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Original Article

EVALUATION OF GLOMERULAR FILTRATION RATE ESTIMATING EQUATIONS IN CKD PATIENTS WITH DIABETES AND HYPERTENSION

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ABSTRACT

Objective: To compare the performance of Cockcroft-Gault and Modification of Diet in Renal Disease (MDRD) equations in estimating kidney function in CKD patients with diabetes and hypertension.

Methods: This study retrospectively reviewed medical records in Hospital Kajang. The GFR was calculated using Cockcroft-Gault and MDRD equations. Kappa Measure of Agreement was used to check the consistency of CKD staging. Wilcoxon signed-ranked tests and Bland-Altman plots were used to determine the difference of both equations. Spearman correlation was used to determine the correlation between blood pressure and blood sugar levels with eGFR.

Results: Data pertaining to a total of 81 patients were extracted. Results showed 22% of the patients were staged differently (Kappa value = 0.644 [P<0.001]) and the majority of them moved down one CKD stage when MDRD equation was used instead of Cockcroft-Gault equation. Wilcoxon signed rank test demonstrated there was a significant difference (P<0.001) in eGFR using CandG and MDRD in patients with diabetes and hypertension. Furthermore, the mean difference observed was 3.78±5.56 [P<0.001]), where the Cockcroft-Gault equation measured 3.78 units higher than MDRD equation. However, the relationship between blood sugar and blood pressure with eGFR were not significant.

Conclusion: There was a significant difference between Cockcroft-Gault and MDRD equations in estimating kidney function CKD patients with diabetes and hypertension.

Keywords: Chronic kidney disease, Estimated glomerular filtration rate, Cockcroft-Gault, Modification of diet in renal disease

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INTRODUCTION

Chronic kidney disease (CKD) was ranked the 18th cause of global deaths [1]. The overall prevalence of CKD in West Malaysia was 9.07 % [2]. Progression of CKD to end-stage renal disease (ESRD) increases the burden of healthcare budgets of the country [3]. The main important risk factors of CKD are diabetes (DM) and hypertension (HTN) [4]. CKD patients are often asymptomatic and the abnormalities were clinically manifested at very late stage [5]. Patients with DM and/or HTN are advised be screened at least yearly for CKD because early detection and intervention of these high-risk groups may prevent the development and progression of CKD [6].

GFR is widely used as an indicator of kidney function [7]. CKD stage is determined based on GFR (table 1). The standard gold method for measuring GFR using exogenous substances for example, inulin is expensive, time-consuming and is not practical for routine clinical practice [8]. As a result, predictive equations were developed based serum creatinine and corrected for gender, weight and age to estimate GFR [9]. The two equations that are widely used and recommended in adults by K/DOQI guidelines in estimating kidney function are the Cockcroft-Gault equation and Modification of Diet in Renal Disease (MDRD) equation [7].

Although the prevalence of CKD is increasing in Malaysia, the screening method of kidney disease is still lacking [10]. Several studies have been undertaken to compare Cockcroft-Gault and MDRD equations either in the general population, in diabetics or in renal impairment patients. However, most of the studies revealed there was a large discrepancy between both equations in estimating renal function [8]. Most of the GFR estimating equations were developed in western countries while there is no unified GFR estimation equation for Asian countries. Inaccurate and inconsistencies estimation of kidney function may contribute to the misclassification of the patient into the appropriate CKD stage, which will indirectly lead to inappropriate treatment for the patient [11].

In Malaysia, however, there is lack of study in comparing both equations in estimating kidney function of CKD patients with DM and HTN. There is also a lack of study on the correlation between blood pressure level or blood sugar level with eGFR since DM and HTN are the leading causes of CKD. Therefore, this preliminary study aimed to study the discrepancy of CKD staging among DM and HTN population.

Therefore, the main objectives of this study were to compare the performance and consistency of Cockcroft-Gault and MDRD equations in staging CKD patients, to compare the difference of eGFR calculated by both equations and to evaluate the relationship between eGFR with blood sugar and blood pressure levels.

MATERIALS AND METHODS

This retrospective study was conducted at Hospital Kajang (HKJ) in Selangor, Malaysia. HKJ is a district hospital, provides dialysis services. This study reviewed the medical records of CKD patients (n = 81) using a specially designed data collection form. A range of data was collected, including age, gender, race, body weight, body height, blood pressure, fasting and non-fasting blood sugar, HbA1c and serum creatinine.

Patient sample

Patients with a diagnosis of CKD admitted to hospital in the last three years (January 2012-August 2015) were identified from medical records. A total of 81 medical records pertaining to those CKD patients with DM and HTN who meet the inclusion criteria were selected. Besides, patients who were excluded were patients with acute kidney injury; the patient's renal damage due to trauma or accident; kidney transplant patients. Patients with incomplete data also were excluded from this study.

Estimation of renal function

eGFR was calculated by Cockcroft-Gault [1] and MDRD [2] equations.

CrCl (ml/min) = [140-age (years)] x weight (kg) x κ

Serum creatinine (μmol/l) [1]

where κ is a constant of 1.23 for men and 1.04 for women [12]

eGFR (ml/min/1.73m^2) = 175 x (SCr[μmol/l])$^{-1}$.[15]^4 x (age[years])$^{-}$ ^{0}.[20]^{3}x 0.742 [if female] x 1.212 [if black] [13]

Statistical analysis

The data were analysed using SPSS software program version 20 (SPSS Inc., Chicago, IL) for windows. Data were presented as means (±SD) or medians (±IQR) for continuous variables and as frequencies (percentages) for categorical variables.

Kolmogorov-Smirnov test revealed the continuous variables were not normally distributed, so non-parametric tests were used to analyse the data. The correlation between analysed values was analysed using Spearman correlation test. Kappa Measure of Agreement was used to compare the consistency of both equations in CKD staging. Additionally, Wilcoxon signed rank test and Bland-Altman plot were used to compare the values of eGFR predicted by two equations. *P* value less than 0.05 was considered as statistically significant.

All aspects of the study protocol were approved by the Medical Research and Ethics Committee of the Malaysia ministry of health (Ref: KKM/NIHSEC/P15-667) and from HKJ Clinical Research Center.

RESULTS

A total of 81 CKD patients were reviewed with a mean age of 60.39±10.72 y, with 46 % of patients aged over 60 y. Majority of patients were males (61.7 %) and most of them were Malay (58 %). The median systolic BP was 145 mmHg while diastolic BP was 80 mmHg. The median non-fasting blood sugar level was 9.0 mmol/l while fasting blood sugar was 7.5 mmol/l. Due to poor documentation of medical records, there was limited data available for HbA1c. The eGFR measured by Cockcroft-Gault was higher than eGFR measured by MDRD. The patients' characteristics were shown in table 2.

The distribution of CKD according to eGFR with Cockcroft-Gault and MDRD equations was shown in fig. 1. The CKD patients were higher in MDRD than Cockcroft-Gault in the advanced CKD stage (stage 5). Results showed that about 22.2 % of patients (18 patients) were staged differently using Cockcroft-Gault and MDRD equations. Additionally, Kappa Measure of Agreement showed moderate agreement between Cockcroft-Gault and MDRD for this subgroup of patients (Kappa value = 0.644, *P*<0.001) (Peat 2001, p.228). Among those who were staged differently, 16 patients moved down one CKD stage; 2 patients moved up one CKD stage when MDRD was used instead of Cockcroft-Gault. The largest restaging was for patients within Cockcroft-Gault stage 4. Of the 32 patients within this stage, 2 were restaged into MDRD stage 3b and 7 were restaged into MDRD stage 5. Table 3 showed the cross-tabulation of Cockcroft-Gault and MDRD staging.

A Wilcoxon signed rank test revealed a statistically significant difference in eGFR using both Cockcroft-Gault and MDRD equations, z = 6.100 with a moderate effect size (r = 0.42). Furthermore, the Bland-Altman plot of comparison of eGFR with Cockcroft-Gault and MDRD was shown in fig. 2. The mean difference of Cockcroft-Gault and MDRD was 3.78±5.56 indicating Cockcroft-Gault measured higher GFR than MDRD.

Results showed the correlation coefficient between both systolic and diastolic BP with eGFR were not significant but were consistently in negative relationship. Besides, for the correlation between blood sugar level and eGFR, the correlation coefficient between both fasting and non-fasting blood sugar with eGFR were not significant however, both relationship showed positive direction.

Table 1: Classification of chronic kidney disease (CKD)

Stage	GFR (ml/min/1.73m^2)	Description
1	≥ 90	Normal or high GFR
2	89-60	Mildly decrease in GFR
3a	59-45	Mildly to moderately decrease in GFR
3b	44-30	Moderately to severely decrease in GFR
4	29-15	Severely decrease in GFR
5	<15	Kidney failure

Table 2: Patient characteristics

Variables	Frequency (%)	Mean (±SD)	Median (IQR)
Age (years)		60.39 (±10.72)	
Age Group	35 (43.2)		
Non-elderly(18-59)	46 (56.8)		
Elderly **(**≥ 60)			
Gender			
Male	50 (61.7)		65.0 (11.0)[a]
Female	31 (38.3)		145 (33.0)[a]
Ethnicity	47 (58.0)		80 (20.0)[a]
Malay	17 (21.0)		7.5 (5.5)[a]
Chinese	17 (21.0)		9.0 (6.7)[a]
Indian			18.94 (17.02)[a]
Body Weight (kg)			13.60 (15.48)[a]
Systolic BP (mmHg)			
Diastolic BP (mmHg)			
Fasting Blood Sugar (mmol/l)			
Non-fasting Blood Sugar (mmol/l)			
eGFR (C**and**G)			
eGFR (MDRD)			

Note: [a]skewed to the right, Abbreviation: blood pressure, BP

Table 3: Crosstabulation of CKD staging using cockcroft-gault and MDRD

		MDRD staging				Total
		Stage 3a	Stage 3b	Stage 4	Stage 5	
Cockcroft-Gault Staging	Stage 2	0	1	0	0	1
	Stage 3a	*3*	2	0	0	5
	Stage 3b	0	*2*	6	0	8
	Stage 4	0	2	*23*	7	32
	Stage 5	0	0	0	*35*	35
Total		3	7	29	42	81

Note: Numbers in italic indicate those subjects who do not change CKD stage on the basis of eGFR assessed with CandG and MDRD. Underlined fig. indicate the numbers of subjects who change into a different CKD stage.

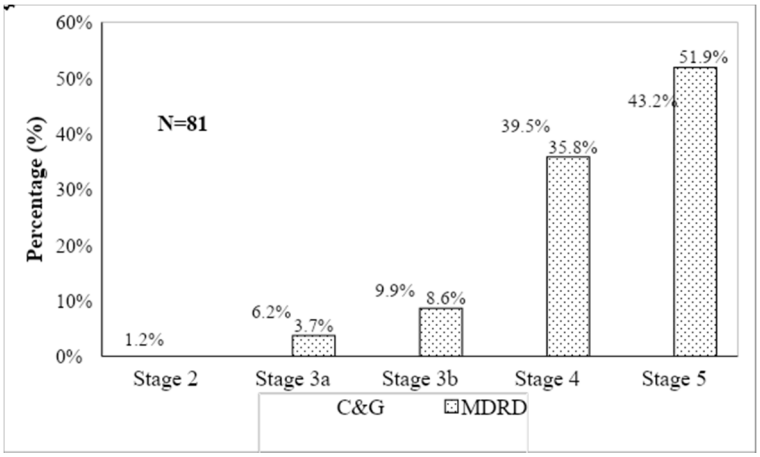

Fig. 1: The percentage of CKD according to C and G and MDRD equations

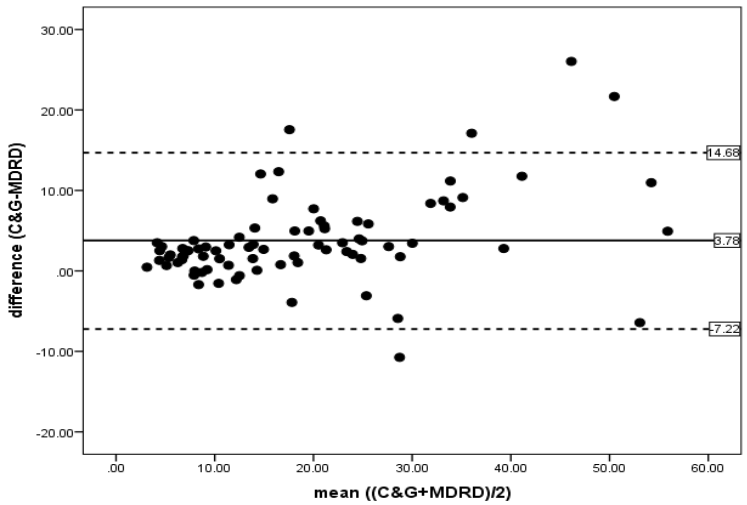

Fig. 2: Bland-altman plot compared the values of eGFR by CandG and MDRD equations

DISCUSSION

In this study, most of CKD patients were in advanced stages (stage 3 to 5) with higher proportion in stage 5. This could be attributed to that majority of the cases recruited in this study were from the hemodialysis unit of hospital Kajang. In addition, some of the CKD patients were under follow up with nephrologist where most of them are also in CKD late stage for monitoring and planning for dialysis initiation.

Estimated GFR (eGFR) was used to stage the study population according to KDOQI classification [14]. We have demonstrated that there was discrepancy in CKD staging using both Cockcroft-Gault and MDRD equations. In line with our findings, studies reported that there was a large discrepancy between both equations in estimating renal function [8, 15]. This may be explained by the underestimation or overestimation of either equation which resulted in different CKD staging. A previous study reported when stage 4 CKD patients were misclassified as stage 3 could delay the initiation of renal replacement therapy while misclassified of stage 2 CKD patients as stage 3 would result in unnecessary assessment of CKD-related complication [11]. Another study also revealed that correct diagnosing and staging of CKD patients was important for initiation of management on complications of CKD [16]. The misclassification of CKD patients may lead to inappropriate management of these patients, thus it is important to determine a single best predictive equation for these populations.

In this study, Cockcroft-Gault estimated higher GFR than MDRD. This was consistent with another study, where CandG median eGFR was 36 ml/min/1.73m^2 while MDRD median eGFR was 32 ml/min/1.73m^2 [17]. Another study also reported that Cockcroft-Gault was found to estimate GFR slightly higher than MDRD [18]. Therefore, all the findings correspond to our study that Cockcroft-Gault estimated higher GFR than MDRD.

This study revealed there was difference between Cockcroft-Gault and MDRD equations among DM and HTN patients. Bland-Altman plot also showed that Cockcroft-Gault measure 3.78 units higher than MDRD. According to a previous study, the difference between CandG and MDRD equations were affected by HTN and DM in which the results reported CandG equation may underestimate those groups of patient [19]. However, it was contrasted with a previous study conducted in diabetic subjects reported that Cockcroft-Gault equation overestimated GFR while MDRD underestimated GFR when compared to gold standard [20]. Additionally, another study reported that decline in renal function in diabetics was better detected by Cockcroft-Gault because it was more accurate in predicting GFR with normal serum creatinine where MDRD was superior than CandG in diabetics with renal impairment [15]. The difference in eGFR in this study was more likely influenced by weight on estimation of renal function. There was 10% overestimation of GFR by Cockcroft-Gault equation in type 2 DM patients which is probably due to influence of weight [20]. Another study also showed that Cockcroft-Gault was inaccurate in estimating renal function in proportion to body weight [21].

The correlation between blood pressure and blood sugar level with eGFR was not significant, this may be attributed to blood pressure and blood sugar levels were only taken once when patient first admitted to the hospital, resulting in underestimation of the strength of the association. In addition, smaller sample of blood sugar levels also may affect the strength of the relationship. However, further research is needed to verify whether the necessary for systemic adjustment for blood glucose or BP when employing these equations to estimate GFR in subjects with DM and/or HTN. Diabetic and hypertensive patients were different from ordinary CKD patients, the parameters such as the course of disease, blood glucose and blood pressure level could affect the progression of renal impairment so these factors might also be included in estimation of GFR.

LIMITATIONS

This was a retrospective study; therefore, not all relevant data was available such as body weight, body height, blood glucose and HbA1c. Besides, this was a single-center study so the results cannot be generalized or represent the whole population in Malaysia. Furthermore, this study evaluated renal function using eGFR formula and not compares to the gold standard of the inulin test. Therefore, this study cannot conclude which formula is more accurately predicting GFR.

CONCLUSION

Our study demonstrates that there is a difference between Cockcroft-Gault and MDRD equations in estimating kidney function among CKD patients with DM and HTN. This study also shows that there is discrepancy in CKD staging and Cockcroft-Gault equation agreed moderately only with MDRD equation. In clinical practice, physicians should be aware of the differences of the two equations and take that into consideration when they estimate renal functions to prevent misclassification and to provide the most appropriate treatment. Since both of GFR estimation equations were originally developed in western countries, therefore, a validated equation should be developed in the future using Malaysia population. The results will be more accurate and precise for our own country.

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Nil

AUTHORS CONTRIBUTIONS

All authors contributed equally to the preparation and final approval of the manuscript.

CONFLICT OF INTERESTS

Declared none

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