

Estimation of Glomerular Filtration Rate Comparison of Equations to Estimate GFR: Cockcroft-Gault, MDRD, CKD - Epi and BIS1

Skalli Zoubair^{1*} and Fatima Bentiss²

¹Provincial Hospital Center August- 20-Ifrane– Hemodialysis Center Azrou, Morocco

²Provincial Hospital Center crown prince -Hemodialysis Center – El Hajeb, Morocco

*Corresponding Author: Dr. SkalliZoubair, Provincial Hospital Center August- 20-Ifrane-Hemodialysis Center Azrou, Morocco, Tel: +212 689099989, E-mail: skallizoubair@gmail.com

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Abstract

Background

Glomerular filtration rate (GFR) estimation is a critical step in clinical nephrology and has important implications in clinical practice, but also in the field of epidemiology and prevention. Commonly used formulas (Cockcroft-Gault, MDRD) have limitations in their relevance at the extremes of age and weight, and at low serum creatinine levels.

The newer formulas, CKD-Epi and BIS1, allow for a more precise estimation of GFR.

Objective: To compare the relevance and limitations of these newer formulas with those of the Cockcroft-Gault and MDRD formulas in a Moroccan population.

Methods

This was a two-center, ambispective study conducted over a six-year period, including 3,578 patients. We collected demographic, clinical, and biological data to determine the GFR for each patient using the four formulas. Descriptive and analytical statistical analyses were performed using standard tests, given that the patient distribution followed a normal distribution.

Results

In our series, the CKD-Epi formula yielded an intermediate GFR value compared to the Cockcroft-Gault and MDRD formulas, particularly in cases of obesity, for normal serum creatinine levels, and in elderly patients. The BIS1 formula is well-suited to the elderly population. It should be noted that there was no significant difference between the MDRD and CKD-Epi formulas in cases of renal insufficiency.

Conclusion

This study demonstrates that the CKD-Epi formula is more relevant. However, the MDRD formula can still be used, especially in cases of kidney failure.

Keywords: Glomerular filtration rate; Cockcroft and Gault; MDRD; CKD-Epi; BIS 1

Introduction

Glomerular filtration rate (GFR) estimation is a critical step in clinical nephrology and has important implications in clinical practice, but also in the field of epidemiology and prevention [1-4]. The measurement of GFR by a so-called reference technique remains fundamental but limited to specialized centers [1,5,6]. The definition of chronic kidney disease (CKD) is based, among other things, on the level of GFR and requires that it can be quickly and easily estimated [7]. In clinical practice, commonly used formulas (Cockcroft and Gault, MDRD) have limitations of relevance for extremes of age and weight and low serum creatinine values. CKD - Epi (Chronic Kidney Disease Epidemiology Collaboration) is a new formula that allows a more accurate estimate of GFR [8].

The purpose of our work is to compare the relevance and limits of the new formulas with Cockcroft and Gault and MDRD formulas in a Moroccan population.

Material and Methods

We conducted a bicentric ambispective study during a six-year from 2009 to 2014 including 3578 patients followed in nephrology consultation for various pathologies, or included as part of an early detection of kidney disease, or during a renal assessment performed for different indications (preoperative assessment, professional recruitment or others).

Patients come from different regions of the kingdom and come from various ethnic origins: Arab, Berber and Sahrawi.

We excluded children (age <16 years), chronic hemodialysis patients, peritoneal dialysis patients and renal transplant patients.

Each patient had a clinical examination with precise determination of the demographic parameters (age, sex, origin, weight) and clinical parameters (blood pressure, blood sugar, renal or general illness known)

The determination of serum creatinine is carried out under the same conditions by a spectrophotometric method for all patients.

For each patient, we determined the GFR according to the 3 formulas: Cockcroft and Gault by simple calculation relative to the body surface, simplified formula MDRD, formula CKD-Epi and the new formula BIS1 for patients over 75 years old thanks to a computer program.

The statistical comparison of the results obtained is carried out using Microsoft Office Excel 2003 software, in particular in elderly or obese patients and in the case of presumed normal renal function (low creatinine).

Cockcroft and Gault Formula

Creatinine Clearance = $(140 - \text{Age}) \times \text{Weight} \times k$ $k = 1.24$ for the man

Serum creatinine ($\mu\text{mol} / \text{l}$) $K = 1.04$ for the woman.

The result is reported at the calculated body surface and expressed in $\text{ml} / \text{min} / 1.73\text{m}^2$

- Simplified MDRD Study Group (for Modification of Diet in Renal Disease):

$$\text{GFR} = 186 \times \text{serum creatinine} (\mu\text{mol} / \text{l})^{-1.154} \times \text{Age}^{-0.203} \times k$$

$K=0.742$ for women, $K=1.21$ for black Americans, $K=0.763$ for Japanese, $K=1.23$ for Chinese

Formula CKD-Epi (for Chronic Kidney Disease Epidemiology):

$$\begin{aligned} \text{Women: } & \begin{cases} \text{if Creatinine} \leq 62 \mu\text{mol} / \text{l}: \text{GFR} = 144 \times (\text{Scr} / 62)^{-0.329} \times (0.993)^{\text{Age}} \\ \text{if Creatinine} > 62 \mu\text{mol} / \text{l}: \text{GFR} = 144 \times (\text{Scr} / 62)^{-1.209} \times (0.993)^{\text{Age}} \end{cases} \\ \text{Men: } & \begin{cases} \text{if Creatinine} \leq 80 \mu\text{mol} / \text{l}: \text{GFR} = 141 \times (\text{Scr} / 80)^{-0.411} \times (0.993)^{\text{Age}} \\ \text{if Creatinine} > 80 \mu\text{mol} / \text{l}: \text{GFR} = 141 \times (\text{Scr} / 80)^{-1.209} \times (0.993)^{\text{Age}} \end{cases} \end{aligned}$$

Formula BIS1

$\text{GFR} = 3,736 \times \text{creatinine}^{-0.87} \times \text{age}^{-0.95}$ specific to the elderly subject.

Definitions

We have retained the definitions and classifications of the ANAES (2002) and the NKF / KDOQI (2002) which are retained by the "High Authority of Health HAS" in its technological evaluation report 2011 (Table I).

Table I: KDOQI 2002 Definition and Staging.

Stage	Description	GFR ($\text{ml}/\text{min}/1.73 \text{ m}^2$)
1	Kidney damage with normal or \uparrow GFR	90
2	Kidney damage with mild \downarrow in GFR	60–89
3	Moderate \downarrow in GFR	30–59
4	Severe \downarrow in GFR	15–29
5	Kidney failure	< 15 (or on dialysis)

- Normal renal function is defined by an estimated GFR according to the simplified formula of the MDRD group greater than or equal to $60 \text{ ml} / \text{min} / 1.73\text{m}^2$.

- The renal insufficiency is defined by a GFR estimated according to the simplified formula of the group MDRD strictly lower than $60 \text{ ml} / \text{min} / 1.73\text{m}^2$.

Results

Demographic Study

The average age of our patients is 48.7 ± 15.6 years with extremes ranging from 16 to 116 years. The distribution of patients by age shows that patients aged over 60 represent 7.8%. We noted a female predominance: sex ratio = 0.57 (about one man for e

two women) (Table II).

Table 2: Repartition of Patients According To Age and Gender.

All patients: 3578					
Men			Women		
1312 (36.7%)			2266 (73.3%)		
Age <30 years	30≤age<60	age≥60	Age <30 years	30≤age<60	age≥60
188 (14.3%)	733 (55.8%)	390 (29.8%)	279 (12.3%)	1522 (67.1%)	465 (20.6%)

Clinical Study

The average weight is 70.6 ± 14.8 kg [18-163].

Obesity, defined by a body mass index: $BMI \geq 30 \text{ kg/m}^2$, is noted in 939 patients or 26.2%. It is more common among women (38.4%) than men (9.3%). We highlighted 3 interesting populations to study: obese subjects, lean subjects and obese elderly subjects (Table 3).

Table 3: Repartition of patients according to BMI

All Patients: 3578 $BMI = \text{Weight} / \text{Height}^2 \text{ (Kg/m}^2\text{)}$		
BMI<25	25≤BMI<30	BMI ≥30
1691 (47.3%)	948 (26.5%)	939 (26.2%)

Patients are included in the study according to different reasons. It is a follow-up of hypertension in 594 patients, an HTA discovered during the screening of 405 patients, a follow-up of diabetes in 601 patients, a diabetes discovered during screening in 409 patients, a follow-up of specific kidney diseases in 977 patients. 592 are included without any particular pathological motive.

Study of Renal Function

General Study

The median serum creatinine is 9.54 mg / l [3-367] or $83.95 \mu\text{mol} / \text{l}$ [26-3230].

The average GFR estimated according to Cockcroft and Gault (relative to body surface area), MDRD and CKD-Epi formulas are respectively: $82.64 \pm 47.81 \text{ ml} / \text{min}$ [3-367], $69.71 \pm 47, 81$ [2-306] and 71.46 ± 33.53 [2-176].

Renal function is normal in 2454 patients or 68.58% (MDRD), while 1124 or 31.42% have renal failure (Table 4).

Table 4: Repartition of Patients According to GFR (MDRD).

Normal renal function		Renal failure		
2454 (68.58%)		1124 (31.42%)		
GFR≥90 ml/min	60≤GFR<90 ml/min	30≤GFR<60 ml/min	15≤GFR<30 ml/min	FRG<15 ml/min
915 (25.58%)	1539 (43%)	540 (15.11%)	223 (6.2%)	361 (10.11%)

It is also observed that standard deviation of the average obtained by CKD-Epi formula is lower than standard deviations of the averages obtained by the two other formulas. ($33.53 < 47.81$)

Therefore, for a given serum creatinine value, CKD-Epi formula gives less scattered GFR estimates than Cockcroft and Gault and MDRD formulas, regardless of age and weight. A notion appears: relevance.

The graphical representation of all the results obtained from the three formulas shows that CKD-Epi formula gives, generally, an intermediate value with respect to those obtained by Cockcroft and Gault and MDRD formulas. Indeed, CKD-Epi gives a value of intermediate GFR in 2092 cases is 58.46% (Figure 1).

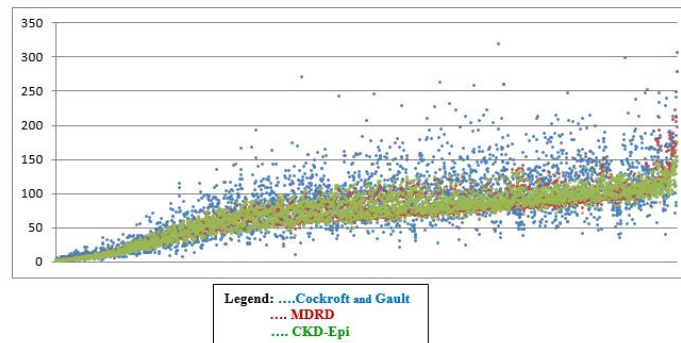


Figure 1: Estimate of GFR by the Three Formulas in the General Group.

We have tried to locate this intermediate value given by the formula CKD-Epi. For this we have calculated for each patient the following ratios: CKD-Epi/MDRD and CKD-Epi/Cockcroft and Gault.

We noted the following results:

Average CKD-Epi /MDRD ratio = 1.0171 ± 0.0743

Average CKD-Epi /Cockcroft and Gault ratio = 0.9496 ± 0.3436

The remarkable difference between the standard deviations of the two ratios shows immediately that the values obtained by CKD-Epi formula and MDRD formula are closer (four and a half times more) compared to the values obtained by CKD-Epi and Cockcroft and Gault formulas. (Figures 2 and 3).

Indeed Cockcroft and Gault formula is very influenced by the weight of the patient.

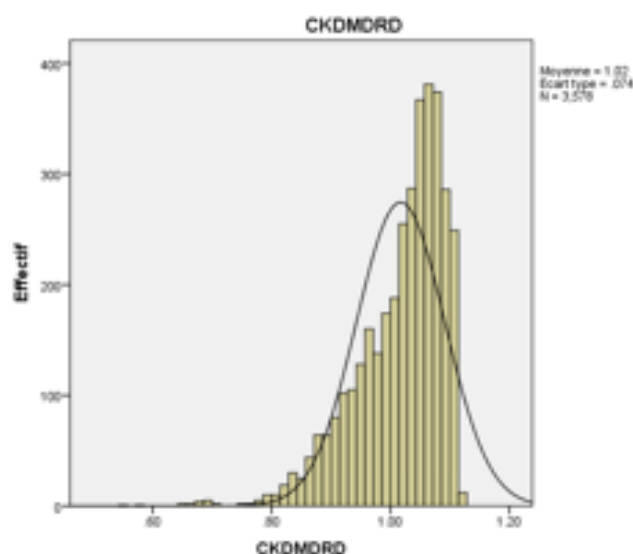


Figure 2: Narrow Gaussian distribution CKD-Epi / MDRD values.

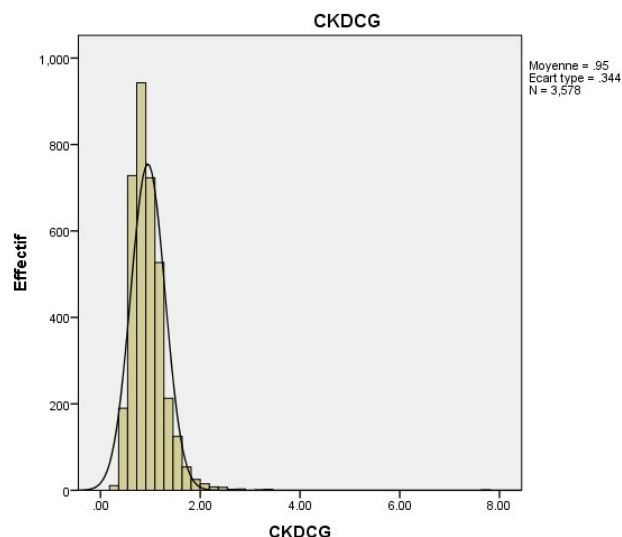


Figure 3: Greater Gaussian distribution of CKD-Epi / Cockcroft-Gault ratio values.

Study of the Particular Populations

According to the GFR

For GFR values <60 ml/min, in 1124 cases (31.4%) MDRD and CKD-Epi formulas are identical with averages of 29.9 ± 19.2 ml/min versus 29.7 ± 19.9 ml/min as shown in figure n° 4. We noticed that the ratio CKD-Epi / MDRD ≈ 1 (Figure 5).

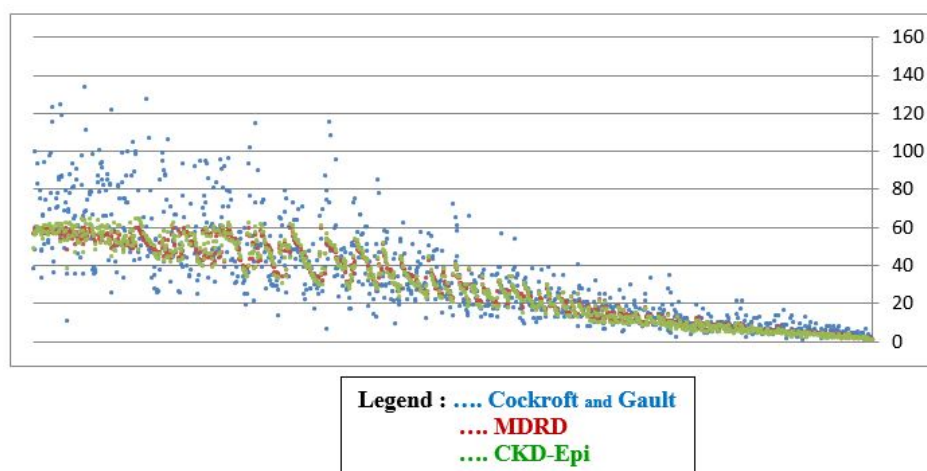


Figure 4: Estimates of GFR by all Three Formulas In Patients With Renal Insufficiency.

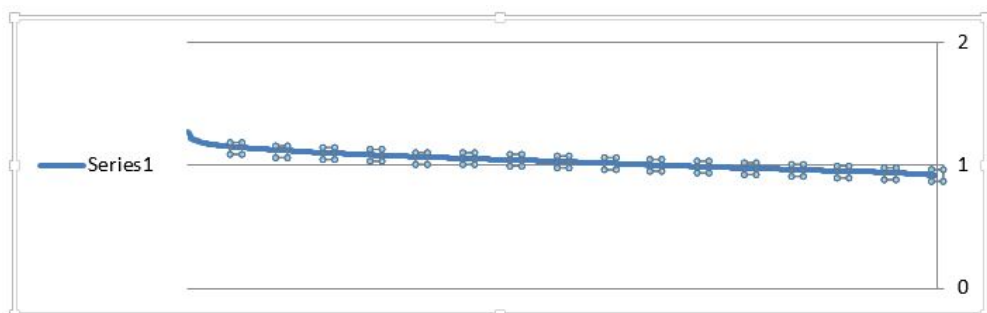


Figure 5: Graphical Representation of the CKD-Epi / MDRD Report

Statistical analysis shows that the discreet difference observed between the averages of the CKD-Epi and MDRD formulas is not significant.

- For higher values of GFR (presumed normal renal function), CKD-Epi formula gives an intermediate value compared to those obtained by Cockcroft and Gault and MDRD formulas (Figure 6).

Cockcroft and Gault = 82.6 ± 47.8 ml / min

MDRD = 69.7 ± 34 ml / min

CKD-Epi = 71.4 ± 33.5 ml / min.

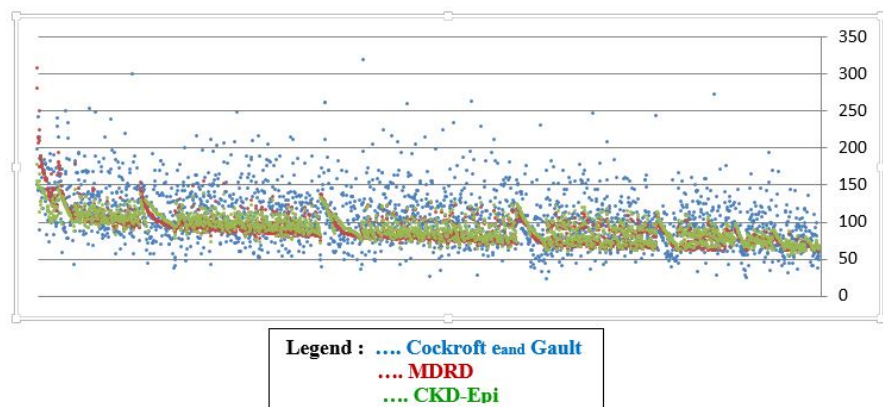


Figure 6: GFR estimates by all three formulas in patients with presumed normal renal function.

We calculated, for each patient, the differences observed between the results obtained by CKD-Epi formula and by Cockcroft and Gault formula on the one hand and between the results obtained by CKD-Epi formula and by MDRD formula on the second hand.

Difference 1 = CKD-Epi - Cockcroft and Gault

Difference 2 = CKD-Epi - MDRD

We compared the means and standard deviations of the two calculated differences.

Average of the difference 1 = 26.8 ± 24.2 ml / min

Average of the difference 2 = 6.1 ± 6.8 ml / min

We note that the average of difference 1 is significantly higher than average of difference 2 ($26.8 \gg 6.1$). As well as standard deviations ($24.2 \gg 6.8$).

This shows that the value obtained by the formula CKD-Epi is intermediate with respect to the other formulas, but it is also closer to the MDRD formula.

This difference is even more accentuated for $GFR > 90$ ml / min.

Thus, if the $GFR > 90$ ml / min the averages obtained are:

$$\text{CKD-Epi} = 108.3 \pm 11.3 \text{ ml / min}$$

$$\text{Cockcroft and Gault} = 122.6 \pm 38.6 \text{ ml / min}$$

$$\text{MDRD} = 108.1 \pm 29.1 \text{ ml / min}$$

It is also observed that standard deviation of the average obtained by CKD-Epi formula is lower than standard deviations of the averages obtained by the two other formulas. ($11.3 < 29.1 < 38.6$)

Therefore, in subjects with serum creatinine levels that are normal or low (normal renal function) the CKD-Epi formula is characterized by a much narrower Gaussian distribution than the MDRD and Cockcroft and Gault formulas. It seems more adapted and more precise in this population (Figure 7).

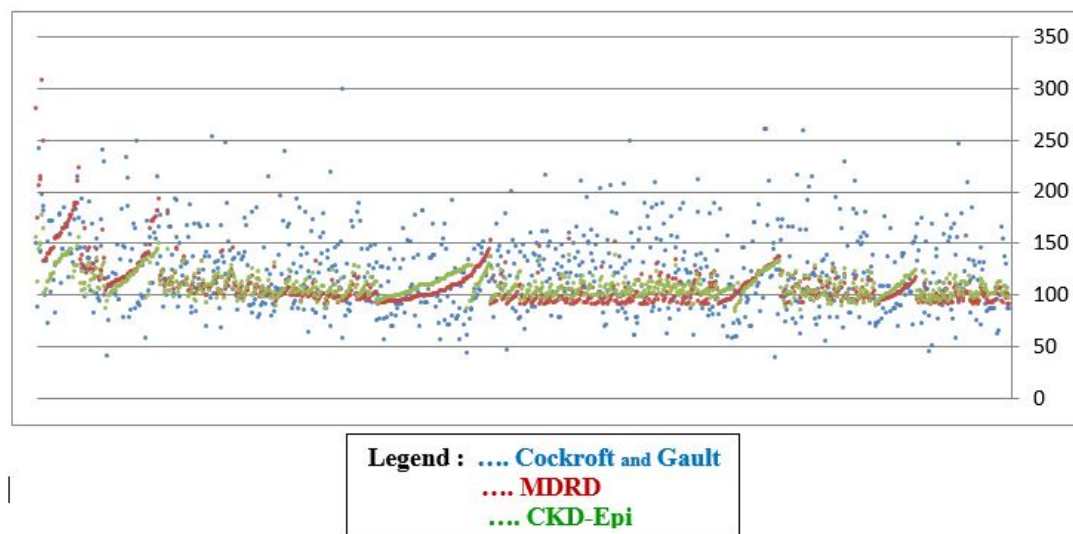


Figure 7: GFR estimates by all three formulas in patients with $\text{GFR} > 90 \text{ ml/min}$.

According To the Weight

- In patients whose $\text{BMI} \geq 30 \text{ Kg / m}^2$, the following averages are observed:

- Average Cockcroft and Gault = $121.7 \pm 42.9 \text{ ml / min}$

- Average MDRD = $76.6 \pm 21.3 \text{ ml / min}$

- Average CKD-Epi = $80.4 \pm 22.4 \text{ ml / min}$

In this population, there is a clear overestimation of GFR by Cockcroft and Gault formula (Figure 8). We also note a high value of standard deviation of the mean of this equation, indicating a significant dispersion of results despite Gaussian model of the population. Indeed, the difference observed between the averages of results obtained by this formula on the one hand and by CKD-Epi and MDRD formulas on the other hand is important and statistically significant (Tables 5 and 6).

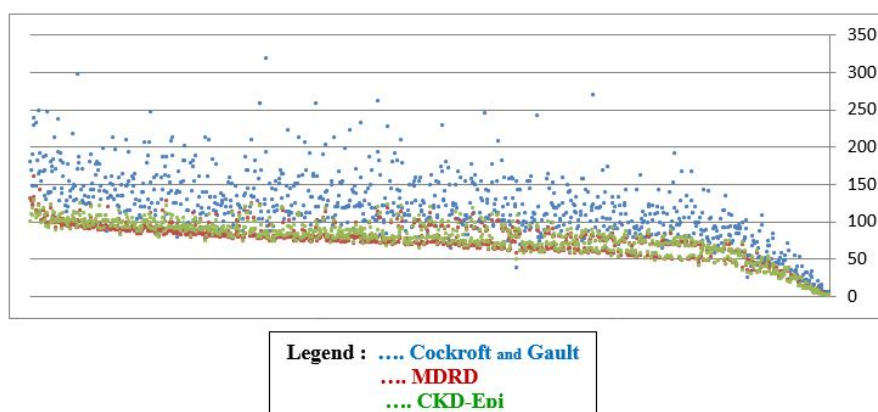


Figure 8: Estimates of GFR by all three formulas in obese patients.

Table 5: Statistical analysis of difference 1.

Cockroft et Gault	CKD-Epi	<i>p (test: t student)</i>
121.7 ± 42.9 ml/min	80.4 ± 22.4 ml/min	<0.001

Table 6: Statistical analysis of difference 2.

Cockroft et Gault	MDRD	<i>p (test: t student)</i>
121.7 ± 42.9 ml/min	76.6 ± 21.3 ml/min	<0.001

Let's calculate these differences and their averages:

- Difference 1 = Cockcroft and Gault - CKD-Epi
- Difference 2 = Cockcroft and Gault - MDRD
- Difference 3 = CKD-Epi - MDRD
- Average of the difference 1 = 41.29 ± 29.6 ml / min
- Average difference 2 = 45.16 ± 30.12 ml / min
- Average of the difference 3 = 3.87 ± 4 ml / min
- In patients who are overweight: $25 \leq \text{BMI} < 30 \text{ Kg} / \text{m}^2$, the following means are observed:
 - Average Cockcroft and Gault = 89.2 ± 37.2 ml / min
 - Average MDRD = 73.1 ± 29.1 ml / min
 - Average CKD-Epi = 76.2 ± 28.9 ml / min

Cockcroft and Gault formula also overestimates GFR in this population, but the importance of this overestimation is lower than in the obese population. However, statistical analysis shows that this difference is still significant (Figure 9).

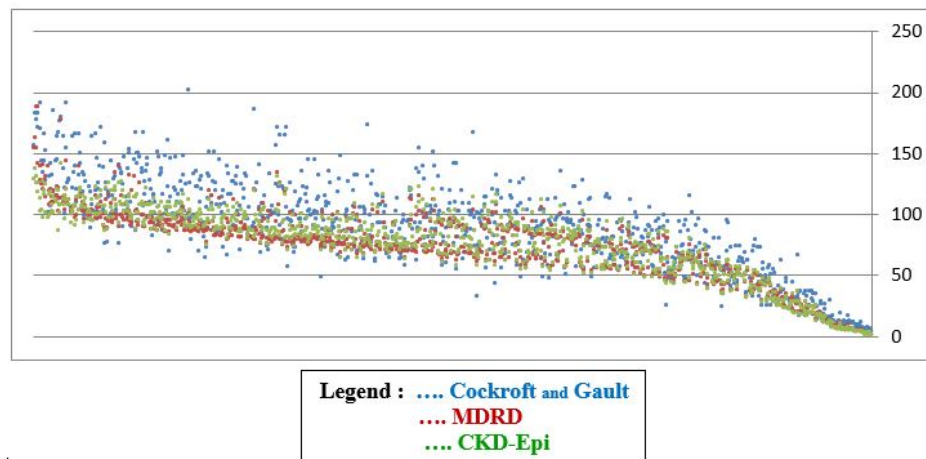


Figure 9: GFR Estimates by All Three Formulas in Patients Who Are Overweight.

- In patients who have a normal weight: $20 \leq \text{BMI} < 25 \text{ kg / m}^2$, the averages are:

- Average Cockcroft and Gault = $59.9 \pm 35.6 \text{ ml / min}$

- Average MDRD = $63.9 \pm 36.8 \text{ ml / min}$

- Average CKD-Epi = $65.1 \pm 33.2 \text{ ml / min}$

The three formulas give similar values without any significant difference.

It is in this population that the Cockcroft and Gault formula gives GFR estimates comparable to those of the other 2 formulas and with a similar standard deviation. In common practice, this formula can be used if the patient has a normal BMI and his or her age is not extreme.

The graphical representation of the results shows a remarkable superposition of the GFR estimation values by the CKD-Epi and MDRD formulas. However, the CKD-Epi equation seems even more accurate as the standard deviation of its mean is lower (Figure 10).

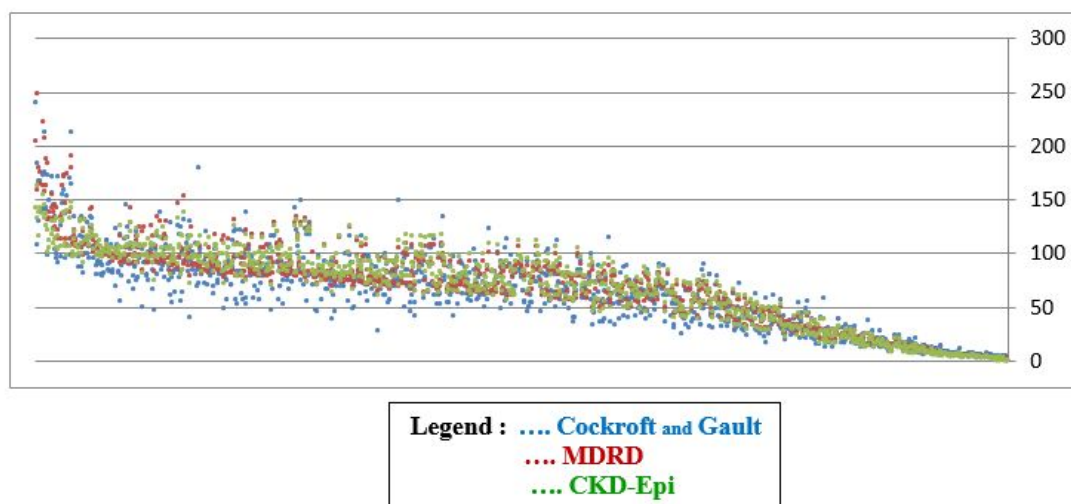


Figure 10: GFR estimates by all three formulas in normal weight patients.

- In patients who had: BMI <20 Kg / m², the following averages can be observed:

- Average Cockcroft and Gault = 41.6 ± 33.2 ml / min

- Average MDRD = 60.7 ± 47.4 ml / min

- Average CKD-Epi = 60.2 ± 42.9 ml / min

Cockcroft and Gault formula is characterized by a remarkable underestimation of GFR compared to other formulas but this underestimation is not statistically significant (Figure 11).

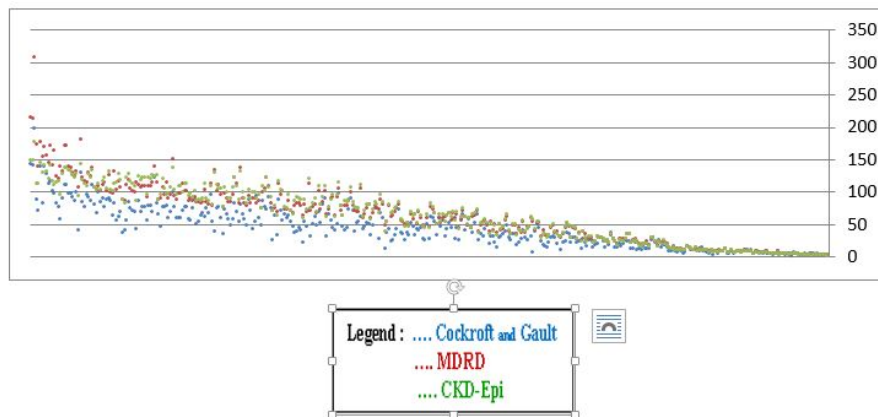


Figure 11: GFR estimates by all three formulas in patients with leanness.

The neutralization of the influence of the patient's weight on this formula in this population results in a narrower Gaussian distribution of results as evidenced by the standard deviation lower than its mean relative to that of the MDRD formula and that of the formula CKD-Epi.

According to Age

In patients older than 75 years, CKD-Epi formula also gives an intermediate value compared to Cockcroft and Gault and MDRD formula.

- A new formula specifically developed to estimate GFR in the elderly patient, called BIS1, gives an intermediate mean value compared to Cockcroft and Gault and MDRD (Figure 12).

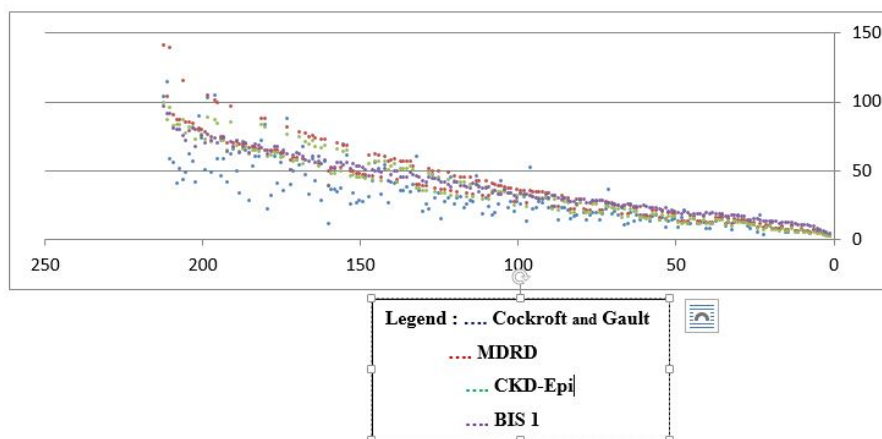


Figure 12: GFR estimates by 4 formulas in elderly patients.

- Average Cockcroft and Gault = 29.9 ± 21.5 ml / min
- Average MDRD = 40.4 ± 27.5 ml / min
- Average CKD-Epi = 36.7 ± 24.6 ml / min
- BIS1 = 38.5 ± 21.1 ml / min

It is observed that Cockcroft and Gault formula gives a significantly lower average value compared to the other formulas. This underestimation of GFR by Cockcroft and Gault is called "classical" and due to a mathematical expression of this formula which subtracts age of a constant (140). As a result, we also understand the less dispersed nature of Gaussian distribution of results in this population.

It is also observed that standard deviation of the average obtained from the formula BIS1 is lower than that of the average obtained from CKD-Epi, formula itself lower than that of the average obtained from MDRD formula. ($21.1 < 24.6 < 27.5$)

Thus, in the elderly, for a given serum creatinine value, the BIS1 formula gives less scattered GFR estimates than the CKD-Epi formula, and this gives less scattered estimates than the MDRD formula.

The difference in underestimation of the Cockcroft and Gault formula with respect to other formulas is determined for each patient:

- Difference 1 = Cockcroft and Gault - MDRD
- Difference 2 = Cockcroft and Gault - CKD-Epi
- Difference 3 = Cockcroft and Gault - BIS1

We compared the means and standard deviations of the 3 calculated differences.

- Average of the difference 1 = -10.5 ± 13.7 ml / min
- Average of the difference 2 = -6.7 ± 11.7 ml / min- Average of the difference 3 = -8.5 ± 10.9 ml / min

Even if the distribution of calculated differences is not Gaussian, the calculated averages are not negligible.

The formula of Cockcroft and Gault seems unadapted and less relevant for the estimation of GFR than the other formulas in the elderly. It underestimates the GFR of a statistically significant value.

BIS1 formula is the most relevant in this population, but failing that, we can use CKD-Epi which gives a rather satisfactory result.

We studied differences in GFR estimation by the 4 formulas in a particular population. These are elderly (over 75) and obese ($BMI > 30$ Kg / m²) patients (Figure 13).

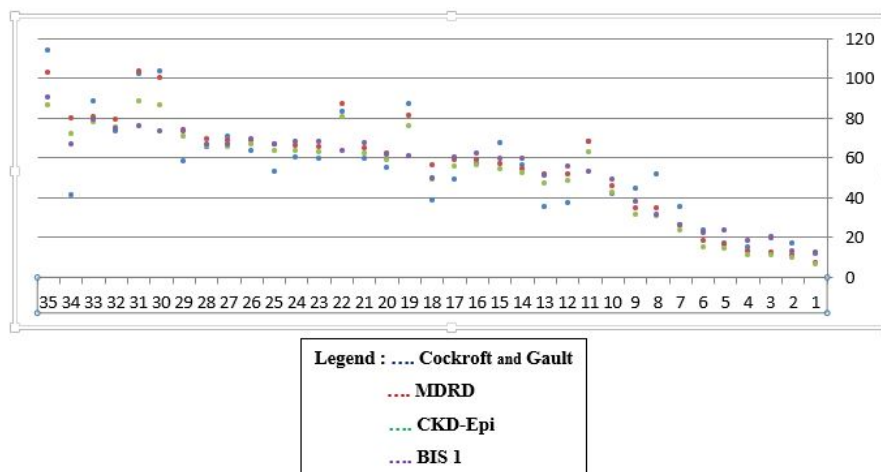


Figure 13: Estimations of GFR by the 4 formulas in elderly and obese patients.

The following results are observed:

- Average Cockcroft and Gault = 54.9 ± 25.7 ml / min
- Average MDRD = 56.9 ± 26.6 ml / min
- Average CKD-Epi = 52.7 ± 24.4 ml / min
- Average BIS1 = 54.1 ± 20.9 ml / min

We observe that the averages of the 4 formulas are similar. For Cockcroft and Gault formula, the "classic" underestimation of GFR in the elderly seems to be "compensated" by being overweight. However, it is noted that the standard deviation of the average obtained from the values of this formula is the highest.

So the formula of Cockcroft and Gault remains less relevant in the elderly subject even in case of excess weight. On the other hand, the standard deviation of the average obtained from the formula BIS1 is the lowest, which confirms the precise and appropriate character of this new equation in the elderly subject.

Discussion

Numerous equations, incorporating serum creatinine as a biological marker of renal function, have been proposed to provide a non-invasive estimate of GFR. These equations incorporate demographic and clinical parameters that influence creatinine concentration such as age and sex to improve the relevance of serum creatinine-based formulas [9]. An established equation should ideally satisfy the quality criterion recommended by the KDOQI guidelines published in 2002 [10]: the aim is to achieve an accuracy margin of 30% compared to measured GFR for more than 90% of patients included in the validation cohort [10]. To improve the accuracy of these equations, a correction for body surface area is recommended [11].

The different equations show the correlation of exponential pace between creatinine and GFR [12-14].

The Cockcroft-Gault Equation

Established in 1976 by Cockcroft-Gault [15] from a population of 249 subjects predominantly male and of European origin without precision of the BMI. [16] with a correction factor for the woman (0.85) that was estimated and not measured. In addition,

the reference method was urinary creatinine clearance and not a measurement of GFR and finally the introduction of age and weight as determinants of serum creatinine attribute too much importance in case of extremes of age or body weight. The KDI-GO recommendations encourage the abandonment of this equation in favor of the CKD-Epi equation.

The MDRD Equation

It was established in an initial cohort of 168 patients (40% female and 12% African-American) with chronic stage 3 or more severe renal disease (mean GFR 40 ± 21 ml / min / 1.73m^2).

It is therefore ideal for monitoring GFR in patients with stage 3 renal failure (<60 ml / min / 1.73m^2) or more severe. 2006 [17] Correlated to a GFR IDMS traceable method measured by the urinary clearance of iothalamate. It integrates age, sex and ethnicity and excludes weight. The MDRD equation has been compared to the Cockcroft and Gault equation in different populations (for example: diabetic patients, renal transplant patients), demonstrating its superiority in terms of precision.

However, it significantly underestimates GFR for values > 60 ml / min / 1.73m^2 [17-19].

It is therefore not recommended for children, patients over 75 years of age, pregnant women or acute situations [20-24].

The Equation of the CKD-EPI Consortium (2009)

The CKD-EPI equation was developed from a truly impressive sample of patients. It is the result of a collaborative work (CKD-EPI Collaboration) whose main leaders are Andrew Levey, Lesley Stevens and Jo Coresh [17]. This working group collected data from 26 studies that measured GFR and used calibrated creatinine. Thus, 5504 patients were included in the cohort to define the formula (development cohort) and 2750 in the cohort to estimate their performance (internal validation cohort).

In both cohorts, GFR was measured by clearance of iothalamate. The equation was then validated in an external validation cohort ($n = 3896$) in which the GFR could be measured by any other reference method.

The mathematical expression of the CKD-Epi equation appears very different from that of the MDRD equation and takes into account the variation of the relationship between creatinine and GFR according to the level of GFR.

This differential weighting specific to the CKD-Epi equation (2009) makes it possible to reduce the bias of the MDRD equation for $\text{GFR} > 60$ ml / min.

However, the overall accuracy (aggregating all GFR levels) of the 2009 CKD-Epi equation does not differ so much from the MDRD equation [18-20]

In 2012, it was proposed for these different reasons to use the CKD-EPI formula at the general population level [24-29].

Equation BIS-1

New equation, always based on plasma creatinine, more precise and specific to the geriatric population (BIS-1) [30]. This minimizes the risks of misclassification for chronic kidney disease and overestimates of GFR in general. However, although it deserves special attention, the BIS-1 equation is not yet recommended by the recommendations.

Our Series

Our series is characterized by a fairly large size (3578 patients) with a satisfactory demographic and clinical distribution (accord-

ing to age, sex, origin and BMI). The series is also characterized by the presence of a large group of subjects with presumed normal renal function and a remarkable number of patients with renal failure at different stages. The importance and diversity of this population allowed us a general statistical analysis and in specific subpopulations conclusive.

We have noticed that the CKD-Epi formula generally gives an estimate of an intermediate value of the GFR compared to the Cockcroft and Gault formulas and MDRD with a less scattered Gaussian distribution of patents. However, this general result does not allow to show a remarkable superiority of relevance of this new formula compared to the MDRD formula, hence the interest of subpopulation analysis.

In fact, the statistical analysis of the group of patients with renal insufficiency (GFR according to MDRD <60 ml / min) does not show a statistically significant difference between the GFR estimation means obtained by the MDRD and CKD-Epi formulas. This is reflected graphically by a remarkable superposition of representative points clouds of the GFR estimated by the two formulas.

On the other hand, for higher GFR values and especially the study of the group of patients whose normal renal function (GFR according to MDRD > 90 ml / min) shows that the CKD-Epi formula gives a value that is likely to be intermediate with respect to other formulas? What is particularly interesting in this group of patients is to note that the CKD-Epi formula gives a much higher estimate than that determined by the MDRD formula and especially much less scattered values (low standard deviation). This demonstrates the remarkable relevance of the CKD-Epi formula when serum creatinine has a normal or low value.

Throughout this study, we note that the Cockcroft and Gault formula is characterized by the largest scatter of GFR values compared to other formulas. This is due to the introduction of the weight parameters in this formula, which makes it very influenced by the variations of the weight even if it is corrected relative to the body surface.

Thus, the Cockcroft and Gault equation overestimates the estimate of GFR in patients who are obese or overweight compared to CKD-Epi and MDRD. Statistical analysis shows that this overestimation is statistically significant.

In lean subjects, on the other hand, the Cockcroft and Gault formula is characterized by a remarkable underestimation of GFR compared to other formulas even if this underestimation is not statistically significant.

When the BMI is in the normal range the three formulas give similar estimates.

The study of the group of patients aged 75 and over shows a particular relevance of the new formula BIS1. This gives an estimate of the GFR of an intermediate value compared to the results obtained by the formulas MDRD and CKD-Epi. The distribution of the results obtained by the formula BIS1 is done according to a Gaussian model characterized by the lowest standard deviation and thus by a scattering of the restricted values. This formula seems the most suitable for the estimation of GFR in the elderly.

While the new BIS1 formula appears to be very relevant in the elderly, the CKD-Epi formula does just as well and gives more accurate and less scattered GFR estimates compared to the MDRD formula. On the other hand, the statistical analysis shows that the difference observed between the averages of the results obtained by the formulas BIS1 and CKD-Epi is not significant.

Summary

Our series confirms the following observations: 1. For normal or low serum creatinine values, approximately $\text{GFR} > 60$ ml / min: The CKD-Epi formula is the most relevant 2. For low values of GFR, $\text{GFR} < 60$ ml / min: The formulas MDRD and CK-

D-Epi are similar.³ In the elderly: The BIS1 formula is particularly interesting and relevant. Note that the accuracy of the CKD-Epi formula is also satisfactory. The formula of Cockcroft and Gault is not recommended.⁴ In obese or overweight subjects: The CKD-Epi formula is more suitable. The MDRD formula can be used. The formula of Cockcroft and Gault is not recommended.

Conclusion

In common practice, the Cockcroft and Gault formula can be used for a quick estimate of GFR without the need for computer equipment, avoiding extremes of age and weight.

International recommendations have clearly favored the CKD-Epi equation [1, 2, 22] compared to the Cockcroft [1, 2, 23] and MDRD equations [1-3, 24].

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