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Infectious Disease Practice

Duration of antimicrobial treatment for uncomplicated streptococcal bacteraemia: Another example of shorter is better

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SUMMARY

Objectives: Duration of treatment for uncomplicated streptococcal bacteraemia is unknown. The study aims to assess clinical outcomes of patients with uncomplicated streptococcal bacteraemia receiving a short course (5–10 days) of antimicrobial treatment compared to those receiving the traditional, longer duration (11–18 days).
Methods: This retrospective study was conducted at the Lausanne University Hospital, Switzerland and included episodes of uncomplicated streptococcal bacteraemia among adult patients from 2015 to 2023. Clinical failure was defined as mortality, recurrence of bacteraemia by the same streptococcal species and development in bone and joint infection within 120 days.
Results: During the study period, 336 episodes of uncomplicated streptococcal bacteraemia were included. The median duration of antimicrobial treatment was 10 days (interquartile range: 7–14); 184 (55%) and 152 (45%) episodes received a short (5–10 days) and long (11–18 days) duration of antimicrobial treatment, respectively. Forty-three (13%) episodes had clinical failure; 120-day mortality was 11% (36 episodes); recurrence of bacteraemia by the same streptococcal species was observed in 8 episodes (2%). No difference in clinical failure was observed between episodes receiving short and long courses of antimicrobial treatment (10% versus 16%; *P* 0.143). The Cox multivariable regression model found that a Charlson comorbidity index >4 (aHR 4.87, 95% CI 3.08–7.71), and septic shock (1.67, 1.04–2.67) were associated with clinical failure; a short course of antimicrobial treatment was not associated with clinical failure (0.90, 0.57–1.12).
Conclusions: This study has shown that a short duration of antimicrobial treatment for cases of streptococcal bacteraemia is effective and safe.

Introduction

Antimicrobial resistance is a significant public health issue.[1] Its emergence results from natural selection, where antimicrobial use creates selective pressure that leads to resistance. The most crucial strategy to prevent resistance is reducing antimicrobial prescriptions, which can be achieved by shortening the duration of antimicrobial courses and thus minimizing overall antibiotic exposure.[2] In the last two decades, many randomized controlled trials compared short-duration treatments with the traditional longer courses and consistently found no difference in efficacy and safety between the two approaches for various infections, such as pneumonia,[3,4] Gram-negative bacteraemia,[5] intraabdominal infections,[6] skin and soft tissue infections,[7] and urinary-tract infections.[8]

Studies on the duration of antimicrobial treatment for Gram-positive bacteraemia primarily focus on *Staphylococcus aureus* bacteraemia,[9,10] with none being randomized clinical trial. There is a scarcity of trials for bacteraemia caused by Gram-positive species other than *S. aureus*.[11] The recommended duration for treating streptococcal bacteraemia varies based on the infection's focus. A complicated course, such as presence of infective endocarditis or bone and joint infections,[12] typically requires prolonged treatment (≥4 weeks). However, no current guidelines address the duration of treatment for uncomplicated streptococcal bacteraemia. In such

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cases, a treatment duration similar to uncomplicated *S. aureus* bacteraemia (14 days) is typically used, based on the rationale that a longer duration is associated with higher success rates and reduced risks of recurrence and metastatic infections.[13] Across all studies on uncomplicated streptococcal bacteraemia, the median duration was 13 days or longer,[14–20] with only 3% of patients in one study receiving antibiotics for less than 10 days.[14]

To date, three retrospective studies have addressed the duration of antimicrobial treatment for uncomplicated bacteraemias caused by *S. pyogenes*,[11] *S. pneumoniae*,[21] and any streptococcal species[22]; all three found that a short course of antimicrobial treatment (≤10 days) was safe and effective.[11] This study aims to fill this knowledge gap by assessing the clinical outcomes of patients with uncomplicated streptococcal bacteraemia receiving a short course of antimicrobial treatment compared to those receiving a longer duration.

Materials and methods

This retrospective study was conducted at Lausanne University Hospital in Switzerland from 2015 to 2023 combining two cohorts: bacteraemia cohort (January 2015 to December 2021), and the cohort of patients with suspected IE (January 2015 to June 2023). The ethics committee of the Canton of Vaud approved the study (CER-VD 2021-02516).

Eligible patients were adults (≥18 years old) with at least one blood culture for *Streptococcus* spp. Patients were excluded if:

- they had formally declined the use of their data
- they were transferred to other hospitals at the onset of infection without follow-up data
- the isolated *Streptococcus* spp. was considered to be a contaminant
- they did not receive appropriate antimicrobial treatment within 48 h from the first positive blood culture
- the infection was categorized as complicated

infection focus warranting a duration of antimicrobial longer than 10 days, such as infective endocarditis, bone and joint infection, deep vein septic thrombophlebitis, vascular graft infections, central nervous system infection, necrotizing fasciitis.

- positive blood cultures at 48 h or later from the first positive blood culture
- neutropenia
- clinically unstable at day five from the first positive blood culture
- polymicrobial bacteraemia with pathogens warranting at least 14 days of antimicrobial treatment, such as *S. aureus* or *Candida* spp.
- source control not achieved within 48 h from the first positive blood culture despite being indicated
- the decision for the total duration of antimicrobial treatment was made after day 7 from the first positive blood culture
- they died or palliative care was instituted within 14 days from the first positive blood culture.

Blood cultures were incubated using the BacT/ALERT System (bioMerieux, Marcy l'Etoile, France) and species identification was performed using matrix-assisted laser desorption-ionization time of flight mass spectrometry (MALDI-TOF MS; Bruker Daltonics, Bremen, Germany). Susceptibility results were assessed in accordance with the EUCAST criteria.[23]

Data on demographics (age, sex), comorbidities, Charlson Comorbidity Index, antimicrobial treatment (intravenous, oral, duration, adverse events), source control, the presence of sepsis or septic shock, and the site of infection were retrieved from patients' electronic health records. In our institution, ID consultants are informed of patients with positive blood cultures after species identification. ID consultation for streptococcal bacteraemia is not mandatory.[24] The realization of cardiac imaging studies was based on the recommendations of the ID consultant, or at the discretion of the treating physician if no ID consultation was solicited.

The primary endpoint of clinical failure was assessed at 120 days from the first positive blood culture and included mortality, recurrence of bacteraemia by the same *Streptococcus* spp. and the development of bone and joint infection. Short antimicrobial treatment duration was defined as 5-10 days, and long duration as 11-18 days. Evaluated adverse events included allergic reactions, interstitial nephritis, and *Clostridioides difficile* infection. The date of collection of the first positive blood culture was defined as the onset of bacteraemia. A new episode was included if more than 120 days had elapsed since the initial bacteraemia. Bacteraemia was classified as community, healthcare-associated, or nosocomial based on Friedman *et al.*[25] Sepsis and septic shock were defined in accordance with the criteria proposed by the Sepsis-3 International Consensus.[26] The determination of the infection focus was based on the assessment by the ID consultant, taking into account clinical, radiological, microbiological, and operative findings. Clinical stability on day 5 was defined as the absence of fever, hemodynamic stability, and no need for supplemental oxygen. The decision regarding the total duration of treatment was recorded in the notes of the ID consultation and in the notes of the treating physician if no ID consultation was provided. Warranted source control interventions were:

- removal of venous catheter in patients with catheter-related bacteraemia or bacteraemia of unknown origin with the presence of a venous catheter
- imaging-guided or surgical drainage of infected collections
- correction of urinary-tract obstruction.

SPSS version 26.0 (SPSS, Chicago, IL, USA) was used for data analyses. Categorical variables were analyzed using the *chi*-square or Fisher exact test and continuous variables with Mann–Whitney *U* test. Univariate logistic regression models were assessed with 120-day primary endpoint as dependent variable. Clinically relevant non collinear covariates, assessed through variance inflation factor, were used in multivariable analysis. After checking Cox assumptions, a multivariable Cox proportional hazards regression models were performed with 120-day primary endpoint as the time-to-event. Adjusted hazard ratios (aHRs) and 95% confidence intervals (CIs) were calculated to evaluate the strength of any association. All statistic tests were 2-tailed and $P < 0.05$ was considered statistically significant. We finally performed Kaplan-Meier curve of the primary endpoint free probability according to duration of antimicrobial treatment.

Results

Among the 1152 non-duplicate episodes of streptococcal bacteraemia from both databases, 336 episodes involving 321 patients were included (Fig. 1); from the 707 episodes of the bacteraemia cohort, 313 (44%) were included. Species belonging to the Mitis Group (apart from *S. pneumoniae*) predominated (111 episodes; 33%). Thirty-one (9%) isolates demonstrated resistance or susceptibility with increased exposure to penicillin.

The most common focus of infection was skin and soft tissue infection (86 episodes; 26%) followed by lower respiratory tract infections (49; 15%) and abdominal infections (44; 13%). The focus of infection was not identified in 59 (18%) episodes. Sepsis or septic shock were present in 110 (33%) episodes, with 35 (10%) episodes presenting with septic shock alone.

ID consultation was provided in 221 episodes (66%). Cardiac imaging to exclude infective endocarditis was conducted in 132

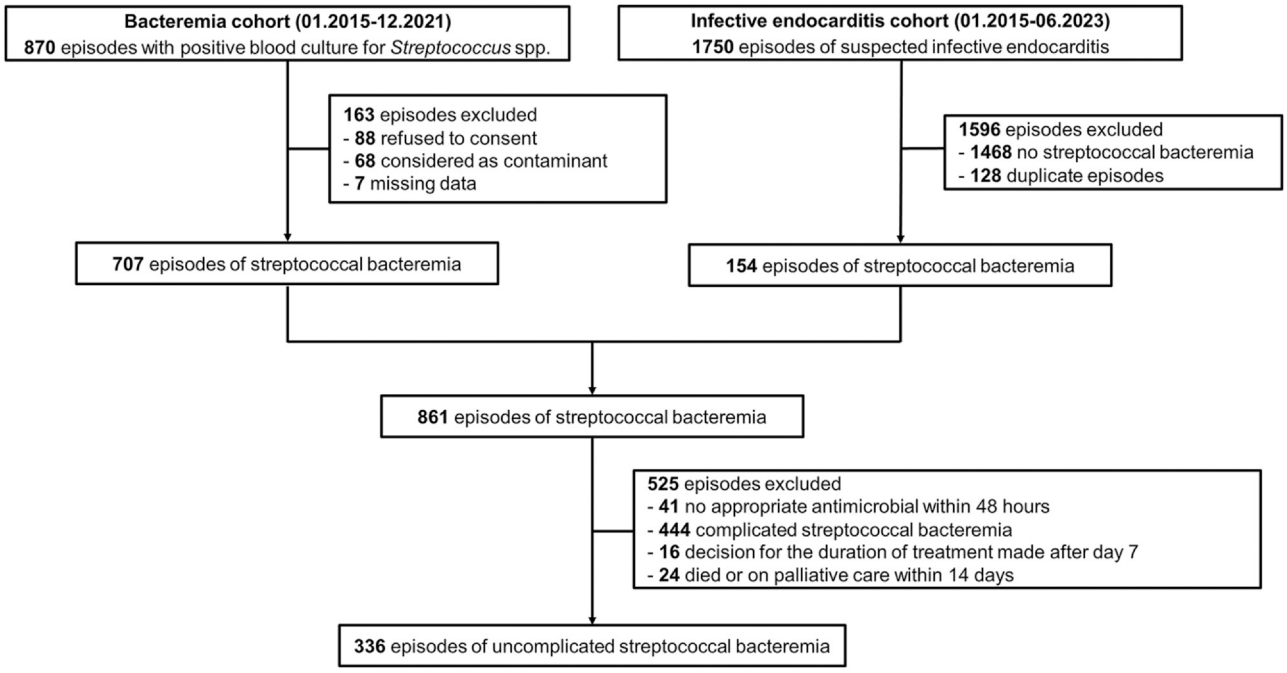

Fig. 1. Flowchart of patients' selection.

episodes (39%), with the first exam conducted within a median of 3 days (interquartile range; IQR: 1–4 days), and the entire diagnostic work-up completed within a median of 4 days (IQR: 2–6 days). Follow-up blood cultures until sterilization were performed in 233 episodes (69%); none had positive blood cultures at 48 h or later from the first positive blood culture.

The median duration of antimicrobial treatment was 10 days (IQR: 7–14); 184 (55%) and 152 (45%) episodes received a short (5–10 days) and long (11–18 days) duration of antimicrobial treatment, respectively. Table 1 shows the comparison of the episodes that received short and long courses of antimicrobial treatment. The median duration of intravenous antimicrobial treatment was 8 days (IQR: 6–13). The rate of antimicrobial-associated adverse was low. Step down oral antimicrobial treatment was performed in 168 (50%) episodes. Supplementary Table 1 shows the different antimicrobials used for targeted intravenous treatment and oral step-down treatment.

The overall 120-day mortality was 11% (36 episodes). Recurrence of bacteraemia by the same *Streptococcus* spp. as the initial episode was observed in 8 episodes (2%), none of which were associated with infective endocarditis. These included 3 episodes of skin and soft tissue infections due to *S. agalactiae*, 3 episodes of cholangitis due to *S. anginosus*, 1 episode of cholangitis due to *S. mitis*, and 1 episode of cholangitis due to *S. salivarius*. No bone and joint infections were observed within the same timeframe. The primary endpoint of clinical failure was met in 43 episodes (13%). No difference in clinical failure was observed between episodes receiving short and long courses of antimicrobial treatment (10% versus 16%; *P* 0.143). Table 2 shows the comparison of episodes that did and did not meet the primary endpoint. The Cox multivariable regression model (Table 3) found that a Charlson comorbidity index >4 (*P* < 0.001; aHR 4.87, 95% CI 3.08–7.71), and septic shock (*P* 0.033; aHR 1.67, 95% CI 1.04–2.67) were associated with clinical failure. Receiving a short duration of antimicrobial treatment was not associated with clinical failure (*P* 0.200; aHR 0.90, 95% CI 0.57–1.12).

Fig. 2 shows Kaplan–Meier curves for primary endpoint free probability for episodes with uncomplicated streptococcal bacteraemia based on the duration of antimicrobial treatment. No significant difference was observed between episodes receiving short and long courses of antimicrobial treatment (log-rank test: *P* 0.140).

Discussion

In this study, no association was found between clinical failure and short course of antimicrobial treatment among episodes of uncomplicated streptococcal bacteraemia.

The median duration of antimicrobial treatment in this study was 10 days, with the majority of patients (55%) receiving a short course (5–10 days). In contrast, previous studies on uncomplicated streptococcal bacteraemias reported longer durations of antimicrobial treatment, with a median of 13 to 15 days,[14–20] and only 3% of patients in one study received antimicrobials for less than 10 days.[14] Only one study previously addressed the duration of antimicrobial treatment for uncomplicated bacteraemia caused by any streptococcal species.[22] Clinical success rates were similar in patients treated with shorter (5–10 days) than longer course.[11–15] However, only 17% of patients received a short course of antimicrobial treatment and the total antimicrobial duration in episodes that received the short course was longer (median of 9 days; IQR: 8–10), compared to the present study (median of 7 days; IQR: 6–8).[22] The two studies that focused on bacteraemia by specific species (*S. pneumoniae* and *S. pyogenes*) found that treatment durations of 10 days or less were safe and effective.[11,21] However, many studies, particularly those on step-down oral treatment for uncomplicated streptococcal bacteraemias, suffered from biases, primarily due to their retrospective nature. This led to a higher risk of allocation bias, as healthier patients were more likely to receive shorter durations of antimicrobial treatment.[11,14–22] To overcome this key bias, we included only episodes where patients were clinically stable on day 5 from the first positive blood cultures and where the decision regarding the total duration of antimicrobial treatment was made within the first 7 days. Another limitation of previous studies was the lack of mention of source control management.[14–18,20,22] Source control is an integral part of managing streptococcal bacteraemias, and failure to perform necessary interventions is associated with worse outcomes.[24] Therefore, we included only patients for whom source control was achieved within 48 h of the first positive blood cultures. Additionally, some studies did not exclude neutropenic patients,[11,14,16,18–20,22] who usually require prolonged antimicrobial treatment influenced by the duration of neutropenia. In this study, we excluded bacteraemias occurring in neutropenic patients.

Table 1
Comparison of episodes with short (5–10 days) and long duration of antimicrobial treatment (11–18 days).

	Short duration (n = 184)	Long duration (n = 152)	P
Demographics			
Male sex	117 (64)	103 (68)	0.489
Age (years)	71 (53–80)	69 (56–77)	0.316
Age > 60 years	126 (69)	100 (66)	0.641
Co-morbidities			
Diabetes mellitus	46 (25)	35 (23)	0.702
Obesity (body mass index ≥30 kg/m^2)	44 (24)	39 (26)	0.799
Chronic kidney disease (moderate or severe)	32 (17)	14 (9)	0.038
Malignancy (solid organ or hematologic)	49 (27)	47 (31)	0.398
Immunosuppression[a]	26 (14)	21 (14)	1.000
Chronic obstructive pulmonary disease	22 (12)	15 (10)	0.702
Cirrhosis	16 (9)	15 (10)	0.762
Congestive heart failure	12 (7)	15 (10)	0.315
IV drug use	3 (2)	6 (4)	0.309
Prosthetic valve	6 (3)	9 (6)	0.293
Cardiac implantable electronic device	8 (4)	10 (7)	0.467
Charlson Comorbidity Index	2 (1–5)	2 (1–4)	0.641
Charlson Comorbidity Index > 4	105 (57)	82 (54)	0.583
Setting of bacteraemia onset			
Community	108 (59)	90 (59)	
Healthcare-associated	35 (19)	22 (15)	
Nosocomial	41 (22)	40 (26)	0.442
Microbiological data			
Two or more positive blood culture sets	69 (38)	83 (55)	0.002
Pathogens			
S. pneumoniae	8 (4)	9 (6)	0.619
S. pyogenes	12 (7)	19 (13)	0.087
S. agalactiae	25 (14)	26 (17)	0.445
S. dysgalactiae	17 (9)	16 (11)	0.716
Mitis group[b]	67 (36)	44 (29)	0.163
Anginosus group	36 (20)	29 (19)	1.000
Other streptococci[c]	30 (16)	17 (11)	0.207
Polymicrobial bloodstream infection[d]	40 (22)	42 (28)	0.251
Increased exposure or resistant to penicillin	15 (8)	16 (11)	0.457
Infection data			
Fever	158 (86)	133 (88)	0.748
Sepsis or septic shock	54 (29)	56 (37)	0.129
Septic shock alone	14 (8)	21 (14)	0.074
Intensive Care Unit admission	32 (17)	32 (21)	0.406
Focus of infection			
Unknown focus	60 (33)	39 (26)	0.187
Catheter-related	3 (2)	5 (3)	0.476
Lower respiratory tract infection	33 (18)	16 (11)	0.063
Abdominal infection	27 (15)	17 (11)	0.417
Skin and soft tissue infection	35 (19)	51 (34)	0.003
Urogenital tract infection	14 (8)	13 (9)	0.841
Ear, nose and throat infection	6 (3)	7 (5)	0.578
Other focus	6 (3)	6 (4)	0.775
Management			
Infectious diseases consultation	108 (59)	113 (74)	0.003
Infectious diseases consultation within 48 h	91 (50)	98 (65)	0.006
Source control			
Not warranted	127 (69)	113 (74)	
Warranted and performed within 48 h	57 (31)	39 (26)	0.332
Antimicrobial treatment			
Step down oral treatment	99 (54)	69 (45)	0.154
Duration of IV antimicrobial treatment	6 (4–8)	13 (8–14)	< 0.001
Total duration of antimicrobial treatment	7 (6–8)	14 (13–15)	< 0.001
Adverse events			
Allergic reaction	1 (0.5)	0 (0)	1.000
Interstitial nephritis	1 (0.5)	1 (0.7)	1.000
Clostridioides difficile infection within 120 days	2 (1)	0 (0)	0.503
Duration of hospitalization	7 (4–13)	10 (6–18)	< 0.001
Primary endpoint at 120 days	19 (10)	24 (16)	0.143
Death	16 (9)	20 (13)	0.216
Recurrence of bacteraemia with the same organism	3 (2)	5 (3)	0.476
New bone and joint infection	0 (0)	0 (0)	-

Data are depicted as number (%) or median (interquartile range).
[a] ongoing immunosuppressive treatment at bacteraemia onset, intravenous chemotherapy in the 30 days prior to bacteraemia onset, AIDS, and asplenia.
[b] without S. pneumoniae.
[c] belonging to Bovis, Mutans, Salivarius, or Sanguinis group.
[d] 49 with aerobic Gram-negative bacteria, 20 with multiple streptococcal species, 15 with aerobic Gram-positive bacteria, 10 with anaerobic Gram-negative bacteria, and one with anaerobic Gram-positive bacteria.

Table 2
Comparison of episodes that did and did not meet the primary endpoint (mortality, recurrence of streptococcal bacteraemia and bone and joint infection within 120 days).

	No primary endpoint (n = 293)	Primary endpoint (n = 43)	*P*
Demographics			
Male sex	190 (65)	30 (70)	0.608
Age (years)	69 (52–78)	75 (70–79)	0.014
Age > 60 years	191 (65)	35 (81)	0.037
Co-morbidities			
Diabetes mellitus	68 (23)	13 (30)	0.341
Obesity (body mass index ≥30 kg/m^2)	77 (26)	6 (14)	0.090
Chronic kidney disease (moderate or severe)	40 (14)	6 (14)	1.000
Malignancy (solid organ or hematologic)	75 (26)	21 (49)	0.003
Immunosuppression[a]	39 (13)	8 (19)	0.349
Chronic obstructive pulmonary disease	31 (11)	6 (14)	0.446
Cirrhosis	25 (9)	6 (14)	0.259
Congestive heart failure	22 (8)	5 (12)	0.366
IV drug use	8 (3)	1 (2)	1.000
Prosthetic valve	9 (3)	6 (14)	0.006
Cardiac implantable electronic device	14 (5)	4 (9)	0.265
Charlson Comorbidity Index	2 (1–4)	4 (2–6)	< 0.001
Charlson Comorbidity Index > 4	152 (52)	35 (81)	< 0.001
Setting of bacteraemia onset			
Community	186 (64)	12 (28)	
Healthcare-associated	44 (15)	13 (30)	
Nosocomial	63 (22)	18 (42)	0.007
Microbiological data			
Two or more blood cultures positive (initial blood cultures)	131 (45)	21 (49)	0.626
Pathogens			
S. pneumoniae	17 (6)	0 (0)	0.143
S. pyogenes	31 (11)	0 (0)	0.021
S. agalactiae	44 (15)	7 (16)	0.821
S. dysgalactiae	31 (11)	2 (5)	0.283
Mitis group[b]	99 (34)	12 (28)	0.492
Anginosus group	49 (17)	16 (37)	0.003
Other streptococci[c]	37 (13)	10 (23)	0.095
Polymicrobial bloodstream infection[d]	66 (23)	16 (37)	0.055
Increased exposure or resistant to penicillin	25 (9)	6 (14)	0.259
Infection data			
Fever	255 (87)	36 (84)	0.630
Sepsis or septic shock	92 (31)	17 (40)	0.299
Septic shock alone	26 (9)	9 (21)	0.028
Intensive Care Unit admission	53 (18)	11 ()26	0.297
Focus of infection			
Unknown focus	79 (27)	20 (47)	0.012
Catheter-related	8 (3)	0 ()0	0.603
Lower respiratory tract infection	40 (14)	9 (21)	0.245
Abdominal infection	37 (13)	7 (16)	0.474
Skin and soft tissue infection	79 (27)	7 (16)	0.189
Urogenital tract infection	26 (9)	1 (2)	0.226
Ear, nose and throat infection	13 (4)	0 (0)	0.387
Other focus	12 (4)	0 (0)	0.376
Management			
Infectious diseases consultation	191 (65)	30 (70)	0.609
Infectious diseases consultation within 48 h	165 (56)	24 (56)	1.000
Source control			
Not warranted	205 (70)	35 (81)	
Warranted and performed within 48 h	88 (30)	8 (19)	0.149
Duration of antimicrobial treatment			
Long duration	128 (44)	24 (56)	0.143
Short duration	165 (56)	19 (44)	

Data are depicted as number (%) or median (interquartile range).
[a] ongoing immunosuppressive treatment at bacteraemia onset, intravenous chemotherapy in the 30 days prior to bacteraemia onset, AIDS, and asplenia.
[b] without *S. pneumoniae*.
[c] belonging to Mutans, Salivarius, or Sanguinis group.
[d] 49 with aerobic Gram-negative bacteria, 20 with multiple streptococcal species, 15 with aerobic Gram-positive bacteria, 10 with anaerobic Gram-negative bacteria, and one with anaerobic Gram-positive bacteria.

Table 3
Cox proportional hazard multivariable regression of 120-day composite endpoint (mortality, recurrence of bacteraemia, new bone and joint infection) among patients with uncomplicated streptococcal bacteraemia.

	P	aHR (95% CI)
Charlson Comorbidity Index > 4	< 0.001	4.87 (3.08–7.71)
Septic shock alone	0.033	1.67 (1.04–2.67)
Bacteraemia by streptococci belonging to Anginosus Group	0.284	1.27 (0.82–1.96)
Unknown focus	0.342	1.19 (0.83–1.71)
Short duration of treatment	0.200	0.90 (0.57–1.12)

CI: confidence interval; aHR: adjusted hazard ratio.

The 120-day mortality among episodes with uncomplicated episodes of streptococcal bacteraemia was 11%, which was higher than previous studies (90-day mortality: 1–7%).[11,14–22] Several factors could explain the higher mortality in the present study. First, the definition of uncomplicated bacteraemia differed among studies. Additionally, active malignancy was more common in our cohort (29%) compared to previous studies (9–18%),[15–17,20] and patients in our cohort were older (median age of 64 years) compared to most other studies (median age of 54–60 years).[11,15,16,19,21] Both age and comorbidities, represented by the Charlson Comorbidity Index, were associated with mortality in this and previous studies on streptococcal bacteraemia[20,24,27,28] Moreover, our cohort comprised more severe infections, with higher rates of Intensive Care Unit (ICU) admission (19% versus 7–15%),[11,17,18] or sepsis (32% versus 15%),[17] and lower rates of skin and soft tissue infections (26% versus 31–74%).[14,17–20] Although ICU admission and sepsis did not influence 90-day mortality in the present study, septic shock was associated with a higher risk of clinical failure. There is growing evidence that patients with septic shock who survive the acute phase have a higher risk of late mortality compared to the general population or patients hospitalized for infection without sepsis.[28–30] The duration of treatment also influenced the length of hospital stay, with patients receiving shorter treatment durations being discharged earlier. Future studies should assess the economic impact of shorter antimicrobial treatment on overall cost reduction.

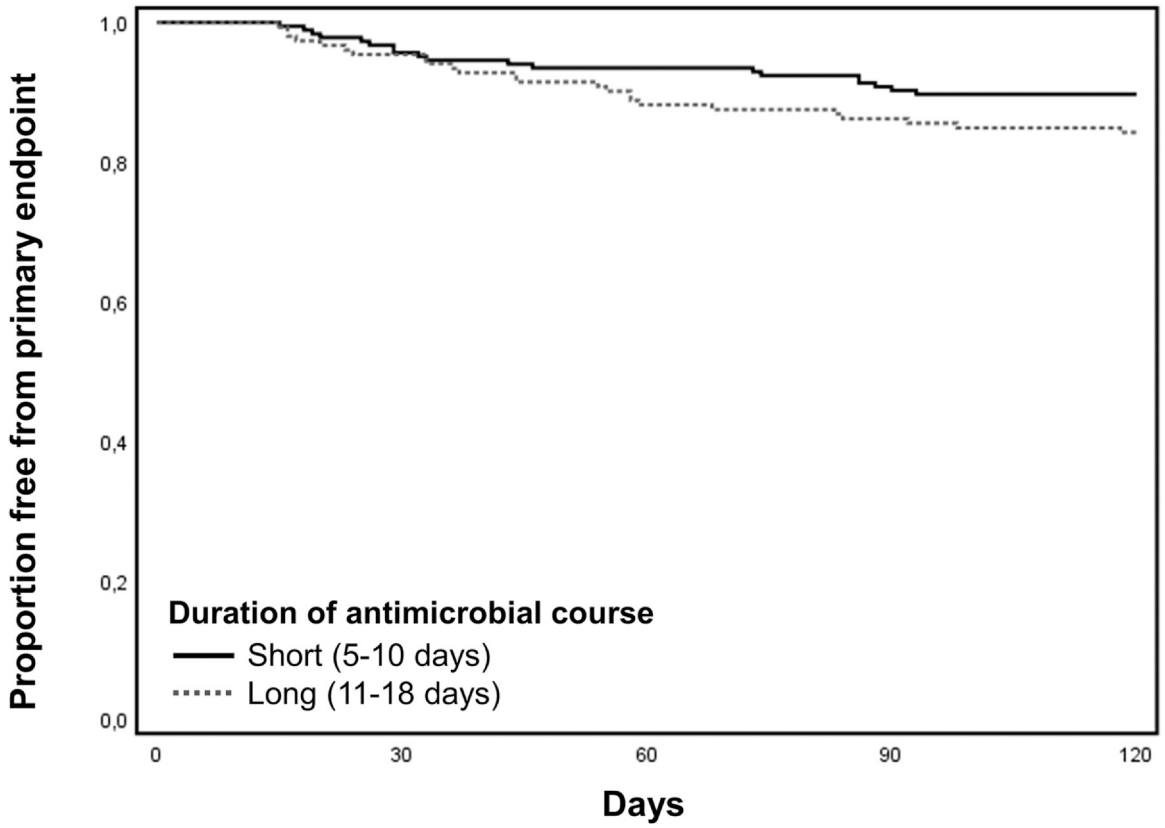

Fig. 2. Kaplan–Meier curves for primary endpoint free probability for episodes with uncomplicated streptococcal bacteraemia based on the duration of antimicrobial treatment (log-rank test: *P* 0.140).

None of the patients in the present study developed bone and joint infections within 120 days from the initial episode, and the risk of recurrence of streptococcal bacteraemia in the same timeframe was low (2%), with no patient developing endocarditis or bone and joint infection, consistent with previous studies.[11,14,15,20] No difference was found between episodes treated with short or long courses of antimicrobial treatment. This finding undercuts the main reason behind the administration of longer duration of treatment among cases with uncomplicated streptococcal bacteraemia, which was the risk of recurrence or metastatic infections such as that found with *S. aureus* bacteraemia.[31]

The focus of infection influenced the duration of antimicrobial treatment, with more patients with skin and soft tissue infections receiving longer courses, whereas patients with lower respiratory tract infections were more often on shorter courses. Guidelines for community-acquired and nosocomial pneumonia recommend a minimum treatment duration of 5 and 7 days, respectively,[32,33] while for skin and soft tissue infections with moderate (presence of systemic signs of infection) or severe infection (hypotension or organ dysfunction), a minimum duration of 7 days is proposed, with the option to extend to 14 days depending on the infection's progression.[34] However, the recommended treatment duration for these infections in the presence of bacteraemia was not addressed. The adherence to these guidelines based on clinical evolution may explain the different management of aforementioned group of patients observed in the present study. Additionally, patients who received an ID consultation were more likely to be placed on a longer course. A prior survey of bacteraemic disease scenarios showed that ID consultants tend to recommend longer treatment durations compared to intensive care physicians[35]; however, the clinical reasoning behind this difference was not explored in that survey. In the present study, a possible explanation is that the decision on the duration of antimicrobial treatment may have been influenced by factors not captured during data collection.

Our study has several limitations. First, it is a retrospective single-center study, and the decision for the duration of antimicrobial treatment might be influenced by factors not documented in the notes of the ID or treating physician. However, the selection of patients was based on clinically relevant criteria, including only those whose treatment did not warrant more than 9 days and whose treatment decision was made by the seventh day at the latest. Second, the lack of a standardized definition for uncomplicated streptococcal bacteraemia is problematic, as each study uses different criteria.[11,14–20] By including stability at day 5 from the first positive blood culture, achievement of source control within 48 h, and absence of persistent bacteraemia for 48 h or more in our definition, our study stands out from prior ones. To address immortal time bias, we excluded all patients who died or had palliative care instituted within 14 days from the first positive blood culture. While these approaches can reduce the risk of bias, randomized controlled trials are still needed. Third, the sample size is modest. However, this study is the second largest to date. Furthermore, no information on readmissions was collected, but the low rates of bacteraemia recurrence, subsequent bone and joint infections, and adverse events suggest that the rate of readmissions related to the bacteraemia itself or to antimicrobial treatment should be low. Additionally, the study was conducted in a tertiary care center with high rates of ID consultation for episodes of streptococcal bacteraemia, which might limit the generalizability of the results. Moreover, although peridental translocation could explain some of the bacteraemias of unknown origin, dental hygiene was not assessed in the included patients. Only four patients in the present study had a diagnosed peridental infection.

In conclusion, this study has shown that a short duration of antimicrobial treatment for cases of uncomplicated streptococcal bacteraemia was effective and safe. No differences in 120-day mortality, bacteraemia recurrence, or antimicrobial treatment-related adverse events were found between episodes treated with short and long courses. Our findings contribute to the growing body of evidence that antimicrobial treatment can be safely shortened in selected patients. Regardless of the duration of treatment, patients who developed septic shock but achieved clinical stability within 5 days were at increased risk of late mortality. A standardized definition of uncomplicated streptococcal bacteraemia is urgently needed, as are randomized controlled studies on the duration of antimicrobial treatment and oral step-down treatment for uncomplicated streptococcal bacteraemias.

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Author contributions

MPO conceived the idea. NF, VZ, LS, MA, and MPO collected the patients' data. BG supervised the project. MPO performed the analysis and interpreted the results. MPO wrote the manuscript. All authors contributed to manuscript revision and read and approved the submitted version.

Data availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Declaration of Competing Interest

None.

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NA.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.jinf.2024.106313.

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