

The occurrence of infective endocarditis with *Staphylococcus lugdunensis* bacteremia: A retrospective cohort study and systematic review

Lemuel R. Non, MD and Carlos A. Q. Santos, MD, MPH

¹Washington University School of Medicine, St. Louis, MO and ²Rush University Medical Center

INTRODUCTION

- Staphylococcus lugdunensis* is a coagulase-negative staphylococcus (CNS) that can cause aggressive tissue-invasive infections similar to *Staphylococcus aureus*
- According to IDSA, IE should be ruled out in cases of *S. aureus* bacteremia (SAB), and the Modified Duke Criteria for Endocarditis includes *S. aureus* in two separate blood cultures as a major criterion for IE. Should this be applied to *S. lugdunensis* bacteremia (SLB) given its comparable virulence to *S. aureus*?
- Our objective was to determine whether the proportion of IE among patients with SLB is comparable to reported proportions of IE among patients with SAB

METHODS

- We conducted a retrospective chart review of patients aged 18 years and older with SLB, defined as at least 1 positive blood culture, admitted to Barnes-Jewish Hospital/Washington University from January 2006 to December 2014
- We identified 75 patients with SLB using the Barnes Medical Informatics Database, and excluded one patient because his chart was not available for review.
- Demographic and clinical characteristics for the cohort were determined at the onset of bacteremia, which was defined as the date of the first positive blood culture
- The Barnes-Jewish Hospital microbiology laboratory used the VersaTREK system for processing of blood cultures for the duration of this study. Matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF) was the primary method of identifying bacteria from 2012 onward
- IE was defined according to the 2000 Modified Duke Criteria. Severity of illness was assessed using the Pittsburgh bacteremia score (PBS) and systemic inflammatory response syndrome (SIRS) criteria
- Descriptive statistics were used to describe the demographic and clinical characteristics of the study population.
- Kaplan-Meier survival analyses and log-rank tests were used to determine differences in overall survival. Onset of bacteremia was defined as the date of the first positive blood culture, and censoring was performed on December 31, 2014.
- Nonparametric bootstrapping methods consisting of random repeated sampling with replacement 1,000 times was performed to determine 95% confidence intervals (CI) for proportions of IE in patients with SLB
- Systematic review of scientific literature was also performed. All original observational studies that determined the proportion of IE among patients with SLB

RESULTS

- Of 391,014 patients admitted to Barnes-Jewish Hospital from January 2006 to December 2014, 75 had SLB yielding an incidence of 18.9 per 100,000 hospitalized patients. Clinical characteristics are presented in Table 1
- Forty-seven percent (35/74) had one positive blood culture with *S. lugdunensis*, while 53% (39/74) had two or more positive blood cultures (Table 2)
- Fifty-four percent (40/74) had an intravascular device, 12% (9/74) had orthopedic hardware in place, and 8% (6/74) had implantable cardiac devices
- Antimicrobial susceptibilities were performed in 90% (67/74) of isolates, and only 15% (10/67) of *S. lugdunensis* isolates were oxacillin-resistant
- Echocardiography was performed in 54% (40/74) of patients, of which 75% (30/40) were transthoracic and 25% were transesophageal
- Fifteen percent (11/74, 95% CI 6.8 – 23.0%) of patients with SLB had IE according to the Modified Duke Criteria, of whom 45% (5/11) had definite IE and 55% (6/11) had possible IE
- Endocardial involvement was documented in only 7% (5/74) of cases: 3 native tricuspid valve, 1 native mitral valve, and 1 bioprosthetic aortic valve (Table 3)
- Eighteen percent (13/74) of patients met the criteria for severe illness by PBS
- The mortality rates were 11% (8/74), 13% (10/74) and 19% (14/74) at 30, 60 and 90 days after the onset of SLB respectively. The one-year mortality of SLB was 25.7% (19/74), while that of *S. lugdunensis* IE was 36% (4/11)
- Systematic review yielded 8 studies; the proportion of IE in those with 2 or more blood cultures ranged from 6.3 – 27.0%

RESULTS

Table 1. Demographic and clinical characteristics of 74 patients with *Staphylococcus lugdunensis* bacteremia

Variables	Result N (%)
Age, years	
Mean ± SD	50.08 ± 15.82
Median (range)	60 (21 – 86)
Female sex (%)	33 (44.59)
Race (%)	
White	41 (55.41)
Black	33 (44.59)
Comorbidities (%)	
Hypertension	47 (63.51)
Diabetes mellitus	25 (33.78)
Active malignancy	17 (22.97)
End-stage renal disease	15 (20.27)
Coronary artery disease	11 (14.86)
Liver cirrhosis	4 (5.41)
Stem cell transplant	3 (4.05)
Devices (%)	
Intravascular	40 (54.05)
Orthopedic	9 (12.16)
Implantable cardiac	6 (8.11)

Table 2. Microbiology and disease severity of 74 patients with *S. lugdunensis* bacteremia

Variables	Result N (%)
Number of positive blood cultures	
1 positive blood culture	35 (47.3)
2 or more	39 (52.7)
Oxacillin-resistance (%)	10 (13.51)
Pittsburgh Bacteremia Score components (%)	
Temperature	
36.1 – 38.9 °C	49 (66.22)
35.1 – 36 or 39 – 39.9 °C	23 (31.08)
< 35 or > 40	2 (2.70)
Hypotension	22 (29.73)
Mechanical ventilation	7 (9.46)
Cardiac arrest	4 (5.41)
Mental status	
Alert	52 (70.27)
Disoriented	13 (17.57)
Stuporous	5 (6.76)
Comatose	4 (5.41)
Severe illness by Pittsburgh Bacteremia Score (%)	13 (17.57)
Systemic inflammatory response syndrome (%)	48 (64.86)

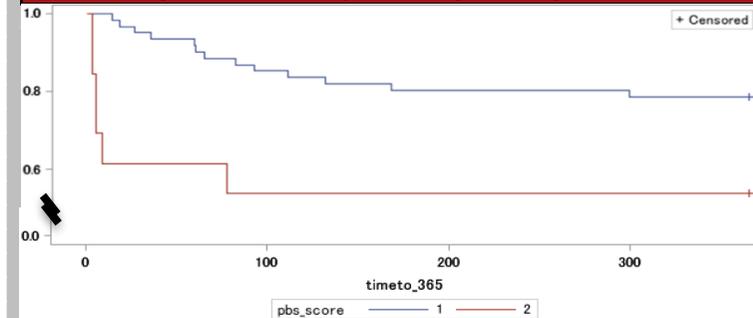
Table 3. Modified Duke Criteria applied to 74 patients with *Staphylococcus lugdunensis* bacteremia

Major criteria (%)	All SLB (N=74)
Blood culture positive for IE	15 (20.27)
Endocardial involvement	5 (6.76)
Minor criteria (%)	
Predisposition	4 (5.41)
Fever	34 (45.95)
Vascular phenomena	1 (1.35)
Microbiologic evidence	57 (77.03)
Possible IE	6 (8.19)
Definite IE	5 (6.76)
Definite or possible IE	11 (14.86)

Systematic Review of Literature

Author, year	Inclusion criteria	Was routine identification of <i>S. lugdunensis</i> performed?	Was Duke criteria used in diagnosis of IE?	Proportion of Possible and definite IE among SLB (number of IE/ number of SLB)
Lin et al, 2014	1 positive blood culture associated with clinical criteria	Yes	Yes	9.7% (4/41)
Byrnes et al, 2014	1 positive blood culture associated with clinical criteria	Not specified	Yes	17.2% (5/26)
Klotchko et al, 2011	At least 1 positive blood culture	Yes	Yes	23.8% (5/21)
Liang et al, 2012	At least 1 positive blood culture	Not specified	Yes	27.0% (3/11)
Fadel et al, 2011	1 positive blood culture only	Yes	Yes	0% (0/29)
Choi et al, 2010	At least 1 positive blood culture	Not specified	Not specified	6.3% (4/63)
Zinkernagel et al, 2008	At least 2 positive blood cultures	Only those with 2 or more positive blood cultures	Yes	46.4%
Ebright, 2003	At least 2 positive blood cultures	Only those with 2 or more positive blood cultures	Yes	5%

One-year survival of patients by severity of illness



CONCLUSIONS

- This is the largest retrospective study and the only systematic review on SLB in the scientific literature
- SLB is associated with a similar proportion of IE as SAB, which suggests that growth of *S. lugdunensis* in two separate blood cultures should prompt consideration of workup for IE
- The proportions of IE yielded by systematic review fell within the 95% confidence intervals yielded by bootstrapping in the retrospective study
- The majority of *S. lugdunensis* isolates are susceptible to anti-staphylococcal beta-lactams.
- SLB is associated with severe illness, which in turn is associated with lower survival at 1 year