**Original Article**

**Staphylococcus lugdunensis Endocarditis: Lower Mortality in the Contemporary Era?**

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**ABSTRACT**

Background: *Staphylococcus lugdunensis* is a virulent coagulase-negative *Staphylococcus* that is a rare cause of infective endocarditis (IE) associated with high mortality. A linear growth of IE has occurred over the past several years in Saskatchewan, with overlapping epidemics of human immunodeficiency virus (HIV)/hepatitis C virus driven by injection drug use (IDU). We hypothesized that given the unique challenges faced by our population with IDU and inequitable healthcare access, our cases of *S. lugdunensis* IE might differ from those in the published literature.

In Saskatchewan, our incidence of IE cases in general, and *S. lugdunensis* IE, is a rare cause of infective endocarditis (IE) associated with high mortality. A linear growth of IE has occurred over the past 10 years, outpacing population growth. This trend is corresponding hospital admissions, has increased linearly over time. In Saskatchewan, our incidence of IE cases in general, and *S. lugdunensis* IE, is a rare cause of infective endocarditis (IE) associated with high mortality. A linear growth of IE has occurred over the past several years in Saskatchewan, with overlapping epidemics of human immunodeficiency virus (HIV)/hepatitis C virus driven by injection drug use (IDU). We hypothesized that given the unique challenges faced by our population with IDU and inequitable healthcare access, our cases of *S. lugdunensis* IE might differ from those in the published literature.

In fact, in clinical practice, *S. lugdunensis* is often compared to *S. aureus*, owing to the fact that they have some common virulence factors, such as adhesion factors and biofilms. In contrast to other coagulase-negative *Staphylococci* that more commonly affect prosthetic valves, *S. lugdunensis* tends to infect native valves and can be associated with valvular destruction, abscess formation, and metastatic infection. In fact, in clinical practice, *S. lugdunensis* can behave as aggressively as *S. aureus*. Although it is usually pan-sensitive to penicillins, the propensity of *S. lugdunensis* to cause invasive infection should prompt early consideration for

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**RESUMÉ**

Contexte : *Staphylococcus lugdunensis* est un staphylocoque à coagulase négative virulent qui, à de rares occasions, est à l’origine de l’endocardite infectieuse associée à une mortalité élevée. Une augmentation linéaire des cas d’endocardite infectieuse a été observée au cours des dernières années en Saskatchewan, accompagnée d’une épidémie d’infections par le virus d’immunodéficience humaine (VIH) / virus de l’hépatite C liées à l’utilisation de drogues injectables. Nous avons formulé l’hypothèse qu’en raison des difficultés particulières auxquelles doit faire face notre population qui
Methods: We retrospectively reviewed the cases of S. lugdunensis endocarditis admitted to our tertiary care hospitals in Saskatoon over a 6-year period and analyzed their baseline characteristics, antimicrobial susceptibility data, management, and outcome data, where available, for each patient.

Results: Of the 24 blood cultures positive for S. lugdunensis, as identified by our laboratory, we verified 6 cases of definite IE, and 2 cases of probable IE, applying the modified Duke’s criteria. A total of 5 of 8 cases involved native valves, with only 1 infection of the bio-prosthetic mitral valve, seen in patient with IDU. A total of 5 of 8 cases involved the left-sided valves, with 1 of 8 involving the tricuspid valve. Only 1 death was recorded.

Conclusions: The male predominance and primarily left-sided valve infection we noted in our review were similar to results in the published literature. We noted a lower rate of surgical intervention and mortality than previously observed, which merits further study. We did not find coinfection with HIV and/or hepatitis C virus as an epidemiologic risk factor, likely owing to the low rate of IDU in our study.

Methods

We conducted a retrospective chart review of all patients > 18 years of age who had blood cultures positive for S. lugdunensis in the preceding 6 years (2013-2018) and were admitted to one of our 2 main local hospitals. The laboratory database included 1 large tertiary academic hospital and 1 large tertiary community hospital. These hospitals are both located in Saskatoon and service the northern half of Saskatchewan. We systematically gathered information, using our data collection tool (see Supplemental Appendix S1). We identified which of these patients met possible or definite criteria for infective endocarditis based on the modified Duke criteria. We gathered the following information: demographic characteristics; admitting and discharge diagnoses; likely portal of entry; first 5 listed comorbidities obtained from the health record; hepatitis C and HIV status; endocarditis location and characteristics of valves involved; presence of an indwelling device (eg, pacemaker); echocardiographic characteristics; penicillin/oxacillin/vancomycin susceptibility; management strategy; and outcome. Information regarding length of stay and need for intensive care unit services were also collected. Mortality will be compared to that in our general IE population and to that in the published literature.

The study was approved by the University of Saskatchewan Biomedical Research Ethics Board, and the need to obtain informed consent was waived. Patients and the public were not involved in the design or reporting of this article.

Results

Of the 24 blood cultures positive for S. lugdunensis that were identified in the database, 3 were excluded from the chart review. Two patients were not hospitalized, making clinical details unavailable, and 1 patient’s blood culture was erroneously included by the laboratory. This exclusion process left 21 patients who underwent chart review, which identified 6 patients with definite IE, and 2 patients with possible IE (see Fig. 1). Demographic information, important comorbidities, and clinical characteristics are outlined by case in Table 1 and summarized in aggregate in Table 2. None of the patients had HIV or hepatitis C coinfection, and none had pacemaker-related infections. A total of 75% of patients had vegetation as seen on transthoracic echocardiography, and the valves involved are described in Table 1. Patient #7 met 1 of the major and several minor criteria for endocarditis, but the more likely source of his bacteremia was an indwelling vascular catheter. As an echocardiogram was not performed, it is not possible to rule out concomitant IE.

One patient had mitral prosthetic valve infection (12.5% of sample). He had a bioprosthetic mitral valve S. lugdunensis vegetation, concomitant IDU, and he died in the intensive care unit after being deemed a nonsurgical candidate. Given that this death was the only one, the overall mortality of our sample was 12.5% (1 of 8). The majority (6 of 8) of S. lugdunensis
isolates were susceptible to penicillin. One isolate was not reported, and the other was penicillin-resistant, with a minimum inhibitory concentration (MIC) > 0.5, and oxacillin-resistant (MIC > 4), but sensitive to vancomycin (MIC < 0.5).

**Discussion**

Our clinical review of 8 cases of *S. lugdunensis* endocarditis demonstrated an in-hospital mortality of 12.5%, compared to 21% in both our general IE population and the published literature. These 8 cases represented 1.3% of our total number of admitted endocarditis cases over the same time frame. Furthermore, among definite cases, 16.7% of patients (1 of 6) had infected prosthetic valves. Both of the surgically managed patients had large vegetations (> 20 mm) and successful valve replacements. The medically managed patients also had good outcomes when they did not have traditional surgical indications for IE.

The most comprehensive recent review of *S. lugdunensis* IE was done by Liu et al. in 2010. The patients in their cohort were

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**Table 1. Clinical characteristics, management, and outcomes**

| Age, y | Sex | Comorbidities | Valve involved, clinical presentation | Complications | Management |
|--------|-----|---------------|---------------------------------------|---------------|------------|
| 33     | M   | History of MV IE ×2, prosthetic MV, chronic pancreatitis, active IDU, depression | MV involved, 27-mm vegetation | ICU admission, persistent bacteremia, shock | Not surgical candidate, started on cloxacillin until death |
| 42     | F   | PE, DM, anxiety | TV involved, 10-mm vegetation, presented with bacteremia | Persistent bacteremia, lung emboli | No surgery; started on vancomycin planned for 6 wk, actual duration unknown |
| 44     | F   | MS, mixed CTD, ILD, chronic pancreatitis, hypothyroidism | MV involved 26 × 20-mm vegetation, presented with right-sided stroke | Brain emboli, immune phenomena, vascular phenomena | Underwent MVR; vancomycin planned for 6 wk, received 7 wk |
| 52     | M   | BAV, congenital VSD, AR, TKA, ex-smoker | AV involved, “small” vegetation | None | No surgery; cefazolin planned for 6 wk; received 6 wk |
| 62     | M   | DM, PVD, BPH, HTN, AF | No vegetation on echo, presented with sepsis | Osteomyelitis | No surgery; cefazolin planned for 6 wk; received 6 wk |
| 63     | M   | MI, CABG, rapid AF with precocious HTN, dystipidemia | MV involved, presented with CHF, 28 × 20-mm vegetation | Persistent bacteremia, vascular phenomena | Underwent MVR, modified De Vega TVR, PFO repair; cloxacillin planned for 6 wk, received 6 wk |
| 66     | M   | HTN, cataracts, AF, anemia | No echo performed; treated per Duke’s as possible IE, admitting diagnosis was multiple myeloma | Persistent bacteremia | No surgery; planned pipsaz for 2 wk, received for 3 wk |
| 89     | M   | AF, COPD, CKD, DM, HTN | AV involved, presented with sepsis, 15 × 3-mm vegetation | Persistent bacteremia, osteomyelitis | Not surgical candidate; cefazolin planned for 6 wk, received 6 wk |

Outcome for all patients was discharge alive with clinical improvement, except for 1 (male, age 33 years) who died in the hospital. AF, atrial fibrillation; AR, aortic regurgitation; AV, aortic valve; BAV, bicuspid aortic valve; BPH, benign prostatic hyperplasia; CABG, coronary artery bypass grafting; CHF, congestive heart failure; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; CTD, connective tissue disease; DLP, dyslipidemia; DM, diabetes mellitus; echo, echocardiography; F, female; HTN, hypertension; ICU, intensive care unit; IDU, injection drug use; IE, infective endocarditis; ILD, interstitial lung disease; M, male; MI, myocardial infarction; MS, multiple sclerosis; MV, mitral valve; MVR, MV replacement; PE, pulmonary embolism; PFO, PV, pulmonic valve; PVD, peripheral vascular disease; TKA, total knee arthroplasty; TV, tricuspid valve; TVR, tricuspid valve replacement; VSD, ventricular septal defect.
Coagulase-negative Staphylococci (S. lugdunensis) suggesting that it is a possible risk factor as it is with other Staphylococci. In addition, one of our patients had injection drug use (IDU), and oxacillin-sensitive. Conversely, we observed a lower rate of surgical interventions in patients with S. lugdunensis compared to previous reports. The rate of surgery and mortality in our sample were low, 68.7% received valve replacement in addition to antibiotics, and greater than 80% of infections were in native valves, mostly left-sided valves (86.6%) were affected, with the mitral valve (40.3%) more commonly involved than the aortic valve (25%). Greater than 80% of patients with S. lugdunensis endocarditis had better outcomes. Medical management patients did not meet standard surgical indications (see Table 5 in Baddour et al.).

The rate of surgery and mortality in our sample were low, in contrast to previous findings. Upon further review, other than having S. lugdunensis bacteremia, most of our medically managed patients did not meet standard surgical indications (see Table 5 in Baddour et al.). Despite being offered medical management only, all of these patients appeared to have good outcomes at the time of discharge from the hospital. Alternatively, our patients with large vegetations, congestive heart failure, shock, and embolic phenomena—when deemed to be surgical candidates—did receive surgery, which also led to good outcomes. In other words, it may be possible to select patients for surgical interventions based on the traditional guideline-driven "clinical and echocardiographic features that suggest potential need for surgical intervention," rather than solely on the presence of S. lugdunensis endocarditis. Our data suggest that a well selected patient with uncomplicated S. lugdunensis endocarditis may do well with medical therapy alone. However, we caution the reader that further studies—ideally prospective ones, including a larger number of patients in high-volume surgical centres—should be undertaken prior to drawing more-definitive conclusions.

The present study has noteworthy limitations, attributable to mainly the small sample size. As a consequence, we cannot make statistical comparisons with previous reviews. That being said, we have contributed several cases to the literature that will serve well in a future systematic review. Furthermore, we are reporting on the experience at 2 centres only. Thus, our data should be interpreted with caution and should be used for hypothesis-generating rather than practice-changing. Finally, we do not have concrete data available on relapses and readmissions for discharged patients, but the absence of subsequent S. lugdunensis blood cultures in studied patients was used as a surrogate for such data.

### Conclusion

*S. lugdunensis* is an uncommon but important cause of IE in the Saskatchewan population. Due to our overall small sample size, with a single patient known to have IDU, HIV and hepatitis C coinfection do not seem to be a significant epidemiologic factor. The principles of medical management of *S. lugdunensis* endocarditis cases should follow the standard of care for treatment of *Staphylococcus* endocarditis. The need for surgical management may be guided more by traditional factors rather than the presence of *S. lugdunensis*, as emphasized in the current literature. More cases with a focus on clinical outcomes should be reported to solidify confidence in this conclusion.

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### Disclosures

The authors have no conflicts of interest to disclose.

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**Supplementary Material**

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