

# Clinical characteristics and prognostic factors of patients with *Stenotrophomonas maltophilia* bacteremia

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*Stenotrophomonas maltophilia* is an important nosocomial pathogen with intrinsic multi-drug resistance. This retrospective study reviewed 84 episodes of *S. maltophilia* bacteremia over a 4-year period from July 1999 to September 2003. *Stenotrophomonas maltophilia* bacteremia was hospital-acquired in 64 patients (76%), and developed after prolonged hospitalization in 48 (57%). Seventy patients (83%) had a central venous catheter (CVC), 64 (76%) had prior antibiotic therapy, 55 (65%) had underlying malignancy, and 43 (51%) were receiving immunosuppressive therapy. Twenty seven percent of the episodes of bacteremia had polymicrobial isolates. The overall and bacteremia-related mortality rates were 44% and 33%, respectively. Forty six percent of the bacteremia-related mortality occurred within 3 days after onset of symptoms. The most common sources of bacteremia were respiratory tract (33%) and CVC (31%), while the source of the bacteremia was unknown in 26% of episodes. The most effective antibiotics in vitro were trimethoprim-sulfamethoxazole, ciprofloxacin, chloramphenicol, and ceftazidime; however, a trend of increasing drug resistance in these agents was identified over the study period. On univariate analysis, nosocomial bacteremia, long-lasting neutropenia (>10 days), bacteremia originating from the respiratory tract, shock, low serum albumin level (<3 g/dL), and thrombocytopenia (platelet count <100,000/mm<sup>3</sup>) were significantly related to mortality ( $p < 0.05$ ). Among these variables, shock and thrombocytopenia were independent factors associated with mortality. In contrast, patients with CVC-related bacteremia had a lower mortality rate (odds ratio, 0.04;  $p < 0.001$ ). Patients treated with appropriate antibiotics had a lower mortality rate, but this difference was not significant ( $p = 0.477$ ). In *S. maltophilia* bacteremia, careful evaluation of CVC was important for identifying the source of bacteremia and predicting prognosis. The source of bacteremia and condition of patients at presentation were the major factors influencing prognosis.

**Key words:** Bacteremia, prognostic factors, risk factors, *Stenotrophomonas maltophilia*

*Stenotrophomonas maltophilia* (formerly called *Xanthomonas maltophilia*), a non-fermentative Gram-negative bacillus, was first identified by Hugh and colleagues in 1958 [1,2]. This organism can cause a wide variety of infections in humans, including respiratory tract, urinary tract, gastrointestinal, skin and soft tissue, bone and joint, and ophthalmologic infections, meningitis, endocarditis and bacteremia [3].

*S. maltophilia* has been an emerging nosocomial pathogen with increasing frequency in recent decades, especially in immunocompromised and

clinically debilitated patients [4-11]. Differentiation of colonization from clinical infection by *S. maltophilia* based on clinical symptoms is difficult. Treatment of infection can be problematic due to debilitated state of patients, and intrinsic resistance of the organism to multiple antimicrobial agents, including carbapenems, and an increasing trend of drug resistance [3-12].

In Taiwan, a high proportion of *S. maltophilia* isolated in intensive care units was resistant to the antimicrobial agents recommended for clinical use [13]. Early recognition of infection by this organism and appropriate antibiotics treatment were crucial for improving survival rate [14]. The objective of this study was to investigate the clinical characteristics, antibiotic susceptibility, antibiotic treatment, outcome and prognostic factors in patients with *S. maltophilia* bacteremia.

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## Materials and Methods

### Patient identification

From July 1999 to September 2003, cases of *S. maltophilia* bacteremia were identified retrospectively from the clinical microbiology laboratory blood culture reports at Taipei Veterans General Hospital, a medical center and teaching hospital comprising about 2900 beds in northern Taiwan. The demographic features, clinical conditions, laboratory data, antimicrobial susceptibility, antibiotic treatment and outcome were recorded from the medical charts and analyzed. Patients less than 18 years old were excluded. There was no apparent outbreak of *S. maltophilia* infection during the period of study.

### Definitions

An episode of significant bacteremia was defined as 1 or more positive blood cultures for *S. maltophilia* with clinical symptoms or signs of infection. Conditions not meeting this definition of bacteremia were considered as contamination and excluded. Multiple episodes that occurred within a 7-day period or without clinical defervescence after the previous episode in the same patient were considered to be the same episode. If the multiple episodes did not fulfill the criteria for the same episode, they were considered as different episodes of bacteremia. The clinical condition, laboratory data and antimicrobial susceptibility of the first episode were recorded for analysis.

Nosocomial bacteremia was defined as bacteremia that occurred 48 hours or more after admission. Prolonged hospitalization was defined as 2 or more weeks hospitalization prior to the development of bacteremia. The source of bacteremia was determined clinically on the basis of the presence of an active infection site coincident with bacteremia or isolation of the organism from other clinical specimens prior to or on the same date as the onset of bacteremia. Types of central venous catheters (CVCs) used included central venous pressure catheter (CVP) and CVC in situ (including Hickman's catheter, port-A catheter, and permanent catheter). CVC-related bacteremia was classified based on isolation of the organism from either the tip of the catheter or purulent discharge, or on the presence of inflammation at the insertion site without other pathogen infection. Shock was defined as systolic blood pressure less than 90 mm Hg or requiring inotropic agents to maintain blood pressure. Prior antibiotic therapy was defined as administration of intravenous

antibiotics for more than 24 hours within 30 days before the onset of bacteremia. Appropriate antibiotic therapy was defined as administering at least an intravenous antibiotic to which the organism tested susceptible within 72 hours after the onset of bacteremia.

Immunosuppressive therapy was defined as the use of cytotoxic agents or corticosteroids (more than 30 mg prednisolone daily or equivalent for 1 week or more). Neutropenia was defined as an absolute neutrophil count  $<500/\text{mm}^3$  and long-lasting neutropenia as a duration of neutropenia  $>10$  days. Thrombocytopenia was defined as a platelet count  $<100,000/\text{mm}^3$ . Bacteremia-related mortality was judged based on the clinical course, response to treatment and severity of underlying disease.

### Microbiology

Blood culture samples were processed by the BACTEC NR-660 system (Becton Dickinson Diagnostic Instrument Systems, Sparks, MD, USA). All positive cultures were Gram-stained and subcultured on blood agar plates and eosin-methylene blue agar plates for further identification. An automatic identification system for Gram-negative rods (ID 32 GN; bioMérieux Vitek, France) was used for identifying *S. maltophilia*. Antibiotic susceptibility was tested by the disk diffusion method as recommended by the National Committee on Clinical Laboratory Standards (NCCLS) [15]. The disk diffusion test of ticarcillin was replaced by piperacillin-tazobactam starting in April 2001, and cefepime and ciprofloxacin were tested starting in October 2000 and July 2001, respectively, in the clinical microbiology laboratory.

### Statistical analysis

The results were analyzed using a commercially available software package (SPSS, version 11.0; SPSS Inc., Chicago, IL, USA). Categorical variables were analyzed using chi-squared or Fisher's exact test as appropriate. Multivariate analysis was performed by logistic regression. All *p* values were 2-tailed and a *p* value  $<0.05$  was considered statistically significant.

## Results

From July 1999 to September 2003, 12,834 positive blood cultures were identified in the clinical microbiologic laboratory. Ninety one (0.7%) of the blood cultures from 84 patients grew *S. maltophilia*. Seven patients were excluded, due to specimen contamination in 4, age  $<18$  years in 1 and unavailable medical charts

**Table 1.** Clinical characteristics of 84 patients with *Stenotrophomonas maltophilia* bacteremia

Characteristic	No. (%)
Age [mean ± SD (years)]	62.3 ± 2.0
Gender	
Female	21 (25)
Male	63 (75)
Underlying disease	
Malignancy	55 (65)
Hematologic malignancy	29 (34)
Solid tumor	26 (31)
Immunosuppressive therapy	43 (51)
Hypertension	25 (30)
Diabetes mellitus	17 (20)
Chronic pulmonary disease	12 (14)
Chronic liver disease	12 (14)
Cerebral vascular accident	11 (13)
Renal insufficiency	8 (10)
Congestive heart failure	5 (6)
Clinical conditions	
Hospitalization days [median (range)]	31.5 (1–202)
Hospitalization days prior to bacteremia [median (range)]	24 (3–100)
Invasive devices	
Presence of CVC <sup>a</sup>	70 (83)
CVP catheter	43 (51)
CVC in situ <sup>b</sup>	32 (38)
Mechanical ventilation	30 (36)
Surgical procedure	19 (23)
Tracheostomy	13 (15)
Prior antibiotic therapy <sup>c</sup>	64 (76)
Nosocomial bacteremia	64 (76)
Prolonged hospitalization <sup>d</sup>	48 (57)
Developed during stay in	
Intensive care unit	28 (33)
General ward	56 (67)
Shock <sup>e</sup>	40 (48)
Neutropenia <sup>f</sup>	30 (36)
Long-lasting neutropenia <sup>g</sup>	23 (27)
Polymicrobial	23 (27)
Source of bacteremia	
Respiratory tract	28 (33)
CVC-related	26 (31)
Unknown	22 (26)
Others <sup>h</sup>	8 (10)

Abbreviations: SD = standard deviation; CVC = central venous catheter; CVP = central venous pressure

<sup>a</sup>Five patients had both types of catheters.

<sup>b</sup>CVC in situ includes Hickman’s catheter, port-A catheter, and permanent catheters.

<sup>c</sup>Intravenous antibiotics used for >24 hours within 30 days prior to bacteremia.

<sup>d</sup>≥14 days of hospitalization prior to bacteremia.

<sup>e</sup>Systolic blood pressure <90 mm Hg or using inotropic agent to maintain blood pressure.

<sup>f</sup>Absolute neutrophil count <500/mm<sup>3</sup>.

<sup>g</sup>Duration of neutropenia >10 days.

<sup>h</sup>Six gastrointestinal tract and 2 urinary tract infections.

in 2. A total of 84 episodes of *S. maltophilia* bacteremia in 77 patients were included in this study. Among these patients, 2 had 3 episodes and 3 had 2 episodes of bacteremia. The 84 “episodes” were considered as 84 “patients” in the analysis. Twenty three episodes of bacteremia (27%) were polymicrobial and the additional isolates included 10 *Enterobacteriaceae*, 6 methicillin-resistant *Staphylococcus aureus* (MRSA), 6 *Acinetobacter* spp., and 1 *Enterococcus* sp.

The clinical characteristics of the patients are summarized in Table 1. Among the 84 patients, 63 (75%) were male and 21 (25%) were female, and the mean age was 62.3 ± 2.0 years. The median duration of hospitalization was 31.5 days (range, 1-202 days). Forty eight patients (57%) had prolonged hospitalization. Sixty four patients (76%) had nosocomial bacteremia and the median duration of hospitalization prior to bacteremia was 24 days (range, 3-100 days). Fifty five patients (65%) had underlying malignancy (34% hematologic malignancy and 31% solid tumor). Forty three patients (51%) had received immunosuppressive therapy. Most patients (83%) had a CVC in place at the onset of bacteremia. Shock developed at the onset of bacteremia in 40 patients (48%). Sixty four patients (76%) had prior antibiotic therapy with aminoglycosides (73%), glycopeptides (47%), first- or second-generation cephalosporins (44%), carbapenems (42%), third- or fourth-generation cephalosporins (36%), or extended-spectrum penicillins (36%). Seventy four percent of patients had an identifiable source of bacteremia, among which the respiratory tract (33%) and CVC-related (31%) were the most common.

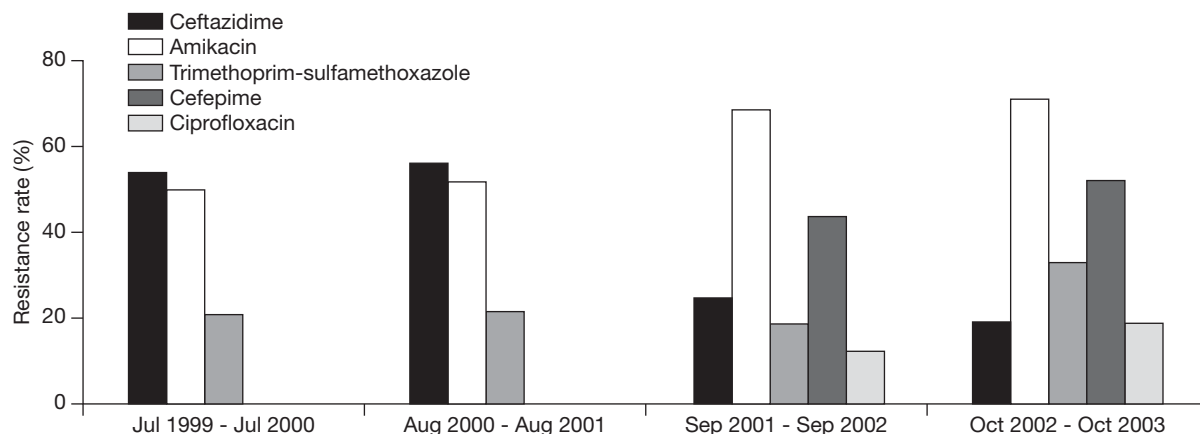
The antimicrobial susceptibility of blood isolates of *S. maltophilia* is summarized in Table 2. All of these isolates were resistant to imipenem. The most active

**Table 2.** Antimicrobial susceptibility<sup>a</sup> of blood isolates of *Stenotrophomonas maltophilia*

Antimicrobial agent (no. tested)	Susceptible no. (%)
Ticarcillin (40)	2 (5)
Piperacillin-tazobactam (44)	13 (30)
Ceftazidime (84)	50 (60)
Cefepime (57)	26 (46)
Imipenem (84)	0 (0)
Ciprofloxacin (47)	39 (83)
TMP-SMX (84)	64 (76)
Amikacin (84)	34 (40)
Tetracycline (84)	16 (19)
Chloramphenicol (84)	60 (71)

Abbreviation: TMP-SMX = trimethoprim-sulfamethoxazole

<sup>a</sup>Disk diffusion method.



**Fig. 1.** Trends of resistance of blood-isolated *Stenotrophomonas maltophilia* to antibiotics during the study period.

antimicrobial agents were ciprofloxacin (83%, 39/47), trimethoprim-sulfamethoxazole (TMP-SMX) (76%, 64/84), chloramphenicol (71%, 60/84), and ceftazidime (60%, 50/84). There was a trend of increasing resistance to the agents used to treat *S. maltophilia* during the study period, except for ceftazidime, which had a trend of decreasing resistance rate (Fig. 1). The overall and bacteremia-related mortality rates were 44% and 33%, respectively. The median duration from onset of bacteremia to death was 4 days (range, 0-26 days) and

46% of the mortality occurred within 3 days after *S. maltophilia* bacteremia developed.

Factors significantly related to mortality on univariate analysis were nosocomial bacteremia ( $p=0.024$ ), long-lasting neutropenia ( $p=0.012$ ), respiratory tract infection in origin ( $p<0.001$ ), shock ( $p=0.001$ ), low serum albumin level ( $<3.0$  g/dL) [ $p=0.034$ ], and thrombocytopenia ( $p=0.001$ ) [Table 3]. Among these factors, only thrombocytopenia (odds ratio [OR], 8.89;  $p=0.001$ ) and shock (OR, 4.85;  $p=0.013$ ) were independent risk

**Table 3.** Univariate analysis of prognostic factors associated with mortality from *Stenotrophomonas maltophilia* bacteremia

Factor	Mortality rate		<i>p</i>
	With factor (%)	Without factor (%)	
Malignancy	20/55 (36)	8/29 (28)	0.57
Hematologic malignancy	11/29 (38)	17/55 (31)	0.685
Solid tumor	9/26 (35)	19/58 (33)	1
Immunosuppressive therapy	18/43 (42)	10/41 (24)	0.143
Clinical conditions			
Long-lasting neutropenia	13/23 (57)	15/61 (25)	0.012
Nosocomial bacteremia	26/64 (41)	2/20 (20)	0.024
Bacteremia at ICU	8/28 (29)	20/56 (36)	0.682
Appropriate antibiotics treatment	9/33 (27)	19/51 (37)	0.477
Prolonged hospitalization	20/48 (42)	8/36 (22)	0.102
Prior antibiotic therapy	25/64 (39)	3/20 (15)	0.085
Polymicrobial bacteremia	5/23 (22)	23/61 (38)	0.261
Shock	21/40 (53)	7/44 (16)	0.001
Source of bacteremia			
Respiratory tract	17/28 (61)	11/56 (20)	<0.001
CVC-related	2/26 (8)	26/58 (45)	0.002
Unknown	5/22 (23)	23/62 (37)	0.334
Laboratory data			
Neutropenia	14/30 (47)	14/54 (26)	0.091
Thrombocytopenia <sup>a</sup>	20/37 (54)	8/47 (17)	0.001
Low serum albumin level (<3 g/dL)	17/37 (46)	8/39 (21)	0.034

Abbreviations: ICU = intensive care unit; CVC = central venous catheter

<sup>a</sup>Platelet count  $<100,000/\text{mm}^3$ .

**Table 4.** Multivariate analysis of prognostic factors associated with mortality from *Stenotrophomonas maltophilia* bacteremia

Factor	Odds ratio (95% CI)	p
CVC-related bacteremia	0.04 (0.007~0.24)	<0.001
Thrombocytopenia	8.892 (2.4~32.8)	0.01
Shock	4.852 (1.4~16.8)	0.013

Abbreviations: CI = confidence interval; CVC = central venous catheter

factors for mortality in the multivariate analysis (Table 4). In contrast, patients with CVC-related bacteremia had lower mortality rate (odds ratio, 0.04;  $p < 0.001$ ). The 33 patients (39%) who were treated with appropriate antibiotics had a lower mortality rate than other patients (27% vs 37%), but this difference was not significant ( $p = 0.477$ ).

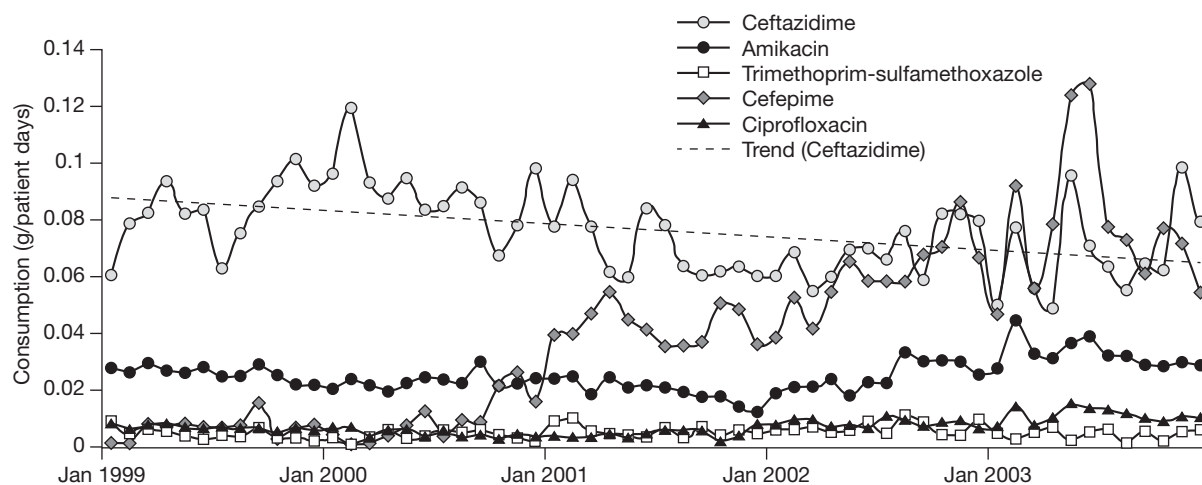
## Discussion

Presence of an indwelling CVC, previous antibiotic therapy, intubation or tracheostomy, prolonged hospitalization, and underlying malignancy have been reported to be predisposing factors for *S. maltophilia* bacteremia [10,14,16-18]. In patients with malignancy, reported risk factors for acquiring *S. maltophilia* bacteremia included profound and long-lasting neutropenia, and severe mucositis [5,19,20]. In the present study, the main characteristics of patients who developed *S. maltophilia* bacteremia were presence of CVC (83%), nosocomially acquired (76%), prior antibiotic treatment (76%), male gender (75%), underlying malignancy (65%), prolonged hospitalization (57%), and receiving immunosuppressive therapy (51%). The predominance of male gender among patients was likely related to the fact that male veterans are the main patient population of the Taipei Veterans General Hospital.

The frequency of polymicrobial bacteremia (27%) was similar to previous studies (23-52%) [11,14,17,20, 21]. Except for a high percentage of *Acinetobacter* spp. (26%, 6/23), the main additional isolates including *Enterobacteriaceae* (43%, 10/23) and MRSA (26%, 6/23) were similar to prior series [14,17]. The increased isolation of *Acinetobacter* spp. may have been due to antibiotic selective pressure. Krcmery et al [11] reported long-lasting neutropenia (>10 days) as a risk factor for polymicrobial *S. maltophilia* bacteremia, but it was not a significant risk factor in this study. The mortality rate of patients with polymicrobial bacteremia in this study was not different from that of patients with

monomicrobial bacteremia (22% vs 38%;  $p = 0.26$ ), as was reported by Muder et al [17]. This may have been due to the high proportion of empiric treatment with aminoglycosides (73%), glycopeptides (47%), and carbapenems (42%), which were active against the additional isolated organisms.

Similar to previous studies [10,14,16-18,21], the most effective antibiotics against blood isolates of *S. maltophilia* in vitro were ciprofloxacin (83%, 39/47), TMP-SMX (76%, 64/84), chloramphenicol (71%, 60/84) and ceftazidime (60%, 50/84). In this study, however, an increasing trend of resistance to these antibiotics was also found over the study period, except for ceftazidime, which had a decreasing trend of resistance rate. The mechanism of developing antibiotic resistance is complex and it was difficult to explain the decreasing resistant rate of ceftazidime in *S. maltophilia* definitively. Interestingly, the trend of increasing resistance was accompanied by a trend of increasing consumption of these antibiotics, while ceftazidime had a decreasing consumption (Fig. 2). This finding may partially explain the resistance pattern of these antibiotics. In previous studies, ticarcillin-clavulanate was generally considered the most effective  $\beta$ -lactam antibiotic against *S. maltophilia* [17,19,22]; however, ticarcillin instead of ticarcillin-clavulanate was tested in this study and only 5% of the isolates were susceptible to ticarcillin. Thirty percent (13/44) of *S. maltophilia* isolates were susceptible to piperacillin-tazobactam. A wide range of susceptibility to this antibiotic (20 to 100%) has been reported [9,19,23]. Fass and Prior [24] reported that clavulanate enhanced the activity of ticarcillin against *S. maltophilia*, but that tazobactam did not significantly enhance the activity of piperacillin. Although piperacillin-tazobactam had modest activity against *S. maltophilia* in this study, it should not replace ticarcillin-clavulanate to treat infection by this organism. In this study, isolates of *S. maltophilia* had a high susceptibility rate to TMP-SMX (76%), which was the antibiotic recommended to treat *S. maltophilia* infection. However, significant numbers of patients were not clinical candidates for this treatment, because of debilitated condition, hypersensitivity, or hematologic cytopenia. Several alternative antibiotics or combination therapies have been suggested, such as ticarcillin-clavulanate combined with aztreonam or TMP-SMX and ciprofloxacin combined with ceftazidime [25,27], but further clinical investigation of their effectiveness is needed. Although the disk diffusion method is not as reliable as agar dilution and



**Fig. 2.** Trends of antibiotic consumption for the treatment of *Stenotrophomonas maltophilia* bacteremia during the study period.

other time-consuming methods, except for TMP-SMX and ciprofloxacin [25,28,29], the latter methods are not clinically practical, universally available or cost-effective.

Several poor prognostic factors of *S. maltophilia* bacteremia were identified in the present study, including nosocomial bacteremia, long-lasting neutropenia (>10 days), origin from respiratory tract infection, shock, low serum albumin level (<3.0 g/dL), and thrombocytopenia (platelet count <100,000/mm<sup>3</sup>). Among these factors, thrombocytopenia and shock were independently associated with poor prognosis. In previous series, profound or long-lasting neutropenia was not only considered a predisposing factor to *S. maltophilia* bacteremia but was also associated with increased mortality [9,17,19]. Similarly, long-lasting neutropenia (>10 days) was a poor prognostic factor in the present study (mortality rate, 57% vs 25%;  $p=0.012$ ). By contrast, underlying malignancy, either hematologic malignancy or solid tumor, was not significantly associated with mortality (mortality rate, 36% vs 28%;  $p=0.57$ ). Thus, our findings suggest that underlying malignancy or neutropenia have less influence on mortality risk than long-lasting neutropenia in patients with *S. maltophilia* bacteremia. Respiratory tract was the most common source (33%) of *S. maltophilia* bacteremia in this study. The incidence of respiratory tract as the source of *S. maltophilia* bacteremia has ranged widely in previous reports, from 10 to 50% [10, 16-19]. In addition, respiratory tract-originating bacteremia was related to mortality (mortality rate, 61% vs 20%;  $p<0.001$ ) in this study, similar to the finding of the Elting and Bodey [10]. This suggests that although

*S. maltophilia* has been considered a low-virulence and opportunistic pathogen [3], it may still cause a high mortality rate if the bacteremia originates from the respiratory tract [30-32]. The presence of a CVC is not only a risk factor for *S. maltophilia* infection but also an important source of bacteremia [9-11,14,17-19]. In contrast to bacteremia originating from the respiratory tract, CVC-related bacteremia was inversely associated with mortality in this study (OR, 0.04;  $p<0.001$ ). This finding is in agreement with previous studies [10,16] and may be attributable to the less complicated nature of catheter-related bacteremia and its good response to removal of the catheter, even without antibiotic treatment. Our results confirm the importance of careful evaluation of CVC because nearly one-third of *S. maltophilia* bacteremia episodes were CVC-related in this study, and removal of the infection source, in addition to appropriate antibiotics treatment, was crucial to infection control. In this study, the outcome of *S. maltophilia* bacteremia with unknown source was not significantly associated with mortality (mortality rate, 23% vs 37%;  $p=0.334$ ), as in previous studies [10,16,19,21] except for the study of Muder et al [17]. This may be due to the low virulence of this organism and potentially to its origination from the CVC, which was correlated to lower mortality rate.

Serum albumin level can be used as an index of general nutrition status and severity of underlying disease, and previous studies found low serum albumin level was associated with mortality [33,34]. In the present study, low serum albumin level (<3 g/dL) was significantly correlated to mortality ( $p=0.034$ ). Low serum albumin level is a consequence of various

mechanisms and it can be used as a marker of poor prognosis of *S. maltophilia* bacteremia. In this study, thrombocytopenia was an independent factor for predicting mortality in patients with *S. maltophilia* bacteremia (OR, 8.89;  $p=0.001$ ). Although the mechanism of thrombocytopenia in sepsis was heterogenous and not clearly clarified, it has been reported to be an early warning sign of sepsis [35] and a poor prognostic factor in septic patients [36,37]. Thrombocytopenia might be a useful clinical predictor of mortality in patients with *S. maltophilia* bacteremia due to its advantages of easy and rapid measure and universal availability. It is not surprising that shock was significantly correlated to mortality in patients with *S. maltophilia* bacteremia in this study (OR, 4.85;  $p=0.013$ ), since the development of septic shock has been shown to be associated with fatal outcome in Gram-negative bacteremia [37-40]. However, few studies of *S. maltophilia* bacteremia have reported that shock was a risk factor associated with death [10,11,19]. Although shock was an uncommon presenting symptom in previous studies of *S. maltophilia* bacteremia, it should be considered as an independent factor predicting poor prognosis.

Only 33 (39%) of our patients were treated with appropriate antibiotics. It was difficult to administer appropriate antibiotics empirically before *S. maltophilia* was identified and susceptibility test results were available because this organism is intrinsically multi-drug resistant to antimicrobial agents including carbapenems. Although the mortality rate of patients treated with appropriate antibiotics was lower than in those without appropriate treatment, this difference was not significant (27% vs 37%;  $p=0.477$ ). This finding is in conflict with previous studies [14,16,18,19]. To investigate possible reasons for this discrepancy, we further analyzed the prognostic factors between patients treated with and without appropriate antibiotics and found no significant difference between these 2 groups. This may suggest that the source of bacteremia (such as respiratory tract in origin) and the condition of patients at the presentation of bacteremia (such as shock and thrombocytopenia) played a more important role in mortality from and response to treatment of *S. maltophilia* bacteremia, as the susceptibility results of the disk diffusion method were not reliable indicators.

This study had several limitations. Due to the lack of a control group, it is difficult to determine whether the results reflect the characteristics of *S. maltophilia* bacteremia or the characteristics of the patient population

in general. Prospective study is needed to confirm our findings. Although ticarcillin-clavunilate was one of the antibiotics used to treat *S. maltophilia* infection in this study, the susceptibility was not routinely tested, and only the disk diffusion susceptibility test results were available for analysis.

In summary, *S. maltophilia* is an emerging nosocomial pathogen with increasing resistance to many antimicrobial agents. Several predisposing and prognostic factors for *S. maltophilia* bacteremia patients were identified in this study. Our results showed that the source of the bacteremia and the condition of patients at the presentation of bacteremia were the major factors influencing prognosis. Antibiotic use based on the disk diffusion results reduced the mortality rate, but this difference was not significant. Further investigation is needed to find a more accurate and reliable susceptibility test, and more effective therapeutic regimens, such as combined therapy, for the treatment of *S. maltophilia* bacteremia.

## References

1. Hugh R, Ryschenkow E. *Pseudomonas maltophilia*, an alcaligenes-like species. J Gen Microbiol 1961;26:123-32.
2. Palleroni NJ, Bradbury JF. *Stenotrophomonas*, a new bacterial genus for *Xanthomonas maltophilia* (Hugh 1980) Swings et al. 1983. Int J Syst Bacteriol 1993;43:606-9.
3. Denton M, Kerr KG. Microbiological and clinical aspects of infection associated with *Stenotrophomonas maltophilia*. Clin Microbiol Rev 1998;11:57-80.
4. Marshall WF, Keating MR, Anhalt JP, Steckelberg JM. *Xanthomonas maltophilia*: an emerging nosocomial pathogen. Mayo Clin Proc 1989;64:1097-104.
5. Labarca JA, Leber AL, Kern VL, Territo MC, Brankovic LE, Bruckner DA, et al. Outbreak of *Stenotrophomonas maltophilia* bacteremia in allogenic bone marrow transplant patients: role of severe neutropenia and mucositis. Clin Infect Dis 2000;30: 195-7.
6. Sanyal SC, Mokaddas EM. The increase in carbapenem use and emergence of *Stenotrophomonas maltophilia* as an important nosocomial pathogen. J Chemother 1999;11:28-33.
7. Morrison AJ Jr, Hoffmann KK, Wenzel RP. Associated mortality and clinical characteristics of nosocomial *Pseudomonas maltophilia* in a university hospital. J Clin Microbiol 1986;24:52-5.
8. Sattler CA, Mason EO Jr, Kaplan SL. Nonrespiratory *Stenotrophomonas maltophilia* infection at a children's hospital. Clin Infect Dis 2000;31:1321-30.
9. Krcmery V, Trupl J, Svetlansky I. Susceptibility to antimicrobial agents of *Stenotrophomonas maltophilia* isolated from patients

- with cancer and bacteremia. *Clin Infect Dis* 2001;32:1656.
10. Elting LS, Bodey GP. Septicemia due to *Xanthomonas* species and non-*aeruginosa Pseudomonas* species: increasing incidence of catheter-related infections. *Medicine (Baltimore)* 1990;69:296-306.
  11. Krcmery V Jr, Pichna P, Oravcova E, Lacka J, Kukuckova E, Studena M, et al. *Stenotrophomonas maltophilia* bacteraemia in cancer patients: report on 31 cases. *J Hosp Infect* 1996;34:75-7.
  12. Vartivarian S, Anaissie E, Bodey G, Sprigg H, Rolston K. A changing pattern of susceptibility of *Xanthomonas maltophilia* to antimicrobial agents: implications for therapy. *Antimicrob Agents Chemother* 1994;38:624-7.
  13. Hsueh PR, Liu YC, Yang D, Yan JJ, Wu TL, Huang WK, et al. Multicenter surveillance of antimicrobial resistance of major bacterial pathogens in intensive care units in 2000 in Taiwan. *Microb Drug Resist* 2001;7:373-82.
  14. Jang TN, Wang FD, Wang LS, Liu CY, Liu IM. *Xanthomonas maltophilia* bacteremia: an analysis of 32 cases. *J Formos Med Assoc* 1992;91:1170-6.
  15. Wayne P. Performance Standards for Antimicrobial Disk Susceptibility Tests: Approved Standards. 7th ed. M100-S10. National Committee for Clinical Laboratory Standards. 1999.
  16. Friedman ND, Korman TM, Fairley CK, Franklin JC, Spelman DW. Bacteraemia due to *Stenotrophomonas maltophilia*: an analysis of 45 episodes. *J Infect* 2002;45:47-53.
  17. Muder RR, Harris AP, Muller S, Edmond M, Chow JW, Papadakis K, et al. Bacteremia due to *Stenotrophomonas (Xanthomonas) maltophilia*: a prospective, multicenter study of 91 episodes. *Clin Infect Dis* 1996;22:508-12.
  18. Senol E, DesJardin J, Stark PC, Barefoot L, Snyderman DR. Attributable mortality of *Stenotrophomonas maltophilia* bacteremia. *Clin Infect Dis* 2002;34:1653-6.
  19. Micozzi A, Venditti M, Monaco M, Friedrich A, Taglietti F, Santilli S, et al. Bacteremia due to *Stenotrophomonas maltophilia* in patients with hematologic malignancies. *Clin Infect Dis* 2000;31:705-11.
  20. Apisarnthanarak A, Mayfield JL, Garison T, McLendon PM, DiPersio JF, Fraser VJ, et al. Risk factors for *Stenotrophomonas maltophilia* bacteremia in oncology patients: a case-control study. *Infect Control Hosp Epidemiol* 2003;24:269-74.
  21. Victor MA, Arpi M, Bruun B, Jonsson V, Hansen MM. *Xanthomonas maltophilia* bacteremia in immunocompromised hematological patients. *Scand J Infect Dis* 1994;26:163-70.
  22. Penzak SR, Abate BJ. *Stenotrophomonas (Xanthomonas) maltophilia*: a multidrug-resistant nosocomial pathogen. *Pharmacotherapy* 1997;17:293-301.
  23. Cohn ML, Waites KB. Antimicrobial activities of gatifloxacin against nosocomial isolates of *Stenotrophomonas maltophilia* measured by MIC and time-kill studies. *Antimicrob Agents Chemother* 2001;45:2126-8.
  24. Fass RJ, Prior RB. Comparative in vitro activities of piperacillin-tazobactam and ticarcillin-clavulanate. *Antimicrob Agents Chemother* 1989;33:1268-74.
  25. Liaw SJ, Teng LJ, Hsueh PR, Ho SW, Luh KT. In vitro activities of antimicrobial combinations against clinical isolates of *Stenotrophomonas maltophilia*. *J Formos Med Assoc* 2002;101:495-501.
  26. Poulos CD, Matsumura SO, Willey BM, Low DE, McGeer A. In vitro activities of antimicrobial combinations against *Stenotrophomonas (Xanthomonas) maltophilia*. *Antimicrob Agents Chemother* 1995;39:2220-3.
  27. Munoz Bellido JL, Munoz CS, Garcia GI, Alonso Manzanares MA, Gutierrez Zufiaurre MN, Garcia-Rodriguez JA. In vitro activities of beta-lactam-beta-lactamase inhibitor combinations against *Stenotrophomonas maltophilia*: correlation between methods for testing inhibitory activity, time-kill curves, and bactericidal activity. *Antimicrob Agents Chemother* 1997;41:2612-5.
  28. Arpi M, Victor MA, Mortensen I, Gottschau A, Bruun B. In vitro susceptibility of 124 *Xanthomonas maltophilia (Stenotrophomonas maltophilia)* isolates: comparison of the agar dilution method with the E-test and two agar diffusion methods. *APMIS* 1996;104:108-14.
  29. Garrison MW, Anderson DE, Campbell DM, Carroll KC, Malone CL, Anderson JD, et al. *Stenotrophomonas maltophilia*: emergence of multidrug-resistant strains during therapy and in an in vitro pharmacodynamic chamber model. *Antimicrob Agents Chemother* 1996;40:2859-64.
  30. Gatell JM, Trilla A, Latorre X, Almela M, Mensa J, Moreno A, et al. Nosocomial bacteremia in a large Spanish teaching hospital: analysis of factors influencing prognosis. *Rev Infect Dis* 1988;10:203-10.
  31. Bisbe J, Gatell JM, Puig J, Mallolas J, Martinez JA, Jimenez de Anta MT, et al. *Pseudomonas aeruginosa* bacteremia: univariate and multivariate analyses of factors influencing the prognosis in 133 episodes. *Rev Infect Dis* 1988;10:629-35.
  32. Brun-Buisson C, Doyon F, Carlet J. Bacteremia and severe sepsis in adults: a multicenter prospective survey in ICUs and wards of 24 hospitals. French Bacteremia-Sepsis Study Group. *Am J Respir Crit Care Med* 1996;154:617-24.
  33. Goldwasser P, Feldman J. Association of serum albumin and mortality risk. *J Clin Epidemiol* 1997;50:693-703.
  34. Dominguez de VE, Mosquera JM, Rubio JJ, Galdos P, Diez BV, de la Serna JL, et al. Association of a low serum albumin with infection and increased mortality in critically ill patients. *Intensive Care Med* 1980;7:19-22.
  35. Cohen P, Gardner FH. Thrombocytopenia as a laboratory sign and complication of gram-negative bacteremic infection. *Arch Intern Med* 1966;117:113-24.

36. Vanderschueren S, De Weerd A, Malbrain M, Vankersschaever D, Frans E, Wilmer A, et al. Thrombocytopenia and prognosis in intensive care. *Crit Care Med* 2000;28:1871-6.
37. Brun-Buisson C, Doyon F, Carlet J, Dellamonica P, Gouin F, Lepoutre A, et al. Incidence, risk factors, and outcome of severe sepsis and septic shock in adults. A multicenter prospective study in intensive care units. French ICU Group for Severe Sepsis. *JAMA* 1995;274:968-74.
38. Uzun O, Akalin HE, Hayran M, Unal S. Factors influencing prognosis in bacteremia due to gram-negative organisms: evaluation of 448 episodes in a Turkish university hospital. *Clin Infect Dis* 1992;15:866-73.
39. Valles J, Leon C, Alvarez-Lerma F. Nosocomial bacteremia in critically ill patients: a multicenter study evaluating epidemiology and prognosis. Spanish Collaborative Group for Infections in Intensive Care Units of Sociedad Espanola de Medicina Intensiva y Unidades Coronarias (SEMIUC). *Clin Infect Dis* 1997;24:387-95.
40. Jang TN, Kuo BI, Shen SH, Fung CP, Lee SH, Yang TL, et al. Nosocomial gram-negative bacteremia in critically ill patients: epidemiologic characteristics and prognostic factors in 147 episodes. *J Formos Med Assoc* 1999;98:465-73.