Association between Vancomycin AUC and Clinical Failure in Patients with Streptococcal Bacteremia

Anna Aycock, PharmD, Jessica M. Smith, PharmD, MBA, BCIDP, Kelci Coe, MPH, Shu-Hua Wang, MD, MPH, PharmD, Erica Reed, PharmD, BCPS, BCIDP

The Ohio State University Wexner Medical Center and Arthur G. James Cancer Hospital and Richard J Solove Research Institute, Columbus, Ohio, USA

Erica Reed, PharmD, BCPS, BCIDP
The Ohio State University
Wexner Medical Center
368 Doan Hall
410 W 10th Ave
Columbus, OH 43210

erica.reed@osumc.edu

THE OHIO STATE UNIVERSITY
WEXNER MEDICAL CENTER

BACKGROUND

- Severe streptococcal infections may require vancomycin (VAN) treatment for 2 to 8 weeks in duration[1,2]
- VAN area under the curve/minimum inhibitory concentration (AUC/MIC) monitoring is the preferred monitoring strategy for severe infections associated with *Staphylococcus aureus*, but the role of VAN AUC/MIC is not well elucidated for other bacterial pathogens[3-5]

Study Objective
Identify a vancomycin AUC that predicts clinical failure in patients with streptococcal bacteremia

METHODS

- **Study Design**: Single-center, retrospective cohort
- **Study Period**: Jan 1, 2011 to Sept 30, 2021

Primary Outcome

- **Composite treatment failure**
  - Persistent streptococcal bacteremia
  - Recurrent bacteremia with *Streptococcus* spp.
  - 30-day readmission
  - 30-day mortality

Secondary Outcomes

- Time to bacteremia clearance
- Hospital length of stay
- Nephrotoxicity

Definitions:

Recurrent bloodstream infection	• Positive blood culture collected ≥ 72h following collection of a negative blood culture
Persistent bacteremia	• Positive blood culture collected ≥ 24h from initial positive blood culture collection
Nephrotoxicity	• Serum creatinine (SCr) ≥ 1.5x baseline SCr or increase in SCr ≥ 0.3 mg/dL

METHODS (continued)

Inclusion Criteria	Exclusion Criteria
Patients 18-89 years old	Protected populations (those < 18 and > 89 years old, inmates, and pregnant patients)
VAN definitive therapy	Alternative/concomitant anti-streptococcal therapy for > 50% treatment course
Streptococcal bacteremia	Concomitant *S. aureus* or *Enterococcus* spp. bacteremia
	Did not have VAN trough collected
	Received renal replacement therapy
	VAN MIC > 2 mcg/mL
	Cystic fibrosis
	Severe burn injury
	Central nervous system infection

Statistical Analysis:

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Demographic and clinical → Descriptive statistics	
Continuous variables → Student's t-test or Wilcoxon rank sum	
Categorical variables → Chi-square or Fisher's exact test	
VAN AUC threshold for predicting clinical failure → Classification and regression tree analysis (CART)	
Secondary outcomes → Groups stratified by AUC threshold	
Performed on SAS Statistical software, version 9.3	

RESULTS

Figure 1. CART analysis of VAN AUC Threshold
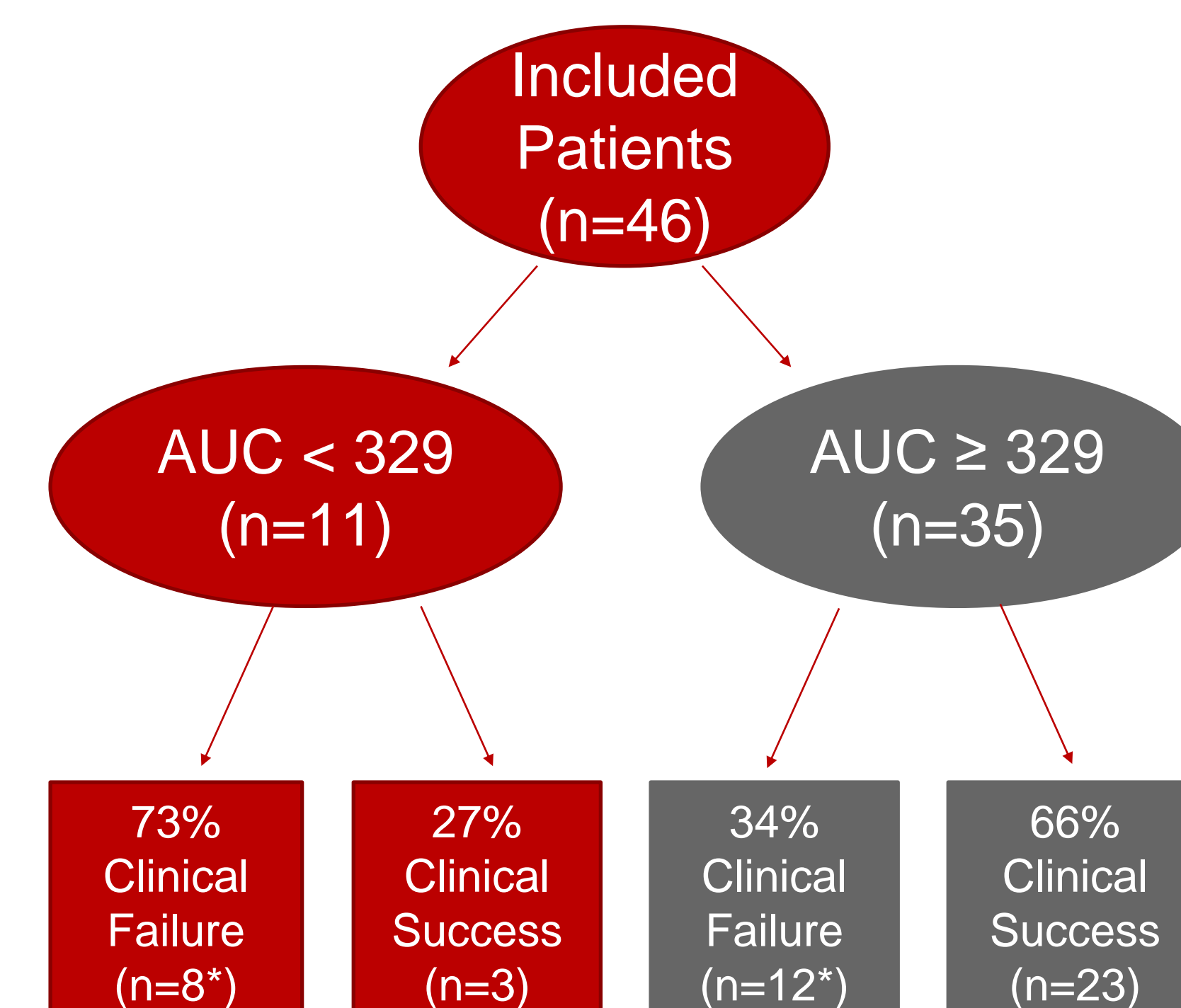
*Of the twenty patients who had clinical failure, eighteen had 60-day all-cause readmission and two had 60-day all-cause mortality

RESULTS (continued)

Table 1: Baseline Characteristics

Characteristic	AUC ≥ 329 (n=35)	AUC < 329 (n=11)	P-value
Age, years	52 [38-62]	62 [48-69]	0.24
Male	15 (43)	6 (55)	0.5
Skilled Nursing Facility/Long Term Assisted Care/Nursing Home	2 (6)	0 (0)	1
Injection Drug Use	10 (29)	0 (0)	0.09
Immunosuppressed	8 (23)	4 (36)	0.44
Charlson Comorbidity Index	3 [2-5.5]	2.5 [2-3]	0.18

Data are presented as number (%) or median [IQR] as appropriate.
Immunosuppressed defined as at least one of the following: active chemotherapy, ≥ 20mg of prednisone equivalents for ≥ 2 weeks, bone marrow or organ transplantation, immune deficiency, or CD4 count < 200.
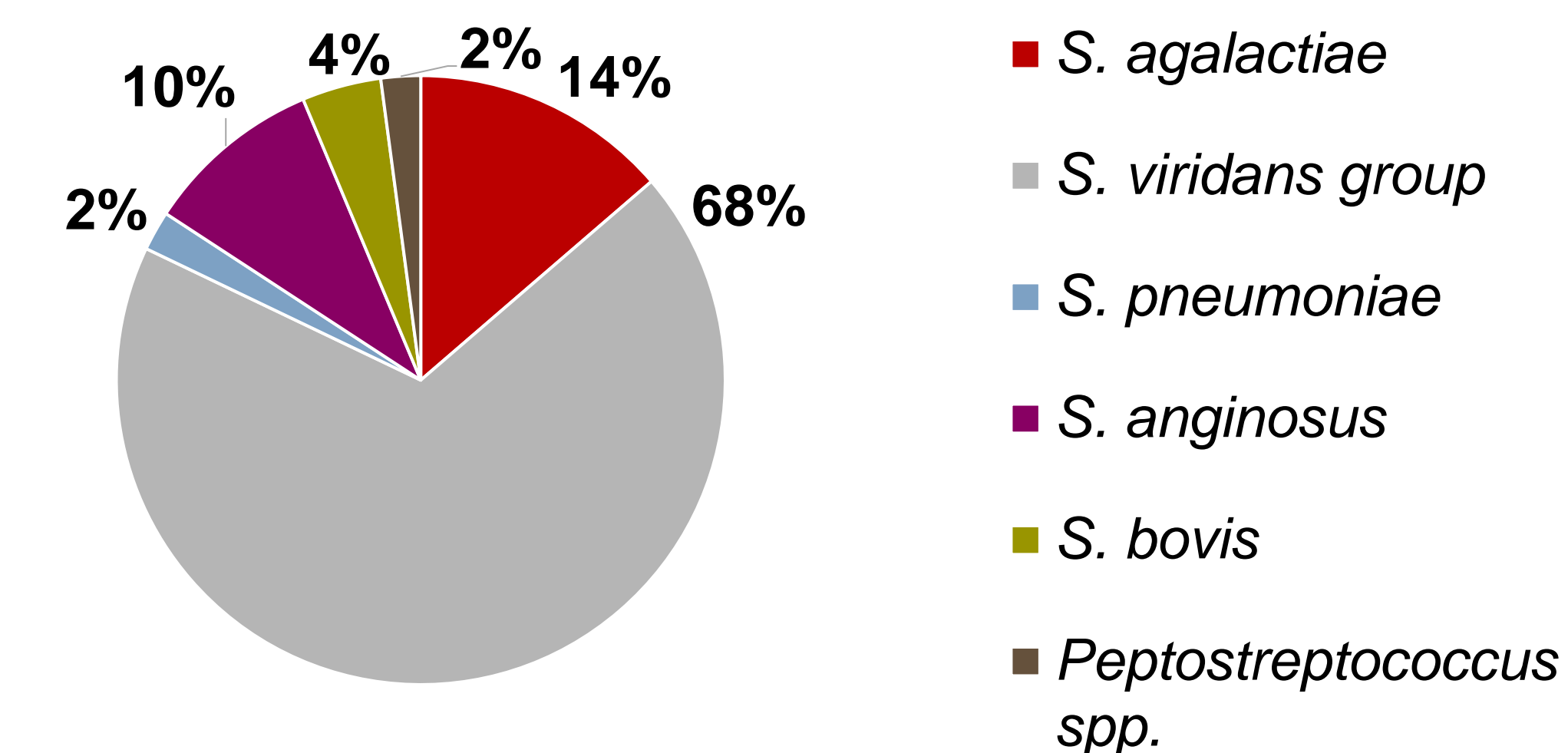
Figure 2: Streptococcal Species

- 68% — S. agalactiae
- 14% — S. viridans group
- 2% — S. pneumoniae
- 4% — S. anginosus
- 10% — S. bovis
- 2% — Peptostreptococcus spp.

Table 2: Clinical Characteristics

Characteristic	AUC ≥ 329 (n=35)	AUC < 329 (n=11)	P-value
Baseline SCr (mg/dL)	0.77 [0.62-0.99]	0.74 [0.53-0.95]	0.37
Peak SCr during VAN (mg/dL)	0.99 [0.84-1.31]	0.95 [0.66-1.33]	0.41
Concurrent nephrotoxin(s)	30 (86)	8 (73)	0.37
Infective endocarditis	7 (20)	0 (0)	0.17
Pitt bacteremia score	2 [0-2]	1 [0-2]	0.20
ICU admission	4 (11)	3 (27)	0.33
Streptococcus VAN MIC			0.23
0.25 mcg/mL	2 (6)	0 (0)	
0.5 mcg/mL	28 (80)	7 (64)	
1 mcg/mL	5 (14)	4 (36)	
Total VAN duration of therapy (days)	21 [14-42]	15 [15-43]	0.74
Initial steady state VAN trough (mcg/mL)	13.2 [11.3-19]	6.3 [5.6-9]	<0.0001

Data are presented as number (%) or median [IQR] as appropriate.
Nephrotoxic agents included aminoglycosides, nonsteroidal anti-inflammatory drugs (NSAIDs), and iodinated contrast given within 72 hours of VAN initiation.
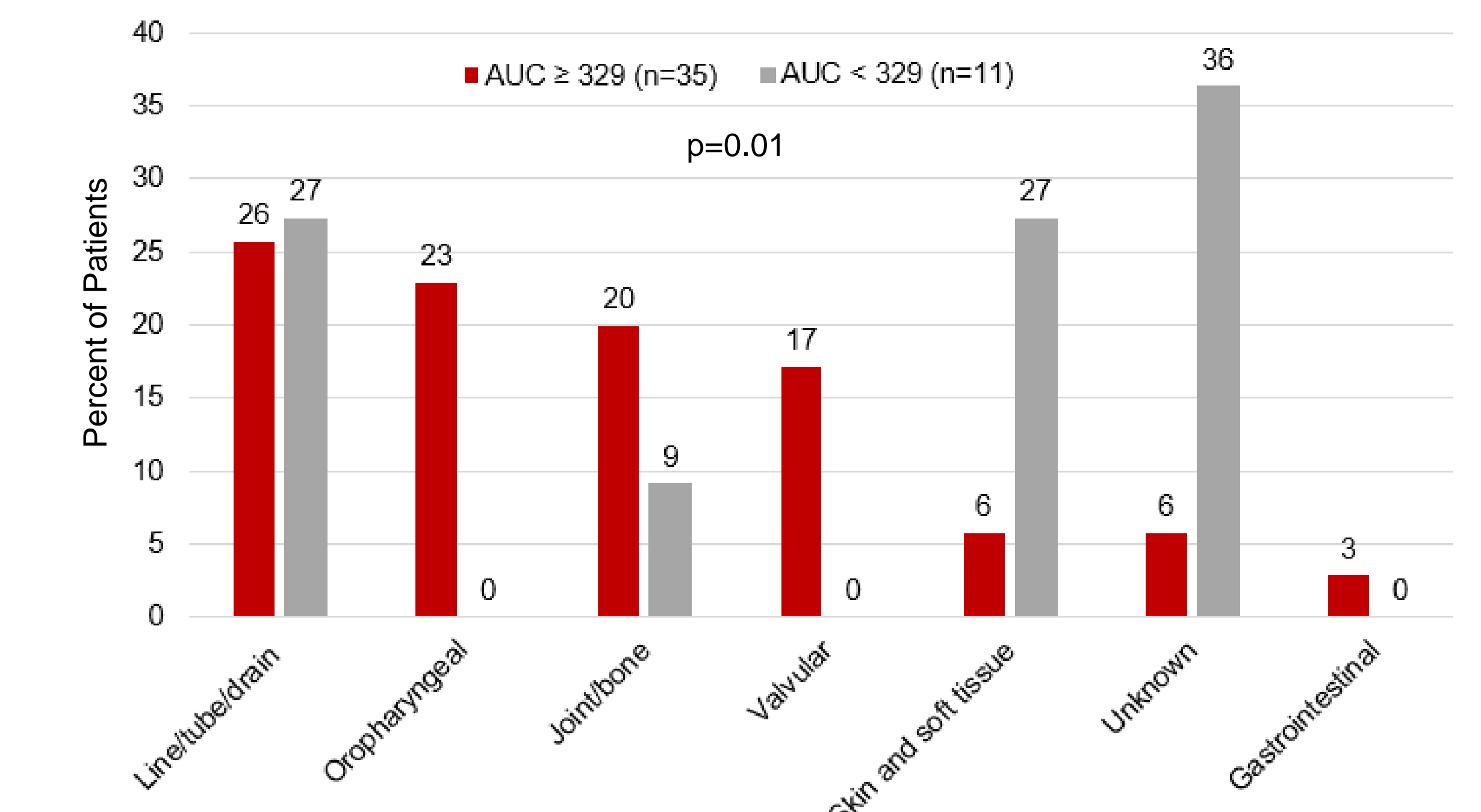
RESULTS (continued)

Figure 3: Bacteremia Source

Figure 4: Secondary Outcomes in Patients with VAN AUC ≥ 329 vs VAN AUC < 329

Hospital length of stay (days)
- 15 [9-22] vs 8 [7-15], p=0.05

Time to bacteremia clearance (hours)
- 29 [22-45] vs 25 [20-29], p=0.15

Nephrotoxicity
- 13 (37%) vs 4 (36%), p=1

Data are presented as number (%) or median [IQR] as appropriate.

DISCUSSION

- Clinical failure was more common in patients with streptococcal bacteremia and VAN AUC less than 329
- No difference in the incidence of nephrotoxicity was identified
- Limitations include small sample size, concomitant antimicrobial agents for <50% of the course, AUC calculation based on first trough only, and data collection limited to OSUWMC electronic medical record
- Larger studies are needed before implementation into clinical practice can be recommended

References
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