Using Two Predictor Scoring Systems Together to Increase the Chance of Identifying the Augmented Renal Clearance Phenomenon: A Cross-sectional Study

Ramin Tolouian,[1] Rezvan Hassanpour,[2] Mohammad Sistanizad,[2,3] Mehran Kouchek,[4] Mir Mohammad Miri,[4] Sara Salarian,[4] Seyedpouzhia Shojaei,[4] Elham Pourheidar[2]

[1]Division of Nephrology and Hypertension, Eastern Virginia Medical School, Norfolk, VA, USA
[2]Department of Clinical Pharmacy, School of Pharmacy, Shahid Beheshti University of Medical Sciences, Tehran, Iran
[3]Prevention of Cardiovascular Disease Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran
[4]Department of Critical Care Medicine, Imam Hossein Medical and Educational Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Keywords. glomerular filtration rate, kidney, critical care, multiple trauma

Introduction. Augmented Renal Clearance (ARC) reflects a measured creatinine clearance (CrCl) of more than 130 ml/min. Also, there are two scoring systems for the prediction of the ARC phenomenon i.e., the ARC score (ARCS) and the Augmented Renal Clearance in Trauma Intensive Care score (ARCTICs). The objectives of the current study were the evaluation the effect of using both scoring systems, on the chance of identifying this phenomenon and evaluating the accuracy of the three commonly used formulas for estimating glomerular filtration rate (eGFR) in ICU patients.
Methods. In this prospective cross-sectional study, the CrCls of all patients admitted to the ICU were evaluated by using ARCS and ARCTICS, and for high-risk subjects based on scoring systems, a 12-hour urine sample was collected to measure CrCl. Besides, daily serum creatinine was recorded to estimate the daily eGFR.
Results. During the study period, 810 subjects were evaluated and 145 were categorized as high-risk using scoring systems. The ARC phenomenon was confirmed in 79 patients on the recruitment day and 81.01 and 18.98% of them were recruited by ARCS and ARCTICS, respectively. The ROC curves showed AUCs > 0.5 for Cockcroft-Gault (C-G) and CKD-EPI with the cut-off of 100.48 and 107.05 mL/min/ 1.73m^2, respectively; to detect the ARC phenomenon.
Conclusion. We recommend using ARCS and ARCTICS simultaneously to assess critically ill patients regarding the possibility of the ARC phenomenon which should be confirmed by using urinary CrCl, as none of the formulas could accurately detect the ARC phenomenon, neither the 12-hour CrCl.

IJKD 2022;16:179-87
www.ijkd.org
DOI: 10.52547/ijkd.6695

Original Paper

INTRODUCTION

Augmented Renal Clearance (ARC) defined as increased Creatinine Clearance (CrCl), is a common phenomenon in critical care settings. The CrCl ≥ 130 mL/min/ 1.73m^2 has been considered as the ARC phenomenon in most studies, although different values have been suggested.[1-10] The incidence of this phenomenon has been reported between 14 to 85%, depending on the population of the studies and the cut-off value of CrCl.[4,10-12] According to the increased elimination rate of drugs in case of existence of ARC, especially for hydrophilic antibiotics, determination of this phenomenon is necessary for adjusting the optimal

treatment to reduce the risk of sub-therapeutic level of medications and the resultant decrease in the length of hospital stay and also improve the clinical outcomes.[4,8,13-15]

The ARC phenomenon is commonly identified by the calculation of the estimated glomerular filtration rate (eGFR) in clinical practice. The eGFR can be calculated by various mathematical equations, such as Cockcroft-Gault (C-G), Modification of Diet in Renal Disease (MDRD), and Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI), which is usually less than the actual CrCl.[16-19] The measurement of urinary CrCl using an 8 to 24 hours period of urine collection (8 to 24-hour CrCl) is a more accurate and reproducible tool to estimate renal function and has been recommended in identifying ARC in critical patients.[16,17,20]

The ARC score (ARCS) and the Augmented Renal Clearance in Trauma Intensive Care (ARCTIC) score are two scoring systems that have been used to predict the occurrence of the ARC phenomenon.[4,7] ARCS is a scoring system that has been developed for critically ill patients while ARCTIC was introduced as a practical screening tool in trauma patients. The sensitivity and specificity of ARCS are 100% and 76% and of the ARCTIC are 84 and 68%, respectively.[4,6,7,9,21-23]

The main aim of this study was to evaluate the value of using both scoring systems i.e., ARCS and ARCTIC together, on the chance of identifying the ARC phenomenon in the ICU setting. The Assessment of the accuracy of the three commonly used formulas for estimating GFR i.e., C-G, MDRD, and CKD-EPI in patients with ARC, and their possible role as an alternative for 12-hour urine collection was also evaluated.

MATERIALS AND METHODS

This was a prospective cross-sectional observational study. The protocol of the study was approved by the Institutional Review Boards of the Ethics Committee of SBMU (IR.SBMU.PHARMACY.REC.1398.164). The study began on July 23, 2018, and was completed on March 19, 2019. We obtained informed written consent from all patients or caregivers.

Setting And Study Population

All patients admitted to the ICU of Imam Hossein Hospital, a tertiary care teaching hospital affiliated with Shahid Beheshti University of Medical Sciences (SBMU), Tehran, Iran, were evaluated on the first day of admission for the risk of developing the ARC phenomenon based on ARCS and ARCTIC scoring systems (Table 1).[4,9]

The patients who were at high risk for developing ARC were included in the study and categorized into three groups according to their scores: patients with an only high ARCS risk score were categorized as group A; patients with an only a high ARCTIC risk score as group B; and patients with both high ARCS and ARCTIC risk scores as group C. Being younger than 18 years old, serum creatinine (SCr) $\geq$ 1.3 mg/dL, lack of urine output, being on dialysis, and pregnancy were considered as exclusion criteria.

Interventions

A 12-hour urine sample (from 5 PM to 5 AM of the next day), was collected, via an indwelling catheter for high-risk patients on days 0, 3, 7, 10, and 14 of the study to identify patients with the ARC phenomenon. Baseline characteristics of the enrolled subjects including age, sex, Acute Physiologic and Chronic Health Evaluation (APACHE) II score, Sequential Organ Failure Assessment (SOFA) score, and diagnosis based on the International Classification of Disease (ICD10) code were recorded.

All patients were followed for 14 days unless

Table 1. The ARC Risk Scoring Systems

	ARC Scoring System	ARCTIC Scoring System
Criteria	● Age 50 or younger = 6 pts ● Trauma = 3 pts ● SOFA score ≤ 4 = 1 pt	● SCr < 0.7 = 3 pts ● Male Sex = 2 pts ● Age < 56 years = 4 pts ● Age: 56 to 75 years = 3 pts
Interpretation*	○ 0 to 6 Points = Low ARC Risk ○ 7 to 10 Points = High ARC Risk	○ ≤6 Points = Low ARC Risk ○ > 6 Points = High ARC Risk

Abbreviations: ARC, augmented renal clearance; ARCTIC, augmented renal clearance in trauma intensive care; SOFA, sequential organ failure assessment score; SCr, serum creatinine concentration (mg/dL); pts, point(s);
*Evaluation the Risk of Developing ARC Phenomenon

they were discharged, transferred out of ICU, or died earlier. Daily SCr of patients was recorded to estimate the daily eGFR. The length of stay in the ICU (ICULS) of all patients was also recorded.

Outcomes

The primary outcome was considered as the impact of using both scoring systems i.e., ARCS and ARCTIC, together, on the chance of identifying the ARC phenomenon in the ICU setting. The power of ARCS and ARCTIC scores to identify critically ill and trauma patients with ARC phenomenon, the occurrence of this phenomenon during 14 days of admission, and its effect on ICULS, the accuracy of the three commonly used formulas for estimating GFR i.e., C-G, MDRD, and CKD-EPI in patients with ARC, and their possible role as an alternative for 12-hr urine collection were also evaluated as secondary outcomes.

Definitions

Arterial Blood Gas (ABG) was not requested routinely for all patients, therefore, we used the SOFA score with some changes including SpO2/FiO2 instead of PaO2/FiO2[24,25] and also using the following correction formula to calculate the Glasgow Coma Scale (GCS) from 15 in all patients, whether intubated or not, whereas GCS in patients who are intubated is usually calculated from 10.[26]

Equation 1: Estimated GCS_{verbal} *(- 0.3756) + (0.5713 × GCS_{motor}) (0.4233 × GCS_{eye})*

Equation 2: C-G (mL/min/ 1.73m^2) =

$$\frac{\left[140-\mathrm{Age(year)}\right]\times \mathrm{Weight(kg)}}{Serum\,Creatinine\left(\frac{mg}{dl}\right)\times 72}\times 0.85(\mathrm{female})$$

eal Body Weight (IBW) was used for calculating CrCl by the C-G formula:

Equation 3: IBW = [Height *(cm)* – 150] × 0.4 + 50 (if male) + 45.5 (if female)

For patients whose height was not recorded in their chart, the length of the ulna was measured and their height was estimated by Malnutrition Universal Screening Tool (MUST) equation.[27]

Equation 4: MDRD (four variables, for non-IDSM SCr, mL/min/ 1.73m^2) =

$$186\times \mathrm{Scr}\left(\frac{\mathrm{mg}}{\mathrm{dL}}\right)^{-1.154}\times \mathrm{Age(y)}^{-0.203}\times 1.212\,(\mathrm{black})\times 0.742(\mathrm{female})$$

uation 5: CKD-EPI (mL/min/ 1.73m^2) =

$$141\times \min\left(\mathrm{Scr}\left(\frac{\mathrm{mg}}{\mathrm{dL}}\right)/\kappa.1\right)^{\alpha}\times \max\left(\mathrm{Scr}\left(\frac{\mathrm{mg}}{\mathrm{dL}}\right)/\kappa.1\right)^{-1.209}$$
$$\times\, 0.993^{\mathrm{Age(y)}}\times 1.159\,(\mathrm{black})\times 1.018\,(\mathrm{female})$$

is 0.7 for females and 0.9 for males, α is -0.329 for females and -0.411 for males, min indicates the minimum of Scr/κ or 1, and max indicates the maximum of Scr/κ or 1.

The confirmed ARC phenomenon was defined as CrCl ≥ 130 mL/min/ 1.73m^2 calculated by the 12-hour urine collection.

12-hour CrCl =

$$\frac{urine\,volume(ml)\times urine\,creatinin\left(\frac{mg}{dl}\right)}{serum\,creatinin\left(\frac{mg}{dl}\right)\times collectin\,time(minutes)}$$

Statistical Analysis

SPSS version 21 was used for statistical analyses. Quantitative data were tested for the normality of distributions running Kolmogorov–Smirnov test, and then compared via a One-way ANOVA test with Tukey, Tamhane's T2 post hoc, Mann-Whitney U, and Kruskal-Willis tests for normally and non-normally distributed data, respectively. Also, categorical data were analyzed using the Chi-square test. Residual plots according to the method of Bland and Altman was used to analyze the matching between the eGFR formulas and the 12-h CrCl. The diagnostic accuracy of the formulas in predicting ARC was assessed by measuring the area under the receiver operating characteristic (ROC) curves. Wilcoxon rank test was used to compare the area under the ROC curves of the eGFR. The best threshold with the corresponding likelihood ratio was defined by Youden's index. All data were presented as mean ± standard deviation (SD) or median (interquartile range [IQR]) for normally and non-normally distributed data, respectively, and mode for categorical data. *P* values < .05 was considered significant.

RESULTS

From a total of 819 patients admitted to the ICU during 9-month screening, 160 patients (19.53%) were considered high risk for developing the ARC phenomenon according to the scoring systems.

Seventy-nine patients were categorized as high-risk by ARCS (group A), 44 patients by ARCTIC risk score (group B), and 37 subjects by both scoring systems (group C). Fifteen patients were excluded due to lack of urine collection (8, 2, and 5 patients in groups A, B, and C, respectively) and finally, data from a total of 145 patients were analyzed, including 71 in group A, 42 in group B and 32 in group C (Figure 1 and Table 2).

All baseline characteristics showed a significant

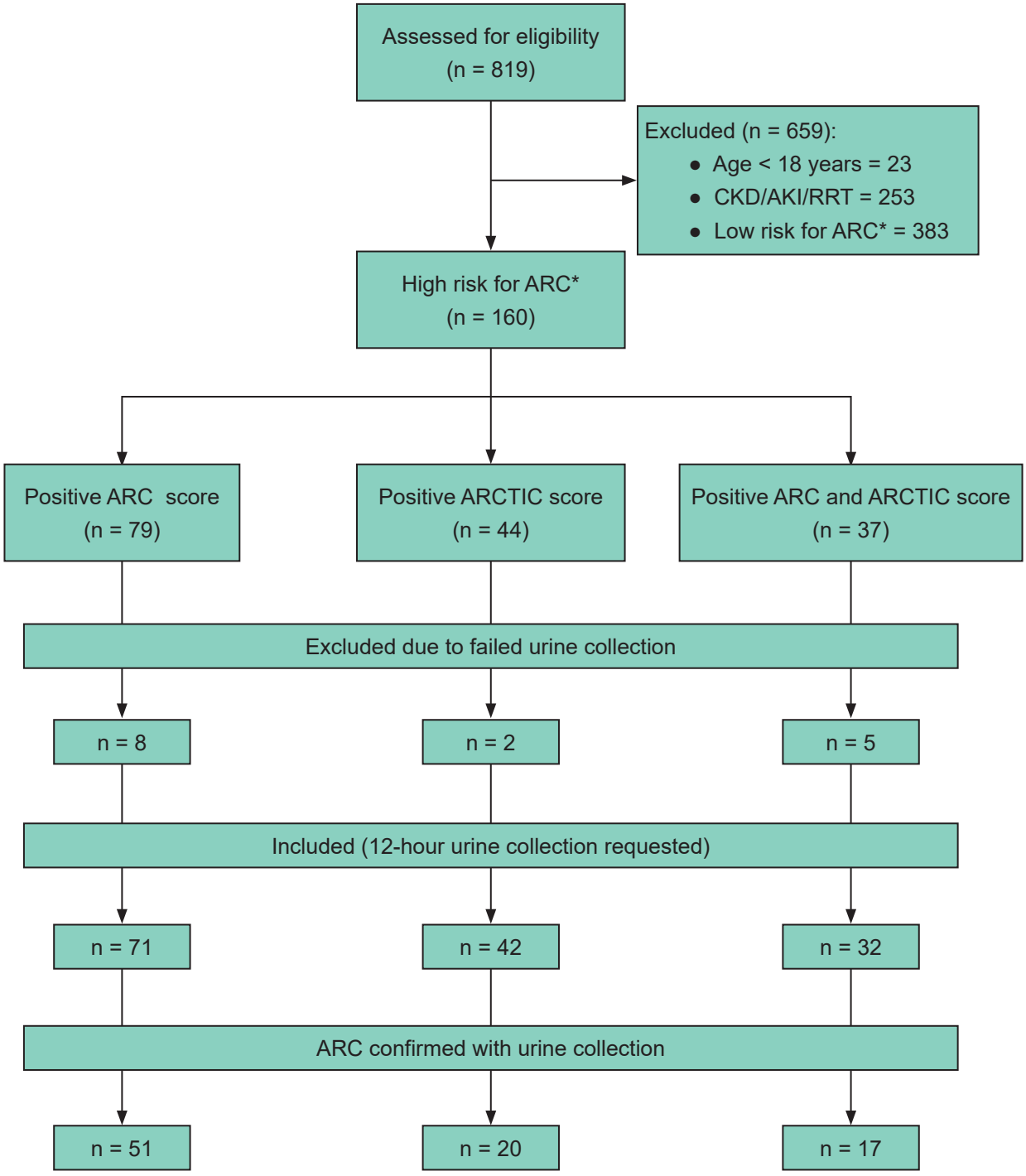

Figure 1. Participant Inclusion Process (Abbreviations: CKD, chronic kidney disease; AKI, acute kidney injury; RRT, renal replacement therapy; ARC, augmented renal clearance; ARCTIC, augmented renal clearance in trauma intensive care)
*Risk Evaluation for ARC Development According to ARC and ARCTIC Scoring System

Table 2. The Number of Patients in Each Group and the Percentage of Them Who Had Confirmed ARC Phenomenon During 14 Days Follow-up

	Day 0			Day 3			Day 7			Day 10			Day 14		
	A	B	C	A	B	C	A	B	C	A	B	C	A	B	C
Total Number	71	42	32	35	30	16	15	19	7	7	16	4	7	9	1
Confirmed ARC[a]	50	15	14	25	8	8	7	1	5	3	0	2	5	2	0
Percent (%)	70.42	35.71	43.75	71.42	26.66	50	46.66	5.26	71.42	42.85	-	50	71.42	22.22	-

Definition: A, patients with only positive Augmented Renal Clearance Score (ARCS); B, patients with only positive Augmented Renal Clearance in Trauma Intensive Care (ARCTIC) score; C, patients with both positive ARCS and ARCTIC scores.
[a]ARC: Confirmed Augmented Renal Clearance (ARC) According to 12-hour Urinary Creatinine Clearance (12h CrCl)

difference between the three groups, except for baseline CrCl, calculated by the C-G and CKD-EPI formulas ($P > .05$) (Table 3).

The ARC phenomenon was confirmed by 12-hour urine collection samples in 79 patients on the recruitment day (day 0), 50 of whom (63.2%) were categorized as high-risk by using ARCS (group A)), 15 by using ARCTIC (18.98%) and 14 by using both methods (17.7%).

Of the total of 79 high risk patients by either of the scoring methods, 43 had been admitted to the ICU due to trauma, 9 of whom (20.93%) were categorized as high-risk using ARCTIC (groups B and C), and by adding ARCS we found 34 patients (79.07%) with confirmed ARC (Table 4).

Three hundred eleven 12-hour urine samples were collected from 145 participants during the 14-day follow-up period and the ARC phenomenon

Table 3. Baseline Characteristics

Variables[d]	Groups			*P* [a,b,c]
	Group A Positive ARCS (n = 71)	Group B Positive ARCTIC Score (n = 42)	Group C Positive Both ARCS and ARCTIC Score (n = 32)	
Sex (n, %)				
Male	52 (73.2)	27 (64.3)	9 (28.1)	< .05
Female	19 (26.8)	15 (35.7)	23 (71.9)	
Age (Median (IQR))	33 (26 to 40)	51 (41.75 to 61.75)	32 (22.75 to 37.5)	< .001*
ICU Diagnosis on Admission Day Based on ICD10 Code[e] (n, %)				
C	8 (11.3)	6 (14.3)	7 (21.9)	< .001
T	39 (54.9)	5 (11.9)	10 (31.3)	
G	4 (5.6)	5 (11.9)	1 (3.1)	
I	6 (8.5)	13 (31)	2 (6.3)	
J	2 (2.8)	3 (7.1)	2 (6.3)	
B	4 (5.6)	5 (11.9)	3 (9.4)	
K	2 (2.8)	5 (11.9)	1 (3.1)	
N	6 (8.5)	0	6 (18.8)	
APACHE IIh (Median (IQR))	14 (6 to 17)	23 (14.75 to 23)	12 (6 to 19.5)	< .05†
SOFAi (Median (IQR))	2 (1 to 4)	5 (4 to 6)	1.5 (1 to 3)	< .001‡
Base C-Gj (mean ± SD)	115.69 ± 30.07	111.14 ± 27.12	124.64 ± 39.40	> .05
Base MDRD	103.23 ± 22.75	130.83 ± 40.44	126.83 ± 27.67	< .05
Base CKD-EPI	105.31 ± 17.47	108.13 ± 17.35	119.43 ± 16.52	> .05

[a]One-way ENOVA test, [b]Kruskal-Willis test, [c]Chi-square.
[d]Values reported as mean ± standard deviation or median (interquartile range: 25%, 75%) for quantitative normal or non-normal distributions data, respectively and Mode for categorical data. [e]ICD 10 code definition: B, Certain infections; C, Malignant neoplasms; G, Diseases of the nervous system; I, Disease of the circulatory system; J, Disease of the respiratory system; K, Disease of the digestive system; N, Pregnancy disorder; T, Injury to a different part of the body region.
*F (142, 2) = 51.42, $P < .05$ group B vs. groups A and C with Tamhane's T2 post hoc test.
†F (78,2) = 6.007, $P < .05$ group B vs. groups A and C with Tukey post hoc test.
‡F (142,2) = 21.32, $P < .05$ group B vs. groups A and C with Tukey post hoc test.
§F (142,2) = 12.89, $P < .05$ group A vs. groups B and C with Tukey post hoc test.
Abbreviations: ARCS, augmented renal clearance score; ARCTIC, augmented renal clearance in trauma intensive care score, SOFA, sequential organ failure assessment; C-G, cockcroft-gault mathematical estimates of creatinine clearance (mL/min/ 1.73m^2), APACHE, acute physiology and chronic health examination.

Table 4. Confirmed Augmented Renal Clearance in traumatic and non-traumatic patients

	Patients with Confirmed ARC[a] on Day Zero (n = 79)	
	Trauma Patients (n = 43)	Non-trauma Patients (n = 36)
Only High ARCS[b] Risk Score	34 (79%)	16 (44.4%)
Only High ARCTIC[c] Risk Score	2 (4.65%)	13 (36.11%)
Both High ARC and ARCTIC Risk Scores	7 (16.28%)	7 (19.44%)

[a]confirmed Augmented Renal Clearance (ARC) according to 12-hour urinary creatinine clearance (12h CrCl).
Abbreviations: ARCS, augmented renal clearance score; ARCTIC, augmented renal clearance in trauma intensive care.

was diagnosed in 88 patients (60.68%) during this period [51 patients in group A (57.95%), 20 in group B (22.72%), and 17 in group C (19.31%)]. Of the 88 patients, 79 patients (89.77%) had confirmed ARC on day 0 while 6 patients (6.82%) developed ARC on the third day and 3 patients (3.41%) between days 3 and 14 of the study. Only four patients had confirmed ARC on all five sampling days. The number of patients in each group and the percentage of patients with confirmed ARC on days 0, 3, 7, 10, and 14 are shown in Table 2.

Of the 145 included patients, 103 patients had high ARCS risk scores (groups A and C) and ARC phenomenon was confirmed in 64 of them (62.13%). Whereas this percentage was 39.19% (29 patients) among the 74 patients who had a high ARCTIC risk score.

Fifty-four patients out of 145 included patients who had been admitted to the ICU due to trauma (Table 1), 15 of whom had a high ARCTIC risk score (group B and C) and the ARC phenomenon was confirmed in 9 patients (60%), while this percentage was 83.67% among the 49 patients who had high ARCS risk score (41 patients).

The mean of ICULS was 9 days (5 to 18.5) in patients without ARC phenomenon and 10.5 days (6 to 21.75) in those with this phenomenon ($P > .05$).

Assessment of the Accuracy of Formulas

As reported in Table 5, the formulas significantly overestimated GFR in patients without the ARC phenomenon whereas in ARC positive group eGFR was significantly lower than 12-h CrCl. We detected a lower bias and higher precision for the C-G in ARC positive group (Table 5). Bland-Altman plots are shown in Figure 2.

The area under the ROC curve (AUC) of formulas used for eGFR was reported in Table 6. In the comparison of ROC curves of formulas, only the AUC of the C-G and CKD-EPI were above 0.5 to detect the ARC phenomenon with the cut-off of 100.48 mL/min/ 1.73m^2 (specificity of 49% and sensitivity of 83%) and 107.05 mL/min/ 1.73m^2 (specificity of 53% and sensitivity of 65%), respectively.

DISCUSSION

This study showed that out of 79 patients who had confirmed ARC on day 0, 64 patients were detected by using ARCS, and the ARCTIC scoring system was able to add 15 more cases (19%) to the pool

Table 5. Glomerular Filtration Rate (GFR) Based on Formulas and Measured by 12h CrCl

	Mean ± SD	Coefficient of Variation (%)	Bias (mL/min/ 1.73m^2)	Precision (mL/min/ 1.73m^2)
ARC Positive				
12h CrCl[a]	174.99 ± 43.81	25.04	-	-
C-G[b]	123.30 ± 28.12	22.80	53.67	43.38
MDRD[c]	114.19 ± 23.98	21	60.81	50.11
CKD-EPI[d]	110.77 ± 15.03	13.57	64.22	45.33
ARC Negative				
12h CrCl[a]	87.67 ± 28.26	32.23	-	-
C-G[b]	108.79 ± 33.19	30.51	-24.31	44.95
MDRD[c]	118.64 ± 40.76	34.36	-30.97	47.81
CKD-EPI[d]	107.42 ± 29.95	19.50	-19.75	32.09

[a]Creatinine Clearance of 12-hour urine collection (mL/min/ 1.73m^2)
[b]Cockcroft-Gault equation (mL/min/ 1.73m^2)
[c]Modification of Diet in Renal Disease equation (mL/min/ 1.73m^2)
[d]Chronic Kidney Disease Epidemiology Collaboration equation (mL/min/ 1.73m^2)

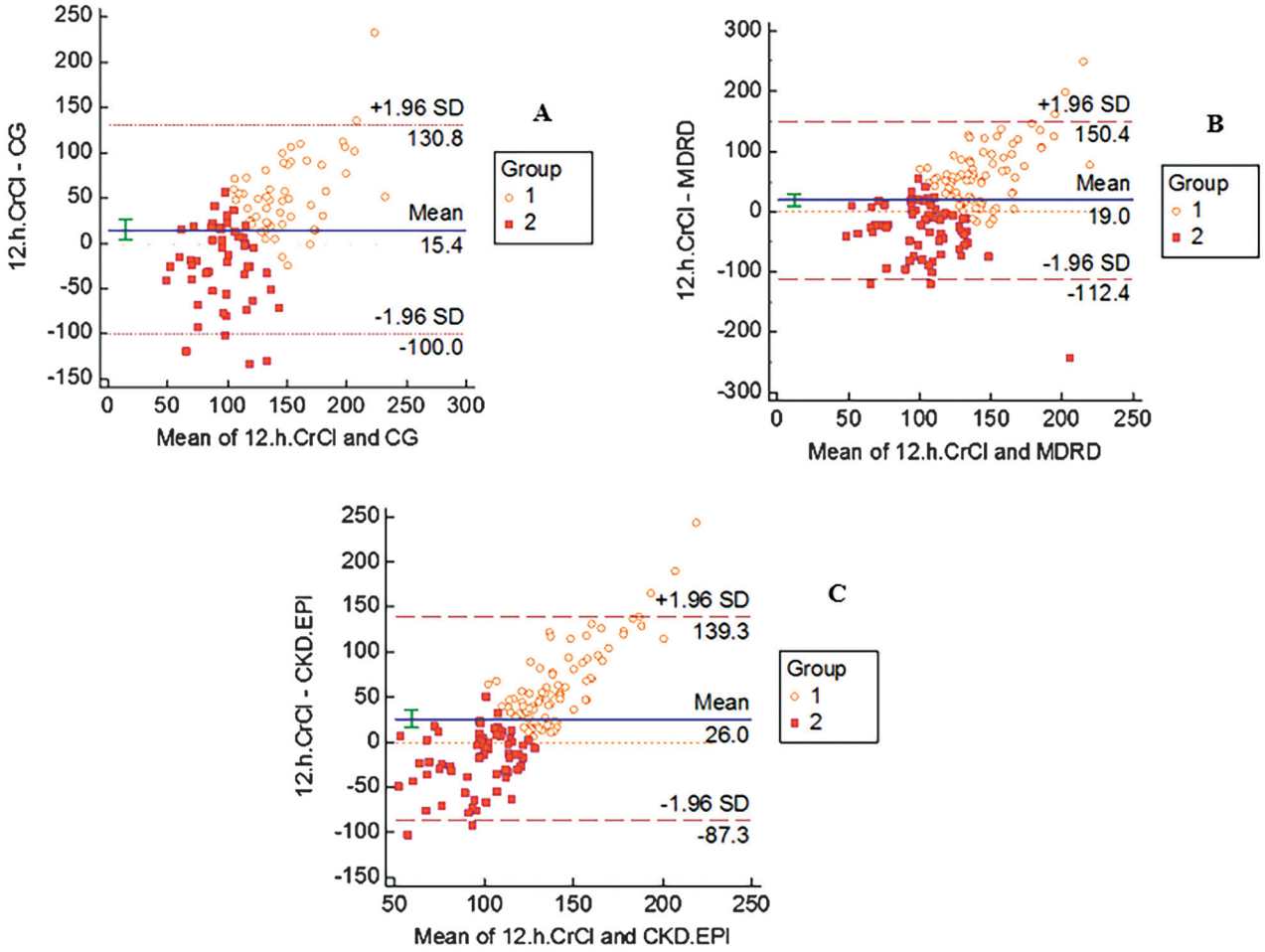

Figure 2. Bland and Altman Plots [Measures of agreement between the eGFR by formulas (A: Cockcroft-Gault equation (CG); B: Modification of Diet in Renal Disease equation (MDRD); C: Chronic Kidney Disease Epidemiology Collaboration equation (CKD-EPI)) and measured 12-h CrCl (Group 1: ARC positive, Group 2: ARC negative)].

Table 6. Accuracy of Formulas to Detect ARC

	AUC[a]	Cut-off	Sensitivity	Specificity
C-G[b]	0.65	≥ 100.48	0.83	0.49
MDRD[c]	0.48	≥ 90.65	0.84	0.30
CKD-EPI[d]	0.54	≥ 107.05	0.65	0.53

[a]Area Under Curve
[b]Cockcroft-Gault equation (mL/min/ 1.73m^2)
[c]Modification of Diet in Renal Disease equation (mL/min/ 1.73m^2)
[d]Chronic Kidney Disease Epidemiology Collaboration equation (mL/min/ 1.73m^2)

of patients with confirmed ARC. In other words, if we had used just ARCS to identify patients with confirmed ARC, almost 20% of the cases would have been missed. The ARCS is reported to have a sensitivity and specificity of 100% and 76%, in critically ill patients, respectively. The ARCTIC scoring system has been proposed as a screening tool to predict augmented renal clearance in trauma patients with a sensitivity of 84% and specificity of 68%.[4,6,7,9,21-23] Of the 43 patients who were admitted to the ICU due to trauma and had confirmed ARC on day 0, 9 patients were categorized as high-risk using ARCTIC and using ARCS found 34 more patients (79.07%) with confirmed ARC. In other words, if we had only used ARCTIC to identify trauma patients with confirmed ARC, almost 80% of the cases would have been missed.

Although the measurement of urinary CrCl is a more accurate and reproducible tool to estimate renal function and has been recommended in identifying

ARC in critical patients,[4,12,16,17,20] this is not a routinely done in all ICUs, especially in rural areas. Therefore, a number of physicians may use the scoring systems to predict the ARC phenomenon without confirming it by measuring urinary CrCl. Our study showed that from 145 patients who were identified as high-risk for developing ARC phenomenon according to scoring systems, ACR was not confirmed in 57 ones (39.31%). So, relying on only scoring systems may result in an over-diagnosis of the ARC phenomenon in 40% of the patients and might expose them to higher doses of mediations.

Some studies have reported that, ARC may remain for weeks, although the exact duration has not been defined.[4,13,28] In our study, 13 patients (16%) had augmented renal clearance after one week and 7 (8.8%) after 2 weeks.

It has been shown that the length of stay in ICU increases from 9 (5 to 18.5) days to 10.5 (6 to 21.75) days when ARC is present ($P > .05$). Studies also noted the importance of identification and diagnosis of ARC as a factor in clinical outcomes and ICULS. [14,15]

We found that none of the formulas used to estimate GFR, accurately detects the ARC phenomenon as good as 12h CrCl. Other studies also showed the poor concordance of eGFR with measured CrCl and emphasized that the accuracy of these equations was significantly lower in patients with ARC. According to the sensitivity and the specificity of the formulas, only the C-G formula, with a cut-off of 100.48 mL/min/ 1.73m^2, was slightly more accurate than the other formulas in critically ill patients. This finding is contrary to that of Ruiz *et al.* who showed that, in French critically ill patients with ARC, C-G, and CKD-EPI formulas were more accurate with a cut-off of 107.5 and 108.1 mL/min/ 1.73m^2, respectively.[11]

This is a single-center experience with relatively small sample size, highlighting the importance of using a proper scoring system in predicting ARC in ICU settings. One of the main limitations of our study was the lack of correct12-hour urine collection, which led to exclusion of a high percentage of our eligible patients. Considering the limitations of this study, a large-scale clinical trial is needed to confirm our findings.

CONCLUSION

Considering to the impact of the ARC phenomenon on the serum concentration of the drugs, where there is no access to measuring the drug levels in the ICU setting, using the ARC scoring system could be a useful method to predict the ARC phenomenon in critically ill patients. Our recommendation is to use both ARCS and ARCTIC scoring systems to identify all high-risk patients for developing the ARC phenomenon, and subsequently confirm the diagnosis with checking the urinary CrCl... Measurement of urinary CrCl is strongly recommended to prevent over-diagnosis of the ARC phenomenon in high-risk patients. None of the formulas used to estimate GFR accurately detect the ARC phenomenon as good as 12-h CrCl, except the C-G formula that was slightly more accurate than the others in critically ill patients with a cut-off of 100.48 mL/min/ 1.73m^2.

ACKNOWLEDGMENT

Funding Support

We did not receive any specific grant or funding for this research.

Conflict of Interests

All authors declare no potential conflicts of interest for this research.

Author Contributions

RT, MS, EP, and RH designed the study. Investigation and Drafting of the proposal were done by EP and RH. EP, RH, MK, MMM, SS, and SPS were involved in collecting data. RH and MS analyzed data. Data interpretation and writing original draft preparation were done by EP and RH. RT and MS reviewed and edited the preparation.

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Correspondence to:
Elham Pourheidar, PhD
Department of Clinical Pharmacy, Shahid Beheshti Medical University, Vali-e-Asr Ave, Niyayesh Junction, Tehran, Postal code: 1991953381, Iran
Tel: 0098 912 041 5025
Fax: 0098 21 8896 5097
E-mail: e.pourheidar@gmail.com
ORCID: 0000-0001-5410-5068

Received January 2022
Revised March 2022
Accepted May 2022