ARTYKUŁ ORYGINALNY/ORIGINAL PAPER
Otrzymano/Submitted: 28.08.2013 • Zaakceptowano/Accepted: 20.09.2013



# The estimation of kidney function with different formulas in overall population

**Katarzyna Wieczorowska-Tobis[1], Zofia I. Niemir[2], Sylwia Kropińska[3]**
[1] Department of Palliative Care, Poznan University of Medical Sciences, Poland
[2] Laboratory for Molecular Nephrology, Poznan University of Medical Sciences, Poland
[3] Departments of Geriatric Medicine and Gerontology, Poznan University of Medical Sciences, Poland

## Abstract

***Background***. The limitations of the laboratory evaluations of kidney function (KF) are well recognized. Therefore, in clinical practice, various mathematical formulas are applied for the bedside estimation of KF. ***Aim***. The aim of this study was to compare the calculated KF function derived from two different formulas i.e. the Cockcroft-Gault (CG) formula and the shorten version of Modification of Diet in Renal Disease (MDRD) formula, in patients at different ages. ***Material and methods***. The study involved three groups of patients at different ages. In all of them serum creatinine was within the reference values. Group A was composed of 40 healthy subjects aged 20-35 years (25.6 ± 4.2 years), group B of 50 elderly subjects at 65-92 years of age (mean age: 74.8 ± 8.2 years), and group C of 50 centenarians aged 100-111 (mean age: 101.7 ± 2.0 years). In all subjects, KF (ml/min/1.73 m2) was estimated based on the CG and the shortened version of the MDRD formula (MDRDs). ***Results***. The comparison of the results obtained with both formulas showed that those calculated using CG were higher in group A (96.0 ± 22.1 vs. 82.0 ± 23.0; $p < 0.0001$). In contrast, this equation gave significantly lower values in subjects from groups B and C (58.4 ± 16.9 vs. 70.0 ± 24.4; $p < 0.0001$ and 33.7 ± 9.0 vs. 82.1 ± 24.1, $p < 0.0001$, respectively). ***Conclusion***. Thus, our results show that the CG formula gives significantly different results than the MDRDs equation and that the difference in the estimated KF is related to the age of the subjects. In the absence of an accurate reference method we cannot say which method gives more reliable results. Until such comparison is made, investigators should be aware of the differences existing. *Geriatria 2013; 7: 137-141.*

*Keywords: kidney function, Cockcroft-Gault formula, MDRD formula*

## Introduction

Limitations of the laboratory evaluations of kidney function are well recognized. Serum creatinine is the simplest way used for estimation of glomerular filtration rate (GFR). However, a dramatic reduction in GFR produces only a small increase in serum creatinine, which is due to nonlinear relationship of these two parameters [1].

Creatinine clearance (CCr), measured based on 24-hour urine collection, is a more precise tool. Nevertheless, this is far from the gold standards, such as inulin clearance or the clearances of radio-labelled substances. Data reported by Burkhard et al. [2] indicated that CCr value of 70 ml/min represents a true GFR between 33.7 and 176.0 ml/min. Moreover, Fliser et al. [3] observed significant differences between the values of CCr and GFR in elderly, whereas in young subjects they were similar. These discrepancies are mainly due to inaccuracies in 24h-urine collection which seem to increase with age due to the presence of co-morbid diseases, e.g. dementia and urine incontinence [4,5].

In clinical practice, various mathematical formulas are applied for the bedside estimation of renal function (reviewed in [6]. These formulas are based on age, body weight, gender, and serum creatinine level. They allow a quick assessment of the severity of renal diseases, as well as the adjustment of the dose of nephrotoxic drugs. Despite growing doubts about the precision and accuracy of the Cockroft and Gault (CG) formula [7,8] it is still widely used and moreover even recommended

for dosage adjustment of the drugs in elderly patients by some authors [9]. On the other hand, nowadays in everyday clinical practice the GFR is estimated with the outcome equation of the multicenter trial of Modification of Diet in Renal Diseases (MDRD) [10].

The aim of this study is to compare the results of KF estimated with the use of two different formulas: the CG and the shortened version of MDRD (MDRDs) in patients at different ages.

## Material and method

- **Studied subjects**

The study involved three groups of patients at different ages. In all of them serum creatinine was within the reference values. Group A was composed of 40 healthy individuals aged 20-35 years (mean age: 25.6 ± 4. 2 years; 25 females and 15 males). Group B included 50 elderly at 65-92 years of age (mean age: 74.8 ± 8.2 years; 38 females and 12 males). The subjects of both groups were volunteers participating in the study of the health status of elderly subjects in Poznan that is one of the biggest cities in western part of Poland. Group C involved 50 individuals aged 100-111 (mean age: 101.8 ± 2.0 years - 41 females and 9 males) who participated in the Polish Centenarians' Study. Both studies (health status of elderly and the Polish Centenarians Study) evaluated health status of these subjects based on a questionnaire, physical examination and assessment of the standard laboratory parameters. The present study considered the following parameters: age, body weight, height, and serum creatinine.

Body surface area (BSA) was calculated in every subject based on body weight and height according to the Dubois and Dubois method [11].

- **Mathematical formulas for the kidney function assessment**

The kidney function (KF) was estimated according to the CG formula and the MDRDs formula. The formulas are as follow:

$$CG = \{(140 - age) \times body\ weight\ (kg)\}/72 \times P_{Cr}$$

[0.85 if patient is female]

$$MDRDs = 186 \times P_{Cr}^{-1.154} \times age^{-0.203}$$

[0.742 if patient is female]

The results of CG were analyzed after adjustment for BSA before the results obtained ith those two formulas was compared.

- **Statistical analysis**

The results are expressed as mean ± SD. Kolmogorov-Smirnoff test revealed that the data distribution was normal in all groups. The statistical analysis was performed with the use of t-Student or ANOVA with the post-hoc test of Kruskall-Wallis test, as appropriate. A p value below 0.05 was considered significant.

## Results

In group A, the mean KF value obtained with the CG formula was 96.0 ± 22.1 ml/min/1.73 $m^2$, whereas that calculated according to the MDRDs equation was significantly lower (82.0 ± 23.0 ml/min/1.73 $m^2$; $p < 0.0001$). The mean difference between both formulas in this group was +13.9 ± 7.1 ml/min/1.73 $m^2$.

In group B, oppositely to the results obtained in group A, KF estimated according to CG was lower than that assessed by MDRDs (58.4 ± 16.9 ml/min/1.73$m^2$ *vs.* 67.0 ± 19.1 ml/min/1.73 $m^2$, $p < 0.0001$), with the mean difference between the results reaching –8.6 ± 11.57 ml/min/1.73 $m^2$.

But the most pronounced difference between the results of both equations was noted in group C. While in this group KF estimated according to CG was only 33.7 ± 9.0 ml/min/1.73 $m^2$, the mean MDRDs value was 68.8 ± 18.3 ml/min/1.73 $m^2$ ($p < 0.0001$), with the negative mean difference between CG and MDRDs reaching –35.1 ± 10.8 ml/min/1.73 $m^2$.

Thus, KF calculated according to CG was higher in group A than in the other two groups ($p < 0.001$), as well as the CG-KF of group B was higher than that in group C ($p < 0.001$). However, the highest mean value of KF calculated with the MDRDs equation was obtained in group A ($p < 0.01$ *vs.* B and C), whereas the results of group B and C were comparable. The individual results obtained in every subject are presented in Figure 1.

The differences between the results obtained with both formulas also differed significantly between the three groups ($p < 0.001$; Figure 2). In group A, the difference was positive in all but one subjects (39 out of 40-97.5%), in group B – in 21 out of 50 subjects (42.0% - $p < 0.0001$ *vs.* A), whereas in group C in none of the examined subjects (0% - $p < 0.0001$ *vs.* A & B).

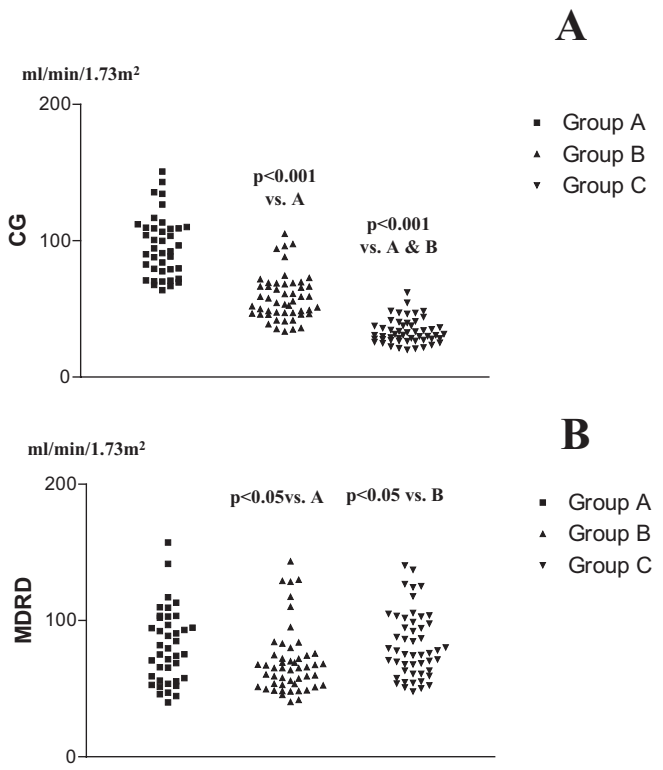


Figure 1A. The individual results of kidney function (KF) calculated in subjects of various ages according to the Cockcroft-Gault formula: group A – subjects aged 20-35 years, group B – subjects aged 65-92 years, group C – subjects aged 100-111 years

Figure 1B. The individual results of kidney function (KF) calculated in subjects of various ages according to the sMDRD formula (short version): group A – subjects aged 20-35 years, group B – subjects aged 65-92 years, group C – subjects aged 100-111 years

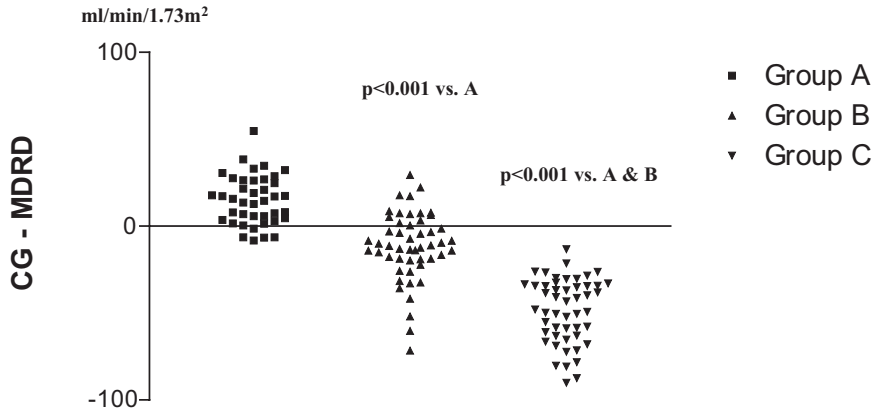


Figure 2. The individual results of the differences between kidney function (KF) calculated in the subjects according to the Cockcroft-Gault formula and sMDRD formula (short version): group A – subjects aged 20-35 years, group B – subjects aged 65-92 years, group C – subjects aged 100-111 years

## Discussion

In the absence of a simple and accurate method of kidney function measurement, mathematical formulas are often used for its estimation. Although several formulas have been presented in the literature during the last 30 years, the most widely used is that of Cockcroft and Gault [12]. Cockcroft and Gault performed their study in the middle of the 1970's using 534 subjects aged 18-92 years. Only 4% of them were females. Eventually, they based their formula on the results of creatinine clearance in 249 males. The remaining subjects were excluded because of differences between repeated serum creatinine measurements. Based on the recommendation of other authors, Cockcroft and Gault decided to adjust their calculated value by -15% in females. Since then, a large body of evidence has appeared which suggest that the CG formula is neither precise nor accurate, especially for elderly subjects [2,8].

MDRD formula has been proposed based on the results of $^{125}$J-iothalamate clearance in 1070 patients who participated in the multicenter randomized trial of Modification of Diet in Renal Disease. These subjects aged 18-70 years had chronic renal diseases and were neither on dialysis nor had kidney engraftment [11]. Then, the authors used this new formula to calculate the GFR in additional 558 subjects with renal diseases and they compared the results with those of iothalamate clearance. The new equation takes into account serum creatinine concentration and demographic data, such as age, sex and ethnicity, as well as other serum parameters including urea nitrogen and albumin concentration. The authors suggested that their formula was more accurate than the CG formula or other widely used equations.

However, more recently Vervoort et al. showed that in subjects with normal or increased GFR the MDRD formula is less accurate than CG formula and thus offers no advantage [13]. According to Van Den Noortgate et al., both the CG and MDRD formulas are comparable markers of renal function in the overall older population [14].

Since MDRD formula requires both the serum concentrations of urea and albumin, it is difficult to compare the results obtained with its use in different parts of the world because of different analytical methods and different reference values. Hence, Levey et al. [15] presented the shorten version of this equation requiring only serum creatinine, age and sex for KF calculation. This shorten version was used in our study.

We compared the results obtained with the CG and the MDRDs in subjects of different ages and showed that KF estimated with MDRDs did not differ between the young subjects and centenarians (Figure 2B). It must be pointed out that the MDRD trial did not include subjects older than 70 years. Furthermore, the equation has not been validated in subjects without renal diseases [10]. Therefore, it is difficult to compare our results with those of the MDRD trial.

Moreover, we showed that the difference between KF calculated with two formulas changes with age (Figure 3). For centenarians, the mean difference was about –50 ml/min/1.73 m$^2$, which means that MDRDs overestimates CG by about 50ml/min/1.73 m$^2$. In contrast, in young adults, this difference was +15, which means that for this group MDRDs underestimated CG by about 15 ml/min/1.73 m$^2$. The observed differences between CG and MDRDs are at least partially caused by mathematical formulas themselves. In case of CG, KF negatively correlates with age, whereas when MDRDs is taken into consideration an opposite relation is observed.

In summary, our results show that the Cockcroft-Gault method gives significantly different results than the MDRD one and that the difference is related to the age of the subject. In the absence of an accurate reference method, we cannot say which method gives results that are more reliable. However, until such a comparison is made, investigators should be aware of the differences and consider them, especially in elderly subjects.

**Conflict of interest**

None

Correspondence address
Prof. Katarzyna Wieczorowska-Tobis
University of Medical Sciences
Department of Palliative Care
Os. Rusa 25 A; 61-245 Poznań, Poland
☎ (+48 61) 873 83 03
kwt@tobis.pl

## References


1. Isles CG, Paterson JR. Serum creatinine and urea: make the most of these simple tests. Br J Hosp Med 1996;55:513-6.
2. Burkhardt H, Bojarsky G, Gretz N, et al. Creatinine clearance, Cockcroft-Gault formula and cystatin C: estimators of true glomerular filtration rate in the elderly? Gerontology 2002;48:140-6.
3. Fliser D, Ritz E. Serum cystatin C concentration as a marker of renal dysfunction in the elderly. Am J Kidney Dis 2001;37:79-83.
4. Fliser D, Bischoff I, Hanses A, et al. Renal handling of drugs in the healthy elderly. Creatinine clerance underestiamtes renal function and pharmacokinetics remain virtually unchanged. Eur J Clin Pharmacol 1999;55:205-11.
5. Rissanen A, Heliovaara M, Knekt P, et al. Risk of disability and mortality due to overweight in a Finnish population. BMJ 1990;301:835-7.
6. Kemperman FAW, Kreidet R, Arisz L. Formula-derived prediction of the glomerular filtration rate from plasma creatinine concentration. Nephron 2002;91:547-58.
7. Waller DG, Fleming JS, Ramsay B, et al. The accuracy of creatinine clearance with and without urine collections as a measure of glomerular filtration rate. Postgrad Med 1991;67:42-6.
8. Glodberg TH, Finkkelstein MS. Difficulties in estimating glomerular filtration rate in the elderly. Arch Intern Med 1987;147:1430-3.
9. Spruill WJ, Wade WE, Cobb HH 3rd. Comparison of estimated glomerular filtration rate with estimated creatinine clearance in the dosing of drugs requiring adjustments in elderly patients with declining renal function. Am J Geriatr Pharmacother 2008;6:153-60.
10. Levey AS, Bosch JP, Lewis JB, et al. A more accurate method to estimate glomerular filtration rate from serum creatinine: a new prediction formula. Ann Intern Med 1999;130:461-70.
11. Dubois D, Dubois EF. Clinical calorimetry. A formula to estimate the approximate surface in height and weight be known. Arch Intern Med 1916;17:863-771.
12. Cockroft DW, Gault MH. Prediction of creatinine clearance from serum creatinine. Nephron 1976;16:31-41.
13. Vervoort G, Willems HL, Wetzels JF. Assessment of glomerular filtration rate in healthy subjects and normoalbuminuric diabetic patients: validity of a new (MDRD) prediction equation. Nephrol Dial Transplant 2002;17:1909-13.
14. Van Den Noortgate NJ, Janssens WH, Delanghe JR, et al. Serum cystatin C concentration compared with other markers of glomerular filtration rate in the old. J Am Geriatr Soc 2002;50:1278-82.
15. Levey AS, Greene T, Kusek JW, et al. A simplified equation to predict glomerular filtration rate from serum creatinine (Abstract). J Am Soc Nephrol 2000;11:A0828.