

Epidemiology and Risk Factors for Primary Bloodstream Infection (pBSI) in Solid Organ Transplant Recipients

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Abstract

Background: Bacteremia is a major cause of morbidity and mortality among solid organ transplant (SOT) recipients. This study aimed to describe the epidemiology and risk factors for pBSI during transplant admissions.

Methods: Retrospective evaluation of all SOT admissions at NewYork-Presbyterian Hospital (NYP) between 2006-2008. Patients without immunosuppressive medication (ISM) records or >1 transplant were excluded. pBSI were defined as central line-associated BSI (CLABSIs) or BSI without another known source.

Results: 1,615 transplant recipients were evaluated: 222 heart transplant (HT), 132 lung transplant (LT), 330 liver transplant (LT), 928 renal transplant (RT), and 3 intestinal transplant (IT). 108 episodes of pBSI occurred in 88 patients. Incidence rates of pBSI ranged from 1.23/1000 patient days for LT to 17.39/1000 patient days for IT. Median time from all transplants to pBSI was 8 days (IQR 4,19); median time to pBSI was similar between groups (p=0.25). Most common pathogens were coagulase-negative *Staphylococcus*, *Enterococcus* species (spp), and *Klebsiella* spp. 46 (43%) episodes of pBSI were due to resistant isolates. Overall crude mortality was 24%. Risk factors included: HT – intubation (OR=12.1, 95%CI=4.3, 33.8) and rejection (OR=4.7, 95%CI=1.6, 13.5); LT – hospitalization within the past 30 days (OR=3.0, 95%CI=1.3, 7.1), intubation (OR=9.7, 95%CI=4.2, 22.3), ≥2 major diagnostic procedures (OR=5.6, 95%CI=1.0, 30.0), and ≥2 major therapeutic procedures (OR=2.8, 95%CI=1.2, 6.2); RT – hospitalization within the past 30 days (OR=10.1, 95%CI=1.7, 60.9), intubation (OR=6.9, 95%CI=1.9, 25.8), ≥2 major therapeutic procedures (OR=6.0, 95%CI=1.3, 26.2), rejection (OR=8.0, 95%CI=1.8, 35.8), and receipt of mammalian target of rapamycin (mTOR) inhibitors (OR=5.6, 95%CI=1.5, 20.7).

Conclusions: pBSI are a major concern during SOT admissions, and inpatient procedures appear to pose significant risk. Stringent infection control practices are required to reduce morbidity and mortality related to pBSI following SOT.

Background

- Bloodstream infections (BSI) are common following solid organ transplantation (SOT) and are associated with increased graft loss and mortality.
- BSI are frequently secondary infections, and their incidence varies by organ transplanted, affecting 22.4-49% of liver, 3.5-76.7% of renal, 25% of lung, 61-69% of intestinal, and 15.8% of heart transplant recipients.^{1,3}
- In a large Spanish cohort, approximately half of BSI among SOT recipients were catheter-related or from an unknown source.⁴
- Little has been published regarding the epidemiology and risk factors for pBSI in the SOT population.

Methods

- IRB-approved retrospective cohort employing admission data from recipients of 1 SOT and complete ISM at NYP between 2006-2008.
- BSI defined as positive blood culture for any pathogen without cultures positive for the same organism at other body sites within the prior 14 days. With common skin contaminants, included cases for which ≥2 blood cultures obtained on separate occasions were positive within 2 days of each other.
- pBSI defined as CLABSIs or BSI of unknown source.
- Statistical analysis performed using SAS v9.3. Univariable comparisons performed using Chi-squared or Fisher's Exact test for categorical variables and Mann-Whitney test for continuous variables where appropriate (p-value <0.05 statistically significant). Multivariable analyses for determination of risk factors for pBSI performed using logistic regression models.

Results

Table 1: Characteristics Patients with pBSI by Organ Transplanted

	Heart	Lung	Liver	Kidney	Intestine	p-value
Transplants – no. (%)	222 (14)	132 (8)	330 (20)	928 (57)	3 (0.2)	
Patients with pBSI – no. (%)	25 (11)	3 (2)	44 (13)	13 (1)	3 (100)	<0.001
Episodes of pBSI	28	3	58	14	5	<0.001
Incidence Rate of pBSI (per 1000 patient days)	5.37	1.23	10.61	2.36	17.36	<0.001
Median Time to pBSI – days (IQR)	11 (6,28)	11 (2,73)	7 (4,14)	6 (4,9)	8 (8,46)	0.226
BSI Source						0.037
CLABSIs – no. (%)	23 (92)	2 (67)	31 (70)	7 (54)	3 (100)	
Unknown – no. (%)	2 (8)	1 (33)	13 (30)	6 (46)	0 (0)	
Male Gender – no. (%)	18 (72)	2 (67)	31 (70)	8 (62)	2 (67)	0.138
Median Age – yrs. (IQR)	51 (34,60)	55 (36,61)	54 (47,60)	51 (40,61)	0 (0,23)	0.056
Median Admission Charlson Score (IQR)	2 (1,3)	0 (0,2)	3 (1,4)	3 (2,3)	3 (3,3)	<0.001
Hospitalized within 30 days – no. (%)	8 (32)	0 (0)	14 (32)	2 (15)	2 (67)	0.545
Renal Failure – no. (%)	17 (68)	2 (67)	23 (52)	13 (100)	1 (33)	0.006
Hemodialysis – no. (%)	8 (32)	2 (67)	13 (30)	8 (62)	0 (0)	0.114
Diabetes Mellitus – no. (%)	7 (28)	1 (33)	8 (18)	3 (23)	0 (0)	0.636
Malignancy – no. (%)	0 (0)	0 (0)	13 (30)	0 (0)	0 (0)	0.002
Chronic Dermatitis – no. (%)	1 (4)	1 (33)	0 (0)	0 (0)	0 (0)	0.353
Required Intubation – no. (%)	14 (56)	3 (100)	24 (55)	5 (38)	0 (0)	0.539
Cardiac Catheterization – no. (%)	17 (68)	0 (0)	0 (0)	1 (8)	0 (0)	<0.001
Biopsy – no. (%)	22 (88)	1 (33)	12 (27)	2 (15)	1 (33)	<0.001
Median diagnostic procedures – no. (IQR)	0 (0,1)	0 (0,2)	0 (0,4)	0 (0,2)	0 (0,0)	1.000
Median therapeutic procedures – no. (IQR)	3 (2,4)	1 (1,1)	1 (1,2)	1 (1,2)	6 (4,17)	<0.001
CMV Infection – no. (%)	1 (4)	0 (0)	1 (2)	0 (0)	0 (0)	1.000
Rejection – no. (%)	16 (64)	3 (100)	17 (39)	10 (77)	2 (67)	0.013
Immunosuppressive Agent						
Calcineurin Inh – no. (%)	25 (100)	3 (100)	44 (100)	13 (100)	3 (100)	1.000
mTOR Inhibitor – no. (%)	0 (0)	1 (33)	1 (2)	5 (38)	1 (33)	<0.001
Anti-IL-2 Receptor Ab – no. (%)	16 (64)	3 (100)	24 (55)	6 (46)	2 (67)	0.387
Mycophenolate – no. (%)	3 (12)	0 (0)	0 (0)	4 (31)	0 (0)	0.002
Azathioprine – no. (%)	20 (80)	3 (100)	2 (5)	1 (8)	0 (0)	<0.001
Rituximab – no. (%)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	1.000
Crude Mortality – no. (%)	7 (28)	1 (33)	10 (23)	2 (15)	1 (33)	0.726

*Intestinal transplant data not included in statistical analysis

Table 2: Microbiology of pBSI by Organ Transplanted

Organism	Total	Heart	Lung	Liver	Kidney	Intestine
CONS	28 (25.9%)	11 (39.3%)	3 (100%)	10 (17.2%)	4 (28.6%)	0 (0%)
<i>Enterococcus</i> spp	25 (23.1%)	3 (10.7%)	0 (0%)	15 (25.9%)	4 (28.6%)	3 (60%)
<i>Klebsiella</i> spp	15 (13.9%)	4 (14.3%)	0 (0%)	9 (15.5%)	1 (7.1%)	1 (20%)
<i>S. aureus</i>	9 (8.3%)	0 (0%)	0 (0%)	6 (10.3%)	2 (14.3%)	1 (20%)
<i>E. coli</i>	7 (6.4%)	2 (7.1%)	0 (0%)	5 (8.6%)	0 (0%)	0 (0%)
<i>Candida</i> spp	5 (4.6%)	3 (10.7%)	0 (0%)	1 (1.7%)	1 (7.1%)	0 (0%)
<i>Enterobacter</i> spp	3 (2.8%)	1 (3.5%)	0 (0%)	2 (3.4%)	0 (0%)	0 (0%)
<i>Strep anginosus</i>	2 (1.9%)	0 (0%)	0 (0%)	1 (1.7%)	1 (7.1%)	0 (0%)
<i>Bacteroides</i> spp	2 (1.9%)	0 (0%)	0 (0%)	1 (1.7%)	1 (7.1%)	0 (0%)
<i>Morganella</i> spp	2 (1.9%)	1 (3.5%)	0 (0%)	1 (1.7%)	0 (0%)	0 (0%)
<i>Pseudomonas</i> spp	2 (1.9%)	1 (3.5%)	0 (0%)	1 (1.7%)	0 (0%)	0 (0%)
<i>Serratia</i> spp	2 (1.9%)	2 (7.1%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Others	6 (5.6%)	0 (0%)	0 (0%)	6 (10.3%)	0 (0%)	0 (0%)

Organism-specific definitions of resistance as follows: *Staphylococcus* spp - oxacillin; *Streptococcus*, *Actinomyces* and *Bacteroides* spp - penicillin; *Enterococcus* spp - vancomycin; *Enterobacteriaceae* except *Klebsiella* spp and *Aeromonas* spp - third-generation cephalosporins; *Klebsiella* spp - carbapenems; *Pseudomonas* and *Salmonella* spp - levofloxacin; *Acinetobacter* spp - ampicillin-sulbactam; *Candida* and *Cryptococcus* spp - fluconazole

Figure 2: Percentage of Resistant Isolates by Organ Transplanted

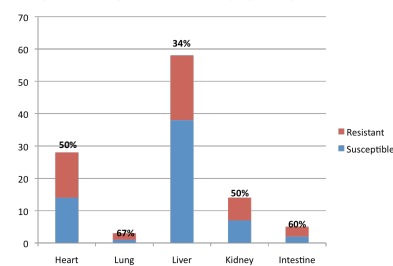


Figure 2: Probability of pBSI by Organ Transplanted

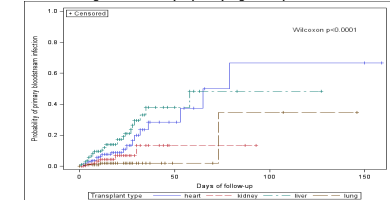


Table 3: Microbiologic Response to Treatment and 3-Month Recurrence Among Treated

Risk Factor for pBSI	OR	95% CI	p-value	Adjusted OR (95% CI)
Heart				
Intubation	9.63	(3.91, 23.72)	<0.001	12.07 (4.31, 33.78)
Rejection	3.53	(1.48, 8.41)	0.004	4.69 (1.63, 13.55)
Hospitalization in Previous 30 Days	1.96	(0.97, 3.94)	0.060	3.02 (1.29, 7.09)
Liver				
Intubation	10.24	(5.07, 20.70)	<0.001	9.69 (4.22, 22.26)
>2 Diagnostic Procedures	11.13	(3.00, 41.24)	<0.001	5.06 (1.04, 30.06)
>2 Therapeutic Procedures	3.05	(1.55, 6.00)	0.001	2.77 (1.23, 6.20)
Hospitalization in Previous 30 Days	5.76	(1.22, 27.22)	0.027	10.11 (1.68, 60.86)
Kidney				
Intubation	19.10	(5.89, 61.96)	<0.001	6.93 (1.86, 25.78)
>2 Therapeutic Procedures	6.80	(1.86, 24.89)	0.003	6.01 (1.38, 26.24)
Rejection	9.22	(2.52, 33.78)	<0.001	8.048 (1.81, 35.80)
mTOR Inhibitor	10.15	(3.21, 32.11)	<0.001	5.644 (1.54, 20.70)

Conclusions

- Risk of post-transplant pBSI varies by organ transplanted, with highest incidence among intestinal transplant recipients.
- Intubation and diagnostic and therapeutic procedures may serve as a proxy for clinical status. Therefore, severity of illness following transplant may increase risk of pBSI.
- Inpatient procedures appear to pose a significant risk for pBSI, underscoring the need for stringent infection prevention practices in procedural areas.

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