REVIEW ARTICLE

Vancomycin Dosing and Pharmacokinetics in Adults Undergoing Continuous Renal Replacement Therapy: A Narrative Review.

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Abstract

Vancomycin is a cornerstone therapy for severe Gram-positive infections, but dosing in critically ill patients on continuous renal replacement therapy (CRRT) is challenging due to significant pharmacokinetic variability. This narrative review synthesizes current evidence on vancomycin pharmacokinetics, dosing strategies, and therapeutic drug monitoring. Twelve articles were included, encompassing 398 adult patients receiving vancomycin across different CRRT modalities, including continuous veno-venous hemofiltration (CVVH), hemodialysis (CVVHD), and hemodiafiltration (CVVHDF). Vancomycin pharmacokinetics during CRRT are influenced by CRRT modality, effluent flow rate, filter integrity, residual renal function, and patient-specific factors such as expanded volume of distribution. Clearance estimates range from 0.7 to 2.6 L/h, with CVVHDF achieving the highest removal (up to 76% of total body clearance). An initial loading dose of 20 to 25 mg/kg is consistently recommended, followed by maintenance dosing of 5-7.5mg/kg every 12 hours, adjusted according to the CRRT intensity. Continuous infusion strategies may offer more stable concentrations but require close monitoring. TDM is essential, with a clear evolution from trough-based monitoring (target 15–20 mg/L) toward AUC_{24}/MIC-guided dosing (target 400–600 mg·h/L), consistent with current guidelines. This review highlights the critical interplay between CRRT parameters and vancomycin clearance, emphasizing the need for individualized, TDM-guided therapy to optimize efficacy and minimize toxicity in this complex patient population.

Keywords: *Continuous renal replacement therapy, pharmacokinetics, vancomycin.*

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Introduction

The pharmacokinetics of vancomycin in critically ill patients undergoing continuous renal replacement therapy (CRRT) is exceptionally complex due to the dynamic interplay of patient-specific physiological changes, the severity of acute kidney injury (AKI), and the variable operational characteristics of different CRRT modalities [1]. Consequently, establishing standardized dosing regimens for vancomycin in this population is challenging, often necessitating individualized therapeutic drug monitoring to ensure optimal drug exposure [2]. Despite these challenges, achieving therapeutic vancomycin levels is crucial, as inadequate dosing can lead to treatment failure and increased mortality, while excessive levels can precipitate nephrotoxicity and ototoxicity. Therefore, a thorough understanding of vancomycin's pharmacokinetic alterations during CRRT is essential for guiding effective and safe antimicrobial therapy in critically ill patients [1]. Vancomycin is used in critically ill patients for the treatment of severe infections, including methicillin-resistant *Staphylococcus aureus* and *Enterococcus* species. Like all antimicrobial drugs, vancomycin has a pharmacokinetic/pharmacodynamic (PK/PD) index associated with effectiveness and toxicity. Vancomycin exhibits time-dependent bacterial killing. The currently considered optimal vancomycin pharmacokinetic/pharmacodynamic index is the ratio of the area under the concentration (AUC) to the minimum inhibitory concentration (MIC) of 400–600 mg*h/L[3]. This review aims to synthesize current literature regarding vancomycin pharmacokinetics in patients undergoing CRRT, exploring the impact of CRRT modalities and patient-specific factors on drug clearance and distribution [2]. The objective is to consolidate existing evidence to provide insights into optimizing vancomycin dosing strategies, particularly focusing on therapeutic drug monitoring (TDM) to improve clinical outcomes and minimize adverse effects [4].

Materials and methods

Literature search

A narrative review approach was adopted. Literature was identified through PubMed/Medline in October 2025, using search terms including "vancomycin," "continuous renal replacement therapy," "CRRT," "pharmacokinetics," "AUC," “adult” and "therapeutic drug monitoring". No cut-off points of search years were applied. Eligible studies included adult patients receiving CRRT with reported pharmacokinetic data, dosing strategies, or TDM outcomes. Key guidelines and consensus statements were also reviewed to provide clinical context. Articles that were short reports, letters, written in languages other than English, or without full-text availability were excluded. Findings were synthesized thematically rather than pooled quantitatively.

Results

Out of the 19 retrieved articles, only 12 met the eligibility criteria. Seven articles were excluded: five because the study subjects were not adults, one because it investigated daptomycin and micafungin, and another because it investigated oral vancomycin, which was outside the scope of this review. No duplicate articles were identified. In total, the reviewed literature encompassed 398 adult patients who received vancomycin while undergoing various CRRT modalities.

Pharmacokinetics of Vancomycin in CRRT

Studies on vancomycin pharmacokinetics in CRRT demonstrate significant variability in parameters such as half-life, clearance, volume of distribution (Vd), and extraction ratios, influenced by the CRRT modality used [5-8,10].

Clearance and Removal by CRRT Modality

More recent data emphasize that vancomycin clearance is strongly influenced by CRRT effluent rate, downtime, and filter integrity, with clearance estimates ranging from 0.7 to 2.6 L/h across studies [2-5,9,11-13]. This variability underscores the challenge of using fixed dosing in heterogeneous CRRT settings. Continuous veno-venous haemodiafiltration (CVVHDF) achieves substantial vancomycin clearance, with reported filter clearance around 1.8 ± 0.4 L/h, accounting for approximately 76% of total body clearance. This modality combines convective and diffusive clearance, leading to greater vancomycin removal compared to others [5].Continuous veno-venous haemofiltration (CVVH) primarily uses convection; vancomycin clearance varies from about 0.7 to 1.1 L/h, depending on ultrafiltration rates and filter types [2,8,13]. Clearance by CVVH is generally lower than CVVHDF. Continuous veno-venous haemodialysis (CVVHD) relies on diffusive clearance, with reported vancomycin clearance rates generally lower than CVVHDF but sometimes comparable to CVVH, depending on dialysis parameters [6].

Half Life

Vancomycin half-life during CVVHDF was approximately 15.6 ± 8.7 hours, longer than in patients with normal renal function but shorter than in conventional hemodialysis or severe renal failure without CRRT. This reflects effective extracorporeal removal while accommodating reduced renal clearance in critically ill patients [5].

Volume of Distribution

In addition to clearance, variability in the Vd was a key determinant of vancomycin pharmacokinetics across studies [4-5,8,12-13]. Reported Vd values generally ranged from 0.38 L/kg to approximately 1.2 L/kg, with most estimates clustering around 0.7–1.0 L/kg. This range aligns with the expanded extracellular fluid volume expected in critically ill patients undergoing CRRT. Factors such as systemic inflammation, capillary leak, hypoalbuminemia, and fluid resuscitation contribute to this expansion, complicating pharmacokinetic predictions. Vancomycin's moderate Vd and minimal protein binding allow relatively efficient removal by CRRT. Vasoactive drugs like dobutamine and dopamine may influence vancomycin pharmacokinetics during CRRT, potentially leading to subtherapeutic drug concentrations due to altered hemodynamics and drug distribution [1].

Vancomycin Dosing in CRRT

Across the 12 studies included (2004–2025), several consistent dosing themes emerged. **Loading doses** were generally recommended in the range of **20–30 mg/kg**, with some studies advocating higher initial doses (up to 35 mg/kg) to rapidly achieve therapeutic concentrations [11]. **Maintenance regimens** varied widely, reflecting differences in CRRT modality and intensity: intermittent dosing typically ranged from **500–1500 mg every 12–24 hours**, while continuous infusion (CI) strategies used **16–35 mg/kg/day** or fixed doses of ~1 g/day [5,8,11].

Continuous Infusion versus Intermittent Dosing

Several studies have explored CI regimens of vancomycin in patients undergoing CRRT to address the challenges of fluctuating serum concentrations seen with intermittent dosing [9,11]. CI, typically following a loading dose, achieves therapeutic vancomycin concentrations more rapidly and reduces episodes of subtherapeutic levels compared to intermittent dosing regimens.

A prospective study involving septic patients treated with CRRT showed that a loading dose of 35 mg/kg vancomycin over 4 hours followed by a continuous daily dose of 14 mg/kg allowed rapid attainment of target drug concentrations (20-30 mg/L) in the majority of patients [11].

Therapeutic Drug Monitoring Approaches

Across the included studies, there has been a clear evolution in TDM strategy for vancomycin in CRRT patients. Earlier studies (2004–2014) almost exclusively relied on trough

concentrations (target 15–20 mg/L) as a surrogate for efficacy, with levels typically measured after 24 hours or even earlier (≥6 hours post-dose in some cohorts) [5,9-11]. These trough-guided approaches highlighted significant variability and often failed to reliably predict therapeutic exposure, particularly in the context of changing CRRT settings.

From 2013 onward, some studies began to explore CI strategies, using steady-state troughs (20–30 mg/L) as more practical markers for maintaining therapeutic exposure [7,11]. More recent investigations (2021–2025) have shifted towards AUC24/MIC-based monitoring as the preferred method, consistent with international guidelines.

The findings of the overall pharmacokinetic profiles, vancomycin dosing, and TDM approaches are summarized in Table 1.

Discussion

In critically ill patients, rapid identification and treatment of bacterial infections are crucial. AKI being a common complication requiring renal replacement therapy, most often managed with CRRT [3,5]. Contemporary CRRT efficiently removes metabolic waste but also clears hydrophilic antimicrobials such as vancomycin. Vancomycin has a molecular weight of approximately 1,448 daltons, is hydrophilic, is minimally bound to plasma proteins (30–55%), and is almost exclusively renally excreted in unchanged form. It also has a relatively small volume of distribution (0.4–1.0 L/kg in adults) [2,5]. These characteristics make vancomycin highly susceptible to extracorporeal clearance during CRRT, where convective and diffusive processes can efficiently remove solutes of this size. CRRT includes three primary variants: CVVH, CVVHD, and CVVHDF [6].

Vancomycin pharmacokinetics during CRRT are influenced by several key factors. The delivered renal dose and the CRRT modality significantly impact vancomycin clearance, as higher effluent rates generally increase drug removal [5]. Additionally, residual kidney function can be substantial in some patients, contributing to overall vancomycin clearance and affecting dosing requirements. The type and integrity of the filter used in CRRT also play a role in determining the extent of extracorporeal drug removal; filter downtime or compromised filter function can reduce vancomycin clearance [7,15]. Furthermore, pathophysiological changes associated with critical illness, including systemic inflammation, capillary leak, fluid resuscitation, and altered plasma protein binding, introduce further pharmacokinetic variability [1]. These conditions often result in an expanded volume of distribution and altered free drug concentrations, complicating the prediction of vancomycin levels and necessitating individualized dosing. The use of vasoactive drugs may also influence vancomycin pharmacokinetics, potentially leading to subtherapeutic concentrations. These determinants complicate achieving and maintaining therapeutic vancomycin exposure in CRRT patients [1].

Notably, vancomycin clearance by CRRT can account for up to 76% of total body clearance [2,5]. This is supported by a study showing that CVVHDF removed nearly three-quarters (76% ± 16.5%) of total vancomycin clearance in critically ill patients [5]. Additionally, CVVHDF removed over half of the administered vancomycin dose during a 12-hour study period, indicating the substantial impact of CRRT on drug elimination. The total body clearance observed also suggests that non-renal pathways contribute to vancomycin elimination to the extent of approximately 25–30%. This significant extracorporeal clearance underlines the importance of dose adjustments and TDM in patients receiving vancomycin during CRRT to avoid subtherapeutic or toxic levels.

Based on the available evidence and the detailed study data summarized, vancomycin dosing during CRRT poses significant challenges due to altered pharmacokinetics stemming from extracorporeal clearance, variability in CRRT modalities and intensities, and patient-specific

factors including residual renal function and critical illness pathophysiology. Most studies recommend an initial loading dose of 20–25 mg/kg to rapidly achieve therapeutic serum concentrations, aligning with consensus guidelines [13,14]. Maintenance doses, however, must be individualized based on CRRT effluent flow rates, with typical regimens ranging from 5 to 7.5 mg/kg every 12 hours. For lower-intensity CRRT (e.g., 20–25 mL/kg/h), doses at the lower end of this range - from 7.5 to 10mg/kg every 12 hours – are used, while higher intensities (>25 mL/kg/h) necessitate more aggressive dosing to compensate for enhanced extracorporeal clearance [14].

TDM is vital given the dynamic and unpredictable pharmacokinetic profiles of patients on CRRT [10]. Early TDM sampling within 6 to 12 hours post-loading dose is critical to identify subtherapeutic or supratherapeutic vancomycin levels and facilitate timely dosage adjustments [10,11]. Target trough concentrations of 15–20 mg/L or AUC/MIC ratios of 400–600 mg*h/L are supported by current guidelines and research to optimize efficacy and minimize toxicity [14]. Several investigations also underscore the potential benefits of continuous infusion dosing to maintain steady therapeutic concentrations, though such approaches still require frequent monitoring due to residual variability in clearance [11].

Incorporating factors such as CRRT downtime, filter integrity, and patient-specific kinetics into dosing decisions through model-informed precision dosing (MIPD) or population pharmacokinetic models can further enhance individualized therapy [3]. Overall, balanced initial dosing combined with responsive TDM-guided adjustments remains the cornerstone of effective vancomycin use in critically ill patients undergoing CRRT.

Most available vancomycin pharmacokinetic studies during CRRT are limited by small, single-center cohorts and significant heterogeneity in CRRT modalities and settings, which restricts the generalizability of findings [2,5,11]. Sample sizes in many reports range from fewer than 10 to around 150 patients, often lacking standardized dosing protocols or consistent TDM strategies. This variability complicates the establishment of universally applicable dosing recommendations and target exposure goals.

Given this, there is a clear need for large, multicentre randomized trials and pragmatic implementation studies to robustly validate dosing strategies, especially AUC-guided dosing approaches, and continuous infusion regimens in diverse critically ill populations on CRRT. Such trials would improve understanding of vancomycin pharmacokinetics across different CRRT machines, filters, modalities, and intensities, while accounting for patient heterogeneity in residual renal function and illness severity.

Conclusion

In summary, multiple factors interplay to influence vancomycin pharmacokinetics in critically ill patients receiving CRRT, making dosing a nuanced and complex task. The evidence consistently indicates that vancomycin clearance during CRRT is predominantly driven by the effluent dose, with higher filtration and dialysate rates leading to increased extracorporeal elimination. This relationship underscores the need to tailor maintenance dosing regimens based on CRRT intensity and modality, ensuring adequate drug exposure despite the variability introduced by extracorporeal clearance and patient-specific factors such as residual renal function and critical illness pathophysiology.

Until large-scale multicentre trials provide more complete data, clinicians should adopt an approach combining appropriate loading doses to rapidly achieve therapeutic levels, effluent flow rate-adjusted maintenance doses, and AUC-based TDM where feasible. Continuous infusion regimens may offer potential advantages by providing more stable vancomycin serum concentrations and reducing peak-trough

fluctuations, but these approaches also demand close monitoring to balance efficacy and safety. Future research priorities include standardizing the reporting of CRRT prescriptions and modalities, validating simplified yet accurate AUC monitoring methods suitable for critically ill populations, and correlating optimized dosing strategies with clinical outcomes. Advancements in model-informed precision dosing hold promise for refining vancomycin therapy during CRRT, ultimately improving patient care in this challenging context.

Conflict of Interest

The authors have no funding or conflicts of interest to disclose. The first author is currently undergoing training under the Malaysia Advanced Clinical Pharmacy Programme (MyACPP - Clinical Pharmacokinetics).

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Authors' Contribution

KLSF performed the literature search and manuscript preparation, while SM was responsible for critical revision of the manuscript for intellectual content. All authors agreed and approved the manuscript for publication.

Table 1. Summary of pharmacokinetic profiles, vancomycin dosing and TDM approaches

Study (First Author, Year)	Design (n)	CRRT Modality (Effluent Rate)	Vancomycin Regimen	PK Findings	TDM Strategy	Clinical/ Interpretive Note
DelDot et al., 2004	Prospective cohort (n=10, ICU)	CVVHDF (25–35 mL/kg/h)	750 mg q12h	CL: 1.8 ± 0.4 L/h; t½: 15.6 ± 8.7 h; Vd: 49.7 ± 29.1 L	Trough	Higher CRRT intensity required higher doses; ~450 mg q12h needed to maintain ~15 mg/L steady-state.
Heintz et al., 2009	Narrative review	CVVH, CVVHD, CVVHDF	LD: 15–20 mg/kg; adjusted per modality /effluent	CL depends on CRRT modality; dosing ranges provided	TDM recommended	Practical early dosing guidance for CRRT.
Lynsay M et al., 2010	Retrospective (n=24)	CVVHD	LD: 1.5 g stat; 1–1.5 g/24 h infusion	CL: 2.4 L/h (1.97–2.92); t½: 22h; Vd: 0.96 L/kg	Trough 15–20 mg/L (24 h)	Standard dosing inadequate; TDM essential; intermittent 1.25–1.5 g q24h may achieve trough 15–20 mg/L.
Chaijarmon W et al., 2011	Prospective open-label (n=7)	CVVH	1 g IV; suggested LD: 25–30 mg /kg, MD: 500–750 mg q12h	CL: 0.73 ± 0.21 L/h; Vd: 0.38 ± 0.18 L/kg;t½: 12.0 ± 7.0 h	Not reported	LD 25–30 mg/kg + MD 500–750 mg q12h achieved trough 15–20 mg/L.
Covajes C et al., 2013	Prospective/ observational (n=85)	CVVHF/CVVHDF (<20–>40 mL/kg/h)	LD: 16.4 mg/kg; Maintenance: 23.5 mg/kg/day	—	Trough Day 1	CI dosing 16–35 mg/kg/day adequate for most critically ill CRRT patients.
Beumier M et al., 2013	Prospective (n=32)	CRRT (25–43 mL/kg/h)	LD: 35 mg/kg over 4 h; MD: 14 mg/kg/day	CL: 0.8–1.8 L/h; Vd highly variable	Trough 20–30 mg/L (≥12 h post-LD)	CI may improve early attainment of therapeutic targets.
Petejova N et al., 2014	Prospective open (n=17)	CVVH (45 mL/kg/h)	LD: 1 g; then 1 g q12h	t½: 4.1–14.2 h	Trough ≥6 h post-dose	Target trough >10 mg/L and AUC24/MIC >400 achievable.
Chen JH et al., 2021	Case reports (n=2)	CVVH (30–59 mL/kg/h)	LD: 25 mg/kg; maintenance ~15 mg/kg q12h	CL: 0.8–0.9 L/h	Trough (24 h)	Suggested LD 25 mg/kg followed by 15 mg/kg q12h to maintain therapeutic levels.
Wang CH et al., 2022	Retrospective cohort (n=159)	CVVH, CVVHD, CVVHDF	LD: ~1 g; Maintenance: 1 g/day	CL: 1.188 L/h; Vd: 107.7 L	AUC24	Optimized regimens: 5 mg/kg q12h (20–25 mL/kg/h) or 7.5 mg/kg q12h (25–45 mL/kg/h).
Smeets TJL et al., 2023	Prospective observational (n=20)	CVVHD/CVVHDF (25–30 mL/kg/h)	LD: 20 mg/kg; Maintenance: 1 g/day	CL: 0.79–0.95 L/h	Trough 10–25 mg/L (24 h)	MIPD with TDM may improve precision dosing; downtime and filter integrity important.
Smeets TJL et al., 2025	Observational (n=18)	CVVHDF (25–30 mL/kg/h)	LD: 20 mg/kg; CI 1 g/day (fixed)	CL influenced by CRRT downtime and filter integrity	TDM after 24 h	Downtime and filter integrity critical for PK; CI may aid dosing in CRRT.
Kirwan M et al., 2025	Retrospective cohort (n=24)	CVVHDF	LD: 25 mg/kg; MD: 15–20 mg/kg daily	CL: 2.59 ± 0.49 L/h; Vd: 1 L/kg	Peak & trough next dose	2 g LD then 750 mg q12h gave ~100% PTA.

CL: Clearance; t½: Half-life, Vd: Volume of distribution, LD: Loading dose, MD: Maintenance dose, AUC: Area under the curve, PTA: Probability of target attainment, MIPD: Model-informed precision dosing

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