

Augmented Renal Clearance in Chinese Intensive Care Unit Patients After Traumatic Brain Injury: Identifying Estimate Glomerular Filtration Rate Cut-off Value as a Risk Factor

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Abstract

Background

Augmented renal clearance (ARC) is common in trauma patients and associated with subtherapeutic antimicrobial concentrations. China has more patients with traumatic brain injury (TBI) than most other countries in the world. However, there were no studies that focus on the ARC in Chinese TBI patients. In this study, we report the incidence of ARC in patients with TBI as well as risk factors for ARC. Besides, we evaluated the ability of four commonly used estimate glomerular filtration rate (eGFR) formulas and other covariates to predict the presence of ARC.

Methods

The prospective observational study was conducted in a 24-bed tertiary level, university-affiliated hospital, and 54 TBI patients with normal serum creatinine enrolled. We measured 24-h creatinine clearance after admission, and ARC defined as measured creatinine clearance ≥ 130 ml/min/1.73 m². Demographic variables were then compared, and multivariate analysis was performed. Receiver operating curve, bias, and precision analyses were conducted to examine eGFR and ARCTIC score accuracy in predicting ARC. Multiple logistic regression analysis was performed to estimate the risk factors contributing to ARC.

Results

The incidence of ARC was 50%. A moderate correlation was shown between measured Crcl and four eGFR (r_s/r was 0.590, 0.499, 0.404, and 0.518, respectively). All of the equations significantly underestimated the measured Crcl, especially in the ARC group. Neither had excellent precision for clinical application in this setting. ARCTIC score can't accurately distinguish ARC either. Multivariable analysis displayed that four factors independently correlated to ARC: male, larger BMI, lower serum creatinine, and without a history of hypertension. Further investigation found eGFR higher than the threshold, without a history of hypertension, and/or bigger BMI were independent risk factors for ARC, and they had good accuracy in predicting the occurrence of ARC.

Conclusions

ARC was frequently observed in Chinese TBI patients. The estimated methods of GFR and ARCTIC score inaccurate and couldn't be directly used as a screening tool to identify ARC in Chinese TBI patients. But if we take the cut-off values of different formulas into account, the estimated GFR could be used as a decisive risk factor in helping to screen the ARC.

Background

The incidence of ARC(Augmented renal clearance) has been reported to range from 14–85%[1], depending on the population studied and the cut-off values used for its definition. As to most patients,

the occurrence of ARC on the first day of ICU admission may predict continued creatinine clearance (CrCl) elevation for one day to several weeks[1, 2].

The occurrence of ARC has a very substantial effect on β -lactam antibiotics PK/PD. Patients with ARC more likely to have very low β -lactam trough concentrations and the reduced probability of reaching the PK/PD target value at the conventional dosage compared with patients without ARC[2-5]. Treatment failure or worse outcome was more frequent in ARC patients, and ARC was significantly associated with recurrent infections[6, 7]. Besides, in logically, ARC is likely to promote the emergence of resistance by incompletely treating infection due to lower serum levels.

It has been reported that the incidence of ARC in traumatic brain injury (TBI) patients as high as 85%[8]. As stated, the rate of nosocomial infections after TBI was 33.3%[9]. And those cleared by the kidney, like beta-lactam antibiotics, were frequently used as anti-infection therapy drugs. Whether the anti-infection therapy successful is one of the critical factors that influence the prognosis of the patient. China has more patients with TBI than most other countries in the world, making this condition a significant public health concern[10]. Unfortunately, the occurrence of ARC in TBI patients didn't get the deserved attention of the Chinese medical staff. As a result, there have been no studies on ARC in patients after TBI in China, and the incidence and risk factors are unknown, not mention to adjust the dosage of the anti-infection drug after ARC. Therefore, it is of great significance to explore the prevalence and risk factors of ARC in Chinese TBI patients.

Until now, although direct measurement of the glomerular filtration rate (GFR) with exogenous substances such as inulin is the gold standard for the assessment of renal function, it is not routinely performed in intensive care units for practical reasons. Instead, one could measure the CrCl from a 24 or 8-h urine collection, which can be realized in ICU but would cost much labor. So a replacement method is using the estimated GFR or identifies the risk factors to screen the ARC patient. In Chinese clinical practice, the GFR is most commonly estimated from the serum creatinine (SCr), using various formulas including Cockcroft-Gault, Modified Chinese MDRD Study equation(CMDRD), and the Chronic Kidney Disease Epidemiology Collaboration for Asian people (CKD-EPI-Asian) and Japanese eGRF equation[11].

In the year 2016, Barletta et al. [12] constructed a scoring system, Augmented Renal Clearance in Trauma Intensive Care scoring system(ARCTIC), which was specifically used to predict the ARC in American trauma patients. Whether this scoring system can be applied to Chinese TBI patients is not yet known.

Thus, the primary aim of the study was to explore the incidence of ARC after traumatic brain injury in Chinese patients, meanwhile to assess the accuracy of 4 commonly used formulas and the ARCTIC scoring system in identifying ARC with normal SCr levels. The secondary aim was to determine risk factors for ARC.

Methods

Setting

This prospective, single-center, observational study was conducted in a 24-bed intensive care unit of the First Hospital of Lanzhou University, a tertiary teaching hospital in Gansu Province, China, from January 2019 to November 2019. This study was approved by the institutional ethics committee (LDYYLL2018-153), and informed consent was obtained from all participants or a surrogate decision-maker.

Study Population

Patients with no evidence of renal impairment (admission SCr > 113 $\mu\text{mol/L}$), no history of renal replacement therapy, and $18 \leq \text{age} \leq 65$ were enrolled. The exclusion criteria for study admission were as follows: age < 18 years, pregnancy, suspicion of rhabdomyolysis, and developing AKI during the treatment (2012 KDIGO Clinical Practical Guideline for Acute Kidney Injury).

Data Collection And Definition

As soon as the patient met the inclusion criteria, 24-hour urine samples and a blood sample were collected for creatinine clearance calculation. Measured CrCl was then calculated using the standard formula: $\text{CrCl} = (\text{UCr} \times \text{UV}) / (\text{SCr} \times 1440)$, where UCr (urine creatinine concentration) and SCr were expressed in $\mu\text{mol/l}$ and UV corresponded to the volume of urine in mL. At the same time, the estimated glomerular filtration rate was calculated using different formulas. We calculated eGFR by using following equations:

Cockcroft–Gault equation (CG) [13]:

Males, $\text{eGFR}(\text{ml}/\text{min}) = (140 - \text{age}) \times \text{Weight} / 72 \times \text{SCr}$

Females, $\text{eGFR}(\text{ml}/\text{min}) = (140 - \text{age}) \times \text{Weight} / 72 \times \text{SCr} \times 0.85$

Modified Chinese Modification of Diet in Renal Disease Study equation (CMDRD) [14]:

Males, $\text{eGFR}(\text{ml}/\text{min}) = 186 \times \text{SCr}^{-1.154} \times \text{age}^{-0.203} \times 1.233$

Females, $\text{eGFR}(\text{ml}/\text{min}) = 186 \times \text{SCr}^{-1.154} \times \text{age}^{-0.203} \times 1.233 \times 0.742$

Chronic Kidney Disease Epidemiology Collaboration equation for Asian people [CKD-EPI-Asian] [15, 16]:

Males, $\text{SCr} \leq 80$, $\text{eGFR}(\text{mL}/\text{min}) = 141 \times (\text{SCr}/0.9)^{-0.411} \times 0.993^{\text{age}} \times 1.057$

Males, $\text{SCr} > 80$, $\text{eGFR}(\text{mL}/\text{min}) = 141 \times (\text{SCr}/0.9)^{-1.209} \times 0.993^{\text{age}} \times 1.057$

Females, $\text{SCr} \leq 62$, $\text{eGFR}(\text{mL}/\text{min}) = 144 \times (\text{SCr}/0.7)^{-0.329} \times 0.993^{\text{age}} \times 1.049$

Females, $\text{SCr} > 62$, $\text{eGFR}(\text{mL}/\text{min}) = 144 \times (\text{SCr}/0.7)^{-1.209} \times 0.993^{\text{age}} \times 1.049$

The Japanese eGFR equation (J-eGFR) [17]

For males: $eGFR \text{ (mL/min)} = 194 \times SCr^{-1.094} \times age^{-0.287}$

For females: $eGFR \text{ (mL/min)} = 194 \times SCr^{-1.094} \times age^{-0.287} \times 0.739$

We calculated body surface area by using following equations[18]:

Males, $BSA = 0.0057 \times Height + 0.0121 \times Weight + 0.0882$

Femals, $BSA = 0.0073 \times Height + 0.0127 \times Weight - 0.2106$

Patient characteristics, clinical features were extracted from medical records. Medical history of high blood pressure(hereinafter referred to as HBP), Acute Physiology And Chronic Health Evaluation (APACHE) II, Glasgow coma scale(GCS) score on the admission-day were calculated from the charts. Data collection began immediately after obtaining informed consent. It was discontinued for death, development of severe renal impairment (measured Crcl < 30 mL/min), initiation of renal replacement therapy, and patient consent withdrawal. ARC was defined as a 24-h Crcl \geq 130 mL/min.

Statistical Analysis

Data that were normally distributed were presented as the means and SDs, and differences between groups were assessed using Student t-tests. Data that were not normally distributed were presented as medians with interquartile ranges, and differences between groups were compared using Mann-Whitney U tests. Categorical variables were presented as numbers with percentages and were analyzed using the χ^2 test or Fisher exact tests. Input and a forward conditional logistic regression model was developed to describe risk factors for ARC in multivariate analysis. To evaluate the relationships between eGFR, which was calculated by different equations, and 24 h creatinine clearance, a receiver operating characteristic curve(ROC) was constructed. The area under the curve and Youden index were also computed to identify the best cut-off value. All statistical analyses were performed using IBM-SPSS (version 26.0) and MedCalc (version 12.7.0.0) statistical software, and differences were considered statistically significant at $P < 0.05$ (2 sided).

The bias and the precision of different formulas compared with the measured CrCl were evaluated according to Sheiner et[19] by the following equations:

$$\text{Bias} = \frac{1}{N} \sum_{i=1}^N (Crcl_{estimated} - Crcl)$$

$$\text{Precision} = \sqrt{\frac{1}{N} \sum_{i=1}^N (Crcl_{estimated} - Crcl)^2}$$

Residual plots analyzed the agreement between the individual eGFRs by the CG, CMDRD, CKD-EPI-Asian, Japanese eGFR equation, and the measured CrCl according to the method of Bland and Altman[20]. The odds ratio (OR) and 95 % confidence intervals (CI) were calculated.

Results

Baselines Characteristics of Study Subjects

The characteristics of the enrolled patients are shown in Table 1. We enrolled 54 patients in this study (median age, 50 years [IQR,40.8-56.5], 63.0% male). Of these, 27 patients (50%) manifesting ARC. ARC occurred less frequently in patients with HBP (3/16, 5.6%) in comparison with the overall incidence of 50% (27/54). The ARC group manifests the lower serum creatinine clearance 56 [IQR, 48.0-66.0] comparison with the patient without ARC 65 [IQR, 58.0-76.0]. The mean 24-h CrCl of patients with ARC was significantly higher : 175.13 ml/min/1.73 m² vs 101.35 ml/min/1.73 m² in patients without ARC (p=0.001).

Accuracy of eGFR and ARCTIC Score system

The eGFR of patients with ARC was significantly higher than that of patients without ARC (p < 0.001) (Fig. 1A, B, D) except the one calculated by CKD-EPI-Asian formula. Analysis to determine the correlation between ARC and eGFR revealed that a moderate correlation was found between measured CrCl and four calculated eGFR, with a Pearson(r)/Spearman coefficient (r_s) of 0.590, 0.499, 0.404 and 0.518 respectively (p<0.01) (Fig.2 A-D).

In the ARC subgroup, each formula underestimated CrCl (Additional eTable 1). For all four methods, a more significant bias and a lower precision were observed in the ARC group (Additional eTable 1).

We also test the ARCTIC score, a predictive model used for screen ARC among the trauma patient. The results showed that a weak positive correlation of 0.269 (p<0.01) between CrCl and ARCTIC scores. The sensitivity of the scoring system as high as 88.9%, but the specificity only 29.6% (Additional eTable 2).

Tools To Screen ARC

The following variables were significantly different between patients with and without ARC: serum creatinine (56.0 vs 65.0, p=0.05), HBP rate (3% vs 13%, p=0.01). Although age, weight, BMI, and BSA showed no difference between the two groups, they were closed to substantial (The p-Value below or close to 0.1). Multiple logistic regression analysis was performed for five variables (Age, Gender, BMI, SCr, HBP). And the result showed that males, BMI, SCr, and without HBP were independent risk factors for ARC (OR, 8.6, 1.3, 0.9, 0.1; 95 % CI, 1.2-62.8, 1.1-1.7, 0.9-1.0, 0.0-0.4, respectively) (Additional eTable 3). The results demonstrate male patient does not has HBP, has a lower serum creatinine, and greater BMI may

have higher risk suffer from ARC. We performed the ROC analysis to evaluate the predictive value of eGFR and ARCTIC score for ARC. The AUROC of eGFR calculated by CG, CMDRD, CKD-EPI-Asian, J-eGFR, and ARCTIC score were 0.77(95 % CI, 0.65-0.90), 0.71(95 % CI, 0.57-0.85), 0.63(95 % CI, 0.47-0.78), 0.70(95 % CI, 0.56-0.84), and 0.59(95 % CI, 0.44-0.75) respectively. The optimal cutoff value of each eGFR and the ARCTIC for ARC was 95.69(sensitivity, 88.9 %; specificity, 59.3 %), 123.70(sensitivity, 81.5 %; specificity, 55.6 %), 94.30(sensitivity, 96.3 %; specificity, 40.7 %), 69.31(sensitivity, 96.3 %; specificity, 44.4 %), and 5.5(sensitivity, 88.9 %; specificity, 29.6 %) (Additional eTable 2). The CG, J-eGFR formula had the highest positive (68.59%) and negative (92.31%) predictive value, respectively. As ROC analysis results showed (Additional eTable 2), only the CG formula presented AUC above 0.75 to detect an ARC, with a cut-off value of 95.69 ml/min/1.73 m². Comparison of ROC curves of the four estimated formulas show no difference between CG, CMDRD, and Japanese eGFR AUCs (Fig. 4), but revealed a significant difference between AUC of CG and CKD-EPI-Asian ($p < 0.05$).

We further tested logistic regression models with significant covariates, in particular, including the cut-off values of ARC detection by four different equations (Table 2).

When including the cut-off values of four eGFR and other risk factors, like BMI, HBP, to a new model, both more accurate than the formula itself alone to predict the ARC. All the Nagelkerke R² above 0.45 and indicated a good fit of the model (Additional eTable 4). They all had good sensitivity, specificity, PPV, and NPV, especially the specificity, improved dramatically (Additional eTable 4).

Discussion

To the best of our knowledge, this is the first study that investigated ARC in China adult patients after TBI. Approximately 50 % of patients suffered TBI with normal SCr levels in the early two days of ICU admission manifested ARC. The eGFR in this report, which was calculated by using CG or CMDRD or Japanese eGFR equation, was significantly different between patients with and without ARC. There was a moderate correlation between the measured Crcl and four calculated GFR, and a weak correlation between Crcl and ARCTIC score. However, unfortunately, we found that none of the four eGFR formulas or ARCTIC score can accurately predict the occurrence of augmented renal clearance in those with normal serum creatinine. Because all equations tended to underestimate the Crcl at high creatinine clearance (Additional eTable 1), so directly using eGFR to identify ARC is not advised. Still, eGFR above the optimal cut-off values as a significant risk factor is strongly recommended to helping identify the ARC.

Until recently, ARC has extensively been studied in general and specific ICU populations, like patients with trauma, burns, traumatic brain injury, polytrauma, sepsis, ventilator-associated pneumonia, or hematological malignancy[3]. In the previous studies[8, 21], the researchers regarding 8 h Crcl above 130 ml/min/1.73 m² as the threshold. In our study, we used a cut-off value for 24 h CrCl of 130 mL/min or greater per 1.73 m² to define ARC. Our results corroborate the data in other literature, reporting ARC prevalence between 14% and 85%[1].

Historically, attention was mostly paid to the decline of renal function and the corresponding necessity of dose adjustments for drugs cleared by the kidney. Recently, the clinical importance of ARC is gradually realized by medical workers, which can be confirmed by the fact that some studies found ARC could affect the pharmacokinetics of many frequently prescribed medications, especially those mainly renally cleared antibacterials. And a number of studies have shown that ARC is a risk factor for not attaining targeted PK/PD targets of antibiotics, thereby causing a potential consequence of therapeutic failure [2, 4, 5] and recurrent infections of the patients[7]. Specifically, these findings remind the clinician that a 'one size fits all' approach to drug dosing in critical illness is flawed and requires adjustment for some variables, least of which is the diagnostic category. Nevertheless, antimicrobial efficacy is not readily clinically evaluable, making underdosing substantially less visible. Thus, an appropriate assessment of renal function is compulsory for identifying patients displaying ARC[7, 11].

Unfortunately, as measuring 24 h urinary CrCl is labor-intensive, as it is not routinely performed in ICU patients. Hence, we tested the identification ability of the ARC of 4 popularly used mathematical equations by the Chinese physician, but none of them can show acceptable sensitivity and specificity. Consider to pathophysiological changes of the traumatic brain injury patients and eGFR formulas that were primarily designed for those non-critically ill patients; the result was not a surprise. In the previous study, ARCTIC was constructed by Jeffrey F. Barletta[12] as a useful tool to help identify the ARC in trauma people, which showed an excellent predictive ability. However, our results demonstrated that the ARCTIC score was not accurate when used to identify ARC in Chinese TBI patients. This finding is most likely due to the different injury mechanisms and ethnicities of patients included in the study.

In the absence of measured CrCl in critically ill patients in daily routine practice and as frequently used eGFR formulas fail to assess renal function, especially for increased renal clearance, evaluating actual kidney function is difficult in this population[22]. Therefore, the identification of predictors for ARC can help the clinicians in recognizing ARC.

Characteristics of ARC patients, like younger age, male sex, bigger BSA, polytrauma, et al., have been extensively described in ICU patients[1, 23]. In this study, we found that male sex, higher BMI, lower serum creatinine, and without a history of HBP were independent risk factors for ARC. When taking the cut-off values of the different formulas into account, the eGFR above the threshold, without HBP, and/or combine with bigger BMI, could be used to identify the ARC more precisely than eGRF alone. The patients with a history of HBP didn't show ARC could be explained by the fact that the HBP does harm to the kidney, and which reduced the GFR and renal tubule excretion. But due to the limited HBP patient number in our study, the results should be interpreted carefully. As to gender, our research found that male patients had a very high risk(OR:8.6[1.2-62.8]) suffer ARC, which was consistent with the found of Claus et al. [6]. But there were also contrary findings, Udy et al. [24]and Minville et al. [25] demonstrated that gender was not a significant covariate predicting ARC. We also found that a bigger BMI was an independent risk factor for ARC, which was exactly contrary to the result of Grootaert et al.[26]. The possible reason for this result is that a considerable portion of the patients included in our study is construction workers. Therefore, high BMI doesn't mean that these patients are obese, but high muscle content and good kidney preserve.

In contrast, the age of patients has been confirmed by other researchers closely related to the occurrence of ARC in critically ill[23, 27]. Still, it did not differ significantly between our ARC versus the non-ARC group. The main reason maybe was the patients in our study were older.

This study has some limitations. First, this was a single-center study with a limited number of cases. Second, the gold standard for the assessment of renal function is by use of an exogenous marker such as inulin or radioisotopes, which undergoing only glomerular filtration without tubular secretion, was not performed in this study, so it is impossible to assess the actual GFR. Therefore, further studies are needed to address the limitations of this study.

Conclusions

ARC is frequently observed in Chinese traumatic brain injury patients. The estimated methods of eGFR inaccurate and couldn't be directly used as a screening tool to identify high CrCl, as is the ARCTIC score. Still, if we treat the cut-off values of eGFR as a risk factor and combine with other characteristics, like lager BMI, and without HBP, it could be used as a helpful tool to screen the patients with ARC.

Abbreviations

IQR: Interquartile range; SD: standard deviation; OR: Odds ratio; 95% CI: Confidence interval; ARC: Augmented renal clearance; TBI: traumatic brain injury ; eGFR: estimate glomerular filtration rate; ARCTIC: Augmented Renal Clearance in Trauma Intensive Care; Crcl: creatinine clearance; SCr: serum creatinine; HBP: Medical history of high blood pressure; CMDRD: Modified Chinese MDRD Study equation; CKD-EPI-Asian: Chronic Kidney Disease Epidemiology Collaboration for Asian people; J-eGFR: Japanese stimatate glomerular filtration rate; AKI: Acute Kidney Injury; CG: Cockcroft–Gault; APACHE II: Acute Physiology And Chronic Health Evaluation II; GCS: Glasgow coma scale; ROC: receiver operating characteristic curve; PPV positive predictive value, NPV negative predictive value;

Declarations

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Authors' contributions

ZLD, HG, and XAW contribute to the literature search, study design, data collection, data analysis, data interpretation, and writing. BL, MHZ, JL, and YHWcontributed to the literature search, study design, data analysis, data interpretation, critical revision, and rewriting of the manuscript. HYQ, ZMD, LZ, LZ, YQC, and

FJL contributed to the critical review and rewriting of the paper. XAW directed the study team. All authors approved the final article.

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Availability of data and materials

Please contact the authors for data requests.

Ethics approval and consent to participate

The institutional ethics committee of The First Hospital of Lanzhou University approved this study (LDYYLL2018-153), and informed consent was obtained from all participants or a surrogate decision-maker.

Consent for publication

N/A

Competing interests

The authors declare that they have no competing interests.

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Tables

Table 1 Demographic and laboratory data

Variable	All Patients(n=54)	Patients with ARC(n=27)	Patients without ARC(n=27)	p Value
Age, median(IQR)	50.0(40.8-56.5)	49.0(33.0-54.0)	51.0(43.0-60.0)	0.174
Male, n(%)	34(63.0)	18(33.3)	16(29.6)	0.573
Height(m), mean(SD)	1.69(0.08)	1.7(0.08)	1.68(0.08)	0.613
Weight(Kg), median(IQR)	65.0(60.0-75.0)	70.0(60.0-76.0)	62.0(60.0-70.0)	0.051
Body mass index(kg/m ²), mean(SD)	23.83(3.85)	24.68(3.89)	22.97(3.68)	0.103
Body surface area(m ²), median(IQR)	1.83(1.76-1.98)	1.9(1.8-2.0)	1.8(1.7-1.9)	0.073
Serum albumin (g/L), mean(SD)	38.6(6)	38.4(6.4)	38.75(5.63)	0.816
Hemoglobin(g/L), mean (SD)	130.4(23.4)	130(20.4)	130.7(26.4)	0.913
Serum Creatinine(μmol/L), median(IQR)	61.5(52.8-72.8)	56.0(48.0-66.0)	65.0(58.0-76.0)	0.05
Fluid balance(ml), mean(SD)	557(1166)	638(1130)	476(1216)	0.613
Mean urine output (ml/kg/h), median(IQR)	1.4(1.0-2.0)	1.4(1.1-1.9)	1.4(1.0-2.2)	0.710
24h Crcl(ml/min/1.73 m ²), mean(SD)	138.24(44.07)	175.13(28.73)	101.35(17.56)	0.001
PMH—High blood pressure, n(%)	16(29.6)	3(5.6)	13(24.1)	0.01
APACHE II, mean(SD)	14(4)	14(4)	14(5)	0.900
First record GCS score, median(IQR)	8(6-11)	8(6-12)	8(6-11)	0.910
Extradural hematoma, n(%)	12(22.2)	4(7.4)	8(14.8)	0.327
Subdural hematoma, n(%)	29(53.7)	15(27.8)	14(25.9)	0.785
Traumatic subarachnoid hemorrhage, n(%)	51(94.4)	27(50.0)	24(44.4)	0.075
Base of skull fracture, n(%)	11(20.4)	6(11.1)	5(9.3)	0.735
Extracranial trauma, n(%)	13(24.1)	6(11.1)	7(13.0)	0.750

PMH, past medical history.

Table 2 Logistic regression for measured creatinine clearance greater than 130 ml/min/1.73 m²

ARC	B	p Value	Odd ratio(IC 95 %)
(A) Taking into account CG equation			
High blood pressure	-2.02	0.012	0.13(0.03-0.65)
ARC detection by CG(\approx 95.69 ml/min/1.73 m ²)	2.46	0.002	11.72(2.56-53.63)
(B) Taking into account CMDRD equation			
BMI	0.34	0.005	1.40(1.10-1.78)
High blood pressure	-2.92	0.002	0.05(0.01-0.35)
ARC detection by CMDRD(\approx 123.70 ml/min/1.73 m ²)	2.51	0.004	12.27(2.20-68.63)
(C) Taking into account CKD-EPI-Asian equation			
BMI	0.28	0.010	1.32(1.07-1.64)
High blood pressure	-2.38	0.010	0.09(0.02-0.56)
ARC detection by CKD-EPI-Asian (\approx 94.30 ml/min/1.73 m ²)	3.06	0.010	21.43(2.08-220.37)
(D) Taking into account Japanese equation			
BMI	0.32	0.007	1.37(1.09-1.73)
High blood pressure	-2.08	0.020	0.13(0.02-0.72)
ARC detection by J-eGFR (\approx 69.31 ml/min/1.73 m ²)	3.45	0.008	31.45(2.51-393.96)

Figures

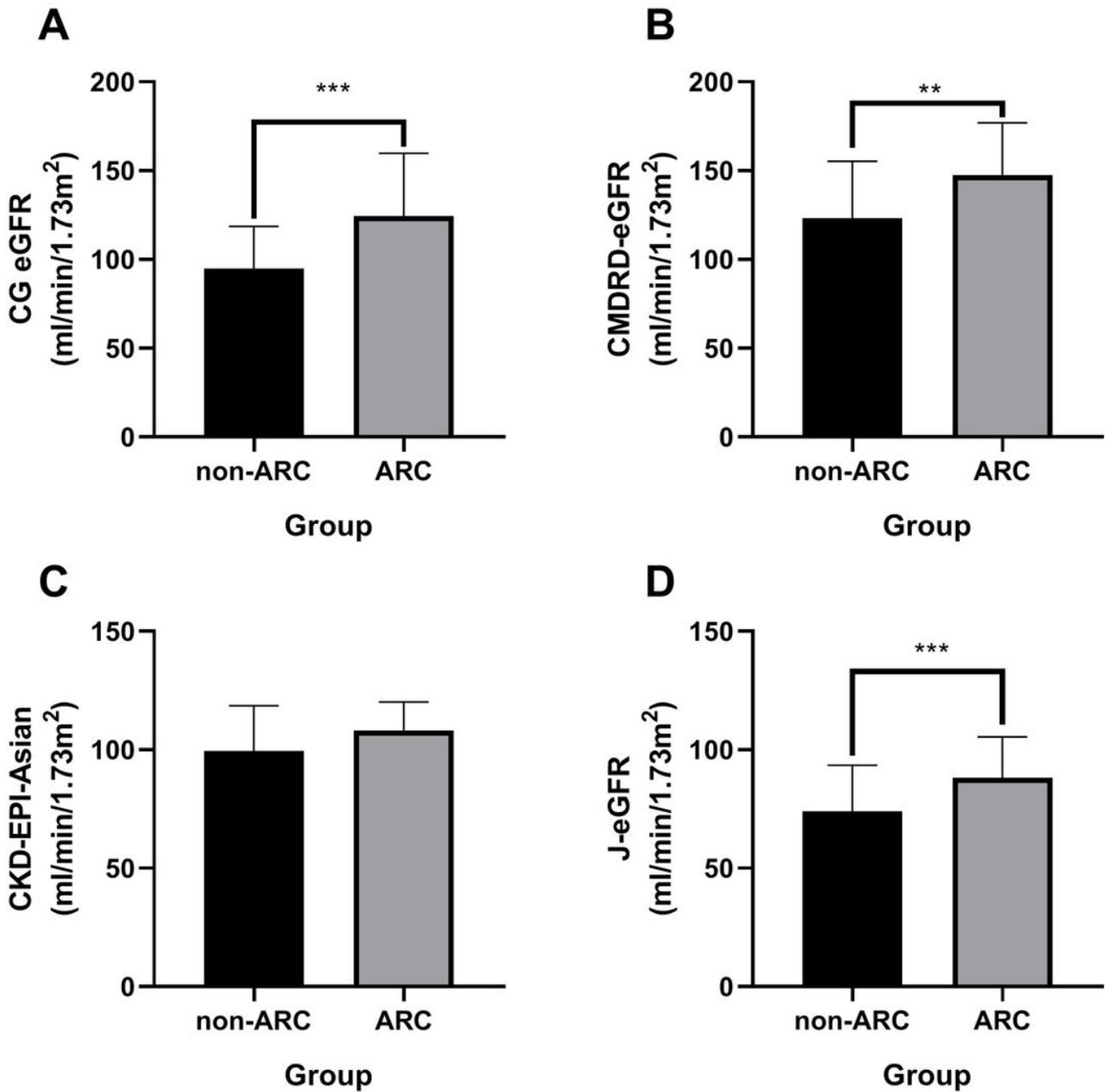


Figure 1

Comparison of the eGFR in patients with and without augmented renal clearance (ARC). The eGFR calculated by CG and CMDRD and Japanese eGFR formula in patients with ARC was significantly higher than that in patients without ARC (***) p < 0.001, ** p < 0.01).

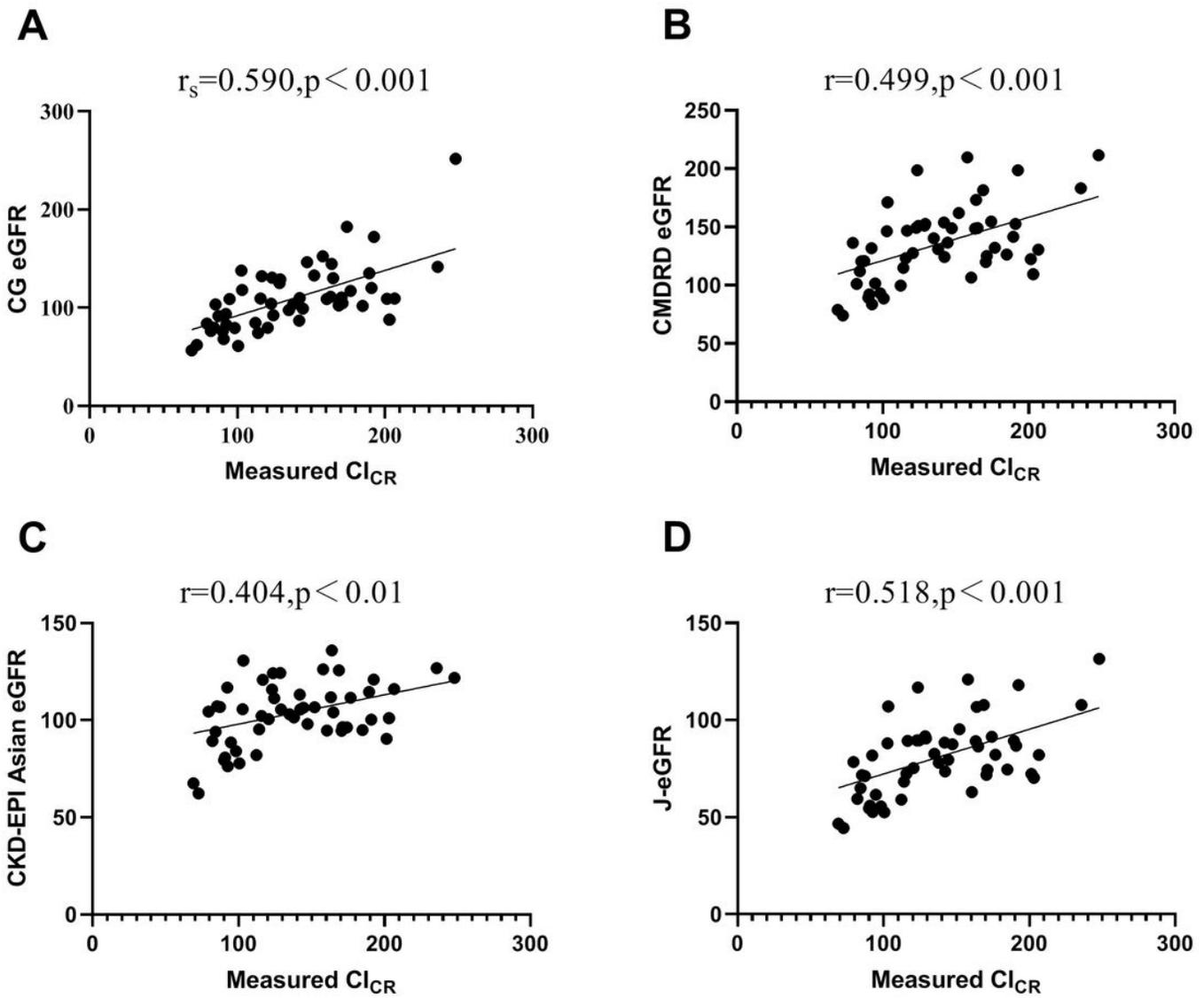


Figure 2

Correlation between the measured 24 h creatinine clearance (Crcl) and eGFR. A moderate correlation was found between measured Crcl and eGFR.

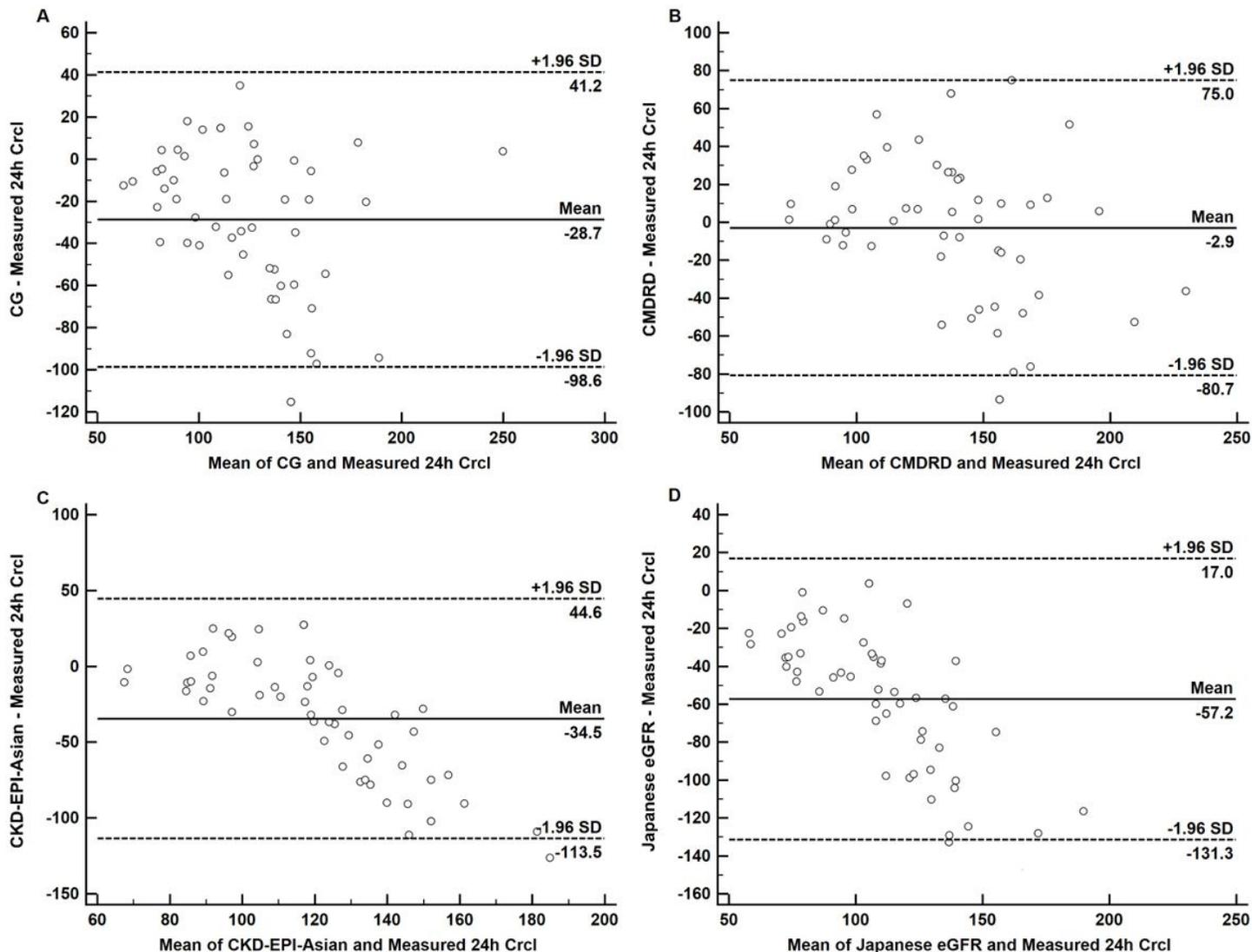


Figure 3

Measures of agreement between the measured 24 h CrCl and eGFR. The solid line indicated the mean of the difference between the results of the eGFR and measured 24 h CrCl. The dashed line shows the 95 % limits of agreement and almost all of eGFR located in the 95 % limits of agreement.

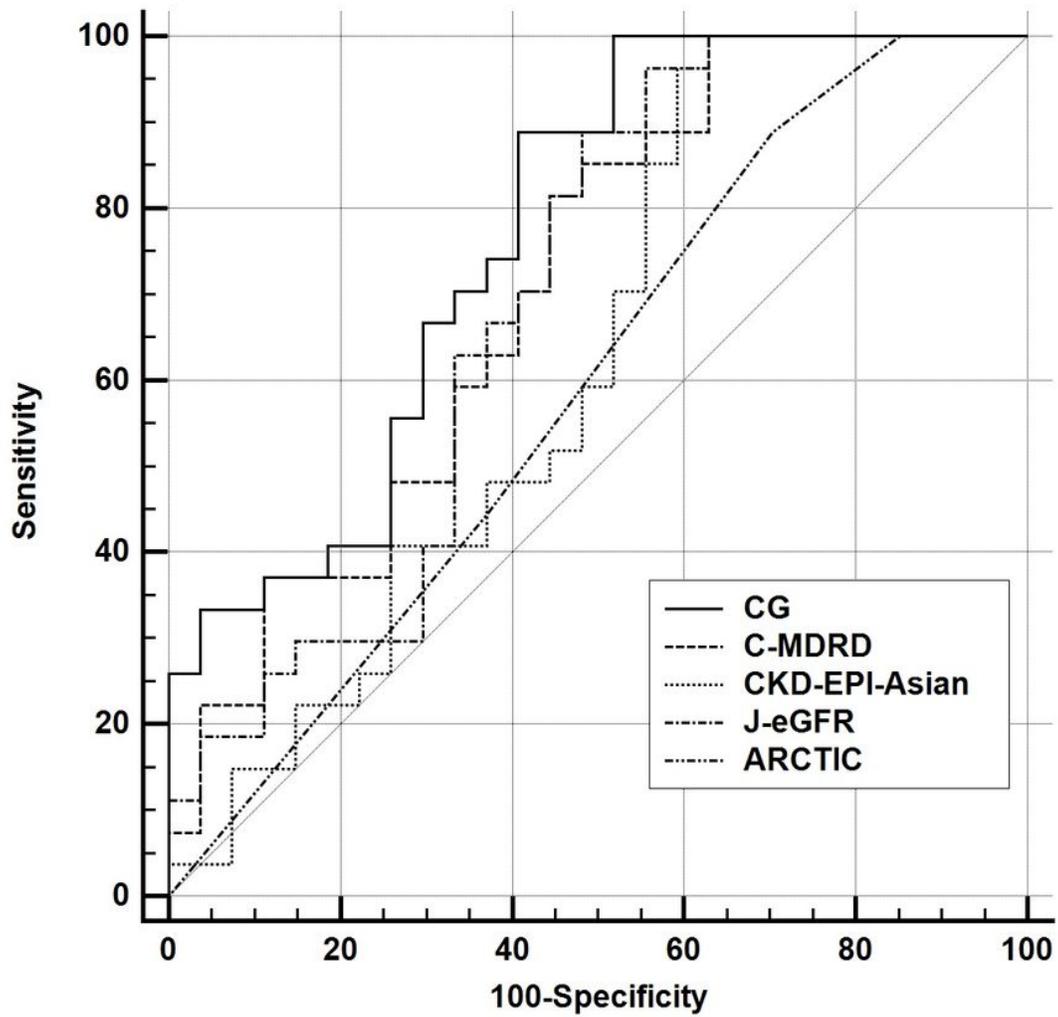


Figure 4

Comparison of ROC curves of four estimated GFR formulas and ARCTIC to detect ARC.

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