



Therapeutic Outcomes Associated with Augmented Renal Clearance in Trauma Patients of the ICU at UGM Academic Hospital

Annafi¹ Nanda Rohmah Utami¹, *Ika Puspitasari^{2,3} and Tri Murti Andayani²

¹Master of Clinical Pharmacy, Faculty of Pharmacy, Universitas Gadjah Mada

²Department of Pharmacology and Clinical Pharmacy, Faculty of Pharmacy, Universitas Gadjah Mada

³Academic Hospital, Universitas Gadjah Mada

*Corresponding Author: ika_tunggul@ugm.ac.id

Submitted: May 2025

Reviewed: October 2025

Published: March 2026

Abstract

Background: Augmented Renal Clearance (ARC) occurs in intensive care units (ICUs) and results in increased drug clearance in critically ill patients. Trauma patients have a twofold higher risk of ARC. ARC can increase the risk of subtherapeutic drug dosing and therapeutic failure. This study aims to determine the characteristics of trauma patients with and without ARC and to investigate the association between ARC and therapeutic outcomes, including length of stay and clinical outcomes, in trauma patients admitted to the ICU at UGM Academic Hospital.

Method: This study is an analytical observational study with a retrospective cohort design. The population in this study consists of adult patients diagnosed with trauma in the ICU at UGM Academic Hospital during the period from January 2021 - April 2024 who met the inclusion and exclusion criteria. Descriptive analysis was used to examine the characteristics of trauma patients in the ICU, with results presented in tables as percentages and mean values. An independent t-test was used to determine the difference in length of stay (LOS) between patients with and without ARC. The Chi-Square test was conducted to assess the association between ARC and clinical outcomes.

Result: The study population comprised 35 trauma patients in the ARC group and 49 in the non-ARC group. Both groups were predominantly male, with the mean age of trauma patients with ARC being younger (34.49 ± 13.38 years). ARC was characterised by lower serum creatinine levels and higher creatinine clearance. Trauma patients with ARC had a higher mean APACHE II score (9.69 ± 6.88) but a lower mean CCI score (0.54 ± 0.74). Trauma patients with ARC showed lower mean initial and final GCS scores (11.23 ± 4.12 and 11.63 ± 5.12 , respectively). The mean leukocyte count in the ARC group was higher ($16.57 \pm 6.45 \times 10^3/\mu\text{L}$), and the group had a higher infection rate (51.4%, $n = 18$). The mean LOS for trauma patients with ARC was longer (11.77 ± 15.35 days), but did not differ significantly from that of patients without ARC ($p = 0.055$). The number of trauma patients with ARC who did not show clinical improvement was significantly higher (28.6%, $n = 10$; $p = 0.005$).

Conclusion: The mean LOS of trauma patients with ARC is longer, showing a tendency towards significance. ARC is associated with worse clinical outcomes in trauma patients in the ICU, as demonstrated by poor clinical outcomes in 10 patients.

Keywords: Augmented renal clearance, clinical outcome, length of stay, trauma patients

1. INTRODUCTION

ARC is a manifestation of increased renal function in critically ill patients. It is defined as an

elevated creatinine clearance exceeding $130 \text{ mL/min/1.73 m}^2$ (1). The pathophysiological mechanism of ARC relates to systemic

inflammatory response syndrome (SIRS). Potential causes of SIRS associated with ARC include trauma, burns, autoimmune disorders, pancreatitis, sepsis, and surgery. SIRS is triggered by relative cellular dysoxia and by the release of endogenous cytokines and inflammatory mediators. These mediators can substantially increase cardiac output. Since renal blood flow correlates with cardiac output, a high-output state increases renal blood flow (2,3). In addition, ARC is associated with younger age, male gender, lower serum creatinine, and trauma conditions (4–7). Notably, trauma on admission has been reported as an independent risk factor for ARC in the ICU, doubling the risk (8).

Trauma is a global concern, contributing to millions of deaths and disabilities. Literature shows that the prevalence of trauma patients admitted to intensive care units (ICUs) is 46.9%. The mortality rate in developed countries ranges from 3.7% to 28.2% (9). Against this backdrop, ARC is common in critically ill patients with severe trauma, posing a risk of subtherapeutic dosing of drugs, electrolytes, and kidney-excreted nutrients. Furthermore, in critically ill patients with infections, ARC can result in low serum concentrations of renally eliminated antibiotics. This can lead to therapeutic failure, recurrent infection, and antibiotic resistance (10). Several studies have demonstrated that ARC is associated with more therapeutic failure, longer stays, and higher mortality in critically ill patients (11,12).

ARC remains a clinical condition that is often underrecognized, and management strategies are still being developed. Given the increasing mortality caused by trauma, analysing the relationship between ARC and clinical outcomes in trauma patients is necessary to raise awareness among healthcare professionals, particularly clinical pharmacists, to select the most appropriate therapy tailored to the patient's condition. Clinical pharmacists play a crucial role in optimising drug dosing in trauma patients experiencing ARC by considering the drug characteristics and pharmacokinetic changes associated with ARC (6).

2. MATERIALS AND METHODS

a. Research Design

This study is an analytical observational study using a retrospective cohort design. Sampling was conducted using a nonprobability purposive sampling method. Data collection was conducted from the patient's electronic health record (EHR) at the Medical Records Department of Universitas Gadjah Mada Academic Hospital.

b. Population and Sample

The subjects in this study were all adult patients in the ICU during the period January 2021 – April 2024 who met the inclusion and exclusion criteria. The inclusion criteria were as follows: patients with a primary diagnosis of trauma, patients aged >18 years, patients with creatinine clearance (CrCl) >130 mL/min for the ARC group and patients with creatinine clearance (CrCl) <130 mL/min for the non-ARC group. The exclusions that apply to this study include Patients who stayed in the ICU for less than 24 hours, those with chronic kidney disease (CKD) and/or undergoing hemodialysis and ARC patients with dose adjustments of renally eliminated drugs.

c. Analysis Method

Descriptive analysis was used to characterise trauma patients in the ICU, including age, gender, body weight, serum creatinine levels, creatinine clearance values, comorbidities, and disease severity. Data are presented in tables using mean values, except for gender data, which are presented as percentages.

Bivariate analysis was used to examine the association between the occurrence of ARC in trauma patients and therapeutic outcomes, namely, length of stay (LOS) and clinical outcomes. Clinical outcome was assessed based on changes in the Glasgow Coma Scale (GCS), leukocyte count, and the presence or absence of infection, and categorised as improved or unchanged. An independent t-test or Mann-Whitney U test is used to assess differences in LOS between trauma patients with and without ARC. The Chi-Square test is used to evaluate the association between ARC and patients' clinical outcomes.

Multivariate analysis assessed the effects of confounding variables —age, sex, comorbidities

(mean Charlson Comorbidity Index [CCI] score), and disease severity (mean APACHE II score)—on dependent variables—length of stay (LOS) and clinical outcomes. The impact of these confounders on LOS was analysed using multiple linear regression, and on clinical outcomes using multiple logistic regression. All analyses were conducted using statistical software at a 5% significance level.

3. RESULTS

In this study, 84 patients met the inclusion criteria, including 35 in the ARC group and 49 in the non-ARC group. Characteristics of the

patients are presented in Table 1. The trauma patient groups with and without ARC were predominantly male, with nearly 80% of patients in both groups being male. The mean age of trauma patients with ARC was younger (34.49 ± 13.38 years). Trauma patients with ARC had a higher mean body weight (65.82 ± 13.77 kg). ARC was characterised by lower serum creatinine levels and higher creatinine clearance. Trauma patients with ARC had a higher mean APACHE II score (9.69 ± 6.88) but a lower mean CCI score (0.54 ± 0.74).

Table 1. Characteristics of trauma patients with and without ARC in the ICU at UGM Academic Hospital

Characteristic	ARC (+), n = 35	ARC (-), n = 49	p
n (%)			
Gender	Male	28 (80)	¹ 0,787
	Female	7 (20)	
Mean ± SD			
Age (y)	34.49 ± 13.38	41.53 ± 16.96	² 0.074
Weight (kg)	65.82 ± 13.77	62.20 ± 11	³ 0.136
SCr (mg/dL)	0.59 ± 0.20	0.77 ± 0.15	³ 0.006
CrCl (mL/min)	167.66 ± 41.71	104.92 ± 8.82	² <0.001
Disease severity (APACHE II score)	9.69 ± 6.88	7.37 ± 4.68	² 0.200
Comorbidity (CCI score)	0.54 ± 0.74	1.02 ± 1.18	² 0.086

¹Chi-Square test, ²Mann-Whitney test, ³Independent sample t-test, APACHE II: Acute Physiology and Chronic Health Evaluation II, CCI: Charlson Comorbidity Index, CrCl: Creatinine clearance, SCr: Serum creatinine, SD: Standard deviation

The distribution of primary diagnoses based on ICD-10 for trauma patients is shown in Table 2. The disease characteristics in the trauma patient groups were predominantly head injuries, with 15

patients (42.86%) in the ARC group and 18 patients (36.73%) in the non-ARC group.

Table 2. Disease characteristics based on ICD-10 in trauma patients

ICD-10	Definition	n (%)	
		ARC (+), n = 35	ARC (-), n = 49
S00 – S09	Injuries to the head	15 (42,86)	18 (36,73)
S10 – S19	Injuries to the neck	4 (11,43)	4 (8,16)
S20-S20	Injuries to the thorax	4 (11,43)	7 (14,29)
S30 – S39	Injuries to the abdomen, lower back, lumbar spine and pelvis	8 (22,86)	6 (12,24)

S40-S49	Injuries to the shoulder and upper arm	0 (0)	2 (4,08)
S70-S79	Injuries to the hip and thigh	1 (2,86)	1 (2,04)
S80-S89	Injuries to the knee and lower leg	1 (2,86)	0 (0)
S90-S99	Injuries to the ankle and foot	0 (0)	1 (2,04)
T00-T07	Injuries involving multiple body regions	0 (0)	8 (16,33)
T20-T32	Burns and corrosions	1 (2,86)	2 (4,08)
T90-T98	Sequelae of injuries, of poisoning and of other consequences of external causes	1 (2,86)	0 (0)

ICD-10: the International Classification of Diseases, 10th Revision

Table 3 presents the clinical parameters of the patients. Trauma patients with ARC showed lower mean initial and final GCS scores (11.23 ± 4.12 and 11.63 ± 5.12 , respectively). The mean leukocyte count in the ARC group was higher ($16.57 \pm 6.45 \times 10^3/\mu\text{L}$), with a higher incidence of infection (51.4%, $n = 18$).

Data on renally excreted medications administered to patients are provided in Table 4. The most common medications given to patients with ARC is Meropenem (42.9%, $n = 15$), followed by Cefazolin, Ceftriaxone, and Levofloxacin (each accounting for 31.4%, $n = 11$).

Table 3. Clinical parameters of trauma patients with and without ARC

Parameter	ARC (+), $n = 35$	ARC (-), $n = 49$	<i>p</i>
Mean \pm SD			
GCS (initial)	11.23 ± 4.12	12.49 ± 3.62	¹ 0.146
GCS (final)	11.63 ± 5.12	14.02 ± 3.15	¹ 0.025
Leukosit ($\times 10^3/\mu\text{L}$)	16.57 ± 6.45	14.56 ± 5.68	¹ 0.122
n (%)			
Infection	18 (51.4)	11 (22.4)	² 0.006

¹Mann-Whitney test, ²Chi-Square test, GCS: Glasgow Coma Scale

Table 4. Renally excreted medication administered to the trauma patients

Medication	n (%)	
	ARC (+), $n = 35$	ARC (-), $n = 49$
Antibiotic, n (%)		
Amikacin	7 (20)	0 (0)
Ampicillin	1 (2,9)	0 (0)
Cefazolin	11 (31,4)	16 (32,7)
Cefixime	2 (5,7)	0 (0)
Cefotaxime	2 (5,7)	1 (2,9)
Ceftazidime	3 (8,6)	0 (0)
Ciprofloxacin	0 (0)	1 (2,9)
Cotrimoxazole	3 (8,6)	0 (0)
Ceftriaxone	11 (31,4)	29 (59,2)

Gentamicin	6 (17,1)	8 (16,3)
Levofloxacin	11 (31,4)	10 (20,4)
Meropenem	15 (42,9)	3 (6,1)
Metronidazole	1 (2,9)	2 (4,1)
Vancomycin	2 (5,7)	0 (0)
Antifungal, n (%)		
Fluconazole	6 (17,1)	0 (0)
Osmotic diuretic, n (%)		
Mannitol	12 (34,3)	20 (40,1)

The association of the ARC with therapeutic outcomes is showed in Table 5. The mean LOS for trauma patients with ARC was longer (11.77 ± 15.35 days). However, the LOS between the two groups did not differ significantly statistically (p = 0.055). Ten (28.6%) trauma patients with ARC did not

show clinical improvement. This number was significantly higher compared to trauma patients without ARC who did not show improvement (p = 0.05).

Table 5. Association between ARC and therapeutic outcomes in trauma patients

Parameter		ARC (+), n = 35	ARC (-), n = 49	p
Mean ± SD				
LOS (days)		11.77 ± 15.35	4.43 ± 3.66	¹ 0.055
n (%)				
Clinical outcome	Improvement	25 (71.4)	46 (93.9)	² 0.005
	No improvement	10 (28.6)	3 (6.1)	

¹Mann-Whitney test, ²Chi-Square test, LOS: Length of stay

4. DISCUSSION

a. Patient and Disease Characteristics

Based on the analysis, the results showed that the characteristics between the trauma patient groups with and without ARC were not significantly different (p > 0.05), except for the SCr (p = 0.006) and CrCl (p < 0.001). SCr is one of the parameters used to calculate CrCl using the Cockcroft-Gault equation. The SCr value is inversely related to CrCl, meaning that the lower the SCr value, the higher the CrCl value. Trauma patients with and without ARC were grouped by CrCl, resulting in significantly different SCr values. Trauma patients with lower SCr levels at ICU admission have a higher risk of experiencing ARC (6).

Trauma patients admitted to the ICU, both in the ARC and non-ARC groups, were predominantly male. The findings of this study are consistent with several previous studies, which indicated that approximately 75% or two-thirds of trauma patients admitted to the ICU are male. This may be due to adult males engaging in more outdoor activities with higher risks, thus increasing the likelihood of trauma (13–15). Male gender has also been associated with higher CrCl, which may be attributed to greater creatinine production in males than in females (4,5,10). ARC was more commonly found in younger male patients. A clear trend was observed: the number of ARC patients decreased with increasing age. The glomerular

filtration rate (GFR) is estimated to decrease by 8 mL/min/1.73 m² per decade after age 40 (16).

In obese patients without primary kidney damage, GFR increases with increasing body weight and is associated with the presence of albuminuria, indicating early kidney damage. The total increase in GFR, known as glomerular hyperfiltration, may lead to long-term kidney dysfunction if left untreated (17). This theory explains the finding that trauma patients with ARC have a higher mean body weight. Studies have shown that there is a higher in-hospital mortality risk in patients with grade 3 obesity following trauma, compared to individuals with a normal body mass index (18).

APACHE II is the most commonly used method for assessing illness severity and predicting therapeutic outcomes, particularly mortality, in critically ill ICU patients. A higher APACHE II score is associated with more severe disease and a higher risk of death (19). The varying APACHE II scores in this study may be influenced by differences in the primary diagnosis or case at ICU admission and the treatment received by patients during the first 24 hours (20). Trauma patients most commonly experience injuries to the head and neck. Spinal cord injuries are associated with significant morbidity and mortality. A study reported that spinal cord injuries are a major cause of severe disability, prolonged hospital stays, and death (21). Trauma patients often have various comorbidities that can complicate treatment and affect therapeutic outcomes. Comorbidities can influence therapeutic outcomes by increasing the risk of complications during and after treatment (22). Trauma patients with comorbid cardiovascular disease, diabetes, liver disease, and kidney disease are associated with higher mortality rates (23).

b. Clinical Presentation of Trauma Patients

GCS is the primary method used to assess the level of consciousness in trauma patients. It is considered the gold standard for evaluating the neurological status of patients with traumatic brain injury (TBI). This method is also the strongest predictor of post-trauma mortality. The GCS assessment of trauma patients treated in the ICU is an independent predictor of patient prognosis,

as lower GCS scores increase the likelihood of poor clinical outcomes (24–26). In this study, a lower initial GCS score was associated with worse final GCS outcomes.

Post-injury leukocytosis is associated with an increased risk of developing multiple organ dysfunction syndrome (MODS). Leukocytosis is also involved as a predictor of the severity of head injury, anaemia due to acute blood loss, and hollow visceral injury in trauma patients (27). In this study, the mean leukocyte count between groups did not differ significantly. However, leukocytosis is a common sign of infection, particularly bacterial infection, and should be monitored to identify other signs and symptoms of infection (28). Based on the results of this study, it was found that the incidence of infection in trauma patients with ARC was higher. Infection in trauma patients is a common finding because, after the initial trauma impact, the integrity of the body's natural barriers, such as the skin, muscles, and bones, is disrupted, and immunity is compromised. Furthermore, invasive devices, such as central venous catheters and thoracic drains, provide a medium for the growth of nosocomial microorganisms (29). This explains the large amount of antibiotic therapy administered to trauma patients in the ICU.

Antibiotic administration for ICU patients should be initiated as early as possible and ensure that optimal serum concentrations are reached for effective infection management. The presence of ARC can accelerate glomerular filtration of drugs eliminated by the kidneys, thereby reducing systemic exposure to these medications (30,31). In this study, the most commonly used antibiotic in trauma patients with ARC was Meropenem, administered to 15 patients (42.9%). On the other hand, the most frequently used antibiotic in trauma patients without ARC was Ceftriaxone, given to 29 patients (59.2%). Both are beta-lactam antibiotics that are eliminated through the kidneys. Based on the increased drug elimination rate in ARC, particularly for hydrophilic antibiotics primarily eliminated by the kidneys, such as beta-lactams, vancomycin, and aminoglycosides, this will impact optimal infection management, LOS, and clinical outcomes. Dose optimisation is

necessary for infections caused by pathogens with low susceptibility, which require higher antibiotic exposure to achieve optimal efficacy (32).

c. The association of the ARC with therapeutic outcomes

It is known from this study that the LOS for trauma patients with ARC is longer. The difference in LOS between trauma patients with and without ARC was not statistically significant (p -value = 0.055), which is slightly above the conventional threshold of 0.05. However, the p -value approaching 0.05 suggests a tendency towards significance. A study with traumatic brain injury (TBI) patients also found that the median ICU LOS was longer for patients with ARC, at 9 (4 – 21) days, compared to patients without ARC, at 4 (2 – 19) days, although statistically insignificant, with a p -value of 0.25 ($p > 0.05$). The longer LOS in patients with ARC may be related to therapy failure associated with antibiotics. Another explanation to consider is that ARC reflects more severe disease, with a higher inflammatory response and a hyperdynamic condition compared to non-ARC patients (33).

The study results indicate that a higher number of trauma patients with ARC did not show clinical improvement. The association between ARC and clinical outcomes was analysed using the Chi-Square test, yielding a p -value of 0.005 ($p < 0.05$). Statistically, this result signifies that ARC is associated with poorer clinical outcomes in trauma patients in the ICU. The high incidence of ARC among critically ill patients with severe traumatic injuries indicates a potential subtherapeutic dose for medications, electrolytes, and nutrients that are eliminated through the kidneys. ARC has a significant impact on the pharmacokinetics/pharmacodynamics (PK/PD) of time-dependent antimicrobials with a short half-life (10,31). Additionally, ARC may be associated with the failure of antibiotic prophylaxis therapy administered to trauma patients, burn victims, post-surgery patients, and immunocompromised individuals (30).

Therapeutic failure in ARC patients is an important outcome that clinicians should closely monitor. Clinical pharmacists must understand the pharmacological properties of drugs that are

eliminated through the kidneys (such as hydrophilicity, molecular size, elimination routes, etc.) that are frequently used in critically ill patients in their respective hospitals, to anticipate the impact of ARC on drug dosing. Moreover, pharmacists should promptly assess and identify patients at risk of developing ARC, and empirically optimise dosages based on clinical presentation. A limitation of this study is that renal function was not assessed using ideal parameters, such as 24-hour urine collection or inulin clearance to calculate CrCl.

5. CONCLUSIONS

Trauma patients with ARC are characterised by a predominance of males, younger age, higher body weight, lower serum creatinine, more severe disease severity, but lower comorbidities. The mean LOS of trauma patients with ARC is longer, showing a tendency towards significance. ARC is associated with worse clinical outcomes in trauma patients in the ICU, with a p -value of 0.005 ($p < 0.05$), as demonstrated by poor clinical outcomes in 10 patients.

6. ACKNOWLEDGEMENT

This original article was supported by the Master of Clinical Pharmacy, University Gadjah Mada. We appreciate the support and facilitation throughout the writing process of this article.

REFERENCES

1. Mahmoud S, Shen C. Augmented Renal Clearance in Critical Illness: An Important Consideration in Drug Dosing. *Pharmaceutics*. 2017 Sep 16;9(3):36.
2. Kanna G, Patodia S, Annigeri RA, Ramakrishnan N, Venkataraman R. Prevalence of Augmented Renal Clearance (ARC), Utility of Augmented Renal Clearance Scoring System (ARC score) and Augmented Renal Clearance in Trauma Intensive Care Scoring System (ARCTIC score) in Predicting ARC in the Intensive Care Unit: Proactive Study. *Indian J Crit Care Med*. 2023 Jun;27(6):433–43.
3. Rhoney DH, Brooks AB, Nelson NR. Augmented Renal Clearance: An Under-Recognized Phenomenon Associated With

- COVID-19. *Critical Care Explorations*. 2022 Feb 4;4(2):e0617.
4. Barletta JF, Mangram AJ, Byrne M, Sucher JF, Hollingworth AK, Ali-Osman FR, et al. Identifying augmented renal clearance in trauma patients: Validation of the Augmented Renal Clearance in Trauma Intensive Care scoring system. *Journal of Trauma and Acute Care Surgery*. 2017 Apr;82(4):665–71.
 5. Mulder MB, Eidelson SA, Sussman MS, Schulman CI, Lineen EB, Iyenger RS, et al. Risk Factors and Clinical Outcomes Associated With Augmented Renal Clearance in Trauma Patients. *Journal of Surgical Research*. 2019 Dec;244:477–83.
 6. Bing E, Archambault K, Sananikone A, Nguyen KD, Fang YT, Jabamikos C, et al. Risk factors associated with augmented renal clearance in a mixed intensive care unit population: a retrospective study. *Int J Clin Pharm*. 2022 Dec;44(6):1277–86.
 7. Ramakrishnan N, Venkataraman R, Patodia S, Annigeri RA, Kanna G. Prevalence of Augmented Renal Clearance (ARC), Utility of Augmented Renal Clearance Scoring System (ARC score) and Augmented Renal Clearance in Trauma Intensive Care Scoring System (ARCTIC score) in Predicting ARC in the Intensive Care Unit: Proactive Study. *Indian Journal of Critical Care Medicine*. 2023 May 31;27(6):433–43.
 8. Baptista L, Moura I, Silva CM, Baptista JP. What is New in Augmented Renal Clearance in Septic Patients? *Curr Infect Dis Rep*. 2023 Nov;25(11):255–72.
 9. Messelu MA, Tilahun AD, Beko ZW, Endris H, Belayneh AG, Tesema GA. Incidence and predictors of mortality among adult trauma patients admitted to the intensive care units of comprehensive specialized hospitals in Northwest Ethiopia. *Eur J Med Res*. 2023 Mar 9;28(1):113.
 10. Dickerson RN, Crawford CN, Tsiu MK, Bujanowski CE, Van Matre ET, Swanson JM, et al. Augmented Renal Clearance Following Traumatic Injury in Critically Ill Patients Requiring Nutrition Therapy. *Nutrients*. 2021 May 15;13(5):1681.
 11. Claus BOM, Hoste EA, Colpaert K, Robays H, Decruyenaere J, De Waele JJ. Augmented renal clearance is a common finding with worse clinical outcome in critically ill patients receiving antimicrobial therapy. *Journal of Critical Care*. 2013 Oct;28(5):695–700.
 12. Hobbs ALV, Shea KM, Roberts KM, Daley MJ. Implications of Augmented Renal Clearance on Drug Dosing in Critically Ill Patients: A Focus on Antibiotics. 2015;35(11):1063–75.
 13. Bayissa BB, Alemu S. Pattern of trauma admission and outcome among patients presented to Jimma University Specialized Hospital, south-western Ethiopia. *Trauma Surg Acute Care Open*. 2021 Jun;6(1):e000609.
 14. Embu HY, Nuhu SI, Isamade ES, Kokong DD, Ozoilo KN, Agbo DO. Characteristics and Outcome of Trauma Patients in a Mixed ICU: A Retrospective Review. *OALib*. 2016;03(07):1–7.
 15. Fokin AA, Wycech Knight J, Gallagher PK, Xie JF, Brinton KC, Tharp ME, et al. Characteristics and outcomes of trauma patients with unplanned intensive care unit admissions: Bounce backs and upgrades comparison. *World J Crit Care Med*. 2025 Jun 9;14(2):101957.
 16. Johnston BW, Perry D, Habgood M, Joshi M, Krige A. Augmented renal clearance: a retrospective, cohort study of urinary creatinine clearance in critically ill patients in the United Kingdom. *J Int Med Res*. 2021 May;49(5):030006052110155.
 17. Basolo A, Salvetti G, Giannese D, Genzano SB, Ceccarini G, Giannini R, et al. Obesity, Hyperfiltration, and Early Kidney Damage: A New Formula for the Estimation of Creatinine Clearance. *The Journal of Clinical Endocrinology & Metabolism*. 2023 Nov 17;108(12):3280–6.
 18. Cromwell PM, Reynolds IS, Heneghan HM, Glasgow SM. Obesity and outcomes in trauma - a systematic review and meta-analysis. *Injury*. 2023 Feb;54(2):469–80.
 19. Tian Y, Yao Y, Zhou J, Diao X, Chen H, Cai K, et al. Dynamic APACHE II Score to Predict the Outcome of Intensive Care Unit Patients. *Front Med*. 2022 Jan 26;8:744907.
 20. Sungono V, Hariyanto H, Soesilo TEB, Adisasmita AC, Syarif S, Lukito AA, et al. Cohort

- study of the APACHE II score and mortality for different types of intensive care unit patients. *Postgraduate Medical Journal*. 2022 Dec 1;98(1166):914–8.
21. Oyediran OO, Ayandiran EO, Olanrewaju TD, Ojo IO, Ogunlade AA, Fajemilehin BR. Prevalence and outcome of care among patients with spinal cord injury in a Nigerian Tertiary Health Institution. *Interdisciplinary Neurosurgery*. 2022 Mar;27:101446.
 22. Talla A, Alshammry N, Alzahrani M, Alshammari A, Almarshadi J, Alshammari A. Influence of comorbidities on outcomes of head trauma patient: a systematic review. *IJMDC*. 2024;2143–9.
 23. Glynn R, Edwards F, Wullschleger M, Gardiner B, Laupland KB. Major trauma and comorbidity: a scoping review. *Eur J Trauma Emerg Surg*. 2025 Dec;51(1):133.
 24. Agorogianni D, Michalopoulos E, Prantzou A, Liaskou C, Stamou A, Kapadochos T, et al. Clinical indicators as prognostic factors of multi-trauma patients in the Intensive Care Unit. *HealthResJ*. 2021 Oct 9;7(4):206.
 25. Agrawal N, Iyer SS, Patil V, Kulkarni S, Shah JN, Jedge P. Comparison of admission GCS score to admission GCS-P and FOUR scores for prediction of outcomes among patients with traumatic brain injury in the intensive care unit in India. *ACC*. 2023 May 31;38(2):226–33.
 26. Han J, Yoon SY, Seok J, Lee JY, Lee JS, Ye JB, et al. Clinical characteristics and mortality risk factors among trauma patients by age groups at a single center in Korea over 7 years: a retrospective study. *J Trauma Inj*. 2023 Dec 31;36(4):329–36.
 27. Hasjim BJ, Grigorian A, Stopenski S, Swentek L, Sun B, Livingston JK, et al. Moderate to severe leukocytosis with vasopressor use is associated with increased mortality in trauma patients. *Journal of the Intensive Care Society*. 2022 May;23(2):117–23.
 28. Riley LK, Rupert J. Evaluation of Patients with Leukocytosis. *Am Fam Physician*. 2015 Dec 1;92(11):1004–11.
 29. Coccolini F, Rausa E, Montori G, Fugazzola P, Ceresoli M, Sartelli M, et al. Risk Factors for Infections in Trauma Patients. *Curr Trauma Rep*. 2017 May 23;3(4):285–91.
 30. Kawano Y, Maruyama J, Hokama R, Koie M, Nagashima R, Hoshino K, et al. Outcomes in patients with infections and augmented renal clearance: A multicenter retrospective study. Lazzeri C, editor. *PLoS ONE*. 2018 Dec 10;13(12):e0208742.
 31. Tesfamariam NS, Aboelezz A, Mahmoud SH. The Impact of Augmented Renal Clearance on Vancomycin Pharmacokinetics and Pharmacodynamics in Critically Ill Patients. *JCM*. 2024 Apr 17;13(8):2317.
 32. Sistanizad M, Hassanpour R, Pourheidar E. Are Antibiotics Appropriately Dosed in Critically Ill Patients with Augmented Renal Clearance? A Narrative Review. Saad K, editor. *International Journal of Clinical Practice*. 2022 Jan 31;2022:1–17.
 33. Campassi ML, Repetto FG, Banegas Litardo DM, Castor R, Gómez G, Tiseyra B, et al. Incidence and determinants of augmented renal clearance in traumatic brain injury: A prospective observational study. *Journal of Critical Care*. 2022 Aug;70:154065.