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Formal Infectious Diseases Specialist Consultation Improves Long-term Outcome of Methicillin-Sensitive *Staphylococcus aureus* Bacteremia

Erik Forsblom,* Hanna Frilander,* Eeva Ruotsalainen, and Asko Järvinen

Division of Infectious Diseases, Inflammation Center, University of Helsinki and Helsinki University Hospital, Helsinki, Finland

Background. Formal infectious diseases specialist (IDS) consultation has been shown to improve short-term outcomes in *Staphylococcus aureus* bacteremia (SAB), but its effect on long-term outcomes lacks evaluation.

Methods. This retrospective study followed 367 methicillin-sensitive (MS) SAB patients for 10 years. The impact of formal IDS consultation on risk for new bacteremia and outcome during long-term follow-up was evaluated. Patients who died within 90 days were excluded to avoid interference from early deceased patients.

Results. Three hundred four (83%) patients had formal IDS consultation, whereas 63 (17%) received informal or no IDS consultation. Formal consultation, compared with informal or lack of consultation, was associated with a reduced risk of new bacteremia caused by any pathogen within 1 year (odds ratio [OR], 0.39; 95% confidence interval [CI], 0.18–0.84; $P = .014$; 8% vs 17%) and within 3 years (OR, 0.39; 95% CI, 0.19–0.80; $P = .010$; 9% vs 21%), whereas a trend toward lower risk was observed within 10 years (OR, 0.56; 95% CI, 0.29–1.08; $P = .079$; 16% vs 25%). Formal consultation, compared with informal or lack of consultation, improved outcomes at 1 year (OR, 0.16; 95% CI, 0.06–0.44; $P < .001$; 3% vs 14%), at 3 years (OR, 0.19; 95% CI, 0.09–0.42; $P < .001$; 5% vs 22%), and at 10 years (OR, 0.43; 95% CI, 0.24–0.74; $P = .002$; 27% vs 46%). Considering all prognostic parameters, formal consultation improved outcomes (HR, 0.42; 95% CI, 0.27–0.65; $P < .001$) and lowered risk for any new bacteremia (OR, 0.45; 95% CI, 0.23–0.88; $P = .02$) during 10 years of follow-up.

Conclusions. MS-SAB management by formal IDS consultation, compared with informal or lack of IDS consultation, reduces risk for new bacteremia episodes and improves long-term prognosis up to 10 years.

Keywords. infectious diseases specialist consultation; long-term outcome; *Staphylococcus aureus bacteremia*.

Staphylococcus aureus causes severe bacteremia (SAB), with mortality ranging up to 30% [1]. Infectious diseases specialist (IDS) consultations improve clinical management of SAB. IDS consultation has been shown to accelerate diagnostics and eradication of infection foci [2–4] and improve choice and duration of antimicrobial therapy [5]. The superiority of formal IDS consultation, compared with informal IDS consultation, has been demonstrated [6]. Above all, IDS consultation improves SAB prognosis, and IDS is advocated as a mandatory practice in SAB management by an increasing number of clinicians [2–8].

Most studies on long-term outcome in SAB have evaluated prognostic factors up to 1 year [9–14], whereas few analyses are available on 2–5 years [15–17] or 10 years of follow-up [18–20]. Parameters linked to shorter survival in these studies have been: older age [9–13, 15–18], underlying conditions [12–17], severe sepsis or septic shock [12, 20], unknown infection focus [10, 14, 18, 20], pneumonia [10, 20] and methicillin-resistant *S. aureus* (MRSA) [11], whereas adequate empiric antibiotic therapy has been connected to improved survival [3, 14]. However, the role of IDS consultation on long-term outcomes in SAB has received surprisingly little attention. Most reports on long-term follow-up of SAB have not included or commented on the role of IDS consultation [10–15, 17, 20]. Five studies provided IDS consultation or an infectious diseases team to 12%–90% of patients, concluding an improved 1-year outcome [3, 18] or improved clinical management [21, 22] whereas 1 report did not specify what clinical or prognostic impact IDS provided [20]. Two of the reports specified IDS consultation as formal or routine [3, 22]. There are no reports on the effect of IDS consultation on long-term outcome beyond 1 year after SAB.

The objective here was to investigate the impact of formal IDS consultation, compared with informal or no IDS consultation,

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*Equal contribution

Correspondence: E. Forsblom, Division of Infectious Diseases, Inflammation Center, Helsinki University Central Hospital, Meilahti Triangle Hospital, Haartmaninkatu 4, Helsinki, P.O. Box 372, FIN-00029 HUS, Finland (erik.forsblom@helsinki.fi).

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on risk for new bacteremia and outcome during 10 years of follow-up after methicillin-sensitive (MS) SAB. Exclusion of patients who died within 90 days enabled evaluation of parameters affecting only long-term outcome. Inclusion of MS-SAB enabled a setting in which each patient received proper nondelayed antibiotics from the first day of SAB, thus avoiding the impact of differences in empirical antibiotic choice.

METHODS

Study Population

The present study included all adult patients with at least 1 positive blood culture for methicillin-sensitive *S. aureus* from Helsinki University Central Hospital in Finland identified during January 1999 to May 1999, January 2000 to August 2002, and 2006 to 2007. Clinical patient data were retrieved from both written (1999–2002) and electronic (2006–2007) patient records. Bacteremia due to MRSA were omitted (altogether 5 cases in 1999–2002 and no cases in 2006–2007). We followed patient records meticulously for 90 days. Data documentation included gender, age, comorbid diseases, infection acquisition, illness severity, antibiotic therapy, radiological and laboratory findings, infection foci, IDS consultation, hospitalization, and outcome. Infection foci were verified by radiological, bacteriological, or pathological investigations or by clinical suspicion. Follow-up continued from hospital records for 10 years after the initial 90 days. Data on date and causative pathogen of any new bacteremia and date of death were recorded. Dead or alive status was retrieved from the Population Register Centre, which includes data on all people in Finland.

Definitions

McCabe's criteria were applied for classification of underlying conditions and comorbid diseases [23]. Patients with McCabe's healthy and nonfatal classification were viewed as lacking severe underlying diseases.

SAB was defined as nosocomial (health care associated) when the first positive blood culture for *S. aureus* was received (i) ≥48 hours after admission to a hospital or (ii) within ≤48 hours of hospital admission with a preceding previous hospital discharge within 7 days. Severe sepsis was categorized as sepsis in combination with hypotension, hypoperfusion, or organ failure [24]. The modified Duke criteria were applied for definition of endocarditis [25]. The Pitt bacteremia score was used for severity of illness evaluation [26]. IDS consultation within 7 days of SAB was categorized as (i) formal IDS, (ii) informal IDS, or (iii) no IDS consultation. Formal consultation was a bedside consultation by the IDS including physical examination, review of patient records, and written directives on clinical management. Informal consultation was recorded when directives given by the IDS on management were given by telephone (or any informal communication) and the treating physician documented the directives in the records. Lack of IDS consultation was defined as no consultation [6].

Outcome

The primary outcome was mortality rate and occurrence of any new bacteremia during 1, 3, and 10 years.

Statistical Analyses

Categorical variables were compared with Pearson's chi-square test, and noncategorical variables with the Student *t* test. Odds ratios (ORs) and hazard ratios (HRs) with 95% confidence intervals (CIs) were calculated. Univariate factors with $P < .1$ were allowed into the Cox regression model (proportional hazards regression) (Table 4) for estimation of prognostic parameters and into multivariate analysis (Table 5) for estimation of parameters predicting risk for new bacteremia. The Kaplan-Meier method was applied for survival estimates. Patients who died within 90 days were excluded from all analyses to enable statistical calculations of long-term prognostic parameters without interference from early deceased patients. Tests were 2-tailed, and $P < .05$ was considered significant. Analyses were done with SPSS 12.0 (SPSS Inc., Chicago, IL, USA).

RESULTS

Patient Characteristics

We identified a total of 440 patients with MS-SAB; however, 73 (17%) patients died during the initial 90 days and were excluded. Formal IDS consultation was received by 304 (83%), whereas 63 (17%) were managed through informal IDS consultation or without consultation. No differences regarding age, gender, or bacteremia acquisition were observed between the 2 groups (Table 1). Patients with formal IDS consultation, compared with patients with informal or lack of IDS consultation, had less hematological malignancy and more injection drug use (IDU), and no other differences were seen regarding other underlying conditions. When comparing patients with formal IDS consultation with patients with informal or lack of IDS consultation, no differences were seen regarding McCabe's healthy, nonfatal, ultimately fatal, or rapidly fatal classification of diseases (Table 1). No differences on severe sepsis, intensive care unit, or Pitt bacteremia scores were seen between patients with formal IDS consultation and those with informal or no IDS consultation (Table 1).

Clinical Management

Altogether, 260 (71%) patients had a deep infection focus. Formal IDS consultation, compared with informal or no IDS consultation, was associated with more radiological examinations, transesophageal echocardiography, computed tomography scans, and leukocyte indium-111 scintigraphy and more deep infection foci. Furthermore, deep infection focus eradication was received by 27% of patients with formal IDS

Table 1. Demographics, Underlying Conditions, and Illness Severity of 367 Methicillin-Sensitive *Staphylococcus aureus* Bacteremia Patients who Survived the First 90 Days; Categorization According to Formal Infectious Specialist Consultation

	Formal Infectious Diseases Specialist Consultation			
Parameters	Present n = 304 (83)	Absent n = 63 (17)	ORs (95% CI)	*P*
Demographics				
Male gender	205 (67)	38 (60)	1.36 (0.78–2.38)	.28
Age >65 y	96 (32)	15 (24)	1.48 (0.79–2.77)	.22
Age, mean ± SD, y	54.5 ± 18	52.4 ± 16	—	.24
Nosocomial bacteremia	143 (47)	38 (60)	0.58 (0.34–1.02)	.06
Underlying conditions				
McCabe's classification[a]				
Healthy	30 (10)	5 (8)	1.27 (0.47–3.41)	.64
Nonfatal	210 (69)	37 (58)	1.57 (0.89–2.74)	.11
Ultimately fatal	62 (20)	19 (30)	0.59 (0.32–1.09)	.089
Rapidly fatal	2 (1)	2 (3)	0.20 (0.03–1.46)	.080
Coronary artery disease	56 (18)	14 (22)	0.79 (0.41–1.53)	.49
Pulmonary disease – acute or chronic	45 (15)	8 (13)	1.19 (0.53–2.68)	.67
Liver disease – acute or chronic	56 (18)	7 (11)	1.81 (0.78–4.17)	.16
Diabetes mellitus	36 (12)	10 (16)	0.71 (0.33–1.52)	.38
Chronic renal failure[b]	34 (11)	9 (14)	0.76 (0.34–1.67)	.49
Malignancy				
Nonhematological	23 (8)	8 (13)	0.56 (0.24–1.32)	.18
Hematological	6 (2)	16 (25)	0.06 (0.02–0.16)	.001
IDU[c]	51 (17)	3 (5)	4.03 (1.22–13.3)	.014
HIV	10 (3)	0	—	—
Severity of illness				
Severe sepsis[d]	19 (6)	6 (10)	0.63 (0.24–1.66)	.35
ICU treatment, within 24 h	55 (18)	13 (21)	0.85 (0.43–1.67)	.64
ICU treatment, with 7 d	77 (25)	17 (27)	0.92 (0.49–1.69)	.78
Pitt score ≥3[d,e]	23 (8)	6 (10)	0.75 (0.29–1.92)	.54
Pitt score, mean ± SD[d,e]	0.59 ± 1.4	0.65 ± 1.6	—	.29

Data are No. (%) of patients. Hazard ratios and 95% confidence intervals are presented.

Abbreviations: CI, confidence interval; ICU, intensive care unit; ORs, odds ratio.

[a]Underlying diseases characterized according to McCabe and Jackson [23].

[b]Chronically elevated serum creatinine (≥180 mmol/L).

[c]Injection drug use within preceding 6 months.

[d]At blood culture collection.

[e]Pitt bacteremia scores [26].

consultation whereas 11% of patients with formal IDS consultation had infected foreign bodies removed. Contrary to this, patients managed by informal IDS or without any IDS did not undergo any infection eradications (Table 2).

Antibiotic Therapy

From the first day of positive blood culture, each patient was treated with an intravenous antimicrobial agent effective in vitro against the *S. aureus* blood isolate. Most patients received an antistaphylococcal penicillin 76%, whereas 17% had cephalosporin and 7% vancomycin, clindamycin, or a carbapenem. Adjunctive fluoroquinolone, rifampicin, or aminoglycoside was received by 51%, 54%, and 16% of patients, respectively. Patients with formal IDS consultation, compared with patients managed by informal IDS consultation or without IDS consultation, had more antistaphylococcal penicillin, more adjunctive rifampicin, and less cephalosporin, vancomycin, clindamycin, or carbapenem therapy, whereas no difference was seen with respect to adjunctive fluoroquinolone or aminoglycoside therapy (Table 2).

Outcome

The 1-, 3-, and 10-year overall mortality rates after exclusion of patients who died within the first 90 days were 5%, 8%, and 30%, respectively. Mortality among patients who received formal IDS consultation, as compared with patients with informal or no IDS consultation, was lower at 1 year, at 3 years, and at 10 years (Table 3). In Cox proportional regression model analysis, prognostic factors at 1, 3, and 10 years were very similar. At the 2 later time points, the only parameter for poor outcome was age >65 years, whereas lack of underlying diseases and formal IDS consultation were connected to better outcome at all 3 time points (Table 4, Figure 1). The Cox proportional regression analyses were re-performed by excluding patients

Table 2. Radiology, Infections, and Antimicrobial Therapy in 367 Methicillin-Sensitive *Staphylococcus aureus* Bacteremia Patients who Survived the First 90 Days; Categorization According to Formal Infectious Diseases Specialist Consultation

	Formal Infectious Diseases Specialist Consultation			
Parameters	Present n = 304 (83)	Absent n = 63 (17)	ORs (95% CI)	*P*
Radiological investigations				
Echocardiography				
Transthoracic	204 (67)	38 (60)	1.34 (0.77–2.35)	.30
Transesophageal	44 (14)	1 (2)	10.5 (1.42–77.6)	.005
Whole-body computed tomography				
≥1 per patient	203 (67)	31 (49)	2.08 (1.12–3.59)	.008
No. per patient, mean ± SD	1.10 ± 1.0	0.49 ± 0.5	—	.004
Magnetic resonance imaging				
≥1 per patient	64 (21)	0	—	—
No. per patient, mean ± SD	0.29 ± 0.6	0	—	—
Leukocyte indium-111 scintigraphy	127 (42)	7 (11)	5.74 (2.53–13.0)	<.001
Infection focus and eradication				
Pneumonia	112 (37)	11 (17)	2.76 (1.38–5.50)	.003
Endocarditis	40 (13)	2 (3)	4.62 (1.09–19.6)	.023
Osteomyelitis and/or septic arthritis	120 (39)	6 (10)	6.23 (2.60–14.9)	<.001
Any deep infection focus	236 (78)	24 (38)	5.64 (3.17–10.0)	<.001
Eradication of deep infection focus[a]	83 (27)	0	—	—
Eradication of infected foreign body	34 (11)	0	—	—
Antimicrobial therapy				
Antistaphylococcal penicillin[b]	255 (84)	25 (40)	7.91 (4.38–14.3)	<.001
Cephalosporine[c]	40 (13)	23 (37)	0.26 (0.14–0.49)	<.001
Other therapy[d]	9 (3)	15 (24)	0.09 (0.04–0.24)	<.001
Vancomycin	7 (2)	3 (5)	0.47 (0.12–1.88)	.28
Fluoroquinolone[e]	159 (52)	27 (43)	1.46 (0.85–2.53)	.17
Aminoglycoside[e]	47 (15)	13 (21)	0.70 (0.36–1.39)	.31
Rifampicin[e,f]	174 (57)	23 (37)	2.33 (1.33–4.08)	.003

Data are No. (%) of patients. Hazard ratios and 95% confidence intervals are presented.

Abbreviations: CI, confidence interval; ORs, odds ratio.

[a]Surgical or radiological eradication.

[b]Cloxacillin.

[c]Cefuroxime or ceftriaxone.

[d]Vancomycin, clindamycin, or a carbapenem.

[e]Adjunctive antimicrobial therapy.

[f]Therapy duration ≥14 days.

with hematological malignancy. The results were very similar to those in Table 4, with formal IDS consultation connecting to a positive prognosis at 1-, 3-, and 10-year follow-up. To further evaluate the long-term prognostic impact of formal IDS consultation, we re-performed the analyses by excluding patients who died within the first 3 years (n = 30). When the prognostic impact of formal IDS consultation on survival during 3–10 years was evaluated, the following results were achieved: OR, 0.66; 95% CI, 0.34–1.29; *P* = .22.

The risk for a new bacteremia episode caused by any pathogen was 9% (34), 11% (41), and 18% (65), and the risk for a new episode of SAB was 4% (14), 4% (15), and 6% (22) at 1-, 3-, and 10-year follow-up, respectively (Table 3). During the 10 years of follow-up, the 3 most common bacteremia pathogens were (1) 22 cases of *Staphylococcus aureus*; (2) 8 cases of various *Streptococci* including 3 cases of *Streptococcus viridans*; 3 cases of *Streptococcus pneumoniae* and 2 cases of *Streptococcus pyogenes*; and (3) 7 cases of *Escherichia coli*.

Formal IDS consultation, compared with informal or no IDS consultation, was connected to a lower risk for new bacteremia episodes at 1 year, at 3 years, and at 10 years (Table 3). However, within 10 years of follow-up, formal IDS consultation, compared with informal or no IDS consultation, presented no reduced risk for a new episode of SAB. In multivariate analysis, factors reducing the risk for any new bacteremia episode within 1 and 3 years were lack of underlying diseases and formal IDS consultation, whereas IDU increased the risk. At 10-year follow-up, IDU increased and formal IDS consultation decreased the risk for any new bacteremia episode (Table 5). The multivariate analyses were re-performed by excluding patients with hematological malignancies. The results were very similar to those in Table 5: Formal IDS consultation reduced the risk for any new bacteremia episode at 1 year, 3 years, and 10 years of follow-up.

Table 3. Risk for New Bacteremia and Outcome in 367 Methicillin-Sensitive *Staphylococcus aureus* Bacteremia Patients who Survived the First 90 Days; Categorization According to Formal Infectious Diseases Specialist Consultation

	Formal Infectious Diseases Specialist Consultation			
Parameters	Present n = 304 (83)	Absent n = 63 (17)	ORs (95% CI)	*P*
Risk for new bacteremia				
Within 1 y				
New bacteremia due to any pathogen	23 (8)	11 (17)	0.39 (0.18–0.84)	.014
SAB relapse	9 (3)	5 (8)	0.77 (0.18–3.29)	.73
Within 3 y				
New bacteremia due to any pathogen	28 (9)	13 (21)	0.39 (0.19–0.80)	.010
SAB relapse	10 (3)	5 (8)	0.89 (0.23–3.46)	.87
Within 10 y				
New bacteremia due to any pathogen	49 (16)	16 (25)	0.56 (0.29–1.08)	.079
SAB relapse	17 (6)	5 (8)	0.69 (0.24–1.94)	.47
Mortality, within				
1 y	8 (3)	9 (14)	0.16 (0.06–0.44)	<.001
3 y	16 (5)	14 (22)	0.19 (0.09–0.42)	<.001
10 y	81 (27)	29 (46)	0.43 (0.24–0.74)	.002

Data are No. (%). Hazard ratios and 95% confidence intervals are presented.

Abbreviations: CI, confidence interval; ORs, odds ratio; SAB, *Staphylococcus aureus* bacteremia.

DISCUSSION

The main observations were that formal IDS consultation, compared with informal or no IDS consultation, improved long-term outcomes in MS-SAB patients. Accounting for all prognostic parameters, MS-SAB patients had a 4–5-fold lower risk for a fatal outcome during 1 and 3 years of follow-up and an almost 2-fold lower risk for a fatal outcome during 10 years of follow-up due to formal IDS consultation. A similar trend was seen for risk of any new bacteremia during long-term follow-up: MS-SAB patients had a 3-fold lower risk during 1 and 3 years of follow-up and an almost 2-fold reduced risk during 10 years of follow-up due to formal IDS consultation.

The importance of deep infection localization and eradication and the potential connection of undiagnosed infection focus with mortality have been demonstrated repeatedly in SAB [27–30]. Identification of deep infection focus has been shown to improve 1- and 5-year prognosis after SAB [10, 14, 18, 20]. Previous reports on long-term outcome in SAB have provided echocardiography to 44%–64% of patients [3, 10, 21, 22] and identified deep infection focus in 11%–38% [3, 9, 10, 14, 22] with endocarditis in 4%–27% [3, 10, 14, 18, 21, 22] and osteomyelitis and/or septic arthritis in 10%–27% of patients [3, 9, 22]. The present study demonstrated a strong connection of formal IDS consultation with radiological investigations, resulting in deep infection focus identification in up to 78%. However, in patients managed through informal IDS consultation or without IDS consultation, deep infection focus was identified in 43% of cases only, and no infection focus eradication was provided.

The impact of IDS consultation–guided clinical management on long-term outcome in SAB has received little attention. Two prospective studies have provided IDS consultation for all SAB patients: 1 report had all patient cases reviewed by 2 infectious diseases specialists [9], and a second report investigated bacteremia of various pathogens (42% SAB) and provided bedside infectious diseases physician evaluation to all cases [16]. A third report had 12% of patients supervised by an infectious diseases team and concluded that lack of supervision was connected to poorer long-term outcome [18]. Another 3 reports provided IDS consultation to 27% [3], 74% [21], and 90% [22] of SAB patients and concluded that IDS consultation improved the 1-year outcome [3] or increased compliance [21, 22]. Contrary to the studies mentioned above, 1 report providing IDS consultation to 25% of SAB patients presented no benefit as a result of the consultation [20]. However, the explicit content and impact of the IDS consultation were not described [9, 16, 18, 20, 21]. Detailed content and impact of the IDS consultation have been specified in only 2 previous studies, which concluded that formal IDS consultation [3] or routine IDS consultation [22] enhanced choice and duration of antimicrobial therapy and increased diagnostics of deep infection focus and endocarditis [3, 22]. However, only 1 of these 2 reports connected formal IDS consultation to improved 1-year outcome [3]. We have previously shown that informal IDS consultation cannot achieve the benefits in short-term survival that have been seen with formal bedside IDS [6]. Hence, despite solid evidence that IDS consultation improves short-term outcome in SAB patients, no reports are available on the detailed content and impact of IDS consultation on a 1–10-year long-term outcome.

The present study excluded patients who died within 90 days to enable statistical analyses without interference from early deceased patients. This enabled evaluation of prognostic parameters that influence outcome after the initial 90 days. Moreover, to further evaluate the long-term prognostic impact of formal IDS consultation, we re-performed the analyses by excluding

Table 4. Cox Proportional Regression Model Analysis for Prognostic Factors for 1-, 3-, and 10-Year Mortality in 367 Methicillin-Sensitive *Staphylococcus aureus* Bacteremia Patients who Survived the First 90 Days

	Univariate Analysis				Multivariate Analysis	
1-y Mortality	Died n = 17 (5)	Survived n = 350 (95)	ORs (95% CI)	*P*	HRs (95% CI)	*P*
Male gender	13 (76)	230 (66)	1.69 (0.54–5.31)	.36	—	—
Age >65 y	9 (53)	102 (29)	2.74 (1.03–7.29)	.037	—	—
Healthy nonfatal disease[a]	6 (35)	276 (79)	0.15 (0.05–0.42)	<.001	0.18 (0.07–0.50)	.001
Nosocomial bacteremia	12 (71)	169 (48)	2.57 (0.89–7.45)	.072	—	—
Severe sepsis[b]	2 (12)	23 (7)	1.89 (0.41–8.79)	.41	—	—
Pneumonia	6 (35)	117 (33)	1.09 (0.39–3.01)	.87	—	—
Endocarditis	0	42 (12)	—	—	—	—
Bedside IDS consultation	8 (47)	296 (85)	0.16 (0.06–0.44)	<.001	0.21 (0.08–0.55)	.001
Telephone or no IDS consultation	9 (53)	54 (15)	6.17 (2.28–16.7)	<.001	—	—
Rifampicin[c]	11 (65)	186 (53)	1.62 (0.59–4.47)	.35	—	—
3-y mortality	Died n = 30 (8)	Survived n = 337 (92)	ORs (95% CI)	*P*	HRs (95% CI)	*P*
Male gender	22 (73)	221 (66)	1.44 (0.62–3.34)	.39	—	—
Age >65 y	15 (50)	96 (28)	2.51 (1.18–5.34)	.014	2.15 (1.02–4.53)	.045
Healthy nonfatal disease[a]	11 (37)	271 (80)	0.14 (0.06–0.31)	<.001	0.19 (0.09–0.42)	<.001
Nosocomial bacteremia	19 (63)	162 (48)	1.87 (0.86–4.04)	.11	—	—
Severe sepsis[b]	3 (10)	22 (7)	1.59 (0.45–5.66)	.47	—	—
Pneumonia	11 (37)	112 (33)	1.16 (0.54–2.53)	.70	—	—
Endocarditis	1 (3)	41 (12)	0.25 (0.03–1.88)	.15	—	—
Bedside IDS consultation	16 (53)	288 (85)	0.19 (0.09–0.42)	<.001	0.23 (0.09–0.44)	<.001
Telephone or no IDS consultation	14 (47)	49 (15)	5.14 (2.36–11.2)	<.001	—	—
Rifampicin[c]	18 (60)	179 (53)	1.32 (0.62–2.83)	.47	—	—
10-y mortality	Died n = 110 (30)	Survived n = 257 (70)	ORs (95% CI)	*P*	HRs (95% CI)	*P*
Male gender	78 (71)	165 (64)	1.36 (0.84–2.21)	.21	—	—
Age >65 y	53 (48)	58 (23)	3.19 (1.98–5.13)	<.001	2.37 (1.61–3.49)	<.001
Healthy nonfatal disease[a]	68 (62)	214 (83)	0.33 (0.19–0.54)	<.001	0.46 (0.31–0.68)	<.001
Nosocomial bacteremia	62 (56)	119 (46)	1.49 (0.96–2.35)	.17	—	—
Severe sepsis[b]	7 (6)	18 (7)	0.99 (0.37–2.22)	.82	—	—
Pneumonia	34 (31)	89 (35)	0.84 (0.52–1.36)	.49	—	—
Endocarditis	8 (7)	34 (13)	0.51 (0.23–1.15)	.10	—	—
Bedside IDS consultation	81 (74)	223 (87)	0.43 (0.24–0.74)	.002	0.42 (0.27–0.65)	<.001
Telephone or no IDS consultation	29 (26)	34 (13)	2.35 (1.35–4.09)	.002	—	—
Rifampicin[c]	58 (53)	139 (54)	0.95 (0.61–1.48)	.81	—	—

Data are No. (%) of patients. Hazard ratios and 95% confidence intervals are presented.

Abbreviations: CI, confidence interval; HRs, hazard ratio; IDS, infectious diseases specialist; ORs, odds ratio.

[a]Underlying diseases characterized according to McCabe and Jackson [23].

[b]At blood culture collection time point.

[c]Adjunctive rifampicin therapy ≥14 days.

patients who died within the first 3 years and investigated parameters affecting survival during 3–10 years. However, when excluding patients who died within the first 3 years, no prognostic impact of formal IDS consultation on 3–10-year survival was observed. Hence, it appears that the major positive prognostic impact of formal IDS consultation is seen within the first 3 years, and for patients who survive past the first 3 years, the outcome during the following years is irrespective of formal IDS consultation. To the best of our knowledge, only 3 studies have excluded early deceased patients, that is, patients who died within 3–30 days [3, 9, 14]. Previous reports on SAB outcome, including studies that excluded early deceased patients, have presented mortality rates of 32%–47% at 1 year, 48% at 3 years, and 76% at 10 years [9, 10, 14, 16, 18, 19]. The mortality rates of the present study are far lower than in these previous reports. However, comparison of mortality figures requires caution, as the present study excluded patients who died early.

The present study connected age and underlying conditions to poorer long-term prognosis at 1, 3, and 10 years of follow-up, which is in line with previous reports [9, 10, 11, 14, 15]. Long-term prognosis in the present report was not affected by severe sepsis, pneumonia, or endocarditis, that is, parameters frequently associated with poorer short-term (30–90 days) outcome [2–6]. These observations are in line with 1 previous report that excluded patients who died within 30 days and support the idea that short-term mortality is mainly influenced by

Table 5. Multivariate Analysis for Factors Predicting the Risk for New Bacteremia due to any Pathogen During 1-, 3-, and 10-Year Follow-up in 367 Methicillin-Sensitive *Staphylococcus aureus* Bacteremia Patients who Survived the First 90 Days

	Univariate Analysis				Multivariate Analysis	
Bacteremia within 1 y	Present n = 34 (9)	Absent n = 333 (91)	ORs (95% CI)	*P*	HRs (95% CI)	*P*
Male gender	23 (68)	220 (66)	1.07 (0.51–2.28)	.85	—	—
Age >65 y	10 (29)	101 (30)	0.96 (0.44–2.08)	.91	—	—
Healthy nonfatal disease[a]	19 (56)	263 (79)	0.34 (0.16–0.69)	.002	0.18 (0.07–0.45)	<.001
Nosocomial bacteremia	19 (56)	162 (49)	1.34 (0.66–2.72)	.42	—	—
IDU[b]	11 (32)	43 (13)	3.23 (1.47–7.08)	.002	8.74 (3.20–23.8)	<.001
Severe sepsis[c]	1 (3)	24 (7)	0.39 (0.05–2.98)	.35	—	—
Pneumonia	12 (35)	111 (33)	1.09 (0.52–2.29)	.82	—	—
Endocarditis	5 (15)	37 (11)	1.38 (0.50–3.78)	.53	—	—
Bedside IDS consultation	23 (69)	281 (84)	0.39 (0.18–0.84)	.014	0.32 (0.14–0.75)	.009
Telephone or no IDS consultation	11 (32)	52 (16)	2.58 (1.19–5.62)	.014	—	—
Rifampicin[d]	17 (50)	180 (54)	0.85 (0.42–1.72)	.65	—	—
Bacteremia within 3 y	Present n = 41 (11)	Absent n = 326 (89)	ORs (95% CI)	*P*	HRs (95% CI)	*P*
Male gender	29 (66)	214 (66)	1.27 (0.62–2.57)	.52	—	—
Age >65 y	10 (24)	101 (31)	0.72 (0.40–1.52)	.39	—	—
Healthy nonfatal disease[a]	24 (59)	258 (79)	0.37 (0.19–0.73)	.003	0.17 (0.07–0.41)	<.001
Nosocomial bacteremia	22 (54)	159 (49)	1.22 (0.63–2.33)	.56	—	—
IDU[b]	15 (37)	39 (12)	4.25 (2.07–8.71)	<.001	12.1 (4.72–30.8)	<.001
Severe sepsis[c]	2 (5)	23 (7)	0.68 (0.15–2.98)	.60	—	—
Pneumonia	14 (34)	109 (33)	1.03 (0.52–2.05)	.93	—	—
Endocarditis	7 (17)	35 (11)	1.71 (0.71–4.15)	.23	—	—
Bedside IDS consultation	28 (68)	276 (85)	0.39 (0.19–0.80)	.009	0.29 (0.13–0.66)	.003
Telephone or no IDS consultation	13 (32)	50 (15)	2.56 (1.24–5.28)	.009	—	—
Rifampicin[d]	20 (49)	177 (54)	0.80 (0.42–1.54)	.51	—	—
Bacteremia within 10 y	Present n = 65 (18)	Absent n = 302 (82)	ORs (95% CI)	*P*	HRs (95% CI)	*P*
Male gender	44 (68)	199 (66)	1.08 (0.61–1.92)	.78	—	—
Age >65 y	17 (26)	94 (31)	0.78 (0.43–1.43)	.43	—	—
Healthy nonfatal disease[a]	46 (71)	236 (78)	0.68 (0.37–1.23)	.20	—	—
Nosocomial bacteremia	34 (52)	147 (49)	1.16 (0.68–1.98)	.59	—	—
IDU[b]	19 (29)	35 (12)	3.15 (1.66–5.98)	<.001	3.63 (1.87–7.02)	<.001
Severe sepsis[c]	5 (8)	20 (7)	1.18 (0.42–3.26)	.76	—	—
Pneumonia	21 (32)	102 (34)	0.94 (0.53–1.66)	.82	—	—
Endocarditis	7 (11)	35 (12)	0.92 (0.39–2.18)	.85	—	—
Bedside IDS consultation	49 (75)	255 (84)	0.56 (0.30–1.08)	.079	0.45 (0.23–0.88)	.02
Telephone or no IDS consultation	16 (25)	47 (16)	1.77 (0.93–3.38)	.079	—	—
Rifampicin[d]	31 (48)	166 (55)	0.75 (0.44–1.28)	.29	—	—

Data are No. (%) of patients. Hazard ratios and 95% confidence intervals are presented.

Abbrevations: CI, confidence interval; HRs, hazard ratio; IDS, infectious diseases specialist consultation; ORs, odds ratio.

[a]Underlying diseases characterized according to McCabe and Jackson [23].

[b]Injection drug use within the preceding 6 months.

[c]At blood culture collection time point.

[d]Adjunctive rifampicin therapy ≥14 days.

severe infection-related complications such as severe sepsis or endocarditis, whereas long-term outcome is dictated by background parameters such as age and comorbidity [9]. Some previous reports have presented severe sepsis, septic shock, and pneumonia as drivers of long-term outcome in SAB [10, 12, 20]. However, these studies have not excluded early deceased patients, and hence the degree to which these parameters impact long-term outcomes is uncertain.

Relapse of SAB is common, and previous reports present relapse rates of 5%–12% during 90 days of follow-up [5, 31–33]. Parameters recognized as independent risk factors for relapse are deep infection focus, endocarditis, unremoved infected central venous line, and vancomycin therapy for MS-SAB [32–34]. Moreover, reports have connected IDS consultation to significantly reduced risk for SAB relapse during a short-term follow-up period of 90 days [5, 31]. To the best of our knowledge, only 1 study has reported a 6% SAB relapse during 1-year follow-up; in this study, each patient was provided IDS consultation [9]. We observed a rate of new SAB episodes of 4% at 1 and 3 years of follow-up and 6% at 10 years of follow-up. In the

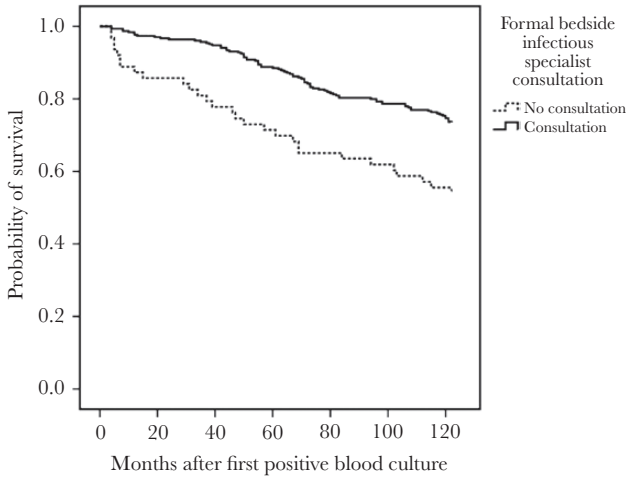

Figure 1. Kaplan-Meier analysis of probability of survival during 10 years of follow-up in 367 patients surviving the first 90 days after methicillin-sensitive *Staphylococcus aureus* bacteremia. Patients are categorized according to formal infectious diseases specialist consultation and informal or no consultation (log-rank $P < .001$).

present study, formal IDS consultation did not impact the risk of a new SAB episode during 1 to 10 years of follow-up. However, a significant reduction in risk for any new bacteremia episode due to formal IDS consultation during 1, 3, and 10 years of follow-up was observed. The association of proper clinical management of SAB, due to formal IDS consultation, and reduced future risk for new bacteremia is difficult to explain. Previous studies have observed that patients who suffer from bacteremia, compared with matched control patients, are more morbid and have higher long-term mortality rates [15, 35]. This excess long-term mortality is not completely understood, and it has been proposed that bacteremia might be a marker of comorbidity or an activator for a low-grade inflammatory response and infection-related inflammation resulting in the development of new diseases or accelerating earlier existing comorbidity, for example, cardiovascular or renal disease [15, 36, 37].

There are weaknesses in the present study that have to be accounted for when interpreting the results. First, the retrospective design includes risk for bias. Patients receiving formal IDS consultation, compared with patients with informal or no IDS consultation, had fewer hematological malignancies. However, analyses were performed twice, both including and excluding hematological malignancies, and the impact of formal IDS consultation on long-term outcome and risk for new bacteremia episodes were almost identical. Second, the present study demonstrated a connection between formal IDS consultation and reduced long-term mortality and risk for new bacteremia episodes, but this does not indicate a causal relationship. There is always the possibility that severely ill patients with presumed poor prognosis did not receive formal IDS consultation. However, the exclusion of patients who died during the first 90 days may have corrected this potential bias. Third, the patient cohort was originally gathered during January–May 1999, January 2000–August 2002, and 2006–2007 for evaluation of the prognostic impact of fluoroquinolones, rifampicin, and IDS consultation in MS-SAB patients [6, 38, 39]. The fluoroquinolone trovafloxacin was initially included but was withdrawn from the market and later replaced by the fluoroquinolone levofloxacin. This explains why no patients were collected during June–December 1999. Considering the time periods of 1999–2002 and 2006–2007, it is plausible to discuss whether the data are valid for current medical practice. However, we wanted to include 2 separate time periods to exclude the possibility of temporary unidentified differences in treatment practices or other factors that are difficult to control for. Furthermore, the possible disadvantage with either information storage pattern was taken into account by including both electronic and paper records.

In conclusion, the study indicates that formal IDS consultation, compared with informal or lack of consultation, improves long-term outcome and reduces risk for new bacteremia episodes. However, the relationship and implication of properly managed SAB and reduced risk of new bacteremia need further evaluation.

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