Yonsei Med J 50(1):112 - 121, 2009
DOI 10.3349/ymj.2009.50.1.112

Epidemiology and Risk Factors for Bacteremia in 144 Consecutive Living-Donor Liver Transplant Recipients

Sang Il Kim,[1] Youn Jeong Kim,[1] Yoon Hee Jun,[1] Seong Heon Wie,[1] Yang Ree Kim,[1] Jong Young Choi,[1] Seung Kyu Yoon,[1] In Sung Moon,[2] Dong Goo Kim,[2] Myung Duk Lee,[2] and Moon Won Kang[1]

Departments of [1]Internal Medicine and [2]Surgery, Kangnam St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, Korea.

Purpose: Bacteremia is a major infectious complication associated with mortality in liver transplant recipients. The causative organisms and clinical courses differ between medical centers due to variations in regional bacterial epidemiology and posttransplant care. Further, living donors in Korea contribute to 83% of liver transplants, and individualized data are required to improve survival rates. **Patients and Methods:** We retrospectively analyzed 104 subjects who had undergone living-donor liver transplant from 2005 to 2007. **Results:** Among the 144 consecutive living-donor liver transplant recipients, 24% (34/144) developed bacteremia, 32% (46/144) developed non-bacteremic infections, and 44% (64/144) did not develop any infectious complications. Forty episodes of bacteremia occurred in 34 recipients. The major sources of bacteremia were intravascular catheter (30%; 12/40), biliary tract (30%; 12/40), and abdomen (22.5%; 9/40). Gram-positive cocci were more common (57.5%; 23/40) than Gram-negative rods (32.5 %; 13/40) and fungi (10%; 4/40). The data revealed that the following factors were significantly different between the bacteremia, non-bacteremic infection, and no infection groups: age ($p = 0.024$), posttransplant hemodialysis ($p = 0.002$), ICU stay ($p = 0.012$), posttransplant hospitalization ($p < 0.0001$), and duration of catheterization ($p < 0.0001$). The risk factors for bacteremia were older than 55 years (odds ratio, 6.1; $p = 0.003$), catheterization for more than 22 days (odds ratio, 4.0; $p = 0.009$), UNOS class IIA (odds ratio, 6.6; $p = 0.039$), and posttransplant hemodialysis (odds ratio, 23.1; $p = 0.001$). One-year survival rates in the bacteremic, non-bacteremic infection, and no infection groups were 73.2%, 91.3%, and 93.5%, respectively. **Conclusion:** Early catheter removal and preservation of renal function should focus for improving survival after transplant.

Key Words: Living-donor liver transplant, bacteremia, risk factor

INTRODUCTION

Bacteremia has been reported to be the main cause of mortality in liver transplant recipients.[1-3] The mortality in bacteremic liver transplant recipients has been found to range between 24% and 36%.[4,5] In a previous study, it was found that the proportion of all infections due to bacteremias increased significantly over time. Furthermore, of other major infections, a trend of fungal infection and cytomegalovirus infection to decrease was noted.[6] Most bacterial infections in liver transplant recipients occur within the first month after transplantation, with the incidence of bacteremia ranging between 21% and 33%.[7,8]

The proportions of types bacterial infections have changed since the early 1990s, and differences have also been noted in the proportions among hospitals. Several centers have reported that the infections due to Gram-negative bacteria constitute 65% of all types of bacterial infections, resulting from intra-abdominal or biliary sources.[7-9] In contrast, some centers have reported that infections due to Gram-positive bacteria, such as staphylococci and enterococci, outnumber those due to Gram-negative bacteria.[10,11] Diabetes and serum albumin levels are significant clinical predictors for bacteremia in liver transplant recipients.[12] However, characteristics of donors, hospital envir-

Received June 2, 2008
Accepted October 22, 2008

This study was supported by a grant of the Korea Health 21 R & D Project, Ministry of Health & Welfare, Republic of Korea (Project No.: A040004).

Reprint address: requests to Dr. Dong Goo Kim, Department of Surgery, Kangnam St. Mary's Hospital, College of Medicine, The Catholic University of Korea, 505 Banpo-dong, Soecho-gu, Seoul 137-701, Korea. Tel: 82-2-590-2724, Fax: 82-2-595-2992, E-mail: kimdg@catholic.ac.kr

onment, antibacterial prophylaxis, regional bacterial epidemiology, and posttransplant managements differ among centers. Further, living donors in Korea contribute to more than 80% of liver transplants.[13-15] Therefore, clinical predictors need to be reassessed to improve the survival.

PATIENTS AND METHODS

Patients

We analyzed 144 patients who had undergone living-donor liver transplant from January 2005 to September 2007 at Kangnam St. Mary's hospital, Seoul, Korea-a 1,000-bed tertiary-care university hospital.

Antimicrobial prophylaxis

The perioperative prophylaxis consisted of cefoperazone/sulbactam (2 g/day, IV) and ampicillin (8g/day, IV) for 5 days. Nystatin (800,000 units/day, oral) was administered for 1 month for fungal prophylaxis. Pneumocystis pneumonia prophylaxis consisted of trimethoprim/sulfamethoxazole (80 mg/400 mg/day, oral). Routine antiviral prophylaxis was not administered.

Immunosuppression

All patients received tacrolimus or cyclosporine, mycophenolate mofetil, and low-dose prednisone as routine immunosuppressive agents. Rejections were treated with a high-dose steroid along with or without change in the immunosuppressive agents to tacrolimus or OKT3.

Definition of bacteremia and infection

We used a previously reported diagnostic definition of infection in transplant recipients.[16] Bacteremia was considered to be present when *Staphylococcus aureus*, *Candida* species, or Gram-negative rods were isolated from at least 1 blood culture. The other pathogens were considered positive when they were isolated from 2 blood cultures from the site considered as the infection site. Primary bacteremia was defined as bacteremia with no physical, radiological, or pathological evidence of a definite infection source. Catheter-related bacteremia was defined when more than 15 colony-forming units of bacteria were cultured from the catheter tip, irrespective of whether the same organism was isolated from the blood culture. Intra-abdominal infection was defined as presence of fever, abdominal pain, tenderness, or elevation of liver function indices with evidence of cholangitis, liver abscess, or infected biloma through radiological examination. These definitions were also stated in the Center for Disease Control criteria.[17]

Statistical analysis

Student's t-test was used to analyze the continuous variables, and chi-square test was used to analyze the categorical variables. We analyzed the risk factors associated with bacteremia by univariate and multivariate logistic regression analyses. Statistical analysis was performed using SPSS for Windows, version 12.0 software package (SPSS Inc, Chicago, IL, USA) and p values less than 0.05 was considered to be statistically significant.

RESULTS

Among the 144 consecutive patients who had undergone living-donor liver transplant from January 2005 to September 2007, bacteremia developed in 23.6% (34/144) of the patients, whereas 31.9% (46/144) of the patients developed non-bacteremic infections. These patients developed infectious complications after the transplant, however, no pathogenic microorganisms were detected from the blood. Infectious complications did not occur in 44% (64/144) of the patients. The number of follow-up days was 525 ± 319 days (mean ± SD). Viral hepatitis with the hepatitis B virus was the predominant underlying liver disease. The mean age of patients with bacteremia was 52.5 years, with non-bacteremic infection was 47.4 years, and without infection was 47.9 years, with a significant difference between the 3 groups ($p = 0.024$) and also between the bacteremia and non-bacteremic infection groups ($p = 0.039$). Combined diseases such as diabetes, tumors, and renal dysfunction did not

Table 1. Demographic and Clinical Characteristics of Living-Donor Liver Transplant Recipients*

	Bacteremia (n = 34)	Non-bacteremic infection (n = 46)	No-infection (n = 64)	*p* value†	*p* value‡
Sex, % of male	76.5% (26/34)	73.9% (34/46)	82.8% (53/64)	0.507	
Age (yrs)	52.5 ± 6.4	47.4 ± 10.1	47.9 ± 9.0	0.024	0.039
Underlying liver disease				0.399	
Alcoholic	8.8% (3/34)	13.0% (6/46)	6.3% (4/64)		
Viral hepatitis					
Hepatitis B	85.3% (29/34)	65.2% (30/46)	76.6% (49/64)		
Hepatitis C	0	2.2% (1/46)	4.7% (3/64)		
NBNC	0	8.7% (4/46)	6.3% (4/64)		
Autoimmune	2.9% (1/34)	2.2% (1/46)	0		
Drug related	2.9% (1/34)	2.2% (1/46)	0		
Unknown	0	6.5% (3/46)	6.3% (4/64)		
Combined disease					
Tumor	55.9% (19/34)	39.1% (18/46)	46.9% (30/64)	0.331	
Diabetes mellitus	29.4% (10/34)	30.4% (14/46)	29.7% (19/64)	0.766	
Renal dysfunction	11.8% (4/34)	6.5% (3/46)	4.7% (3/64)	0.419	
Pre-transplant condition					
MELD score	17.0 ± 9.5	18.3 ± 8.7	15.1 ± 8.2	0.161	
Child-pugh score	9.2 ± 2.6	9.5 ± 2.4	8.9 ± 2.7	0.509	
UNOS class IIA	20.6% (7/34)	10.9% (5/46)	6.3% (4/64)	0.134	

NBNC, non-B non-C; MELD, model for end-stage liver disease; UNOS, united network of organ sharing.
*Data are presented as percent (no.) or mean ± SD.
†Chi-square test was used to analyze categorical variables between three groups and ANOVA for continuous variables.
‡Student's t-test was used between bacteremia group and non-bacteremic infection group.

differ between the 3 groups. Pre-transplant parameters such as the Model for End-Stage Liver Disease (MELD) scores, Child-Pugh scores, and United Network of Organ Sharing (UNOS) classes did not significantly differ between the 3 groups (Table 1).

Sources and causes of bacteremia

Of the 144 patients, 34 had 40 episodes of bacteremia, and 17% (6/34) of these patients experienced an additional bacteremia episode during the study period. None of these patients showed relapse or recurrence of bacteremia, and each episode was considered a different case. Among 40 episodes of bacteremia, 22.5% (9/40) occurred within 14 days of operation and 77.5% (31/40) occurred later than 14 days after transplantation.

The 3 most common sources of bacteremia were intravascular catheter (30%; 12 of 40 episodes), biliary tract (30%; 12 of 40 episodes), and abdomen (22.5%; 9 of 40 episodes). The sources and pathogens in bacteremic patients are listed in Table 2. Catheter-related bacteremia in the majority of the cases was caused by staphylococci (75.0%; 9 of 12 episodes). Of them, 88.9% (8 of 9 organisms) were methicillin-resistant. Two patients died due to catheter-related bacteremia caused by *Candida albicans* and *Acinetobacter lwoffii*.

The data revealed that Gram-positive cocci (57.5 %; 23 of 40 episodes) were more common than Gram-negative rods (32.5%; 13 of 40 episodes).

Table 2. Sources and Pathogens Associated with Bacteremia in Study Patients

Source (No. of episodes)	Pathogen	No. of episodes	Sensitivity to major antibiotics (No. of episodes)
Catheter related (n = 12)	Coagulase-negative *Staphylococci*	7	
	Staphylococcus epidermidis	4	MR (4)
	Staphylococcus hominis	2	MR (1), MS (1)
	Staphylococcus haemolyticus	1	MR (1)
	Staphylococcus aureus	2	MR (2)
	Acinetobacter lwoffii	1	CS (1)
	Candida albicans	1	FS (1)
	Candida parapsilosis	1	FR (1)
Biliary (n = 12)	*Enterococcus faecium*	3	VR (2), VS (1)
	Enterococcus casseliflavus	1	VR (1)
	Klebsiella pneumoniae	3	ESBL (1), non-ESBL (2)
	Escherichia coli	2	non-ESBL (2)
	Pseudomonas aeruginosa	1	non-ESBL (1)
	Enterobacter cloacae	1	ESBL (1)
	*Candida species**	1	
Abdomen (n = 9)	*Enterococcus faecium*	5	VR (3), VS (2)
	Escherichia coli	2	non-ESBL (2)
	Acinetobacter baumannii	1	CS (1)
	Candida glabrata	1	FR (1)
Pneumonia (n = 2)	*Streptococcus pneumoniae*	1	CS (1)
	Chryseobacterium meningosepticum	1	CR (1)
Wound (n = 1)	*Staphylococcus aureus*	1	MR (1)
Urinary tract (n = 1)	*Enterococcus faecium*	1	VS (1)
Unknown (n = 3)	*Staphylococcus epidermidis*†	2	MR (1), MS (1)
	Empedobacter brevis	1	CR (1)

MR, methicillin resistant; MS, methicillin sensitive; CS, cephalosporin sensitive; CR, cephalosporin resistant; FS, fluconazole sensitive; FR, fluconazole resistant; VR, vancomycin resistant; VS, vancomycin sensitive; ESBL, extended-spectrum beta lactamase positive; non-ESBL, extended-spectrum beta lactamase negative.
*Species were not demonstrated at the point of detected.
†Both 2 episodes fulfilled the definition for primary bacteremia.

Among the Gram-positive cocci, methicillin-resistant coagulase-negative staphylococci (30.4%; 7/23) were the most common, followed by vancomycin-resistant enterococci (26.1%; 6/23), vancomycin-sensitive enterococci (17.4%; 4/23), methicillin-resistant *S. aureus* (13%; 3/23), methicillin-sensitive coagulase-negative staphylococci (8.7%; 2/23), and penicillin-resistant pneumococci (4.3%; 1/23). Overall, 26.1% (6 of 23 Gram-positives) of the Gram-positive cocci were resistant to vancomycin. None of the enterococci were resistant to linezolid.

The most common Gram-negative rod was *Escherichia coli* (30.8%; 4/13), followed by *Klebsiella pneumoniae* (23.1%; 3/13) and *Acinetobacter baumannii*

(15.4%; 2/13). Among the Gram-negatives, 46.2% (6/13) demonstrated resistance to third-generation cephalosporins such as ceftazidime, ceftriaxone, and cefoperazone. Furthermore, most of the organisms that were resistant to third-generation cephalosporins also showed resistance to piperacillin-

Table 3. Pre-operative Variables with Bacteremia Compared to Non-Bacteremic Infections and No-Infection*

	Bacteremia (n = 34)	Non-bacteremic infection (n = 46)	No-infection (n = 64)	*p* value†
Donor relationship				0.912
Offspring	47.1% (16/34)	43.5% (20/46)	43.8% (28/64)	
Sibling	20.6% (7/34)	21.7% (10/46)	15.6% (10/64)	
Parent	0	2.2% (1/46)	1.6% (1/64)	
Distant family	0	4.3% (2/46)	6.3% (4/64)	
Conjugal	11.8% (4/34)	8.7% (4/46)	15.6% (10/64)	
Unrelated	20.6% (7/34)	19.6% (9/46)	17.2% (11/64)	
Positive lymphocyte crossmatch	6.9% (2/34)	11.8% (4/46)	3.4% (2/64)	0.300
History of Previous operation	11.8% (4/34)	13.0% (6/46)	9.4% (6/64)	0.825
Pre-operational infectious disease				
Fever of unproven source	11.8% (4/34)	17.4% (8/46)	7.8% (5/64)	0.307
Infectious disease				0.309
SBP	17.6% (6/34)	15.2% (7/46)	4.7% (3/64)	
Pneumonia	0	0	3.1% (2/64)	
Sinusitis	5.9% (2/34)	4.3% (2/46)	7.8% (5/64)	
Cholecystitis	2.9% (1/34)	0	0	
Tuberculosis	0	2.2% (1/46)	1.6% (1/64)	
Others	5.9% (2/34)	6.5% (3/46)	1.6% (1/64)	
None	67.6% (23/34)	71.7% (33/46)	81.3% (52/64)	
Pre-operational non-infectious variables				
Acute hepatic failure	23.5% (8/34)	26.1% (12/46)	18.8% (12/64)	0.645
Portal vein thrombosis	14.7% (5/34)	8.7% (4/46)	20.3% (13/64)	0.246
Small graft size	0	6.5% (3/46)	7.8% (5/64)	0.259
Laboratory findings				
White blood cell count (/mm^3)	4,264 ± 3,181	4,089 ± 2,894	3,649 ± 2,498	0.529
Creatinine (mg/dL)	0.96 ± 0.74	0.81 ± 0.38	1.03 ± 1.32	0.502
Total bilirubin (mg/dL)	11.6 ± 13.4	10.9 ± 11.9	7.2 ± 10.3	0.116
Albumin (mg/dL)	3.2 ± 0.5	3.1 ± 0.5	3.2 ± 0.5	0.987
SGPT (IU/L)	50 ± 41	57 ± 77	48 ± 51	0.709
INR	1.6 ± 0.4	1.9 ± 1.0	1.6 ± 0.5	0.067

SBP, spontaneous bacterial peritonitis; SGPT, serum glutamate pyruvate transaminase; INR, international normalized ratio.
*Data are presented as percent(no.) or mean ± SD.
†Chi-square test was used to analyze categorical variables between three groups and ANOVA for continuous variables.

tazobactam (data not shown). Fungi caused 10% (4 of 40 episodes) of the episodes, and 50% of these fungi were resistant to fluconazole.

Predictors of bacteremia

The perioperative clinical and laboratory variables predictive of post-transplant bacteremia were compared between bacteremia, non-bacteremic infection, and no infection groups (Table 3). No difference was noted between the groups with regard to preoperative variables such as donor relationship, positive lymphocyte cross-match, history of previous surgery, presence of preoperative infectious disease, and laboratory findings. The intraoperative and postoperative variables of the recipients are listed in Table 4. Surgery duration and the amount of transfusion did not differ between groups. However, bacteremic patients were significantly more likely to have undergone posttransplant hemodialysis ($p = 0.002$), and to have longer duration of ICU stay ($p = 0.012$) and longer period of intravascular catheterization ($p < 0.0001$). Postoperative hospitalization period was longer in bacteremic patients than in patients with non-bacteremic infection ($p = 0.005$).

Risk factors for bacteremia and mortality

Univariate analysis revealed that age above 55 years ($p = 0.014$), intravascular catheterization for more than 8 days ($p = 0.003$), UNOS class IIA ($p = 0.044$), and hemodialysis ($p = 0.001$) were significant risk factors for bacteremia (Table 5). Multivariate analysis revealed an association between bacteremia and age (odds ratio, 6.05; 95% confidence interval, 1.86 to 19.66; $p = 0.003$), catheterization for more than 22 days (odds ratio, 3.97; 95% confidence interval, 1.4 to 11.22; $p = 0.009$), UNOS class IIA (odds ratio, 6.59; 95% confidence interval, 1.1 to 39.37; $p = 0.039$), and posttransplant hemodialysis (odds ratio, 23.12; 95% confidence interval, 3.78 to 141.55; $p = 0.001$).

Of the 144 patients, 11.8% (17/144) died. Of these, 52.9% (9/17) had episodes of bacteremia, 23.5% (4/17) had episodes of non-bacteremic infec-

Table 4. Intra-Operative and Post-Operative Variables of Bacteremic Group Compared to Non-Bacteremic Infection and No Infection*

	Bacteremia (n = 34)	Non-bacteremic infection (n = 46)	No-infection (n = 64)	p value†	p value‡
Intraoperative variables					
Operative duration (min, min ± SD)	640 ± 94	645 ± 103	613 ± 72	0.150	
RBC transfusion (packs, min ± SD)	15.3 ± 8.4	15.2 ± 10.4	12.4 ± 6.7	0.143	
Post-operative variables					
Re-operation	8.8% (3/34)	15.2% (7/46)	6.3% (4/64)	0.288	
Hemodyalisys	26.5% (9/34)	10.9% (5/46)	3.1% (2/64)	0.002	
ICU stay (days)	15.6 ± 23.6	10.0 ± 7.1	7.6 ± 2.0	0.012	0.009
Catheter days (days)	29.6 ± 22.6	17.5 ± 6.2	16.6 ± 6.4	< 0.0001	< 0.0001
Biliary complication	26.5% (9/34)	37.0% (17/46)	18.8% (12/64)	0.102	
Duration of hospitalization					
Post-operation	38.9 ± 22.1	35.7 ± 21.4	25.3 ± 6.6	< 0.0001	< 0.005

ICU, intensive care unit.
*Data are presented as percent (no.) or mean ± SD.
†Chi-square test was used to analyze categorical variables between three groups and ANOVA for continuous variables.
‡Student's t-test was used between bacteremia group and non-bacteremic infection group.

Table 5. Logistic Regression Analysis of Risk Factors for Bacteremia after Living-Donor Liver Transplant

Risk factors		Percentage of bacteremia with risk factor (No.*)	*p* value (univariate)	*p* value (multivariate)	OR (95% CI)
Preoperational variables					
Age (yrs)	≥ 55	36.2% (17/47)	0.014	0.003	6.05 (1.86-19.66)
	< 55	17.5% (17/97)			
Diabetes	Yes	21.9% (7/32)	0.793		
	No	24.1% (27/112)			
UNOS class	IIA	43.8% (7/16)	0.044	0.039	6.59 (1.10-39.37)
	IIB or III	21.1% (27/128)			
Child class	C	22.1% (17/77)	0.642		
	A or B	25.4% (17/67)			
MELD score	≥ 25	29.0% (9/31)	0.422		
	< 25	22.1% (25/113)			
Tumor	Yes	28.4% (19/67)	0.211		
	No	19.5% (15/77)			
History of previous surgery	Yes	25.0% (4/16)	0.890		
	No	23.4% (30/128)			
Renal dysfunction	Yes	40.0% (4/10)	0.206		
	No	22.4% (30/134)			
Portal vein thrombosis	Yes	22.7% (5/22)	0.916		
	No	23.8% (29/122)			
Intra- and post-operational variables					
Duration of operation (h)	≥ 10	22.4% (19/85)	0.670		
	< 10	25.4% (15/59)			
Re-operation	Yes	21.4% (3/14)	0.840		
	No	23.8% (31/130)			
Posttransplant hemodialysis	Yes	56.3% (9/16)	0.001	0.001	23.12 (3.78 - 141.55)
	No	19.5% (25/128)			
Bilary complication	Yes	23.7% (9/38)	0.990		
	No	23.6% (25/106)			
ICU stay(d)	≥ 8	22.6% (14/62)	0.800		
	< 8	24.4% (20/82)			
Catheter days	≥ 22	39.1% (18/46)	0.003	0.009	3.97 (1.40 - 11.22)
	< 22	16.3% (16/98)			

OR, odd ratio; CI, confidence interval; UNOS, united network of organ sharing; MELD, model for end-stage liver disease; ICU, intensive care unit.
*No. of bacteremia/No. of patients with risk factors.

tions, and 23.5% (4/17) did not have any infectious complication. The mortality rates were 26.5% (9/34) in bacteremia group, 8.7% (4/46) in non-bacteremic infection group, and 6.3% (4/64) in no infection group, respectively. The causative organisms related to death in bacteremia group were 4 enterococci including 2 vancomycin-resistant strains, 2 *Acinetobacter* species, 1 *E. coli*, and 3

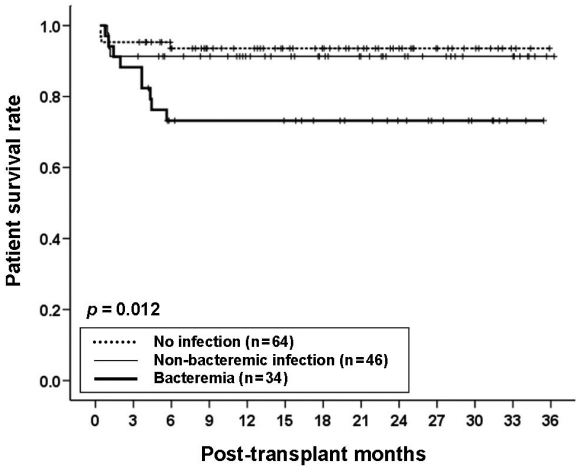

Fig. 1. Survival curves of study groups; the survival rate at 1 month: bacteremia group, 94.1%; non-bacteremic infection group, 95.7%; and no infection group, 95.3%, the survival rate at 12 months: bacteremia group, 73.2%; non-bacteremic infection group, 91.3%; and no infection group, 93.5%. It was statistically different between the groups as follows: bacteremia vs. no infection, $p = 0.006$; bacteremia vs. non-bacteremic infection, $p = 0.044$. No difference was noted between the no infection and non-bacteremic infection groups ($p = 0.65$).

candidemias. One patient developed *Candida* and enterococci bacteremia simultaneously. Of the 46 patients in the non-bacteremic infection group, 4 died: 1 due to multi-drug resistant *Acinetobacter* pneumonia, 1 due to *Aspergillus* pneumonia, 1 due to refractory shock with pneumonia and infected hematoma, and 1 due to pneumonia with ischemic heart disease. Of 64 patients in the no infection group, 4 died: 1 due to primary graft failure, 2 due to varix bleeding, and 1 due to cardiac ischemia.

The survival rate at 1 month was as follows: bacteremia group, 94.1%; non-bacteremic infection group, 95.7%; and no infection group, 95.3% (Fig. 1). However, the survival rate at 12 months was as follows: bacteremia group, 73.2%; non-bacteremic infection group, 91.3%; and no infection group, 93.5%. It was statistically different between the groups as follows: bacteremia vs. no infection, $p = 0.006$; bacteremia vs. non-bacteremic infection, $p = 0.044$. No difference was noted between the no infection and non-bacteremic infection groups ($p = 0.65$).

DISCUSSION

In this study, patients who developed bacteremia after liver transplantation had a decreased 1-year survival rate compared to patients who developed non-bacteremic infection ($p = 0.044$) or who did not develop any infectious complications ($p = 0.006$). No difference was noted in the survival rate between the patients who developed non-bacteremic infection and those who did not develop any infection ($p = 0.650$). Even though all the cases of mortality did not occur because of bacteremia, major causes of death were infectious complications with bacteremia rather than rejection, surgical complications, and non-bacteremic infections. Despite improvements in surgical technique, prolonged graft function, and progress in therapeutic options, the rate of major infectious complications remains high.[2] Technical complexity due to the high rate of bile leakage has been the main factor responsible for infectious complications.[18] Our data revealed that the biliary tract was one of the most common sources of bacteremia (Table 2). In the present study, biliary complications were not significantly different between the groups, however, reduction of biliary complications is thought to be important in reducing bacteremia, especially in living-donor liver transplantation, because biliary trees are one of the most common entries of bacteria and surgical technique is complex.

Liver transplant recipients are generally immunocompromised.[1] Furthermore, the pretransplant conditions between patients are considerably variable, and therefore, can be minimally controlled. Except for age, the uncontrollable pretransplant variables such as underlying liver disease, donor relationship, lymphocyte mismatch, and history of surgery did not differ between the groups. Moreover, pretransplant conditions such as laboratory findings and presence of infectious and non-infectious diseases, including portal vein thrombosis, did not differ between the groups. These results indicated that posttransplant managements, short duration of ICU stay, early catheter removal, and short duration of hospital stay are important factors in reducing the rate of bacteremia. However, these results differ from those of a previous study in which diabetes, pretransplant renal dysfunction, and hypoalbuminemia were found to be independently significant predictors of bacteremia in liver transplant recipients.[12] An improvement in the general care or change in the posttransplant care

could have led to these differences.

In our study, patients who developed bacteremia had undergone posttransplant hemodialysis more frequently than other patients and had longer duration of ICU stay and longer period of intravascular catheterization. These results are not very different from those observed in a larger study.[9,12] The independent risk factors for bacteremia were age above 55 years, catheterization for more than 22 days, UNOS class IIA, and posttransplant hemodialysis. However, in a previous study, only diabetes mellitus and serum albumin level were found to be the risk factors for bacteremia.[12] This indicates that our medical center performs catheterization for a longer period and needs to improve posttransplant care. In a previous study, age above 65 years, donor age above 50 years, male gender recipient, re-transplant, and pretransplant MELD score greater than 25 were associated with poor patient and graft survival.[19] Furthermore, a high MELD score was found to be indicative of poor outcome and showed maximal impact during the first year posttransplant. Our data also revealed that bacteremic patients tended to have a higher MELD score than other patients, nevertheless it was not a significant risk factor. Therefore, we analyzed 4 variables of the MELD score separately to determine which factors were directly related to bacteremia. In the above mentioned study,[19] recipients above the age of 65 years showed significantly lower survival rates, whereas age above 55 years was found to be a significant risk factor for bacteremia in our study. However, old age is a well-known risk factor for bacteremia even in non-transplant patients.[20] Combined tumor, largely hepatoma, was more common in bacteremic patients than in other patients, however, was not significant.

Catheter-related infection was the main cause of bacteremia; this has also been reported in a previous study.[12] However, the common etiologic organisms such as methicillin-resistant *S. aureus* and coagulase-negative staphylococci differ between centers.[12,21,22] At our center, coagulase-negative staphylococci were found to be more common than *S. aureus*. Clinically, it is of importance to note that 88% of the staphylococci were methicillin-resistant. Therefore, it can be suggested that, whenever a patient develops fever, glycopeptide should be added empirically during the pending blood culture in addition to removing the catheter. Furthermore, 26.1% of the Gram-positive cocci were vancomycin-resistant enterococci, therefore, linezolid can be considered when a patient is febrile 48 to 72 hours after glycopeptide administration even when no growth is detected in the blood culture.

One-year survival rate showed a significant difference between the 3 groups, whereas 1-month survival rate did not differ between the 3 groups: bacteremia group 94.1%; non-bacteremic infection group, 95.7%; and no infection group, 95.3% (Fig. 1). Majority of the deaths occurred between 1 and 6 months. Posttransplant infection within 1 month occurs primarily due to surgical and technical complexity, wound infection, urinary tract infection, catheter-related infection, and pneumonia.[1,2] Our data revealed that a large percentage of events related to bacteremia occurred within 1 month, although death occurred between 1 and 6 months after transplant. Furthermore, long hospital stay along with hemodialysis or catheterization could be another factors responsible for bacteremia that contribute to the decreased survival rate in liver transplant recipients.[23] The limitations of our data are that, since this is a retrospective analysis, we could not identify the precise operational breakage during the transplant that could have an effect on the posttransplant clinical course and also could not evaluate biliary variation in donors, which could be an important factor. A large prospective study in the future can provide more informative data.

In conclusion, posttransplant bacteremia decreases the 1-year survival rate in liver transplant recipients. To reduce the occurrence of bacteremia, recipients with older than 55 years of age and UNOS class IIA need to be carefully monitored for bacteremia, and antibacterial agents should be changed or added for resistant organisms based on the epidemiologic data. Early catheter removal and preservation of renal function could improve posttransplant survival.

REFERENCES

1. Fishman JA, Rubin RH. Infection in organ-transplant

recipients. N Engl J Med 1998;338:1741-51.
2. Snydman DR. Infection in solid organ transplantation. Transpl Infect Dis 1999;1:21-8.
3. Kwak EJ, Kusne S. Risks and epidemiology of infections after liver transplantation. In: Bowden RA, Ljungman P, Paya CV, editors. Transplant infection. 2nd ed. Philadelphia: Lippincott Williams & Wilkins; 2003. p.120.
4. Wade JJ, Rolando N, Hayllar K, Philpott-Howard J, Casewell MW, Williams R. Bacterial and fungal infections after liver transplantation: an analysis of 284 patients. Hepatology 1995;21:1328-36.
5. Singh N, Gayowski T, Wagener MM, Marino IR. Predictors and outcome of early-versus late-onset major bacterial infections in liver transplant recipients receiving tacrolimus (FK506) as primary immunosuppression. Eur J Clin Microbiol Infect Dis 1997;16:821-6.
6. Singh N, Wagener MM, Obman A, Cacciarelli TV, de Vera ME, Gayowski T. Bacteremias in liver transplant recipients: shift toward gram-negative bacteria as predominant pathogens. Liver Transpl 2004;10:844-9.
7. George DL, Arnow PM, Fox AS, Baker AL, Thistlethwaite JR, Emond JC, et al. Bacterial infection as a complication of liver transplantation: epidemiology and risk factors. Rev Infect Dis 1991;13:387-96.
8. Kusne S, Dummer JS, Singh N, Iwatsuki S, Makowka L, Esquivel C, et al. Infections after liver transplantation. An analysis of 101 consecutive cases. Medicine (Baltimore) 1988;67:132-43.
9. Wagener MM, Yu VL. Bacteremia in transplant recipients: a prospective study of demographics, etiologic agents, risk factors, and outcomes. Am J Infect Control 1992;20:239-47.
10. Paya CV, Hermans PE, Washington JA 2nd, Smith TF, Anhalt JP, Wiesner RH, et al. Incidence, distribution, and outcome of episodes of infection in 100 orthotopic liver transplantations. Mayo Clin Proc 1989;64:555-64.
11. Kawecki D, Chmura A, Pacholczyk M, Lagiewska B, Adadynski L, Wasiak D, et al. Etiological agents of bacteremia in the early period after liver transplantation. Transplant Proc 2007;39:2816-21.
12. Singh N, Paterson DL, Gayowski T, Wagener MM, Marino IR. Predicting bacteremia and bacteremic mortality in liver transplant recipients. Liver Transpl 2000; 6:54-61.
13. Korean Network for Organ Sharing. Annual Report 2007. Available from: URL: http://www.konos.go.kr accessed 1 June 2008.
14. Cho WH, Kim YS. Landmarks in clinical transplantation in Korea. Yonsei Med J 2004;45:963-7.
15. Moon DB, Lee SG. Adult-to-adult living donor liver transplantation at the Asan medical center. Yonsei Med J 2004;45:1162-8.
16. Chang FY, Singh N, Gayowski T, Wagener MM, Marino IR. Fever in liver transplant recipients: changing spectrum of etiologic agents. Clin Infect Dis 1998;26:59-65.
17. Garner JS, Jarvis WR, Emori TG, Horan TC, Hughes JM. CDC definitions for nosocomial infections, 1988. Am J Infect Control 1988;16:128-40.
18. Simon DM, Levin S. Infectious complications of solid organ transplantations. Infect Dis Clin North Am 2001; 15:521-49.
19. Habib S, Berk B, Chang CC, Demetris AJ, Fontes P, Dvorchik I, et al. MELD and prediction of post-liver transplantation survival. Liver Transpl 2006;12:440-7.
20. Mellors JW, Horwitz RI, Harvey MR, Horwitz SM. A simple index to identify occult bacterial infection in adults with acute unexplained fever. Arch Intern Med 1987;147:666-71.
21. Candel FJ, Grima E, Matesanz M, Cervera C, Soto G, Almela M, et al. Bacteremia and septic shock after solid-organ transplantation. Transplant Proc 2005;37:4097-9.
22. Bedini A, Codeluppi M, Cocchi S, Guaraldi G, Di Benedetto F, Venturelli C, et al. Gram-positive bloodstream infections in liver transplant recipients: incidence, risk factors, and impact on survival. Transplant Proc 2007;39:1947-9.
23. Al Riyami D, Alam A, Badovinac K, Ivis F, Trpeski L, Cantarovich M. Decreased survival in liver transplant patients requiring chronic dialysis: a Canadian experience. Transplantation 2008;85:1277-80.