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Effects of Rapid Detection of Bloodstream Infections on Length of Hospitalization and Hospital Charges

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Current automated continuous-monitoring blood culture systems afford more rapid detection of bacteremia and fungemia than is possible with non-instrument-based manual methods. Use of these systems has not been studied objectively with respect to impact on patient outcomes, including hospital charges and length of hospitalization. We conducted a prospective, two-center study in which the time from the obtainment of the initial positive blood culture until the Gram stain was called was evaluated for 917 cases of bloodstream infection. Factors showing univariate associations with a shorter time to notification included higher body temperature and respiratory rate and higher percentage of immature neutrophils. Multiple linear regression models determined that the primary predictors of both increased microbiology laboratory and total hospital charges for patients with bloodstream infection were nonmicrobiologic and included length of stay and host factors such as the admitting service and underlying illness score. Significant microbiologic predictors of increased charges included the number of blood cultures obtained, nosocomial acquisition, and polymicrobial bloodstream infections. Accelerated failure time regression analysis demonstrated that microbiologic factors, including time until notification, organism group, and nosocomial acquisition, were independently associated with length of hospitalization after bacteremia, as were the factors of admitting service, gender, and age. Our data suggest that an increased time to notification of bloodstream infection is independently associated with increased length of stay. We conclude that the time to notification is an obvious target for efforts to shorten length of stay. The newest generation of automated continuous-monitoring blood culture systems, which shorten the time required to obtain a positive result, should impact length of hospitalization.

Bloodstream infections (BSIs) are now ranked as the 10th leading cause of death in the United States, with a recent increase in age-adjusted death rates (19). BSIs also have been associated with increased rates of hospitalization (2, 18), increased length of stay (23, 25), and increased hospital costs (1, 7, 21). The earliest possible identification of BSI allows for prompt optimization of antimicrobial therapy and diminished need for additional diagnostic studies, which in turn may serve to decrease both length of stay and cost.

Current automated continuous-monitoring blood culture systems afford more rapid detection of bacteremia and fungemia than is possible with non-instrument-based manual methods (5, 13, 14, 24, 27). Detection with continuous-monitoring systems has been estimated to be 1 to 1.5 days sooner than with instrumented blood culture systems that do not employ continuous monitoring (17). While such a decrease in detection time may seem intuitively important, use of these systems has not been studied objectively with respect to impact on patient outcomes, including hospital charges and length of hospitalization. Additionally, although the species of microorganism is known to affect the time to detection (8), other determinants of a shorter time to detection have not been examined. The intent of the present investigation was to explore factors associated with a shorter time to detection of BSI and to examine the impact of these factors on the outcomes of charges and length of stay. Our group has reported factors associated with the outcomes of antimicrobial therapy (20) and mortality (D. J. Diekema, S. E. Beekmann, K. C. Chapin, K. A. Morel, E. Munson, and G. V. Doern, submitted for publication) elsewhere.

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MATERIALS AND METHODS

Setting. This prospective study was conducted at the University of Iowa Hospitals and Clinics (UIHC) and at the Lahey Clinic Medical Center from February 1999 to July 2000. UIHC is an 813-bed tertiary referral teaching hospital with 41,460 admissions per year and serves Iowa and the border areas of surrounding states. The Lahey Clinic Medical Center is a 249-bed community-based teaching hospital with 16,703 admissions per year and serves eastern Massachusetts.

Patient eligibility. All patients admitted to the UIHC or Lahey Clinic Medical Center between February 1999 and July 2000 who had a positive blood culture by the BacT/Alert system were eligible for enrollment based on the first positive culture for each bacteremic or contamination episode.

A patient was eligible to be enrolled more than once if a new microorganism(s) was detected as part of a distinct septic episode. Patients with false-positive signals (no organisms on Gram stain or subculture from blood culture bottle), patients younger than 16 years of age, patients not admitted to the hospital, autopsy blood cultures, and blood cultures referred from other hospitals (where the patient was not admitted to one of the study centers) were excluded from the study.

Study methods. An experienced reviewer examined medical records for each enrolled patient. All patient and microbiologic data were recorded onto a standardized collection sheet. Based on clinical parameters at the time of infection, the number of positive blood cultures out of the total number drawn, results of other cultures, pathology findings, imaging results, and clinical course, each positive culture was classified as being clinically significant or not. Outcome measures included length of stay and hospital charges. Length of stay was calculated based on the dates and times of admission and discharge or death as recorded in the patient care

computer system. Hospital charges were obtained from the business office computer system; physician charges were excluded from these analyses.

Definitions. An episode of BSI was defined from the time the first positive blood culture was obtained (designated T0). The time to notification of patient care staff (calculated as the number of hours between T0 and the time when a blood culture Gram stain result was called) was divided into four categories: <24, 24 to 47, 48 to 71, and ≥72 h. Time to notification was used as the predictor variable rather than time to detection because no patient care decisions could be made (potentially affecting the outcomes) until the blood culture results were made available to patient care staff. We utilized the Charlson index (4) to assign an underlying illness score for each patient. The index assigned points based on the ICD-9 codes for the relevant admission.

Microbiologic laboratory processing. Both centers used the BacT/Alert 3D microbial detection system (bioMérieux, Marcy l'Etoile, France) with FAN aerobic and standard anaerobic bottles. This system monitors carbon dioxide production within each bottle every 10 min 24 h per day. Bottles identified as positive were immediately removed from the instrument between the hours of 7 a.m. and 11 p.m., and an aliquot was taken for Gram stain and subculture onto appropriate solid media. Bottles signaling positive between 11 p.m. and 7 a.m. were processed during the period from 7 to 8 a.m. Negative bottles were discarded after 5 days of incubation.

Statistical methods. All statistical analyses were restricted to clinically significant cases, to adults older than 16 years of age, and to patients who were still alive at the time the Gram stain was called. A second set of statistical analyses was performed using only the first episode from each patient and excluding all second and subsequent episodes. Univariate analyses (see Table 2) were performed using the nonparametric Kruskal-Wallis test for the dependent variable and a single independent classification variable. The continuous classification variables were analyzed using Spearman correlation to determine the strength of the linear association. All statistical analyses were performed using the SAS software program, version 8.2 (SAS Institute, Cary, N.C.).

To adjust for covariates, the multiple regression models were constructed in three stages. First, potential correlates of the outcomes were grouped into two categories: patient level variables and microbiology level variables. Second, preliminary models were run to determine significant factors from both categories. Third, all independent variables in each model associated with the outcome variable ($P < 0.1$) were retained and evaluated in a final combined model. Variables significant at an alpha of 0.05 were retained.

Univariate analyses of the charge outcomes were performed using a one-way analysis of variance test for an unbalanced design. All charge (dependent) variables underwent log transformation to linearize the regression model since distribution of residuals was positively skewed. Multiple linear regression models were constructed using PROC GLM with stepwise variable selection.

The SAS LIFEREG procedure was used to apply survival analysis based on parametric accelerated failure time regression to examine the influence of the explanatory variables on time to discharge from the hospital or on time to death in the hospital. In the former situation, patients were censored at the time of discharge, while in the latter situation, patients were censored at time of death. With either outcome, the regression models having a parametric Weibull residual hazard distribution fit the duration data significantly better than did the comparable exponential models, and all inferences concerning the explanatory variables are based on the Weibull models.

RESULTS

A total of 1,800 positive blood culture episodes were considered. Exclusion of 768 contaminated samples, 103 children, and 12 patients who died before the Gram stain could be called resulted in a study population of 917 cases of BSI that could be evaluated. Thirty-seven of the 917 cases were repeat (second or subsequent) bacteremias in the same patient. The distribution of organisms and the cumulative percentages of positive results called to the attention of patient care providers within 24, 48, and 72 h are shown in Table 1. Gram-positive pathogens caused the majority of BSIs, with *Staphylococcus aureus* being the most common pathogen overall, followed by *Escherichia coli* and coagulase-negative staphylococci. The mean time from T0 until the Gram stain was called (notification) was 27.6 h (range, 5.1 to 127.5 h). Selected demographic, clinical, and outcome variables for patients with BSI categorized by time to notification are presented in Table 2.

TABLE 1. Clinically significant microorganisms detected in index positive blood cultures and cumulative percentages of positive results called to the attention of patient care providers within 24, 48, and 72 h

Organism (no.)	% called in less than:		
	24 h	48 h	72 h
Staphylococcus aureus (182)	62	93	98
Escherichia coli (153)	75	92	98
Coagulase-negative staphylococci (111)	31	92	99
Enterococcus spp. (103)	75	96	99
Klebsiella pneumoniae (62)	82	96	98
Pseudomonas aeruginosa (50)	54	96	98
Streptococcus pneumoniae (41)	78	97	100
Alpha-hemolytic streptococci (19)	79	95	100
Candida albicans (19)	5	53	89
Enterobacter cloacae (18)	61	89	94
Proteus mirabilis (14)	78	100	100
Group B streptococci (12)	83	100	100
Serratia marcescens (11)	64	73	100
Bacteroides fragilis (10)	0	50	70
Klebsiella oxytoca (10)	50	70	80
Candida glabrata (8)	0	25	75
Yeast, unspeciated (6)	17	67	100
Beta-hemolytic streptococci (5)	60	100	100
Clostridium perfringens (5)	100	100	100
Candida tropicalis (4)	0	100	100
Clostridium spp. (4)	0	50	50
Diphtheroids (4)	50	100	100
Bacillus spp. (3)	67	100	100
Group A streptococci (3)	67	100	100
Enterobacter aerogenes (3)	33	66	66
Lactobacillus spp. (3)	33	66	100
Other (54)	37	67	94
Gram-positive group (507)	59	93	98
Gram-negative group (346)	69	91	97
Anaerobe group (25)	20	52	76
Yeast group (39)	5	51	87
Total (917)	60	90	97

Factors showing univariate associations with a shorter time to notification among patients with BSI included admission to general medicine or hematology-oncology departments, higher body temperature and respiratory rate, higher percentage of immature neutrophils (bands), and an absence of any indwelling lines or tubes (Table 3). Total white blood cell count did not achieve a statistically significant univariate association with shorter time to notification ($P = 0.14$).

Multiple linear regression models were constructed to examine factors associated with microbiology laboratory and total hospital charges. Length of stay and host factors, including admitting service, presence of an endotracheal tube, and underlying illness score, were significant predictors of both increased microbiology laboratory and total hospital charges (Tables 4 and 5). Microbiologic factors associated with higher charge outcomes included the number of blood cultures obtained, nosocomial acquisition of BSI (as defined by the Centers for Disease Control and Prevention [10]), and polymicrobial BSI. Gender was an independent predictor of total hospital charges only.

These models were repeated when only the first episodes of bacteremia were included and were essentially unchanged (data

TABLE 2. Relation of demographic, clinical, and outcome variables for patients with BSI to time to notification[a]

Variable	Time (h) to notification			
	<24 (n = 546)	24–47 (n = 275)	48–71 (n = 69)	≥72 (n = 27)
Hospital				
Lahey Clinic[c]	255 (55)	146 (32)	45 (10)	15 (3)
UIHC	291 (64)	129 (28)	24 (5)	12 (3)
Mean age (yr)	60 (17–98)	59 (17–91)	63 (23–91)	63 (27–87)
Female	255 (63)	100 (25)	37 (9)	10 (2)
Male	291 (56)	175 (34)	32 (6)	17 (3)
Admitting service[c]				
General medicine	283 (64)	112 (25)	34 (8)	12 (3)
Hematology/oncology	95 (66)	38 (26)	8 (5)	2 (1)
General surgery	47 (57)	29 (35)	3 (4)	3 (4)
Cardiology	25 (61)	11 (27)	5 (12)	0
Neurosurgery	12 (46)	13 (50)	0	1 (4)
Solid organ Transplant	18 (58)	7 (23)	4 (13)	2 (6)
Neurology	5 (29)	10 (59)	2 (12)	0
Bone marrow Transplant	17 (48)	14 (40)	3 (9)	1 (3)
Cardiovascular surgery	7 (47)	7 (47)	1 (7)	0
Urology	11 (44)	8 (32)	4 (16)	2 (8)
Vascular surgery	4 (44)	4 (44)	0	1 (11)
Orthopedic surgery	4 (33)	5 (42)	2 (17)	1 (8)
Obstetrics and gynecology	6 (75)	2 (25)	0	0
Burns	3 (37)	3 (37)	1 (12)	1 (12)
Other	9 (37)	12 (50)	2 (8)	1 (4)
Location at T0[b]				
ICU	227 (37)	284 (46)	69 (11)	31 (5)
Floor	498 (43)	457 (40)	122 (11)	80 (7)
Fever within 24 h of T0[b]	383 (62)	175 (28)	44 (7)	15 (2)
No fever	161 (54)	100 (34)	25 (8)	12 (4)
Temperature at T0[b]				
<36°C	25 (57)	10 (23)	7 (16)	2 (5)
36–38.5°C	271 (56)	158 (32)	41 (8)	17 (3)
>38.5°C	250 (65)	107 (28)	21 (5)	8 (2)
Endotracheal tube at T0[d]	60 (46)	53 (40)	15 (11)	3 (2)
No endotracheal tube	486 (62)	222 (28)	54 (7)	24 (3)
White blood cell count at T0				
<1,000	70 (57)	40 (33)	11 (9)	1 (1)
1,000–4,499	53 (69)	17 (22)	6 (8)	1 (1)
4,500–12,499	203 (59)	98 (28)	31 (9)	14 (4)
12,500–19,999	133 (58)	77 (34)	11 (5)	8 (3)
≥20,000	87 (61)	43 (30)	10 (7)	3 (2)
Charlson index score:				
0	203 (59)	109 (32)	21 (6)	11 (3)
1	84 (56)	50 (33)	13 (9)	3 (2)
2	130 (65)	50 (25)	17 (9)	3 (2)
3, 4, 5	87 (57)	45 (30)	11 (7)	6 (4)
≥6	42 (56)	21 (28)	7 (9)	4 (5)
Hospital acquired	257 (55)	163 (35)	36 (8)	14 (3)
Community acquired	289 (65)	112 (25)	33 (7)	13 (3)
Ever admitted or transferred to ICU	239 (56)	136 (32)	37 (9)	11 (3)
Mean no. of total blood cultures[d]	4.87 (0–20)	6.03 (0–20)	6.07 (0–20)	5.96 (1–20)
Mean no. of blood cultures with same organism[b]	1.10	1.05	1.04	0.96
Polymicrobial	61 (60)	30 (30)	7 (7)	3 (3)
Monomicrobial	485 (59)	245 (30)	62 (8)	24 (3)
Length of stay (days)[c]	18.1 (0–144)	22.2 (0.1–135)	21.8 (0.9–102)	26.6 (0.3–115)
Length of stay from T0 to discharge (days)[b]	13.1 (0–101.2)	14.9 (0–117.0)	16.6 (0–101.1)	18.2 (0.4–85.6)
Total hospital charges (dollars)[c]	59,150	84,022	73,820	92,305
Death	128 (60)	61 (28)	17 (8)	8 (4)

[a] Unless otherwise specified, values in table represent the numbers of patients. Single values in parentheses indicate percentages, and values separated by dashes indicate ranges.
[b] $P < 0.05$.
[c] $P < 0.01$.
[d] $P < 0.001$.

not shown). Presence of a central venous catheter at T0 was associated with increased microbiology laboratory charges in addition to the other factors previously shown. Gender no longer predicted total hospital charges and was replaced as a factor by organism group, with the highest total hospital charges being associated with bacteremias caused by anaerobic and gram-positive organisms (data not shown).

Accelerated failure time regression analysis demonstrated that

TABLE 3. Univariate analysis ($P < 0.10$) of variables associated with a shorter time to notification

Variable	*P* value
Demographic variables at admission and at T0	
Admission to general medicine	0.0161
Admission to hematology/oncology	0.0503
Presence of fever within 24 h of T0	0.0187
Higher temperature at T0	0.0024
Higher respiratory rate at T0	0.0109
Higher percentage of bands at T0	0.0094
Immunosuppressed patients	0.0824
Absence of arterial line at T0	0.0004
Absence of endotracheal tube at T0	0.0008
Absence of indwelling urinary catheter at T0	0.0093
Absence of surgical drain at T0	0.0749
Location on floor at T0 (not ICU)	0.0155
Shorter time from admission to T0	0.0039
Microbiologic variables	
Bacteremia with *E. coli*	0.0001
Bacteremia with *Klebsiella* spp.	0.0020
Bacteremia with pneumococci	0.0100
Bacteremia with enterococci	0.0004
Bacteremia with group B streptococcus	0.0772
Bacteremia with gram-negative organisms	<0.0001
More blood cultures with the same organism	0.0270
Bacteremia source of respiratory tract	0.0580
Community-acquired bacteremia	0.0064
Outcome variables	
Shorter time from T0 to discharge	0.0331
Shorter total length of stay	0.0016
Fewer antibiotics given	0.0027
Fewer total blood cultures drawn	0.0003
Never admitted to ICU	0.0869
Never intubated	0.0002
Fewer mean days of intubation	0.0814
Fewer mean days with central venous catheter	0.0556
Never with arterial line	0.0102
Fewer mean days with art line	0.0017
Never received total parenteral nutrition	0.0442
Never with indwelling urinary catheter	0.0021
Fewer infectious diseases consults performed	0.0016
Decreased antibiotic charges	0.0092
Decreased pharmacy charges	0.0332
Decreased microbiology charges	<0.0001
Decreased laboratory charges	0.0023
Decreased total charges	0.0011

TABLE 4. Multiple linear regression analysis of independent predictors of microbiology laboratory charges[a]

Factor	*F* value	*P* value	Cost ratio	Least squares mean of charges (dollars)[b]
Total no. of blood cultures drawn				
Linear term	329.47	<0.0001	1.21	
Quadratic term	90.34	<0.0001	0.99	
Length of stay	100.62	<0.0001	1.01	
Presence of endotracheal tube at T0	49.70	<0.0001		
No				844
Yes				1,200
Acquisition	11.13	0.0009		
Community acquired				946
Hospital acquired				1,070
Admitting service	5.31	<0.0001		
Obstetrics and gynecology				704
General medicine				907
Urology				866
General Hematology/ Oncology				806
Cardiology				683
Neurology				845
Other (including psychiatry)				927
Vascular surgery				1,299
Solid organ transplant				1,270
Burn unit				1,838
General surgery				961
Bone marrow transplant				1,062
Cardiovascular surgery				1,098
Orthopedic surgery				1,288
Neurosurgery				1,051
Polymicrobial	4.13	0.0424		
No				955
Yes				1,060
Charlson index score	2.64	0.0325		
0				1,064
1				1,036
2				936
3, 4, 5				958
≥6				1,044

[a] $R = 0.75$.
[b] Adjusted for mean values of covariables, i.e., length of stay = 19.7 days and no. of blood cultures drawn = 5.25.

the admitting service, gender, and age had significant association with length of stay after the index positive blood culture (T0 to time of discharge or death) (Table 6). Microbiologic factors, including time from T0 until notification, organism group, and nosocomial acquisition, were strongly associated with length of stay after T0 for patients with BSI. While none of the organism group subset analyses were significant, infection with anaerobes or gram-negative organisms was associated with a shorter time to notification than was infection with yeasts or gram-positive organisms. Nosocomial acquisition of BSI resulted in the largest duration ratio, with length of stay being significantly extended, by 1.56 times, compared with that associated with community acquisition of BSI. A second accelerated failure time regression analysis restricted to patients who died demonstrated that host factors and severity of illness at T0, including a white blood cell count of less than 1,000, presence of an endotracheal tube, lower body temperature, older age, and tachypnea, were strongly associated with shorter time to death (data not shown). Organism group was also significantly associated with shorter time to death; patients with a yeast BSI died more quickly than did those with a bacterial BSI. Finally, this analysis was repeated with only the first episodes of bacteremia included and the results were found to be unchanged (data not shown).

DISCUSSION

This prospective study of over 900 episodes of BSI is one of the largest recent studies examining clinical outcomes related

TABLE 5. Multiple linear regression analysis of independent predictors of total hospital charges[a]

Factor	*F* value	*P* value	Cost ratio	Least squares mean of charges (dollars)[b]
Length of stay	491.17	<0.0001	1.03	
Total no. of blood cultures drawn			1.21	
Linear term	222.30	<0.0001		
Quadratic term	141.33	<0.0001	0.99	
Acquisition	90.64	<0.0001		
Community acquired				46,879
Hospital acquired				71,385
Presence of endotracheal tube at T0	41.49	<0.0001		
No				47,666
Yes				70,206
Polymicrobial	6.41	0.0115		
No				53,520
Yes				62,528
Admitting service	4.79	<0.0001		
Obstetrics and gynecology				35,198
General medicine				46,167
Urology				48,154
General Hematology/ Oncology				50,232
Cardiology				51,045
Neurology				53,508
Other (including psychiatry)				55,231
Vascular surgery				59,621
Solid organ transplant				61,557
Burn unit				62,016
General surgery				63,494
Bone marrow transplant				66,299
Cardiovascular surgery				69,563
Orthopedic surgery				78,356
Neurosurgery				78,795
Gender	4.49	0.0343		
Female				55,487
Male				60,311
Charlson index score	2.71	0.0290		
0				52,376
1				58,703
2				54,967
3, 4, 5				59,077
≥6				64,887

[a] $R = 0.79$.
[b] Adjusted for mean values of covariables, i.e., length of stay = 19.7 days and no. of blood cultures drawn = 5.3.

TABLE 6. Accelerated failure time regression analysis of independent effects of risk factors on length of stay after the index positive blood culture (from T0 until discharge)[a]

Risk factor variable	χ^2	*P* value	Duration ratio	95% confidence interval
Admitting service	77.602	<0.0001		
Acquisition (hospital versus community)	51.541	<0.0001	1.56	1.38, 1.76
Organism group (versus yeast)	19.443	0.0002		
Anaerobes	0.670	0.4130	0.83	0.53, 1.30
Gram negatives	1.327	0.2493	0.83	0.61, 1.14
Gram positives	0.349	0.5545	1.10	0.81, 1.48
Age	11.608	0.0007	0.994	0.990, 0.997
Time from T0 until Gram stain called (per hour of time)	5.345	0.0208	1.004	1.001, 1.008
Gender (female versus male)	5.233	0.0222	1.15	1.02, 1.29

[a] Weibull loglikelihood, −1287.90; Weibull scale, 0.864.

to BSIs (6, 9, 15, 16, 22, 31). Since none of the previously published prospective studies examined either length of stay or hospital charges as an outcome variable, our data provided a unique opportunity to study these patient care outcomes as they related to microbiologic predictors in a diverse population in hospitals from two different regions of the country.

While there was no control group for which a nonautomated continuous-monitoring blood culture system was used, the differential times to notification among the 917 patients included in the study afforded an opportunity to examine the effects of a shorter time to notification on outcomes. Surprisingly, we found that microbiologic factors had a minimal association with microbiology laboratory and total hospital charges for patients with BSI. However, microbiologic factors, including time to notification, were significantly correlated with length of hospital stay for patients with BSI.

On univariate analysis, we determined that a shorter time to notification was found for patients with clinical evidence of infection (i.e., fever, tachypnea, or presence of more immature neutrophils) and a higher organism burden (i.e., more positive blood cultures with the same organism). Additionally, patients without invasive devices and not in intensive care units (ICUs) had a shorter time to notification.

Analysis of factors associated with higher microbiology laboratory and total charges for patients with BSI indicated that length of stay was one of the primary predictors, as was the total number of blood cultures drawn during hospitalization. Although the number of blood cultures drawn may be a partial surrogate for length of stay, this factor was an independent predictor of charges even with length of stay included in the model. The Charlson index was an independent predictor of both microbiology laboratory and total hospital charges, indicating that severity of illness was a potential confounder and an important covariate, as previously reported by others (3, 25, 28). Interestingly, host factors serve an important role in predicting both microbiology laboratory and hospital charges, while microbiologic factors, which included polymicrobial and nosocomial BSIs, have only a subsidiary role. Polymicrobial BSIs have been associated with poorer outcome, independent of the patient's underlying disease or the organism group caus-

ing the infection (22, 30). Nosocomial BSIs often are confounded by underlying disease status and severity of illness.

Microbiologic factors play a much more important predictive role in the length of time from bacteremia until discharge. Time from T0 until notification was a significant predictor of length of stay from T0 to discharge. This time period encompasses transit time from the location of the blood draw to the microbiology laboratory, processing of the bottles, incubation until the machine signals a positive result, waiting overnight until day shift staff arrive to pull the bottle, Gram stain of the bottles, and calling of patient care staff. The machine incubation almost always accounted for the vast majority of this time period, indicating that the earliest possible detection of microbial growth is associated with shorter lengths of stay. While the duration ratio of 1.004 indicates that the magnitude of this effect is small (length of stay is increased by 1.004 per hour of time to notification), a shorter time to detection is a significant independent predictor of length of stay even with organism group in the regression equation.

The results of our study are consonant with those from a number of published reports indicating that BSI is associated with increased length of stay (7, 21, 23, 29) and with increased costs (7, 21, 23, 26, 28). Our study, which was not designed to include a control group, cannot assess the relative contribution of BSI to length of stay or charges within the context of underlying or preexisting illness. Our data indicate that time to notification significantly impacts length of stay for patients with BSI, with overall length of stay ($P = 0.0016$) as well as length of stay after diagnosis of BSI ($P = 0.0331$) being increased in stepwise fashion with length of time to notification. We also found that microbiology laboratory charges ($P < 0.0001$) and total charges ($P = 0.0011$) increased in a similar stepwise fashion for patients with BSI.

One potential criticism of this study relates to our use of the Charlson index (4) to assess severity of underlying illness. This standardized score index was initially developed for outcomes of noninfectious diseases (11). Nevertheless, the Charlson index was chosen because it was developed to assess underlying illness in a general medicine population rather than acuity of current illness. Most acuity of illness scores were developed for ICU patients and do not predict nosocomial infection rates well (12).

Another potential limitation is that our sample may not be representative of the overall population of patients with bacteremia. All patients with bacteremia in the two hospitals between February 1999 and July 2000 were enrolled. The two hospitals were located in geographically diverse areas, served different primary patient populations, and had different academic affiliations. In addition, a complete range of patient care services was offered between the two institutions. Nevertheless, hospital charges and length of stay vary considerably within and between regions, and these data may not be representative of other facilities in the United States.

Additionally, hospital charges were utilized rather than actual cost. Hospital charges are obviously greater than either costs or revenue, and thus our charge data may not be directly comparable to other published data examining costs (7, 21, 23). Differences, however, should be randomly distributed and applicable to all patients enrolled in our study, making the analysis of charges viable.

Our data suggest that increased time to notification of BSI is independently associated with increased length of stay. While host factors most often cannot be changed, time to notification can be improved. We conclude that time to notification of BSI is an obvious target for focused strategies aimed at decreasing this period of time. Clearly, use of the newest generation of automated continuous-monitoring blood culture systems, which shortens the period of time needed to obtain a positive result, should impact length of hospitalization. Additionally, microbiology laboratories should focus on other methods to decrease time to notification, including decreasing transit time from patient care areas to the laboratory, prioritizing processing of blood cultures and Gram stain results (including during night shifts), and communicating Gram stain results immediately to patient care staff.

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