Acute Kidney Injury Following Antibiotic-Laden Spacer Placement in Two-Stage Revision Arthroplasty

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INTRODUCTION

- The most common cause of revision arthroplasty is prosthetic joint infection (PJI).
- Chronic PJI is commonly treated with two-stage exchange arthroplasty, which involves the placement of an antibiotic-laden cement spacer (ACS) in the first stage, often containing nephrotoxic antibiotics, including vancomycin and tobramycin.
- Many patients with chronic PJI often have significant medical comorbidity burdens and can cause acute kidney injury (AKI)
- This systematic review aims to assess the current literature to identify the incidence of AKI following the first-stage of exchange arthroplasty and associated risk factors.

METHODS

- An electronic search was performed of the PubMed database from inception to 1/21/2022 of all studies involving patients undergoing ACS placement for chronic PJI.
- Studies assessing AKI rates and risk factors were screened by two authors independently
- Significant heterogeneity of included studies prevented meta-analysis. **See Table 1**

TABLE 1

Study	LoE	Country	Age (yrs) Mean (SD)	BMI (kg/m²) Mean (SD)	Female (%)	CKD (%)	Preop Cr Mean (SD)	N (%)		Inclusion Criteria	Exclusion Criteria
								Hip ACS	Knee ACS		
Aeng 2015 (1)	3	Canada	66 (13)	NR	NR	NR	0.86 (0.79-1.01)*	32 (64)	18 (36)	Age > 18, ACS with tobramycin powder +/- vancomycin powder in PMMA cement for first-stage revision of infected TKA/THA	Hemodialysis dependence or development of AKI prior to surgery
Berliner 2018 (2)	3	USA	67 (11)	31.3 (7.3)	48	NR	0.95 (0.53)	0 (0)	75 (100)	Static or articulating ACS for infected TKA	NR
Dagneaux 2021 [4]	3	USA	67 (11)	33 (8.0)	47	72 (16)	1.0 (0.5)	0 (0)	455 (100)	Chronic PJI following TKA treated with 2-stage exchange involving resection and ACS implantation	Total femoral constructs, bilateral TKA PJI, simultaneous PJI of TKA and another joint, ACS implanted at a different institution, resection only
Dagneaux 2021 [3]	3	USA	65 (12)	30 (7.0)	45	41 (16)	1.0 (0.3)	256 (100)	0 (0)	Chronic PJI following THA treated with 2-stage exchange involving resection arthroplasty and ACS implantation	Total femoral constructs, hemiarthroplasties, age <18, bilateral hip PJI, simultaneous PJI of THA and another joint, ACS placed at different institution, resection only
Edelstein 2018 (5)	2	USA	67 (13)	32 (9.0)	41	NR	0.9 (0.2)	17 (46)	20 (54)	Infected primary TKA/THA treated with two-stage exchange involving resection arthroplasty and placement of ACS	Vancomycin/aminoglycoside allergy, no baseline Cr data, repeat spacer exchange required prior to second stage of revision, parenteral aminoglycoside given to reduce AKI risk unrelated to ACS
Geller 2017 (6)	3	USA	64 (12)	30 (7.0)	52	NR	1.0 (0.7)	91 (37)	156 (63)	Hip or knee PJI treated with two-stage revision procedure	Missing information on antibiotic type/dosage in ACS, missing preoperative Cr or postoperative hemoglobin
Menge 2012 (7)	3	USA	63* (NR)	NR	55	NR	0.9 (0.8-1.2)*	0	84 (100)	TKA resection and ACS placement, Cr value <30 days before ACS placement, Cr value available within 90 days after ACS placement	NR
Theil 2021 (8)	3	Germany	NR	29* (NR)	52	NR	0.9 (0.7-1.2)*	144 (52)	135 (48)	Chronic PJI following TKA/THA treated with two-stage revision using PMMA ACS. PJI defined based on MSIS 2011 criteria	Single stage revision for early PJI or aseptic revision, reconstruction following tumor resection, no ACS placement in revision, girdlestone procedures

LoE = Level of Evidence; SD = standard deviation; BMI = body mass index; ACS = antibiotic-laden cement spacer; NR = not reported; PMMA = polymethyl methacrylate; TKA = total knee arthroplasty; THA = total hip arthroplasty; AKI = acute kidney injury; USA = United States of America; MSIS = Musculoskeletal Infection Society; PJI = prosthetic joint infection; Cr = serum creatinine

*: mean not reported; median reported in its place (interquartile range in parentheses)
†: differential of THA vs. TKA not reported within ACS subset
‡: not reported for ACS subset

RESULTS

- Eight observational studies consisting of 540 knee PJIs and 943 hip PJIs met the inclusion criteria for this review.
- There were 309 (21%) cases involving postoperative AKI.
- Most common risk factors included perfusion-related factors (lower preoperative hemoglobin, perioperative transfusion requirement or hypovolemia), older age, increased comorbidity burden, and perioperative non-steroidal anti-inflammatory drug consumption.
- Two studies found increased risk with greater ACS antibiotic concentration (>4g vancomycin and >4.8g tobramycin per spacer in one study, >3.6g of vancomycin per batch or >3.6g of aminoglycosides per batch in the other). **See Table 2**

TABLE 2

Study	AKI Definition	Incidence of AKI N (%)	Predictive Univariate Risk Factors Identified	Multivariate Risk Factors
Aeng 2015 (1)	KDIGO Cr increase ≥50% from baseline within 7 days of surgery	10 (20)	Premanufactured ACS Intraoperative Transfusion Postoperative NSAIDs	NR
Berliner 2018 (2)	KDIGO >50% Cr increase from baseline (within 30 days preoperatively) to ≥1.4mg/dL	11 (15)	Lower preoperative hemoglobin	Lower preoperative hemoglobin*
Dagneaux 2021 (3)	KDIGO Stage 1: Cr ≥1.5 times baseline or increase of ≥0.3 mg/dL within 48 hour period Stage 2: Cr ≥2 times baseline Stage 3: Cr ≥3 times baseline or increase to ≥4.0 mg/dL or acute dialysis	81 (19) Without pre-existing CKD: n = 52 (14) With pre-existing CKD: n = 29 (45)	Without pre-existing CKD: BMI ≥30 kg/m2; Hypertension; Inflammatory arthritis; Nonarticulating spacer; >3.6 g/batch vancomycin; >3.6 g/batch aminoglycosides; Perioperative hypovolemia; ICU requirement; Acute atrial fibrillation; Urinary tract infection With pre-existing CKD: Diabetes; Hydronephrosis; Postoperative hypovolemia	Hypertension Perioperative hypovolemia Acute atrial fibrillation
Dagneaux 2021 (4)	KDIGO Stage 1: Cr ≥1.5 times baseline or increase of ≥0.3 mg/dL within 48 hour period Stage 2: Cr ≥2 times baseline Stage 3: Cr ≥3 times baseline or increase to ≥4.0 mg/dL or acute dialysis	23 (10) Without pre-existing CKD: n = 13 (7) With pre-existing CKD: n = 10 (28)	Without pre-existing CKD: Diabetes; Inflammatory rheumatism; Chronic NSAID use; Nephrotoxic agents; Postoperative hypovolemia; ICU requirement; Acute atrial fibrillation With pre-existing CKD: Prostatic disease/surgery; Bladder tumor/surgery; Postoperative hypovolemia	No significant predictors of AKI on multivariate regression
Edelstein 2018 (5)	RIFLE Risk: increase in Cr 1.5 times baseline or decrease in GFR of 25% Injury: increase in Cr 2 times baseline or decrease in GFR of 50% Failure: increase in Cr 3 times baseline or decrease in GFR of 75% Loss of kidney function: complete loss of kidney function for >4 weeks	10 (27)	No significant predictors of AKI on univariate regression	No significant predictors of AKI on multivariate regression
Geller 2017 (6)	KDIGO Cr ≥1.5 times baseline within one week or increase of ≥0.3 mg/dL within 48 hour period	65 (26)	Age; Male gender; BMI; Baseline hemoglobin (per 1 g/dL decrease); Hemoglobin drop; Vancomycin dose; Tobramycin dose; Comorbid condition (including one of diabetes mellitus, CKD, cardiovascular disease, and hypertension); IV vancomycin	BMI Baseline hemoglobin (per 1 g/dL decrease) Comorbid condition (including one of diabetes mellitus, CKD, cardiovascular disease, and hypertension)
Menge 2012 (7)	KDIGO Increase of ≥50% in Cr from preoperative baseline (within 30 days of ACS placement) to a level ≥1.4 mg/dL	14 (17)	>4g vancomycin >4.8g tobramycin	NR
Theil 2021 (8)	KDIGO Stage 1: Cr ≥1.5-1.9 times baseline or increase of ≥0.3 mg/dL Stage 2: Cr ≥2-2.9 times baseline Stage 3: Cr ≥3 times baseline or acute dialysis requirement	95 (33)	Higher median patient age Higher median Charlson comorbidity index Lower preoperative hemoglobin Higher median number of units of blood transfused	Higher age Higher baseline creatinine

AKI = acute kidney injury; CI = confidence interval; β = beta coefficient; Cr = creatinine; ACS = antibiotic-laden cement spacer; NSAID = nonsteroidal anti-inflammatory drug; NR = not reported; KDIGO = Kidney Disease Improving Global Outcomes; CKD = chronic kidney disease; BMI = body mass index; ICU = intensive care unit; RIFLE = Risk, Injury, Failure, Loss of kidney function, and End-stage kidney disease; IV = intravenous;
*: multivariate regression for percent change in creatinine

DISCUSSION/CONCLUSIONS

- Patients undergoing ACS placement for chronic PJI are at an increased risk for AKI.
- Knowing and minimizing risk factors preoperatively can lead to better multidisciplinary care and safer outcomes for chronic PJI patients.

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