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Galaxy Publication

Intravenous Vancomycin for Periprosthetic Joint Infection: Do We Reach the Desired Target Levels?

Fatima Zahra Amrani[1]*, Youssef Benali[1]

[1]Department of Pharmacotherapy and Clinical Practice, Faculty of Medicine and Pharmacy, Mohammed V University, Rabat, Morocco.

***E-mail** ✉ fatima.amrani@gmail.com

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ABSTRACT

Vancomycin is frequently administered for treating periprosthetic joint infection (PJI), with serum trough levels routinely monitored to ensure therapeutic adequacy. However, the extent to which measured concentrations actually remain within the desired range during treatment is not well defined. In addition, the frequency of necessary dose modifications and patient characteristics that contribute to subtherapeutic or supratherapeutic levels have not been sufficiently explored. Accordingly, the primary objectives of this study were (1) to evaluate whether serum vancomycin concentrations in PJI patients fall within the recommended therapeutic range, and (2) to determine the number of trough measurements and dose adjustments required during standard treatment. This single-center cohort analysis included 108 patients who underwent surgical management for PJI followed by postoperative intravenous vancomycin therapy. Cases were identified through a local arthroplasty registry, and supplementary clinical data were extracted from electronic health records. The study population consisted of 41% women, with a median age of 71 years (IQR 63–79). Hip infections were predominant (73%). Before vancomycin therapy, 54% of patients had undergone a DAIR (debridement, antibiotics, and implant retention) procedure, and 39% had received vancomycin-enriched bone cement during previous revision surgery. Across 791 trough measurements, only 58.2% were within the therapeutic target range of 15–20 mg/L, while 18.5% were below and 23.4% exceeded it. Overall, 71% of patients required at least one dose adjustment, and the median treatment duration was 8 days. Vancomycin trough levels showed moderate positive correlations with age (Spearman's rho = 0.35, $P < 0.001$) and baseline creatinine (Spearman's rho = 0.34, $P < 0.001$). No significant difference was observed between patients who received vancomycin-loaded cement and those who did not. A considerable proportion of vancomycin serum levels in PJI patients fall outside the recommended therapeutic window despite guideline-based dosing. Elderly patients and those with impaired renal function appear particularly vulnerable to abnormal concentrations. These findings support consideration of alternative broad-spectrum antibiotics that require less intensive therapeutic drug monitoring.

Keywords: Antibiotic-loaded cement, Trough value, Drug monitoring, Therapeutic range, Periprosthetic joint infection, Vancomycin

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Introduction

Periprosthetic joint infection (PJI) represents one of the most serious complications after arthroplasty surgery. Its reported incidence after hip or knee replacement is typically between 1% and 2%, although several studies indicate that this figure may be underestimated and that rates are increasing, particularly in Nordic populations [1-4]. The infection develops when microorganisms adhere to prosthetic surfaces, a process that can occur through hematogenous spread, perioperative contamination, or postoperative infection, most often associated with surgical site infections [5].

Diagnostic criteria for PJI have been proposed by multiple groups, with the European Bone and Joint Infection Society (EBJIS) definition now being widely adopted [6]. This system integrates clinical findings, laboratory parameters, microbiological results, histopathology, and imaging, and classifies cases into three categories: (1) "infection unlikely," indicating absence of evidence; (2) "infection likely," defined by at least two supportive findings; and (3) "infection confirmed," based on at least one definitive diagnostic criterion [7].

Depending on the timing of symptom onset, PJI is further divided into three clinical patterns. Early postoperative infection occurs within 1 month of surgery and is usually contiguous in origin. Acute hematogenous infection occurs after an initially uneventful postoperative period due to bloodstream spread of bacteria. Chronic PJI develops beyond the early postoperative phase and persists for more than three weeks, with both hematogenous and contiguous mechanisms potentially contributing to its development [8].

Management of PJI requires a combination of surgical intervention and antimicrobial therapy. Surgical strategies include debridement with implant retention (DAIR) and one-stage or two-stage revision procedures [8]. DAIR is mainly suitable for early postoperative infections and selected acute hematogenous cases of limited duration, whereas chronic infections typically require implant removal and staged reconstruction. Antibiotic therapy is guided by microbiological cultures, infection classification, surgical approach, and clinical judgment when cultures are inconclusive. Empirical broad-spectrum antibiotics are routinely initiated following DAIR or revision surgery until pathogen identification is confirmed through culture, sonication, or molecular diagnostics, and vancomycin is frequently selected at this stage due to its broad activity against Gram-positive organisms.

Vancomycin is a tricyclic glycopeptide antibiotic that inhibits bacterial cell wall synthesis. It binds specifically to the D-alanyl-D-alanine terminal of peptidoglycan precursors, preventing polymerization of cell wall components [9, 10]. Its antimicrobial spectrum includes staphylococci, such as methicillin-resistant Staphylococcus aureus (MRSA) and coagulase-negative staphylococci (CoNS), as well as enterococci. Because oral absorption is poor, vancomycin is administered intravenously [5]. The drug has approximately 55% plasma protein binding, a half-life of 4–6 hours, and reaches steady-state concentrations within about two days. It is not metabolized and is primarily eliminated via renal glomerular filtration.

Therapeutic monitoring relies on measuring trough serum concentrations immediately before the next dose, with a target range of 15–20 mg/L according to local protocols based on Swedish national guidelines [5]. In patients with normal renal function, treatment typically begins with a loading dose of 30 mg/kg (often 2 g), followed by 1 g every 8 hours. Dosing adjustments are subsequently made based on measured trough levels, with changes in dose and interval used to maintain concentrations within the therapeutic range [10].

In addition to systemic therapy, vancomycin is also commonly incorporated into antibiotic-loaded bone cement (ALBC) during revision surgery. In one-stage exchanges and in the second stage of two-stage procedures, definitive implants are frequently fixed using vancomycin-containing cement. In the first stage of two-stage revisions, spacers—either articulating or non-articulating—are often constructed using antibiotic-loaded cement. This results in simultaneous systemic and local exposure to vancomycin in patients with PJI.

Patients with PJI are typically elderly and have multiple comorbidities, yet relatively little evidence exists regarding how reliably systemic vancomycin concentrations remain within the therapeutic range in this population [11]. Moreover, the combined effect of intravenous vancomycin administration and local release from bone cement on serum trough concentrations has not been thoroughly investigated.

Accordingly, the primary objectives of this study were (1) to evaluate whether serum vancomycin concentrations in PJI patients fall within the recommended therapeutic range, and (2) to determine the number of trough measurements and dose adjustments required during standard treatment. Secondary objectives included analysis of correlations between vancomycin trough levels and serum creatinine, BMI, age, and sex, as well as assessment of whether additional exposure from vancomycin-loaded bone cement influences systemic vancomycin concentrations in patients receiving intravenous therapy.

Materials and Methods

Study design and patient selection

We conducted an observational, longitudinal cohort study at a single tertiary referral center, including patients who received intravenous vancomycin for hip or knee PJI between 23 November 2017 and 4 August 2023. The inclusion period was defined based on a major update to the electronic medical record medication module in

October 2017, which enabled reliable continuous recording of vancomycin dosing and dosing intervals from that point onward.

Using the local arthroplasty registry, 158 surgically treated PJI patients who had received IV vancomycin were initially identified. After applying inclusion criteria and excluding cases mainly due to prior vancomycin exposure and incomplete or erroneous documentation, the final study cohort consisted of 108 patients. None of these patients developed bacteremia following the index surgical procedure **(Figure 1).**

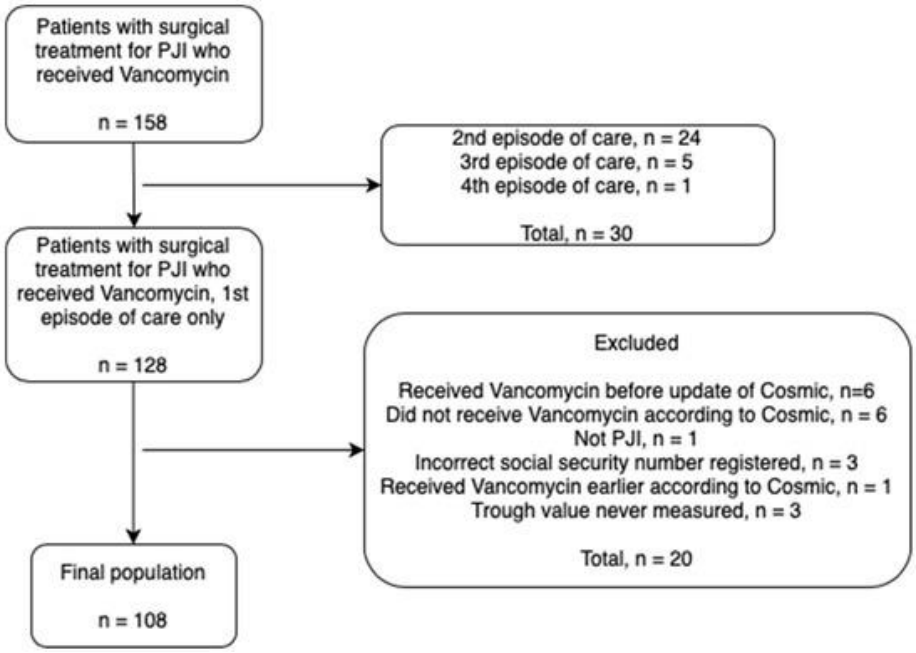

Figure 1. Study cohort flow diagram. Cosmic refers to the electronic medical record platform used at our institution.

Antibiotic-loaded bone cement

At our institution, the most frequently used antibiotic-loaded bone cement is Copal G+V® (Heraeus, Wehrheim, Germany). Each 43 g package of cement powder contains 2 g vancomycin and 0.5 g gentamicin. The required number of cement packs per patient depends on the prosthetic reconstruction. For cemented procedures, a minimum of two packs is generally used—one for the acetabular component and one for a standard primary femoral component. In more extensive revision cases, particularly those involving long-stem femoral implants, the number may increase to 4 packs, including 1 for the acetabulum and up to 3 for the femoral reconstruction.

Variables and data collection

Clinical and demographic variables—age, sex, BMI, date of surgery, involved joint (hip or knee), revision category, and ALBC use at the index procedure—were collected from the local arthroplasty register. To complement this, additional information was retrieved from electronic health records and merged with the registry dataset. These included the timing of vancomycin initiation, the daily vancomycin dose, the number of trough-level assessments, measured vancomycin serum concentrations, details of dose adjustments, and overall treatment duration. Laboratory data were likewise obtained from the medical charts and comprised eGFR, serum creatinine, CRP, ESR, leukocyte count, and cystatin C.

Vancomycin concentration measurements

Vancomycin therapy necessitates close therapeutic monitoring to maintain serum levels within the recommended 15–20 mg/L range [12, 13]. At Uppsala University Hospital, institutional protocol dictates that trough concentrations are obtained immediately before the third dose, along with assessment of eGFR. Monitoring is continued until pharmacokinetic stability is reached, defined as three consecutive trough measurements within the target range without any changes to dose or dosing interval. Although local guidelines permit extending the

monitoring interval to every 7 days once stability has been achieved, trough sampling is often performed more frequently in routine practice due to concerns about potential deviation from the therapeutic window [12].

Ethics

The research adhered to the ethical principles described in the Declaration of Helsinki. The Regional Ethical Review Board in Uppsala, Sweden, gave its initial approval (Dnr 2016/214; 15 June, 2016). A subsequent amendment, which allowed review of medical records for the specified cohort, received clearance from the Swedish Ethical Review Authority (Dnr 2024-02581-02; 26 April, 2024).

Statistics

All data files were stored securely on the Uppsala University Hospital intranet, with an additional layer of password protection. Statistical analyses were performed after importing the dataset into R (version 4.3.2; 2023-10-31) and RStudio (version 2023.09.1+494). Descriptive results for quantitative variables were presented using tables, boxplots, and bar charts. Associations between out-of-range vancomycin trough measurements and BMI or age were evaluated using Spearman's rank correlation coefficient. The same approach was used to examine the relationship between the initial vancomycin trough concentration and serum creatinine. Group comparisons, including sex-based differences and differences between patients treated with or without ALBC regarding out-of-range trough levels, were assessed using the Wilcoxon rank-sum test. Given that most variables were not normally distributed, non-parametric statistical methods were applied throughout. A two-sided P-value < 0.05 was considered statistically significant.

Results and Discussion

Description of the study population

The study population consisted of 108 individuals, with a median age of 71 years and a median BMI of 27.4 **(Table 1).** Most infections involved hip prostheses, representing 73% of cases. Before vancomycin therapy, the most frequently performed revision procedure was debridement with implant retention (DAIR), performed in 54% of patients.

Use of antibiotic-loaded bone cement containing vancomycin (Copal G+V®) was documented in 42 patients (39%). In contrast, 61% did not receive any cement augmentation. This group mainly included patients managed with DAIR, where only modular components were exchanged, as well as cases in which uncemented prosthetic components were used during revision surgery.

During the clinical course, 22 patients were discharged while still receiving intravenous vancomycin, with therapy continued at their referring institutions. The median duration of intravenous treatment was 8 days, ranging from 1 to 24 days.

Microbiological assessment of intraoperative tissue cultures showed that *Staphylococcus epidermidis* was the predominant pathogen.

Table 1. Summary of baseline features of the study cohort. 1 Median (IQR); n (%).

Characteristic	Value (n = 108)
Age[1]	71 (63, 79)
Sex	
• Female	44 (41%)
• Male	64 (59%)
BMI[1]	27.4 (25.1, 31.1)
• Missing data	7
Affected Joint	
• Hip	79 (73%)
• Knee	29 (27%)
Surgical procedure before vancomycin use	
• Alternative surgical procedure	2 (1.9%)
• DAIR	58 (54%)
• Single-stage exchange	19 (18%)
• Two-stage exchange (stage 1)	24 (22%)

• Two-stage exchange (stage 2)	3 (2.8%)
• Open biopsy	1 (0.9%)
• Missing data	1
Bone cement usage	
• Containing vancomycin	42 (39%)
• No cement applied	66 61%)

Trough concentrations

A dataset of 791 vancomycin trough measurements was evaluated. Of these readings, 58.2% were within the intended therapeutic window, while 18.5% fell below the target limits and 23.4% exceeded them **(Figures 2 and 3).** In the overall cohort, 69% of patients had at least one supratherapeutic trough value, and 66% had at least one subtherapeutic trough value. Age showed a positive relationship with the proportion of elevated trough concentrations (rho = 0.35; P < 0.001); **(Figure 4).** Likewise, higher baseline serum creatinine levels were associated with increased vancomycin trough concentrations (rho = 0.34; P < 0.001); **(Figure 5).** No meaningful association was detected between BMI and out-of-range trough levels. Moreover, initial trough concentrations did not differ significantly between patients treated with vancomycin-loaded ALBC and those without this intervention (P = 0.84). Mean trough levels were 16.39 (SD = 0.19) in the ALBC group and 16.12 (SD = 0.19) in the non-ALBC group.

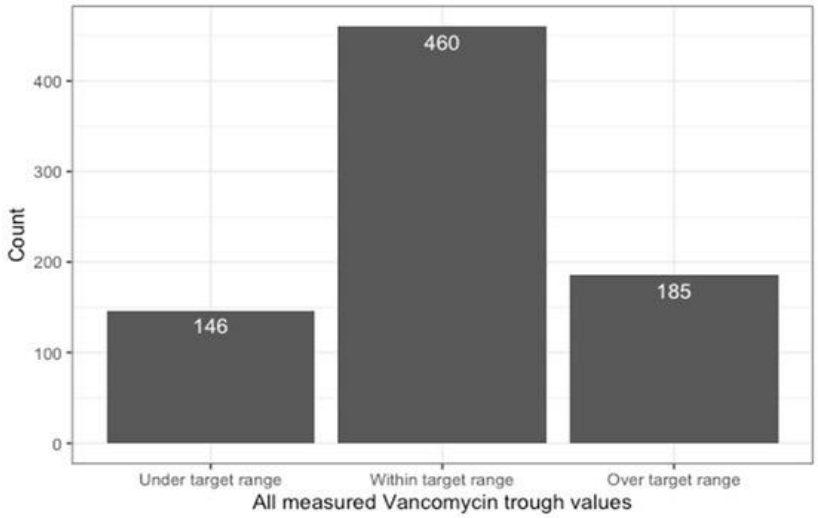

Figure 2. Overview of all vancomycin trough concentration measurements across the study population.

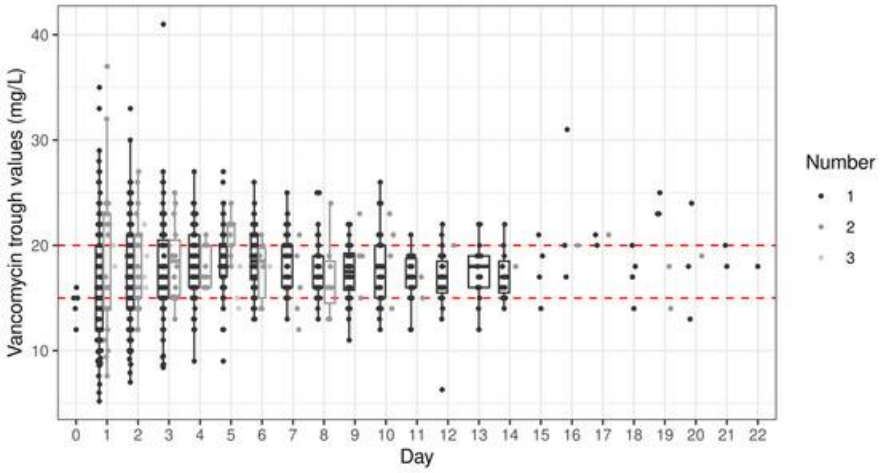

Figure 3. Vancomycin trough levels (mg/L) plotted by day after the index procedure. In cases where more than one sample was taken on the same day (for example, day 1), individual readings are labeled 1–3 in the legend and displayed in different shades of gray. The red reference lines mark the therapeutic target interval, and values plotted beyond the whiskers represent outliers.

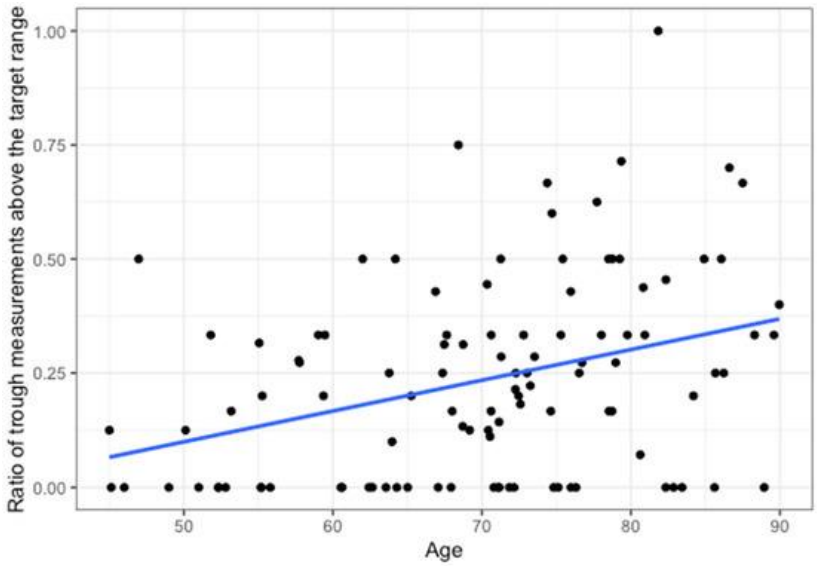

Figure 4. Association between patient age and the fraction of vancomycin trough values above the therapeutic range (Rho = 0.35, P < 0.001). The blue curve depicts the linear regression fit.

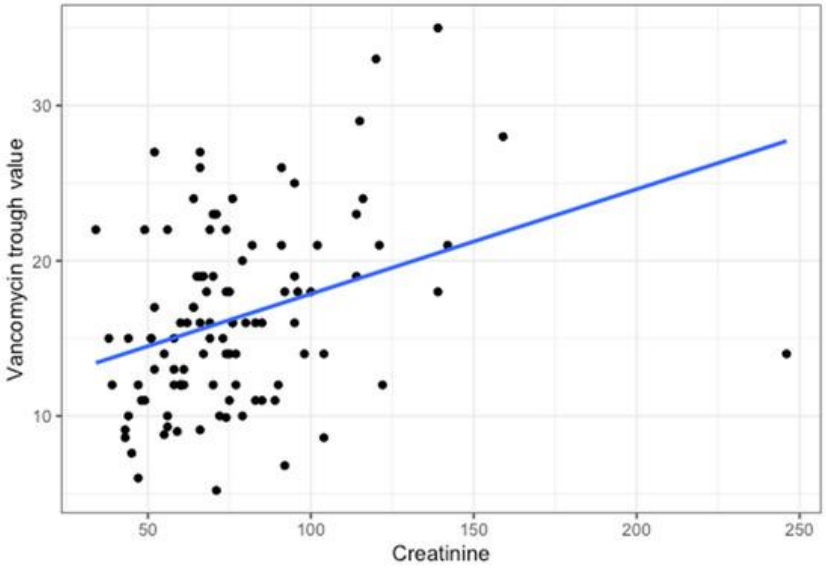

Figure 5. Association between serum creatinine (µmol/L) and the first recorded vancomycin trough concentration (µmol/L) obtained on the same day (Rho = 0.34, P < 0.001). The blue line shows the linear regression fit.

Dose changes

Vancomycin dosing was often adjusted during therapy, with only 29% of patients remaining on the initial standard regimen without modification **(Table 2).** On average, patients underwent 1.2 dose changes each.

Table 2. Frequency of dose modifications among patients.

Number of dose changes	n (%)
0	31 (29%)
1	44 (41%)
2	22 (20%)
3	5 (4.6%)
4	(3.7%)

5	2(1.9%)

Renal function

Renal function was assessed in all patients using repeated creatinine measurements over time. Values above 150 µmol/L were mainly observed during the first 6 days of vancomycin administration, whereas similarly elevated levels became uncommon thereafter **(Figure 6).** Given the low number of readings above the reference limit, a multivariable regression analysis to explore determinants of elevated creatinine could not be conducted.

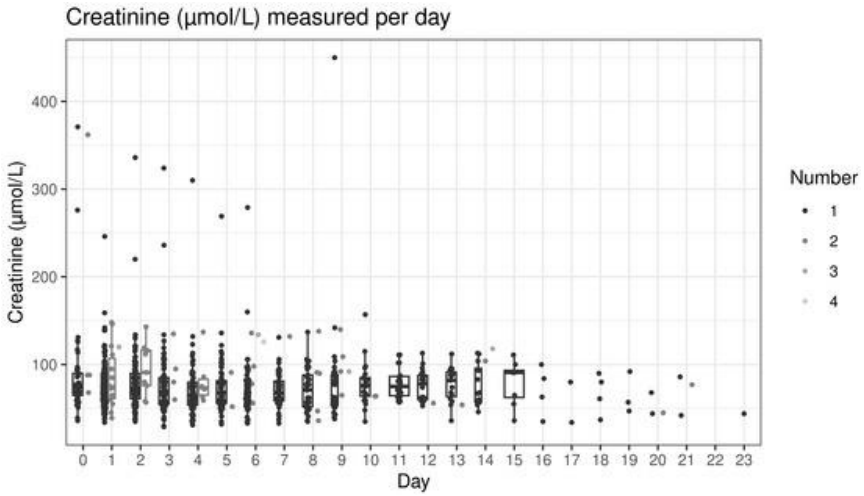

Figure 6. Creatinine (µmol/L) measurements were recorded across days after the index procedure. In instances where multiple samples were taken on the same day (e.g., day 1), these are labeled 1-4 in the legend and visualized with varying gray tones.

Treatment costs

We performed a cost estimation for vancomycin therapy in patients with PJI. In the regional healthcare setting, vancomycin powder vials (0.5 g and 1 g) are priced at SEK 66 and SEK 88, respectively, not including dispensing charges. One ready-to-administer dose is estimated to cost SEK 220, while each trough concentration test costs SEK 94. Costs related to nursing and pharmacy workload, protective equipment, consumables, and vascular access were excluded from the calculations. Using this simplified model, an 8-day treatment course with 1 g of vancomycin administered three times daily results in a drug cost of SEK 5282, with an additional SEK 754 for monitoring. When inpatient stay costs are included, the total estimated expenditure is SEK 86,684, roughly equivalent to USD 8,000 [14].

Vancomycin is widely used in the management of PJI due to its activity against Gram-positive pathogens, including MRSA. In this indication, administration is primarily intravenous, although adjunctive local delivery strategies—such as vancomycin-impregnated bone cement—may also be used to obtain high concentrations at the infection site.

In our cohort, trough levels frequently fell outside the desired therapeutic window, and most patients required a dose adjustment; approximately 10% needed 3 or more adjustments. Higher age and impaired renal function (reduced eGFR) were associated with an increased likelihood of supratherapeutic concentrations. By contrast, concomitant exposure to systemic and locally delivered vancomycin did not result in higher serum trough levels than systemic therapy alone.

Limitations and strengths

Because this was a retrospective study based on electronic health record review, missing data, incomplete documentation, and occasional recording errors were expected. Consequently, around one-third of all eligible cases were excluded due to insufficient or incorrect information. Even within the final dataset, several clinically relevant variables could not be fully assessed, including the incidence of common adverse reactions associated with vancomycin.

Rapid administration of vancomycin may lead to infusion-related reactions, including phlebitis, histamine-mediated pseudoallergic reactions, and upper-body flushing (“red-person syndrome”). More frequently reported

adverse effects (≥ 1/100 to <1/10) include hypotension, dyspnea, stridor, pruritus, urticaria, skin rash, mucosal irritation, and impaired renal function. Less common events (≥ 1/1000 to < 1/100) include transient or permanent hearing loss [9]. Nephrotoxicity remains a key safety concern due to renal elimination and potential kidney injury. Published incidence rates vary considerably; Filippone *et al*. [15] reported values ranging from 0% to more than 40%. Recognized risk factors include elevated trough concentrations, obesity, pre-existing renal dysfunction, severe illness, and concomitant nephrotoxic agents. Horey *et al*. [16] demonstrated a direct association between increasing vancomycin trough levels and higher nephrotoxicity risk. Evidence on ototoxicity is inconsistent: Humphrey *et al*. [17] observed an incidence of approximately 8% among nearly 100 patients, mostly with mild to moderate hearing impairment, whereas Forouzesh *et al*. [18] reported a 12% incidence, with all affected patients older than 52 years, suggesting age as a potential risk factor. Nevertheless, the Swedish Medical Products Agency classifies ototoxicity as an uncommon adverse effect (≥ 1/1000 to < 1/100) [9].

No severe adverse outcomes such as profound hypotension, acute renal failure, or clinically relevant hearing loss were documented in our cohort. Longitudinal creatinine trends also did not suggest any episodes of acute kidney failure. However, the absence of documentation of mild adverse events cannot be interpreted as evidence of their nonoccurrence; therefore, these outcomes were not formally analyzed.

As the dataset was derived from a single institutional registry and local electronic records, an additional limitation is the inability to track patients who were transferred back to their referring hospitals while still receiving vancomycin therapy. For these patients, post-transfer trough levels and total treatment duration were not available, and follow-up was censored at the time of transfer.

Being a single-center study limits generalisability. Institutional protocols, clinical routines, and resource availability may have influenced treatment patterns and outcomes, and these factors may not be directly applicable to other healthcare settings. This should be considered when interpreting the findings.

Focusing exclusively on trough concentrations is debatable. Vancomycin requires close therapeutic monitoring to balance efficacy and toxicity, with recommended trough targets of 15–20 mg/L [12, 13]. At our institution, trough levels and estimated glomerular filtration rate are routinely monitored before every third dose [12]. However, Álvarez *et al*. [18] have proposed that the area under the curve to MIC ratio (AUC/MIC) provides a more accurate pharmacokinetic target. Despite this, AUC/MIC-based monitoring is more complex and resource-intensive, whereas trough-based monitoring is simpler and remains the standard practice locally, although its limitations are acknowledged [19, 20]. Recent work by Chen *et al*. [20] using machine learning suggests that daily dose and GFR alone may accurately predict vancomycin trough concentrations, potentially simplifying dosing strategies without requiring AUC/MIC estimation.

The study also has notable strengths. Vancomycin is widely recommended for infections caused by oxacillin-resistant staphylococci and enterococci, and is an accepted alternative in streptococcal PJI according to international guidelines and consensus statements [21, 22]. Thus, its use in our cohort reflects established clinical practice. Monitoring routines used in this study align with national recommendations [23, 24], although newer Infectious Diseases Society of America guidelines advocate AUC/MIC-based monitoring to reduce nephrotoxicity and improve efficacy [25]. Finally, all PJI diagnoses were made according to strict EBJIS criteria, and all patients had infection confirmed by at least 2 positive intraoperative cultures obtained during index surgery.

Accord and discord with previous studies

The observation that a considerable proportion of patients treated with vancomycin received concentrations outside the therapeutic window, despite strict compliance with local and national dosing recommendations, is not unique. This issue has been particularly explored in obese populations, where a systematic review has shown that even with adjusted or extensively modified dosing strategies, a substantial number of patients still present with initial trough levels outside the desired range [26]. Furthermore, vancomycin trough concentrations demonstrate only a moderate relationship with AUC, with an R^2 of 0.51 reported in one study [27]. Nevertheless, AUC- or AUC/MIC-based monitoring has been proposed as a more precise approach for therapeutic drug monitoring [18]. The associations we observed between age, serum creatinine, and vancomycin trough concentrations are consistent with previous literature. These variables have also been incorporated jointly into dosing nomograms to improve the selection of initial vancomycin regimens [28].

We did not identify any local or systemic adverse effects associated with locally administered vancomycin in ALBC, consistent with earlier studies [29, 30]. In the investigation by Kendoff *et al*. [29], 20 patients received industrially produced Copal G+V® bone cement during hip arthroplasty revision for established PJI. The highest

reported systemic vancomycin concentration in that study was 0.74 mcg/mL, well below therapeutic levels achieved with systemic therapy. Similarly, Oe *et al*. [30] reported peak serum concentrations up to 3 mcg/mL, which also remained far below therapeutic thresholds. These findings are consistent with our observation that adjunctive local vancomycin delivery via ALBC does not lead to excessive systemic trough concentrations in patients already receiving intravenous vancomycin for PJI. To our knowledge, no formal analysis correlating local and systemic vancomycin levels after ALBC use has been published. However, some studies have evaluated vancomycin concentrations in wound drainage fluid and serum [29]. It has also been demonstrated that vancomycin levels in peri-spacer tissue correlate with the quantity of antibiotic-loaded cement used in spacer fabrication [31].

Although our study was not designed to evaluate economic outcomes, the observed frequency of trough monitoring, repeated dose adjustments, and prolonged hospitalization associated with intravenous vancomycin prompted an exploratory cost consideration. Using a simplified calculation, we estimated that an 8-day course of 1 g vancomycin administered three times daily results in total costs of approximately SEK 86,000, including inpatient care. In comparison, dalbavancin is considerably more expensive per administered dose, at SEK 21,564 per ready-to-use dose. Rappo *et al*. [32] demonstrated that two doses of 1500 mg dalbavancin, administered on days 1 and 8, achieved outcomes comparable to those of 4–6 weeks of intravenous vancomycin therapy in patients with osteomyelitis. This regimen may reduce or eliminate the need for hospitalization solely for intravenous vancomycin administration. However, the referenced trial included only 80 patients, used a 7:1 randomization in favor of dalbavancin, and involved osteomyelitis rather than PJI, limiting its direct applicability. To date, no large randomized controlled trials have evaluated dalbavancin in this context. Despite this, dalbavancin has been used selectively in PJI cases at our institution, enabling earlier discharge following surgical intervention and potentially shortening hospital stay. In addition, unlike vancomycin, dalbavancin does not require intensive therapeutic drug monitoring; the Swedish Society of Infectious Diseases recommends monitoring only when available, with a single sample suggested after 3–5 weeks, depending on eGFR [5]. Overall, substituting a 3–5-day inpatient vancomycin regimen with dalbavancin treatment would result in estimated costs of SEK 51,807-73,371, excluding monitoring expenses [12], and may therefore offer both economic and logistical advantages.

Daptomycin represents another intravenous alternative for PJI management. Its once-daily dosing allows outpatient administration and potential hospital discharge. However, in the Swedish healthcare context, its implementation requires considerable logistical coordination, including agreements with municipal home care services to manage drug administration, vascular access care, and blood sampling. In addition, routine creatine kinase monitoring is necessary to detect potential rhabdomyolysis [5]. Overall, while daptomycin facilitates outpatient therapy, its practical implementation appears more complex from an organizational standpoint

Conclusion

A substantial proportion of vancomycin trough levels in patients with PJI did not fall within the intended therapeutic window, with just over half remaining outside the target range. Increasing age and higher baseline creatinine were both associated with progressively higher trough concentrations. Given the frequent need for dose modifications and prolonged treatment courses, alternative therapies such as dalbavancin may be worth considering to improve treatment efficiency and potentially reduce hospital stay.

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Conflict of Interest: N.P.H. has received institutional support, along with honoraria and lecture fees, from Waldemar Link (Hamburg, Germany), Zimmer Biomet (Warsaw, IN, USA), DePuy Synthes (Stockholm, Sweden), and Heraeus Medical (Wehrheim, Germany). Additionally, he has a licensing arrangement with Waldemar Link (Hamburg, Germany). The remaining co-authors have no competing interests to declare.

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Ethics Statement: This investigation adhered to the ethical guidelines of the Declaration of Helsinki. The first approval was issued by the Regional Ethical Review Board in Uppsala, Sweden (reference number 2016/214,

approved 15 June, 2016). A later approval was then secured from the Swedish Ethical Review Authority (reference number 2024-02581-02, approved 26 April, 2024).
In line with the Ethical Review Board's decision, this retrospective observational study was granted a waiver of informed consent.

References

1. Lindgren V, Gordon M, Wretenberg P, Kärrholm J, Garellick G. Deep infection after total hip replacement: a method for national incidence surveillance. Infect Control Hosp Epidemiol. 2014;35:1491-6.
2. Thompson O, W-Dahl A, Lindgren V, Gordon M, Robertsson O, Stefánsdóttir A. Similar periprosthetic joint infection rates after and before a national infection control program: a study of 45,438 primary total knee arthroplasties. Acta Orthop. 2022;93:3-10.
3. Wildeman P, Rolfson O, Wretenberg P, Nåtman J, Gordon M, Söderquist B, et al. Effect of a national infection control programme in Sweden on prosthetic joint infection incidence following primary total hip arthroplasty: a cohort study. BMJ Open. 2024;14:e076576.
4. Dale H, Fenstad AM, Hallan G, Overgaard S, Pedersen AB, Hailer NP, et al. Increasing risk of revision due to infection after primary total hip arthroplasty: results from the Nordic Arthroplasty Register Association. Acta Orthop. 2023;94:307-15.
5. Sörstedt E. Vårdprogram för led- och skelettinfektioner. Rev. 2023. Available from: https://www.google.com.ua/url?sa=i&url=https%3A%2F%2Finfektion.net%2Fwp-content%2Fuploads%2F2023%2F07%2Fvardprogram_led_och_skelettinfektioner_2023_07_11.pdf&psig=AOvVaw0RVWcpDJcUYQfNIWk0KdO4&ust=1734486365507000&source=images&cd=vfe&opi=89978449&ved=0CAYQrpoMahcKEwiwsICy162KAxUAAAAAHQAAAAAQBA (accessed on 15 December 2024).
6. Aboltins CA, Antoci V, Bhattacharyya S, Cross M, Ducheyne P, Freiberg AA, et al. Hip and Knee Section, Prevention, Prosthesis Factors: Proceedings of International Consensus on Orthopedic Infections. J Arthroplasty. 2019;34:S309-20.
7. McNally M, Sousa R, Wouthuyzen-Bakker M, Chen AF, Soriano A, Vogely HC, et al. The EBJIS definition of periprosthetic joint infection: a practical guide for clinicians. Bone Joint J. 2021;103-B:18-25.
8. Zimmerli W. Clinical presentation and treatment of orthopaedic implant-associated infection. J Intern Med. 2014;276:111-9.
9. Vancomycin Viatris. FASS Vårdpersonal. Available from: https://www.fass.se/LIF/product?userType=0&nplId=20220328000023#pharmacodynamic
10. Antibiotika—Glykopeptider. Internetmedicin. Available from: https://www.internetmedicin.se/infektionssjukdomar/antibiotika-glykopeptider
11. Persson A, Sköldenberg O, Mohaddes M, Eisler T, Gordon M. Increased mortality after total hip prosthetic joint infection is mainly caused by the comorbidities rather than the infection itself. Acta Orthop. 2023;94:484-9.
12. Vancomycin Concentration Monitoring—Department of Orthopedics.pdf. Available from: https://www.google.com.ua/url?sa=t&source=web&rct=j&opi=89978449&url=https://orto.nu/books/pms/2022/Region%2520Uppsala/Vancomycinkoncentrations%2520%25C3%25B6vervakning%2520-%2520Vo%2520Ortopedi.pdf&ved=2ahUKEwjb8975162KAxUmMtAFHUgNI5cQFnoECB4QAQ&usg=AOvVaw1Rcvuj6aFM_1456SYWuGlz (accessed on 15 December 2024). [in German]
13. Álvarez R, López Cortés LE, Molina J, Cisneros JM, Pachón J. Optimizing the clinical use of vancomycin. Antimicrob Agents Chemother. 2016;60:2601-9.
14. Parliden JN. Pris- och produktkatalog 2024—Akademiska Sjukhuset, Lasarettet i Enköping samt Primärvård och Habilitering Region Uppsala. Uppsala: Region Uppsala; 2024.
15. Filippone E, Kraft W, Farber J. The nephrotoxicity of vancomycin. Clin Pharmacol Ther. 2017;102:459-69.
16. Horey A, Mergenhagen KA, Mattappallil A. The relationship of nephrotoxicity to vancomycin trough serum concentrations in a veteran's population: a retrospective analysis. Ann Pharmacother. 2012;46:1477-83.
17. Humphrey C, Veve MP, Walker B, Shorman MA. Long-term vancomycin use had low risk of ototoxicity. PLoS One. 2019;14:e0224561.

18. Forouzesh A, Moise PA, Sakoulas G. Vancomycin ototoxicity: a reevaluation in an era of increasing doses. Antimicrob Agents Chemother. 2009;53:483-6.
19. Cusumano JA, Klinker KP, Huttner A, Luther MK, Roberts JA, LaPlante KL. Towards precision medicine: therapeutic drug monitoring-guided dosing of vancomycin and β-lactam antibiotics to maximize effectiveness and minimize toxicity. Am J Health Syst Pharm. 2020;77:1104-12.
20. Chen Y, Lin X, Huang C, Wu W, Lin W, Chen S, et al. Vancomycin trough concentration in adult patients with periprosthetic joint infection: a machine learning-based covariate model. Br J Clin Pharmacol. 2024;90:2188-99.
21. Osmon DR, Berbari EF, Berendt AR, Lew D, Zimmerli W, Steckelberg JM, et al. Diagnosis and management of prosthetic joint infection: clinical practice guidelines by the Infectious Diseases Society of America. Clin Infect Dis. 2013;56:e1-25.
22. Saeed K, McLaren AC, Schwarz EM, Antoci V, Arnold WV, Chen AF, et al. 2018 international consensus meeting on musculoskeletal infection: summary from the biofilm workgroup and consensus on biofilm related musculoskeletal infections. J Orthop Res. 2019;37:1007-17.
23. Bremell D, Edlund C, Edquist P, Eliasson E, Giske C, Hanberger H, et al. Antibiotikakompendium. Reference group for antibiotics issues RAF. 2022. Available from: https://www.sls.se/globalassets/raf/ovriga-dokument/raf-antibiotikakompendium.pdf (accessed on 27 February 2024)
24. Rybak MJ, Lomaestro BM, Rotschafer JC, Moellering RC Jr, Craig WA, Billeter M, et al. Vancomycin therapeutic guidelines: a summary of consensus recommendations from the Infectious Diseases Society of America, the American Society of Health-System Pharmacists, and the Society of Infectious Diseases Pharmacists. Clin Infect Dis. 2009;49:325-7.
25. Rybak MJ, Le J, Lodise TP, Levine DP, Bradley JS, Liu C, et al. Therapeutic monitoring of vancomycin for serious methicillin-resistant Staphylococcus aureus infections: a revised consensus guideline and review by the American Society of Health-System Pharmacists, the Infectious Diseases Society of America, the Pediatric Infectious Diseases Society, and the Society of Infectious Diseases Pharmacists. Am J Health Syst Pharm. 2020;77:835-64.
26. Durand C, Bylo M, Howard B, Belliveau P. Vancomycin dosing in obese patients: special considerations and novel dosing strategies. Ann Pharmacother. 2018;52:580-90.
27. Bel Kamel A, Bourguignon L, Marcos M, Ducher M, Goutelle S. Is trough concentration of vancomycin predictive of the area under the curve? A clinical study in elderly patients. Ther Drug Monit. 2017;39:83-7.
28. Thalakada R, Legal M, Lau TTY, Luey T, Batterink J, Ensom MHH. Development and validation of a novel vancomycin dosing nomogram for achieving high-target trough levels at 2 Canadian teaching hospitals. Can J Hosp Pharm. 2012;65:180-7.
29. Kendoff DO, Gehrke T, Stangenberg P, Frommelt L, Bösebeck H. Bioavailability of gentamicin and vancomycin released from an antibiotic containing bone cement in patients undergoing a septic one-stage total hip arthroplasty revision: a monocentric open clinical trial. Hip Int. 2016;26:90-6.
30. Oe K, Iida H, Ueda N, Nakamura T, Okamoto N, Ueda Y. In vivo serum concentration of vancomycin in antibiotic-loaded acrylic cement for the treatment and prevention of periprosthetic hip infection. J Orthop Sci. 2017;22:710-4.
31. Klinder A, Zaatreh S, Ellenrieder M, Redanz S, Podbielski A, Reichel T, et al. Antibiotics release from cement spacers used for two-stage treatment of implant-associated infections after total joint arthroplasty. J Biomed Mater Res B Appl Biomater. 2019;107:1587-97.
32. Rappo U, Puttagunta S, Shevchenko V, Shevchenko A, Jandourek A, Gonzalez PL, et al. Dalbavancin for the treatment of osteomyelitis in adult patients: a randomized clinical trial of efficacy and safety. Open Forum Infect Dis. 2019;6:ofy331.