

ESTIMATES OF GLOMERULAR FILTRATION RATE BASED ON CREATININE, CYSTATIN C AND COMBINATION OF CREATININE AND CYSTATIN C EQUATIONS IN CRITICALLY ILL PATIENTS

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ABSTRACT

Introduction: Accurate assessment of renal function in the critically ill is important for the diagnostic and prognostic utility to guide clinical management. It is usually estimated from various estimate glomerular filtration rate (eGFR) equations. We evaluated eGFR based on Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation using serum creatinine (Cr), Cystatin C (CysC), and its combination, against 24-hour creatinine clearance (CrCl). We aimed to find the most accurate, precise, and less biased equation for GFR estimation.

Methods: Critically ill patients, older than 18 years who stayed longer than 24 hours were included in the study. Urinary creatinine, serum Cr, and CysC were measured at three-time points (8, 24, and 72 hours). We then compared eGFR from Cr (eGFR_{Cr}), CysC (eGFR_{CysC}) and combined CKD-EPI (eGFR_{Cr-CysC}) to the measured 24-hour CrCl.

Results: A total of 43 patients were recruited. eGFR_{Cr} had the highest correlation to CrCl, with correlation of 0.81 and 0.73 at 24 and 72 hours, respectively, and was the most precise and accurate equation compared to eGFR_{CysC} and eGFR_{Cr-CysC} at all-time points. The bias was lowest for eGFR_{CysC} equation. The Area Under Curve of eGFR_{Cr} in diagnosing acute kidney injury (AKI) was 0.93 and 0.84 at 24 and 72 hours, respectively. Neither the eGFR equations nor CrCl played a role in the prediction of in-hospital mortality.

Conclusion: eGFR_{Cr} had the highest correlation to CrCl and was the most accurate and precise equation, however, eGFR_{CysC} had lowest bias. Most of the equations contributed to the diagnosis of AKI. However, none on contributed to the prediction of in-hospital mortality.

Keywords: *Estimated Glomerular Filtration Rate, Serum Creatinine, Serum Cystatin C, Intensive Care Unit.*

INTRODUCTION

Accurate assessment of kidney function in critically ill patients is important for correct drug dosing, fluid requirement, adequacy of nutrition, and early detection of kidney injury (AKI) (1,2). A standard measure for renal

function calculation is estimates of glomerular filtration rate (eGFR) (3). Measurement of glomerular filtration rate (GFR) can be performed either by the clearance of exogenous filtration markers such as inulin or by the clearance of endogenous filtration markers such as serum creatinine (Cr), or serum Cystatin C (CysC) (4,5). However, these are not usually used in daily practice and research due to challenges in sample assortment, expense, inconvenience, and time consumption (8,9,10). More common in the clinical setting is the measurement using 24-hour creatinine clearance (CrCl) (9). However, the challenges for 24-hour CrCl include difficulty of a scheduled urine collection and failure in obtaining a

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perfect specimen (10).

Estimation of GFR is usually focused on endogenous compounds, as it is more accessible and convenient (11). Various eGFR equations are available since the first equation introduced in 1957(9,12). However, most were developed in non-critically ill populations. Serum Cr is insensitive to rapidly changing GFR, and is influenced by age, sex, muscle mass, diet, and tubular secretion of creatinine (13,14,15). CysC is a 13kDA molecule which is freely filtered from glomerulus and is catabolised from the proximal renal tubule (16). CysC is not influenced by muscle mass and dietary protein intake, hence is a better filtration marker than Cr (17).

Equations based on CysC have been introduced for diagnosis of kidney disease because of its independence from many factors that affect Cr. (7). However, in ICU patients the actual advantage of CysC over Cr equations in estimating true GFR still remains unclear (18,19) eGFR estimates from the combination of Cr and CysC have been shown to be more advantageous than eGFR based on either marker alone (20). The National Kidney Foundation Disease Outcomes Quality Initiative (KDOQI) recommended the use of estimates of GFR calculated from predicting equations based on Cr, CysC and their combination (4). To date, there are few studies investigating Cr and CysC based equation for estimating GFR in critical care patients. We aimed to evaluate which of these equations performed best in our critically ill patients, and if there is any difference in patients with AKI and those without AKI.

MATERIALS AND METHOD

This is a single center, cross-sectional observational study in critically ill patients of Sultan Ahmad Shah Medical Centre, Islamic University of Malaysia (SASMEC@IIUM). This study has been approved by IIUM Research Ethical Committee (IREC Number 2019-185). Consent was obtained from the patient or legally-approved representative. All critically ill patients older than 18 years, who stayed in the ICU for more than 24 hours with a urinary catheter in place were included in the study. Patients on diuretics, dialysis, with thyroid dysfunction, post elective surgery, and pregnant females were excluded from the study. In addition, anuric patients were excluded due to lack of urine collection for CrCl measurement.

Blood samples were centrifuged at 3600 rpm for 15 minutes and the plasma were stored at -80°C for batch analysis. Serum and urinary creatinine measured at 8, 24 and 72 hours, were assayed using Modified JAFFA

method Chemistry Analyzer (Cobas Integra 400 plus, Roche, Indianapolis, USA). Serum CysC, measured at 12 and 24 hours were assayed using Fine Care CysC Rapid Test (Wondfo Biotech). Urine was collected over 24 hours on day 1 and day 3, and the total volume collected was recorded. Urinary creatinine and plasma creatinine were measured at these time points. From these, 24-hour CrCl were calculated for day 1 and day 3. GFR was estimated based on the Chronic Kidney Disease Epidemiologic Collaboration (CKD-EPI) equations based on Cr (eGFR_{Cr}), CysC (eGFR_{CysC}), and their combination (eGFR_{Cr-CysC}) Other data collected include age, sex, height, weight, ethnicity, medical or surgical admission, primary admission diagnosis, co-morbidities, length of ICU and hospital stay, and mortality. The baseline Acute Physiology and Chronic Health Evaluation (APACHE) II and Sequential Organ Failure Assessment (SOFA) scores were used to assess severity of illness in each patient. AKI was defined based on baseline creatinine value at the time of admission based on the Kidney Disease Improving Global Outcome (KDIGO) guideline. Patients were followed-up until discharged from the hospital to determine the outcome parameters studied.

STATISTICAL ANALYSIS

Statistical analyses were performed using SPSS® Statistics version 25 (IBM, New York, USA for the statistical analysis). Sample size was calculated using MedCalc® Software version 18.11.6. Comparison of variables between two groups were analysed using the independent t-test for normally distributed variables, or the Mann-Whitney U test for non-normally distributed variables. Categorical variables were compared using the Chi-square test. Pearson correlation was used for the analysis of normally distributed variables, and Spearman correlation for non-normally distributed variables. Bland Altman analysis was performed using 95% limits of agreement that were calculated as the mean difference \pm 1.96 SD. The mean difference between estimated GFR and measured CrCl was defined as bias, while precision was expressed as the SD of this difference. The proportion of eGFR within 30 percent of the measured CrCl was described as accuracy. The receiver operating characteristic (ROC) curve of the sensitivity verse 1-specificity was used to diagnostic and predictive ability of eGFR equations to assess area under curve (AUC).

RESULT

One hundred sixty-two patients were screened between 1st October 2019 to 20th March 2020. Patients less than 18 years (n=6), post elective surgery (n=41), with no consent (n=25), no urine output (n=23), technical problem in urine collection (n=10), ICU admission of less than 24 hours (n=7), and patient with dialysis (n=7) were excluded. Of

screened patients, 43 were enrolled in the study. Of this 26 stayed for more than 72 hours, and 13.9% died in the hospital (Figure 1). All patients recruited have a complete 24-hour urine collection for CrCl measurement on day 1. However, CrCl measurements were not available in 17 (39.5%) of patients in day 3 as they were already discharged from the ICU.

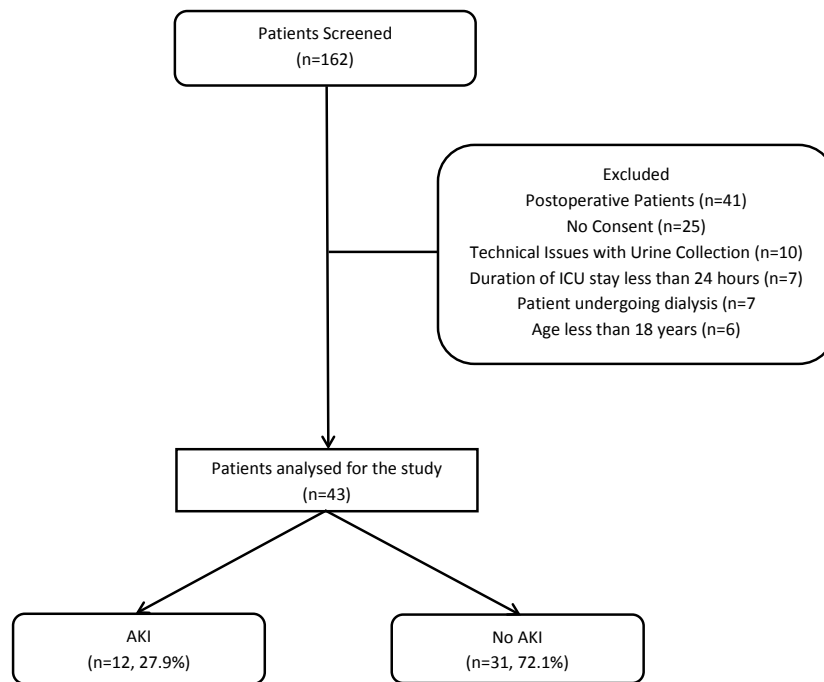


Figure 1: Plain chest radiograph showing bilateral heterogenous patchy opacities

Demographic, Clinical Characteristics and Outcomes

Table I compares the baseline demographic, clinical characteristics and outcome for patients with AKI and without AKI. Of the 43 patients recruited, 26 (60.4%) patients stayed in the ICU for more than 3 days. The median length of ICU stay was 6 days (IQR 3 days). Majority of our study patients was of medical category (88.3%), with infective disease (34.9 %) and respiratory disease

(27.9%) as the leading causes of admission. Patients with AKI were older and had higher APACHE II and SOFA scores on ICU admission compared to those without AKI. There were no differences in other parameters. Six patients (13.9%) died during the hospital admission, and there were no differences in AKI and No AKI group. There were no differences in age, and severity score of SOFA and APACHE II in survivor and non-survivor.

Table 1: Demographic, clinical characteristics, and patient outcome

Variables	All patients n=43	AKI n=12	No-AKI n=31	P-value
Age (years)	61.0 (17.0)	68.0 (14.0)	59.0 (18.0)	0.041
Ethnicity				
• Malay	38.0 (88.4)	11.0 (91.7)	27.0 (87.1)	0.644
• Indian	3.0 (7.4)	0.0 (0.0)	2.0 (6.5)	
• Chinese	2.0 (4.2)	1.0 (8.3)	2.0 (6.5)	
Gender (male)	27.0 (62.7)	9.0 (75.0)	18.0 (58.1)	0.308
Height (m)	162.0 (14.0)	162.0 (11.0)	163.0 (14.0)	0.989
Weight (kg)	70.0 (26.0)	75.0 (29.0)	70.0 (30.0)	0.221
Sepsis	39.0 (91.7)	12.0 (100)	27.0 (87.1)	0.197
		0.0 (0.0)	4.0 (12.9)	
Admission Category				0.679
• Medical	38.0 (88.4)	11.0 (91.7)	27.0 (87.1)	
• Surgical	5.0 (11.6)	1.0 (8.3)	4.0 (12.9)	
SOFA score				
• Day 1	5.5 (4.0)	6.0 (5.0)	3.0 (5.0)	0.076
• Day 3	5.0 (3.0)	5.0 (3.0)	4.5 (4.0)	0.231
APACHE II scores				
• Day 1	14.0 (6.0)	17.0 (10.0)	12.0 (5.0)	0.018
• Day 3	11.0 (5)	15.0 (10.0)	11.0 (2.0)	0.023
Length of Hospital Stay (days)	11.0 (11.0)	12.5 (22.0)	11.0 (10.0)	0.232
Length of Stay, ICU (days)	6.0 (9.0)	5.0 (7.0)	8.0 (6.0)	0.254
Discharge status				0.508
• Alive	37.0 (86.0)	11.0 (91.7)	26.0 (83.9)	
• Dead	6.0 (13.9)	1.0 (8.3)	5.0 (16.1)	
Primary Diagnoses				0.732
• Endocrine/Metabolic	2.0 (4.7)	0.0 (0.0)	2.0 (6.5)	
• Renal	5.0 (11.6)	3.0 (25.0)	2.0 (6.5)	
• Neurological	3.0 (7.0)	1.0 (8.3)	2.0 (6.5)	
• Respiratory	12.0 (27.9)	3.0 (25.0)	9.0 (29.0)	
• Connective tissue / Auto-immune	1.0 (2.3)	0.0 (0.0)	1.0 (3.2)	
• Cardiovascular	5.0 (11.6)	1.0 (8.3)	4.0 (12.9)	
• Infective	15.0 (34.9)	4.0 (33.3)	11.0 (35.5)	
Baseline co-morbidities				
• Myocardial infarction	6.0 (14.0)	2 (16.67)	4 (12.9)	0.752
• Congestive heart failure	10.0 (23.3)	5 (41.6)	5 (16.1)	0.079
• Solid tumor	2.0 (4.7)	1 (8.3)	1 (3.2)	0.118
• Moderate to severe CKD	9.0 (20.9)	5 (41.6)	4 (12.9)	0.040
• Diabetes Mellitus	20.0 (44.2)	3 (25)	16 (51.6)	0.420
• Hemiplegia	3.0 (7.0)	1 (8.3)	2 (6.4)	0.830
• Connective tissue disease	2.0 (4.7)	1 (8.3)	1 (3.2)	0.481
• Peptic ulcer disease	2.0 (4.7)	0	2 (6.4)	0.373
• PVD	2.0 (4.7)	1 (8.3)	1 (3.2)	0.481
• COPD	2.0 (4.7)	1 (8.3)	1 (3.2)	0.481
• CVA-TIA	5.0 (11.6)	1 (8.3)	4 (12.9)	0.679

Data expressed as median (IQR) or n (%), ICU, Intensive Care Unit; SOFA, Sepsis-related Organ Failure Assessment; APACHE, Acute Physiological Assessment and Chronic Health Evaluation; AKI, Acute Kidney Injury; PVD, Peripheral Vascular Disease; COPD, chronic obstructive pulmonary disease; CVA-TIA, Cardiovascular Accident-Transient Ischemic Attack.

Correlation Analyses

All eGFR equations were significantly correlated to the CrCl (Table II). At 24 hours, eGFR_{Cr} had the highest and strong positive correlation to CrCl, with correlation coefficient of 0.810. eGFR_{CysC} had the weakest correlation to

CrCl. At 72 hours, eGFR_{Cr} had highest positive correlation compared to other equations with correlation coefficient of 0.733, followed by eGFR_{Cr-CysC} with correlation coefficient of 0.648.

Table II: Spearman correlation analysis of CrCl with estimated GFR equations

Time		Variables	Correlation coefficient (r)	P value
All Patients (n=43)	CrCl			
8 hours	CrCl	eGFR _{Cr}	0.775	<0.0001
24 hours	CrCl	eGFR _{Cr}	0.810	<0.0001
	CrCl	eGFR _{CysC}	0.433	0.0004
72hrs	CrCl	eGFR _{Cr-CysC}	0.651	<0.0001
	CrCl	eGFR _{Cr}	0.733	<0.0001
	CrCl	eGFR _{CysC}	0.510	0.0008
CrCl	eGFR _{Cr-CysC}	0.648	<0.0001	
AKI Patients (n=12)				
8 hours	CrCl	eGFR _{Cr}	0.799	0.002
24 hours	CrCl	eGFR _{Cr}	0.942	<0.0001
	CrCl	eGFR _{CysC}	0.296	0.351
72hrs	CrCl	eGFR _{Cr-CysC}	0.620	0.031
	CrCl	eGFR _{Cr}	0.955	<0.0001
	CrCl	eGFR _{CysC}	0.562	0.091
CrCl	eGFR _{Cr-CysC}	0.812	0.004	
No AKI Patients (n=31)				
8 hours	CrCl	eGFR _{Cr}	0.545	0.002
24 hours	CrCl	eGFR _{Cr}	0.492	0.005
	CrCl	eGFR _{CysC}	0.425	0.017
	CrCl	eGFR _{Cr-CysC}	0.425	0.017
72hrs	CrCl	eGFR _{Cr}	0.473	0.064
	CrCl	eGFR _{CysC}	0.373	0.154
	CrCl	eGFR _{Cr-CysC}	0.439	0.089

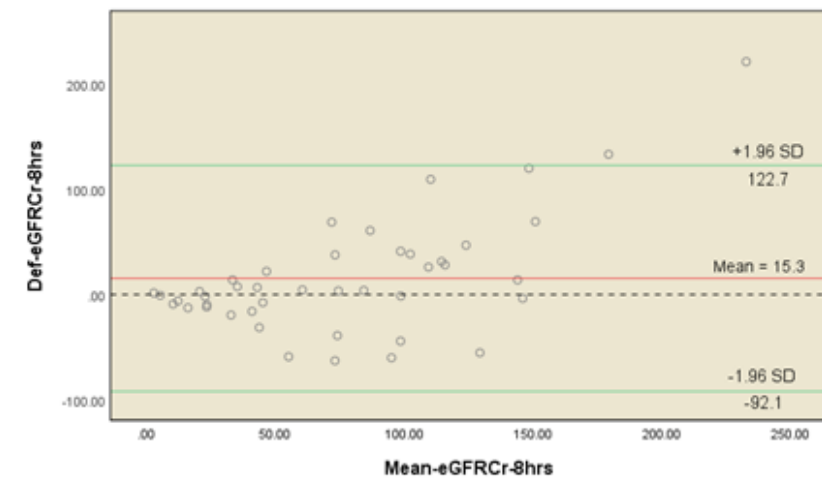
eGFR, estimated glomerular filtration; CrCl, Creatinine clearance; Cr, creatinine; CysC, Cystatin C

Accuracy, Bias, And Precision Analyses

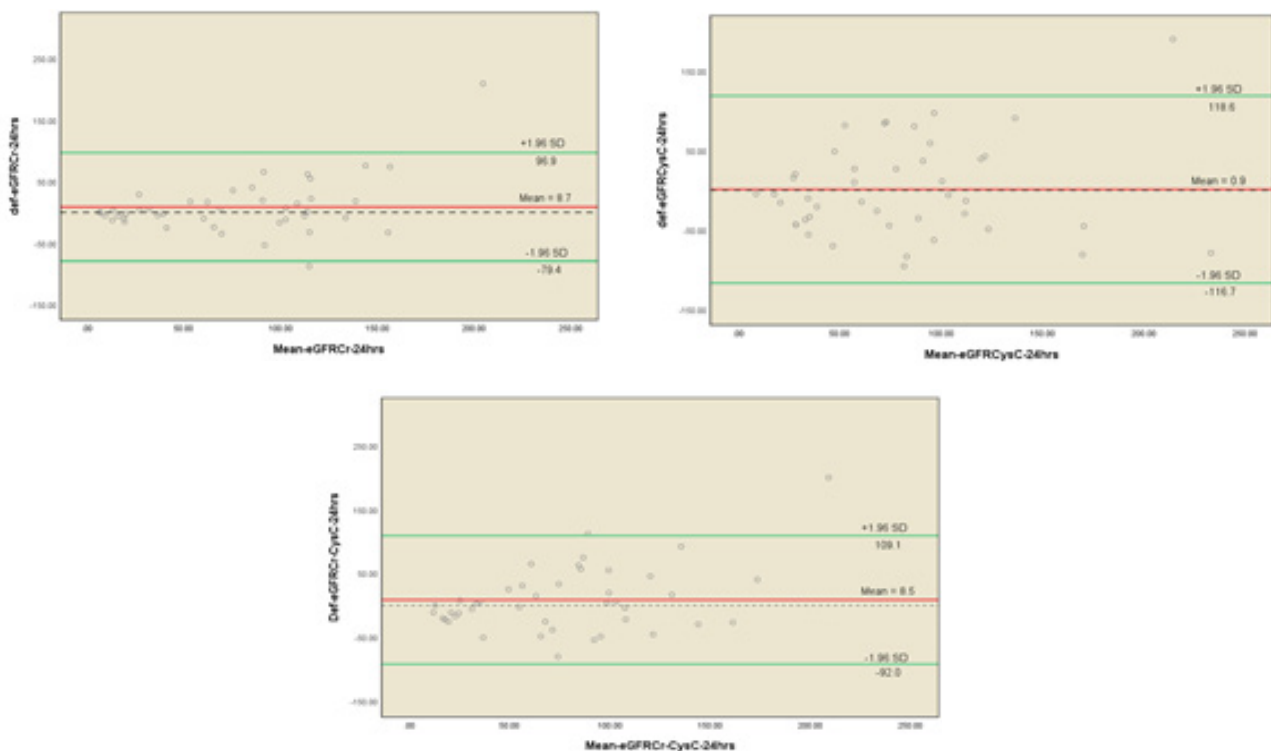
Bias, precision, and accuracy of each eGFR equations to CrCl are shown in Table III and Figure 2. At 24 hours, eGFR_{Cr} had the highest accuracy with 30% and 50% accuracy of 53.5 and 74.4, respectively. The lowest accuracy was observed in eGFR_{CysC} with accuracy within 30% and 50% of 18.6 and 46.5, respectively. At 72 hours,

eGFR_{Cr} had the highest accuracy within 30% and 50% of 60.04 and 51.32, respectively. eGFR_{Cr} was also the most precise with the lowest SD mean bias of 45, However, eGFR_{CysC} had the lowest bias with the mean difference of 0.9 at 24 hours, and 1.1 at 72 hours.

(A): Bland Altman plots at 8 hrs



(B): Bland Altman plots at 24 hrs



(C): Bland Altman plots at 72 hrs

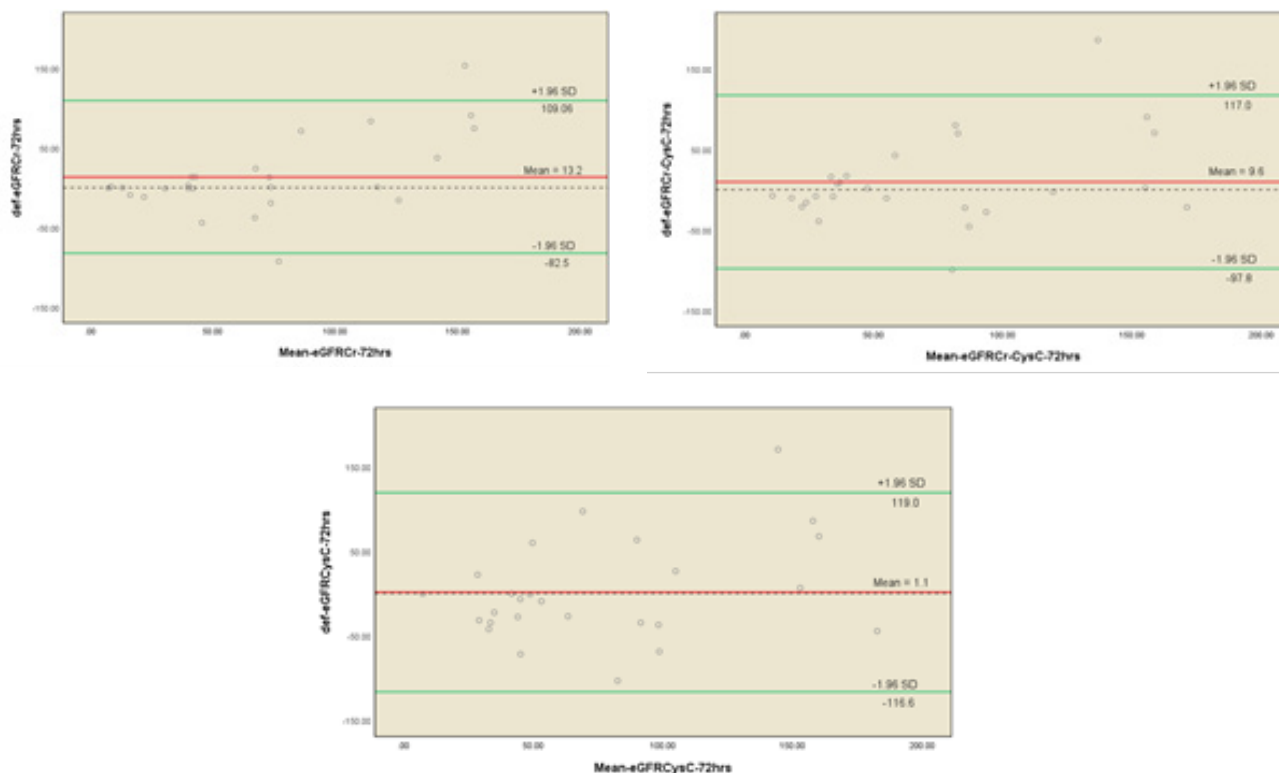


Figure 2: Bland-Altman plots of the CrCL and $eGFR_{Cr}$, $eGFR_{CysC}$, and $eGFR_{Cr-CysC}$ (ml/min), showing the limits of agreement. The difference of CrCL was plotted against the mean of CrCL and eGFR. The mean difference was shown as a dotted horizontal line whereas the 95% limit of agreement was shown as the horizontal green lines. $eGFR_{CysC}$ showed the least bias among three equations. (A) $eGFR_{Cr}$ at 8 hrs (B) $eGFR_{Cr}$, $eGFR_{CysC}$, and $eGFR_{Cr-CysC}$ at 24 hrs (C) $eGFR_{Cr}$, $eGFR_{CysC}$, and $eGFR_{Cr-CysC}$ at 72 hrs.

Subset Analysis of Patients with AKI and without AKI patients

Of the 43 patients recruited, 12 (27.9%) had AKI based on KDIGO criteria. We evaluated the eGFR equations separately in patients with AKI and without AKI patients. Generally, eGFR equations correlated well with 24-hour CrCl in AKI patients only, but not in patients without AKI

(Table II). Of all equations, $eGFR_{Cr}$ correlated best with 24-hour CrCl at all time points, with r of 0.799, 0.942 and 0.955 at 8, 24 and 72 hours respectively. In AKI patients, $eGFR_{Cr}$ were the least biased and most precise at 24 and 72 hours compared to $eGFR_{CysC}$ and $eGFR_{Cr-CysC}$ (Table III). In patients without AKI, $eGFR_{CysC}$ was the least bias, however $eGFR_{Cr}$ was still the most precise.

Table III: Bias, accuracy, and precision of estimated glomerular filtration rate (eGFR)

Time	Equation	Mean difference (bias)	SD of mean Bias	(Precision)	Accuracy within	
					Precision	r2
8 hrs	eGFR _{Cr}	15.3	54.81	0.43	34.88	55.81
24 hrs	eGFR _{Cr}	8.7	45.00	0.48	53.49	74.42
	eGFR _{CysC}	0.9	60.04	0.23	18.60	46.51
	eGFR _{Cr-CysC}	8.5	51.32	0.33	37.21	53.49
72 hrs	eGFR _{Cr}	13.2	48.87	0.44	57.69	69.23
	eGFR _{CysC}	1.1	60.11	0.22	30.77	46.15
	eGFR _{Cr-CysC}	9.6	54.80	0.31	30.77	57.69

eGFR, estimated glomerular filtration; CrCl, Creatinine clearance; Cr, creatinine; CysC, Cystatin C

The Diagnostic and Predictive Performance of eGFR Equations

eGFR_{Cr} at 24 hours strongly diagnosed AKI at 24 hours and 72 hours (Table IV). eGFR_{Cr} performed best in detecting AKI compared to the other two equations, with highest

AUC of 0.938 and 0.844, respectively. eGFR_{Cr-CysC} fare moderately with AUC 0.847 and 0.738 at 24 and 72 hours, respectively. All eGFRs were not predictive of mortality (Table IV).

Table IV: Area Under Curve (AUC) of the Receiver Operating Characteristic (ROC) Curve for Diagnosis of Acute Kidney Injury and Prediction of Mortality

Time	Equation	AUROC (95% CI)	Lower bound	Upper bound	P value
Diagnosis of AKI					
8hrs	CrCl	0.777	0.586	0.967	0.005
	eGFR _{Cr}	0.774	0.589	0.960	0.006
24hrs	CrCl	0.879	0.733	1.000	0.000
	eGFR _{Cr}	0.938	0.852	1.000	0.000
	eGFR _{CysC}	0.688	0.518	0.859	0.058
72hrs	eGFR _{Cr-CysC}	0.847	0.707	0.987	0.000
	CrCl	0.706	0.478	0.935	0.082
	eGFR _{Cr}	0.844	0.684	1.000	0.004
	eGFR _{CysC}	0.700	0.499	0.901	0.092
	eGFR _{Cr-CysC}	0.738	0.543	0.932	0.045
Prediction of Mortality					
8 h	CrCl	0.536	0.311	0.761	0.779
	eGFR _{Cr}	0.360	0.144	0.576	0.277
24 h	CrCl	0.423	0.185	0.662	0.551
	eGFR _{Cr}	0.446	0.208	0.684	0.674
	eGFR _{CysC}	0.450	0.156	0.745	0.700
72 h	eGFR _{Cr-CysC}	0.464	0.184	0.743	0.779
	CrCl	0.432	0.109	0.754	0.670
	eGFR _{Cr}	0.432	0.187	0.676	0.670
	eGFR _{CysC}	0.602	0.288	0.916	0.522
	eGFR _{Cr-CysC}	0.580	0.278	0.881	0.619

CI, confidence Interval; AUROC, Area Under Receiver Operating Characteristic Curve; eGFR, estimated glomerular filtration; CrCl, Creatinine clearance; Cr, creatinine; CysC, Cystatin C

DISCUSSION

The main aim of this study was to investigate which of the three CKD-EPI equations based on Cr (eGFR_{Cr}), CysC (eGFR_{CysC}) or combination of Cr and CysC (eGFR_{Cr-CysC}) best estimate measured GFR by 24-hour CrCl. Of the three equations, eGFR_{Cr} had the highest correlation, accuracy, and precision with CrCl at 24 and 72 hours. The finding was similar in subset of patients with AKI (n=12). All equations contributed to the diagnosis of AKI, however none predicted in-hospital-mortality.

Previous studies that compared eGFR using CKD-EPI equations based on CysC and Cr with measured GFR showed conflicting results (4). eGFR_{CysC} was shown to be more reliable for GFR assessment and clinical decision-making, as well as a better risk indicator for cardiovascular disease and mortality compared to eGFR_{Cr} and eGFR_{Cr-CysC} (21-24). Other studies showed that eGFR_{Cr-CysC} has the greatest accuracy compared to eGFR_{Cr} and eGFR_{Cr-CysC}. (25, 26,27). In a local study, eGFR_{Cr} was shown to have the highest precision and accuracy to measured GFR by 51Cr-EDTA clearance compared to eGFR_{Cr-CysC} and eGFR_{CysC}. (15). This finding was consistent with our study which showed that eGFR_{Cr} equation had the highest correlation and highest accuracy with CrCl compared to eGFR_{CysC}, eGFR_{Cr-CysC} at 24 and 72 hours. When patients were grouped in AKI and no AKI, this relationship was maintained in AKI patients only.

CysC is a potent inhibitor of cysteine proteases and is upregulated by corticosteroids suggesting that it could be upregulated in critically ill patients with the systemic inflammatory response syndrome (28). In our study most of our patients' primary diagnosis was infection (34.9%), indicating that CysC might be upregulated in these patients, and this partly explained the reason why CysC did not perform well. Another postulation of the poor performance of eGFR_{CysC} is that CrCl that was considered as reference, was based on Cr hence resulting in a better result for eGFR_{Cr} equation. In addition, CysC's volume of distribution varies in ICU patients with the volume status, hence further affecting its performance. We also postulate that eGFR_{Cr} performed best in our ICU as most of our ICU patients had short stay, hence reduction in muscle mass did not influence eGFR_{Cr}.

We showed that CrCl and eGFR equations were strongly diagnostic of AKI. The AUC of eGFR_{Cr} in predicting AKI was higher compared to CrCl, eGFR_{CysC} and eGFR_{Cr-CysC} at all time points. This finding is consistent with a study involving 203 emergency department patients, which showed that eGFR_{Cr} was diagnostic of AKI with AUC of

0.70 (29). CrCl was also diagnostic of AKI, similar to a study on 484 ICU patients which showed that 4-hour CrCl helps in diagnosis of AKI with AUC of 0.87 (30). We postulate that the main reason that CysC based equations did not performed well is because AKI was diagnosed using creatinine definition, hence eGFR_{Cr} performed best. In investigating the prognostic value of the eGFR, we observed that none of the equations predicted in hospital mortality in our study. This might be because of low sample size as it was not powered to the detection of mortality. This differs from the finding of a study on 3,298 participants that showed better performance of eGFR_{CysC} compared to eGFR_{Cr} in predicting 5-year and 10-year mortality (31).

Limitations of the study

There were several limitations of the current study. First, the data originated from a single center with a small sample size. Second, the study lacked the gold standard of GFR measurement using tracer such as inulin or radioisotope clearance due to financial and technical limitations. Since the current available measurement for GFR which is available clinically in the ICU setting is 24-hour CrCl, we utilised it in this study. There is a limitation of overestimation of eGFR due to creatinine secretion with CrCl measurement. Third, anuric patients were excluded due to lack of urine for 24-hour CrCl measurement. Finally, the CKD-EPI equation was developed in CKD patients, but not in critically ill patients, hence further study developing or revising an equation in this population is warranted (32).

CONCLUSION

eGFR_{Cr} had the highest correlation to 24-hour CrCl and was the most accurate and precise equation. eGFR_{CysC} equation had the lowest bias compared to eGFR_{Cr} and eGFR_{Cr-CysC} at 24 and 72 hours. However, these comparisons are invalid in patients with anuric AKI due to lack of urine to allow for CrCl measurement. Hence future study utilising a tracer clearance as gold standard is important to evaluate the equations. Using ROC analysis, most of the equations contributed to diagnose AKI, however, none of the equation predicted in-hospital-mortality.

ACKNOWLEDGEMENT

The authors would like to acknowledge and thanks, the research nurse (Nur Hafizah Zarudin) who helped in consent taking and all ICU nurses for their help. This work was supported by Ministry of Higher Education Fundamental Research Grant Scheme (FRGS/1/2019/SKK02/UIAM/02/1, FRGS19-184-0793). The study has been presented as an eposter presentation in, 4th Kuantan research day 2020.

CONFLICT OF INTEREST

None

ABBREVIATIONS

eGFR: Estimated glomerular filtration rate
 CKD-EPI: Chronic Kidney Disease Epidemiology Collaboration
 Cr: Creatinine
 CysC: Cystatin C
 CrCl: Creatinine clearance
 eGFR_{Cr}: Estimate glomerular filtration rate from serum creatinine
 eGFR_{CysC}: Estimate glomerular filtration rate from serum Cystatin C
 KDOQI: National Kidney Foundation Disease Outcomes Quality Initiative
 APACHE II: Acute Physiology and Chronic Health Evaluation II
 SOFA: Sequential Organ Failure Assessment
 KDIGO: Kidney Disease Improving Global Outcome
 MDRD: Modified Diet in Renal Disease
 ICU: Intensive Care Unit

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