Brief Report

Prevalence and Factors Associated with Prosthetic Joint Infections in Patients with *Staphylococcus aureus* Bacteraemia: A 7-Year Retrospective Study

Matthais Papadimitriou-Olivgeris 1,2,* , Laurence Senn 1,2, Claire Bertelli 3, Bruno Grandbastien 2, Sylvain Steinmetz 4 and Noémie Boillat-Blanco 1

1 Infectious Diseases Service, Lausanne University Hospital and University of Lausanne, 1011 Lausanne, Switzerland
2 Infection Prevention and Control Unit, Lausanne University Hospital and University of Lausanne, 1011 Lausanne, Switzerland
3 Institute of Microbiology, Lausanne University Hospital and University of Lausanne, 1011 Lausanne, Switzerland
4 Department of Orthopaedics and Traumatology, Lausanne University Hospital and University of Lausanne, 1011 Lausanne, Switzerland

* Correspondence: matthais.papadimitriou-olivgeris@chuv.ch; Tel.: +41-795-565-695

Abstract: Background: *Staphylococcus aureus* is the main cause of haematogenous prosthetic joint infections (PJI). We aimed to describe the prevalence and factors associated with PJI in patients with documented *S. aureus* bacteraemia. Methods: Adult patients with *S. aureus* bacteraemia and presence of prosthetic joint hospitalized in Lausanne University Hospital during a seven-year period (2015–2021) were included. Results: Among 135 patients with *S. aureus* bacteraemia and prosthetic joints, 38 (28%) had PJI. Multivariate analysis revealed that the presence of PJI was associated with knee arthroplasty (*P* 0.029; aOR 3.00, 95% CI 1.12–8.05), prior arthroplasty revision (*P* 0.034; aOR 3.59, 95% CI 1.10–11.74), community-acquired bacteraemia (*P* 0.005; aOR 4.74, 95% CI 1.61–14.01) and age < 70 years (*P* 0.007; aOR 9.39, 95% CI 1.84–47.85). Conclusions: PJI was common among patients with documented *S. aureus* bacteraemia. PJI was associated with characteristics of the prosthesis, such as prior arthroplasty revisions and knee prosthesis.

Keywords: *Staphylococcus aureus*; bloodstream infection; prosthetic joint infection; arthroplasty; community-acquired infection

1. Introduction

Prosthetic joint infection (PJI) is a significant complication of arthroplasties, leading to multiple admissions, increased healthcare costs and associated with increased morbidity and mortality [1–3]. Although the risk of PJI after arthroplasty remains low (up to 2.2%), the increase in PJIs can be attributed to the continual rise in number of total joint arthroplasties and an older and more comorbid population [4,5]. Several risk factors for PJI development after total joint arthroplasty are identified and include increased body mass index, diabetes mellitus, immunosuppression, knee arthroplasty and prior joint surgery [6,7].

A significant proportion of PJIs are due to haematogenous seeding usually occurring more than 3 months after arthroplasty [8,9]. Haematogenous PJIs presents as an abrupt onset of joint symptoms following a symptom-free period, ranging from 3 months to several years. Such symptoms include joint pain, erythema, swelling and drainage [1]. An increase in bacteraemic PJIs has been observed over the last three decades [5]. *Staphylococcus aureus* is the most common pathogen implicated in haematogenous PJIs [9]. In patients with prothetic joints and occurrence of *S. aureus* bacteraemia, the prevalence of PJIs ranges between 20% and 42%, but these results are mostly from studies with low patient numbers [8,10–12].
The aim of this study was to describe the prevalence and factors associated with PJI in patients with documented S. aureus bacteraemia in a Swiss university hospital.

2. Results

A total of 151 patients with S. aureus bacteraemia and presence of a prosthetic joint were identified, from which 16 were excluded (bacteraemia occurrence within 3 months after prosthesis implantation or revision). Hence, 135 patients with 208 joint prostheses (117 hip, 89 knee and 2 shoulder; 73 patients had more than one prosthesis) were included. Of these 208 prostheses, 24 had prior revision; 22 for mechanical reasons (loosening of the prosthesis without signs of infection, metallosis, etc.) and two for PJI by another pathogen.

A total of 39 (19%) PJI cases were diagnosed at the time of S. aureus bacteraemia in 37 (25%) patients (two patients had two PJIs at the same time). Only one patient (3%) was not diagnosed clinically with a PJI at the time of S. aureus bacteraemia; indeed, a collection on CT scan was documented 5 days after S. aureus bacteraemia. Perioperative cultures were positive for S. aureus in 37 (93%) cases and 36 (95%) patients. Orthopaedic characteristics of the joint arthroplasties among patients with PJIs and those without are shown in Table 1.

### Table 1. Orthopaedic characteristics of the joint arthroplasties.

| Localization of prosthesis | No PJI (n = 168) | PJI (n = 40) | P  |
|----------------------------|------------------|-------------|----|
| Hip | 102 (61%) | 15 (38%) | 0.007 1 |
| Knee | 64 (38%) | 25 (63%) | 0.001 |
| Other | 2 (1%) | 0 (0%) | |

| History of revisions | No PJI (n = 168) | PJI (n = 40) | P  |
|----------------------|------------------|-------------|----|
| None | 156 (93%) | 28 (70%) | <0.001 |
| One or more | 12 (7%) | 12 (30%) | 0.355 |

| Months from last revision | No PJI (n = 168) | PJI (n = 40) | P  |
|--------------------------|------------------|-------------|----|
| Asymptomatic | 137 (82%) | 1 (3%) | <0.001 |
| Joint pain | 25 (15%) | 39 (98%) | <0.001 |
| Swelling | 4 (2%) | 20 (50%) | <0.001 |
| Periarticular warmth | 3 (2%) | 10 (25%) | <0.001 |
| Periarticular erythema | 3 (2%) | 13 (33%) | <0.001 |
| Drainage | 0 (0%) | 1 (3%) | 0.192 |

Data are depicted as number and percentage or median and Q1-3. 1 Knee arthroplasty compared to other sites (hip, shoulder).

Among patients with PJI, the median duration of local symptoms before documentation of S. aureus bacteraemia was 3 days (range: 1–40 days), while the median duration of fever (among 33 patients with fever) was 2 days (range: 1–3). Joint pain was present in all 39 initially symptomatic prostheses (Table 1). Swelling was present in 20 (51%) prostheses, periarticular warmth in 13 (33%), periarticular erythema in 10 (26%), and drainage in one (3%). Among patients without PJI, 18% of prosthetic joints presented at least one symptom, with joint pain being the most prominent. Upon bacteraemia onset, no patient was actively receiving antibiotic treatment.

Among the 97 patients who did not have PJI diagnosed at the time of S. aureus bacteraemia, 6-month follow-up information was available for 64 patients (66%) of whom only one developed S. aureus PJI (at 98 days from S. aureus bacteraemia) and 20 patients died in the interval (range 3–131 days after S. aureus bacteraemia) without sign of PJI. For 13 patients, the last follow-up occurred earlier (range 24–124 days after S. aureus bacteraemia).

PJI upon initial hospitalization was associated with younger age, community-acquired bacteraemia, presence of knee prosthesis, prior revision, higher CRP and lower rate of malignancy (Table 2). On multivariate analysis, PJI was associated with knee arthroplasty (P 0.029; aOR 3.00, 95% CI 1.12–8.05), prior arthroplasty revision (P 0.034; aOR 3.59, 95% CI 1.10–11.74), community-acquired bacteraemia (P 0.005; aOR 4.74, 95% CI 1.61–14.01) and age < 70 years (P 0.007; aOR 9.39, 95% CI 1.84–47.85).
Table 2. Characteristics of patients with *S. aureus* bacteraemia in the presence of prosthetic joint according to the presence or absence of prosthetic joint infection (PJI).

| Univariate Analysis | Multivariate Analysis |
|---------------------|-----------------------|
| No PJI (*n* = 97)   | PJI (*n* = 38)        | *P*    | aOR (95% CI) | *P*    |
| Demographics        |                       |        |              |        |
| Male sex            | 67 (69%)              | 26 (68%) | 0.941        |        |
| Age (years)         | 78 (69–84)            | 71 (63–77) | 0.001        |        |
| Age < 70 years old  | 27 (28%)              | 19 (50%) | 0.025        | 9.39 (1.84–47.85) | 0.007 |
| Co-morbidities      |                       |        |              |        |
| Arterial hypertension | 58 (59%)            | 26 (68%) | 0.352        |        |
| Coronary disease    | 27 (28%)              | 5 (13%)  | 0.071        |        |
| Congestive heart failure | 8 (8%)               | 0 (0%)   | 0.105        |        |
| Chronic obstructive pulmonary disease | 12 (12%) | 2 (5%)  | 0.348        |        |
| Cirrhosis           | 11 (11%)              | 3 (8%)   | 0.757        |        |
| Diabetes mellitus   | 33 (34%)              | 9 (24%)  | 0.303        |        |
| Chronic kidney disease (moderate or severe) | 27 (28%) | 8 (21%) | 0.419        |        |
| Malignancy (solid organ or haematologic) | 21 (22%) | 2 (5%)  | 0.023        |        |
| Obesity             | 27 (28%)              | 16 (42%) | 0.109        |        |
| Autoimmune disease  | 15 (16%)              | 7 (18%)  | 0.676        |        |
| Immunosuppression   | 21 (22%)              | 4 (11%)  | 0.217        |        |
| Setting of infection onset |              |        |              |        |
| Community-acquired  | 64 (66%)              | 37 (97%) | <0.001       | 4.74 (1.61–14.01) | 0.005 |
| Nosocomial          | 33 (34%)              | 1 (3%)   |              |        |
| Microbiological data|                       |        |              |        |
| Two or more blood cultures positive | 75 (77%) | 32 (84%) | 0.482        |        |
| Polymicrobial bacteraemia | 8 (8%) | 1 (3%) | 0.444        |        |
| Methicillin-resistance | 11 (11%) | 1 (3%) | 0.178        |        |
| Persistent bacteraemia (≥48 h) | 22 (23%) | 14 (37%) | 0.094        |        |
| Antibiotic treatment (upon bacteraemia onset) | 0 (0%) | 0 (0%) | -            |        |
| Clinical presentation|                       |        |              |        |
| Temperature (°C)    | 38.4 (38.0–39.0)      | 38.6 (37.8–39.0) | 0.892 |        |
| Fever (temperature >38 °C) | 81 (84%) | 33 (87%) | 0.630        |        |
| Sepsis              | 45 (46%)              | 12 (32%) | 0.117        |        |
| Septic shock        | 14 (14%)              | 5 (13%)  | 1.000        |        |
| SOFA score          | 3 (1–5)               | 2 (1–4)  | 0.449        |        |
| Localization of prosthesis |              |        |              |        |
| Hip                 | 68 (70%)              | 19 (50%) | 0.020        | 3.00 (1.12–8.05) | 0.029 |
| Knee                | 42 (43%)              | 25 (68%) |              |        |
| Shoulder            | 2 (2%)                | 0 (0%)   |              |        |
| Multiple joint prosthesis | 44 (45%) | 29 (50%) | 0.624        |        |
| Months since implantation | 71 (37–139) | 103 (53–143) | 0.368 |        |
| Prior revision (more than 3 months before) | 9 (9%) | 12 (32%) | 0.003        | 3.59 (1.10–11.74) | 0.034 |
| Months since last revision | 71 (37–139) | 84 (19–122) | 0.845 |        |
| Laboratory data     |                       |        |              |        |
| C-reactive protein (mg/L) | 229 (118–307) | 337 (243–388) | <0.001 |        |
| C-reactive protein ≥ 220 mg/L | 50 (52%) | 29 (76%) | 0.011        |        |

Data are depicted as number and percentage or median and Q1-3. 1 Knee arthroplasty compared to other sites (hip, shoulder); 95% CI: 95% confidence interval; aOR: adjusted odds ratio; SOFA: Sequential Organ Failure Assessment.

3. Discussion

Our results showed that PJI diagnosis is frequent among patients with *S. aureus* bacteraemia in the presence of prosthetic joints (28%); this rate is similar to that reported in
the literature (20–42%) [8,10,11]. This diagnosis must always be sought in the absence of another obvious source.

Consistent with previous studies, community as opposed to nosocomial acquisition of *S. aureus* bacteremia is associated with PJI [10,11,13]. The duration of nosocomial bacteremia before diagnosis and treatment initiation is probably most often short and prevents such a complication. In this study, age < 70 years was also associated with PJI. This is in line with a previous study which showed that among patients with bacteremia, patients with PJI were younger than those without [15]. However, most studies did not show any age difference [8,10,11]. Younger patients were closer to the date of last revision (median of 66 vs. 74 months; *P* 0.584); in previous studies PJI related to bacteremia was higher during the first year after operation (implantation or revision) [8,14]. Another explanation could be the type of prosthesis implanted, but such information was not collected.

Prosthetic joint characteristics play an important role in PJI development. Indeed, prior revision (more than 3 months before infection) was associated with *S. aureus* bacteraemic PJI. Although prior revision was previously reported [11,13,15], this association with PJI was not universally found [8,10]. Another prosthesis characteristic associated with PJI was presence of a knee prosthesis; such an association was found in some, but not all previous studies with haematogenous *S. aureus* PJIs [4,13,16]. Knee prostheses are usually more difficult to implant than hip prostheses and knee arthroplasty usually results in bone loss, which necessitates a larger prosthesis to compensate for the loss and in turn increases the prosthetic material surface prone to bacterial adhesion [15]. In contrast to Tande et al. [11], the presence of multiple joint prostheses was not associated with PJI in the present study.

Only a minority of PJI were diagnosed in a second step, which reinforces previously published data that in the absence of clinical signs of PJI at the time of *S. aureus* bacteremia, the risk of PJI is extremely low, and no additional diagnostic investigations are necessary [11,17]. As previously shown, the most prominent local symptom was pain, which was universally present in our study, followed by joint swelling, warmth and erythema [11]. As previously shown, in patients without diagnosis of PJI a small percentage of prostheses will become symptomatic upon bacteremia, with the most prominent symptom being joint pain [11].

Only one patient (2%) who did not have PJI diagnosed at the time of *S. aureus* bacteremia (follow-up for 6 months) developed metachronous PJI (124 days after *S. aureus* bacteremia). This finding was in line with previous studies that showed low risk for metachronous PJI. Tande et al. found four (8%) metachronous PJI among 50 patients in 3.4 years follow-up (174 to 670 days after *S. aureus* bacteremia). This higher percentage can be explained by the longer follow-up period (3.4 years); indeed, among these four PJIs only one occurred within 6 months from *S. aureus* bacteremia [11]. In another study, no metachronous infection was diagnosed in 19 patients within a 12-month follow-up after *S. aureus* bacteremia [10].

The present study has several limitations. First, it was a single centre retrospective study with a limited number of patients; in contrast to previous studies [4,10,11,13], upon *S. aureus* bacteremia all patients were evaluated by a specialized team, thus limiting the number of undiagnosed cases. However, the study size is comparable to the largest study to date [13] and significantly higher than most previous studies [8,10,11]. Second, we may have missed PJIs that occurred at a later stage as 6-month follow-up information was missing for 13% of the patients. Third, the prevalence of PJIs among patients with *S. aureus* bacteremia and presence of prosthetic joint could be lower in other settings, since our centre is a tertiary referral hospital. Last, the type of prosthesis implanted was not collected, thus its impact was not assessed.

4. Materials and Methods

This was a retrospective study conducted at Lausanne University Hospital, Lausanne, Switzerland over a seven-year period (1st January 2015 to 31st December 2021). Lausanne
University Hospital is a 1100-bed primary and tertiary care hospital and has a dedicated Septic Surgery Unit.

Inclusion criteria were adults (age ≥ 18 years), *S. aureus* bacteraemia and the presence of at least one prosthetic joint. Exclusion criteria were patients’ written refusal of the use of data and bacteraemia occurrence within 3 months after prosthetic joint implantation or revision (considered to have primary postsurgical PJI) [1,9].

We decided on a 3-month cut-off for the characterization of an *S. aureus* PJI as primary versus haematogenous based on previous studies [1,9]. Since *S. aureus* is highly virulent, its perioperative inoculation leads to local signs development within days or weeks from joint implantation or revision, and rarely after 3 months.

*S. aureus*-positive blood cultures were extracted from the database of the microbiological laboratory. Blood cultures were collected during routine care. Information on the presence or absence of a prosthetic joint was extracted from the patients’ electronic health records.

Data regarding demographics (age, sex), comorbidities (arterial hypertension, coronary disease, congestive heart failure, chronic obstructive pulmonary disease, cirrhosis, diabetes mellitus, chronic kidney disease, malignancy, obesity, autoimmune disease, immunosuppression), number of positive blood cultures, polymicrobial bacteraemia, persistent bacteraemia, C-reactive protein, presence of sepsis or septic shock, prostheses characteristics (timing of implantation, site of prosthetic joint, prior revision), presence of joint symptoms or fever were retrieved from patients’ electronic health records. Study data were collected and managed using REDCap by an infectious disease specialist. REDCap electronic data capture tools is hosted at Lausanne University Hospital. REDCap (Research Electronic Data Capture) is a secure, web-based software platform designed to support data capture for research studies [18,19].

The date of collection of the first positive blood culture was defined as infection onset. Bacteraemia was characterized as community-acquired according to Friedman et al. [20]. PJI was defined upon initial hospitalization according to the European Bone and Joint Infection Society [16]. Diagnosis of PJI the time of bacteraemia was based on at least one positive intraoperative sample (synovial fluid or tissue culture), positive aspiration fluid culture and cytologic/histologic findings. Infection was categorized as sepsis or septic shock according to the definition proposed by the Sepsis-3 International Consensus [21]. C-reactive protein level with a cut-off of ≥220 mg/L was used, because it was previously found to be associated with PJI among patients with *S. aureus* bacteraemia [13]. Malignancy was considered as active solid tumour or haematologic cancer or during the first year from complete remission. Patients’ records were reviewed until the latest clinical visit or death to assess for the occurrence of *S. aureus* PJI not diagnosed at the time of initial hospitalization.

SPSS 26.0 (SPSS, Chicago, IL, USA) was used for data analysis. Categorical variables were depicted as counts and percentages, while continuous with medians and interquartile ranges (IQRs). Differences between patients with and without PJI were analysed by Fisher’s exact test and Mann–Whitney U test, as appropriate. We investigated factors associated with PJI with multivariate logistic regression using backward selection including non-collinear variables. All statistical tests were two-tailed and *P* < 0.05 was considered statistically significant.

5. Conclusions

PJI was common among patients with documented *S. aureus* bacteraemia, particularly for community-acquired bacteraemia, and almost always clinically conspicuous at the time of bacteraemia diagnosis. PJI was associated with characteristics of the prosthesis, such as prior arthroplasty revisions and knee prosthesis. The risk of metachronous PJI was low.

Author Contributions: Conceptualization: M.P.-O., N.B.-B.; methodology: L.S., B.G., S.S.; formal analysis and investigation: L.S., C.B., S.S.; writing—original draft preparation: M.P.-O.; writing—review and editing: L.S., C.B., B.G., S.S., N.B.-B.; supervision: N.B.-B. All authors have read and agreed to the published version of the manuscript.
**Funding:** This research received no external funding.

**Institutional Review Board Statement:** The study was approved by the ethics committee of the Canton of Vaud (CER-VD 2021-02516).

**Informed Consent Statement:** The Ethical Committee waived the need for informed consent.

**Data Availability Statement:** The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

**Conflicts of Interest:** The authors declare no conflict of interest.

**References**

1. Zimmerli, W.; Trampuz, A.; Ochsner, P.E. Prosthetic-joint infections. *N. Engl. J. Med.* 2004, 351, 1645–1654. [CrossRef] [PubMed]
2. Boddaert, V.; Fu, M.C.; Mayman, D.J.; Su, E.P.; Sculco, P.K.; McLawhorn, A.S. Revision Total Knee Arthroplasty for Periprosthetic Joint Infection Is Associated with Increased Postoperative Morbidity and Mortality Relative to Noninfectious Revisions. *J. Arthroplast.* 2018, 33, 521–526. [CrossRef] [PubMed]
3. Fischbacher, A.; Borens, O. Prosthetic-joint Infections: Mortality over the Last 10 Years. *J. Bone Jt. Infect.* 2019, 4, 198–202. [CrossRef] [PubMed]
4. Kurtz, S.; Ong, K.; Lau, E.; Mowat, F.; Halpern, M. Projections of primary and revision hip and knee arthroplasty in the United States from 2005 to 2030. *J. Bone Jt. Surg. Am. Vol.* 2007, 89, 780–785. [CrossRef]
5. Tande, A.J.; Patel, R. Prosthetic joint infection. *Clin. Microbiol. Rev.* 2014, 27, 302–345. [CrossRef]
6. Kunutsor, S.K.; Whitehouse, M.R.; Blom, A.W.; Beswick, A.D.; Team, I. Patient-Related Risk Factors for Periprosthetic Joint Infection after Total Joint Arthroplasty: A Systematic Review and Meta-Analysis. *PLoS ONE* 2016, 11, e0150866. [CrossRef]
7. Peel, T.N.; Dowsey, M.M.; Daffy, J.R.; Stanley, P.A.; Choong, P.F.; Buisin, K.L. Risk factors for prosthetic hip and knee infections according to arthroplasty site. *J. Hosp. Infect.* 2011, 79, 129–133. [CrossRef]
8. Honkanen, M.; Jamsen, E.; Karppein, M.; Huttunen, R.; Eskelinen, A.; Syrjanen, J. Periprosthetic Joint Infections as a Consequence of Bacteremia. *Open Forum Infect. Dis.* 2019, 6, ofz218. [CrossRef]
9. Wouthuyzen-Bakker, M.; Sebillotte, M.; Lomas, J.; Taylor, A.; Palomares, E.B.; Murillo, O.; Parvizi, J.; Shohat, N.; Reinoso, J.C.; Sanchez, R.E.; et al. Clinical outcome and risk factors for failure in late acute prosthetic joint infections treated with debridement and implant retention. *J. Infect.* 2019, 78, 40–47. [CrossRef]
10. Sendi, P.; Banderet, F.; Graber, P.; Zimmerli, W. Periprosthetic joint infection following *Staphylococcus aureus* bacteremia. *J. Infect.* 2011, 63, 17–22. [CrossRef]
11. Tande, A.J.; Palraj, B.R.; Osmun, D.R.; Berbari, E.F.; Baddour, L.M.; Lohse, C.M.; Stockelberg, J.M.; Wilson, W.R.; Sohail, M.R. Clinical Presentation, Risk Factors, and Outcomes of Hematogenous Prosthetic Joint Infection in Patients with *Staphylococcus aureus* Bacteremia. *Am. J. Med.* 2016, 129, 221.e11–221.e20. [CrossRef] [PubMed]
12. Murdoch, D.R.; Roberts, S.A.; Fowler, V.G.; Jr.; Shah, M.A.; Taylor, S.L.; Morris, A.J.; Corey, G.R. Infection of orthopedic prostheses after *Staphylococcus aureus* bacteremia. *Clin. Infect. Dis. Off. Publ. Infect. Dis. Soc. Am.* 2001, 32, 647–649. [CrossRef] [PubMed]
13. Dufour, S.; Piroth, L.; Chirouze, C.; Tattevin, P.; Becker, A.; Braquet, P.; Ferry, T.; Duval, X.; le Moing, V.; Group, V.A.S. *Staphylococcus aureus* Bloodstream Infection in Patients with Prosthetic Joints in the Prospective VIRSTA Cohort Study: Frequency and Time of Occurrence of Periprosthetic Joint Infection. *Open Forum Infect. Dis.* 2019, 6, ofz215. [CrossRef] [PubMed]
14. Pulido, L.; Ghanem, A.; Yoshi, A.; Purtill, J.J.; Parvizi, J. Periprosthetic joint infection: The incidence, timing, and predisposing factors. *Clin. Orthop. Relat. Res.* 2008, 466, 1710–1715. [CrossRef] [PubMed]
15. Rakow, A.; Perka, C.; Trampuz, A.; Renz, N. Origin and characteristics of haematogenous periprosthetic joint infection. *Clin. Microbiol. Infect. Off. Publ. Eur. Soc. Clin. Microbiol. Infect. Dis.* 2019, 25, 845–850. [CrossRef]
16. McNally, M.; Sousa, R.; Wouthuyzen-Bakker, M.; Chen, A.F.; Soriano, A.; Vogely, H.C.; Clauss, M.; Higuera, C.A.; Trebse, R. The EBIS definition of periprosthetic joint infection. *Bone Jt. J.* 2021, 103-B, 18–25. [CrossRef]
17. Wouthuyzen-Bakker, M.; Sebillotte, M.; Arcueux, C.; Fernandez-Sampedro, M.; Senneville, E.; Barbero, J.M.; Lora-Tamayo, J.; Aboltins, C.; Trebse, R.; Salles, M.J.; et al. How to Handle Concomitant Asymptomatic Prosthetic Joints During an Episode of Hematogenous Periprosthetic Joint Infection, a Multicenter Analysis. *Clin. Infect. Dis. Off. Publ. Infect. Dis. Soc. Am.* 2021, 73, e3820–e3824. [CrossRef]
18. Harris, P.A.; Taylor, R.; Thielke, R.; Payne, J.; Gonzalez, N.; Conde, J.G. Research electronic data capture (REDCap)—A metadata-driven methodology and workflow process for providing translational research informatics support. *J. Biomed. Inform.* 2009, 42, 377–381. [CrossRef]
19. Harris, P.A.; Taylor, R.; Minor, B.L.; Elliott, V.; Fernandez, M.; O’Neal, L.; McLeod, L.; Delacqua, G.; Delacqua, F.; Kirby, J.; et al. The REDCap consortium: Building an international community of software platform partners. *J. Biomed. Inform.* 2019, 95, 103208. [CrossRef]
20. Friedman, N.D.; Kaye, K.S.; Stout, J.E.; McGarry, S.A.; Trivette, S.L.; Briggs, J.P.; Lamm, W.; Clark, C.; MacFarquhar, J.; Walton, A.L.; et al. Health care—Associated bloodstream infections in adults: A reason to change the accepted definition of community-acquired infections. *Ann. Intern. Med.* 2002, 137, 791–797. [CrossRef]

21. Singer, M.; Deutschman, C.S.; Seymour, C.W.; Shankar-Hari, M.; Annane, D.; Bauer, M.; Bellomo, R.; Bernard, G.R.; Chiche, J.D.; Coopersmith, C.M.; et al. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). *JAMA* 2016, 315, 801–810. [CrossRef] [PubMed]