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Variation in Antibiotic Prophylaxis Selection for Coronary Artery Bypass Graft Procedures in an Era of Rising Methicillin Resistant *Staphylococcus aureus* Prevalence

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Approximately 400,000 coronary artery bypass graft (CABG) procedures are performed annually in the US.¹ Infection is the second most-common complication, but appropriate pre-operative antibiotic prophylaxis reduces risk of surgical site infections (SSI).²

There is no consensus on routine vancomycin use for CABG prophylaxis. National guidelines from Infectious Diseases Society of America (IDSA), Society for Healthcare Epidemiology (SHEA) and others state, “there is no clear evidence to support the use of vancomycin, alone or in combination ... for routine antimicrobial prophylaxis in institutions that have a high prevalence of MRSA.”³ The IDSA/SHEA reserves vancomycin for individual patients at high-risk for MRSA infection.³ In contrast, the Society for Thoracic Surgery (STS) guidelines state, “it would appear most reasonable to employ a cephalosporin as the primary prophylactic agent ... [and vancomycin as] an adjuvant agent ... where there is a high prevalence of MRSA isolates from infections.”⁴ To understand current practice, we conducted a survey of antibiotic prophylaxis for CABG among California hospitals. We surveyed all medical centers that perform CABG surgery in California. Questions relating to

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prophylaxis included; i) Which antibiotics are standard for isolated CABG; ii) What is the duration of prophylaxis; iii) Are any individual patients given broader-spectrum prophylaxis to prevent infection; iv) What is the frequency of broader-spectrum prophylaxis; and v) Which antibiotics are used for broader-spectrum prophylaxis. Broader-spectrum prophylaxis was defined as anti-MRSA prophylaxis, anti-pseudomonal cephalosporins, carbapenems or double gram-negative prophylaxis. Broader-spectrum prophylaxis excluded changes due to allergy. Respondents included healthcare professionals familiar with clinical practices.

We collected hospital information from the California Department of Public Health (CA-DPH) ⁵ and the California Office of Statewide Health Planning and Development (OSHPD). ⁶ Hospitals were classified as high, normal, or low MRSA burden facilities using hospital MRSA-BSI rates, as described by CA-DPH.⁵ We collected the number of CABG procedures performed from 2009 to 2010, the geographic location of hospitals, and teaching hospital versus community.⁶

Bivariate analyses were performed using two-sided Pearson's chi-squared test, Fisher's exact test, Student's t-test or one-way ANOVA. We used logistic regression to model i) predictors of routine vancomycin use, and ii) predictors of prophylaxis including vancomycin for individual patients. Variables significant at $\alpha=0.20$ were included and p-values ≤ 0.05 were considered significant.

Eighty of 120 medical centers (67%) responded, including 70 community and 10 teaching hospitals. Surveys were completed by STS database managers (41%), cardiac surgery nurse-practitioners (37%), infection control (20%), and surgeons (2%). Respondents performed a mean of 140 procedures per year (min 18, max 793) with a mean hospital size of 358 beds (min 60, max 900). Seven hospitals (9%) had high MRSA-BSI incidence, 62 hospitals (83%) had normal incidence, and 6 hospitals (8%) had low incidence.

The majority of hospitals (63/80, 79%) used a cephalosporin alone for routine CABG prophylaxis (cefazolin $n=61$, ceftriaxone $n=2$). Few hospitals (17/80, 21%) used vancomycin routinely; vancomycin alone ($n=3$) and 14 vancomycin combined with a cephalosporin ($n=14$; vancomycin/cefazolin $n=9$, vancomycin/ceftriaxone $n=2$, vancomycin/cefuroxime $n=3$).

In bivariate analysis, routine vancomycin was associated with higher case volume ($p=0.05$), and inversely associated with Southern California ($p=0.05$). Low-burden MRSA hospitals were more likely to use vancomycin (67%, $n=4/6$) than normal (18%, $n=11/62$) or high-burden (29%, $n=2/7$) hospitals ($p=0.03$).

In the multivariable model, routine vancomycin use was independently associated with teaching hospital status (O.R. 5.9, 95% CI 1.0–38.7) and inversely associated with Southern California location (O.R. 0.15, 95% CI 0.02–0.7). Hospital MRSA burden was not associated with routine vancomycin use in the multivariable model.

Thirty-three hospitals that use cefazolin for routine prophylaxis changed CABG prophylaxis for individual patients ($n=33/58, 57\%$). Vancomycin monotherapy was used in 18/33 centers (55%), vancomycin and a cephalosporin in 15/33 (45%; vancomycin/cefazolin $n=14$,

vancomycin/cefepime n=1) and daptomycin in 2/33 (6%). Hospital characteristics were not associated with vancomycin prophylaxis for individual patients. (data not shown)

Pre-operative antibiotic prophylaxis is a cornerstone of infection prevention for CABG.² Findings from our large sample of cardiac surgery centers demonstrate heterogeneity in clinical practice and systematic deviations from guideline recommendations.

We were surprised to find twenty-one centers using vancomycin alone, either routinely or in select patients. The use of vancomycin alone is not recommended by IDSA/SHEA or STS guidelines because of the known risk of gram-negative mediastinitis.^{3,4}

We identified 29 centers that combine vancomycin with a cephalosporin, either routinely or in select patients. Dual-agent prophylaxis is consistent with STS guidelines, but has not been formally studied.⁴ Theoretically, dual-agent prophylaxis prevents SSI due to MSSA and gram-negative pathogens from the cephalosporin component and will reduce MRSASSI by the inclusion of vancomycin.^{7,8} Conversely, the dual-agent approach may result in more side effects, including emergence of resistance and *Clostridium difficile* infections, without measurable benefit. Formal evaluation of the cost, benefits, and antimicrobial stewardship implications of the dual-agent approach are warranted.

A clinical trial of β -lactam prophylaxis compared to dual-agent prophylaxis is needed. A randomized trial, based on the STS Adult Cardiac Surgery registry, could provide a cost-effective infrastructure for data collection and quicker enrollment than a traditional multi-center trial.^{9,10} A randomized registry trial could be adequately powered to capture rare events, such as emergence of resistance after broader prophylactic strategies.^{9,10}

Our investigation demonstrates significant variation in clinical practice. The variation may reflect limited clinical data and discrepancies between national guidelines. However, the heterogeneity in practice, particularly monotherapy with vancomycin, raises significant patient safety and healthcare quality concerns.

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Table 1

Characteristics of Hospitals that Use a Cephalosporin Alone Compared to Hospitals that use Vancomycin (Alone or in Combination) for Routine Prophylaxis of CABG procedures.

Hospital Characteristics	Cephalosporin Alone n=58	Vancomycin Alone or in Combination n=17	P-value
	n (%) Mean $\pm$ SD	n (%) Mean $\pm$ SD	
MRSA-BSI Incidence¹	0.59 $\pm$ 0.43	0.56 $\pm$ 0.57	0.84
MRSA-BSI Incidence Categories²			0.02
High	5 (71%)	2 (29%)	
Normal	51 (82%)	11 (18%)	
Low	2 (33%)	4 (67%)	
Bed size	356 $\pm$ 163	362 $\pm$ 172	0.9
Geography			
Northern California	18 (72%)	7 (28%)	0.07
Central California	11 (65%)	6 (35%)	
Southern California*	34 (89%)	4 (11%)	
Hospital type			0.21
Community	57 (81%)	13 (19%)	
Teaching*	6 (60%)	4 (40%)	
Number of procedures	127 $\pm$ 93	188 $\pm$ 169	0.05

* Multivariate Analysis found that vancomycin use for CABG prophylaxis was associated with teaching hospitals status (O.R. 5.9, 95% CI 1.0–38.7) and inversely associated with Southern California location (O.R. 0.15, 95% CI 0.02–0.7).