

Background

- Bacterial bloodstream infections (BSIs) are one of the leading causes of death among infections in the United States^{1,2}
- Gram-positive bacteria are predominant pathogens in BSIs^{1,2}
- Highly bioavailable oral antibiotics have similar clinical outcomes when compared to standard IV therapy for gram-negative BSIs^{3,4}
- A recent study showed significantly shorter length of hospital stay and lower mortality associated with step-down oral antibiotics against IV only antibiotic therapy for the treatment of *Streptococcus* spp. BSIs⁵
- Evidence supporting the management of *Streptococcus* spp. BSIs with oral antibiotics is scarce

Objective

- To compare efficacy and safety of step-down IV-to-PO antibiotic therapy to IV-only treatment of uncomplicated Streptococcal BSIs

Methods

Study Design: Single-center, retrospective observational cohort of adult patients with Streptococcal spp. BSI who were treated at the University of New Mexico Hospital, a tertiary care academic medical hospital with 565 beds, from January 1, 2017 to December 31, 2019.

Inclusion Criteria: (1) Age ≥ 18 years, (2) *Streptococcus* spp. identified from one or more blood specimens obtained by culture, and (3) Active IV antibiotic therapy initiated within 48 hours of blood culture collection

Exclusion Criteria: (1) Positive blood culture treated as contaminant by provider, (2) Polymicrobial BSI, (3) Subjects with cystic fibrosis, (4) Active diagnosis of endocarditis, osteomyelitis, or septic arthritis, (5) Total duration of treatment greater than 14 days from last negative blood culture, (6) Death within 48 hours of presentation or a life expectancy of less than three months

Primary Outcome: Clinical failure, defined as having one or more of the following criteria:

- Persistent bacteremia
- 30-day reinfection at any site or new onset sepsis
- 30-day BSI recurrence
- 30-day all-cause mortality

Secondary Outcomes:

- 30-day all-cause readmission
- 30-day antibiotic-related side effects
- 30-day *Clostridium difficile* infection
- Hospital length of stay

Definitions:

- Active antibiotic: IV or oral antibiotic with confirmed in-vitro activity
- Immunodeficiency: HIV stage 3, asplenia, solid organ or bone marrow transplant on immunosuppressive therapy, chemotherapy within 90 days, ≥10mg of prednisone 2 weeks prior to onset of infection, absolute neutrophil count <1500cells/μL
- Microbiological cure: negative blood culture at the end of therapy or on active IV or oral antibiotic therapy
- Persistent bacteremia: positive blood culture at day 3 or after despite active antibiotic therapy

Results

Figure 1. Study Participants

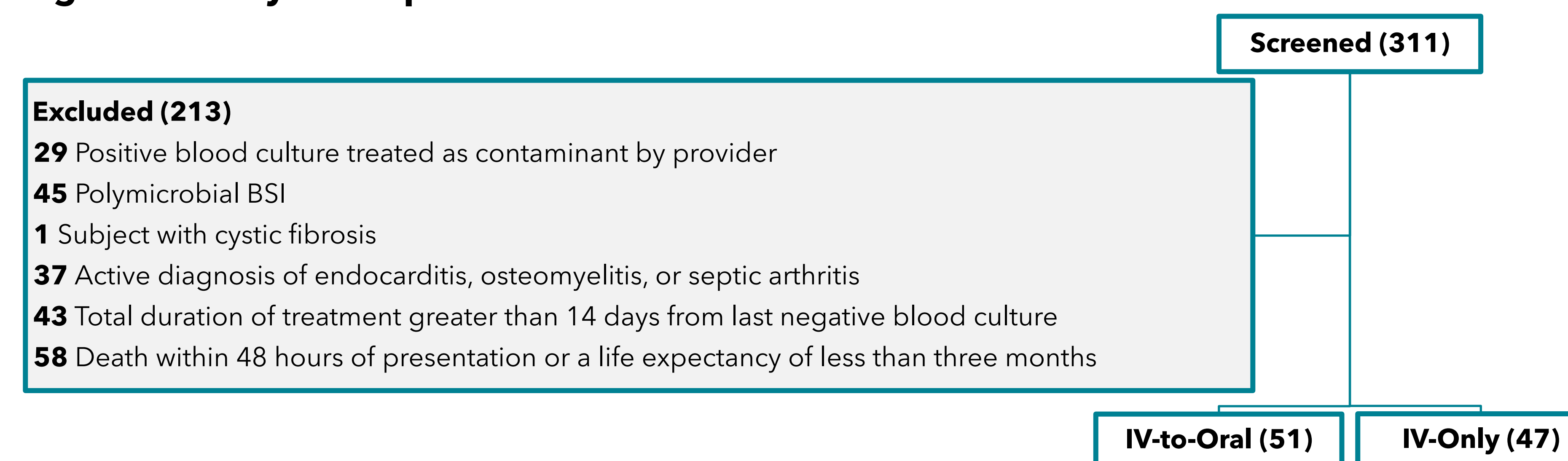


Table 1. Baseline Characteristics

Variable	IV-to-PO (n=51)	IV-Only (n=47)	p-value
Age (years) [mean (SD)]	56.6 (17.3)	59.0 (18.5)	0.455
Male [no. (%)]	32 (62.7)	32 (68.1)	0.579
Co-morbid conditions [no. (%)]			
Diabetes	15 (29.4)	15 (31.9)	0.788
Malignancy	6 (11.8)	12 (25.5)	0.079
Immunodeficiency	2 (3.9)	5 (10.6)	0.255
COPD	4 (7.8)	5 (10.6)	0.734
CKD on dialysis	2 (3.9)	3 (6.4)	0.598
Cirrhosis	6 (11.8)	9 (19.1)	0.310
IV drug use	8 (15.7)	5 (10.6)	0.462
Source of infection [no. (%)]			0.279
Respiratory System	17 (33.3)	7 (14.9)	
Skin/soft Tissue	8 (15.7)	11 (23.4)	
Intra-abdominal	6 (11.8)	4 (8.5)	
Unknown	16 (31.4)	20 (42.6)	
Pitt bacteremia score [median (IQR)]	2 (0-3)	2 (1-4)	0.056
Total antibiotic duration (days) [median (IQR)]	13 (9-14)	15 (13-16)	0.001
Total IV-antibiotic duration (days) [median (IQR)]	4 (3-6)	15 (13-16)	<0.001
Microbiological cure [no. (%)]	42 (82.4)	45 (95.7)	0.036
ICU admission [no. (%)]	10 (19.6)	20 (42.6)	0.014
Streptococcal organism from blood culture [no. (%)]			
Group A <i>Streptococcus</i>	13 (25.5)	7 (14.9)	0.193
Group B <i>Streptococcus</i>	7 (13.7)	9 (19.1)	0.468
Group C and Group G <i>Streptococcus</i>	3 (5.9)	7 (14.9)	0.188
<i>S. anginosus</i> Group	3 (5.9)	1 (2.1)	0.545
<i>S. mitis</i> Group	2 (3.9)	10 (21.3)	0.012
<i>S. pneumoniae</i>	19 (37.3)	10 (21.3)	0.083
<i>S. salivarius</i>	5 (9.8)	1 (2.1)	0.207
<i>S. viridans</i>	3 (5.9)	3 (6.4)	1.00

S. anginosus Group: *S. anginosus*, *S. constellatus*, *S. intermedius*; *S. mitis* Group: *S. mitis*, *S. gordonii*, *S. oralis*, *S. parasanguinis*

Results (continued)

Table 2. Primary Outcome

Variable	IV-to-PO (n=51)	IV-Only (n=47)	p-value
Clinical Failure [no. (%)]			
Persistent Bacteremia	0 (0)	9 (19.1)	0.001
30-day reinfection at any site or new-onset sepsis	0 (0)	8 (17.0)	0.002
30-day BSI recurrence	0 (0)	1 (2.1)	0.480
30-day all-cause mortality	0 (0)	1 (2.1)	0.474

Table 3. Secondary Outcomes

Variable	IV-to-PO (n=51)	IV-Only (n=47)	p-value
30-day all-cause readmission [no. (%)]	6 (11.8)	8 (17.0)	0.458
30-day antibiotic-related side effects [no. (%)]	3 (5.9)	1 (2.1)	0.348
30-day <i>Clostridium difficile</i> infection [no. (%)]	0 (0)	1 (2.1)	0.295
Hospital length of stay (days) [median (IQR)]	5 (4-7)	12 (7-16)	< 0.001

Discussion/Conclusions

- IV-to-oral step-down therapy appears to be safe and effective alternative for treating uncomplicated Streptococcal BSIs in patients who are otherwise clinically stable
- Patients in the IV-to-oral step-down group had shorter duration of therapy and decreased hospital length of stay
- Clinical failure was not statistically different when assessed for co-morbidities, source of infection, Pitt bacteremia score, documented BSI clearance, ICU admission or pathogen
- Beta-lactam antibiotics were used in the majority (94%) of the IV-to-oral group
- This was a single-center, observational cohort study; larger randomized controlled trials are needed to better determine the efficacy and safety of step-down IV-to-PO antibiotic therapy to IV-only for the treatment of uncomplicated Streptococcal BSIs

References

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Disclosure: Authors of this presentation have nothing to disclose concerning possible financial or personal relationships with commercial entities that may have a direct or indirect interest in the subject matter of this presentation.

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