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Original article

Staphylococcus lugdunensis prosthetic joint infection: A multicentric cohort study

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SUMMARY

Objectives: To describe *Staphylococcus lugdunensis* prosthetic joint infection (PJI) management and outcome.

Methods: Adults with proven *S. lugdunensis* PJI were included in a multicentric retrospective cohort. Determinants for failure were assessed by logistic regression and treatment failure-free survival curve analysis (Kaplan-Meier).

Results: One hundred and eleven patients were included (median age 72.4 [IQR, 62.7–79.4] years), with a knee ($n = 71$, 64.0%) or hip ($n = 39$, 35.1%) PJI considered as chronic in 77 (69.4%) cases. Surgical management consisted in debridement, antibiotic with implant retention (DAIR; $n = 60$, 54.1%), two-stage ($n = 28$, 25.2%) or one-stage ($n = 15$, 13.5%) exchange. Total duration of antimicrobial therapy was 13.1 (IQR, 11.8–16.9) weeks. After a median follow-up of 99.9 (IQR, 53.9–178.1) weeks, 22 (19.8%) *S. lugdunensis*-related treatment failures were observed. Independent determinants for outcome were diabetes (OR, 3.741; $p = 0.036$), sinus tract (OR, 3.846; $p = 0.032$), DAIR (OR, 3.749; $p = 0.039$) and rifampin-based regimen (OR, 0.319; $p = 0.043$). Twenty-four (40.0%) of the 60 DAIR-treated patients experienced treatment failure, with hip location (OR, 3.273; $p = 0.048$), delay from prosthesis implantation (OR, 1.012 *per* month; $p = 0.019$), pre-surgical CRP level >115 mg/L (OR, 4.800; $p = 0.039$) and mobile component exchange (OR, 0.302; $p = 0.069$) constituting additional determinants of outcome.

Conclusions: *Staphylococcus lugdunensis* PJI are difficult-to-treat infections, with pivotal roles of an optimal surgical management.

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Introduction

Staphylococcus lugdunensis is a coagulase-negative staphylococci (CoNS) colonizing skin flora of 30% to 50% of individuals [1]. In the last decade, the use of matrix-assisted laser desorption ionization–time of flight mass spectrometry (MALDI-TOF-MS) for routine bacterial identification has raised awareness of the prevalence of invasive infections related to this species, until then often misidentified as *S. aureus* due to the production of clumping factor foiling the slide coagulase test [2]. As a result, *S. lugdunensis* has been increasingly described in bacteremia and infective endocarditis of particular virulence, and seems particularly associated with bone and joint infections [3,4]. Among those, it generates prosthetic joint infection (PJI) with clinical characteristics and outcome more akin to those of *S. aureus* than its other CoNS counterparts [5,6]. This might rely on various virulence factors associated with bone and joint infection (BJI), including a large panel of adhesion proteins – which can trigger bone tissue colonization, biofilm formation and internalization within host cells [7,8] –, and its ability to form small colony variants [9,10].

Data regarding the specific management of *S. lugdunensis* PJI are limited to small retrospective cohorts, restricting conclusions of therapeutic outcome analysis to the need of aggressive surgical strategies and prolonged intravenous antimicrobial therapy [11–13]. In order to refine these findings, we designed a large multicentric cohort study describing clinical characteristics, management and outcome of patients with *S. lugdunensis* PJI.

Materials and methods

Ethical statement

The study (ClinicalTrials.gov registration number NCT04409392) received the approval of the Scientific and Ethical Committee of Hospices Civils de Lyon, France (reference number 21_068). In accordance with French legislation regarding retrospective observational studies, all patients received written information about the study and their possibility to decline to participate, but the need for written informed consent was waived.

Study design and included population

All patients diagnosed with a *S. lugdunensis* PJI in the 11 study centers (including three tertiary care centers and eight general hospitals in South-East France) were included in a retrospective cohort study (2010–2020). Patients were identified by cross-reviewing databases of clinical centers and results of orthopedic sample cultures of the laboratories of bacteriology. Clinical, biological and bacteriological data were retrospectively collected from the medical records in an anonymous case report form.

Definitions

The European Bone and Joint Infection Society (EBJIS) definition of PJI was used to include “likely” or “confirmed” infections, according to the presence of clinical, radiological and/or histological signs of infection, associated with gold-standard bacteriological sample(s) (i.e., deep intraoperative fluid or tissue sample) positive in culture for *S. lugdunensis* [14]. As *S. lugdunensis* is an uncommon contaminant and virulent microorganism, one positive sample was considered as sufficient for the diagnosis of PJI in the presence with other evidence. Duration of progression from the presumed date of inoculation (i.e., date of device implantation for postoperative infections, or date of symptom/bacteremia for haematogenous infections) up to diagnosis differentiated acute (≤4 weeks) vs. chronic (>4 weeks) infections. Time from prosthetic implantation to infection categorized early (≤3 months), delayed (3–12 months) and late (> 12 months) infections [15].

Patient’s comorbidities were summarized according to the ASA score and the modified Charlson’s comorbidity index.

The surgical strategies considered as optimal were: (i) debridement, antibiotic therapy with implant retention (DAIR) with mobile element exchange for acute PJI; and (ii) one- or two-stage exchange for chronic PJI [16]. Other strategies were considered as “not optimal”. A non-optimal surgery with long-term suppressive antimicrobial therapy was considered as an appropriate medico-surgical strategy.

Treatment failure included infection persistence under treatment, relapse after treatment discontinuation, need for unplanned additional surgery for septic reason, superinfection (i.e., new surgical site infection documented to a different pathogen than the original one), and infection-related death. Patients requiring long-term suppressive antimicrobial therapy with no sign of active infection at the end of follow-up were not considered as failures. Documented superinfections were not considered as *S. lugdunensis*-related treatment failures.

Statistical analysis

Studied variables were described as percentages for dichotomous variables and as medians with interquartile range (IQR) for continuous variables. In percentage calculation, the number of missing values was excluded from the denominator. Nonparametric tests were used to compare groups (Fisher exact and Mann-Whitney U tests), as appropriate. Variation of some variables were assessed using Chi square test for trends over the study period. Kaplan-Meier curves were compared between groups using the log-rank (Mantel-Cox) test. Determinants of treatment failure were assessed using stepwise binary logistic regression, and expressed as odd ratios (ORs) with their 95% confidence intervals (95%CI). Non-interacting variables with medical meaning and p-values obtained in univariate analysis <0.15 were included in the final multivariate model. A p-value <0.05 was considered significant. All analyses were performed using SPSS v19.0 (SPSS, Chicago, IL, USA) and GraphPad-Prism v5.03 (GraphPad, San Diego, CA, USA) softwares.

Results

Included population

After exclusion of two individuals who declined to participate, 111 patients were included (75 males [67.6%], median age 72.4 [IQR, 62.7–79.4] years), presenting a knee ($n = 71$, 64.0%), hip ($n = 39$, 35.1%) or shoulder ($n = 1$, 0.9%) *S. lugdunensis* PJI. Main prosthesis indications were arthrosis ($n = 89$, 80.9%), fracture ($n = 9$, 8.2%) and revision of a previous arthroplasty ($n = 8$, 7.3%). Thirty-seven (42.0%) were cemented prosthesis. Patient and infection characteristics are presented in Table 1. The most frequent comorbidities were obesity (boddy mass index [BMI] > 30 kg/m²; $n = 40$, 37.0%), congestive heart failure ($n = 27$, 24.3%) and diabetes ($n = 23$, 20.7%).

Isolates of *S. lugdunensis* had mostly a multisusceptible profile, with only 4 (3.6%) isolates being resistant to methicillin. Resistance to rifampin, erythromycin, clindamycin and fluoroquinolones was noted in 4 (3.6%), 9 (8.1%), 8 (7.2%) and 6 (5.4%) cases, respectively. Infection were plurimicrobial in 38 (34.2%) cases, *S. lugdunensis* being mostly associated with other CoNS ($n = 20$, 18.0%), *S. aureus* ($n = 8$, 7.2%), enterococci ($n = 6$, 5.4%), streptococci ($n = 5$, 4.5%) and/or *Enterobacteriaceae* ($n = 5$, 4.5%).

Table 1
Description of the included population, comparison of patients without or with treatment failure, and determinants of *S. lugdunensis*-related treatment failure (univariate analysis).

	Descriptive statistics			Univariate analysis		
	All patients ($n = 111$)	Treatment success ($n = 89$)	Treatment failure ($n = 22$)	p-value	OR (95%CI)	p-value
Demographics, comorbidity scores						
Age (years)	72.4 (62.7–79.4)	71.3 (63.8–79.0)	74.3 (58.3–83.1)	0.845	0.998 (0.678–1.471)[1]	0.993
Sex (male)	75 (67.6%)	62 (69.7%)	13 (59.1%)	0.343	0.629 (0.240–1.647)	0.345
Modified Charlson comorbidity index	4 (2.5–6)	4 (2–5)	4 (3–6.8)	0.404	1.096 (0.918–1.309)	0.312
ASA score	2 (2–3)	2 (2–3)	2 (2–3)	0.325	1.462 (0.685–3.117)	0.326
Infection characteristics						
Mechanism of acquisition						
Inoculation	83 (74.8%)	69 (77.5%)	14 (63.6%)	1.179	0.507 (0.186–1.380)	0.184
Haematogenous	18 (16.2%)	13 (14.6%)	5 (22.7%)	0.355	1.719 (0.540–5.472)	0.359
Chronology						
Delay from implantation to diagnosis (months)	16.1 (1.4–52.5)	15.0 (1.2–48.6)	31.6 (3.7–85.9)	0.093	1.005 (0.999–1.011)	0.089
Early infection ($\leq$ 3 months)	33 (29.7%)	28 (31.5%)	5 (22.7%)	0.422	0.641 (0.215–1.911)	0.425
Delayed infection (3–12 months	12 (10.8%)	9 (10.1%)	3 (13.6%)	0.702	1.404 (0.346–5.686)	0.635
Late infection ($>$ 12 months)	66 (59.5%)	52 (58.4%)	14 (63.6%)	0.656	1.245 (0.474–3.270)	0.656
Delay from inoculation to management (weeks)	20.9 (3.0–90.1)	20.9 (3.0–88.6)	21.6 (2.9–99.4)	0.953	1.000 (0.998–1.001)	0.730
Chronic infection ($>$ 4 weeks)	77 (69.4%)	62 (69.7%)	15 (68.2%)	0.893	0.933 (0.342–2.548)	0.893
Diagnosis						
Clinical arthritis	44 (41.9%)	33 (39.3%)	11 (52.4%)	0.277	1.700 (0.650–4.448)	0.280
Wound abnormalities	34 (31.8%)	24 (28.2%)	10 (45.5%)	0.122	2.118 (0.809–5.548)	0.127
Abscess	18 (16.7%)	13 (15.1%)	5 (22.7%)	0.393	1.652 (0.518–5.261)	0.396
Sinus tract	18 (17.0%)	10 (11.9%)	8 (36.4%)	0.007	4.229 (1.420–12.592)	0.010
Radiological loosening	23 (23.7%)	16 (21.3%)	7 (31.8%)	0.309	1.721 (0.600–4.935)	0.313
Pre-surgical CRP level (mg/L)	52.0 (15.1–103.5)	18.0 (0.0–71.0)	31.4 (0.0–112.1)	0.185	1.033 (0.984–1.084)[2]	0.194
Surgical management						
Abstention	2 (1.8%)	2 (2.2%)	0 (0%)	1.000	NC	NC
DAIR	60 (54.1%)	43 (48.3%)	17 (77.3%)	0.015	3.637 (1.235–10.714)	0.019
Partial removal/exchange	3 (2.7%)	2 (2.2%)	1 (4.5%)	0.488	2.071 (0.179–23.940)	0.560
1-stage exchange	15 (13.5%)	14 (15.7%)	1 (4.5%)	0.296	0.255 (0.032–2.054)	0.199
2-stage exchange	28 (25.2%)	27 (30.3%)	1 (4.5%)	0.013	0.109 (0.014–0.855)	0.035
Ablation	2 (1.8%)	0 (0%)	2 (9.1%)	0.038	NC	NC
Non-optimal surgical strategy	54 (50.0%)	38 (43.7%)	16 (76.2%)	0.007	4.126 (1.387–12.272)	0.011
Antimicrobial therapy						
Total duration of curative antimicrobial therapy (weeks)	13.1 (11.8–16.9)	13.1 (12.3–17.0)	12.0 (9.1–16.2)	0.191	0.989 (0.927–1.056)	0.741
Parenteral antimicrobial therapy	106 (95.5%)	85 (95.5%)	21 (95.5%)	1.000	0.988 (0.105–9.308)	0.992
Duration of parenteral therapy (days)	17.5 (10.0–38.0)	18.0 (10.0–40.0)	16.0 (8.0–34.8)	0.473	0.992 (0.975–1.011)	0.410
Rifampin-based regimen	79 (71.2%)	68 (76.4%)	11 (50.0%)	0.014	0.309 (0.117–0.813)	0.017
Duration of rifampin (days)	73.0 (32.5–89.0)	50.0 (5.0–85.0)	2.0 (0.0–32.3)	0.113	0.886 (0.806–0.974)[3]	0.012

[1] calcultated for 10 additional years
[2] calcultated for 10 additional mg/L
[3] calculated for every additional week.

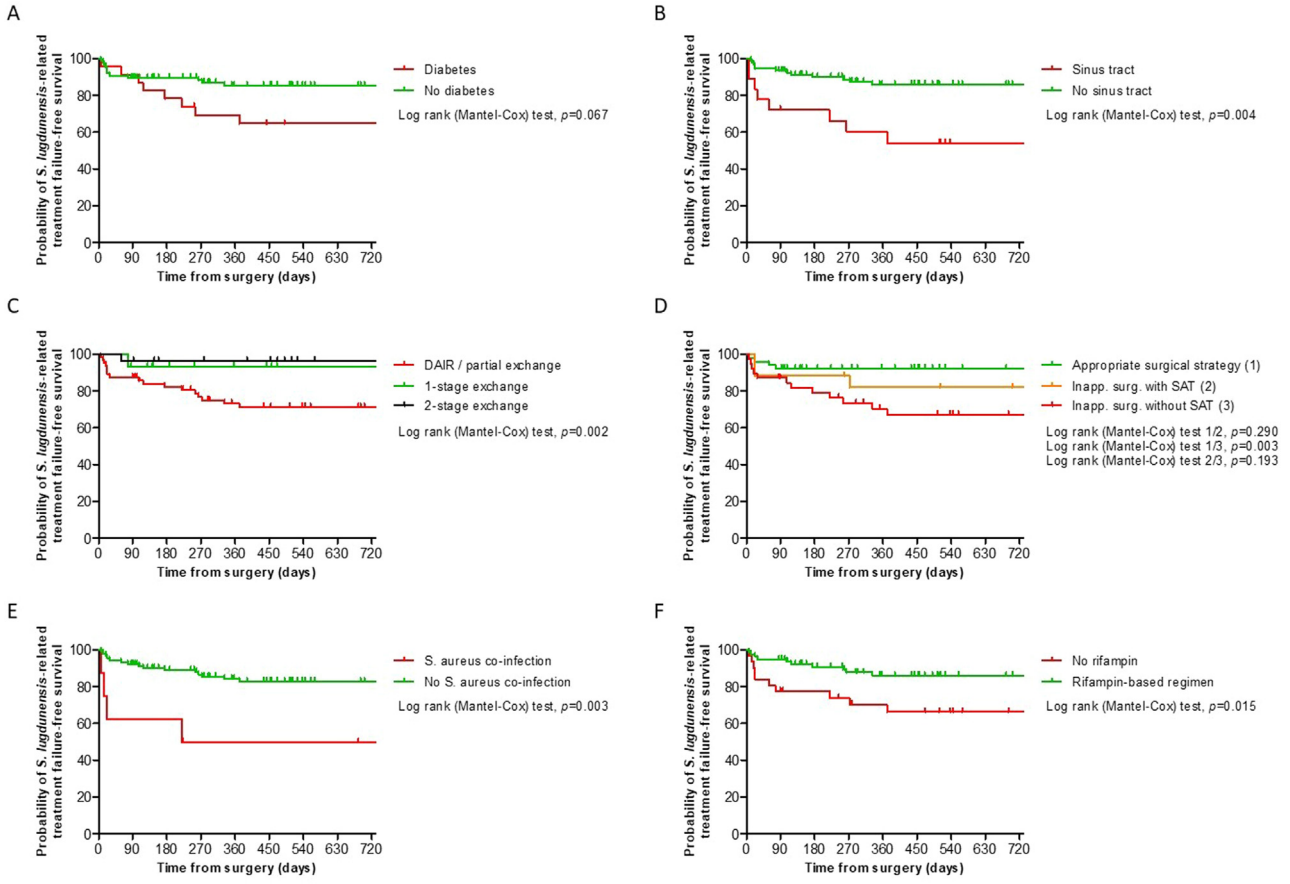

Fig. 1. Kaplan-Meier survival curve for probability of survival without *S. lugdunensis*-related failure in all patients with PJI, according to the main determinants of outcome. *DAIR, Debridement, antimicrobial therapy and implant retention; SAT, Suppressive antimicrobial therapy.*

Patient management

All but two patients benefited from surgery, mostly consisting in DAIR ($n=60$, 54.1%), two-stage ($n=28$, 25.2%) or one-stage ($n=15$, 13.5%) exchanges. The surgical strategy was considered as non-optimal in 54 (50.0%) cases. Total duration of antimicrobial therapy was 13.1 (IQR, 11.8–16.9) weeks, including 17.5 (IQR, 10.0–38.0) days of intravenous treatment. After the initial empirical antimicrobial therapy, the intravenous molecule was mainly an anti-staphylococcal beta-lactam ($n=78$, 70.3%) or vancomycin ($n=23$, 20.7%). An oral switch was proposed in 101 (91.8%) patients. The main oral regimens were rifampin-fluoroquinolone ($n=69$, 68.3%) and clindamycine-fluoroquinolone ($n=15$, 14.9%). Rifampin (median dose, 12.6 [IQR, 10.5–14.4] mg/kg/day) was introduced in 79 (71.2%) patients with no significant variation over the study period ($p=0.829$), in a median of 9.0 (3.0–19.5) days after surgery, and for a duration of 73.0 (IQR, 32.5–89.0) days. Seventeen (15.3%) patients required long-term suppressive antimicrobial therapy, consisting in doxycycline ($n=8$, 47.1%), cotrimoxazole ($n=4$, 23.5%), beta-lactam ($n=4$, 23.5%) or pristinamycin ($n=1$, 5.9%).

Outcome

After a median follow-up of 99.9 (IQR, 53.9–178.1) weeks, 38 (34.2%) treatment failures were observed, including 15 (13.5%) infection persistence, 15 (13.5%) relapses, 15 (13.5%) superinfections, and/or 4 (3.6%) infection-related deaths. Twenty-six (23.4%) patients required unplanned additional surgical procedure for septic reason, including 3 (7.9%) limb amputations. Four (3.6%) patients had no prosthesis reimplantation. Excluding superinfections as the only reason for failure, 22 (19.8%) *S. lugdunensis*-related treatment failures were suspected, including 10 (45.5%) microbiologically confirmed. Of note, no significant variation of failure rate was observed over time (Chi square for trends, $p=0.280$).

Focusing on *S. lugdunensis*-related treatment failures, the only comorbidity associated with outcome was diabetes, present in 15 (16.9%) and 8 (36.4%) patients without and with failure, respectively ($p=0.043$), and was significantly associated with outcome in univariate analysis (OR, 2.819; 95%CI, 1.006–7.903; $p=0.049$). Plurimicrobial infection had no impact on the outcome, but *S. aureus* co-infection was more frequent in the subset of patients with failure (4 [18.2%] versus 4 [4.5%]) and was a predictor of poor outcome (OR, 4.722; 95%CI, 1.079–20.667). Non-optimal surgical strategy was associated with failure (OR, 4.126; 95%CI, 1.387–12.272; $p=0.011$). Patients treated with DAIR were more likely to fail (OR, 3.637; 95%CI, 1.235–10.714; $p=0.019$). Conversely, two-stage exchange was protective (OR, 0.109; 95%CI, 0.014–0.855; $p=0.035$). Considering only the 54 patients who benefited from an optimal surgical strategy, only 5 (9.3%) failures were observed. Among medical management, a rifampin-based regimen was the only predictor for treatment success (OR, 0.309; 95%CI, 0.117–0.813; $p=0.017$) (Fig. 1), with no impact of its introduction time after surgery (OR, 0.891; 95%CI, 0.698–1.136). The use of vancomycin as the IV molecule over anti-staphylococcal beta-lactam had no significant impact (OR, 2.129; 95%CI, 0.747–6.070; $p=0.157$). In multivariate analysis, independent predictors of treatment failure remained diabetes (OR, 3.741; 95%CI, 1.088–12.864; $p=0.036$), presence of a sinus tract (OR, 3.846; 95%CI, 1.120–13.204; $p=0.032$) and DAIR strategy (OR, 3.749; 95%CI, 1.066–13.181; $p=0.039$). The use of rifampin was associated with favorable outcome (OR, 0.319;

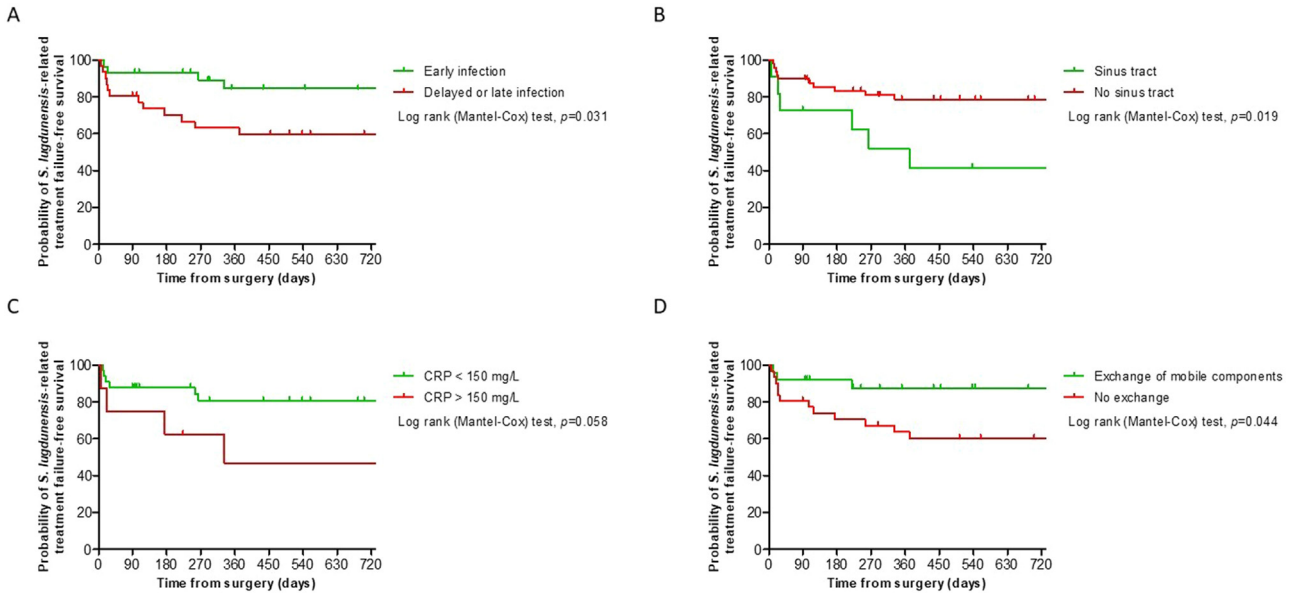

Fig. 2. Kaplan-Meier survival curve for probability of survival without *S. lugdunensis*-related failure in patients treated with DAIR, according to the main determinants of outcome.

95%CI, 0.105–0.967; $p = 0.043$). Of note, only three out of the 17 (17.6%) patients under suppressive antimicrobial therapy experienced treatment failure, in a median follow-up of 3.3 (IQR, 1.9–3.8) years.

DAIR-treated patients

The 60 patients treated with a DAIR strategy are presented in Table 2. Mobile components were exchanged in 25 (44.6%) patients, with no significant variation over the study period ($p = 0.268$). After a follow-up of 120.2 (IQR, 69.9–188.4) weeks, 24 (40.0%) treatment failures were observed, including 17 (28.3%) related to *S. lugdunensis*. Among patients and infection characteristics, diabetes ($n = 12$, 20.0%) tended to be associated with failure (OR, 3.364; 95%CI, 0.902–12.549; $p = 0.071$). Hip location ($n = 20$, 33.3%; OR, 3.273; 95%CI, 1.013–10.578); $p = 0.048$), delay from prosthesis implantation to debridement (OR, 1.012 *per* month; 95%CI, 1.002–1.022; $p = 0.019$), the presence of a sinus tract (OR, 4.036; 95%CI, 1.031–15.796; $p = 0.045$) and a pre-surgical CRP level >115 mg/L (OR, 4.800; 95%CI, 1.086–21.218; $p = 0.039$) were determinants of treatment outcome. Mobile component exchange tended to be associated with better outcome (OR, 0.302; 95%CI, 0.083–1.096; $p = 0.069$) (Fig. 2). The use of rifampin (OR, 0.710; 95%CI, 0.214–2.350) and its introduction time after surgery (OR, 1.072; 95%CI, 0.759–1.515) were not associated with *S. lugdunensis*-related treatment failure in univariate analysis.

Discussion

This study represents the largest series of *S. lugdunensis* PJI available to date. Its retrospective design begets some inherent limitations, including the heterogeneity of patients and their management over time, impeding definitive conclusions regarding the optimal surgical and medical management of *S. lugdunensis* PJI. In particular, standard principles for surgical management of PJI have substantially changed over the study period, including DAIR indications and the need for mobile element exchange, and might not have been implemented similarly by all study centers. However, failure rate did not vary over time, and our results provide insights into diagnosis and management of this emerging and difficult-to-treat BJI.

Demographics of patients were consistent with the usual spectrum of PJIs, with a male predominance, and a median age of 70 years [15,17]. Almost two thirds of cases concerned a knee prosthesis, strengthening the already described overrepresentation of knee location compared to *S. aureus*, with no pathophysiological explanation [5,7,12,13,18].

Staphylococcus lugdunensis appeared as a difficult-to-treat infection, with a specific treatment failure rate of 20%. Of note, defining failures specifically related to *S. lugdunensis* is challenging. In addition to documented *S. lugdunensis* failures, negative culture cases were also included, possibly leading to an overestimation of treatment failure rate. However, our finding was consistent with other series of orthopedic device-related *S. lugdunensis* infection, highlighting failure rates ranging from 6% to 43% [5,11,13,18].

As for all PJI, an optimal surgical management appeared to be a cornerstone for treatment outcome. Using a strict definition, surgical management proposed for half of patients was non-optimal, constituting a major determinant of failure. DAIR also appeared as a risk factor for poor outcome, but this result must be considered with caution given that 50% of infections were lasting for more than 4 weeks, and that mobile elements have been exchanged in less than 50% of patients, which also negatively influenced outcome. Indeed, the impact of mobile element exchange has been well demonstrated for *S. aureus* PJI treated by DAIR [19], and has been included in the CRIME80 prognostic score for late acute PJI [20], but has never been shown for *S. lugdunensis*. Of note, in a retrospective cohort gathering 28 *S. lugdunensis* PJI mainly managed by DAIR (32%) or two-stage exchange (46%), Masood et al. also concluded in favor of aggressive surgical strategies [13]. This statement remains controversial, as other series found no difference in outcome according to surgical strategies [5], but patients with *S. lugdunensis* PJI who might benefit from a DAIR strategy should probably be carefully selected. Finally, other prognosis factors for DAIR-treated *S. aureus* PJI turned to also influence *S. lugdunensis* PJI outcome, including the presence of a sinus tract [21], a high preoperative CRP level [20,22], and delayed or late infection [23]. Unfortunately, the number of patients included in our series did not allow to balance the failure rate according to surgical procedure, or to assess determinant of outcome in each subset

Table 2
Description of the 60 patients treated by DAIR, comparison of patients without or with treatment failure, and determinants of *S. lugdunensis*-related treatment failure (univariate analysis).

	Descriptive analysis			Univariate analysis		
	All patients ($n=60$)	Treatment success ($n=43$)	Treatment failure ($n=17$)	p-value	OR (95%CI)	p-value
Demographics						
Age (years)	72.4 (62.3–80.2)	72.5 (65.1–79.7)	72.3 (56.8–80.2)	0.450	0.845 (0.560–1.275)[1]	0.422
Sex (male)	42 (70.0%)	32 (74.4%)	10 (58.8%)	0.235	0.491 (0.150–1.605)	0.239
Modified Charlson comorbidity index	3 (2–4)	3 (2–3.5)	3 (1–4)	0.766	1.005 (0.819–1.234)	0.961
ASA	2 (2–3)	2 (2–3)	2 (2–3)	0.931	0.902 (0.355–2.289)	0.828
Infection characteristics						
Mechanism of acquisition						
Inoculation	45 (75.0%)	34 (79.1%)	11 (64.7%)	0.324	0.485 (0.141–1.671)	0.252
Haematogenous	12 (20.0%)	7 (16.3%)	5 (29.4%)	0.293	2.143 (0.572–8.026)	0.258
Chronology						
Delay from implantation to diagnosis (months)	3.3 (0.7–47.5)	1.3 (0.7–28.6)	36.2 (2.8–120.5)	0.007	1.012 (1.002–1.022)	0.019
Early infection ($\leq$ 3 months)	29 (48.3%)	24 (55.8%)	5 (29.4%)	0.065	0.330 (0.099–1.100)	0.071
Delayed infection (3–12 months	6 (10.0%)	4 (9.3%)	2 (11.8%)	1.000	1.300 (0.215–7.855)	0.775
Late infection ($>$ 12 months)	25 (41.7%)	15 (34.9%)	10 (58.8%)	0.145	2.667 (0.843–8.435)	0.095
Delay from inoculation to management (weeks)	4.1 (2.4–20.2)	3.7 (2.4–11.7)	12.3 (2.0–25.0)	0.426	1.003 (0.998–1.008)	0.299
Chronic infection ($>$ 4 weeks)	31 (51.7%)	21 (48.8%)	10 (58.8%)	0.485	1.497 (0.481–4.661)	0.487
Diagnosis						
Clinical arthritis	28 (50.0%)	18 (45.0%)	10 (62.5%)	0.237	2.037 (0.621–6.686)	0.241
Wound abnormalities	29 (49.2%)	21 (50.0%)	8 (47.1%)	0.838	0.889 (0.288–2.747)	0.838
Abscess	15 (25.4%)	10 (23.8%)	5 (29.4%)	0.654	1.333 (0.377–4.710)	0.655
Sinus tract	11 (18.6%)	5 (11.9%)	6 (35.3%)	0.037	4.036 (1.031–15.796)	0.045
Radiological loosening	5 (9.1%)	2 (5.3%)	3 (17.6%)	0.165	3.857 (0.581–25.601)	0.162
Pre-surgical CRP level (mg/L)	73.0 (42.5–125.0)	42.5 (0.0–94.5)	53.0 (0.0–140.0)	0.237	1.028 (0.974–1.085)[2]	0.323
CRP $>$ 115 mg/L	12 (29.3%)	6 (20.0%)	9 (54.5%)	0.031	4.800 (1.086–21.218)	0.039
CRP $>$ 150 mg/L	8 (19.5%)	4 (13.3%)	4 (36.4%)	0.099	3.714 (0.737–18.727)	0.112
Surgical management						
Exchange of mobile components	25 (44.6%)	21 (52.5%)	4 (25.0%)	0.079	0.302 (0.083–1.096)	0.069
Non-optimal surgical strategy	46 (80.7%)	31 (75.6%)	15 (93.8%)	0.154	4.839 (0.566–41.377)	0.150
Antimicrobial therapy						
Total duration of curative antimicrobial therapy (weeks)	13.1 (12.3–16.3)	13.1 (12.6–16.0)	13.1 (10.0–16.3)	0.380	0.951 (0.863–1.048)	0.313
Parenteral antimicrobial therapy	58 (96.7%)	42 (97.7%)	16 (94.1%)	0.490	0.381 (0.022–6.462)	0.504
Duration of parenteral therapy (days)	17.5 (9.8–35.8)	18.0 (11.0–34.5)	17.0 (8.0–35.0)	0.812	1.006 (0.979–1.033)	0.680
Rifampin-based regimen	42 (70.0%)	31 (72.1%)	11 (64.7%)	0.574	0.710 (0.214–2.350)	0.575
Duration of rifampin (days)	74.0 (33.0–86.8)	52.0 (0.0–83.5)	15.0 (0.0–75.0)	0.103	0.925 (0.836–1.023)[3]	0.128

[1] calcultated for 10 additional years.
[2] calcultated for 10 additional mg/L.
[3] calculated for every additional week.

of surgical strategies and specifically in patients receiving optimal surgical treatment.

The only determinant of outcome among medical treatment was the use of rifampin. Its excellent antistaphylococcal activity and bone penetration, along with its antibiofilm and intracellular activities, make it a drug of choice in BJI [24,25]. Indeed, various studies have shown the superiority of rifampin-based combination therapies in *S. aureus* PJI treated by DAIR [26,27]. The ability of *S. lugdunensis* isolated from BJI to rapidly form biofilm advocates for the use of such molecules [7]. While our results highlighted a superiority of rifampin for the whole cohort, they failed to show a significant benefit in case of implant retention, for which the antibiofilm activity is believed to be the most important. Although this last statement has never been demonstrated, this negative finding could result from the relatively small size of this subset of patients, and the overpowering impact of the non-optimal surgical strategy for a large part of the patients. Additionally, an in vitro study showed that biofilm bactericidal concentrations of rifampin against clinical isolates of *S. lugdunensis* were relatively high (64 mg/L), even if it remained the second more active drug after moxifloxacin [28]. The combination of rifampin and fluoroquinolone was used in 61% of the patients described by Lourtet-Hascoët et al. with a success rate of 89% [5]. Duration of parenteral antimicrobial therapy is also questionable. In most series, a prolonged use of intravenous treatment was proposed, mostly ranging from 4 to 6 weeks [12,18]. In our study, the shorter IV treatment duration of 2–3 weeks did not appear as a determinant of treatment failure. This finding is in line with the recent randomized trial including 639 metalware-related infections showing no superiority of prolonged IV treatment over early (7 days) oral switch [29]. Total duration of antimicrobial therapy was 3 months. Even if one series described good success rates with shorter (7 weeks) courses of treatment [5], most studies reported longer durations [11,12], three months having recently been shown to be the appropriate length of treatment in PJI [30]. Of note, long-term suppressive antimicrobial therapy seemed an efficient strategy when optimal surgical management could not be performed, with a success rate exceeding 80%, which appeared higher than general results for other PJI [31].

In summary, *Staphylococcus lugdunensis* PJI are associated with a high rate of treatment failure, of which the main determinant is the surgical strategy. In particular, indication for DAIR should include mobile element exchange, and be restricted to acute PJI in patients with no other risk factor of failure, including sinus tract. Rifampin-based combination therapy must be proposed as first line medical treatment in patients with no contraindication. In situations in which surgical strategy cannot be optimal, suppressive antibiotic treatment appears as an acceptable alternative.

Transparency declaration

The study was performed as part as our routine work and did not receive any final support.

Conflict of interest

None of the authors has commercial or other associations that might pose a conflict of interest for this manuscript.

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