Impact of short-incubation MALDI-TOF MS on empiric antibiotic therapy in bloodstream infections caused by *Pseudomonas aeruginosa*, *Enterococcus* spp. and AmpC-producing Enterobacteriaceae

Mika Halavaara [a,*], Annika Nevalainen [b], Timi Martelius [a], Pentti Kuusela [b], Veli-Jukka Anttila [a]

[a] *Department of Infectious Diseases, Inflammation Center, Helsinki University Hospital and University of Helsinki, Finland*
[b] *Division of Clinical Microbiology, HUSLAB, Helsinki University Hospital and University of Helsinki, Finland*

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ABSTRACT

The impact of the short-incubation matrix-assisted laser desorption ionization time-of-flight (si-MALDI-TOF) mass spectrometry technique was evaluated in the treatment of bloodstream infections (BSIs) caused by *Pseudomonas aeruginosa*, *Enterococcus* spp., and Amp-C producing Enterobacteriaceae. A total of 124 bacteremia episodes were divided into 2 groups: i) si-MALDI-TOF group ($n = 69$) and ii) control group ($n = 55$). Identification by si-MALDI-TOF resulted in 12.8% increase in cases receiving appropriate antibiotic treatment within 48 h from blood culture draw. The importance of the rapid identification was emphasized in BSIs caused by enterococci ($n = 62$), where si-MALDI-TOF led to appropriate antibiotic treatment in 87.9% of cases (versus control group 65.5%, $P = 0.036$). Implementation of si-MALDI-TOF technology for microbial identification was associated with increased proportion of patients receiving effective antibiotic treatment within 48 h from blood culture draw. The effect was most significant in BSIs caused by enterococcal species and in a subgroup of immunosuppressed patients.

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1. Introduction

The cornerstone of the management of bloodstream infections (BSIs) is rapid identification of the causative organism (Seifert, 2009). This will enable timely and appropriate antibiotic treatment, which is the most important predictor of a better outcome in patients with BSI (Ibrahim et al., 2000; Leibovici et al., 1998). This issue is relevant because BSIs cause a significant burden of disease with an increasing incidence (Skogberg et al., 2012).

Matrix-assisted laser desorption ionization time-of-flight (MALDI-TOF) mass spectrometry has changed the field of rapid microbial identification in clinical microbiology, especially in bacteremias (Drancourt, 2010). This technique allows a shorter time from blood culture draw to organism identification in patients with BSI compared with traditional methods (Bizzini and Greub, 2010; Martiny et al., 2013). Several studies have shown this technique's benefit on antibiotic treatment in patients with BSI (Clerc et al., 2013; Huang et al., 2013; Vlek et al., 2012). Combined with antimicrobial stewardship team intervention, it has been associated with reduced mortality and shorter hospital stay in patients with BSI (Huang et al., 2013). In addition, combined with antimicrobial stewardship team intervention, it has been shown to be cost-effective (Patel et al., 2016; Perez et al., 2013). MALDI-TOF analysis

combined with a short subculture time of positive blood cultures (si-MALDI-TOF) is an improvement of this technique, allowing even shorter time to pathogen identification with a positive effect on antibiotic therapy (Idelevich et al., 2014; Kohlmann et al., 2015), and is also associated with reduced length of hospital stay and mortality in patients with BSI (Delport et al., 2017).

In BSIs caused by *Pseudomonas aeruginosa*, *Enterococcus* spp., and AmpC-producing Enterobacteriaceae, empiric antibiotic therapy is likely to be inappropriate due to their natural resistance profile. This stresses the need for a faster recognition of these pathogens in bloodstream, especially since the benefit of timely and appropriate antibiotic treatment has been demonstrated also with these pathogens (Huang et al., 2013; Kang et al., 2003; Zasowski et al., 2016). An increase in mortality was observed in patients with delay in receiving appropriate antibiotic therapy over 48 h from blood culture draw (Lodise et al., 2007; Zasowski et al., 2016). Previous studies have also suggested particular benefit of MALDI-TOF in bacteremias caused by these pathogens (Clerc et al., 2013; Osthoff et al., 2016). However, in most studies, the impact of MALDI-TOF analysis is evaluated in combination with antimicrobial stewardship team and/or infectious disease (ID) consultation.

In the present study, we investigate the impact of si-MALDI-TOF on antibiotic treatment of BSIs caused by *Pseudomonas aeruginosa*, *Enterococcus* spp., and AmpC-producing Enterobacteriaceae. We hypothesized that si-MALDI-TOF would enable patients to receive appropriate antibiotic treatment faster. Time from blood culture draw to the receipt of

* Corresponding author. Tel.: +358-504270202.
E-mail address: mika.halavaara@hus.fi (M. Halavaara).

appropriate antibiotic therapy is a good indicator of the possible benefits of si-MALDI-TOF (Timbrook et al., 2017). Therefore, the primary outcome of the study was the percentage of patients receiving appropriate antibiotic therapy within 48 h after the blood culture draw.

2. Materials and methods

2.1. Patients and study design

This was a retrospective, observational study of adult patients with BSIs caused by *Pseudomonas aeruginosa*, *Enterococcus* spp., and AmpC-producing Enterobacteriaceae (including *Enterobacter* spp., *Serratia* spp., and *Morganella morganii*) between March 2014 and December 2015 at Helsinki University Hospital (HUH). Patients were identified from the clinical microbiology laboratory database at Helsinki University Hospital Laboratory (HUSLAB). Only the first BSI episode of patients with multiple episodes of the same bacteria during the study period was included.

HUH is a tertiary hospital serving population about one and a half million in the Hospital District of Helsinki and Uusimaa. The prevalence of multidrug-resistant *Pseudomonas aeruginosa* is low (65 cases year 2015). Also, the prevalence of vancomycin-resistant enterococci (VRE) is low (under 20 cases annually past few years). The research board of the Inflammation Center at the Helsinki University Hospital approved the study protocol.

2.2. Identification of bacteria

The si-MALDI-TOF identification was done from all blood culture bottles (BacT/Alert FA Plus, FN/PF Plus, FA, SN, and PF; bioMérieux) which flagged positive between 8 p.m. and 11 a.m. (si-MALDI-TOF group). For the analysis, 50–100 μl of blood culture content was applied on chocolate agar plates, which were incubated for 3–4 h at $+35$ °C in CO_2. After incubation, a sample for the MALDI-TOF analysis was taken by streaking the application area on the chocolate agar. One spot was inoculated for each sample. The analysis (Vitek MS; bioMérioux) was performed even if no growth was visible. Simultaneously with the si-MALDI-TOF analysis, another sample from blood culture bottle was Gram stained and subcultured on agar plates for susceptibility and identification confirmatory testing. Additionally, a sample from a positive blood culture bottle was used for conventional bacterial identification (in-house identification set containing 10 biochemical tests, as well as chromogenic plates). On the next day, a conventional MALDI-TOF was performed in cases giving unreliable identification in conventional biochemical analysis. The si-MALDI-TOF results were reported between 11 a.m. and 2 p.m., and the results for the control group were reported on the next day between 9 a.m. and 11 a.m. As a consequence, identification by si-MALDI-TOF resulted in initial identification roughly 22–24 h earlier than the one achieved by conventional MALDI-TOF and biochemical identification methods.

2.3. Data collection and statistics

An infectious disease specialist (M.H.) reviewed medical records of each patient. Demographic and clinical data were collected. Demographic data were analyzed using descriptive statistics. Categorical variables were analyzed using Chi-square analysis or Fisher's exact test when appropriate. Mann–Whitney U test was used in continuous variables if data were not normally distributed; otherwise, a 2-tailed Student t test was used. Kaplan–Meier method and log-rank test were used to analyze survival (type) data. P value <0.05 was considered statistically significant. Statistical analyses were performed using SPSS software, version 22.0 (SPSS, Inc., Chicago, IL).

2.4. Study definitions

Index bacteria mean one of the bacteria that are included in the study. Index bacteria are *Pseudomonas aeruginosa*, *Enterococcus* spp., and AmpC-producing Enterobacteriaceae (*Enterobacter* spp., *Serratia* spp., and *Morganella morganii*). Polymicrobial bacteremia was defined as the isolation of more than 1 bacterial species during the same bacteremia episode, except when the second microorganism was considered to be a contaminant. The focus or source of BSI was assessed on the basis of medical records.

Immunosuppressive treatment included antirejection medication, cancer chemotherapy, prednisolone more than 10 mg/day, and antirheumatic medications including biological medications (Table 1). Patients in this group are similar in a way that they all receive or have received immunosuppressive medication and are in a close follow-up of appropriate specialty. So, in their case, immunosuppression is clearly defined and is due to medication and comorbidity also. Patients with a disease associated with varying degree of immunosuppression (e.g., diabetes or liver disease) are a more heterogeneous group and harder to define. Thus, patients with these comorbidities are not included in the subgroup analysis including immunosuppressed patients.

2.5. Study definitions about antibiotic therapy

Appropriate antibiotic therapy was defined as an antibiotic regimen (i) to which the index bacterium was susceptible in vitro, (ii) considered standard treatment according to Helsinki University Hospital's antimicrobial treatment guide, and (iii) delivered intravenously (with the exception of fluoroquinolones). For example, antipseudomonal beta-lactam or fluoroquinolone for *Pseudomonas aeruginosa* BSI was considered appropriate, while monotherapy with aminoglycosides was inappropriate. Similarly, first-, second-, and third-generation cephalosporins and monotherapy with aminoglycosides were considered inappropriate for AmpC-producing *Enterobacteriaceae*. Time to the appropriate antibiotic

Table 1
Patient characteristics and focus or source of infection.

	Whole study group ($n = 124$)	Si-MALDI-TOF Group ($n = 69$)	Control group ($n = 55$)	P value
Patient characteristics				
Age, years (mean; SD)	61.3; 15.2	62.7; 15.6	59.6; 14.7	0.257
Gender, male; n (%)	74 (59.7)	42 (60.9)	32 (58.2)	0.762
Chronic heart disease	14 (11.3)	9 (13.0)	5 (9.1)	0.490
Chronic kidney disease	22 (17.7)	11 (15.9)	11 (20.0)	0.557
Dialysis	4 (3.2)	2 (2.9)	2 (3.6)	>0.99
Liver cirrhosis	5 (4.0)	4 (5.8)	1 (1.8)	0.381
Chronic lung disease	18 (14.5)	11 (15.9)	7 (12.7)	0.614
Diabetes	26 (21.0)	14 (20.3)	12 (21.8)	0.835
Blood malignancy[a]	14 (11.3)	10 (14.5)	4 (7.3)	0.207
Acute leukemia	15 (12.1)	9 (13.0)	6 (10.9)	0.717
Stem cell transplant	5 (4.0)	2 (2.9)	3 (5.5)	0.654
Solid organ malignancy	32 (25.8)	16 (23.2)	16 (29.1)	0.456
Solid organ transplant	18 (14.5)	10 (14.5)	8 (14.5)	0.993
Immunosuppressive treatment[b]	70 (56.5)	44 (63.8)	26 (47.3)	0.066
Neutropenia[c]	21 (16.9)	14 (20.3)	7 (12.7)	0.265
Infection focus or source				
Pulmonary	5 (4.0)	2 (2.9)	3 (5.5)	0.654
Urinary tract	21 (16.9)	13 (18.8)	8 (14.5)	0.526
Skin/musculoskeletal	7 (5.6)	5 (7.2)	2 (3.6)	0.461
Abdominal cavity	55 (44.4)	28 (40.6)	27 (49.1)	0.343
Central nervous system	1 (0.8)	1 (1.4)	0	>0.99
Heart	2 (1.6)	1 (1.4)	1 (1.8)	>0.99
Indwelling catheter	5 (4.0)	1 (1.4)	4 (7.3)	0.170
Unknown	28 (22.6)	18 (26.1)	10 (18.2)	0.296

[a] Other than acute leukemia.
[b] Antirejection medication, cancer chemotherapy, prednisolone more than 10 mg/day, and antirheumatic medications including biological medications.
[c] Absolute neutrophil cell count less than 0.5×10^5 neutrophils/mL.

therapy was calculated from the time of the first positive blood culture draw to the delivery of first dose of appropriate antibiotic.

2.6. Exclusion criteria

Patient exclusion criteria were i) transfer to another hospital before receipt of appropriate antibiotic therapy or lack of verified clinical details (data could not be obtained) ($n = 25$), ii) patient did not receive appropriate antibiotic treatment at all by the decision of the treating physician (e.g., due to poor prognosis) ($n = 6$), iii) bacteremia episodes during the appropriate antibiotic treatment ($n = 5$), and iv) blood culture result ruled as a contamination by the treating physician ($n = 4$; in these cases, blood culture was drawn through a catheter and did not correlate with clinical situation).

3. Results

3.1. General

A total of 164 episodes of bacteremia caused by the index bacteria were identified. According to exclusion criteria, 40 episodes were excluded (as shown in more detail is Subsection 2.6.), and resulting 124 bacteremia episodes originating from 120 patients were included in the study. One patient had 2 separate bacteremias of different index bacteria during the study period. Three patients had a polymicrobial bacteremia caused by 2 of the index bacteria. Consequently, both these findings were analyzed as separate episodes. The number of polymicrobial bacteremias including only 1 of index bacteria was 15.

One hundred twenty-four bacteremia episodes were divided into 2 groups: i) si-MALDI-TOF group ($n = 69$), i.e., si-MALDI-TOF was used for bacterial identification with a positive result, and ii) control group ($n = 55$), i.e., identification was done by means of conventional methods (including those cases where si-MALDI-TOF was done but was negative). For more details, see Subsection 2.2.

The site of acquisition of the blood culture was emergency room in 33.9% ($n = 42$), intensive care unit in 12.9% (16), internal medicine (including pulmonology and neurology) ward in 4.8% (6), hematology ward in 13.7% (17), surgical ward in 25.8% (32), gynecology ward in 3.2% (4), and oncology ward in 5.6% (7) of cases.

Baseline demographic characteristics were similar in both study groups (Table 1). HUH is the only national center for solid organ transplantations and also responsible for the majority of stem cell transplantations nationally. This explains the quite high number of hematological comorbidities in this study. Patients in the si-MALDI-TOF group had immunosuppressive medication more often than the ones in the control group (63.8% versus 47.3%, $P = 0.066$). None of the patients had an HIV infection. The most common source of bacteremia was abdominal cavity (44.4%), with second being urinary tract (16.9%) (Table 1). Seven-day mortality was 2.4% ($n = 3$) and 30-day mortality was 12.9% ($n = 16$), with no statistically significant difference between study groups (data not shown).

3.2. Microbiology and si-MALDI-TOF results

Pseudomonas aeruginosa caused 21 (16.9%) bacteremia episodes, *Enterococcus* spp. 62 (50%), and AmpC-producing Enterobacteriaceae 41 (33.1%). These results are shown in more detail in Table 2. Of all 103 monobacteremias, si-MALDI-TOF was done in 65 and yielded a result in 62 (3 bacteremias without a result: 1 *E. faecium*, 2 *E. cloacae*). Of polymicrobial bacteremias ($n = 21$), si-MALDI-TOF was done in 14 and yielded a result in 7 (for the index bacteria).

3.3. Early initiated empiric antibiotic treatment

In 75.8% ($n = 94$) of bacteremia episodes caused by the index bacteria, antibiotic treatment was either started or changed within 12 h after

Table 2
Number of bacteremic episodes according to the causative bacteria ($n = 124$).

	All episodes	Si-MALDI-TOF group	Control group	P value
Pseudomonas aeruginosa	21	14	7	0.265
Enterococcus spp.	62	33	29	0.588
E. faecalis	22	11	11	
E. faecium	37	21	16	
E casseliflavum	3	1	2	
AmpC-producing Enterobacteriaceae	41	22	19	0.754
E. aerogenes	2	1	1	
E. cloacae	21	11	10	
Serratia liquefaciens	1	1	0	
Serratia marcescens	13	6	7	
Morganella morganii	4	3	1	

the positive blood culture draw; in 19.4% ($n = 24$), no change was made to the ongoing inappropriate antibiotic treatment; and 6 patients received no antibiotic treatment at all. Subsequently, early initiated empiric antibiotic treatment was appropriate only in 22.6% ($n = 28$) of the bacteremia episodes in this study, and in the remaining episodes, treatments were inappropriate.

3.4. Impact of si-MALDI-TOF analysis on antibiotic treatment

In 72.6% ($n = 90$) of all bacteremia episodes, patients received appropriate antibiotic treatment within 48 h from the first positive blood culture draw. In si-MALDI-TOF group, this percentage was 78.3% ($n = 54$) and in control group 65.5% ($n = 36$); $P = 0.112$ by univariate analysis (Table 3). A similar trend was seen in Kaplan–Meier survival analysis (Fig. 1). However, in BSIs caused by *Enterococcus* spp. ($n = 62$), a significantly higher percentage of cases received appropriate antibiotic therapy within 48 h in si-MALDI-TOF group (87.9% versus 65.5% in the control group, $P = 0.036$). Results for different subgroups according to the index bacteria are shown in Table 3.

A significant benefit of si-MALDI-TOF identification was seen in the treatment of bacteremic episodes in patients with immunosuppressive medication ($n = 70$). In si-MALDI-TOF group, 86.4% ($n = 38/44$) and, in control group, 57.7% ($n = 15/26$) cases had appropriate antibiotic treatment within 48 h from blood culture draw ($P = 0.007$), as shown in Fig. 2.

In general, median time from blood culture draw to receipt of appropriate antibiotic treatment was 33.5 h (interquartile range [IQR] 19.3–49.5). In si-MALDI-TOF group versus control group, median times were 31.9 h (IQR 14.9–46.8) and 39.7 h (IQR 21.2–61.4), respectively ($P = 0.230$).

4. Discussion

In this study, we showed that enhanced MALDI-TOF analysis, si-MALDI-TOF, was valuable in guiding the antibiotic treatment of bacteremia episodes caused by *Pseudomonas aeruginosa*, *Enterococcus* spp., and AmpC-producing Enterobacteriaceae. Si-MALDI-TOF increased the proportion of appropriate antibiotic treatment within 48 h from the blood culture draw by 12.8%. Significant improvement in proportion of patients with appropriate treatment was seen in *Enterococcus* spp. group (22.4%, $P = 0.036$). Of all cases, the antibiotic treatment was appropriate only in 22.6% of cases within 12 h from the blood culture draw but was improved to 72.6% within 48 h. In patients with immunosuppressive medication, si-MALDI-TOF significantly increased the percentage of cases receiving appropriate antibiotic treatment within 48 h from blood culture draw.

In a study by Vlek and colleagues, it was demonstrated that, in 218 patients with BSI, rapid MALDI-TOF was associated with an 11.3% increase in the proportion of appropriate antibiotic treatment after 24 h

Table 3
Number of bacteremia episodes (BE) on appropriate antibiotic treatment within 48 h from the first positive blood culture draw.

		Total number n (%)	Si-MALDI-TOF group	Control group	P value
All bacteremia episodes in study group		90/124 (72.6)	54/69 (78.3)	36/55 (65.5)	0.112
BE caused by	*Pseudomonas aeruginosa*	16/21 (76.2)	11/14 (78.6)	5/7 (71.4)	>0.99
	Enterococcus spp.	48/62 (77.4)	29/33 (87.9)	19/29 (65.5)	0.036
	Amp-C producing Enterobactariaceae	26/41 (63.4)	14/22 (63.6)	12/19 (63.2)	0.975

of blood culture positivity (64.0% vs. 75.3%) (Vlek et al., 2012). This result is in line with our study, although for *Enterococcus* spp., the impact of si-MALDI-TOF was greater (65.5% vs. 87.9%), suggesting special benefit in that group.

In another study by Clerc et al. including 202 episodes of gramnegative bacteremias, enhanced MALDI-TOF analysis had an impact on empiric antibiotic therapy in 35.1% of bacteremia episodes and in 59.3% of the episodes caused by AmpC-producing Enterobacteriaceae ($n = 27$) (Clerc et al., 2013). Compared to our study, the number of bacteremias caused by the *Enterobacter* spp. and other AmpC-producing Enterobacteriaceae was lower. In spite of the higher number of BSIs caused by AmpC-producing Enterobacteriaceae, we could not detect any difference between the study groups. One possible explanation is that, in the study by Clerc et al., only patients for whom ID consultation was performed were included.

In a recent study, the benefit of rapid MALDI-TOF identification was evaluated in a setting with preexisting antimicrobial stewardship team program (Osthoff et al., 2016). Although it did not have an impact on the duration of intravenous antibiotic therapy, it led to lowered admission frequency to the intensive care unit after BSI onset. The MALDI-TOF analysis seemed to offer an extra benefit in a subgroup that included AmpC-producing Enterobacteriaceae and *Enterococcus* spp. In the 2 studies, additional benefit of MALDI-TOF method was suggested in treating patients with BSIs caused by the index bacteria in our study (Clerc et al., 2013; Osthoff et al., 2016).

In the recent study by Jeon et al., the use of MALDI-TOF alone did not significantly reduce the time to effective therapy (Jeon et al., 2018). This is in contrast to our study, which adds to the body of evidence on benefits of si-MALDI-TOF on antibiotic treatment of patients with BSIs caused by the index bacteria in our study. However, further studies will be needed, as noted in a recent meta-analysis, which also emphasized that earlier information should also lead to an appropriate clinical response (Dixon et al., 2015). This idea is further supported in a recent study on 239 BSI patients showing that MALDI-TOF method combined with antimicrobial stewardship intervention was more powerful than MALDI-TOF MS alone (Beganovic et al., 2017).

An interesting finding is the impact of si-MALDI-TOF in a subgroup of patients with immunosuppressive medication. In this group of patients, the proportion on appropriate antibiotic treatment within 48 h from the blood culture draw was significantly larger in the si-MALDI-TOF group than in the control group. This finding is difficult to explain. Looking only at bacteremic episodes in patients with immunosuppressive medication with inappropriate initial empiric antibiotic therapy, the difference remains ($n = 54$, 81.8% vs. 46.7%, $P = 0.008$). The proportions of different bacteria are also the same (e.g., *Enterococcus* spp. 52.9%, rest of the data not shown). One possible explanation is that the treating
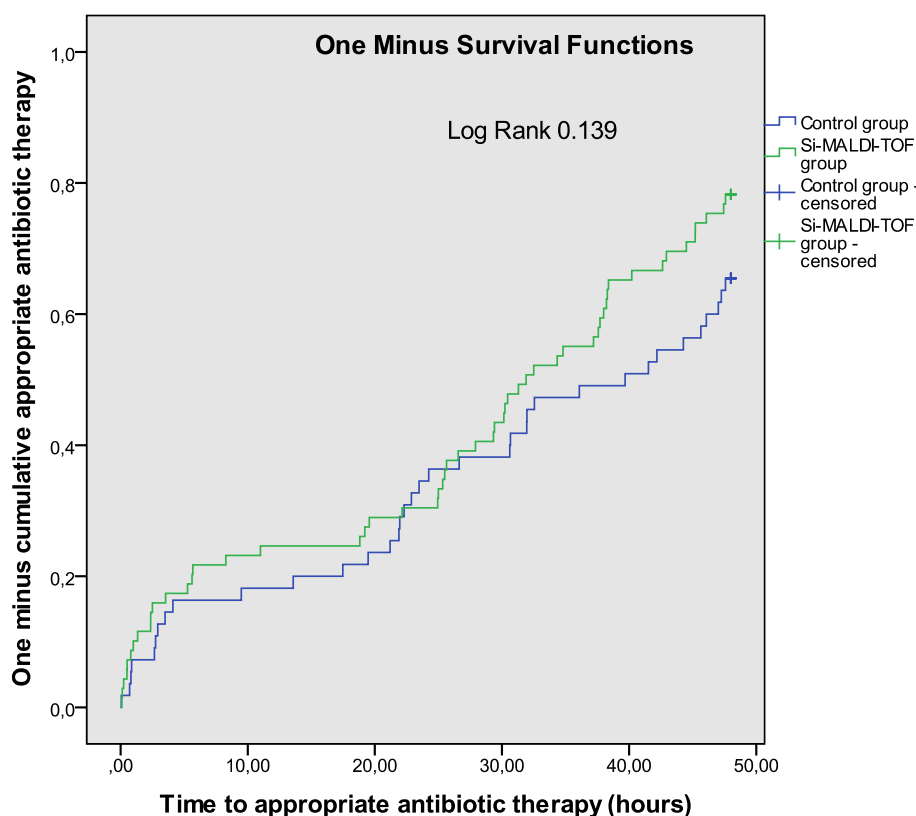

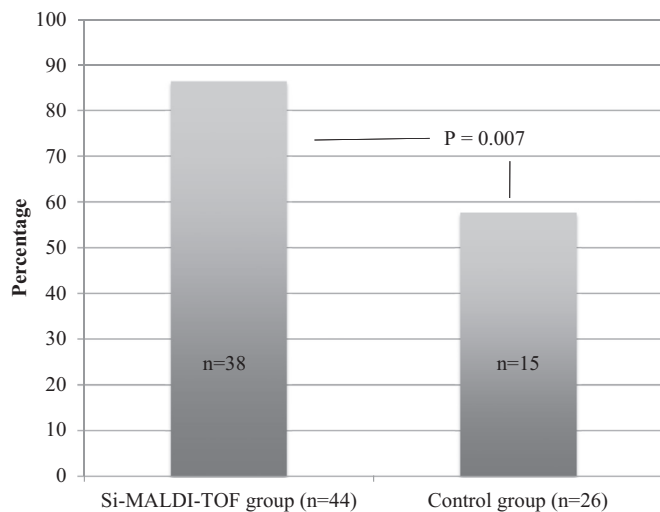**Fig. 1.** Kaplan–Meier survival analysis (log rank) between the 2 study groups, censored at 48 h.

Fig. 2. Percentages of appropriate antibiotic treatment within 48 h in bacteremic episodes of patients with immunosuppressive medication ($n = 70$).

physicians observe this group of patients more vigilantly and take full advantage of the information provided by the rapid diagnostics.

In clinical work, the antibiotic treatment is usually initiated after blood culture draw; in this study in 75.8% of cases. However, the antibiotic treatment was appropriate only in 22.6% of bacteremic episodes within 12 h after the blood culture draw. Empiric antibiotic therapy is often not changed until further microbial or clinical evidence is obtained, which usually takes at least 48 h. This highlights the importance of methods like si-MALDI-TOF that speed up the identification of bacteria in patients with BSI. Indeed, in clinical routine, information acquired from short-incubation MALDI-TOF method led to a change in empiric antibiotic treatment in 20% of patients with bacteremia (179 antibiotic prescriptions analyzed), and three quarters of these changes were considered rational by the authors (Kock et al., 2017).

The most plausible explanation why si-MALDI-TOF analysis brought a statistically significant benefit particularly in enterococcal bacteremias is the natural resistance profile of these microbes. Antibiotics effective also against enterococci are seldom included in empiric (in HUH often second- or third-generation cephalosporin) as well as in second-line antibiotic treatment (often a more broad spectrum beta-lactam). This is especially highlighted in BSI caused by *E. faecium*, which is often resistant to beta-lactams and requires vancomycin implemented in the regimen. Indeed, in 83.9% ($n = 52$) of all enterococcal bacteremias, the early empiric therapy was inappropriate. An effective coverage was obtained by expanding the regimen with either vancomycin or linezolid (67.3%, $n = 35$) or, alternatively, with enterococcal beta-lactam (32.7%, $n = 17$). This was seen clearly in *E. faecium* bacteremias ($n = 37$) where vancomycin was needed in 86.5% ($n = 32$) of cases in order to make the antibiotic therapy effective.

The strength of this study is its focus on the group of bacteria requiring special attention towards antibiotic therapy. Another strength is that the impact of si-MALDI-TOF information on antibiotic treatment could be evaluated independently of antimicrobial stewardship team since it was introduced to a routine clinical setting (i.e., real-world data). Although this is a single-center study, patient population was quite wide and diverse. Advantage of a single-center study is that all samples were analyzed in a single microbial university laboratory (HUSLAB).

There are several limitations in our study. It is a single-center study and is retrospective. Bacteremia episodes were divided into 2 study groups as described above, so presence of confounding factors is possible. If si-MALDI-TOF did not recognize the index bacteria from positive blood culture, clinicians did not receive any microbial information earlier, and hence, these bacteremia episodes were placed in the control group. Additionally, appropriate de-escalation of antibiotic therapy was not evaluated. Importantly, quite a high number of patients had neutropenia or were otherwise immunosuppressed, and in many cases, the source of infection was the abdominal cavity. These are situations where de-escalation is often not plausible even when bacteria in blood are recognized. In addition, the natural resistance profile of the bacteria in our study often necessitates the use of broad-spectrum antibiotics. In polymicrobial infections, the appropriateness of antibiotic therapy was assessed from the perspective of the index bacteria. However, in every polymicrobial bacteremia episode, appropriateness of antibiotic therapy was reached when index bacteria were covered. Si-MALDI-TOF provides faster recognition to species level but no further information about antimicrobial susceptibility of the bacteria. Thus, our findings might not be generalizable to a setting where prevalence of more resistant bacteria (e.g., VRE, MDR *Pseudomonas*) is higher. The number of cases was too low to properly assess this method's impact on mortality. However, as noted in a recent meta-analysis, true mortality benefits may be difficult to detect when assessing the benefits of molecular rapid detection test, and time to appropriate antibiotic therapy is a better indicator (Timbrook et al., 2017).

5. Conclusion

Si-MALDI-TOF is a useful tool in the treatment of patients with bloodstream infections. It increases the number of patients receiving appropriate antibiotic treatment within 48 h from blood culture draw. A statistically significant impact was observed in patients with BSI caused by *Enterococcus* spp. and in a subgroup of patients with immunosuppressive medication.

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Declaration of interest

Authors report no conflict of interest relevant to this study. MH has received conference invitation from Astellas and a speaker honorarium from MSD and Ratiopharm and has recent consultancies with Pfizer. AN has received a congress invitation from MSD. TM has received a speaker honorarium from CSL Behring and Octapharma; congress invitation from Pfizer, CSL Behring, and Gilead; and a grant from Sanguin. PK has received a speaker honorarium from MSD. VJA has received a speaker honorarium from Astellas, Roche, MSD, and Pfizer and has recent consultancies with MSD and Pfizer and study participation with Astellas and MSD.

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