

Comparison of CKD-EPI estimated glomerular filtration rate and measured creatinine clearance in critically ill patients with normal plasma creatinine

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Abstract

Introduction: Accurate assessment of renal function is a priority in the management of critically ill patients. Assessment of renal function helps in guiding drug dosing, optimize fluid, acid–base, and electrolyte management. Evidence based medicine in the form of research studies have shown that there exists a poor correlation between CKD-EPI eGFR and creatinine clearance in patients with normal plasma creatinine. Currently there is a paucity of data in India as to whether examining whether eGFR could be used in place of conventional measures for such a purpose, particularly in the critical care environment. The study was done to compare CKD-EPI eGFR with measured urinary CLCR, in recently admitted critically ill patients with normal plasma creatinine concentrations.

Material and Methods: The study was a prospective observational study which consisted of recently admitted critically ill patients with normal plasma creatinine concentrations admitted to the ICU of A. J. Institute Of Medical Sciences Hospital, Mangalore on f 100 patients who met a pre-defined criteria done over a period of 2 years from October 2014 to November 2016 after obtaining ethical clearance committee of the institution and informed consent of the patient and/or their legal heir. This was a prospective observational study that was conducted in the intensive care unit Patients who were recently were admitted to the intensive ICU admission, plasma creatinine concentration \leq 1.2mg/dL and no history of prior CKD. CKD-EPI eGFR was compared against 8-hour measured urinary CLCR. Data was collected within 48 hours of admission. The collected data was transferred to a master- chart and analyzed for

Results: The mean age in our study was 55.43 years, the mean height was 164.55cms, the mean weight was 69.19 kg and the mean BSA was 1.7759 males predominated the study cases 62%. males predominated the study cases 62%. 16 % cases in our study needed mechanical ventilation On comparison of the mean values of 24 HR Cr CL and CKD-EPI the mean values of CKD-EPI is higher with a difference of 0.9727 is statistically not significant with a p value of 0.726. At a GFR of 90-119.99 ml/min On comparison of the mean values of 24 HR Cr CL and CKD-EPI the mean values of 24 HR Cr CL is higher with a difference of 22.229 is statistically significant with a p value of $<$ 0.001. On comparison of the mean values of 24 HR Cr CL and MDRD the mean values of 24 HR Cr CL is higher with a difference of 21.7355 is statistically significant with a p value of $<$ 0.001. On comparison of the mean values of 24 HR Cr CL and CG-Cr CL the mean values of 24 HR Cr CL is higher with a difference of 19.29194 is statistically significant with a p value of $<$ 0.001.

Conclusion: In conclusion, this study has examined CKD-EPI eGFR in comparison to 8-hr measured CLCR in a cohort of recently admitted critically ill patients with normal plasma CR concentrations. Our results suggest poor agreement between these techniques in this population. Whether this represents a true limitation of CKD-EPI eGFR, or an intuitive discrepancy based on the problems with endogenous CLCR, remains uncertain. Notwithstanding this, until additional data are available on the utility of CKD-EPI eGFR for drug dose adjustment, particularly in identifying ARC, we would recommend clinicians consider using CLCR for this purpose.

Keywords: Glomerular filtration rate, Renal Disease, CKD-EPI.

Introduction

Accurate assessment of renal function is a priority in the management of critically ill patients. Assessment of renal function helps in guiding drug dosing, optimize fluid, acid–base, and electrolyte management. Though plasma creatinine concentrations are within the reported reference range the normal values in the critically ill have been associated with both augmented creatinine clearance (CLCR),¹ and occult acute kidney injury (AKI).²

The most commonly applied formula developed to estimate the glomerular filtration rate (eGFR) is the Modification of Diet in Renal Disease (MDRD),³ newer CKD Epidemiology Collaboration (CKD-EPI)⁴ equations and Cockcroft Gault Creatinine Clearance.

Though MDRD and CKD-EPI equations improved the quality of care for patients with CKD, there is a concern about the ubiquitous application of eGFR, particularly in dose modification.⁹

Evidence based medicine in the form of research studies have shown that there exists a poor correlation between CKD-EPI eGFR and creatinine clearance in patients with normal plasma creatinine.¹⁰

Currently there is a paucity of data in India as to whether examining whether eGFR could be used in place of conventional measures for such a purpose, particularly in the critical care environment. The aims and objectives of the study was to compare CKD-EPI eGFR with measured urinary CLCR, in recently admitted critically ill patients with normal plasma creatinine concentrations.

Materials and Methods

The study was a prospective observational study which consisted of recently admitted critically ill patients with normal plasma creatinine concentrations admitted to the ICU of A. J. Institute Of Medical Sciences Hospital, Mangalore on f 100 patients who met a pre-defined criteria done over a period of 2 years from October 2014 to

November 2016 after obtaining ethical clearance committee of the institution and informed consent of the patient and/or their legal heir.

Method of collection of data

It was a hospital based prospective observational study done on recently admitted critically ill patients with normal plasma creatinine concentrations admitted in the ICU of AJ Institute of Medical Science.

A study of 100 patients was done over a period of 2 years from October 2014 to November 2016

These were the pre-defined criteria:

Inclusion Criteria

1. Recent ICU admission
2. Plasma creatinine \leq 1.2mg/dL
3. No history of prior CKD

Exclusion Criteria

1. < 18 years
2. Pregnancy
3. Rhabdomyolysis
4. Admission plasma creatinine kinase > 5000IU/L (RIFLE criteria)

Methodology

1. This was a prospective observational study that was conducted in the intensive care unit
2. Patients who were recently were admitted to the intensive ICU admission, plasma creatinine concentration \leq 1.2mg/dL, and no history of prior CKD.

Table 3: Admission type

Admission type	Frequency	Percentage
Elective	10	10
Emergency	69	69
Surgical emergency	10	10
Trauma	11	11

Table 4: Variation of creatinine in the various admissions

		Mean	N	Std. Deviation	BIAS		t Value for paired T -Test	P value	R	P value of correlation
					Mean Difference	Std. Deviation				
Overall	24 HR Cr CL	102.131	100	29.2996						
	Pair 1 CKD-EPI	80.035	100	19.5258	22.096	25.2185	8.762	<0.001	0.528	<0.001
	Pair 2 MDRD	80.238	100	20.2887	21.893	27.106	8.077	<0.001	0.45	<0.001
	Pair 3 CG-Cr CL	81.4239	100	26.8346	20.7071	31.39529	6.596	<0.001	0.377	<0.001
Elective	24 HR Cr CL	96.76	10	23.4835						
	Pair 1 CKD-EPI	82.08	10	17.2427	14.68	9.4965	4.888	0.001	0.937	<0.001
	Pair 2 MDRD	82.51	10	17.2926	14.25	9.9865	4.512	0.001	0.924	<0.001
	Pair 3 CG-Cr CL	88.048	10	22.51076	8.712	19.27077	1.43	0.187	0.65	0.042

3. CKD-EPI eGFR was compared against 8-hour measured urinary CLCR.
4. Data was collected within 48 hours of admission.
5. The collected data was transferred to a master- chart and analyzed.

Statistical Analysis

Statistical analysis was done using SPSS software version 23.0. A 'p' value less than 0.05(p<0.05) is considered significant.

The collected information was summarized as percentage and proportions.

To study the prevalence of work related musculoskeletal disorders frequency and percentage was used.

The rest collected data was analyzed using mean, mode for demographic data and frequency percentage for the analysis of the clinical data.

Results and Observations

Table 1: Demographic data

	Mean	Standard Deviation
Age	55.43	16.00332
Height	164.55	8.079623
Weight	69.19	10.24911
BSA	1.7759	0.158516

Table 2: Gender

		Count	%
Gender	F	38	38
	M	62	62

Emergency		24 HR Cr CL	103.201	69	29.1065						
	Pair 1	CKD-EPI	79.826	69	18.3704	23.3754	27.838	6.975	<0.001	0.383	0.001
	Pair 2	MDRD	80.381	69	19.4445	22.8203	30.3593	6.244	<0.001	0.268	0.026
	Pair 3	CG-Cr CL	78.4075	69	25.40345	24.79391	32.10593	6.415	<0.001	0.312	0.009
Surgical emergency		24 HR Cr CL	86.88	10	39.1336						
	Pair 1	CKD-EPI	69.41	10	23.7316	17.47	22.6428	2.44	0.037	0.852	0.002
	Pair 2	MDRD	68.74	10	23.7441	18.14	22.6343	2.534	0.032	0.852	0.002
	Pair 3	CG-Cr CL	76.451	10	33.26813	10.429	31.55659	1.045	0.323	0.631	0.051
Trauma		24 HR Cr CL	114.164	11	20.8498						
	Pair 1	CKD-EPI	89.145	11	22.2823	25.0182	19.6663	4.219	0.002	0.586	0.058
	Pair 2	MDRD	87.727	11	22.987	26.4364	18.8262	4.657	0.001	0.635	0.036
	Pair 3	CG-Cr CL	98.8436	11	28.69385	15.32	33.48948	1.517	0.16	0.114	0.738

Table 4: Various laboratory parameters

Plasma Creatinine Concentration (µmol/L)	0.981	0.173901
Plasma Creatinine Concentration (µmol/L) + 24hrs plasma creatinine	0.997	0.148021
Apache II	9.11	4.607624
Modified SOFA	3.75	2.540083
ICU Stay (days)	4.72449	2.99064
CKD-EPI	80.035	19.52579
MDRD	80.238	20.2887
CG-Cr CL	81.4239	26.8346
24 HR U Cr	85.99	17.8402
24 HR Cr CL	102.131	29.2996

Overall

On comparison of the mean values of 24 HR Cr CL and CKD-EPI the mean values of 24 HR Cr CL is higher with a difference of 22.096 is statistically significant with a p value of <0.001.

On comparison of the mean values of 24 HR Cr CL and MDRD the mean values of 24 HR Cr CL is higher with a difference of 21.893 is statistically significant with a p value of <0.001.

On comparison of the mean values of 24 HR Cr CL and CG-Cr CL the mean values of 24 HR Cr CL is higher with a difference of 20.7071 is statistically significant with a p value of <0.001.

Elective

On comparison of the mean values of 24 HR Cr CL and CKD-EPI the mean values of 24 HR Cr CL is higher with a difference of 14.68 is statistically significant with a p value of 0.001.

On comparison of the mean values of 24 HR Cr CL and MDRD the mean values of 24 HR Cr CL is higher with a difference of 14.25 is statistically significant with a p value of 0.001.

On comparison of the mean values of 24 HR Cr CL and CG-Cr CL the mean values of 24 HR Cr CL is higher with a

difference of 8.712 is statistically not significant with a p value of 0.187.

Emergency

On comparison of the mean values of 24 HR Cr CL and CKD-EPI the mean values of 24 HR Cr CL is higher with a difference of 23.3754 is statistically significant with a p value of <0.001.

On comparison of the mean values of 24 HR Cr CL and MDRD the mean values of 24 HR Cr CL is higher with a difference of 22.8203 is statistically significant with a p value of <0.001.

On comparison of the mean values of 24 HR Cr CL and CG-Cr CL the mean values of 24 HR Cr CL is higher with a difference of 24.79391 is statistically significant with a p value of <0.001.

Surgical Emergency

On comparison of the mean values of 24 HR Cr CL and CKD-EPI the mean values of 24 HR Cr CL is higher with a difference of 17.47 is statistically significant with a p value of 0.037.

On comparison of the mean values of 24 HR Cr CL and MDRD the mean values of 24 HR Cr CL is higher with a difference of 18.14 is statistically significant with a p value of 0.032.

On comparison of the mean values of 24 HR Cr CL and CG-Cr CL the mean values of 24 HR Cr CL is higher with a difference of 10.429 is statistically not significant with a p value of 0.323.

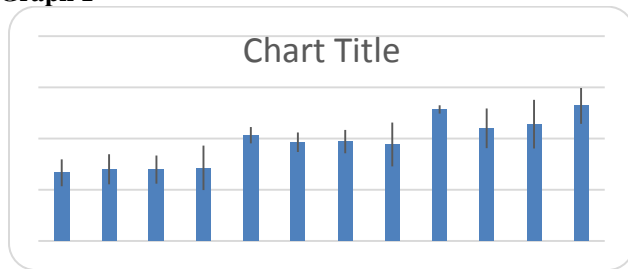
Trauma

On comparison of the mean values of 24 HR Cr CL and CKD-EPI the mean values of 24 HR Cr CL is higher with a difference of 25.0182 is statistically significant with a p value of 0.002.

On comparison of the mean values of 24 HR Cr CL and MDRD the mean values of 24 HR Cr CL is higher with a difference of 26.4364 is statistically significant with a p value of 0.001.

On comparison of the mean values of 24 HR Cr CL and CG-Cr CL the mean values of 24 HR Cr CL is higher with a difference of 15.32 is statistically not significant with a p value of 0.16.

Graph 1



Discussion

Accurate assessment of renal function is a priority in the management of critically ill patients. Clinicians regularly utilize such information to help guide drug dosing, optimize fluid, acid-base, and electrolyte management, tailor nutritional requirements, and assess the need for renal replacement therapy (RRT). Rising plasma creatinine (CR) concentrations often trigger clinical interventions, including dose reduction of renally eliminated agents. In contrast, plasma CR concentrations within the reported reference range appear to be less useful. Normal values in the critically ill have been associated with both augmented creatinine clearance (CL_{CR}), and occult acute kidney injury (AKI). In ICU patients with normal serum creatinine (SCr), a state of increased renal drug excretion has been described (creatinine clearance ≥ 130 ml/min/1.73 m²), and named augmented renal clearance (ARC). In ICU patients, the accuracy of GFR estimates is insufficient. Currently there is a paucity of data in India as to whether examining whether eGFR could be used in place of conventional measures for such a purpose, particularly in the critical care environment. In our study titled "comparison of CKD-EPI estimated glomerular filtration rate and measured creatinine clearance in critically ill patients with normal plasma creatinine" we aimed to compare CKD-EPI eGFR with measured urinary CLCR, in recently admitted critically ill patients with normal plasma creatinine concentrations.¹⁰

Admission Type

In our study the admission type was elective 10, emergency 69, surgical emergency 10, trauma 11.

Andrew A Udy et al.¹⁰ had Admission type, n (%) Elective 15(13.6) Emergency 33(30.0) Surgical emergency, 37(33.6) - Trauma 25(22.7).

Need for mechanical ventilation

16 % cases in our study needed mechanical ventilation In a study by Stéphanie Ruizet al 270(75 %) of the patients were mechanically ventilated.

In a study by Andrew A Udy et.al Mechanical ventilation, was needed inn 63(57.3%)

Variations of Creatinine

Stéphanie Ruizet al¹¹ showed that ICU patients can exhibit important variations of their measured CrCl, despite a normal SCr with the CrCl being higher than 130 ml/min/1.73 m² (ARC) in more than 33 % of the cases.

This finding was similar to our finding in which the ICU patients exhibit important variations of their measured CrCl, despite a normal SCr 35%. In our study on comparison of the mean values of 24 HR Cr CL and CKD-EPI the mean values of 24 HR Cr CL is higher with a difference of 22.096 is statistically significant with a p value of <0.001.

Drugs Given

In a study by Andrew A Udy et al¹⁰ the drugs given are comparable with our study Intravenous contrast administration, n (%) (n=109) 30(27.3) Frusemide administration, n (%) 13(11.8) Mannitol administration, n (%) 4(3.6) Vasopressors, n (%) 33(30.0).

In 28 critically ill patients with normal SCr, Hoste¹² demonstrated that the Cockcroft-Gault and MDRD formulas were not adequate in assessing renal function and we have previously shown similar findings in 36 burn patients.

Conclusion

Acute renal compromise appears to be common in intensive care critically ill patients. This study suggests the CKD-EPI equation could allow a first screening of patients with Acute renal compromise. In conclusion, this study has examined CKD-EPI eGFR in comparison to 8-hr measured CLCR in a cohort of recently admitted critically ill patients with normal plasma CR concentrations. Our results suggest poor agreement between these techniques in this population. Whether this represents a true limitation of CKD-EPI eGFR, or an intuitive discrepancy based on the problems with endogenous CLCR, remains uncertain. Notwithstanding this, until additional data are available on the utility of CKD-EPI eGFR for drug dose adjustment, particularly in identifying ARC, we would recommend clinicians consider using CLCR for this purpose.

Conflict of Interest: None.

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