Correlation Between the C-G and MDRD Equations in Comparison to the CKD-EPI Equations in Geriatric Patients

Muhamad Wirawan Adityo[a]*, Tiene Rostini[a]

official email address: drwira1@gmail.com
[a]Clinical Pathology Resident, Faculty of Medicine, Universitas Padjadjaran, West Java, Indonesia
[b]Clinical Pathology Staff, Faculty of Medicine, Universitas Padjadjaran, West Java, Indonesia

Abstract

Decreased kidney function will occur along with an increase in a person's age which usually starts from the age of 40 years and this phenomenon increases in Geriatrics. Indirect assessment of kidney function can be achieved by calculating the estimated Glomerular Filtration Rate (eGFR) utilizing the Cockroft-Gault (C-G), Modification of Diet in Renal Disease (MDRD), or Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equations. **Method:** This descriptive correlation research employed a cross-sectional design using retrospective data by tracing the medical record data of the patients at the Geriatric polyclinic Dr. Hasan Sadikin Hospital, Bandung, from January - June 2021. The analysis used was the Shapiro Wilk test and the Spearman correlation test which was processed using SPSS 25.0. **Result:** The number of subjects who met the inclusion criteria were 47 people. There is a strong correlation between the C-G and MDRD equations in comparison to the CKD-EPI equation, with r values of 0.992 and 0.876 ($p < 0.001$), respectively. Discussion: MDRD has greater accuracy and less precision than C-G against CKD-EPI equation. Overall, MDRD is better than C-G equation. **Conclusion:** A significant correlation exists between eGFR values based on the C-G and MDRD to CKD-EPI equation for patients at the Geriatric Internal Medicine Polyclinic, Dr. Hasan Sadikin Bandung Hospital.

Keywords: Geriatric; eGFR; C-G; MDRD; CKD-EPI

1. Background

As life expectancy continues to rise, there has been a noticeable surge in the elderly population, particularly those aged 60 years and older. Globally, the elderly population is projected to nearly triple in size, transitioning from 743 million individuals in 2009 to an estimated two billion by 2050. In Indonesia, of the total population, there are around 8.9% are people aged over 60 years based on Basic Health Research (Riskesdas) data in 2018. Projections suggest that by 2025, the elderly population in Indonesia will witness a significant increase of 41.4% compared to the situation in 2010 (NKF KDOQI., 2015; Riskesdas., 2018; Permenkes., 2014).

Schlanger et al through their research in the United States in 2015 revealed that as a person ages, there will be a decrease in kidney function. This decline in kidney function usually starts from the age of 40 years. Research conducted in Japan by Miyatake et al in 2015 revealed that as many as 20% of adults aged > 50 years had kidney damage or an eGFR value of <60 mL/minute/1.73m^2 (Schlanger L., 2015; Miyatake N., 2015).

Assessment of kidney function involves the assessment of serum creatinine levels and the computation of the estimated Glomerular Filtration Rate (eGFR). This rate corresponds to the rate at which blood undergoes filtration within the kidney's glomerulus (Gaspari et al., 2013; Raman et al., 2017). This metric holds significant importance when predicting kidney function, especially within the geriatric population, and offers insights into the count of operational nephrons. A low eGFR value indicates that fewer nephrons are functioning properly (Pottel et al., 2017; Denic et al., 2017; Stevens et al., 2009).

Several biomarkers can be used to measure GFR, including exogenous biomarkers such as Chromium-51-EDTA and Inulin as well as endogenous biomarkers such as Cystatin C, β-traceprotein, and β-microglobulin. Measuring GFR directly with exogenous or endogenous biomarkers is difficult and impractical in practice, so the eGFR equation is currently calculated using serum creatinine levels (Stevens et al., 2009; Stevens et al., 2010).

The estimated Glomerular Filtration Rate (eGFR) is a valuable instrument for evaluating both the stage and progression of kidney disease. eGFR can be determined through the application the Cockroft-Gault (C-G), Modification of Diet in Renal Disease (MDRD), or Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equations (Stevens et al., 2010).

Utilizing the Cockroft-Gault (C-G) equation for eGFR calculations proves to be a straightforward and pragmatic approach in clinical settings, as it eliminates the need for factoring in race variables. In contrast, the MDRD equation has been adapted to the body surface area, rendering it more precise when compared to eGFR calculations using the C-G equation. However, in patients with severe kidney damage, the use of the MDRD equation remains questionable. This is different from the CKD-EPI equation created in 2009 which calculates eGFR using serum creatinine, age, gender, and race variables (Levey et al., 1999; Killeen., 2013). Research conducted by Al-Maqbali et al. (2016) in Iran proved that the CKD-EPI equation yields results that closely align with measurements of measured GFR (Rule., 2011). Similarly, research undertaken by Johnson et al. (2017) in the United States affirmed the suitability of the CKD-EPI equation in estimating eGFR values for geriatric patients afflicted by Chronic Kidney Disease (CKD).

2. Method

This research employed a descriptive correlation with a cross-sectional approach utilizing retrospective data. Retrospective data collection was carried out by tracing patient medical record data and the Laboratory Information System (LIS) archives.

A descriptive analysis was conducted to investigate the distribution of eGFR variables based on the C-G and MDRD equations in comparison to the CKD-EPI equation. The formulas employed to measure eGFR were as follows:

1. C-G = (140 - age) × BW / (serum creatinine × 72) (× 0.85 if female).
2. MDRD = 175 × serum creatinine -1.154 × age -0.203 (× 0.742 if female).
3. CKD-EPI = 141 × min (serum creatinine / k,1) α × max (serum creatinine / k,1) -1.209 × 0.993 age (× 1.018 if female), where k = 0.7 for females and 0.9 for males, and α is -0.329 for females and -0.411 for males.

The normality of research data was assessed using the Shapiro-Wilk test to determine whether the data exhibited a normal or abnormal distribution. Subsequently, the Pearson correlation test was applied if the data adhered to a normal distribution. Conversely, in cases of non-normal distribution, the Rank Spearman correlation test was utilized. The Statistical Product and Service Solution (SPSS) software for Windows version 25.0 facilitated data analysis.

3. Results

In this study, the initial subject count was 63 individuals. However, 16 participants had to be excluded due to incomplete data, which means the final sample size was 47 individuals with an average age of approximately 60 years (Standard Deviation: 3 years) and a sex distribution of 48.9% females and 51.1% males. Their median Body Mass Index (BMI) stood at 24.6 kg/m², ranging from 16.4 kg/m² to 35.5 kg/m². The serum urea levels exhibited a median value of 31.0 mg/dl, ranging from 12.8 mg/dl to 201.0 mg/dl, with most cases falling into the abnormal range (83.0%). Conversely, the serum creatinine levels had a median value of 1.0 mg/dl, ranging from 0.6 mg/dl to 4.8 mg/dl, with a predominant presence in the normal range (70.2%). The comprehensive overview of the research subject characteristics is presented in Table 1 below.

Table 1. Characteristics of the Research Subjects

Characteristics	n=47
Age (years)	
Average ±SD	66 ± 3
Gender	
Male	24 (51.1%)
Female	23 (48.9%)
BMI (kg/m^2)	
Median (range)	24.6 (16.4 – 35.5)
BMI Criteria	
Underweight	1 (2.1%)
Normoweight	25 (53.2%)
Overweight	16 (34.0%)
Obese	5 (10.6%)
Ureum (mg/dl)	
Median (range)	31.0 (12.8 – 201.0)

The median eGFR values for CKD-EPI, MDRD, and C-G were recorded at 71, 80, and 58, respectively. Notably, significant differences were observed between MDRD, CKD-EPI, and C-G ($p < 0.001$), with particularly pronounced distinctions between MDRD and CKD-EPI ($p < 0.001$), and between C-G and CKD-EPI ($p = 0.001$). When assessing the bias against CKD-EPI, it was found that MDRD exhibited a bias of 10.1, whereas C-G demonstrated a bias of -6.0. The highest bias was in MDRD and the smallest was in CG. The precision of MDRD and C-G against CKD-EPI was 4.2 and 15.0. It was seen that MDRD was better than CG. Furthermore, a significant difference was observed in the mean bias and precision between MDRD and C-G (p < 0.001). Interestingly, the accuracy within a 30% margin of difference was identical for MDRD and C-G (91.5% for both, p = 0.001). For a comprehensive overview of the comparison between CKD-EPI and C-G with the MDRD equation, please refer to Table 3.2.

Table 2. The Comparison Of CKD-EPI and C-G With MDRD Equation.

	MDRD	CG	P
Median (min-max)	80 (15 – 163)	58 (13 – 114)	**<0.001**
Bias	10.1	-6.0	**0.001**
Precision	4.2	15.0	
Accuracy in 30%	91.5%	70.2%	**<0.001**

Analyze using validation test

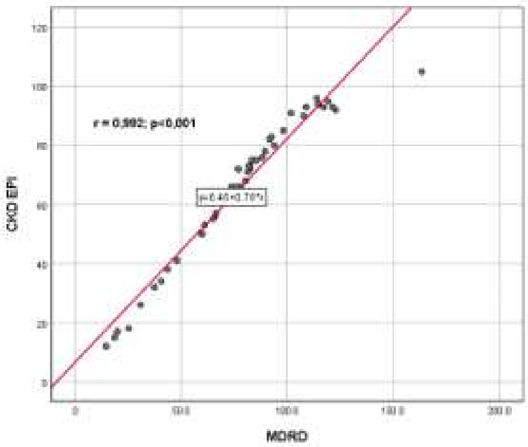
Table 3.3 illustrates the correlation between the C-G and MDRD equations in comparison to the CKD-EPI equation. It is noteworthy that both MDRD and C-G exhibit robust correlations with CKD-EPI, with r values of 0.992 and 0.876, respectively (p < 0.001).

Tabel 3. Correlation between the C-G and MDRD equations in Comparison to the CKD-EPI Equation.

Variable	**CKD-EPI**	
	r coefficient	**P value**
MDRD	0.992	<0.001
C-G	0.876	<0.001

Analyzed using the Rank Spearman correlation test

Based on the scatterplot from Figure 3.1 we can see that the MDRD and C-G equations have a strong correlation with CKD-EPI equation with r = 0.992 and 0.876 (p < 0.001) respectively. MDRD has a stronger correlation than C-G to CKD-EPI, but C-G has a smaller bias or difference than MDRD to CKD-EPI. Overall, MDRD compares favorably with C-G.



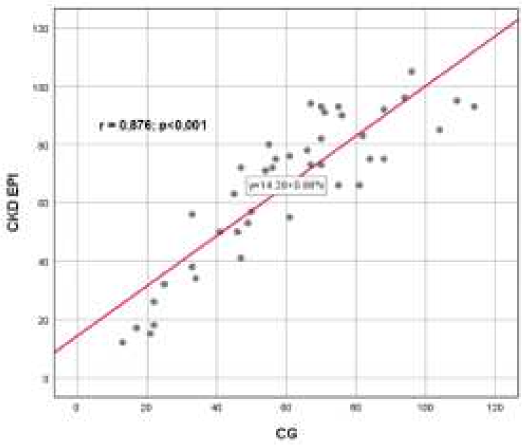


Figure 1. Suitability between the C-G and MDRD Equations in Comparison to the CKD-EPI Equation

4. Discussion

The findings presented in Table 3.2 reveal notable disparities, including a significant difference between MDRD and C-G ($p < 0.001$) and between MDRD and CKD-EPI ($p < 0.001$). These results are inconsistent with research conducted by Agaba et al in 2009 which states that there is no significant difference in calculating eGFR using C-G and MDRD (Agaba et al., 2009).

The MDRD and C-G biases for CKD-EPI are -10.1 and -6.0 respectively. The highest bias was found in C-G and the smallest in MDRD. Notably, a significantly different mean bias between CKD-EPI and C-G ($p = 0.001$) was observed. MDRD performance is better than C-G because it has greater accuracy and lower precision than C-G (97.1% vs 70.2%, $p < 0.001$). In contrast to research conducted by Michels et al. in 2010 which stated that the smallest mean bias was found in MDRD. MDRD has the highest accuracy compared to CKD-EPI and C-G, although not significantly different (Michels et al., 2010).

MDRD's superior performance over C-G due to its higher accuracy and lower precision (97.1% vs. 70.2%, $p<0.001$) aligns with the results of research conducted by by Jessani et al. in 2014 on populations in South Asia where CKD-EPI is better than C-G because it has greater accuracy and smaller precision. (Jessani et al.,2014).

Regarding the correlation analysis presented in Table 3.3, it is noteworthy that both MDRD and C-G exhibited strong correlations with CKD-EPI, with correlation coefficients (r values) of 0.992 and 0.876, respectively ($p < 0.001$). However, these results are inconsistent with those reported by Al-Osali et al. in 2014, whose research suggested that MDRD and C-G had a moderate correlation with CKD-EPI, with r values of 0.701 and 0.605, respectively ($p<0.001$) (Al-Osali et al., 2018).

5. Conclusion

In conclusion, a strong correlation was observed between the eGFR values of the patients receiving care at the Geriatric Internal Medicine Clinic of Hasan Sadikin Hospital in Bandung calculated using the C-G and MDRD equations in comparison to the CKD-EPI equation. The overall performance of these two equations was quite similar, with MDRD exhibiting slightly greater accuracy compared to C-G. This suggests that both the C-G and MDRD equations can serve as effective tools in reducing the necessity for complex and costly in-person GFR assessments. Future research is advised to explore further the correlation of eGFR estimations based on the C-G, MDRD, and CKD-EPI equations with measured GFR examinations utilizing Inulin.

Reference

Agaba EI, Wigwe CM, Agaba PA, Tzamaloukas AH. Performance of the Cockcroft- Gault and MDRD Equations in Adult Nigerians with Chronic Kidney Disease. Int Urol Nephrol. 2009;41:635–42.

Al-Osali, M.E., Al-Qassabi, S.S., Al-Harthi, S.M. 2014. Assessment of Glomerular Filtration Rates by Cockcroft-Gault and Modification of Diet in Renal Disease Equation in a Cohort of Omani Patients, Sultan Qaboos University Med J 14, p. 72–9.

Denic, A., Mathew, J., Lerman, L.O., Lieske, J.C., Larson, J.J., Alexander, M.P. 2017. Single-Nephron Glomerular Filtration Rate in Healthy Adults, The New England Journal of Medicine 376, p. 2349-57.

Gaspari, F., Ruggenenti, P., Porrini, E., Motterlini, N., Cannata, A., Carrara F. 2013. The GFR and GFR Decline Cannot be Accurately Estimated in Type 2 Diabetics.. Kidney Int 84, p. 164-73.

Jessani S, Levey AS, Bux R, Inker L a, Islam M, Chaturvedi N, et al. Estimation of GFR in South Asians: a Study from the General Population in Pakistan. American Journal of Kidney Diseases: 2014.

Killeen A. A., Ashwood E. R., Ventura C. B., Styer P. Recent Trends in Performance and Current State of Creatinine Assays. Arch Pathol Lab Med. 2013;137(4):496-502.

Levey A. S., Bosch J. P., Lewis J. B., Greene T., Rogers N., Roth D. 1999. A More Accurate Method to Estimate Glomerular Filtration Rate from Serum Creatinine: a New Prediction Equation. Modification of Diet in Renal Disease Study Group. Annals of internal medicine 130, p. 461-70.

Michels WM, Grootendorst DC, Verduijn M, Elliott EG, Dekker FW, Krediet RT. Performance of the Cockcroft-Gault, MDRD, New CKD-EPI Formulas in Relation to GFR , Age , and Body Size. Clin J Am Soc Nephrol. 2010;5:1003–9.

Miyatake, N., Shikata, K., Makino, H. 2015. Decreasing Systolic Blood Pressure is Associated with Improving Estimated Glomerular Filtration Rate (eGFR) with Lifestyle Modification in Japanese Women, Acta Medica Okayama 64, p. 339-343.

National Kidney Foundation Kidney Disease Outcome Quality Initiative (NKF KDOQI) Clinical Practice Guideline. Glomerular Filtration Rate. 2015.

Peraturan Menteri Kesehatan Republik Indonesia Nomor 79 Tahun 2014. Kementerian Kesehatan. Jakarta: 2014.

Pottel, H., Delanaye, P., Weekers, L., Selistre, L., Goffin, K., Gheysens, O. 2017. Age-Dependent Reference Intervals for Estimated and Measured Glomerular Filtration Rate, Clin Kidney J 10, p. 545-51.

Raman, M., Middleton, R. 2017. Estimating Renal Function in Old People: an in-Depth Review Int, Urol Nephrol, Nature Publishing Group 49, p. 1979–1988.

Riset Kesehatan Dasar (Riskesdas). Kementerian Kesehatan. Jakarta: 2018.

Rule A. D., Cornell L. D., Poggio E. D. Senile Nephrosclerosis--Does It Explain The Decline In Glomerular Filtration Rate With Aging? Nephron Physiol. 2011;119(1):6-11.

Schlanger, L. 2015. Kidney Senescene. American Society of Nephrology.

Stevens, L. A., Schmid, C. H., Greene, T., Zhang, Y. L., Beck, G. J., Froissart, M. 2010. Comparative performance of the CKD Epidemiology Collaboration (CKD-EPI) and the Modification of Diet in Renal Disease (MDRD) Study Equations for Estimating GFR Levels Above 60 mL/min/1.73 m2, Am J Kidney Dis 56, p. 486-95.

Stevens, L.A., Levey, A.S. 2009. Measured GFR as a Confirmatory Test For Estimated GFR, J Am Soc Nephrol 20, p. 2305-13.