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The effect of duration of antimicrobial treatment for bacteremia in critically ill patients on in-hospital mortality – Retrospective double center analysis

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ABSTRACT

Purpose: Excessive duration of antibiotic treatment is a major factor for inappropriate antibiotic consumption. Although in some instances shorter antibiotic courses are as efficient as longer ones, no specific recommendations as to the duration of antimicrobial treatment for bloodstream infections currently exist. In the present study, we investigated the effect of antibiotic treatment duration on in-hospital mortality using retrospective data from two cohorts that included patients with bacteremia at two Swiss tertiary Intensive Care Units (ICUs).

Materials and methods: Overall 8227 consecutive patients requiring ICU admission were screened for bacteremia between 01/2012–12/2013 in Lausanne and between 07/2016–05/2017 in Bern. Patients with an infection known to require prolonged treatment or having single positive blood culture with common contaminant pathogens were excluded. The primary outcome of interest was the time from start of antimicrobial treatment to in-hospital death or hospital discharge, whichever comes first. The predictor of interest was adequate antimicrobial treatment duration, further divided into shorter (≤10 days) and longer (>10 days) durations. A time-dependent Cox model and a cloning approach were used to address immortality bias. The secondary outcomes were the median duration of antimicrobial treatment for patients with bacteremia overall and stratified by underlying infectious syndrome and pathogens in the case of secondary bacteremia.

Results: Out of the 707 patients with positive blood cultures, 382 were included into the primary analysis. Median duration of antibiotic therapy was 14 days (IQR, 7–20). Most bacteremia (84%) were monomicrobial; 18% of all episodes were primary bacteremia. Respiratory (28%), intra-abdominal (23%) and catheter infections (17%) were the most common sources of secondary bacteremia. Using methods to mitigate the risk of confounding associated with antibiotic treatment durations, shorter versus longer treatment groups showed no differences in in-hospital survival (time-dependent Cox-model: HR 1.5, 95% CI (0.8, 2.7), $p = 0.20$; Cloning approach: HR 1.0, 95% CI (0.7,1.5) $p = 0.83$). Sensitivity analyses showed that the interpretation did not change when using a 7 days cut-off.

Conclusions: In this restrospective study, we found no evidence for a survival benefit of longer (>10 days) versus shorter treatment course in ICU patients with bacteremia.

Trial registration: The study was retrospectively registered on clinicatrials.gov (NCT05236283), 11 February 2022. The respective cantonal ethics commission (KEK Bern # 2021–02302) has approved the study.

Abbreviations: APACHE, Acute Physiology And Chronic Health Evaluation; BSI, Bloodstream infections; COPD, Chronic Obstructive Pulmonary Disease; CI, Confidence Interval; eCRF, electronic Case Report Form; ICU, Intensive Care Unite; IFIK, Institute of Infectious Diseases; IPT, Inverse Probability of Treatment; IQR, Interquartile Range; PDMS, Patient Data Monitoring System; RCT, Randomized Control Trial.

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1. Introduction

Bloodstream infections (BSI) inflict a considerable burden to patients and healthcare systems. They are among the most common infections within intensive care units (ICUs) [1-5], affecting up to 15% of critically ill patients [5] with an up to 3-fold increase in mortality compared with patients without BSI [6-9]. Patients with bloodstream infections stay up to 2–3 additional weeks in the hospital, increasing hospital costs by $25,000–40,000 [10-13]. In addition, bloodstream infections are major contributors of antibiotic overconsumption within the ICUs as most of them are often managed with long antibiotic treatment courses [14,15]. Reducing treatment duration of bacteremia within the ICU is one approach to control for antibiotic overconsumption [15-17].

Shorter duration of antibiotic treatment (≤7 days) has been shown to be as effective as longer duration treatment for infectious syndromes such as ear, bladder kidney, abdominal infections, as well as for community-acquired [18] or ventilator-associated pneumonia [19,20]. However, evidence is lacking to guide the duration of treatment in the case of blood stream infection. A shorter regime of systemic antibiotic treatment duration may be sufficient for uncomplicated catheter related bloodstream infection [21], gram-negative bacteremia [22] or even in sepsis [23]. Nevertheless, most guidelines regarding infections commonly encountered in ICU, including pneumonia [24,25], intra-abdominal infection [26], catheter-related bloodstream infection [27], pyelonephritis [28], and skin and soft tissue infection [29,30] provide no specific guidance as to the optimal duration of therapy for ICU patients with secondary bacteremia.

In the absence of guidelines, the current management of patients with bacteremia on the ICU is highly variable [31-34]. A national survey of Canadian infectious diseases and critical care physicians explored what durations of antibiotic treatment they typically recommend for common scenarios of bacteremia among critically ill patients [35]. Overall, the single most common recommendation was 14 days of antibiotics, but durations of 7 or 10 days were recommended by half of respondents. A multicenter, retrospective study of antibiotic treatment duration for 1202 patients with bacteremia across ICUs in 14 Canadian hospitals in 11 cities and 6 provinces revealed a median duration of treatment of 14 days independently of underlying infection [36]. Neither patient demographics, age, severity of illness, comorbidities, or immune status affected antibiotic treatment duration. Treatment duration was not associated with a difference in survival [36]. Results from an ongoing international, multicenter randomized controlled trial which investigates the effect of shorter (7 days) vs longer (14 days) antibiotic treatment on 90-day survival are still pending [17].

The primary objective of this study was to investigate the association of shorter (≤10 days) or longer (>10 days) treatment duration on hospital mortality using retrospective data from two Swiss ICUs using several analysis strategies. Secondary objectives included determining the median duration of antimicrobial treatment for patients with bacteremia overall and stratified by underlying infectious syndrome for secondary bacteremia. We perform several sensitivity analyses with changing eligible study populations and with a shorter treatment duration of 7 days.

2. Methods

2.1. Setting

Retrospective double center analysis of data from critically ill patients with confirmed bacteremia while staying at the Lausanne University Hospital (CHUV) ICU between 01/2012–12/2013 and at the Bern University hospital (Inselspital) ICU between 07/2016–05/2017.

The study was registered on clinicatrials.gov (NCT05236283). The respective cantonal ethics commission (KEK Bern # 2021–02302) has approved the study.

2.2. Patient selection

Extraction of all positive blood cultures diagnosed over the study periods was performed by the microbiology laboratories of each university hospital. The search was restricted to patients with ICU stays according to data from the ICU's Patient Data Monitoring System (PDMS) (Metavision in Lausanne, General Electric Centricity Software in Bern).

2.3. Inclusion criteria

Patients admitted to the ICU with a documented positive blood culture with a pathogenic organism and either treated in the ICU at the time of blood culture collection or admitted to ICU in the 48 h after blood culture collection were included for further analysis.

2.4. Exclusion criteria

Patients who had a focus of infection with known need of very long treatment, e. g. osteomyelitis, spondylodiscitis or endocarditis as well as those with undrainable abscesses or unremovable foreign body material were excluded. Additionally, patients with just one single positive blood culture with a common contaminant organism (*coagulase negative staphylococci*, *Bacillus* spp., *Corynebacterium* spp., *Propionibacterium* spp., *Aerococcus* spp., *Micrococcus* spp) were also excluded.

2.5. Definitions

Antimicrobial treatment duration was arbitrarily dichotomized as shorter (≤ 10 d) and longer (> 10 d) duration as previously performed by Daneman et al. [36]. The duration of adequate treatment was defined as the number of consecutive days during which the patient received an antimicrobial to which the index blood culture isolate(s) was/were all susceptible [36]. In sensitivity analyses we used a duration cut-off of 7 days. Bacteremia was classified as primary (i.e. no focus identified) or secondary (i.e. focus identified). In the case of secondary bacteremia, the following infection sites were recorded: (i) catheter-related, (ii) pneumonia, (iii) urinary tract infection, (iv) intra-abdominal, (v) hepatobiliary, and (vi) skin/soft tissue.

2.6. Data collection

To identify study patients, we first performed an extraction of all positive blood cultures diagnosed in the Bern University Hospital over the study period from the Institute of Infectious Diseases (IFIK) microbiology database. Next, eligible patients who stayed in the Bern ICU during the recruiting period were identified using the Bern ICU Patient Data Monitoring System (PDMS) Database (General Electric Centricity Software). Finally, among all patients with a positive blood culture, we only included those having stayed in the Bern University Hospital ICU. Data acquisition in Lausanne followed a similar procedure.

Data were introduced into a secure electronic case report form (eCRF), which checked automatically for missing or invalid data. The case report form included admission (hospital admission/discharge and ICU admission/discharge), demographics (age, comorbidities) and severity scores (SAPS II, APACHE-II) as well as outcome data (mortality, length of stay and duration of bacteremia).

Demographic, medical and treatment data are extracted from the Bern University Hospital electronic medical record system (iPDOS), from the ICU PDMS and from the IFIK database, in Lausanne, the extraction was performed accordingly. Data management was performed in Toronto using iDataFax for data etry and checking and SAS software for data analysis.

2.7. Outcomes

The primary outcome of interest was the time from start of antimicrobial treatment to in-hospital death or hospital discharge, whichever comes first. Secondary outcomes were the median duration of antimicrobial treatment for patients with bacteremia overall and stratified by underlying infectious syndrome for secondary bacteremia.

2.8. Predictor of interest and confounders

The primary predictor of interest was adequate antimicrobial treatment duration, arbitrarily divided into shorter (≤10 days) vs longer (>10 days) duration. We a priori identified the following potential confounders: age, sex, an age-corrected APACHE-II, comorbidities (heart disease, diabetes, renal disease, chronic obstructive pulmonary disease, liver disease, leukemia/lymphoma, immunosuppression) and study site (Bern, Lausanne). Because age is an item of the APACHE-II score we constructed an age-corrected APACHE-II score - by subtracting the corresponding age constants - for modelling.

2.9. Statistical methods

Characteristics of the study population were described by counts (n), percentages (%), or median and interquartile range (IQR) whenever appropriate. We compared groups defined by shorter or longer adequate antimicrobial treatment duration (shorter [≤10 days] vs longer [>10 days]) with Pearson's Chi-squared test for categorical variables, or a Kruskal-Wallis test for continuous variables. Since treatment assignment happened after eligibility criteria, survival estimates might be affected by immortal time bias - patients need to be alive long enough to have received therapy for the post-hoc duration definition, potentially leading to an association of higher mortality for 'short' treatment durations among those dying early, and an association of lower mortality for those who survive sufficiently long to have received a longer course of therapy [37]. To address this issue, two different analysis strategies were performed.

First, we analyzed the treatment duration group as a time-dependent covariate (see e.g. [38,39]) using a time-dependent Cox model, in which patients switched to the longer treatment duration group after 10 days until end of follow-up. Because treatment is not randomly assigned, we performed an inverse probability of treatment weighting (IPTW) approach to address confounding [40]. We used a logistic regression model with 'being on short duration treatment' as outcome and predictors site, age, sex, APACHE-II and number of comorbidities (heart disease, diabetes, renal disease, chronic obstructive pulmonary disease, liver disease, leukemia/lymphoma and immunosuppression) as predictors to construct IPT weights.

For the second analysis strategy, we used a cloning approach as suggested by Hernán [37], and created two pseudo-populations with same baseline characteristics. In brief, patients are copied ('cloned') so that they are also represented in the (actual) not observed treatment group. Patients who deviate from their actual treatment group are censored. For example, patient A who actually received a longer treatment duration of 15 days is observed until death (S-Fig. 1). Her or his clone is censored at 10 days and assigned to a shorter treatment duration group in a cloning population. Thus, each patient receives the other treatment than actually observed one, represented by a clone. This artificial censoring is addressed by the construction of inverse probability weights similar to that described above. In both analysis strategies time zero is the start of antimicrobial treatment.

2.10. Sensitivity analyses

To create the situation comparable to a RCT [17], we exclude patients with a predefined follow-up time in a sensitivity analysis. The eligibility criteria mimics the timing of randomization similar to the ongoing BALANCE randomized controlled trial (Daneman et al. [17]), where patients were randomized after 7 days into a 'prolonged' treatment (14 days group) or to stop treatment (7 days group). In our case we used a cut-off at 10 days, that is, patients are eligible for analysis if they had a follow-up time of at least 10 days. All analyses were similarly performed for a antimicrobial treatment duration cut-off of 7 days. Time zero for sensitivity analyses was either 10 days after start of antimicrobial treatment, or 7 days, respectively.

3. Results

3.1. Study population

Among the 8227 consecutive patients admitted to both Swiss tertiary ICUs - 3845 patients between 01/2012 to 12/2013 in Lausanne and 4382 patients between 07/2016 to 02/2017 in Bern, we identified a total of 707 ICU patients with at least one positive blood culture during their hospital stay. After exclusion of 325 patients (see exclusion criteria in Fig. 1), 382 were considered for further analysis. We excluded nine patients with missing information about the adequate antibiotic duration, 1 patient with an unknown discharge date and 3 patients with a missing hospital outcome, leading to a total of 382 patients for the primary analysis (Fig. 1). For sensitivity analyses, either 91 patients (23.8%) were excluded because they died or were discharged within 10 days (43 died (47.3%); 48 patients (52.7%) were discharged) or within 7 days (58 patients of whom 35 died (60.3%) and 23 patients (39.7%) were discharged) after start of treatment. The sample sizes for the sensitivity analyses were 291 patients (10 days cut-off) or 324 patients (7 days cut-off), respectively.

3.2. Patient characteristics

Median age of the study population was 64 (IQR [51, 73]); 255 patients (67%) were male (Table 1). All patients were severely ill (median APACHE II score of 18 [14,25]). About half of the patients had a previous heart condition (46%), one third suffered from not further specified renal disease (32%). Patients suffering from leukemia or lymphoma were infrequent (13%), yet 23% of patients had a chemically depressed immune system and >8% of the overall study population were neutropenic. 1 patient (0.3%) had a missing in value in gender. 26 patients (6.9%) had a missing value in APACHE-II. 10 patients (2.6%) had missing values in all comorbidities. These were replaced by its median or highest frequency. A supplemental table (S-Table 1) provides a comparison of antibiotic treatment regimen of the two university hospitals.

3.3. Primary outcome analysis

3.3.1. The effect of shorter (≤10 days) vs longer (>10 days) treatment duration on in-hospital mortality

3.3.1.1. Naïve approach. 62 (44%) patients died in the shorter duration group compared to 110 (29%) in the longer duration group. A naïve analysis approach showed strong evidence for a difference between the survival curves (p value from Cox model: $p < 0.001$) (S-Fig. 2). Patients in the shorter duration group had a 4.4, 95% CI (3.0, 6.5), higher hazard of dying compared to the longer duration group. These estimates are affected by an immortal time bias.

3.3.1.2. Models addressing immortal time bias. Fig. 2 shows the survival curves from two approaches that addressed the immortal time bias: (i) a time-dependent Cox model (Panel A) and (ii) a cloning approach (Panel B) respectively. When corrected for immortal time bias, we did not find consistent evidence for a difference in survival between both antibiotic treatment duration groups (Time-dependent Cox model: HR 1.5, 95% CI (0.8, 2.7), $p = 0.20$; Cloning approach: HR 1.0, 95% CI (0.7, 1.5), $p =$

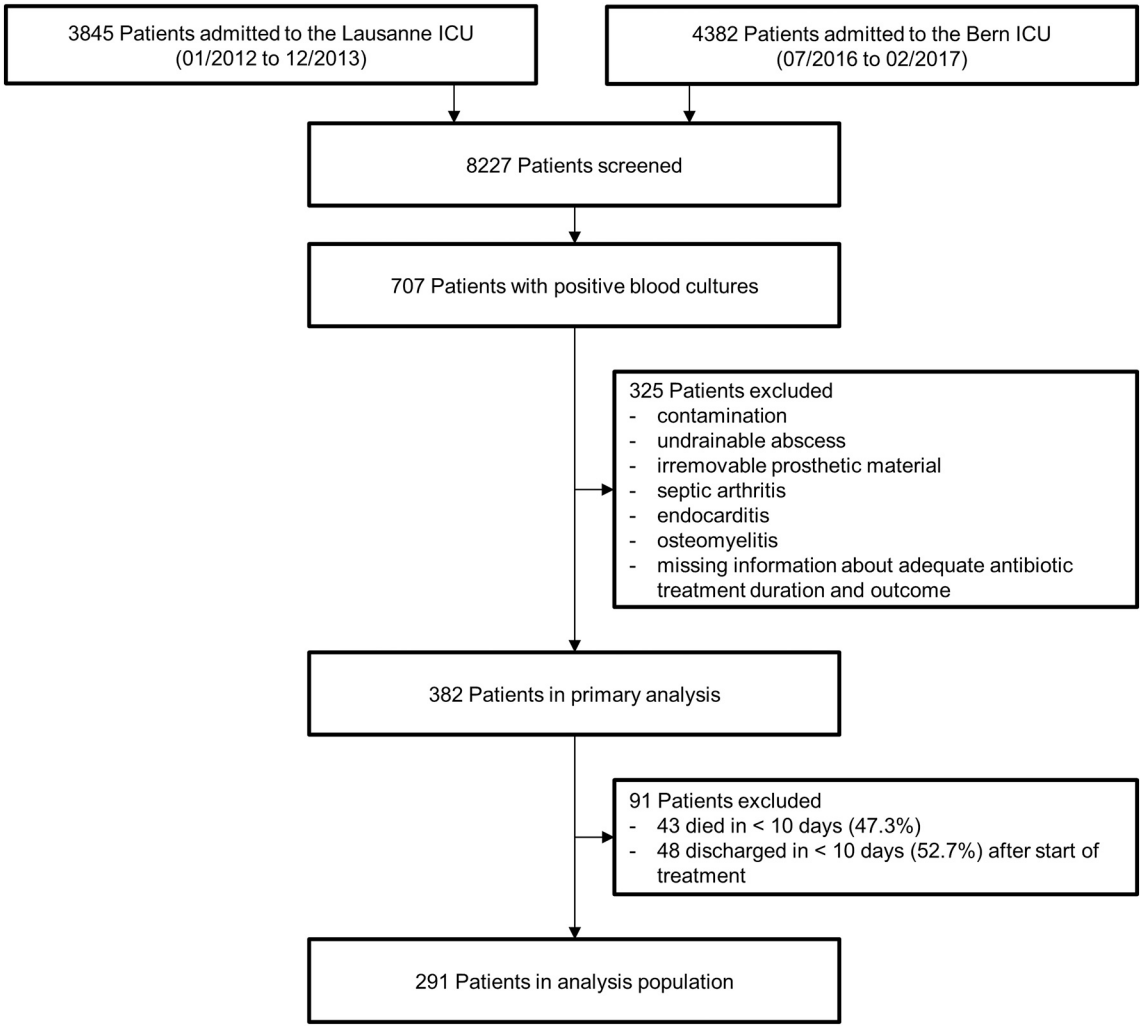

Fig. 1. Study flow chart.

0.83).

3.3.1.3. Sensitivity analyses. S-Fig. 3 shows the survival curves from a time-dependent Cox model (Panel A) and from a cloning approach (Panel B) restricted to patients with a follow-up time of at least 10 days. Similar to the main results, we found no difference in survival between groups (Time-dependent Cox model: HR 1.3, 95% CI (0.7, 2.5), $p = 0.42$; Cloning approach: HR 1.6, 95% CI (0.9, 2.7), $p = 0.11$). Interpretation of our findings do not change when we use a shorter treatment duration of 7 days. While the time-dependent Cox model (Panel A, S-Fig. 4) showed evidence for a survival difference, all other approaches showed no survival difference.

3.4. Secondary outcomes analysis

3.4.1. Duration of adequate antibiotic treatment

Overall, the median duration of antibiotic therapy was 14 days (IQR, 7–20). We observed a large variability, with treatment durations reaching up to 60 days (Fig. 3). Median treatment duration among secondary bacteremia based on infection source varied from 12 days (for hepato-bilary infection) to 20 days (for peripheral venous catheter infection) (Table 2).

3.4.2. Characteristics of bacteremia episodes

Less than one fifth (18%) of all bloodstream infections were primary bacteremia, whereas respiratory (28%), intra-abdominal (23%) and catheter infections (17%) were the most common sources of secondary bacteremia (Table 1). Most of bacteremia were monomicrobial (84%), with an almost equal distribution of gram-positive (234) and gram-negative microorganisms (213) (S-Table 2). The most frequently isolated bacteria were *Escherichia coli* (45% of gram-negative bacteria), *coagulase-negative staphylococci* (30% of gram-positive bacteria) followed by *Staphylococcus aureus* (19% of gram-positive bacteria), *Enterococcus faecium* (12% of gram-positive bacteria), *Streptococcus pneumoniae* comprised 9% of gram-positive bacteria and *Klebsiella pneumoniae (12%)* with *Pseudomonas aeruginosa* (9%) the second and third most frequent bacteria found in the group of gram-negative microorganisms.

4. Discussion

This retrospective observational two center study analyzed the treatment duration of bacteremia occurring in 382 critically ill patients admitted over a one-year timeframe to two Swiss tertiary ICUs. We used statistical approaches which attempt to address immortal time bias, to compare the association of shorter versus longer duration of adequate antibiotic treatment on in-hospital mortality. Using a cut-off of 10 days, we did not find evidence for a survival difference between patients with a shorter and longer antimicrobial treatment duration. The interpretation of results did not change when using a 7 days cut-off in sensitivity analyses. Our findings are in line with previously published data [36].

We observed a median adequate treatment duration of 14 days but

Table 1
Overall study population.

Characteristic	Overall (*N* = 382)	Longer duration (*N* = 241)	Shorter duration (*N* = 141)	*p*-value*
Age	64 (51, 73)	63 (51, 72)	65 (49, 74)	0.61
Gender				0.19
Female	127 (33%)	86 (36%)	41 (29%)	
Male	255 (67%)	155 (64%)	100 (71%)	
Baseline APACHE-II	18 (14, 25)	18 (13,23)	19 (15, 26)	0.061
Heart disease	175 (46%)	121 (50%)	54 (38%)	0.024
Diabetes	78 (20%)	57 (24%)	21 (15%)	0.04
Renal disease	124 (32%)	79 (33%)	45 (32%)	0.86
COPD	59 (15%)	42 (17%)	17 (12%)	0.16
Liver disease	84 (22%)	50 (21%)	34 (24%)	0.44
Leukemia/Lymphoma	51 (13%)	37 (15%)	14 (9.9%)	0.13
Immunosuppression	87 (23%)	55 (23%)	32 (23%)	0.98
Sum of comorbities				
0	81 (21%)	41 (17%)	40 (28%)	
1	105 (27%)	66 (27%)	39 (28%)	
2	87 (23%)	58 (24%)	29 (21%)	
3	70 (18%)	51 (21%)	19 (13%)	
4	28 (7.3%)	20 (8.3%)	8 (5.7%)	
5	9 (2.4%)	4 (1.7%)	5 (3.5%)	
6	2 (0.5%)	1 (0.4%)	1 (0.7%)	
Length of stay in ICU (days)	7 (2,20)	8 (2, 25)	6 (2, 15)	0.007
Length of stay in hospital (days)	26 (13, 44)	31 (20, 52)	15 (7, 32)	<0.001
Adequate antimicrobial treatment duration	14 (7, 20)	18 (14, 26)	5 (2, 8)	<0.001
Re-admitted to ICU	63 (17%)	54 (22%)	9 (6.4%)	<0.001
Unknown	1	0	1	
Death at hospital	110 (29%)	48 (20%)	62 (44%)	<0.001
Death at ICU	77 (20%)	25 (10%)	52 (37%)	<0.001
Bacteremia				0.3
1 monomicrobial	320 (84%)	198 (82%)	122 (87%)	
ge 2 polymicrobial	61 (16%)	42 (18%)	19 (13%)	
Unknown	1	1	0	
Primary bacteremia (site unknown)	68 (18%)	31 (13%)	37 (26%)	<0.001
Secondary bacteremia: Catheter	66 (17%)	46 (19%)	20 (14%)	0.22
Secondary bacteremia: Pneumonia/respiratory infections	107 (28%)	67 (28%)	40 (28%)	0.91
Secondary bacteremia: Urinary/pyelonephritis	36 (9.4%)	26 (11%)	10 (7.1%)	0.23
Secondary bacteremia: Intra-abdominal infections	89 (23%)	56 (23%)	33 (23%)	0.97
Secondary bacteremia: Hepato-biliary infection	36 (9.4%)	23 (9.5%)	13 (9.2%)	0.92
Secondary bacteremia: Skin and/or soft tissue	26 (6.8%)	19 (7.9%)	7 (5.0%)	0.27
Secondary bacteremia: Other infection	25 (6.5%)	21 (8.7%)	4 (2.8%)	0.025
Microorganism				0.37
Both	62 (16%)	43 (18%)	19 (13%)	
Fungi	9 (2.4%)	5 (2.1%)	4 (2.8%)	
Gram negative	157 (41%)	103 (43%)	54 (38%)	
Gram positive	154 (40%)	90 (37%)	64 (45%)	

Values are median (interquartile range) or counts (percentage)
* p-value from Fisher's exact test, Pearson's Chi-squared test or Wilcoxon-rank sum test

with a high variability in antibiotic treatment durations (IQR, 7–20). Similar treatment durations of bacteremia have been reported by others [41-45]. Yet, there is a strong rationale to study reduced treatment courses, as durations >14 days are decreasingly recommended for most non-bacteremic infections [19].

Our results might open the way to intervention aiming at actively reducing antibiotic consumption, as antibiotic overconsumption is associated with potential harms. First, antibiotics are the most common cause of serious adverse drug events [46,47], affecting about 5–10% of inpatient recipients [48,49], with sometimes-harmful consequences such as allergy, anaphylaxis, neutropenia, hepatitis, seizures, renal failure, or even death [50,51]. Second, antibiotic overuse is causing a high financial burden to the healthcare system [52]. Finally, antibiotic overconsumption has since long been recognized as a leading cause of antibiotic resistance by exerting a selection pressure on patients' microbiota. Organisms that develop resistance to antibiotics may become the cause of future infections, which are less likely to be adequately treated, and more likely to result in death [53].

Escherichia coli and *Staphylococcus* spp. were the most frequent isolated microorganisms, responsible together for more than the half of all bacteremia episodes. This observation is line with reports from others [54,55]. Predominance of *E. coli* bacteremia might be related to the high number of urinary and hepatobiliary infections as sources of secondary bacteremia. The high number of coagulase negative bacteremia we reported, despite the restrictive inclusion criteria we used, might reflect a higher rate of catheter-related infections compared to other studies.

Our study has several strengths. It includes consecutive critically ill patients from two tertiary medical-surgical ICUs, collecting relevant data from severely critically ill patients including baseline information about demographics and comorbidities. Data was collected for multiple organisms including date and time of blood culture assessment. We used state-of-the-art approaches to address immortal time bias, a bias which is common in observational data investigating survival outcomes [34]. Naïve analyses - which do not address immortal time bias - might lead to biased results, such that the use of different analysis strategies allows a direct comparison between different methods.

Because of its retrospective and observational nature, this study also suffers from certain limitations. First, data presented in this study dates back to 2012 and might not reflect current practice guidelines. Second, the group assignment based on the duration of adequate antimicrobial treatment was defined retrospectively, which ultimately leads to biases (among others, confounding and immortal time bias) in the investigation of a mortality effect. Despite our efforts to correct for such biases, relevant information to address confounding (for example, decision-relevant factors from medical doctors or infection information during treatment course) were missing. Third, we have no data on the exact clinical patient condition at the cut-off days and cannot compare their clinical presentation at dichotomization. Fourth, we only investigated in-hospital mortality, which likely underestimates true survival effects. Fifth, our study covers only two tertiary study centers. Since guidelines for antimicrobial treatment are missing, a large between-hospital variation might exist. Inclusion of more study centers in our analysis could strengthen our findings. Sixth, patients were followed up until hospital discharge. Therefore, lack on follow-up data might have led to mortality underestimation and/or bias otherwise not accounted for.

The results of our analysis don't show clear survival benefit of long versus short antibiotic treatment of bacteremia in patients hospitalized on intensive care units. We believe, however, that the only way to overcome the mentioned limitations and gain the best knowledge in this field is to perform a prospective randomized control trial, evaluating shorter versus longer durations of antibiotic treatment [17].

5. Conclusions

Using different analysis strategies that attempt to adjust for confounding and immortal time bias inherent in treatment duration studies,

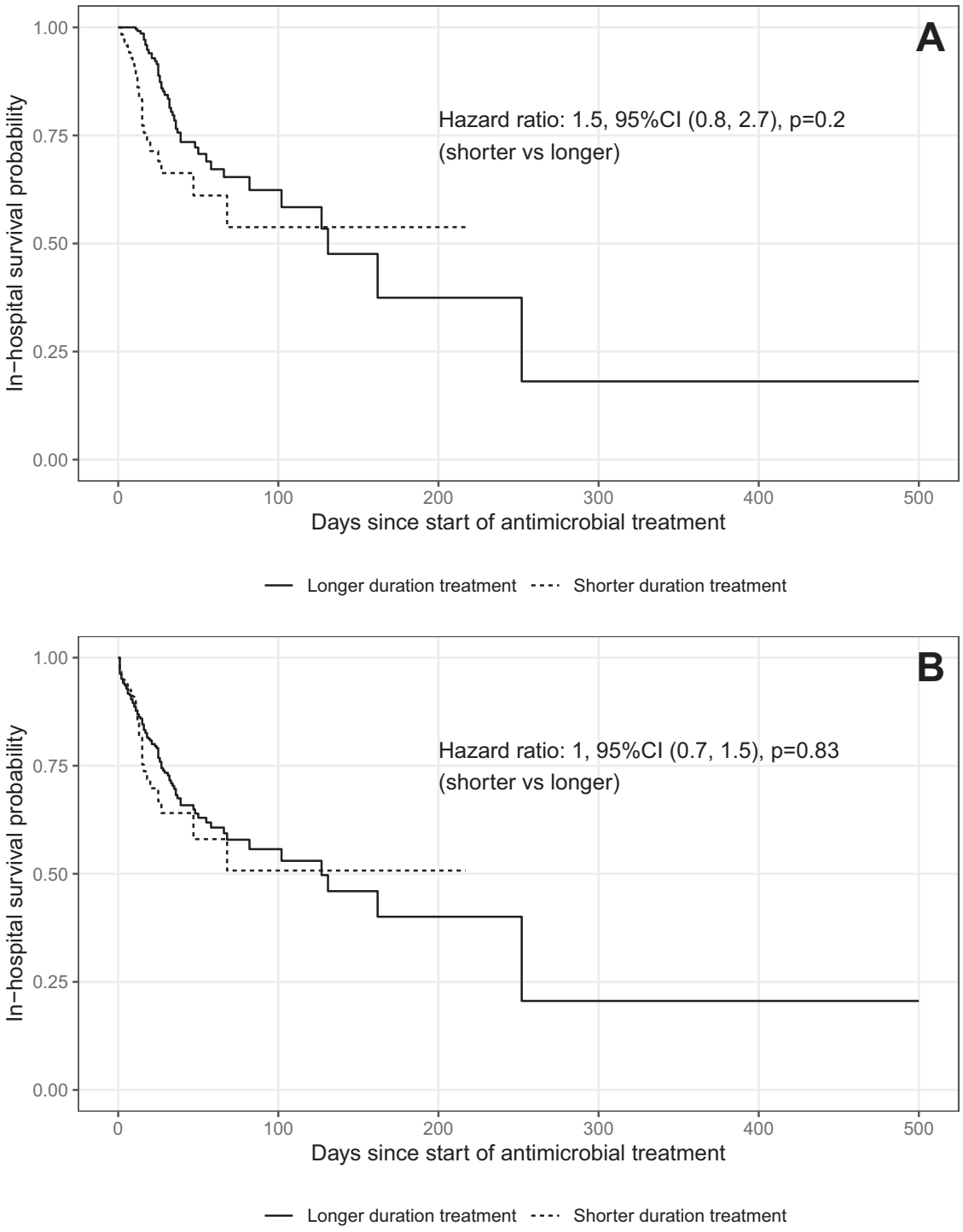

Fig. 2. Models addressing immortal time bias (Panel A: Time-dependent Cox model; Panel B: Cloning approach).

we did not find evidence for a survival difference between patients with a shorter (≤10 days) or longer (>10 days) antimicrobial treatment of bacteremia. However, the safety of shorter duration of antibiotic treatment in patients with bacteremia must be confirmed in adequately powered randomized control trials.

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jcrc.2023.154257.

Ethics approval

The Cantonal Ethical Committee of the State of Bern (#2022–02302) reviewed and approved the protocol of this double-centre study in 2022; the respective ethical committees approved both specific studies previously. This study was conducted with the support of the Data promotion unit of the CHUV. The study was retrospectively registered on clinicaltrials.gov (NCT05236283), 11 February 2022. Consent to participate NA. The Declaration of Helsinki and its subsequent revisions were followed.

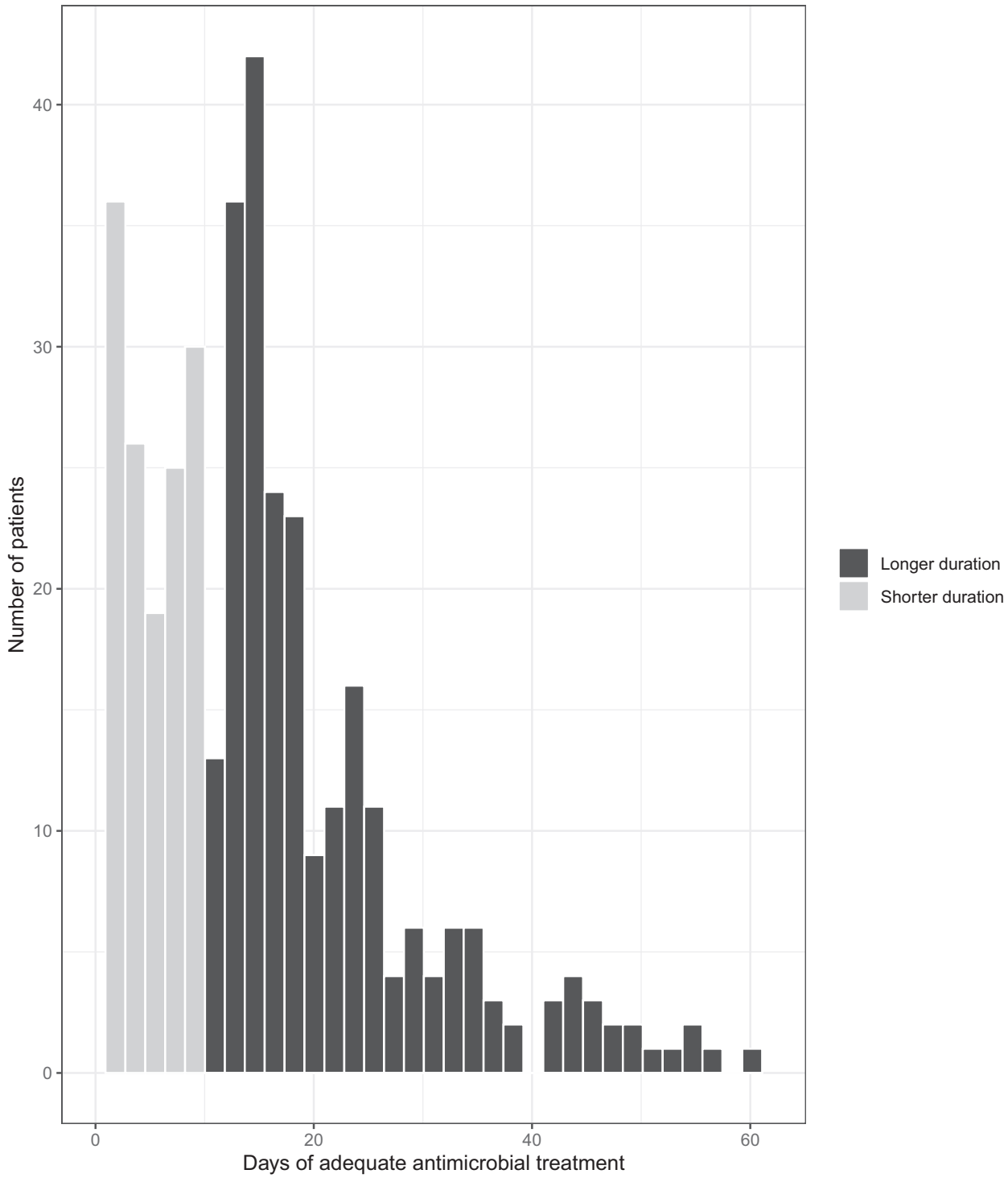

Fig. 3. Overall distribution of antimicrobial treatment durations received by critically ill patients with bacteremia, including those defined as shorter duration (≤10 days; light gray bars) and longer duration (>10 days; dark gray bars).

Consent to participate

NA

Consent for publication

NA

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Table 2
Median duration of antimicrobial treatment according to underlying source of bacteremia.

Secondary bacteremia	Median	Interquartile range
Catheter	16	(10, 20.8)
Venous cath - central	16	(10,21)
Venous cath - periph	19.5	(17.8, 23.8)
Artherial cath - cent	16	(15, 18)
Arterial cath - periph	16.5	(11.5, 23.8)
Pneumonia /respiratory infections	13	(8, 16.5)
Urinary/pyelonephritis	14	(7.75, 18.2)
Intra-abdominal infections	13	(7, 24)
Hepato-biliary infection	12	(8.5, 20.5)
Skin and/or soft tissue	18.5	(10.2, 30.5)
Other infection	16	(13, 27)

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Author contributions

PZ, AM, JP, and YAQ designed the study. MF, PE and JLP collected the raw data. AM performed the statistical analysis. AM, PZ, JP, MF, JLP, RF, ND, NB, PE and YAQ analyzed the data, JP, PZ, AM and YAQ wrote the manuscript. All authors reviewed and accepted the manuscript. All named authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship for this article, take responsibility for the integrity of the work as a whole, and have given their approval for this version to be published.

Declaration of Competing Interest

Patrick Zuercher, André Moser, Michael C. Frey, Jean-Luc Pagani, Niccolo Buetti, Philippe Eggimmann, Nick Daneman, Rob Fowler, Yok-Ai Que. and Josef Prazak have no conflict of interest to declare.

Data availability

The Corresponding author has acces to all data included into the analysis. Requests should be submitted to the corresponding author in the first instance.

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NA

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