KF. According to Fliser et al. [5], significant differences between the values of  $C_{cr}$  and GFR could particularly be observed in the older population. In our study, the results obtained with CG were the lowest. This could suggest that the CG formula underestimates KF in centenarians.

The results obtained using the equation of Baracska et al. [8] showed the difference between females and males. The difference was probably noticed due to the fact that this equation, as the only one known, has no multiplier for women. The Baracska et al. formula was created based on the measurement of KF in elderly subjects with iothalamate clearance (<sup>125</sup>I iothalamate) [8]. The study involved only 41 subjects and these were predominantly females (32 females and only 9 males). Since the number of males was very small, it seems obvious that the sex impact on the GFR was not noticed. We have already reported on the difference between the results calculated using CG and B in centenarians [12]. As far as we know, the formula of Baracska et al. [8] has never been validated on a bigger group of elderly subjects.

In the present study, KF calculated according to the MDRD formula was the highest one (Fig. 1 & 2). The MDRD formula was created based on the results of <sup>125</sup>I-iothalamate clearance in 1070 patients aged 18-70 years [9]. Because there were no very old subjects in the examined group, the accuracy and precision of this formula for such a population was not validated at all. Recently, Lamb et al. [13] have demonstrated that in subjects

aged 65-92 years the MDRD equation may slightly overestimate the GRF.

In summary, our results showed that KF calculated with the CG, B and MDRD formulas significantly differed in the centenarians examined. Thus, further studies, which include a reference standard, are necessary to answer the question which of these mathematical formulas is the most reliable for the calculation of KF in the elderly.

## References

1. Guay DRP, Artz MB, Hanlon JT, Schmader K. The pharmacology of aging. In: Tallis RC, Fillit HM, editors. Geriatric medicine and Gerontology. 3<sup>rd</sup> ed. McGraw-Hill, Inc; 1994, p. 155-62.
2. Goldberg TH, Finkelstein MS. Difficulties in estimating glomerular filtration rate in the elderly. Arch Intern Med, 1987; 147: 1430-3.
3. Hajd-Aissa A, Dumarest C, Maire P, Pozet N. Renal function in the elderly. Nephron, 1990; 54: 364-5.
4. Cockcroft DW, Gault MH. Prediction of creatinine clearance from serum creatinine. Nephron, 1976; 16: 31-41.
5. Fliser D, Bischoff I, Hanses A, Block S, Joest M, Ritz E, Mutschler E. Renal handling of drugs in the healthy elderly. Creatinine clearance underestimates renal function and pharmacokinetics remain virtually unchanged. Eur J Clin Pharmacol, 1999; 55: 205-11.
6. Van Den Noortgate NJ, Janssens WH, Delanghe JR, Afschrift MB, Lameire NH. Serum Cystatin C concentration compared with other markers of glomerular filtration rate in the old. J Am Ger Soc, 2002; 50: 1278-82.
7. Burkhardt H, Bojarsky G, Greta N, Gladisch R. Creatinine clearance, Cockcroft-Gault formula and cystatin C: estimators of true glomerular filtration rate in the elderly? Gerontology, 2002; 48: 140-8.
8. Baracska D, Jarjoura D, Cugino A, Blend D, Rutecki GW, Whittier FC. Geriatric renal function: estimating glomerular filtration in an ambulatory elderly population. Clin Nephrol, 1997; 47: 222-8.
9. Levey AS, Bosch JP, Lewis JB, Greene T, Rogers N, Roth D. A more accurate method to estimate glomerular filtration rate from serum creatinine: a new prediction equation. Ann Intern Med, 1999; 30: 461-9.
10. Mossakowska M, Puzianowska-Kuznicka M, Barcikowska M, Chiron-Jouan S, Czyzewski K, Derejczyk J, Franceschi C, Gabryelewicz T, Galus K, Grodzicki T, Gross R, Klich-Rączka A, Łuczywek E, Passeri G, Pfeffer A, Pruszyński J, Radziszewska E, Sikora E, Sosnowski M, Styczyńska M, Wasiak B, Wieczorowska-Tobis K, Życzkowska J, Kuźnicki J. Program badania polskich stulatków "PolStu99" – poszukiwanie czynników sprzyjających długowieczności. Gerontologia Polska, 2000; 8: 35-9.
11. Dubois D, Dubois EF. Clinical calorimetry. A formula to estimate the approximate surface in height and weight be known. Arch Intern Med, 1916; 17: 863-71.
12. Wieczorowska-Tobis K, Mossakowska M, Niemir Z, Breborowicz A, Oreopoulos DG. Discrepancies in creatinine clearance in centenarians when calculated by two different mathematical formulas. Nephrol Dial Transplant, 2002; 17: 2274-5.
13. Lamb EJ, Webb MC, Simpson DE, Coakley AJ, Newman DJ, O'Riordan SE. Estimation of glomerular filtration rate in older patients with chronic renal insufficiency: is the modification of diet in renal disease formula an improvement? J Am Geriatr Soc, 2003; 51: 1012-7.