Estimation of renal function in adult outpatients with normal serum creatinine

Temesgen Fiseha*, Tizita Mengesha, Rahel Girma, Edosa Kebede and Angesom Gebreweld*

Abstract

Objective: The aim of this study was to estimate the prevalence of renal insufficiency using estimated glomerular filtration rate (eGFR) among adult outpatients with normal SCr.

Results: A total of 414 patients with normal SCr were included in the study. Mean GFR (ml/min/1.73 m²) was 116.8 ± 43.5 using the MDRD equation and 90.5 ± 33.1 by the C–G formula. According to the MDRD formula, mild renal insufficiency (i.e. eGFR 60–89.9 ml/min/1.73 m²) was found in 21.5% of the patients and moderate renal insufficiency (i.e. eGFR 30–59.9 ml/min/1.73 m²) was found in 7.7%. According to the Cockcroft–Gault (C–G) formula, mild renal insufficiency was found in 38.2% and moderate renal insufficiency in 16.9% of the patients with normal SCr. In multivariate analysis, older age, female sex, a family history of kidney disease or other chronic diseases and high systolic blood pressure were associated with prevalent renal insufficiency depending on the formula used to estimate GFR. This study demonstrates the substantial prevalence of impaired renal function among Ethiopian adult outpatients with normal SCr. Including calculated estimates of GFR in routine laboratory reporting may help to facilitate the identification and thus optimal management of patients with renal insufficiency.

Keywords: Serum creatinine, Renal function, Estimated glomerular filtration rate

Introduction

Kidney disease, even when renal function is only mildly or moderately altered, is an established risk factor for all-cause and cardiovascular mortality in high-risk patients, as well as in the general population [1–4]. Impaired renal function is also associated with an increased risk of several complications, such as anemia and bone mineral metabolism disorders, and poor outcomes, including cardiovascular events and progression to renal failure; requiring renal replacement therapy [5–7]. Early detection of renal impairment is, therefore, crucial to facilitate the employment of measures that can prevent or delay disease progression and reduce the risk of adverse outcomes [8]. Glomerular filtration rate (GFR) is accepted as the best indicator of renal function in both health and disease. GFR can be measured directly by clearance studies of ideal exogenous markers, such as inulin. However, none of these procedures are practical or economical for routine use and serum levels of endogenous filtration markers have traditionally been used to estimate renal function [9].

Serum creatinine (SCr) is the most widely used endogenous filtration marker for assessing renal function in clinical practice. However, SCr is insensitive to detect early renal disease, and levels could remain within the normal range even when renal function is significantly impaired; making the recognition and thus the optimal management of renal impairment at earlier stages more difficult [10, 11]. Current guidelines therefore recommend the use of prediction equations, such as the Modification of Diet in Renal Disease (MDRD) equation [12] and the Cockcroft–Gault equation [13], to estimate GFR (eGFR) whenever SCr is measured to facilitate early recognition of renal disease [14, 15]. In agreement with these guidelines, several studies provided evidence that incorporating eGFR into screening for renal impairment would identify individuals earlier in the natural history of the disease and enable the timely initiation of treatment.
to slow progression of renal disease and improve patient outcomes [16–18].

Most outpatient laboratories in Ethiopia do not routinely report estimated GFR when SCr is measured, and renal function is usually estimated by inspection of SCr levels in the primary care settings. Despite this, the under-ascertainment of impaired renal function among the Ethiopian adult outpatients with normal SCr has not been reported. Such information will be useful in establishing the clinical relevance and need of providing automated eGFR reporting for adult outpatients in the country. The aim of this study was to determine the prevalence of renal insufficiency using estimated GFR (eGFR) among adult outpatients with normal SCr at a hospital in Northeast Ethiopia.

**Main text**

**Methods**

**Study design, setting and population**

This cross-sectional study was conducted at the outpatient department of Debre Berhan Referral Hospital in North Shoa zone of Amhara regional state, which is located 130 km north of the capital Addis Ababa, Ethiopia. Adult outpatients (aged 18 years or more) referred by physicians for SCr measurements during the period from January to April 2018 were included in the study. Patients were excluded if they were treated with dialysis, hospitalized, have acute illnesses (fever) and if their SCr levels were abnormal (men > 1.5 mg/dl and women > 1.3 mg/dl). After applying exclusion criteria, 422 consecutive patients with normal SCr were qualified for the study.

**Sample size determination**

The sample size was calculated using single proportion formula on the basis of the following assumptions: a 95% confidence level; 5% margin of error; expected renal impairment prevalence of 50% and by adding 10% non-response rate. Respondents who did not participate in the examination component (n = 8) were excluded from the analysis. The final sample therefore included 414 individuals.

**Data collection**

Participants were interviewed for collecting demographic and other risk factor variables. Weight, height and blood pressure were measured at the time of the clinical examination performed. Body mass index (BMI) was calculated as weight square (kg) to height (meters), and participants were grouped into normal (BMI < 25 kg/m²), overweight (BMI = 25–29.9 kg/m²) and obese (BMI ≥ 30 kg/m²). Blood pressure (BP) was measured in the right upper arm in the sitting posture, after a 5 min rest and three measurements were averaged. Hypertension was defined as systolic BP ≥ 140 mmHg and/or diastolic BP ≥ 90 mmHg and/or use of antihypertensive medication. A blood sample was collected for SCr measurement using a modified Jaffe method as mg/dl with calibration traceable to IDMS reference material NIST SRM 909B level 2.

**Measurement of renal function**

Renal function was estimated according to the 4-variable Modification of Diet in Renal Disease (MDRD) study equation as eGFR = 186 × SCr (mg/dl)⁻¹.154 × age (years)⁻⁰.203 × 0.742 (if female) × 1.210 (if black) [12] and the Cockcroft–Gault (C–G) formula [13] normalized for the body surface area (BSA): (140-age) × Weight (kg) × 0.86 (if female) × 1.73/72 × SCr (mg/dl) × BSA (m²). Patients were categorized as having normal renal function when the eGFR was ≥ 90 ml/min/1.73 m², and mild, moderate and severe renal insufficiency when the eGFR was 60–89.9, 30–59.9 and 15–29.9 ml/min/1.73 m², respectively [14, 19]. Moderate renal insufficiency was further categorized into G3a (eGFR 45–59.9 ml/min/1.73 m²) and G3b (eGFR 30–44.9 ml/min/1.73 m²) [19].

**Statistical analysis**

Statistical analyses were carried out using SPSS version 20.0 software (SPSS Inc., Chicago, IL, USA). Data were expressed as mean ± standard deviation (SD) or percentage. Comparisons between groups were done by Chi square (χ²) test or t-test as appropriate. Multivariate logistic regression was conducted and the corresponding adjusted odds ratios (AOR) and 95% confidence intervals (CI) were used to identify factors independently associated with renal insufficiency. P < 0.05 was used to indicate statistical significance.

**Results**

A total of 414 patients who had SCr level within the normal range participated in this study. Mean age was 48.9 ± 17 years, and 216 (52.2%) were males. Of the total participants, 83 (20.0%) were diabetic, 89 (21.5%) were hypertensive, 32 (7.7%) had cardiovascular disease and 29 (7.0%) were HIV positive patients. Majority, 372 (89.9%) of the participants had no a family history of kidney disease (FH-KD). Mean BMI was 21.82 ± 2.56 kg/m². Mean systolic and diastolic BP (mmHg) were 124 ± 10 and 79 ± 10, respectively. Mean SCr was 0.88 ± 0.26 mg/dl. The mean eGFR (ml/min/1.73 m²) of the participants were 116.8 ± 43.5 and 90.5 ± 33.1 according to the MDRD and C–G equations, respectively (Table 1).

Estimation of renal function in patients with normal SCr using the MDRD and C–G equations are presented in Table 2. In patients with normal SCr, according to the MDRD equation mild renal insufficiency (eGFR
60–89.9 ml/min/1.73 m²) was found in 21.5% of the patients and moderate renal insufficiency (eGFR 30–59.9 ml/min/1.73 m²) was found 7.7%. According to the C–G formula, mild renal insufficiency was found in 38.2% of the patients and moderate renal insufficiency (eGFR 30–44.9 ml/min/1.73 m²) was found in 16.9% of the patients with normal SCr. Thirty-two (7.7%) and 38 (9.2%) of patients with normal SCr had mild to moderately impaired renal function (eGFR 45–59.9 ml/min/1.73 m²) according to the MDRD and C–G equations, respectively. In addition, 32 (7.7%) patients had moderate to severely impaired renal function (eGFR 30–44.9 ml/min/1.73 m²) despite normal SCr when renal function was estimated using the C–G formula (Table 2).

Characteristics of patients with and without clinically significant renal insufficiency (eGFR < 60 ml/min/1.73 m²) according to the MDRD equation are shown in Table 3. Patients with renal insufficiency were significantly older, females, had low educational status, family history of kidney disease or other chronic disease (diabetes, hypertension or CVD), medical history of hypertension, high systolic and diastolic BP, higher BMI and SCr when compared with patients with eGFR ≥ 60 ml/min/1.73 m². Except for gender and BMI, the same pattern was found when C–G formula was used.

In multivariate analysis, older age (AOR = 10.81, 95% CI 4.05–28.83, P < 0.001), female sex (AOR = 32.00, 95% CI 7.99–128.13; P < 0.001), a family history of kidney disease, HTN, DM or CVD, medical history of hypertension, high systolic and diastolic BP, higher BMI and SCr when compared with patients with eGFR ≥ 60 ml/min/1.73 m². Except for gender and BMI, the same pattern was found when C–G formula was used.

Table 1 Demographic and clinical characteristics of study subjects with normal serum creatinine (n = 414)

| Characteristics                  |   |   |
|----------------------------------|---|---|
| **Age (year), mean ± SD**        | 48.9 ± 17 |
| **Age group, n (%)**             |   |   |
| 18–30                            | 84 (20.3) |
| 31–40                            | 71 (17.1) |
| 41–50                            | 69 (16.7) |
| 51–60                            | 79 (19.1) |
| > 60                             | 111 (26.8) |
| **Sex, n (%)**                   |   |   |
| Male                             | 216 (52.2) |
| Female                           | 198 (47.8) |
| **Education, n (%)**             |   |   |
| < High school                    | 292 (70.5) |
| ≥ High school                    | 122 (29.5) |
| **Family history, n (%)**        |   |   |
| Kidney disease                   | 42 (10.1) |
| Hypertension, diabetes or CVD    | 90 (21.7) |
| **Medical history, n (%)**       |   |   |
| Diabetes                         | 83 (20.0) |
| Hypertension                     | 89 (21.5) |
| Cardiovascular disease           | 32 (7.7) |
| HIV                              | 29 (7.0) |
| **Current smoker, n (%)**        | 23 (5.6) |
| **Body mass index (Kg/m²), mean ± SD** | 21.82 ± 2.56 |
| **Systolic BP (mmHg), mean ± SD** | 124 ± 12 |
| **Diastolic BP (mmHg), mean ± SD** | 79 ± 10 |
| **Serum creatinine (mg/dl), mean ± SD** | 0.88 ± 0.26 |
| **eGFRMDRD (ml/min/1.73 m²), mean ± SD** | 116.8 ± 43.5 |
| **eGFRC–G (ml/min/1.73 m²), mean ± SD** | 90.5 ± 33.1 |

BP blood pressure, CVD cardiovascular disease, eGFR estimated glomerular filtration rate

Table 2 Estimation of renal function in patients with normal serum creatinine using the simplified MDRD and Cockcroft–Gault formulas

| GFR (ml/min/1.73 m²) | Description | MDRD, n (%) | Cockcroft–Gault, n (%) |
|----------------------|-------------|-------------|------------------------|
| ≥ 90                 | Normal or high GFR | 293 (70.8) | 186 (44.9) |
| 60–89.9              | Mildly ↓ GFR | 89 (21.5) | 158 (38.2) |
| 30–59.9              | Moderate ↓ GFR | 32 (7.7) | 70 (16.9) |
| 45–59.9              | Mild to moderate ↓ GFR | 32 (7.7) | 38 (9.2) |
| 30–44.9              | Moderate to severe ↓ GFR | – | 32 (7.7) |

GFR glomerular filtration rate

Table 3 Characteristics of patients with and without renal insufficiency (eGFRMDRD < 60 ml/min/1.73 m²)

|                        | eGFR < 60 ml/min/1.73 m² | eGFR ≥ 60 ml/min/1.73 m² |
|------------------------|--------------------------|--------------------------|
| Age above 60 yearsb, % | 68.8                     | 23.3                     |
| Female sexb, %         | 90.6                     | 44.2                     |
| Education: < High schoola, % | 87.5                  | 69.1                     |
| Family history, %      |                          |                          |
| Kidney diseaseb        | 28.1                     | 8.4                      |
| HTN, DM or CVDb        | 50.0                     | 19.4                     |
| Medical history, n (%) |                          |                          |
| Hypertensiona          | 43.8                     | 19.6                     |
| Diabetes mellitus      | 31.2                     | 19.1                     |
| Cardiovascular disease | 9.4                      | 7.6                      |
| HIV                    | 6.2                      | 7.1                      |
| Current smoker         | 9.4                      | 5.2                      |
| Antihypertensive drug intakeb, % | 40.6             | 13.6                     |
| Systolic BP (mm Hg)b   | 134.1 ± 11.60            | 123.2 ± 11.56            |
| Diastolic BP (mm Hg)b  | 85.6 ± 8.51              | 78.7 ± 9.52              |
| Hypertensionb, n (%)   | 65.6                     | 27.5                     |
| BMI (kg/m²)b           | 22.87 ± 3.0              | 21.73 ± 2.5              |
| Serum creatinine (mg/dlb) | 1.34 ± 0.07             | 0.84 ± 0.23              |
| eGFR (ml/min/1.73 m²)b | 52.34 ± 2.65             | 122.19 ± 40.91           |

| AHR hypertension, DM diabetes mellitus, CVD cardiovascular disease, BP blood pressure, BMI body mass index, eGFR estimated glomerular filtration rate |
|---------------------------------------------------------------------------------------------------------------------------------------------|
| a Differences or associations significant at P < 0.05                                                                                     |
| b Differences or associations significant at P < 0.001                                                                                    |
other chronic diseases (AOR = 3.06, 95% CI 1.19–7.86, 
\( P = 0.020 \)), and high systolic BP (AOR = 1.07, 95% CI 
1.03–1.12, \( P = 0.002 \)) were independently associated 
with increased risk of renal insufficiency according to the 
MDRD equation. However, only older age (AOR = 14.06, 
95% CI 7.39–26.77; \( P = 0.001 \)) and a FH-KD (AOR = 2.80, 
95% CI 1.21–6.48, \( P = 0.017 \)) were independently associ-
ated with prevalent renal insufficiency when using C–G 
formula.

Discussion

In this study, we found a high prevalence of abnormal 
renal function up to 55% on the basis of eGFR in adult 
out-patient with normal SCr. Clinically significant renal 
insufficiency (as defined by eGFR < 60 ml/min/1.73 m²) 
was found in 7.7–16.9% of the study participants depend-
ing on the formula used to estimate GFR. In previous 
Studies, a considerable number of out-patients ranging 
from 5.3 to 19.3% have shown to have significantly 
impaired renal function (eGFR < 60 ml/min/1.73 m²) 
with normal SCr [20–23]. Another study also found that 
13.9% of out-patients with normal range SCr levels had 
substantially abnormal calculated GFR, with C–G values < 50 ml/min [10]. These findings suggest that if SCr 
is used instead of eGFR as a measure of renal function, 
there is a likely chance of missing a significant number of 
patients with renal insufficiency.

This study shows that a large proportion of females 
and older persons with impaired renal function are not 
diagnosed if clinicians rely only on normal SCr levels as 
evidence of normal renal function. This is supported by 
the results of related studies and by the fact that SCr pro-
duction is dependent on lean body mass and therefore 
may not be an accurate reflection of GFR, especially in 
older subjects and females because they have a reduced 
muscle mass [10, 16, 23–27]. The above studies have also 
demonstrated that inclusion of eGFR calculated by using 
equations which attempt to correct for factors affecting 
the muscle mass, such as age, sex and body size may facil-
itates the early identification and intervention of these 
subgroup of patients with renal impairment.

The finding of significantly prevalent renal insuf-
Cficiency in patients with a FH-KD, a family history of 
other chronic diseases (diabetes, hypertension or CVD) 
and high systolic BP, suggests that a substantial propor-
tion of cardiovascular at risk patients whose SCr levels 
fall within the normal range would not have been iden-
tified as having abnormal renal function without use of 
the GFR equations to estimate renal function. This is 
consistent with previous findings which documented 
that renal function should be assessed by using eGFR 
than SCr alone to facilitate the identification of high-
risk patients with renal insufficiency at a time sufficient 
to ensure proactive care to delay disease progression and 
 improve outcomes [21, 28, 29]. This was also supported 
by the NKF K/DOQI guidelines, which recommend 
using a GFR estimating equations to derive GFR from 
SCr (eGFR) rather than relying on SCr alone in at-risk 
populations [30].

Estimates of GFR using prediction equations provide 
substantial improvements over the measurement of SCr 
alone in the clinical assessment of renal function [31]. 
Several creatinine-based GFR prediction equations were 
developed in the past for estimating renal function, but 
the most commonly used are the MDRD [12, 32] and 
the C–G equations [13]. The MDRD equation that was 
developed using data from patients with established renal 
insufficiency as measured by 125I-iothalamate clearance 
adjusted for BSA is the most widely used in clinical prac-
tice today. Since it relies on age, sex, race and SCr only, 
this equation is quick and easy to calculate on all patients 
using data routinely provided when requesting a SCr 
measurement. It has been generally shown to provide a 
more accurate estimates of GFR than measured creati-
nine clearance or the C–G equation [12, 33]. The C–G 
equation, which predicts creatinine clearance [13], is a 
simple and recommended means to assess renal func-
tion. Unlike the MDRD equation, it requires a measure 
of height and computation of BSA (making it a less con-
venient method for routine use). However, eGFR derived 
from the C–G equation is superior to SCr alone in the 
asessment of renal function [33].

Conclusions

In conclusion, this study demonstrates a substantial 
prevalence of renal impairment among Ethiopian adult out-
patients identified as having normal SCr levels. A large 
proportion of the elderly, women and cardiovascular at 
risk patients will not be recognized as having impaired 
renal function if clinicians rely on normal SCr as evi-
dence of normal renal function. Including calculated esti-
mates of GFR in routine laboratory reporting may help to 
facilitate the early identification and thus optimal man-
agement of patients with renal impairment.

Limitations

The use of calculated GFR but not measured GFR, which 
is not the gold standard, to estimate renal function is the 
first limitation. Secondly, we used the MDRD study equa-
tion, the validation of which is lacking among Ethiopian 
adults. Third, the measurement of serum creatinine was 
not standardized; this might influence the performance 
of eGFR equations, particularly at higher values. This 
also limited us from using the popular Chronic Kidney 
Disease Epidemiology (CKD–EPI) equation, as recom-
Ended by the KDIGO guidelines. Finally, the estimation
of abnormal GFR is based on a single measurement of SCr which might lead to over or under estimating patients with abnormal GFR.

Abbreviations
AOR: adjusted odds ratio; BMI: body mass index; BP: blood pressure; C–G: Cockcroft–Gault; CI: confidence interval; eGFR: estimated glomerular filtration rate; FF–KD: family history of kidney disease; GFR: glomerular filtration rate; MDRD: modification of diet in renal disease.

Acknowledgements
The authors would like to acknowledge data collectors, and staff of Debre Berhan Referral Hospital for collecting the data.

Authors' contributions
TF and AG were involved in the conception, design, analysis, interpretation, report writing and manuscript writing. TM, RG and EK had been involved in the design, analysis, and critically reviewing the manuscript. All authors read and approved the final manuscript.

Funding
This study did not receive any official funding.

Availability of data and materials
The date of this study can’t be shared publicly due to presence of sensitive information. The data are available from the corresponding author on reasonable request.

Ethics approval and consent to participate
Study protocol was approved by the Institutional Review Board of College of Medicine and Health Sciences, Wollo University. An informed verbal as well as written consent was obtained from each study participants. Moreover, confidentiality was assured for all the information provided and personal identifiers were not included on questionnaire.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

Received: 7 February 2019 Accepted: 17 July 2019 Published online: 29 July 2019

References
1. Henry RM, Kostense PJ, Bos G, Dekker JM, Nipels G, Heine RJ, et al. Mild renal insufficiency is associated with increased cardiovascular mortality: the Hooorn Study. Kidney Int. 2002;61:1402–7.
2. Muntner P, He J, Hamm L, Loria C, Whelton PK. Renal insufficiency and subsequent death resulting from cardiovascular disease in the United States. J Am Soc Nephrol. 2002;13:745–53.
3. Leocinini G, Viazzi F, Parodi D, Ratto E, Vettoretti S, Vaccaro V, et al. Mild renal dysfunction and cardiovascular risk in hypertensive patients. J Am Soc Nephrol. 2004;15:588–90.
4. Oh SW, Baek SH, Kim YC, Goo HS, Heo NJ, Na K, et al. Mild decrease in estimated glomerular filtration rate and proteinuria are associated with all-cause and cardiovascular mortality in the general population. Nephrol Dial Transpl. 2012;27:2284–90.
5. Inker LA, Coresh J, Levey AS, Tighiouart H, Stone K, Delakas D, et al. Level of kidney function as a risk factor for atherosclerotic cardiovascular outcomes in the community. J Am Coll Cardiol. 2003;41:47–55.
6. Manjunath G, Tighiouart H, Ibrahim H, Macleod B, Salem DN, Griffith JL, et al. Level of kidney function as a risk factor for atherosclerotic cardiovascular outcomes in the community. J Am Coll Cardiol. 2003;41:47–55.
7. So WY, Kong APS, Ma RCW, Ozaki R, Szeto CC, Chan NN, et al. Glomerular filtration rate, cardioaerial end points, and all-cause mortality in type 2 diabetic patients. Diabetes Care. 2006;29:2046–52.
8. Johnson DW. Evidence-based guide to slowing the progression of early renal insufficiency. Intern Med. 2004;34:50–7.
9. Lesley A, Coresh J, Greene T, Andrew S. Assessing kidney function—measured and estimated glomerular filtration rate. N Engl J Med. 2006;354:2473–83.
10. Duncan L, Heathcote J, Djurdjev O, Levin A. Screening for renal disease using serum creatinine: who are we missing? Nephrol Dial Transpl. 2001;16(5):1042–6.
11. Hommel K, Madsen M, Kamper A-L. The importance of early referral for the treatment of chronic kidney disease: a Danish nationwide cohort study. BMC Nephrol. 2012;13:108.
12. Levey AS, Greene T, Kusek JW, Beck GJ. A simplified equation to predict glomerular filtration rate from serum creatinine. J Am Soc Nephrol. 2000;11:155A (Abstract).
13. Cockcroft DW, Gault MH. Prediction of creatinine clearance from serum creatinine. Nephron. 1976;16:31–41.
14. Levey AS, Eckardt K-U, Tsukamoto Y, Levin A, Coresh J, Rossert J, et al. Definition and classification of chronic kidney disease: a position statement from Kidney Disease: Improving Global Outcomes (KDIGO). Kidney Int. 2005;67(6):2089–100.
15. MacGregor GS, Taal MW. Renal Association Clinical Practice Guideline on detection, monitoring and management of patients with CKD. Nephron Clin Pract. 2011;118(Suppl 1):c71–100.
16. Akbari A, Swedko PJ, Clark HD, Hogg W, Lemelin J, Magner P, et al. Detection of chronic kidney disease with laboratory reporting of estimated glomerular filtration rate and an educational program. Arch Intern Med. 2004;164:1788–92.
17. Jain AK, Cuerden MS, McLeod I, Hemmelmang B, Akbari A, Tonelli M, et al. Reporting of the estimated glomerular filtration rate was associated with increased use of angiotensin-converting enzyme inhibitors and angiotensin-II receptor blockers in CKD. Kidney Int. 2012;81:1248–53.
18. Wang V, Hammad BG, Maciejewski ML, Hall RK, Scyoc LV, Garg AX, et al. Impact of automated reporting of estimated glomerular filtration rate in the veterans health administration. Med Care. 2015;53(2):177–83.
19. KDIGO 2012 Clinical practice guideline for the evaluation and management of chronic kidney disease. Kidney Int. 2013;83(Suppl):1–163.
20. Wu M-J, Shu K-H, Liu P-H, Chang P-H, Cheng C-H, Chen C-H, et al. High risk of renal failure in stage 3b chronic kidney disease is under-recognized in standard medical screening. J Chin Med Assoc. 2010;73(10):515–22.
21. Lu Z, Yin J, Zhang G, Wu R, Zhao Q, Wang N, et al. Underestimated incidence of kidney disease in nonrenal outpatient. Ren Fail. 2017;39(1):328–32.
22. Lorente DG, Lorente JG, Usach TS. Repeated serum creatinine measurement in primary care: not all patients have chronic renal failure. Nefrologia. 2015;35:395–402.
23. Kannapiran M, Nisha D, Madhusudhana Rao A. Underestimation of impaired kidney function with serum creatinine. Ind J Clin Biochem. 2010;25(4):380–4.
24. Labrador PJ, Mengotti T, Jiménez M, Macias M, Vicente F, Labrador J, et al. Occult renal failure in primary care. A women’s problem? Nefrologia. 2007;27(6):716–20.
25. Swedko PJ, Clark HD, Parnasothy K, Akbari A. Serum creatinine is an inadequate screening test for renal failure in elderly patients. Arch Intern Med. 2003;163(3):356–60.
26. Duru OK, Vargas RB, Kermah D, Nissenson AR, Norris KC. High prevalence of stage 3 chronic kidney disease in older adults despite normal serum creatinine. J Gen Intern Med. 2008;23(11):186–92.
27. Giannelli SV, Patel KV, Windham BG, Rizzello F, Ferrucci L, Guralnik JM. Magnitude of underascertainment of impaired kidney function in older adults with normal serum creatinine. J Am Geriatr Soc. 2007;55:S16–23.
28. Rodrigo MP, Andrés MR. Evaluation of hidden renal insufficiency by abbreviated-MRD equation. Nefrología. 2006;26(3):339–43.
29. Fácia L, Bertomeu-González V, Bertomeu V, González-Juanatey JR, Maçón P, Morillas P; RICAR group. Importance of recognizing occult renal disease in hypertensive patients. Rev Esp Cardiol. 2009;62(Suppl):282–7.
30. National Kidney Foundation. K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. Ann Intern Med. 2002;139(2):S1–266.
31. Bostom AG, Kronenberg F, Ritz E. Predictive performance of renal function equations for patients with chronic kidney disease and normal serum creatinine levels. J Am Soc Nephrol. 2002;13:2140-4.

32. 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. Modification of Diet in Renal Disease Study Group. Ann Intern Med. 1999;130(6):461-70.

33. Coresh J, Stevens LA. Kidney function estimating equations: where do we stand? Curr Opin Nephrol Hypertens. 2006;15:276-84.

Publisher’s Note
Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.