

Mortality Predictors of Bloodstream Infections in Solid-Organ Transplant Recipients

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Abstract

Objectives: Bloodstream infections are of great concerns and a major cause of mortality in solid-organ transplant recipients. This study investigated the possible predictors influencing survival among solid-organ transplant recipients with bloodstream infections.

Materials and Methods: We performed a retrospective analysis of bloodstream infections in patients who underwent solid-organ transplant between January 2002 and November 2011. During the study, 133 episodes of bloodstream infections occurred in 98 solid-organ transplant recipients. The predictors were identified by univariate and multivariate logistic regression analyses.

Results: The mean age for the 98 enrolled patients was 42.3 years (42.3 ± 12.8 y). The majority of infections were nosocomial (79.6%), and the bloodstream infection-related mortality rate was 39.8% (39 of 98 patients). The univariate analysis identified the following variables as predictors of bloodstream infection-related mortality: intra-abdominal/biliary focus ($P = .011$), polymicrobial infection ($P < .001$), liver transplant ($P = .002$), platelet count $< 50\,000 \times 10^9/L$ ($P < .001$), lymphocyte count $< 300 \times 10^9/L$ ($P = .027$), and septic shock ($P < .001$). The multivariate logistic regression analysis identified platelet count $< 50\,000 \times 10^9/L$ and septic shock as independent predictors of mortality.

Conclusions: The predictors significantly associated with increased mortality in solid-organ transplant recipients with bloodstream infections included decreased platelet count and septic shock. Even with appropriate antimicrobial therapy, bloodstream infections, accompanied by septic shock or decreased platelet count, are associated with high mortality rates. Therefore, steps must be taken to reduce the incidence of bloodstream infections in solid-organ transplant patients.

Key words: Bloodstream infections, Mortality, Predictors, Solid-organ transplant

Introduction

Bloodstream infections are a serious concern worldwide. The mortality rates in solid-organ transplant patients with bloodstream infections range from 3% to 33% in heart, 10% to 27.8% in liver, and 2.5% to 11% in kidney transplant recipients.¹⁻⁶ Several previous studies have identified independent demographic and clinical predictors of bloodstream infection-related mortality among solid-organ transplant recipients. Few studies have evaluated whether laboratory variables had effect on mortality in the transplant setting. Thus, the effect of laboratory variables on outcomes of solid-organ transplant recipients associated with bloodstream infections has not been clearly established. In this study, we aimed to identify laboratory values (eg, creatinine levels, serum albumin levels, platelet counts, white blood cell counts, and lymphocyte counts), demographic factors, and clinical factors that influence survival. We used bloodstream infection-related mortality as the main outcome among solid-organ transplant patients with bloodstream infections.

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Materials and Methods

Study population

Between January 2002 and November 2011, one hundred thirty-three episodes of bloodstream infections in 98 patients who underwent solid-organ transplant were documented at the Third Affiliated Hospital, Central South University in Changsha, China. These patients' demographic, clinical, and laboratory records were analyzed. All protocols were approved by the ethics committee of the institution before the study began, and the protocols conformed with the ethical guidelines of the 1975 Helsinki Declaration. Written, informed consent was obtained from all patients.

Study design and data collection

A retrospective study was conducted to determine the predictors of bloodstream infection-related mortality. We collected information on clinical characteristics, including age, sex, peak body temperature, time of bloodstream infection onset, nosocomial origin of infection, site of primary infection, empirical antimicrobial therapy, type of organism, type of transplant, septic shock, and laboratory data. For intra-abdominal/biliary sepsis, there was not any case with biliary tract problem or hepatic artery thrombosis. The laboratory variables were collected in the first 24 hours after the blood culture was drawn, including serum creatinine levels, serum albumin levels, white blood cells counts, platelet counts, and lymphocyte counts.

Definitions

Antimicrobial use was considered appropriate if 1 or more antimicrobial agents with in vitro activity against the causative organisms was administered at an adequate dosage via an appropriate route within 24 hours after obtaining results of the blood culture. Cases that did not meet these criteria were considered to have inappropriate antimicrobial use. The nosocomial origin of infection and the sites of infection (eg, lungs, intra-abdomen/bile duct, and intravascular catheter) were evaluated using the criteria established by Centers for Disease Control.⁷ Bloodstream infections also were defined on the basis of the criteria proposed by Centers for Disease Control.⁷ Isolation of bacteria other than common skin flora (eg, coagulase-negative staphylococci,

bacillus spp., and diphtheroids) from 1 single blood culture with the presence of clinical features consistent with sepsis, or the isolation of an organism from more than 1 blood culture accompanied by signs of systemic infection, including fever, chills, or hypotension. The bloodstream infections were defined as *polymicrobial* if 2 or more different organisms were observed in blood cultures. Patients were diagnosed with septic shock owing to bloodstream infection if their blood cultures were positive and they exhibited persistent dysfunction of at least 1 organ that could only be explained by hypoperfusion despite adequate fluid resuscitation.⁸ Mortality was considered bloodstream infection-related when death was associated with clinical signs of active infection without evidence of any other cause.

Statistical analyses

Continuous variables are expressed as means $\pm$ standard deviation. Chi-square analysis or Fisher exact test was used to compare categorical data. For the final multivariate model, only variables that were statistically significant in the univariate analyses were included, and a multivariate forward logistic regression model was used to identify predictors of mortality caused by bloodstream infections. A 2-sided value of $P < .05$ was considered statistically significant. Statistical analyses were performed with SPSS software (SPSS: An IBM Company, version 13.0, IBM Corporation, Armonk, NY, USA).

Results

The present study included 98 solid-organ transplant patients with bloodstream infections with a mean age of 42.3 years (range, 12-66 y), including 41 liver, 54 kidney, 1 heart, 1 combined liver-kidney, and 1 combined kidney-pancreas transplants. Among these patients, 67 were male and 31 were female. Fever and septic shock developed in 92% and 39.8% of patients. Bacteremia was designated nosocomial in 79.6% of cases. The rate of bloodstream infection-related mortality was 39.8% (39 of 98 patients). The rate of mortality increased sharply to 79.5% in patients with septic shock.

Thirty out of 98 cases (30.6%) received inappropriate antibiotic treatment. The lungs (41.8%), intra-abdomen/bile ducts (24.5%), and intravascular catheter (16.3%) were the 3 most-

common sites of primary infection. Seventy-four patients (75.5%) experienced a single episode of bloodstream infections, 16 (16.3%) experienced 2 episodes, and 8 (8.2%) experienced 3 or more episodes. There were 28 patients with gram-positive bacteremia, 43 with gram-negative bacteremia, 4 with fungemia, and 23 with polymicrobial bloodstream infections. The demographic, laboratory, and clinical characteristics of the patients are listed in Table 1. On univariate analysis (Table 2), intra-abdominal/biliary focus, polymicrobial infection, liver transplant, platelet count $< 50\,000 \times 10^9/L$, lymphocyte count $< 300 \times 10^9/L$, and septic shock were significantly associated with mortality. The multivariate analysis identified 2 independent predictors of mortality caused by bloodstream infections: platelet count $< 50\,000 \times 10^9/L$ (OR 6.292 [1.873-21.142]; $P = .03$) and septic shock (OR 10.671 [3.291-34.603]; $P < .001$).

Discussion

Bloodstream infections still hinder the success of transplant. Previous studies^{3, 9-13} have demonstrated that in bacteremic recipients of solid-organ transplants, the factors significantly associated with greater mortality included advanced age (≥ 50 y), nosocomial acquisition, intensive care unit stay at the time of bacteremia, pulmonary focus, polymicrobial infection, certain types of isolates, the absence of fever or chills, inadequate empirical therapy, liver transplant, greater serum bilirubin level or prothrombin time, and the need for mechanical ventilation. The present study, which was aimed at solid-organ transplant recipients, suggests that septic shock constitutes an independent predictor of bloodstream infection-related mortality.

Several studies^{3, 9, 11} in the transplant setting suggest similar findings, and these are concordant with the findings of the present study. There is a strong agreement of the association of septic shock with increased mortality, and a related mortality rate can reach up to 54% when bacteremias are accompanied with septic shock.⁹ In the present study, the mortality rate was 79.5% among patients with septic shock. The present study also suggests that a platelet count $< 50\,000 \times 10^9/L$ constitutes another independent predictor of bloodstream infection-related mortality in solid-organ transplant recipients. To the best of our knowledge, this is the first study

Table 1. Demographic, Laboratory, and Clinical Variables of 98 Solid-Organ Transplant Patients with Bloodstream Infections

Characteristics	Value
Age, mean y $\pm$ SD	42.3 $\pm$ 12.8
Sex, number of male/number of female patients	67/31
Temperature of 40°C or higher/number of cases	27/98
Nosocomial origin/number of cases	78/98
Inappropriate antimicrobial use/number of cases	30/98
Septic shock/number of cases	39/98
The type of transplant, number of cases (%)	
Liver	41 (41.8)
Kidney	54 (55.2)
Heart	1 (1)
Liver-kidney	1 (1)
Kidney-pancreas	1 (1)
Site of primary infection, number of cases (%)	
Lungs	41 (41.8)
Intra-abdomen/bile duct	24 (24.5)
Intravascular catheter	16 (16.3)
Intestinal tract	6 (6.1)
Urinary tract	4 (4.2)
Unknown	7 (7.1)
Time of onset (posttransplant), number of cases (%)	
Within 8 wk	51 (52)
More than 8 wk	47 (48)
Type of organisms, number of cases (%)	
Gram-positive	28 (28.6)
Gram-negative	43 (43.9)
Fungal	4 (4.1)
Polymicrobial	23 (23.4)
Laboratory variables, number of cases (%)	
Platelet count $< 50\,000 \times 10^9/L$	16 (16.3)
Lymphocyte count $< 300 \times 10^9/L$	34 (34.7)
Albumin level < 30 g/L	32 (32.7)
White blood cells count $< 4000 \times 10^9/L$	3 (3.1)
Creatinine level > 265 μ mol/L	24 (24.5)

Table 2. Predictors of Mortality in Solid-Organ Transplant Recipients with Bloodstream Infections

	OR (95% CI)	P Value
Univariate analysis		
Age > 50 y	NS	NS
Sex	NS	NS
Temperature of 40°C or higher	NS	NS
Nosocomial origin	NS	NS
Inappropriate antimicrobial use	NS	NS
Septic shock	24.703 (8.416-72.514)	$< .001$
Liver transplant	3.953 (1.679-9.309)	.002
Intra-abdominal/biliary focus	3.472 (1.331-9.060)	.011
Polymicrobial infection	6.367 (2.548-18.285)	$< .001$
Platelet count $< 50\,000 \times 10^9/L$	15.619 (5.399-45.184)	$< .001$
Lymphocyte count $< 300 \times 10^9/L$	2.667 (1.117-6.364)	.027
Albumin level < 30 g/L	NS	NS
White blood cell count $< 4000 \times 10^9/L$	NS	NS
Creatinine level > 265 μ mol/L	NS	NS
Multivariate analysis		
Septic shock	10.671 (3.291-34.603)	$< .001$
Platelet count $< 50\,000 \times 10^9/L$	6.292 (1.873-21.142)	.003

reporting that a decreased platelet count has an adverse influence on clinical outcome among solid-organ transplant patients with bloodstream infections.

The present study has some limitations, including a small sample size and its retrospective nature. We

found that, even with appropriate antimicrobial treatment, bloodstream infections accompanied by septic shock or decreased platelet count were associated with high mortality rates. Therefore, in the transplant setting, it is essential to use effective measures for reducing the incidence of bloodstream infections.

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