Multicenter evaluation: Predictors for *Pseudomonas aeruginosa* surgical site infections after head/neck cancer microvascular reconstruction

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Introduction

Surgical site infections (SSI) in head/neck cancer microvascular reconstruction remain a significant post-operative complication, despite the increased use of post-operative antibiotic prophylaxis (POABP). The role of *Pseudomonas aeruginosa* (PSA) SSI in this population has not been well established, but perceived PSA risk factors are extrapolated from traditional variables found in other disease states (e.g. immunosuppression, diabetes). Consequently, some clinicians prefer to use antipseudomonal POABP in this setting. Optimal POABP durations are also unknown, and combined with overuse of extended spectrum antimicrobials, can lead to poor outcomes, selection for resistant organisms, or severe adverse reactions (e.g. *Clostridioides difficile*-associated diarrhea).

The objective of this study was to characterize SSI microbiology and identify PSA risk factors for patients who receive head/neck cancer microvascular reconstruction among eleven North American institutions.

Methods

Study Design
This was an IRB approved cross sectional study with a nested case-case-control, conducted at eleven North American tertiary-care centers.

Study Population
The study population included hospitalized patients who received head/neck cancer microvascular reconstruction from January 2003 to December 2015.

Inclusion Criteria	Exclusion Criteria
• Age ≥ 18 years • Documented oncologic disease	• Patients with existing infection prior to surgery • Patients requiring an infection-related operating room visit within 48-hours post-operation of initial surgery • Surgical intervention on an existing tumor within 90-days prior to microvascular reconstruction

Data Collection
Data collected included: patient demographics (e.g. American Society of Anesthesiologists [ASA] classification system), select comorbid conditions (e.g. diabetes mellitus, smoking and alcohol status, previous radiation therapy), surgery and infection characteristics (POABP spectrum and durations, 30-day SSI per CDC/NHSN criteria, unexpected return to operating room), and SSI microbiology. All species identification was completed by individual institution in accordance to Clinical & Laboratory Standards Institute (CLSI) standards. Data were collected using a standardized electronic case report form.

> **Key Definitions**
> POABP was categorized *a priori* based on bacterial spectrum of activity, as determined by blinded infectious diseases pharmacists:
> **Narrow**: Gram-positive with anaerobic coverage only
> **Broad**: Gram-positive, enteric Gram-negative, and anaerobic coverage
> **Antipseudomonal**: Gram-positive, anti-pseudomonal, and anaerobic coverage

Statistical Analyses
Descriptive statistics were used to identify the incidence of 30-day SSI. Baseline patient characteristics were compared using bivariate analyses: categorical variables were compared by the Pearson's χ^2 or Fisher's exact test, continuous variables were compared by the student's *t*-test or the Mann-Whitney U-test; *P*-values <0.05 were considered statistically significant. Cases were defined as patients with PSA SSI and with non-PSA SSI; controls were patients without SSI. Multiple comparisons were performed in case-case-control fashion. All statistics were performed using IBM SPSS Statistics version 23.0.
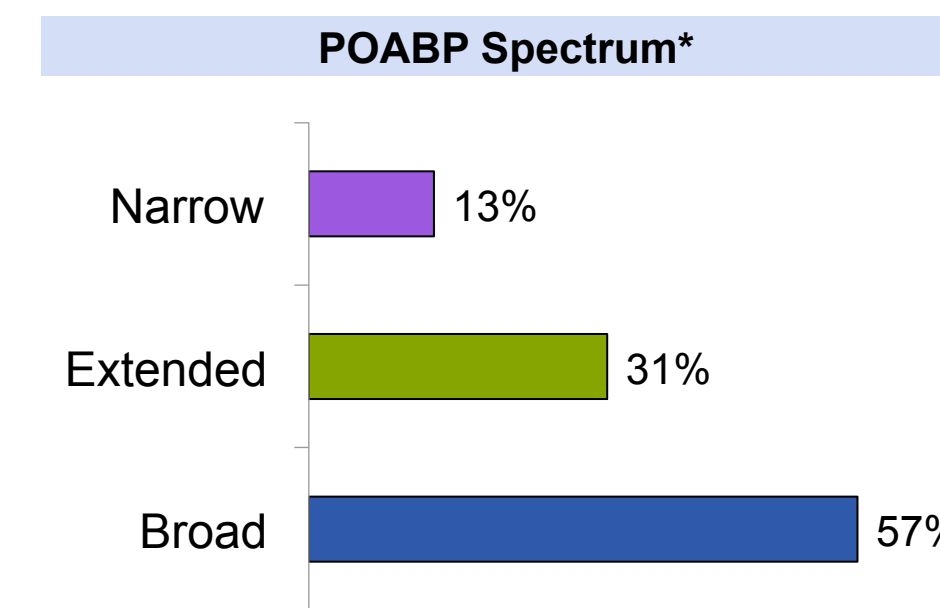
Results

Patient and Antibiotic Characteristics

Covariate n (%) or median (IQR)	n = 1307
Median age, years	62 (53-70)
Sex, male	894 (68%)
Diabetes mellitus	205 (16%)
Previous radiation therapy	452 (35%)
Smoking status, current	375 (29%)
Median surgery duration, hrs	9.6 (7.9-12.1)

POABP Spectrum*

Narrow 13%
Extended 31%
Broad 57%

*The median [IQR] duration of all POABP was 6 days [3-7]

Infection Characteristics

Surgical Site Incidence per Year

	Pre-'04	'05	'06	'07	'08	'09	'10	'11	'12	'13	'14	'15
n Surgeries/year	1	87	78	33	13	33	202	200	104	186	214	156
n Infections/year	0	8	3	0	6	6	22	28	21	17	45	33
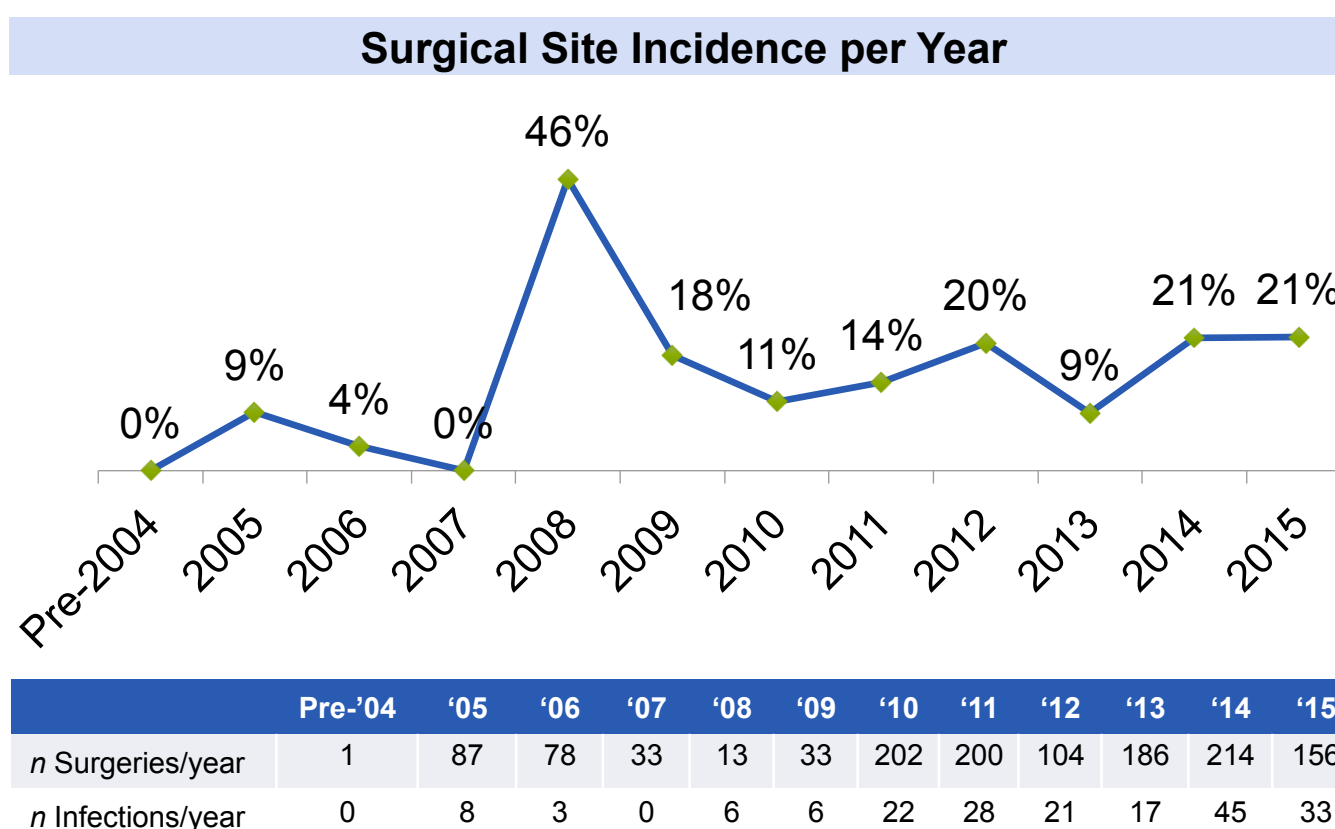
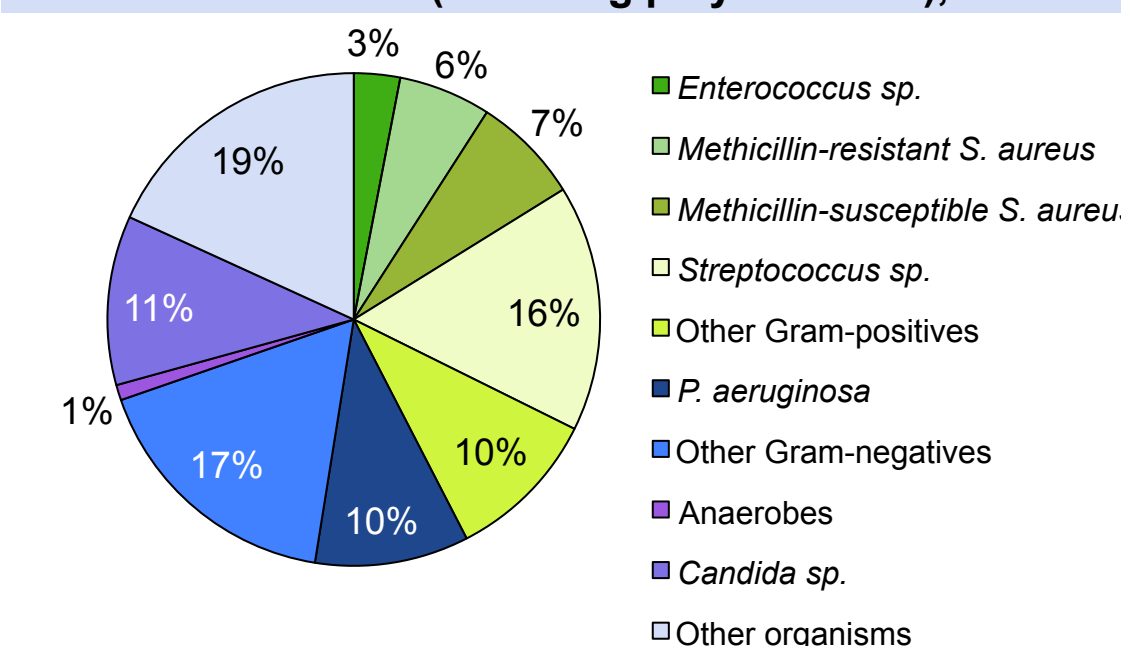| Covariate	n (%) or median (IQR)
30-day SSI	189 (15%)
Time to SSI, days	11.5 (7-17)
Unexpected 30-day OR return	261 (20%)

Microbiology

• *P. aeruginosa* was isolated from 17 (9%) of the 189 patients who developed 30-day SSI.

SSI Cultures, *n* = 189

- Gram-positive, single organism 16%
- Gram-positive, polymicrobial 2%
- Gram-negative, single organism 10%
- Gram-negative, polymicrobial 2%
- Polymicrobial, mixed 5%
- Polymicrobial, other 11%
- Other cx 13%
- No/negative cx 41%
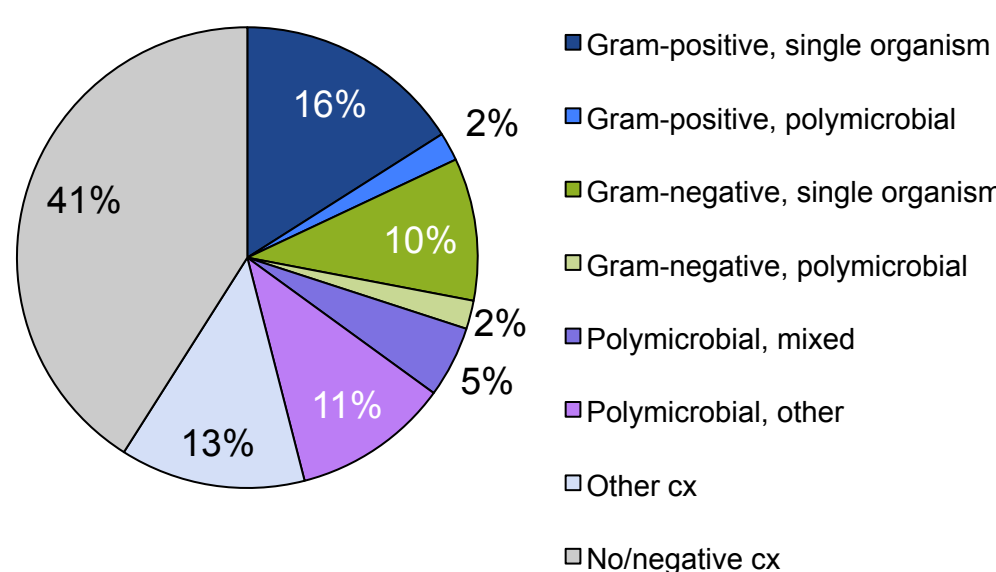
Individual Isolates (including polymicrobial), *n* = 175

- Enterococcus sp. 3%
- Methicillin-resistant S. aureus 6%
- Methicillin-susceptible S. aureus 7%
- Streptococcus sp. 16%
- Other Gram-positives 10%
- P. aeruginosa 10%
- Other Gram-negatives 17%
- Anaerobes 1%
- Candida sp. 11%
- Other organisms 19%

Comparison of Post-operative Antibiotic Prophylaxis

Covariate n (%) or median (IQR)	Narrow n = 125	Broad n = 565	Antipseudomonal n = 309	P-value*
Median age, years	62 (52-69)	61 (53-71)	63 (55-71)	0.63
Sex, Male	72 (58%)	402 (71%)	210 (68%)	0.005
30-day chemotherapy use	6 (5%)	48 (9%)	35 (11%)	0.09
ASA Classification ≥ III	96 (77%)	446 (79%)	293 (95%)	0.02
Diabetes mellitus	14 (11%)	88 (16%)	57 (18%)	0.12
Previous radiation therapy	42 (34%)	190 (34%)	109 (35%)	0.89
Smoking status, current	29 (23%)	172 (30%)	96 (31%)	0.09
Alcohol intake, current	56 (45%)	252 (45%)	118 (38%)	0.6
Median POABP duration, days	3 (1-7)	5 (3-7)	7 (5-8)	< 0.001
30-day SSI	44 (35%)	80 (14%)	61 (20%)	< 0.001

*Narrow POABP used as reference group

Risk Factors for *P. aeruginosa* Surgical Site Infections

Covariate	PSA SSI to non-PSA SSI UnadjOR (95% CI)	PSA SSI to controls UnadjOR (95% CI)
ASA Classification ≥ III	2.8 (0.36-22.4)	3.2 (0.43-24.4)
Previous radiation therapy	1.8 (0.66-4.9)	1.7 (0.64-4.4)
Smoking status, current	0.56 (0.18-1.8)	0.8 (0.26-2.5)
Alcohol intake, current	0.76 (0.27-2.1)	0.74 (0.27-2.0)
Diabetes mellitus	0.75 (0.16-3.47)	0.71 (0.16-3.1)
Antipseudomonal POABP	0.59 (0.19-1.9)	0.70 (0.22-2.2)

Summary

• *P. aeruginosa* was uncommonly isolated from surgical site infections
  • Antipseudomonal POABP spectrum and other traditional risk factors were also not associated with *P. aeruginosa* surgical site infections
• Antimicrobial stewardship interventions that limit unnecessary exposure to antimicrobials can have beneficial outcomes for patients and prevent the emergence of resistant organisms