

G. Van Pottelbergh^{1,3}, N. Gurina², J. Degryse^{1,3}, E. Frolova²**PREVALENCE OF IMPAIRED RENAL FUNCTION IN THE ELDERLY
IN THE ST. PETERSBURG DISTRICT: RESULTS OF THE CRYSTAL STUDY**¹ Institute of Health and Society, Université Catholique de Louvain, Clos Chapelle-aux-Champs 30, bte 3005, 1200 Brussels, Belgium;² St. Petersburg Medical Academy for Postgraduate Studies, 45 pr. Prosvescheniya, St. Petersburg 194291;³ Department of Primary Health Care, Katholieke Universiteit Leuven, Leuven, Belgium; e-mail: jan.degryse@med.kuleuven.be

Chronic kidney disease (CKD) has a high prevalence in the elderly. It has been recognized as an independent cardiovascular risk factor and detecting CKD is also important to ensure the appropriate dose of medication and to prevent further damage by limiting the use of potential harmful drugs. The aim of the research was to study the prevalence of CKD in elderly (≥ 65 years) in a St. Petersburg district and to study the impact of using different methods to estimate the GFR on the prevalence of different stages of CKD. The cross-sectional analysis of prospective population based study in the district of Kolpino was conducted. All creatinine measurements were performed in the same laboratory. Renal function was assessed calculating the eGFR using different creatinine based formulas. 611 elderly (65–91 years) were examined. Using the MDRD formula a prevalence of CKD stage III–V for males of 11% was found in stratum 1 and of 15% in stratum 2 and for females prevalence was 14 and 29%, respectively. A considerable mismatch in classification of stages of CKD was found when comparing the MDRD based estimations with the CG-based ones. Compared to what has been reported internationally in other studies a considerable lower prevalence of CKD stage IV–V was found in both age groups. Thus, the prevalence of an impaired renal function in elderly in the St. Petersburg district is relatively low, especially in the subgroup of males aged 75 years and over compared to what been reported in other studies. The CG and MDRD formula generate significantly different results when they are used to classify the population of elderly according to the stages of CKD.

Key words: chronic kidney disease, elderly, glomerular filtration rate, MDRD-equation

Classification and prevalence of chronic kidney disease worldwide

Chronic kidney disease (CKD) is increasingly recognized as an important problem of public health for several reasons. First, the disease is highly prevalent in Europe and the USA [18] and the prevalence of impaired renal function increases with advancing age.

Second, CKD is an independent cardiovascular risk factor, in that a low estimated glomerular filtration rate (eGFR) is associated with increased mortality, a higher rate of cardiovascular events, and more hospitalizations. A study by A. S. Go et al. in 2004 [6] suggested that a GFR of < 29 mL/min corresponds to

an adjusted hazards ratio for cardiovascular events of 2.8, a GFR of 30–44 mL/min to a ratio of 2.0, and a GFR of 45–59 mL/min to a ratio of 1.4. Although only a very small subgroup of all patients with CKD will develop end-stage renal failure [8], the costs of dialysis and kidney transplant are very high for a society.

CKD is defined as structural or functional renal damage and/or reduced renal function for at least three months. The most commonly used classification of kidney function is that of the American Kidney Foundation (*tabl. 1*). In this classification, the diagnosis of CKD is based not only on the eGFR but also on the presence of proteinuria or hematuria. Therefore, it is also important to measure proteinuria, rather than screening for CKD simply by calculating the eGFR.

Table 1

Classification of CKD according to the American Kidney Foundation

Stage	Description	GFR (mL/min/1.73 m ²)
I	Kidney damage* with normal or increased GFR	> 90
II	Kidney damage with mild reduction in GFR	60–89
IIIA	Moderate reduction in GFR	45–59
IIIB	Moderate reduction in GFR	30–44
IV	Severe reduction in GFR	15–29
V	End-stage kidney failure	< 15 or dialysis

Signs of kidney damage:

- Persistent proteinuria
- Persistent hematuria (after exclusion of other possible etiologies)
- Structural kidney abnormalities, such as polycystic kidneys and reflux nephropathy
- Chronic glomerulonephritis

* National Kidney Foundation. Amer. J. Kidney Dis. 2002. Vol. 39 (2 Suppl. 1). P. S1–S266

Detecting CKD is important not only because of the risk of end-stage renal failure or the higher

cardiovascular risk involved but also to ensure the appropriate dose of medication and to prevent further renal damage by limiting the use of potentially harmful medications, like nonsteroidal anti-inflammatory drugs [12, 13, 17].

Two formulas are frequently used to estimate the GFR based on age, sex, serum creatinine, and other parameters, such as weight and race. Multiple studies using a correct gold standard (for an overview, see reference [9] have shown that the Modification of Diet in Renal Disease (MDRD) formula generates a better estimate than the Cockcroft–Gault (CG) formula, especially in patients with a GFR below 60 mL/min/1.73 m². A recent systematic review [16] of studies that used the gold standard to validate the creatinine- or cystatin-based equations in the elderly revealed that only a limited number of small studies in people aged 65 years and over have been published. The evidence from these studies shows that the MDRD formula and CG formula estimate the GFR more accurately than do other equations. However, no clear conclusion has been drawn regarding the use of the CG or MDRD formula in elderly patients.

Life expectancy and cardiovascular disease (CVD) in Russia

The average life expectancy at birth in Russia currently lags behind that of the European Union by as much as 14 years. By 2007, the life expectancy at birth in Russia was 67.5 years, whereas in Belgium, for example, it was 76.6 years for men and 82.3 years for women (www.statbel.fgov.be). Russia is the first country in the history of modern nations to experience such a significant peace-time reduction in life expectancy.

Russia's CVD death rate was 833 per 100,000 people in 2008, one of the world's highest (www.gks.ru). By comparison, the CVD death rate was 336 per 100,000 in Belgium. CVD accounts for 57% of deaths in Russia, compared with 34.9% in Belgium. Russia's high mortality among working-age men is mainly attributable to CVD. Such statistics led a 2004 World Bank report to conclude that Russia could gain 6.7 years in life expectancy by matching the European Union's CVD mortality rates. This would result in a growing population of elderly survivors of cardiovascular disease and would generate a particular epidemiological context in which to study aging from a scientific perspective.

The first aim of our study was to investigate the prevalence of CKD in elderly Russians and to compare it with the prevalence reported internationally. Our

second aim was to study the impact of using different methods to estimate the GFR in an elderly population on the (mis)classification of the CKD in different stages.

Methods

This paper reports a cross-sectional analysis of the data available from the «Crystal» (Хрусталь) study, which was designed as a population-based prospective cohort study. The research took place in the Kolpino district of St Petersburg.

The study included all patients over 65 years who lived at home and were registered at Polyclinic no. 95 ($n=10,986$), 41.6% of whom ($n=4,567$) were older than 75 years. The elderly population from the Polyclinic register was first stratified by age into two groups: 65–74 years old and ≥ 75 years old. A representative random sample was selected from each group: 462 people from the first stratum and 452 from the second stratum.

The selected persons were invited by telephone to participate. This strategy was used to ensure that the nurse who took care of the patients daily was responsible for the invitation, the examination, and the interview. Some people who were unable to attend the Polyclinic were examined at home. All participants gave their written informed consent.

A portfolio was designed for the data collection. It included a comprehensive geriatric assessment as the major domain. All research data were collected during the period between March and December 2009.

Details of past and current medical problems collected were based on anamnesis or on information available in medical records. The following medical conditions or diseases were documented systematically: angina pectoris, myocardial infarction, arrhythmias, obstructive pulmonary diseases or asthma, peripheral artery disease, diabetes mellitus, stroke, cancer, osteoarthritis and rheumatoid arthritis, incontinence, and vision or hearing decline.

All creatinine measurements were performed in the same clinical diagnostic laboratory. A modified kinetic Jaffé colorimetric method was used with a Hitachi-912 analyzer. The reference value for creatinine was 53–106 $\mu\text{mol/L}$ in males and 44–88 $\mu\text{mol/L}$ in females. The coefficient of analytical variation was determined as 2.14.

We used the CG [2] and MDRD [10] formulas to estimate the GFR and corrected the CG formula for a body surface area (BSA) of 1.73 m² using the equation of D. Du Bois [4].

Cockcroft–Gault formula:

$$eC_{Cr} = \frac{(140 - \text{Age}) \times \text{Mass (kg)} \times \text{Constant}}{\text{Serum Creatinine } (\mu\text{mol/l})}$$

MDRD formula:

$$e\text{GFR (mL/min/1.73 m}^2) = 32788 \times \text{Serum Creatinine}^{-1.154} \times \text{Age}^{-0.203} \times [1.210 \text{ if Black}] \times [0.742 \text{ if Female}]$$

Results

Six hundred eleven adults aged 65–91 years were examined. The response rate was 66.2% among the younger participants (65–74 years old) and 67.9% in the older group (75 years and older). To test the representativeness of the sample, those who participated in the study and those who were invited to do so were compared. No significant differences were found in their sex or age distributions (data not shown).

In stratum 1 (aged 65–74 years), 100 males and 205 females participated; in stratum 2 (aged 75 years and older), 73 males and 233 females participated. No blood samples were obtained for 17 patients in this group during the data collection. Therefore, the total study population contained 594 patients.

eGFR by age and formula

The estimated GFR calculated with the CG and MDRD formulas, and the classification of the stages of CKD based on this eGFR are shown in *tabl. 2*. The prevalence of CKD stages III–V using the BSA-corrected CG formula was 21% for males in stratum 1 and 18% for those in stratum 2. For females, the prevalence was 52% in both age groups. When we used the MDRD formula, the prevalence was 11

and 15%, respectively, in males and 14 and 29%, respectively, in females (see *tabl. 2*).

Patients with diabetes mellitus had a lower mean GFR than patients without diabetes mellitus, except for the males in the older age group, where this relationship was reversed.

It is clearly shown in *Fig. 1* and *2* that the mean GFR decreased with increasing age and that the mean eGFR decreased more with increasing age when we used the CG formula than when we used the MDRD formula. The mean eGFRs calculated by the two formulas are significantly different for the patients aged 75 years and over.

Mismatch between the formulas

We analyzed the mismatch by comparing the MDRD-based classification of stages of CKD with the CG-based classification (*tabl. 3*). We performed this mismatch analysis for the whole population. This mismatch was up to 44%, depending on the stage of CKD. Most of the mismatch occurred in stages IIIA and IIIB. In contrast, patients who were classified as stage IV by one formula were always classified as stage IIIB or stage IV by the other formula.

We also constructed a Bland–Altman plot (see *fig. 2*), showing the relative differences in the eGFRs estimated with the BSA-corrected CG formula and with the MDRD formula against the average of these two values. The plot shows that the eGFR estimated with the MDRD formula was generally higher than the eGFR estimated with the CG formula and that the major differences in the eGFR values occurred at an eGFR of 50 mL/min/1.73 m² or more.

Table 2

Estimated GFR by age group and by formula: Modification of Diet in Renal Disease (MDRD) formula and Cockcroft–Gault formula corrected for body surface area (CGbsa)

Subgroup	Stratum 1 (65–75 years)				Stratum 2 (75+ years)			
	male, n=98		female, n=194		male, n=72		female, n=230	
Mean creatinine (SD), $\mu\text{mol/L}$	88.97 (21.29)		73.46 (19.17)		91.08 (30.91)		76.96 (17.82)	
GFR average (SD), mL/min	CGbsa	MDRD	CGbsa	MDRD	CGbsa	MDRD	CGbsa	MDRD
	73.4 (16.4)	82.8 (20.4)	75.4 (17.2)	76.7 (18.5)	62.3 (16.2)	80.7 (21.6)	50.5 (14.8)	70.4 (17.1)
CKD stage 0–II	79%	89%	82%	86%	56%	85%	48%	71%
CKD stage IIIA	15%	8%	15%	11%	32%	10%	39%	25%
CKD stage IIIB	5%	3%	2%	2%	8%	4%	12%	3%
CKD stage IV	0%	0%	1%	2%	3%	1%	1%	1%
Mean GFR without diabetes	73.6	84.0	75.2	77.2	62.1	80.5	59.6	70.9
Mean GFR with diabetes	71.8	75.8	76.4	73.9	65.2	82.7	58.9	67.7

Discussion

The results of various other cross-sectional studies performed in different parts of the world are presented in *tabl. 4*. Comparing these data with our results leads to the conclusion that the prevalence of stage III–V CKD in stratum 1 and the prevalence in all stages of CKD among females in stratum 2 are similar to the prevalence found elsewhere.

In contrast, the prevalence of CKD stages III–V in males in stratum 2 (15%), calculated using the MDRD formula, is clearly lower than the prevalence reported in the studies of A. X. Garg et al. [5] (17.3 to 32.1%), J. Coresh et al. [3] (24.9%), and M. Cirillo [1] (34.5%). Surprisingly, in this group of males aged 75 years or older, a higher mean GFR was found in the subgroup of patients with diabetes compared with that in the subgroup without diabetes.

Another difference is apparent in the prevalence of CKD stages IV–V. The prevalence of CKD stages IV–V in our Russian cohort was lower in both age groups in both males and females compared with those reported in the study [5]. Moreover, we found no patient with stage V renal failure in our Russian cohort. We have no clear explanation for these differences. One explanation is that because of the high CVD-related mortality in Russia, and particularly the high cardiovascular mortality among males, elderly Russians with a low GFR die early. This could explain why we found very few elderly people with CKD stage IV or V. Diabetes and hypertension have been reported in most countries in the Western world as the main etiologies of CKD [1].

This could also explain why the males in stratum 2 had a relatively good average eGFR and a low prevalence of CKD stages III–V. They might be the few survivors of a very severe selection process that eliminated most male patients with impaired renal function before they reached the age of 75 years. Another possible explanation might be that because of the high cardiovascular mortality, patients and particularly males die before they have accumulated enough (hypertension- and diabetes-related) kidney damage to impair their GFR.

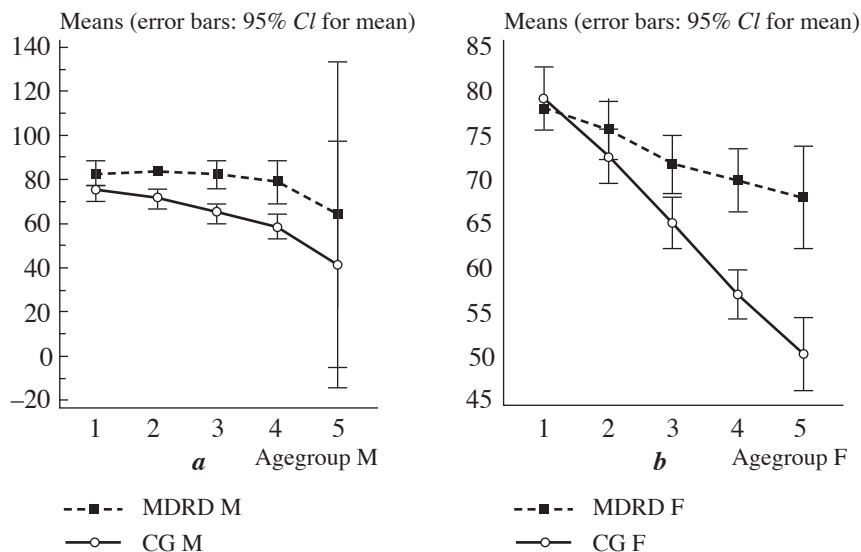


Fig. 1: a — mean eGFR calculated by the CG and MDRD formulas for the male patients in the study population divided into five-year age groups (1=65–69 years, 2=70–74 years, 3=75–79 years, 4=80–84 years, 5=85 years and older). The confidence interval (CI) for age group 5 is very wide because of the limited sample size (n=4); b — mean eGFR calculated with the CG and MDRD formulas for the female patients in the study population, divided into five-year age groups (1=65–69 years, 2=70–74 years, 3=75–79 years, 4=80–84 years, 5=85 years and older)

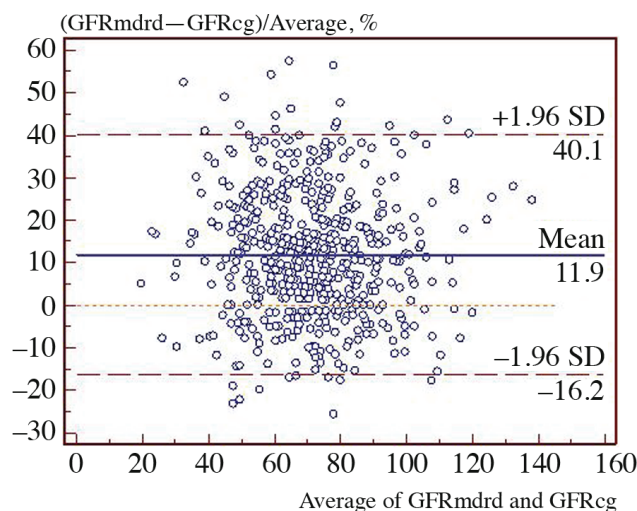


Fig. 2. Bland–Altman plot showing the relative differences in eGFR estimated with the BSA-corrected CG formula and the MDRD formula relative to the average of these two values

The difference in eGFR values generated by the CG and MDRD formulas increases with age (see fig. 1, a, b). This phenomenon has also been reported in other studies (see *tabl. 4*). It can probably be explained by the different weight attributed to the age factor in the two equations and to the fact that the MDRD equation does not include body weight.

Table 3

Match or mismatch between CG- and MDRD-based eGFRs and CKD classification, %

MDRD	CGbsa			
	Stage II <60 ml/min	Stage IIIA 45– 60 ml/min	Stage IIIB 30– 45 ml/min	Stage IV 15– 30 ml/min
Stage II <60 ml/min	80	19	1	0
Stage IIIA 45–60 ml/min	7	65	29	0
Stage IIIB 30–45 ml/min	0	28	56	17
Stage IV 15–30 ml/min	0	0	20	80

Our results illustrate once more that estimating the GFR in the elderly is problematic. The CG formula and the MDRD formula are both frequently used, but they produce significant and clinically relevant differences in eGFR. Neither of these formulas has been well validated using gold standard methods [8]. There are other promising methods for estimating GFR in the elderly, including cystatin-C-based equations [7, 14] and the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula [11] but these methods also lack validation in elderly populations.

The strength of this study is that we recruited a representative sample of the elderly in Russia within

the framework of a prospective study. However, we had only single creatinine values, so we cannot really speak about the prevalence of chronic kidney disease given the fact that by definition, the eGFR should be below 60 mL/min for more than three months before a patient can be classified as suffering from CKD, and given that we have no data on the presence of proteinuria or other signs of kidney damage. However, we are convinced that our data offer an interesting insight into the magnitude of the problem. More research is required to increase our understanding of the natural history of impaired renal function in the elderly.

Conclusion

The prevalence of impaired renal function in elderly in the St. Petersburg region is relatively low, especially in the subgroup of males aged 75 and over, compared with that reported internationally in other studies. The Cockcroft–Gault and MDRD formulas generate significantly different results when they are used to classify study populations according to the stages of CKD.

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Table 4

The prevalence of chronic kidney disease reported internationally in other studies

Author	Country	Age groups, years	Prevalence based on the MDRD formula by stage	Prevalence based on the CG formula by stage
A. X. Garg et al. [5]	Canada	65–69	M: III–V (6.9%), IV–V (2.3%) F: III–V (20.1%), IV–V (2.7%)	M: III–V (14.9%), IV–V (2.3%), F: III–V (31.0%), IV–V (3.8%)
		70–74	M: III–V (12.5%), IV–V (2.4%) F: III–V (21%), IV–V (2.8%)	M: III–V (26.9%), IV–V (3.0%), F: III–V (44.6%), IV–V (4.1%)
		75–79	M: III–V (17.3%), IV–V (4.4%) F: III–V (25.4%), IV–V (3.8%)	M: III–V (37.8%), IV–V (5.8%), F: III–V (57.5%), IV–V (7.4%)
		80–85	M: III–V (24.9%), IV–V (2.6%) F: III–V (32.1%), IV–V (3.1%)	M: III–V (55.7%), IV–V (7.0%), F: III–V (70.3%), IV–V (12.6%)
		85–90	M: III–V (29.2%), IV–V (3.6%) F: III–V (32.1%), IV–V (3.1%)	M: III–V (66%), IV–V (11.3%), F: III–V (70.1%), IV–V (22.3%)
J. Coresh et al. [3]	USA	60–69 70+	7.6% stage III–V 24.9% stage III–V	10.5% stage III–V 49.2% stage III–V
M. Cirillo [1]	Italy	65–74 75+	M: 15.0%, F: 11.0% stage III–V M: 34.5%, F: 31.6% stage III–V	
L. Van Heden et al. [15]	Belgium	60–79 80+	M: 15%, F: 24% stage III–V M: 43.0%, F: 48.0% stage III–V	M: 18%, F: 31% stage III–V M: 78%, F: 86% stage III–V
«Crystal» study	Russia	65–75 75+	M: 11%, F: 14% stage III–V M: <1%, F: 2% stage IV–V M: 15%, F: 29% stage III–V M: 1%, F: 1% stage IV–V	M: 21%, F: 18% stage III–V M: <1%, F: 1% stage IV–V M: 44%, F: 52% stage III–V M: 3%, F: 1% stage IV–V

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Успехи геронтол. 2011. Т. 24. № 1. С. 108–113

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РАСПРОСТРАНЕННОСТЬ НАРУШЕННОЙ ФУНКЦИИ ПОЧЕК У ПОЖИЛЫХ В ОДНОМ ИЗ РАЙОНОВ САНКТ-ПЕТЕРБУРГА: НЕКОТОРЫЕ РЕЗУЛЬТАТЫ ПРОЕКТА «ХРУСТАЛЬ»

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Хроническая болезнь почек (ХБП) широко распространена у лиц пожилого возраста. Она признана независимым фактором риска развития заболеваний системы кровообращения. Выявление ХБП также имеет значение для определения оптимальной дозы назначаемых лекарств и предотвращения дальнейшего ущерба почечной функции путем ограничения потенциально опасных препаратов. Цель исследования — изучение распространенности ХБП у пожилых (65 лет и старше) в одном из районов Санкт-Петербурга и оценка зависимости показателя от метода оценки скорости клубочковой фильтрации. Проведено одномоментное изучение популяции пожилых людей в Колпино в проспективном исследовании. Уровень креатинина сыворотки крови определяли в одной лаборатории. Функцию почек оценивали с помощью формул для расчета скорости клубочковой фильтрации, основанных на уровне креатинина. Обследованы 611 пожилых пациентов (возраст 65–91 год). С использованием формулы, полученной в исследовании MDRD (Modification of Diet in Renal Disease Study), установлено, что распространенность ХБП III–V стадии у мужчин 65–74 лет — 11%, старше 74 лет — 15%; у женщин — 14 и 29%, соответственно. Установлено значительное несоответствие классификаций стадий ХБП, основанных на различных формулах, в данном случае при сравнении формул MDRD и Кокрофта–Голта. В нашем исследовании распространенность ХБП IV–V стадии в обеих возрастных группах была значительно ниже, чем установлено в других международных исследованиях. Распространенность нарушенной функции почек у пожилых людей в одном из районов Санкт-Петербурга по сравнению с данными, полученными в других исследованиях, относительно низка, особенно у мужчин 75 лет и старше. Формулы MDRD и Кокрофта–Голта дают противоречивые показатели, когда используются для классификации разных стадий ХБП у пожилых людей.

Ключевые слова: хроническая болезнь почек, пожилые, скорость клубочковой фильтрации, MDRD-формула