J Microbiol Immunol Infect.
2009;42:243-250

Original Article

Clinical significance of and outcomes for *Bacteroides fragilis* bacteremia

Chun-Wen Cheng, Huang-Shen Lin, Jung-Jr Ye, Chien-Chang Yang, Ping-Cherng Chiang, Ting-Shu Wu, Ming-Hsun Lee

Division of Infectious Diseases, Department of Internal Medicine, Chang Gung Memorial Hospital, Chang Gung University College of Medicine, Taoyuan, Taiwan

Received: March 10, 2008 Revised: June 5, 2008 Accepted: July 7, 2008

Background and purpose: *Bacteroides fragilis* is a virulent anaerobic pathogen, resulting in considerable mortality. This study was conducted to investigate the clinical characteristics, significance of polymicrobial bacteremia, and treatment outcomes of *B. fragilis* bacteremia.

Methods: This retrospective analysis enrolled 199 adult patients with *B. fragilis* bacteremia, who were admitted to hospital between January 2004 and May 2007. Chi-squared and Fisher's exact tests were used for comparison. A p value of <0.05 was considered statistically significant.

Results: 142 patients with *B. fragilis* bacteremia (71.4%) had at least 1 underlying disease. Malignancy was the commonest comorbidity (n = 62; 31.2%). Intra-abdominal infection accounted for 49.3% of the infection sources. Seventy seven patients (38.7%) had polymicrobial bacteremia and *Escherichia coli* was the most common concurrent isolate (n = 24). There was no significant difference in septic shock incidence and clinical outcome between the monomicrobial and polymicrobial groups. The overall 30-day crude mortality rate was 30.7%. Inappropriate early antimicrobial therapy did not affect outcome, but a higher mortality rate was noted for patients who never received appropriate antimicrobial therapy (55.2% vs 26.5%; p = 0.002). Independent risk factors for mortality were age 65 years and older (p = 0.010), malignancy (p = 0.001), shock (p < 0.001), thrombocytopenia (p = 0.026), and lack of surgical intervention (p = 0.035).

Conclusions: *B. fragilis* bacteremia causes a high mortality rate, especially for elderly people and patients with cancer. Clinicians should be alert to the infectious focus, and appropriate surgical intervention may be necessary to improve outcomes.

Key words: Bacteremia; Bacteria, anaerobic; *Bacteroides fragilis*

Introduction

Anaerobic bacteremia accounts for a relatively low incidence (0.5% to 12.0%) of all bacteremia, but is associated with a high mortality rate [1-3]. A decrease in the incidence of anaerobic bacteremia was reported during the 1970s and 1990s [2,4], which was explained by the routine use of bowel preparation, prophylactic antibiotics for abdominal surgery, and new broad-spectrum antibiotics with activity against anaerobic bacteria. However, the incidence of anaerobic bacteremia has increased considerably at the Mayo Clinic since the late 1990s [5]. Complex underlying diseases, especially malignancy, bone marrow transplantation, and an increase in the number of elderly patients are responsible for the re-emergence of anaerobic bacteremia.

Bacteroides fragilis is the commonest anaerobic blood isolate, with this group accounting for 45% to 65% of clinically important bacteremia, both nosocomial and community acquired [4,6-9]. Factors predisposing to *B. fragilis* group bacteremia include malignancy, recent gastrointestinal (GI), obstetric, or gynecologic surgery, intestinal obstruction, decubitus ulcer, diabetes mellitus, hematological disorders, and the use of cytotoxic agents or corticosteroids [10]. The

Corresponding author: Dr. Ming-Hsun Lee, Division of Infectious Diseases, Department of Internal Medicine, Chang Gung Memorial Hospital, 5 Fu-Shin St, Gueishan 333, Taoyuan, Taiwan.
E-mail: lmh1016@adm.cgmh.org.tw

overall mortality rate associated with *B. fragilis* bacteremia ranges from 20% to 31% [1,11]. In Taiwan, there are limited clinical data of *B. fragilis* bacteremia [9,12,13]. Thus, this study was conducted to evaluate the clinical characteristics, risk factors, and outcomes for adult patients with *B. fragilis* bacteremia, including the significance of polymicrobial bacteremia.

Methods

Setting

The study was performed at Chang Gung Memorial Hospital, Taoyuan, Taiwan. The hospital is a university teaching hospital, comprising 3300 beds and providing primary and tertiary health care in northern Taiwan. A central microbiology laboratory is responsible for the management of all clinical specimens.

Patients

Adult patients older than 18 years with blood cultures positive for one or more *B. fragilis* isolates from January 2004 to May 2007 were identified retrospectively from microbiology laboratory records. The medical records were reviewed and patients who were not admitted to hospital were excluded.

Design

Information obtained from the medical records of patients enrolled in the study included demographic characteristics, underlying diseases, clinical presentation, recent surgery or invasive procedures, use of corticosteroids or immunosuppressants, laboratory data, bacteriology data, infection source, antibiotic regimens, surgical intervention or drainage, and outcomes.

Definitions

The presence of an underlying disease was based on the medical record made by the treating physician. Only surgical or invasive procedures performed within 2 weeks before the onset of infection were considered recent. Previous antibiotic therapy was defined as use of an antimicrobial agent for at least 3 days within the 7 days preceding the onset of infection. The source of infection was determined by radiological, surgical, or microbiological evidence of barrier compromise or an infectious pathology, such as abscess or necrosis. Polymicrobial bacteremia was defined as one or more additional bacteria species isolated from blood simultaneously with *B. fragilis.* Other isolates, such as *Propionobacterium* spp., coagulase-negative staphylococci, and *Bacillus* spp., were regarded as contaminants [14,15]. Such isolates were excluded unless the organism was isolated from ≥2 consecutive blood cultures.

Fever was defined as an ear temperature of >38°C. Hypothermia was defined as a body temperature of <36°C. Leukocytosis was defined as a leukocyte count of >10,000/μL and leukopenia was defined as a leukocyte count of <4000/μL. Thrombocytopenia was defined as a platelet count of $<150 \times 10^3$/μL. Shock was defined as systolic blood pressure ≤90 mm Hg measured on the same day as the collection of blood cultures and unrelated to other possible causes of shock, such as hypovolemic and cardiogenic shock.

Antimicrobial therapy was considered to be appropriate if the agents used for therapy had activity against *B. fragilis* by in vitro susceptibility testing. Antimicrobial therapy started within 48 h of the onset of infection and used for at least 3 days was considered to be early treatment. Crude mortality was defined as all-cause fatality within 30 days of the emergence of bacteremia.

Microbiology

Blood samples were inoculated into both aerobic and anaerobic broth media for processing with the BACTEC 9240 blood culture system (Becton, Dickinson and Company, Madison, WI, USA). Identification of *B. fragilis* was based on the recognition of Gram-negative bacilli with good growth on *Bacteroides* bile esculin agar plate; resistance to vancomycin, kanamycin, and colistin antibiotic disks; negative spot indole test; presence of catalase production; absence of fermentation of trehalose, arabinose, rhamnose, and salicin; and positive fermentation of sucrose [16]. The antimicrobial susceptibility testing was performed by the agar dilution method recommended by the Clinical and Laboratory Standards Institute (CLSI), with the use of Wilkins-Chalgren medium [17]. Briefly, 5 antimicrobial agents were used for susceptibility testing: penicillin G, ampicillin-sulbactam, clindamycin, metronidazole, and piperacillin. The inoculum of isolates was prepared by suspending colonies from anaerobic sheep blood agar into Schadler broth and adjusting to the density of McFarland standard 0.5. An inoculum of 10^5 colony-forming units per well was then delivered by a Steers replicator to the antibiotic-containing Wilkins-Chalgren agar plates. All plates were incubated at 35°C anaerobically for 48 h. The susceptibility breakpoints employed were based on the recommendations of the CLSI [17]. A reference strain

of *B. fragilis* American Type Culture Collection 25285 was used for quality control.

Statistical analysis

Comparisons between categorical variables were calculated using chi-squared or Fisher's exact tests, as appropriate. Continuous variables were compared by Student *t* test. Odds ratios and 95% confidential intervals were calculated to evaluate the strength of any association, as well as the precision of the estimate of the effect in the outcome analysis. Univariate analysis was conducted first to determine the association between potential risk factors and mortality. Variables with a 2-tailed *p* value of <0.05 were included in the multiple logistic regression analysis to determine the independent risk factors for mortality associated with *B. fragilis* bacteremia. A *p* value of <0.05 was considered statistically significant for the multivariate analysis. All statistical calculations were done with the standard programs of the Statistical Package for the Social Sciences for Windows, version 13.0 (SPSS, Inc., Chicago, IL, USA).

Results

During the 41-month study period, there were 199 episodes of bacteremia in 199 patients. The demographics, clinical features, and laboratory data are summarized in Table 1. The mean ± standard deviation (SD) age of the patients was 61.1 ± 16.9 years (range, 19-94 years) and the male to female ratio was 1.14 (106 men and 93 women). 142 patients (71.4%)

Table 1. Demographics, predisposing factors, clinical characteristics, and treatment outcomes for patients with polymicrobial and monomicrobial *Bacteroides fragilis* bacteremia.

Variable	All patients (n = 199) No. (%)	Polymicrobial group (n = 77) No. (%)	Monomicrobial group (n = 122) No. (%)	p^a
Age (years)				
Mean ± SD	61.1 ± 16.9	61.5 ± 18.5	60.8 ± 15.8	0.789
≥65	102 (51.3)	42 (54.5)	60 (49.2)	0.461
<65	97 (48.7)	35 (45.5)	62 (50.8)	
Sex				
Men	106 (53.3)	42 (54.5)	64 (52.5)	0.774
Women	93 (46.7)	35 (47.5)	58 (47.5)	
Recent surgery	36 (18.1)	6 (7.8)	30 (24.6)	0.003
Previous antibiotic therapy	40 (20.1)	8 (10.4)	32 (26.2)	0.007
Comorbid conditions				
Malignancy	62 (31.2)	15 (19.5)	47 (38.5)	0.005
Diabetes mellitus	61 (30.7)	26 (33.8)	35 (28.7)	0.449
Liver cirrhosis	18 (9.0)	6 (6.5)	13 (10.7)	0.319
End-stage renal disease	16 (8.0)	8 (10.4)	8 (6.6)	0.333
Heart failure	9 (4.5)	4 (5.2)	5 (4.1)	0.737
Collagen vascular disease	2 (1.0)	1 (1.3)	1 (0.8)	1.000
Steroid	6 (3.0)	2 (2.6)	4 (3.3)	1.000
Immunosuppressant	8 (4.0)	2 (2.6)	6 (4.9)	0.489
Presentations and laboratory data				
Fever (>38°C)	139 (69.8)	54 (70.1)	85 (69.7)	0.945
Hypothermia (<36°C)	9 (4.5)	2 (2.6)	7 (5.7)	0.487
Shock	41 (20.6)	13 (16.9)	28 (23.0)	0.303
Leukocytosis (>10,000/μL)	124 (62.3)	48 (62.3)	76 (62.3)	0.995
Leukopenia (<4000/μL)	16 (8.0)	8 (10.4)	8 (6.6)	0.333
Thrombocytopenia (<150 x 10^3/μL)	76 (38.2)	35 (45.5)	41 (34.5)	0.123
Treatment and outcome				
Appropriate early antimicrobial therapy	72 (36.2)	23 (29.9)	49 (37.7)	0.141
Surgical intervention	109 (54.8)	44 (57.1)	65 (53.3)	0.594
Mortality	61 (30.7)	25 (32.5)	36 (29.5)	0.659

[a]Comparison between patients with polymicrobial and monomicrobial bacteremia by univariate analysis.
Abbreviation: SD = standard deviation.

had at least 1 underlying disease. Malignancy was the most common comorbidity (n = 62; 31.2%), followed by diabetes mellitus (n = 61; 30.7%) and liver cirrhosis (n = 18; 9.0%). GI neoplasm accounted for more than half of the malignancies (40/62; 64.5%). Forty patients (20.1%) had previous antibiotic therapy, and 7 of the regimens (17.5%) contained antibiotics with anaerobic activity. Patients with cancer had a higher rate of previous antibiotic use than those without malignancy (25.8% vs 17.5%; $p = 0.177$). Seventy two patients (36.2%) received appropriate early treatment, and antimicrobial agents were modified for 113 patients (56.7%) after antimicrobial susceptibility results became available. 170 patients (85.4%) received appropriate antimicrobial therapy throughout the course of their infection. Sixty one patients died, accounting for a crude mortality rate of 30.7%.

The sources of *B. fragilis* bacteremia are shown in Table 2. The GI tract was the most common source of infection (n = 59; 29.6%), followed by skin and soft tissue (n = 56; 28.1%), and liver and biliary tree (n = 39; 13.9%) infections. No definite focus of infection could be detected in 27 patients (13.6%). Seventy seven patients (38.69%) had polymicrobial bacteremia, with 102 concurrent blood isolates other than *B. fragilis* isolated. Two species were isolated in 55 patients (71.4%), 3 species in 19 (24.7%), and 4 species in 3 (3.9%). *Escherichia coli* was the most common concurrent microorganism (n = 24) [Table 3]. Other *Enterobacteriaceae*, streptococci, and Gram-negative anaerobic bacteria were also common concurrent pathogens.

Higher rates of recent surgery (24.6% vs 7.8%; $p = 0.003$), previous antibiotic therapy (26.2% vs 10.4%; $p = 0.007$), and underlying malignancy (38.5% vs 19.5%; $p = 0.005$) were associated with patients with monomicrobial bacteremia than with patients with polymicrobial bacteremia (Table 1). There was no significant difference between the monomicrobial and polymicrobial bacteremia groups in septic shock incidence and clinical outcome. In the polymicrobial bacteremia group, a trend towards higher mortality was observed in those with more than 2 concurrent isolates than in those with ≤2 isolates (45.5% vs 27.3%), but this was not statistically significant ($p = 0.124$) [Table 4]. Univariate analysis showed that age older than 65 years ($p = 0.017$), malignancy ($p < 0.001$), end-stage renal disease ($p = 0.043$), hypothermia ($p = 0.025$), shock ($p < 0.001$), leukopenia ($p = 0.001$), thrombocytopenia ($p < 0.001$), GI tract infection ($p = 0.005$), inappropriate antimicrobial therapy throughout the infection course ($p = 0.002$), and lack of surgical intervention ($p < 0.001$) were associated with higher mortality (Table 5). Appropriate early antimicrobial therapy did not affect the clinical outcome in this study. Multivariate analysis identified age older than 65 years ($p = 0.010$), malignancy ($p = 0.001$), shock ($p < 0.001$), thrombocytopenia ($p = 0.025$), and lack of surgical intervention ($p = 0.025$) as independent predictors for mortality in *B. fragilis* bacteremia.

Table 2. Infection source of patients with *Bacteroides fragilis* bacteremia (n = 199).

Source	No. of patients (%)
Gastrointestinal tract	59 (29.6)
Bowel perforation	15
Gastrointestinal malignancy	15
Appendicitis	14
Diverticulitis	6
Ischemic bowel	3
Other colitis	2
Ileus	2
Enterocutaneous fistula	1
Necrotizing pancreatitis	1
Skin and soft tissue	56 (28.1)
Decubitus ulcer infection	30
Diabetic foot infection	14
Wound infection	9
Perianal infection	2
Necrotizing fasciitis	1
Liver/biliary tree	39 (19.6)
Cholangitis	30
Cholecystits	6
Liver abscess	3
Reproductive system	8 (4.0)
Tubo-ovarian abscess	4
Endometritis	3
Pelvic inflammatory disease	1
Bone and joint	5 (2.5)
Osteomyelitis	4
Septic arthritis	1
Pulmonary	2 (1.0)
Lung abscess	1
Empyema	1
Others	3 (1.5)
Brain epidural abscess	1
Arterial venous graft infection	1
Retroperitoneal abscess	1
Unknown	27 (13.6)

Discussion

Although *B. fragilis* accounts for only 0.5% of human colonic flora, it is the most commonly isolated anaerobic

Table 3. Concurrent pathogens in patients with polymicrobial bacteremia (n = 77).

Pathogen	No. of isolates
Gram-negative bacilli	
Escherichia coli	24
Proteus mirabilis	6
Klebsiella pneumoniae	5
Pseudomonas aeruginosa	5
Morganella morgannii	3
Proteus penneri	1
Stenotrophomonas maltophilia	1
Haemophilus influenzae, non-serotype B	1
Glucose non-fermenting Gram-negative bacilli	1
Chryseobacterium indologenes	1
Citrobacter diversus	1
Acinetobacter baumannii	1
Gram-positive cocci	
Viridans streptococci	9
Streptococcus constellatus	6
Enterococcus spp.	5
Staphylococcus aureus	5
β-*Streptococcus* group non-A, B, or D	3
Streptococcus anginosus	1
Streptococcus pneumoniae	1
Coagulase-negative staphylococci	1
Anaerobes	
Gram-positive bacilli, non-spore forming	7
Fusobacterium spp.	6
Other *Bacteroides* spp.	3
Prevotella spp.	2
Pasteurella spp.	1
Clostridium spp.	1
Yeast	
Candida albicans	1
Total	102

pathogen and most virulent *Bacteroides* sp. [18]. Mucosal barrier disruption of the GI wall due to perforation, malignancy, surgical wound, or deep wound abscess will predispose to *B. fragilis* infection. As shown in previous studies [1,10,11], this study demonstrated that intra-abdominal infection (GI tract and liver/biliary tree) constituted the most common infection sources (98/199; 49.27%). Decubitus ulcer infection and diabetic foot infection were 2 common sources of skin and soft tissue infection in this study. Decubitus ulcer is usually near to the perianal area, which is vulnerable to *B. fragilis* infection. Polymicrobial infection is well documented in diabetic foot infection and anaerobic pathogens play an important role, especially in patients with ischemic or gangrenous changes [19].

Underlying diseases are reported frequently as potential risk factors for anaerobic bacteremia, particularly malignancy, diabetes mellitus, immunosuppression, renal failure, liver failure, decubitus ulcer, and previous GI surgery [7,9,10,14,15]. Malignancy, diabetes mellitus, and previous surgery were the 3 most common underlying conditions in this study. GI neoplasm accounted for more than half of the patients with malignancy. GI neoplasm associated with mucosal disruption, bowel obstruction, tumor necrosis, chemotherapy-related mucositis, and complications after a surgical procedure increase the risk for *B. fragilis* bacteremia. Diabetes mellitus could predispose patients to anaerobic infection because of diabetic foot ulcer, and impaired phagocytosis and chemotaxis [20].

Table 4. Number of blood isolates in patients with polymicrobial bacteremia and treatment outcome (n = 77).

No. of isolates	Mortality No. (%)	p^a
2 (n = 55)	15 (27.3)	0.124
>2[b] (n = 22)	10 (45.5)	

[a]Chi-squared test.

[b]Isolates >2 include 3 isolates in 19 patients and 4 isolates in 3 patients.

There were 77 patients with polymicrobial bacteremia (38.7%) in this study, and *E. coli* (24/102; 23.5%) was the most common microorganism found in combination with *B. fragilis*. *Enterobacteriaceae* and anaerobic Gram-negative bacilli are endogenous flora of the bowel. This could explain their predominance of 40 of 102 concurrent isolates (39.2%). Aerobic Gram-positive cocci, which are important pathogens in skin and soft tissue infection, were also commonly seen in polymicrobial bacteremia. In comparison with the polymicrobial bacteremia group, the monomicrobial group had a higher rate of recent surgery, previous antibiotic therapy, and underlying malignancy. The higher rate of recent surgery for patients with monomicrobial bacteremia was also observed in a study of anaerobic bacteremia in patients with cancer [21]. At the Chang Gung Memorial Hospital, surgeons usually use first-generation cephalosporins as prophylactic antibiotics before clean-contaminated surgery, and this practice may reduce the incidence of postoperative aerobic bacteremia. The higher rate of previous antibiotic therapy in patients with cancer probably contributed to the lower rate of polymicrobial bacteremia. In this study, the incidence of septic shock was 20.6% (41/199), which is similar to that of previous studies of anaerobic or *B. fragilis* bacteremia (20.0%

Table 5. Risk factors for mortality in patients with *Bacteroides fragilis* bacteremia (n = 199).

Variable	Mortality No. (%)	Univariate *p*	Multivariate	
			Odds ratio (95% confidence interval)	*p*
Sex				
Men (n = 106)	33/106 (31.1)	0.876		
Women (n = 93)	28/93 (30.1)			
Age (years)				
≥65 (n = 102)	39/102 (38.2)	0.017	3.137 (1.313-7.494)	0.010
<65 (n = 97)	22/97 (22.7)			
Recent surgery				
Yes (n = 36)	9/36 (25.0)	0.416		
No (n = 163)	52/163 (31.9)			
Type of bacteremia				
Polymicrobial (n = 77)	25/77 (32.5)	0.659		
Monomicrobial (n = 122)	36/122 (29.5)			
Comorbid conditions				
Malignancy (n = 62)	30/62 (48.4)	<0.001	4.188 (1.781-9.850)	0.001
Liver cirrhosis (n = 18)	5/18 (27.8)	0.781		
Diabetes mellitus (n = 61)	16/61 (26.2)	0.368		
End-stage renal disease (n = 16)	9/16 (56.3)	0.043	3.615 (0.995-13.132)	0.051
Heart failure (n = 9)	3/9 (33.3)	1.000		
Collagen vascular disease (n = 2)	2/2 (100.0)	0.093		
Steroid (n = 6)	4/6 (66.7)	0.073		
Immunosuppressant (n = 8)	4/8 (50.0)	0.252		
Presentation and laboratory data				
Fever (n = 139)	41/139 (29.5)	0.590		
Hypothermia (n = 9)	6/9 (66.7)	0.025	0.784 (0.127-4.827)	0.793
Shock (n = 41)	30/41 (73.2)	<0.001	9.269 (3.337-25.746)	<0.001
Leukocytosis (n = 124)	36/124 (29.0)	0.524		
Leukopenia (n = 16)	11/16 (68.8)	0.001	2.760 (0.611-12.466)	0.187
Thrombocytopenia (n = 76)	35/76 (46.1)	<0.001	2.719 (1.136-6.504)	0.025
Treatment and outcome				
Appropriate early antimicrobial therapy				
Yes (n = 72)	22/72 (30.6)	0.982		
No (n = 127)	39/127 (30.7)			
Appropriate antimicrobial therapy during the course				
Yes (n = 170)	45/170 (26.5)	0.002	0.548 (0.165-1.821)	0.326
No (n = 29)	16/29 (55.2)			
Surgical intervention				
Yes (n = 109)	20/109 (18.3)	<0.001	0.383 (0.166-0.888)	0.025
No (n = 90)	41/90 (45.6)			

to 31.8%) [2,10,15,21]. The difference in the incidence of septic shock was not statistically significant between the polymicrobial and monomicrobial groups (16.9% vs 23.0%; $p = 0.303$), although this result differs from previous reports [21]. It is well known that circulating Gram-negative bacterial endotoxin triggers an inflammatory reaction and induces hemodynamic changes. Endotoxin in *B. fragilis* has an unusual structure and is 10 to 1000 times less toxic than that of *E. coli* [19]. An experimental primate model suggested that *B. fragilis* bacteremia has a minor role in promoting septic shock syndrome [22]. Surprisingly, the incidence of septic shock does not correlate with the increasing aerobic Gram-negative bacteria predominant in polymicrobial blood isolates. Therefore, synergy or asynergy between multiple organisms needs to be further elucidated to better understand the roles that each plays. The number of organisms in polymicrobial bacteremia did not impact on clinical outcome in this and other studies [21]. There was no difference in the mortality rate between patients with polymicrobial or monomicrobial bacteremia in this

study. This finding is consistent with several studies of anaerobic bacteremia [6-9,14].

The crude mortality rate in this study was 30.1% (61/199), which is comparable to previous studies in which the rate ranges from 20% to 31% [1,11]. A matched-pair controlled study showed that the attributable mortality rate associated with *B. fragilis* group bacteremia was 19.3%, with a mortality risk ratio of 3.2 and a 16-day longer duration of hospital stay [10]. Risk factors for poor outcome by univariate analysis included old age, underlying malignancy, renal failure, septic shock, hypothermia, leukopenia, thrombocytopenia, inappropriate antimicrobial therapy throughout the course, and lack of surgical intervention. Previous studies of anaerobic bacteremia also found liver disease [14], polymicrobial bacteremia [21], treatment in an intensive care unit [6], and an Acute Physiology And Chronic Health Evaluation II score of >15 [11] were poor prognostic factors. The different study populations and inconsistent methodology for determining mortality between this study and previous studies might explain the differences. A study conducted by Wilson et al [14] demonstrated that underlying liver disease is an independent risk factor for mortality in anaerobic bacteremia. The increased mortality rate for patients with concurrent liver disease and anaerobic bacteremia probably reflected the strong association between cirrhosis and *Clostridium* bacteremia [23], which was not included in this study.

Only 72 patients (36.2%) received appropriate antimicrobial agents within 48 h of infection onset. However, inappropriate early antimicrobial therapy did not affect clinical outcome in this study or in other studies [6,11,15]. This may be explained by the fact that anaerobic pathogens usually begin to predominate in the second stage of infection, after sufficient oxygen has been removed by the aerobic bacteria (approximately 20 h) [18]. However, failure to pay attention to the results of antimicrobial susceptibility of anaerobic pathogens and to modify an ineffective regimen may have serious consequences [6,8,11]. There were 29 patients (14.6%) in this study who never received appropriate antimicrobial agents throughout their treatment course. Patients without appropriate antimicrobial therapy had a higher mortality rate than those who received appropriate antimicrobial therapy (55.2% vs 26.5%; $p = 0.002$). Antimicrobial susceptibility testing was not available for 13 of the 29 patients before they died, and this should be taken into consideration when interpreting the statistical results. In the multivariate analysis, age older than 65 years, malignancy, shock, thrombocytopenia, and the lack of surgical intervention were independent risk factors for mortality due to *B. fragilis* bacteremia.

In conclusion, although *B. fragilis* bacteremia is not common, it causes significant mortality, especially in elderly people and patients with cancer. Appropriate action must be taken to search out the infectious foci when *B. fragilis* bacteremia is clinically evident. Surgical intervention or drainage of the infectious process has a critical role in improving outcomes. *B. fragilis* is not necessarily treated by empirical antimicrobial agents, so clinicians should be aware of the antimicrobial susceptibility results.

References

1. Goldstein EJ. Anaerobic bacteremia. Clin Infect Dis. 1996;23(Suppl 1):97-101.
2. Lombardi DP, Engleberg NC. Anaerobic bacteremia: incidence, patient characteristics, and clinical significance. Am J Med. 1992;92:53-60.
3. Arzese A, Trevisan R, Menozzi MG, Botta GA, on behalf of the Italian Anaerobe Study Group. Anaerobe-induced bacteremia in Italy: a nationwide survey. Clin Infect Dis. 1995; 20(Suppl 2):230-2.
4. Dorsher CW, Rosenblatt JE, Wilson WR, Ilstrup DM. Anaerobic bacteremia: decreasing rate over a 15-year period. Rev Infect Dis. 1991;13:633-6.
5. Lassmann B, Gustafson DR, Wood CM, Rosenblatt JE. Reemergence of anaerobic bacteremia. Clin Infect Dis. 2007;44:895-900.
6. Salonen JH, Eerola E, Meurman O. Clinical significance and outcome of anaerobic bacteremia. Clin Infect Dis. 1998;26:1413-7.
7. Blairon L, Gheldre YD, Delaere B, Sonet A, Bosly A, Glupczynski Y. A 62-month retrospective epidemiological survey of anaerobic bacteremia in a university hospital. Clin Microbiol Infect. 2006;12:527-32.
8. Zahar JR, Farhat H, Chachaty E, Meshaka P, Antoun S, Nitenberg G. Incidence and clinical significance of anaerobic bacteremia in cancer patient: a 6-year retrospective study. Clin Microbiol Infect. 2005;11:724-9.
9. Hung MN, Chen SY, Wang JL, Chang SC, Hsueh PR, Liao CH, et al. Community-acquired anaerobic bacteremia in adults: one-year experience in a medical center. J Microbiol Immunol Infect. 2005;38:436-43.
10. Redondo MC, Arbo MD, Grindlinger J, Snydman R. Attributable mortality of bacteremia associated with the *Bacteroides fragilis* group. Clin Infect Dis. 1995;20:1492-6.
11. Nguyen MH, Yu VL, Morris AJ, McDermott L, Wagener

MW, Harrell L, et al. Antimicrobial resistance and clinical outcome of *Bacteroides* bacteremia: findings of a multicenter prospective observational trial. Clin Infect Dis. 2000;30:870-6.
12. Lee CS, Hwang B, Chung RL, Tang RB. The assessment of anaerobic blood cultures in children. J Microbiol Immunol Infect. 2000;33:49-52.
13. Tsao YT, Lin SH, Cheng CJ, Chang FY. Pylephlebitis associated with acute infected choledocholithiasis. Am J Med Sci. 2006;332:85-7.
14. Wilson JR, Limaye AP. Risk factors for mortality in patients with anaerobic bacteremia. Eur J Clin Microbiol Infect Dis. 2004;23:310-6.
15. Vazquez F, Mendez FJ, Perez F, Mendoza MC. Anaerobic bacteremia in a general hospital: retrospective five-year analysis. Rev Infect Dis. 1987;9:1038-43.
16. Murray PR, Baron EJ, Pfaller MH, Tenover FC, Yolken RH. Manual of clinical microbiology. 8th ed. Herndon: ASM Press; 2003; 835-900.
17. National Committee for Clinical Laboratory Standards. Methods for antimicrobial susceptibility testing of anaerobic bacteria. Approved standard. 5th ed. NCCLS document M11-A5. Wayne: National Committee for Clinical Laboratory Standards; 2001.
18. Wexler HM. *Bacteroides*: the good, the bad, the nitty-gritty. Clin Microbiol Rev. 2007;20:593-621.
19. Lipsky BA, Berendt AR, Deery HG, Embil JM, Joseph WS, Karchmer AW, et al. Diagnosis and treatment of diabetes foot infection. Clin Infect Dis. 2004;39:885-910.
20. Repine JE, Clawson CC, Goetz FC. Bactericidal function of neutrophils from patients with acute bacterial infection and from diabetes. J Infect Dis. 1980;142:869-75.
21. Fainstein V, Elting LS, Bodey GP. Bacteremia caused by non-sporulating anaerobes in cancer patients: a 12-year experience. Medicine. 1989;68:151-62.
22. Simon GL, Gelfand JA, Connolly RA, O'Donnell TF, Gorbach SL. Experimental *Bacteroides fragilis* bacteremia in a primate model: evidence that *Bacteroides fragilis* does not promote the septic shock syndrome. J Trauma. 1985; 25:1156-62.
23. Chen YM, Lee HC, Chang CM, Chuang YC, Ko WC. *Clostridium* bacteremia: emphasis on the poor prognosis in cirrhotic patients. J Microbiol Immunol Infect. 2001;34: 113-8.