Low incidence of acute kidney injury with combined intravenous and topical antibiotic infusions in periprosthetic joint infection after total knee arthroplasty

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Aims

This study aimed to assess the risk of acute kidney injury (AKI) associated with combined intravenous (IV) and topical antibiotic therapy in patients undergoing treatment for periprosthetic joint infections (PJIs) following total knee arthroplasty (TKA), utilizing the Kidney Disease: Improving Global Outcomes (KDIGO) criteria for classification.

Methods

We conducted a retrospective analysis of 162 knees (162 patients) that received treatment for PJI post-TKA with combined IV and topical antibiotic infusions at a single academic hospital from 1 January 2010 to 31 December 2022. The incidence of AKI was evaluated using the KDIGO criteria, focussing on the identification of significant predictors and the temporal pattern of AKI development.

Results

AKI was identified in 9.26% (15/162) of the cohort, predominantly presenting as stage 1 AKI, which was transient in nature and resolved prior to discharge. The analysis highlighted moderate anaemia and lower baseline serum creatinine levels as significant predictors for the development of AKI. Notably, the study found no instances of severe complications such as wound dehiscence, skin erosion, or the need for haemodialysis following treatment.

Conclusion

The findings suggest that the combined use of IV and topical antibiotic therapy in the management of PJIs post-TKA is associated with a low incidence of primarily transient stage 1 AKI. This indicates a potentially favourable renal safety profile, advocating for further research to confirm these outcomes and potentially influence treatment protocols in PJI management.

Article focus

- Evaluating the incidence and predictors of acute kidney injury (AKI) in patients treated with combined intravenous (IV) and topical antibiotic therapy for PJIs post-total knee arthroplasty (TKA).
- Understanding the renal safety of combined antibiotic therapy in the context of PJI management.
- Analyzing the implications of AKI development on postoperative outcomes and treatment efficacy.

Key messages

- The incidence of AKI among patients treated for PJIs post-TKA with combined antibiotic therapy is relatively low, primarily involving transient stage 1 AKI.

- Factors such as moderate anaemia and lower baseline serum creatinine levels significantly predict AKI development in this patient population.
- The study's outcomes support the consideration of combined antibiotic therapy as a renal-safe alternative in the management of PJIs, highlighting its potential benefits over traditional methods such as antibiotic-loaded bone cement.

Strengths and limitations

- This investigation is among the pioneering studies to examine the renal consequences of combined IV and topical antibiotic therapy in treating PJIs, offering critical insights into its safety and efficacy.
- The retrospective design and single-centre nature of the study may limit the generalizability of the findings across different populations and healthcare settings.
- While the study meticulously used Kidney Disease: Improving Global Outcomes (KDIGO) criteria for AKI assessment, enhancing the reliability of its results, it did not account for all potential confounding factors, such as preoperative medication and intraoperative anaesthetic use, which may have influenced outcomes.

Introduction

The global incidence of periprosthetic joint infections (PJIs) following primary total knee arthroplasty (TKA) ranges from 1% to 4%, with revision procedures presenting a slightly higher rate of 2% to 4%. Specifically, PJIs are the culprit in 16.8% of knee revision arthroplasties.[1,2] As the frequency of TKA escalates, a corresponding rise in PJI-related revisions is projected, potentially increasing by 170% by the year 2030.[3] The economic and clinical consequences of knee PJIs are considerable. In the USA, the financial burden attributed to PJIs was approximately $1 billion in 2017, with expectations to approach $2 billion by 2030.[4] Moreover, PJI can cause serious health issues, increase mortality, and inflate healthcare costs due to longer hospital stays and more complications.[5]

PJIs are notably difficult to treat due to limited blood supply to the bone and the protective nature of biofilms, which significantly increase antibiotic resistance. The concentrations of antibiotics needed to disrupt biofilms far exceed those that kill free-floating bacteria, making systemic delivery via an intravenous (IV) route problematic due to toxicity risks.[6] Topical delivery methods, such as antibiotic beads, sponges, antibiotic-loaded bone cement (ALBC), intraosseous routes, and direct infusion, are preferred for the benefit of delivering high doses of antimicrobials to the site of infection directly.[7,8] However, it may still inadvertently result in systemic absorption and increased toxicity risk, especially when paired with IV antibiotics.[9] It is noted that postoperative renal complications associated with ALBC are not uncommon, with instances of acute kidney injury (AKI) following spacer implantation reported in up to nearly half of patients in some studies.[10–12]

Our practice of combining intra-articular antibiotic infusions with debridement, antibiotics and implant retention (DAIR) protocols and single-stage revisions for knee PJIs has shown efficacy, especially in complex cases such as culture-negative infections, polymicrobial infections, or those with prior failed surgeries. This method has led to promising mid- to long-term outcomes and high infection-free recovery rates, highlighting its value in treating challenging PJIs.[7,13–16] However, the cumulative impact of such topical regimens when used in tandem with IV antibiotics on renal function during the management of infected TKA has not been thoroughly examined, as evidenced by the scarcity of related studies in the literature.

The main goal of our research is to investigate the frequency of AKI in patients undergoing treatment for knee PJI at our institution, where both DAIR and single-stage revision surgeries are enhanced by the administration of intra-articular antibiotic infusions. By conducting this analysis, we seek to enrich the current understanding of how these localized antibiotic strategies impact renal health in the context of managing knee PJI.

Methods

Approved by the ethics committee of First Affiliated Hospital of Xinjiang Medical University, a retrospective review of patient records at this hospital from 1 January 2010 to 31 December 2022 was conducted. The review focused on individuals who underwent PJI treatment involving DAIR or single-stage revision complemented by antibiotic infusion for infected TKA. Inclusion criteria were based on the Musculoskeletal Infection Society's 2011 guidelines for diagnosing PJI of the knee.[17] We excluded cases of bilateral knee PJI, concurrent PJI involving the knee, and other joints such as the hip, fungal PJI, or mycobacterial PJI. Cases where patients underwent amputation subsequent to PJI post-TKA were also omitted.

A total of 162 knees treated with antibiotics infusion were included. The median age at the time of index surgery was 69 years (IQR 63.2 to 74), the mean BMI was recorded at 25.85 kg/m^2 (SD 3.74), and males represented 32.10% (n = 52) of the patient population. Overall, 44 patients received DAIR and 118 underwent single-stage revision surgery. Of these, seven patients (4.32%) had a history of chronic kidney disease (CKD). Patients who experienced AKI had a higher incidence of moderate anaemia, lower baseline serum creatinine levels, and BMI ≥ 30 kg/m^2 (Table I).

As previously outlined, the broad indications and minimal contraindications for DAIR or single-stage revision have been established.[20] For surgical intervention, a midline incision paired with a medial parapatellar approach is standard. Removal of pre-existing skin scars and sinus tracts is performed to reduce infection sources. Intraoperative collection and analysis of joint fluid are sent for culture to identify the responsible microorganisms. The cornerstone of infection control is comprehensive debridement, which includes the excision of all potentially infected bone, necrotic tissue, and non-viable fibrous tissue, along with the resection of inflamed synovium within the surgical field. Achieving a clean surgical boundary characterized by fresh, bleeding soft-tissue is essential. Chemical debridement follows, utilizing a sequential lavage with normal saline, 0.5% aqueous povidone-iodine, 3% hydrogen peroxide, and additional saline to ensure an environment inhospitable to microorganisms. During DAIR procedures, liners are routinely replaced, and a dual setup is consistently employed in all PJI cases. All knee revisions employ cemented fixation without the use of antibiotics. For DAIR procedures, antibiotics were administered

Table I. Baseline demographics.

Characteristic	Overall (n = 162)	Non-AKI (n = 147)	AKI (n = 15)	p-value
Median age, yrs (IQR)	69 (63.2 to 74)	69 (64 to 73)	75 (62.5 to 78.5)	0.176*
Sex, n (%)				0.391†
Female	110 (67.90)	98 (66.67)	12 (80)	
Male	52 (32.10)	49 (33.33)	3 (20)	
Ethnicity, n (%)				0.643†
Han	113 (69.75)	100 (68.03)	13 (86.67)	
Kazakh	11 (6.79)	10 (6.80)	1 (6.67)	
Hui	5 (3.09)	5 (3.40)	0 (0)	
Mongol	2 (1.23)	2 (1.36)	0 (0)	
Uyghur	31 (19.14)	30 (20.41)	1 (6.67)	
Mean BMI, kg/m^2 (SD)	25.85 (3.74)	25.69 (3.68)	27.47 (4.12)	0.080‡
BMI grade, n (%)				0.035†
< 30	140 (86.42)	130 (88.44)	10 (66.67)	
≥ 30	22 (13.58)	17 (11.56)	5 (33.33)	
Median CCI[18] score (IQR)	3 (2 to 3)	3 (2 to 3)	3 (2 to 3)	0.433*
ASA grade,[19] n (%)				0.475†
1	1 (0.62)	1 (0.68)	0 (0)	
2	72 (44.44)	67 (45.58)	5 (33.33)	
3	89 (54.94)	79 (53.74)	10 (66.67)	
Hypertension, n (%)				0.135†
No	89 (54.94)	84 (57.14)	5 (33.33)	
Yes	73 (45.06)	63 (42.86)	10 (66.67)	
Diabetes, n (%)				0.179†
No	130 (80.25)	120 (81.63)	10 (66.67)	
Yes	32 (19.75)	27 (18.37)	5 (33.33)	
Preoperative CKD, n (%)				0.500†
No	155 (95.68)	141 (95.92)	14 (93.33)	
Yes	7 (4.32)	6 (4.08)	1 (6.67)	
Previous surgeries, n (%)				0.430†
1	114 (70.37)	103 (70.07)	11 (73.33)	
2	42 (25.93)	39 (26.53)	3 (20.00)	
3	3 (1.85)	3 (2.04)	0 (0)	
4	3 (1.85)	2 (1.36)	1 (6.67)	
Type of surgery, n (%)				0.071†
DAIR	44 (27.16)	43 (29.25)	1 (6.67)	
Single-stage revision	118 (72.84)	104 (70.75)	14 (93.33)	
Side, n (%)				> 0.999†
Right	76 (46.91)	69 (46.94)	7 (46.67)	
Left	86 (53.09)	78 (53.06)	8 (53.33)	
Mean duration of IV antibiotics, days (SD)	13.31 (1.59)	13.27 (1.59)	13.73 (1.62)	0.281‡
Mean duration of topical antibiotics infusion, days (SD)	13.59 (1.63)	13.56 (1.65)	13.87 (1.46)	0.486‡

(*Continued*)

(*Continued*)

Characteristic	Overall (n = 162)	Non-AKI (n = 147)	AKI (n = 15)	p-value
Type of antibiotics, n (%)				0.909†
Vancomycin for IV and topical infusion	108 (66.67)	97 (65.99)	11 (73.33)	
Carbapenem for IV and topical infusion	14 (8.64)	13 (8.84)	1 (6.67)	
Vancomycin for IV, vancomycin and carbapenem for topical infusion	40 (24.69)	37 (25.17)	3 (20)	
Perioperative transfusion, n (%)				0.179†
No	130 (80.25)	120 (81.63)	10 (66.67)	
Yes	32 (19.75)	27 (18.37)	5 (33.33)	
Transfusion before surgery, n (%)				0.325†
No	158 (97.53)	144 (97.96)	14 (93.33)	
Yes	4 (2.47)	3 (2.04)	1 (6.67)	
Transfusion during surgery, n (%)				0.593†
No	153 (94.44)	139 (94.56)	14 (93.33)	
Yes	9 (5.56)	8 (5.44)	1 (6.67)	
Transfusion after surgery, n (%)				0.280†
No	135 (83.33)	124 (84.35)	11 (73.33)	
Yes	27 (16.67)	23 (15.65)	4 (26.67)	
Median haemoglobin, g/l (IQR)	119 (108 to 128)	120 (108.5 to 129)	114 (107.5 to 120)	0.060*
Grading of anaemia, n (%)				0.0203†
No	102 (62.96)	94 (63.95)	8 (53.33)	
Mild (male: 91 to 120 g/l; female: 91 to 110 g/l)	49 (30.25)	46 (31.29)	3 (20)	
Moderate (61 to 90 g/l)	11 (6.79)	7 (4.76)	4 (26.67)	
Median baseline serum creatinine, μmol/l (IQR)	60.2 (50 to 74)	62 (51 to 74.75)	45 (38 to 54)	0.001*
Baseline serum creatinine (μmol/l), n (%)				< 0.001†
Normal range (male: 53 to 115 μmol/l; female: 46 to 92 μmol/l)	125 (77.16)	120 (81.63)	5 (33.33)	
Below the lower limit of normal range	33 (20.37)	23 (15.65)	10 (66.67)	
Above the upper limit of normal range	4 (2.47)	4 (2.72)	0 (0)	

*Mann-Whitney U test.
†Chi-squared test.
‡Independent-samples *t*-test.
AKI, acute kidney injury; ASA, American Society of Anesthesiologists; CCI, Charlson Comorbidity Index; CKD, chronic kidney disease; DAIR, debridement, antibiotics, and implant retention; IV, intravenous.

based on intraoperative findings without waiting for preoperative culture results. For single-stage revision surgeries, we waited for preoperative culture results if fluid was obtained via aspiration; otherwise, we proceeded immediately. For all patients, if preoperative culture results were not available, we initially treated the cases as culture-negative and adjusted based on intraoperative culture results. Antibiotics administration included an intraoperative powder combined with postoperative infusion and IV therapy, followed by oral delivery. In single-stage revision surgeries, the antibiotics powder was applied into the femoral and tibial canals before final prosthesis implantation in knee surgeries, and into the femoral canal and acetabulum in hip surgeries. Topical antibiotics powder was administered before closing the joint capsule in knee surgeries and the tensor fasciae latae in hip surgeries. All patients had surgical drainage. The drainage was closed before antibiotics infusion and remained closed for 20 hours, reopening three hours before the next infusion. Antibiotics were injected into the joint after aspirating the joint fluid through a T-branch pipe for hip surgeries or a syringe for knee surgeries in a sterile manner. The drainage was removed if the fluid volume was less than 50 ml, and the T-branch pipe was removed once intra-articular antibiotic therapy was completed (Figure 1).

Serum creatinine levels were measured preoperatively and then at a minimum of twice weekly during their hospitalization for all patients. AKI was classified in accordance with the Kidney Disease: Improving Global Outcomes (KDIGO)

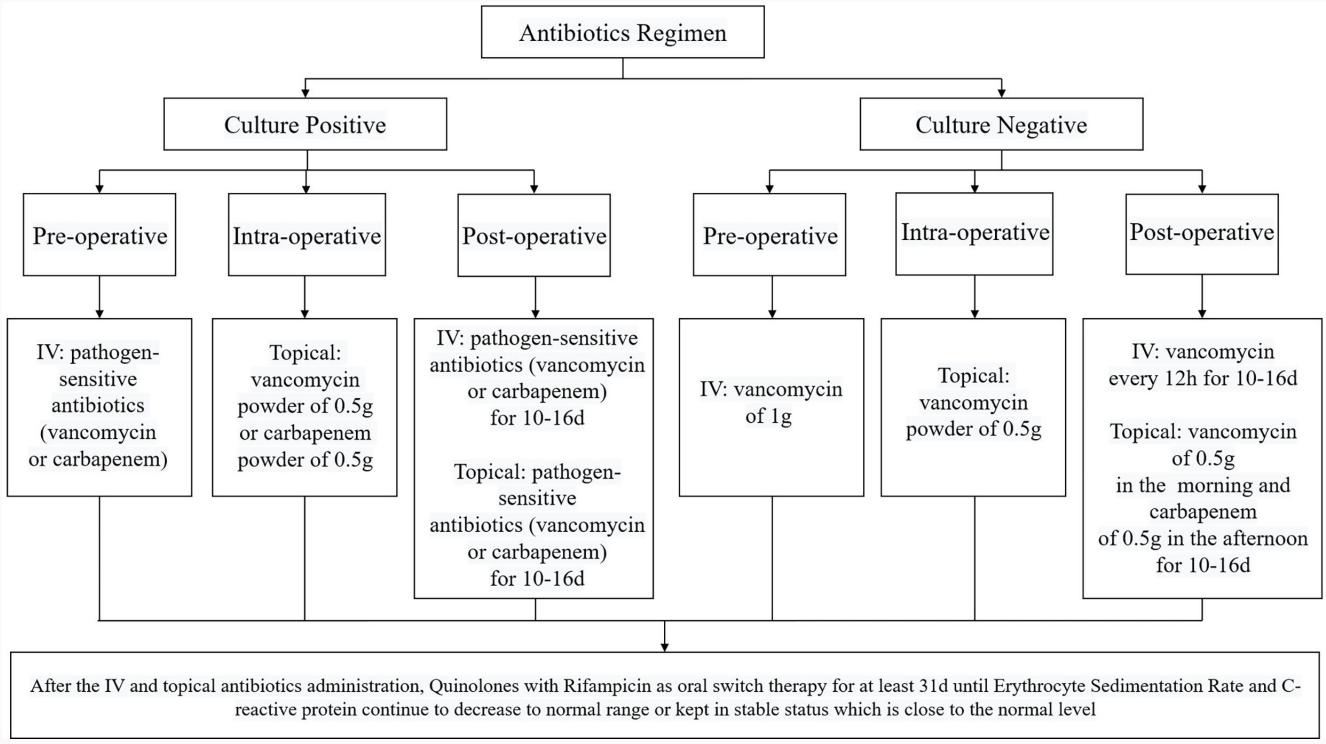

Fig. 1
Antibiotics regimen for patient with periprosthetic joint infection. d, days; IV, intravenous.

Table II. Classification of acute kidney injury following Kidney Disease: Improving Global Outcomes (KDIGO) criteria.

Stage	Criteria
1	Increase in serum creatinine (SCr) by ≥ 0.3 mg/dl (≥ 26.5 μmol/l) within 48 hours, or increase in SCr to 1.5 to 1.9 times baseline within the last 7 days, or urine volume < 0.5 ml/kg/hr for 6 to 12 hours
2	Increase in SCr to 2.0 to 2.9 times baseline
3	Increase in SCr to 3.0 times baseline or increase in SCr by ≥ 4.0 mg/dl (≥ 353.6 μmol/l) or initiation of renal arthroplasty therapy or in patients < 18 years, decrease in eGFR to < 35 ml/min/1.73 m^2

eGFR, estimated glomerular filtration rate.

guidelines, as depicted in Table II.[21] Furthermore, basic demographic data, notable comorbidities, and the Charlson Comorbidity Index (CCI) scores were extracted from the patients' digital records.[18] Preoperative CKD was indicated by a glomerular filtration rate (GFR) of less than 60 ml/min/1.73 m^2 for three months or longer. Incidence of blood transfusions administered during hospital care was also documented.

Statistical analysis

All statistical analyses were performed using R (V.4.2.1; R Foundation for Statistical Computing, Austria) and RStudio (V.2023.09.1-494; Posit, USA). Categorical variables were described using ORs and analyzed using the chi-squared test. Quantitative variables conforming to a normal distribution were described using means and SDs, and analyzed with the independent-samples *t*-test. Quantitative variables not following a normal distribution were described using medians (IQR), and analyzed using the Mann-Whitney U test. Independent risk factors for AKI were initially screened using univariate binary logistic regression, with variables having a p-value < 0.1 considered as potential significant predictors. These preliminarily screened variables were subsequently included in a multivariate logistic regression model, to assess which factors remained significantly associated with the risk of AKI after controlling for other variables. Receiver operating characteristic (ROC) curves were constructed to evaluate the performance of the risk prediction model for AKI. Statistical significance was set at $p < 0.05$, and 95% CIs were calculated for each estimate. All p-values were two-sided.

Results

In this cohort analysis, AKI was observed in 9.26% (15/162) of the participants. Median AKI onset occurred at around day 4 postoperative (IQR 2 to 7). Among these cases, stage 1 AKI was the most common, affecting 66.67% (10 out of 15 individuals). Specifically, eight patients with stage 1 AKI showed transient conditions and recovered to non-AKI status before discharge. Five patients, accounting for 33.33%, had stage 2 AKI, of whom

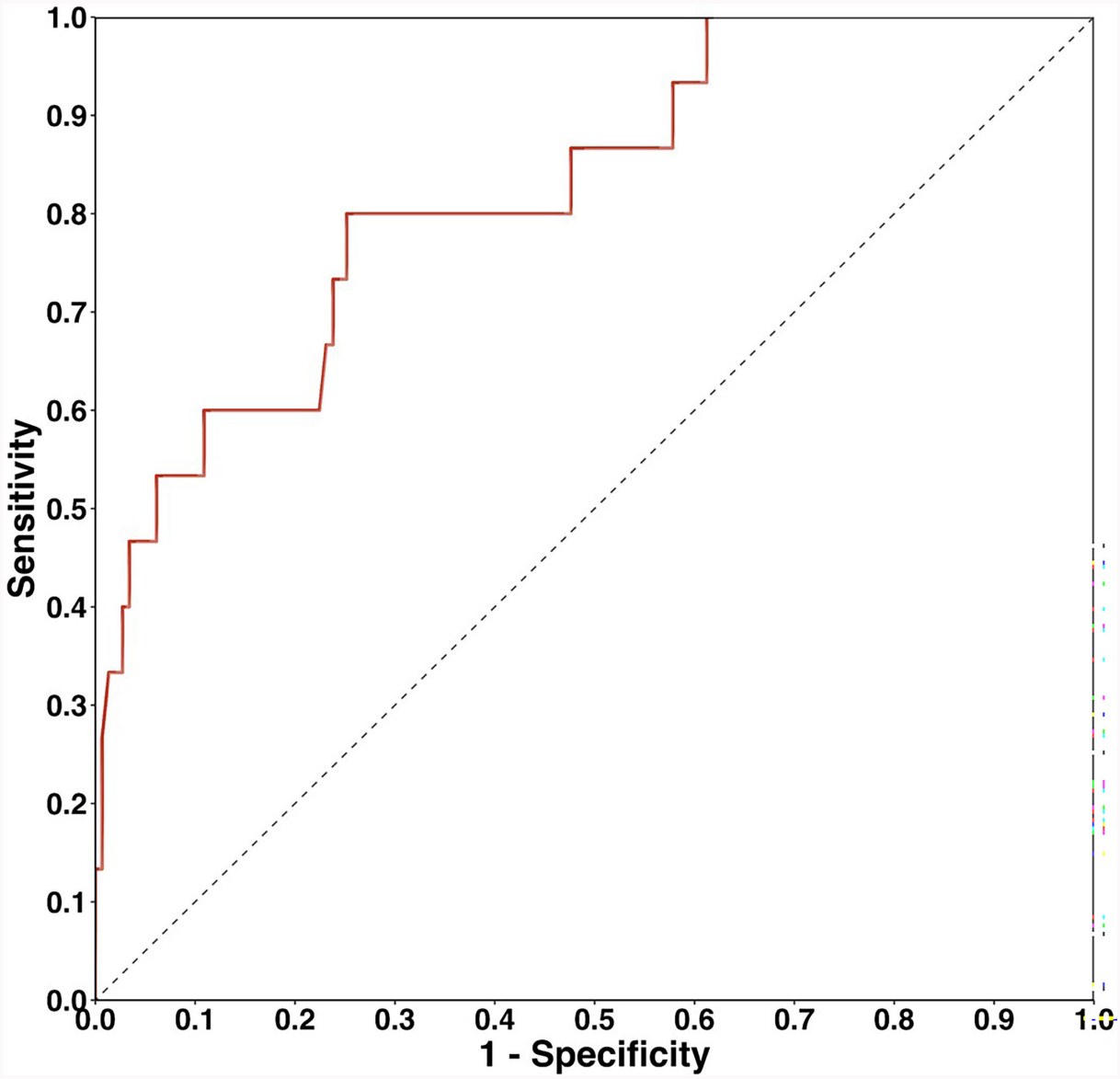

Fig. 2
Receiver operating characteristic curve for the risk prediction model of acute kidney injury.

two also exhibited temporary AKI and returned to non-AKI status by the time of discharge.

Perioperative factors were scrutinized for associations with AKI incidence. Univariate analysis indicated that a preoperative BMI of ≥ 30 kg/m^2, moderate anaemia, and low baseline serum creatinine levels significantly increased the odds of developing AKI (BMI: odds ratio (OR) 3.824, 95% CI 1.086 to 12.200, p = 0.027; moderate anaemia: OR 6.714, 95% CI 1.507 to 27.812, p = 0.009; low baseline serum creatinine: OR 1.069, 95% CI 1.025 to 1.125, p = 0.004) (Table III). Multivariate analysis confirmed moderate anaemia and low baseline serum creatinine levels as independent risk factors (moderate anaemia: OR 7.840, 95% CI 1.270 to 49.997, p = 0.025; low baseline serum creatinine: OR 1.063, 95% CI 1.017 to 1.124, p = 0.015) (Table IV). The area under the receiver operating characteristic (AuROC) of the combined variables was 0.824 (95% CI 0.700 to 0.826) (Figure 2).

The postoperative period was devoid of complications such as wound dehiscence, skin erosion, or red man syndrome, and none of the patients required haemodialysis following treatment for PJI.

Discussion

Our study highlights a novel approach to PJI management post-TKA, exploring the renal safety of combined IV and topical antibiotic infusions. With an AKI incidence of 9.26%, our results are substantially lower than those associated with ALBC. This suggests that topical antibiotics, used alone or in combination, may be a safer alternative, possibly reducing AKI risks and informing future treatment guidelines.

Administering antibiotics directly at the surgical site achieves high intra-articular concentrations while maintaining minimal systemic exposure. In the USA, ALBC application is common for combating and preventing PJI. However, AKI incidence following ALBC implantation in knee procedures varies. Initial studies reported low AKI prevalence (5% to 10%),[22–24] but recent research shows higher rates (17% to

Table III. Univariate analysis for risk factors of acute kidney injury.

Risk factor for AKI	OR	95% CI	p-value
Age	1.046	0.982 to 1.129	0.213
Sex			
Female	Reference	Reference	Reference
Male	0.500	0.110 to 1.662	0.300
BMI ≥ 30 kg/m^2	3.824	1.086 to 12.200	0.027
ASA grade	1.734	0.599 to 5.743	0.330
CCI score	1.177	0.739 to 1.854	0.484
Hypertension	2.667	0.901 to 8.920	0.087
Diabetes	2.222	0.649 to 6.808	0.174
CKD	1.679	0.086 to 10.841	0.643
Previous history of surgery	1.141	0.446 to 2.381	0.750
Type of surgery			
DAIR	Reference	Reference	Reference
Single-stage revision	5.788	1.110 to 106.515	0.095
Side			
Right	Reference	Reference	Reference
Left	1.011	0.346 to 3.021	0.984
Duration of IV antibiotics (days)	1.213	0.863 to 1.750	0.280
Duration of topical antibiotics infusion (days)	1.129	0.813 to 1.619	0.484
Type of antibiotics			
Vancomycin for IV and topical infusion	Reference	Reference	Reference
Carbapenem for IV and topical infusion	0.678	0.036 to 3.946	0.721
Vancomycin for IV, vancomycin and carbapenem for topical infusion	0.715	0.155 to 2.444	0.621
Perioperative transfusion	2.222	0.649 to 6.808	0.174
Transfusion before surgery	3.429	0.164 to 28.890	0.300
Transfusion during surgery	1.241	0.065 to 7.515	0.844
Transfusion after surgery	1.960	0.509 to 6.309	0.283
Grading of anaemia			
No	Reference	Reference	Reference
Mild	0.766	0.162 to 2.789	0.704
Moderate	6.714	1.507 to 27.812	0.009
Low baseline serum creatinine	1.069	1.025 to 1.125	0.004

AKI, acute kidney injury; ASA, American Society of Anesthesiologists; CCI, Charlson Comorbidity Index; CKD, chronic kidney disease; DAIR, debridement, antibiotics, and implant retention; IV, intravenous.

Table IV. Multivariate analysis for risk factors of acute kidney injury.

Risk factor for AKI	OR	95% CI	p-value
BMI ≥ 30 kg/m^2	2.632	0.583 to 11.008	0.189
Hypertension	1.851	0.518 to 7.035	0.345
Type of surgery			
DAIR	Reference	Reference	Reference
Single-stage revision	4.345	0.730 to 83.960	0.181
Grading of anaemia			
No	Reference	Reference	Reference
Mild	0.800	0.158 to 3.256	0.766
Moderate	7.840	1.270 to 49.997	0.025
Low baseline serum creatinine	1.063	1.017 to 1.124	0.015

AKI, acute kidney injury; DAIR, debridement, antibiotics, and implant retention.

26%).[25–28] Variations in AKI definitions and spacer types may contribute to these discrepancies.[10,29]

When employing the KDIGO criteria, which offer enhanced sensitivity, the rates of ALBC-associated AKI have been reported to be between 19% and 33%, with stage 3 AKI accounting for 4.7% to 12%.[12,26,30] Our results, however, indicate a lower incidence of AKI at 9.26%, with no cases progressing to stage 3. Vancomycin, used alone or with carbapenems for culture-negative and polymicrobial infections, shows a favourable AKI risk profile. Our findings align with research on fracture-related infections, noting reduced AKI risk with combined vancomycin and meropenem use.[31] Cumulative doses of vancomycin powder were not associated with an increased risk of drug-induced AKI among fracture patients, supporting the safety profile of topical vancomycin delivery.[32]

A recent clinical trial reported higher AKI rates in patients with ALBC during the first stage of two-stage revision compared to single-stage revision.[30] Systematic reviews reveal a dose-dependent trend in vancomycin-induced nephrotoxicity, with nephrotoxicity occurring in 10% to 20% of cases at lower doses and escalating to 30% to 40% at higher

doses.[33,34] Spacer-associated risks increase when antibiotic dosages exceed 3.6 g per batch of cement.[10] Research by Menge et al[25] highlighted that vancomycin doses over 4 g and tobramycin doses above 4.8 g nearly increased six-fold the odds for AKI. Edelstein et al[28] found that in their PJI patient cohort treated with high-dose vancomycin in cement spacers, 27% developed stage 1 or stage 2 AKI, and 5% developed stage 3. Vancomycin dosages exceeding 4 g per day and extended treatments beyond a week increase the risk of toxicity.[35] Supporting this dose-dependent risk, research by Dagneaux et al[26] revealed a doubling in AKI risk with each increment of vancomycin or aminoglycosides beyond 3.6 g per batch of cement. In the present study, the intra-articular regimen consisted either of 0.5 g of vancomycin (or carbapenem) administered once-daily or a combination of 0.5 g vancomycin with 0.5 g of carbapenems. Despite the prolonged treatment duration of ten to 16 days, the daily dosage was kept low, resulting in an AKI incidence of only 9.26%. This suggests that lower, sustained dosing may mitigate the risk of nephrotoxicity associated with ALBC.

Savas et al's[36] study showed that over half of AKI cases post-DAIR or Stage 1 revision surgery appeared within a week, while Edelstein et al[28] reported a 27% AKI incidence within two months postoperation in ALBC-treated patients. Theil et al[12] found renal recovery in AKI patients after second-stage reimplantation, which Berliner et al[29] support, emphasizing the need for renal monitoring due to long-term risks such as CKD and increased mortality. Dagneaux et al[26] noted that most AKIs after knee PJI treatment with ALBC occurred within 48 hours, with some progressing to CKD or requiring dialysis after six years. In our study, AKI typically manifested at a median four days post-surgery, with most cases resolving before discharge. This aligns with findings on rapid vancomycin clearance from the knee joint, supporting our observation of no vancomycin detected in synovial fluid post-standard IV doses, indicating a reduced AKI risk window post-administration.[37–39] This is particularly relevant in light of the American Society of Health-System Pharmacists (ASHP) 2020 guidelines[40] on therapeutic drug monitoring for vancomycin, highlighting the limitations of serum trough levels as surrogates for 24-hour area under the concentration-time curve (AUC24) and their association with increased AKI risk at elevated concentrations. He et al[39] presented lower serum trough levels for intra-articular vancomycin, with most remaining below the critical 15 to 20 μg/ml threshold, even with a higher IV dose (1 g every 12 hours). These results suggest that our protocol provides a safer profile, potentially lowering AKI risk without compromising efficacy. Despite not tracking long-term creatinine, no patients required dialysis on follow-up, indicating a minimal long-term renal impact.

Chronic comorbidities, particularly CKD, increase the risk of AKI following ALBC use due to their negative effects on renal vascular health. Conditions such as CKD, diabetes, cardiovascular disease, and hypertension impair renal blood flow and oxygenation, weakening the kidneys' defence against nephrotoxic substances.[12,26,30,36,41–43] Hence, patients with CKD or similar chronic issues must be carefully managed to prevent AKI from additional renal stressors. Surgeons should be cautious about introducing further nephrotoxic agents to those with pre-existing CKD to prevent additional renal damage.

Traditionally, lower baseline serum creatinine levels suggest superior preoperative renal function and lower AKI risk. However, our findings reveal a more complex relationship between low baseline serum creatinine levels and AKI risk. Serum creatinine is influenced by factors like muscle mass and diet, making it an imperfect marker of renal function. Patients with reduced muscle mass or malnutrition might present with lower serum creatinine levels, which do not necessarily indicate better renal function.[44,45] This underscores the need for detailed preoperative renal evaluations, incorporating additional biomarkers or risk stratification tools, to provide a more accurate assessment of true renal health and AKI risk.[46–48]

Low preoperative haemoglobin is a recognized risk factor for AKI among PJI patients, with hypertension and diabetes also contributing. Even modestly lower haemoglobin levels can signal a higher risk for renal function decline, due to insufficient oxygen supply to the kidneys from anaemia or blood transfusions. Blood transfusions might introduce additional AKI risks through haemolytic reactions and reperfusion injuries.[12,49–52] Despite some studies showing no clear connection between blood loss during surgery, transfusions, and kidney issues, careful attention to preoperative anaemia and strategic blood management are needed to lower AKI risk.[30] Our study supports this, showing an association between moderate anaemia and postoperative AKI. Therefore, vigilant monitoring and management of anaemia preoperatively are imperative.

This study's limitations include its single-centre design, which may not reflect the diversity of a broader patient population, thus limiting the generalizability of the results. The retrospective nature introduces potential confounding variables. Nephrotoxic risks from preoperative, routine, and intraoperative medications were not controlled, which may affect outcomes. The lack of a control group limits comparative conclusions. Post-discharge renal function was not adequately monitored, indicating a gap in the detection and management of potential chronic renal issues. Although the majority of AKI cases were transient and resolved prior to discharge, we did not have post-discharge serum creatinine measurements for all patients. Long-term renal function monitoring is needed in future studies. Moreover, our study did not specifically measure blood loss, although perioperative transfusion data were collected as an indirect indicator. The study aimed to identify associative factors for AKI rather than establish causality. Renal biopsy could verify tubular necrosis and clarify AKI origins. Multicentre studies are needed to validate these findings.

In conclusion, our study offers new insights into the renal safety of using topical antibiotic infusions, specifically a combined vancomycin and carbapenem protocol, in the management of PJI following TKA. This innovative approach to directly infuse antibiotics into the joint space represents a method that our findings suggest could reduce the incidence of AKI associated with PJI treatment. The potential for a safer alternative to current treatment methods is highlighted by our observations of a relatively low incidence of primarily transient AKI. These results lay a foundation for further prospective studies aimed at validating these findings and potentially influencing the standard protocols for PJI management.

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Data sharing

The datasets generated and analyzed in the current study are not publicly available due to data protection regulations. Access to data is limited to the researchers who have obtained permission for data processing. Further inquiries can be made to the corresponding author.

Ethical review statement

The study was conducted in accordance with the Declaration of Helsinki, and approved by the First Affiliated Hospital of Xinjiang Medical University Ethics Committee (K202401-08).

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