

# Acute Kidney Injury with Tobramycin-Impregnated Bone Cement in Prosthetic Joint Infections: A Quality Assurance Controlled Study

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## Background

- Incidence of infected prosthetic joint arthroplasties is 0.5-3%
- At VGH, two-stage revision surgery is standard treatment for infection of prosthetic joint arthroplasties:
  - Stage 1: Removal of infected prosthetic joint and insertion of antibiotic-impregnated bone cement spacer (ACS)
    - Tobramycin ± vancomycin added to ACS
    - Followed by IV antibiotics x 6 weeks
  - Stage 2: Removal of ACS and insertion of new prosthetic joint
- A retrospective trial of 84 patients noted 17% incidence of acute kidney injury (AKI) with use of tobramycin ACS
- Incidence of AKI with ACS at VGH is uncertain

## Objectives

- To evaluate incidence of AKI in patients receiving Stage 1 procedure with tobramycin ± vancomycin ACS
  - AKI = increase in serum creatinine ≥ 50% from baseline
- To assess tobramycin serum levels after implantation of ACS
- To determine risk factors associated with AKI

## Inclusion & Exclusion Criteria

- Inclusion Criteria:**
  - Patients ≥ 18 years of age
  - Tobramycin Group:** Two-stage revision of hip or knee joint arthroplasty with tobramycin ± vancomycin ACS
  - Control Group:** Revision of non-infected hip arthroplasty
- Exclusion Criteria:**
  - Systemic tobramycin given post-operatively days (POD) 0-7

## Methods

- Prospective, observational, controlled quality assurance study conducted at VGH between Nov, 2011 and Feb, 2013
- Sample Size Calculation:
  - n = 45/group, power = 0.80, alpha < 0.05, difference = 25%
- Data Collection:
  - Baseline (BL): serum creatinine (SCr), hemoglobin
  - POD 1, 3, 5, 7: serum tobramycin ± vancomycin levels (if not on IV vancomycin), SCr and BUN
- Statistical significance: p-value < 0.05
  - T-test (continuous variables), Chi-square (non-continuous)
  - Univariate and multivariate analysis

Table 1. Baseline Characteristics

Variable	Tobramycin Group n = 50	Control Group n = 69	p-value
Age, yrs (mean ± SD)	66.0 ± 13.0	66.1 ± 12.4	0.97
Weight, kg (mean ± SD)	82.8 ± 18.4	79.7 ± 17.4	0.35
Sex, male, n (%)	27 (54.0)	25 (36.2)	0.06
<b>Comorbidities, n (%)</b>			
Hypertension	19 (38.0)	25 (36.2)	0.85
Diabetes	7 (14.0)	6 (8.7)	0.39
↑ SCr, umol/L	7 (14.0)	5 (7.2)	0.36
<b>Nephrotoxin PTA, n (%)</b>			
ACEI or ARBs	16 (32.0)	19 (27.5)	0.68
NSAIDs	10 (20.0)	18 (26.1)	0.51
SCr, umol/L (mean ± SD)	82.1 ± 29.2	76.2 ± 24.3	0.23
Hemoglobin, g/L (mean ± SD)	118.7 ± 17.9	136.9 ± 11.3	<0.0001
Procedure, Hip/Knee (n/n)	32/18	69/0	
<b>Antibiotic Dose in ACS, g, (median, IQR)</b>			
Tobramycin (n = 50)	7.2 (7.2-7.2)	-	
Vancomycin (n = 45)	3.0 (3-3.5)	-	
Gentamicin (in pre-packaged cement) (n = 18)	1.0 (0.5-1.0)	-	

Table 2. Outcomes, According to Treatment Groups

	Tobramycin	Control	p-value
AKI, n (%)	10 (20.0)	3 (4.3)	<b>OR 5.5 (95%CI 1.4-21.1)</b>
AKIN Stage, n (%)			<b>0.03</b>
1 ↑SCr ≥ 150-200% from BL	5 (10.0)	2 (2.9)	
2 ↑SCr ≥ 200-300% from BL	2 (4.0)	1 (1.4)	
3 ↑SCr > 300% from BL	3 (6.0)	0 (0)	
Day AKI First Occurred (mean ± SD)	3.2 ± 1.9	3.0 ± 2.7	0.88
Length of Hospital Stay, day (mean ± SD)	13.34 ± 10.0	7.6 ± 6.2	<b>0.0002</b>
Lowest Hgb, g/L (mean ± SD)	84.7 ± 13.5	98.1 ± 14.2	<b>&lt;0.0001</b>
Received PRBC POD 1-7, n (%)	11 (22.0)	2 (2.9)	<b>0.0017</b>

Figure 1: Median Change in SCr and Tobramycin Levels (Tobramycin Group)

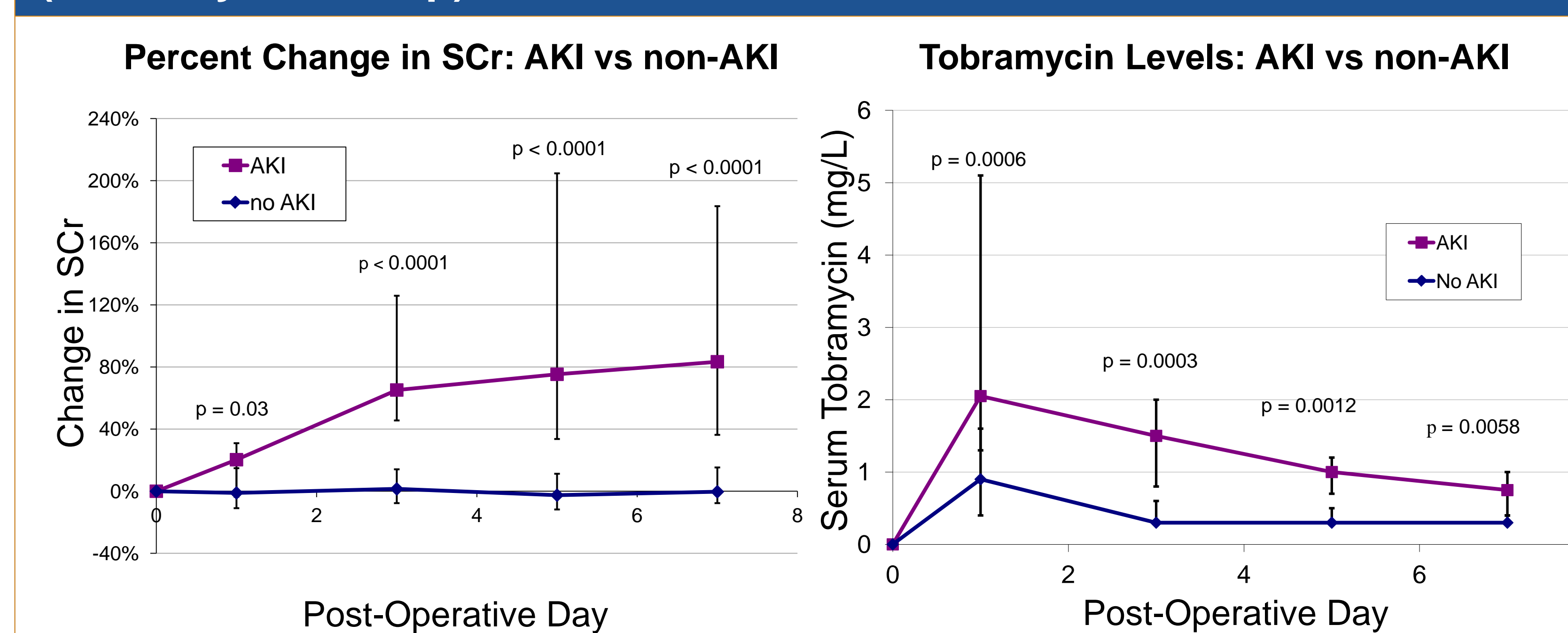


Figure 2: Pathogens (Tobramycin Group, n=50)

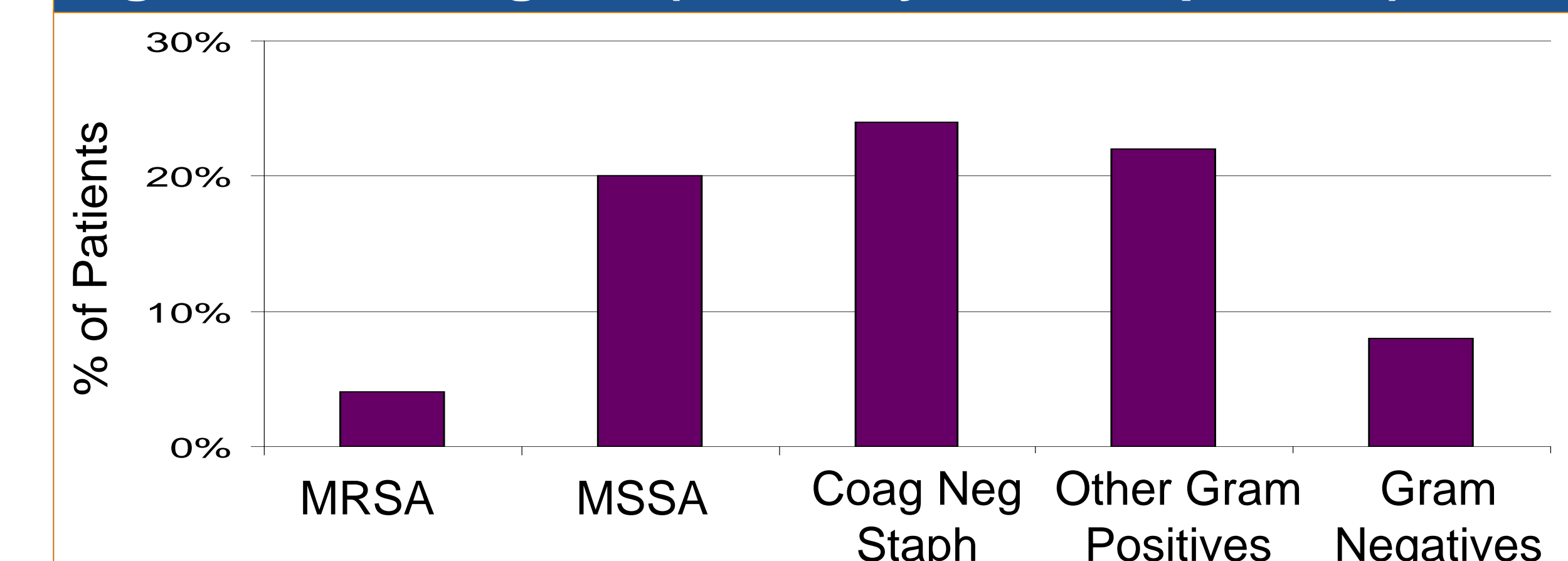


Table 3. Risk Factors for AKI

Risk Factors (post-op) % (n)	AKI	No AKI	OR (95% CI)	p-value
Gentamicin* (in pre-packaged cement)	70.0% (7/10)	27.5% (11/40)	6.2 (1.4 - 28.1)	<b>0.02</b>
Received Blood Transfusion	53.8% (7/13)	5.7% (6/106)	19.4 (5.0-76.3)	<b>&lt; 0.0001</b>
ACEI/ARBs	53.8% (7/13)	22.6% (24/106)	4.0 (1.2-13.0)	<b>0.04</b>
Vancomycin IV	53.8% (7/13)	17.9% (19/106)	5.3 (1.6-17.7)	<b>0.0076</b>
NSAIDs	53.8% (7/13)	55.7% (59/106)	-	1.00

\* Also shown to be significant in multivariate analysis

## Discussion

- Tobramycin AKI incidence 20% vs control 4.3% (p=0.04)
  - Similar to literature (J Arthroplasty 2012)
- AKI patients had higher tobramycin serum levels
  - No difference in vancomycin levels (AKI vs non-AKI)
- Risk factors for AKI: transfusions, ACEI/ARBs, vancomycin IV, using gentamicin pre-packaged cement

## Limitations

- Observational study – OTCs not assessed PTA
- Too few events for multivariate analysis
- Some patients discharged before POD 5
  - 4% Tobramycin group; 41% control group
- First SCr preop assumed to represent BL renal function

## Conclusions

- Incidence of AKI in infected hip or knee arthroplasties is greater than in routine total hip arthroplasties
- Strategies aimed at minimizing AKI risk and early detection appear warranted. These may include:
  - Avoid pre-packaged gentamicin in Stage 1 procedure
  - Avoid ACEI/ARBs within first 72 hours post-op
  - Stop NSAIDs as soon as AKI noted
  - Monitor SCr closely in patients requiring transfusions or concomitant vancomycin IV