European Journal of Clinical Microbiology & Infectious Diseases (2021) 40:1103–1106
https://doi.org/10.1007/s10096-020-04134-w

BRIEF REPORT

Endocarditis due to *Staphylococcus lugdunensis*—a retrospective national registry–based study

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Received: 15 October 2020 / Accepted: 16 December 2020 / Published online: 30 December 2020

Abstract

We present characteristics of infective endocarditis (IE) caused by *Staphylococcus lugdunensis* and compare with IE caused by *Staphylococcus aureus* and other CoNS, in the National Swedish Registry of IE (2008–2018). Thirty episodes of *S. lugdunensis* IE were registered, of which 21 cases affected native valves, and 7 patients were subjected to surgery. The mortality rate at 30 days was significantly higher for *S. lugdunensis* IE (20%, $n = 6$), than for IE caused by other CoNS (7%) or *S. aureus* (9%) $p = 0.016$. Septic embolisation was only reported in two cases (7%). The most common treatment was isoxazolyl penicillin ($n = 18$).

Introduction

Staphylococcus lugdunensis belongs to the group of CoNS and was first described in 1988 [1–3]. Since then, *S. lugdunensis* has attracted increasing interest as a cause of infective endocarditis (IE). It is known to infect native valves to a larger extent than other CoNS, and to have a clinical presentation more similar to *S. aureus* [4]. Several case reports indicate that *S. lugdunensis* can cause severe IE with rapid destruction of heart valves and massive septic embolisation [5–9], and many studies have emphasised the importance of early surgical intervention [7, 8, 10]. *S. lugdunensis* is also often susceptible to narrow-spectrum antibiotics including penicillin, and recent reports have indicated that benzyl penicillin may be a better alternative for susceptible isolates than standard treatment with isoxazolyl penicillin or vancomycin [11–13].

Our aim was to describe the clinical presentation of IE caused by *S. lugdunensis*, and to compare it with the clinical presentation of IE caused by other CoNS and *S. aureus*. A secondary aim was to present the antibiotic treatment of *S. lugdunensis* IE.

Material and methods

We retrospectively reviewed cases of IE caused by *S. lugdunensis*, *S. aureus* and other CoNS from the Swedish Registry of Infective Endocarditis between 2008 and 2018.

Cases were classified according to Duke's criteria [14, 15]. If information about comorbidities were missing, we interpreted it as a negation of that condition. For other missing data, no imputations were made. Treatment delay was defined as days from onset of symptoms until start of IE treatment. Definite antibiotic treatment was defined as the antibiotic given more than 50% of the treatment time. Antibiotic susceptibility data were received by personal contact with the local microbiological department at each site. Antibiotic susceptibility testing was performed according to EUCAST guidelines [16].

Comparisons between groups were made with chi-squared test when testing categorical variables and Mann-Whitney *U* test for continuous data. Survival data were calculated with a Kaplan-Meier survival curve and log-rank test. Two-tailed $p < 0.05$ was regarded as

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statistically significant. Analyses were performed using the SPSS software, version 25 (SPSS, Armonk, NY, USA).

The study was approved by the Medical Ethics Committee (Institutional Review Board) of Lund University (Dnr 2017/1002).

Results and discussion

In total, we found 30 cases of IE caused by *S. lugdunensis*, 262 cases of IE caused by other CoNS and 1892 cases of IE caused by *S. aureus*. Clinical characteristics of the different groups are summarised in Table 1. Patients with *S. lugdunensis* IE were significantly older than patients with IE caused by *S. aureus* (73 vs 66 years, $p = 0.01$). When iv-drug users were excluded, the median age of *S. aureus* cases increased to 69.5 years, and the age difference between the groups was no longer significant ($p = 0.44$). In agreement with previous reports, 21 patients (70%) in the *S. lugdunensis* group had native valve IE, and the most common localisation was the aortic valve (60%) [7, 17]. The proportion of native valve IE in the *S. lugdunensis* group was similar to that in *S. aureus* IE, but significantly higher than for other CoNS (70% vs 35%, $p = 0.0001$).

Table 1 Patient characteristics and outcome data

Bacteria (*n*)	*S. lugdunensis* *n* = 30	CoNS *n* = 262	*P* value CoNS *vs S. lugdunensis*	*S. aureus* *n* = 1892	*P* value *S. aureus vs S. lugdunensis*
Background data					
Age (years); median (IQR)	*73 (65–84)*	72 (61–80)		66 (45–79)	$p = 0.01$
Gender-female	*11 (37%)*	86 (33%)		725 (38%)	
Diabetes	*9 (30%)*	58 (22%)		349 (18%)	
Cancer last 5 years	*6 (20%)*	46 (18%)		173 (9%)	$p = 0.042$
IV drug users	*0 (0%)*	9 (3%)		448 (24%)	$p = 0.002$
Prosthetic valve	*8 (27%)*	115 (44%)		255 (14%)	$p = 0.037$
Pacemaker/ICD	*1 (3%)*	74 (28%)	$p = 0.031$	324 (17%)	$p = 0.046$
Native valve disease	*5 (17%)*	55 (21%)		222 (12%)	
Treatment delay, days median (IQR)	*9 (4-15)*	10 (3–26)		5 (2-9)	$p < 0.001$
Dukes criteria					
Definite	*27 (90%)*	194 (74%)		1544 (82%)	
Possible	*3 (10%)*	67 (26%)		338 (18%)	
Localisation					
Aortic	*18 (60%)*	121 (46%)		577 (31%)	$p = 0.001$
Mitral	*10 (33%)*	76 (29%)		596 (32%)	
Tricuspid	*1 (3%)*	22 (8%)		441 (23%)	$p = 0.01$
Type of infection					
Prosthetic IE	*6(20%)*	110 (42%)	$p = 0.02$	245 (13%)	
Pacemaker/ ICD IE	*1(3%)*	48 (18%)	$p = 0.01$	179 (9%)	
Native valve IE	*21 (70%)*	90 (35%)	$p = 0.0001$	1103 (58%)	
Community acquired	*25 (83%)*	179 (68%)		1543 (82%)	
Outcome					
Antibiotic treatment, median days (IQR)	*31 (18–37)*	35 (28–42)	$p = 0.046$	30 (28-40)	
Embolisation	*2 (7%)*	62 (24%)	$p = 0.033$	907 (48%)	$p < 0.001$
Surgical intervention	*7 (23%)*	111 (42%)	$p = 0.044$	455 (24%)	
Day of surgery, median (IQR)	*5 (1–9)*	12 (5-20)		12 (7-23)	
Mortality at 30 days	*6 (20%)**	17(7%)		166 (9%)	
In-hospital mortality	*7 (23%)*	49 (19%)		268 (14%)	
Day of death in hospital, Median (IQR)	*9 (8–23)*	36 (28–47)	$p = 0.007$	25 (14-39)	$p = 0.016$

Data are presented as number and (%) unless otherwise stated. Survival data calculated with Kaplan-Meier survival curve and log-rank test

ICD intracardiac device, *IQR* interquartile range

*$p = 0.016$

There was a significantly lower occurrence of septic embolisation in patients with *S. lugdunensis* IE (7%, $n = 2$), both compared with the *S. aureus* group (48%, $p < 0.001$) and the other CoNS group (24%, $p = 0.033$). This is in contrast to earlier published studies, reporting a high frequency of severe septic embolisation [5, 6, 8, 9]. This discrepancy could be a result of previous publication bias, unthorough clinical examination or failure to report correctly to the database registry. Speaking against the latter is that the embolisation frequency for *S. aureus* was in line with previously published data [18].

Moreover, earlier studies have reported a need of surgical intervention in a large proportion of cases [5, 7, 19], but only seven patients with *S. lugdunensis* IE (23%) underwent surgery in our cohort. This was similar to the *S. aureus* group (24%) but lower than for other CoNS cases (42% vs 23%, $p = 0.044$), which can probably be attributed to the high proportion of prosthetic valve IE in the other CoNS group.

In-hospital mortality was comparable between the groups. However, death occurred after a median time of 9 days in the *S. lugdunensis* group, which was significantly earlier than both the groups of *S. aureus* (median 25 days, $p = 0.016$) and other CoNS (median 36 days, $p = 0.007$) as visualised in Fig. 1 and Table 1. This makes all-cause mortality at 30 days significantly higher in the *S. lugdunensis* group (20%, $n = 6$) compared with other CoNS (7%, $n = 17$) and *S. aureus* (9%, $n = 166$), $p = 0.016$. This indicates, as previously reported, that *S. lugdunensis* on some occasions can cause an aggressive form of IE, which supports the importance of early identification and early surgical intervention for this pathogen [7, 8, 10].

The most common antibiotic treatment of *S. lugdunensis* IE, given to 18 cases (60%), was an isoxazolyl penicillin. All isolates were reported susceptible to isoxazolyl penicillin, except for two isolates where data were missing. Despite this, 7 patients (23%) received treatment with different antibiotic combinations, and only one of these patients had a prosthetic valve IE. Only one isolate was tested for penicillin G even though *S. lugdunensis* is known to have a conserved susceptibility to most antibiotics [5, 12, 20]. Recent research has suggested penicillin to be the preferred treatment of *S. lugdunensis* infections [12], and reliable methods for susceptibility testing are available [21].

The most important weakness of this study is the small number of *S. lugdunensis* IE cases. Given the few cases of *S. lugdunensis* IE, this study was underpowered to detect any small differences between the groups, and statistically significant differences have to be interpreted with caution. Even so, this is to our knowledge the largest *S. lugdunensis* IE cohort described, and the registry-based design of the study adds important knowledge about the clinical presentation of *S. lugdunensis* IE.

Acknowledgements The authors wish to thank the Swedish Registry of Infective Endocarditis.

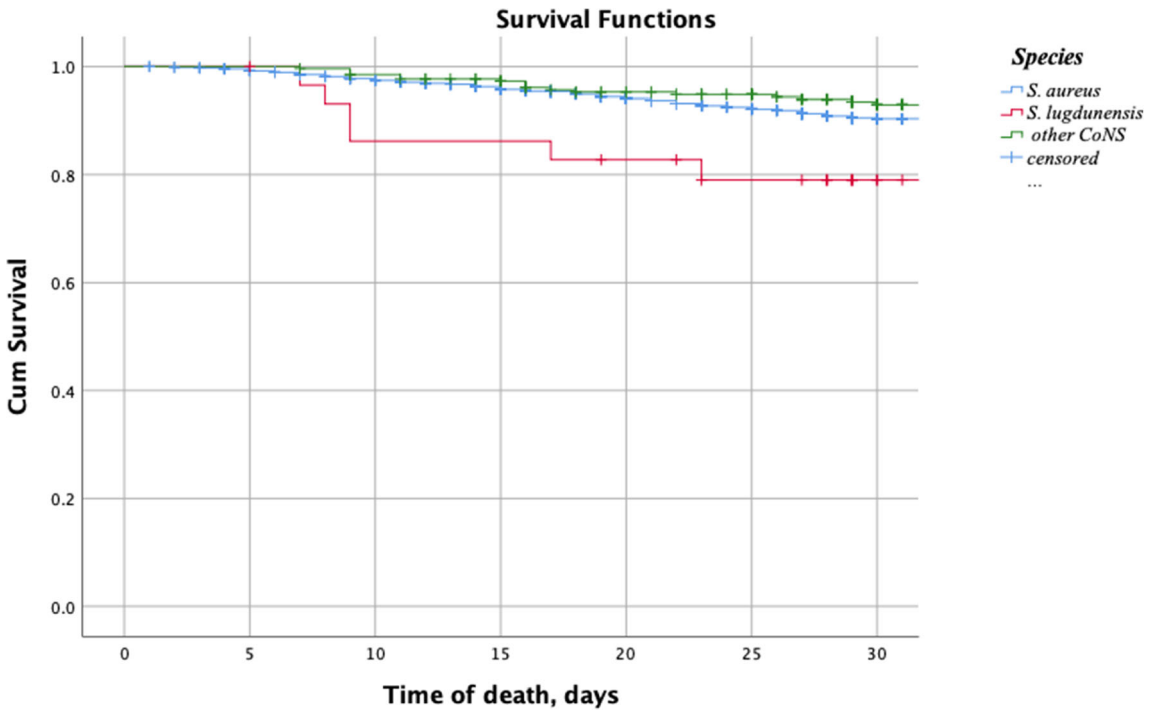

Fig. 1 Kaplan-Meier plot survival after hospitalisation with IE caused by different staphylococci

Funding Open Access funding provided by Lund University. This work was funded by the Regional Research Funds, grant numbers 40231 and 40284; Skåne University Hospital Foundations, grant number 91202; MIMS Clinical Research Fellows, grant number 81226; and The Knut and Alice Wallenberg foundation, the Medical Faculty at Lund University and Region Skåne, grant number 81234.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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