Clinical Significance of Donor-Unrecognized Bacteremia in the Outcome of Solid-Organ Transplant Recipients

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We evaluated the clinical significance of unrecognized bacteremia in the organ donor (i.e., blood culture results that were reported to be positive after transplantation) on the outcome of transplant recipients. Twenty-nine of 569 liver and heart donors (5%) had bacteremia at the time of organ procurement, but there were no documented instances of transmission of the isolated bacteria from the donor to the recipient. Unrecognized bacteremia in the donor does not have a negative clinical impact on the outcome of organ transplant recipients.

Nowadays, the shortage of suitable organ donors is the most important obstacle in the field of organ transplantation [1]. Some medical conditions, including the presence of an active infection in the donor, are important hindrances to organ donation. Donor-transmitted bacterial infections have been described extensively; in some cases, these infections have had an important impact on the outcome of the organ transplant recipient [2]. Bacteremia and sepsis at the time of the donor’s death introduce the risk of transmission of infection to the recipient, and, in most cases, prohibit the organs from being transplanted [3]. Several reports in the literature have described the grave consequences of transmission of bacterial infections from donors to recipients, including the development of arterial anastomotic disruption, graft infection, and sepsis in the recipients [4–8]. On the other hand, some authors have reported a low rate of infectious complications for patients who have received potentially infected grafts, which suggests that a less restrictive organ donation policy could be implemented [9, 10].

Bacterial infection is not unusual in potential organ donors. Use of medical devices (e.g., orotracheal tubes, intravascular catheters, urinary tubes), treatment of patients in areas of the hospital that have significant rates of bacterial contamination (such as intensive care units [ICUs]), and, most importantly, the presence of certain medical conditions in the potential organ donor are important factors that facilitate bacterial infection.

The present study was performed to investigate the influence of unrecognized bacteremia in the donor (determined by the results of cultures of blood samples that were obtained at the time of organ retrieval and that turned positive after transplantation) on the outcome of the recipient. Specifically, we searched for evidence of transmission of bacterial infection during the procedure; in addition, we assessed whether such infection had a deleterious influence on graft function or led to early morbidity and mortality.

Patients and methods. From January 1990 through March 1998, 569 patients underwent liver (n = 408) or heart (n = 161) transplantation at our institution. Serial blood samples were routinely obtained for culture from all donors at the time of organ procurement; they were also obtained from the recipient, following the protocol, at days 1, 7, 14, and 21 after transplantation and when clinically indicated. Blood samples were inoculated and processed in an automated blood culture testing system (BacT Alert, Organon Teknika; or BACTEC, Becton Dickinson Microbiological Systems). Blood cultures that yielded such organisms as Propionibacterium species, coagulase-negative staphylococci, Corynebacterium species, Veillonella parvula, Bacillus species, and Peptostreptococcus species were only considered indicative of true bacteremia if the same organism was isolated from at least 2 different blood cultures.

All donors were retrospectively reviewed for isolates recovered from blood cultures, patient age, duration of stay in the ICU, mean dose of dopamine and dobutamine, use of noradrenaline, presence of fever (temperature, ≥38.2°C), and antibiotic use during the 24 h before organ retrieval. The following information was retrospectively obtained from recipients whose donors had bacteremia at the time of organ retrieval: patient age and sex, presence of positive blood culture results, type of transplant (heart or liver), severity of underlying liver or heart disease, need for an urgent transplant procedure, occurrence...
of primary graft failure or thrombosis, need for surgical re-
tervention, duration of stay in the hospital and ICU, occurrence
of episodes of acute rejection, need for retransplantation, mean
levels of aspartate aminotransferase (AST) and creatinine during
the first 60 days after transplantation, and severe infections.
The same information was also obtained from a control group
that consisted of transplant recipients who were randomly cho-
sen from among patients who received transplants obtained
from a donor who did not have bacteremia (ratio of case pa-
tients to control subjects, 1:5). “Severe infection” was defined
as an infection with serious associated morbidity and mortality
that necessitated specific therapy and included the following:
bacteremia, peritonitis, abscess, pneumonia, meningitis, invasive
fungal infection and symptomatic cytomegalovirus disease.

Vancomycin and ceftazidime were administered to liver
transplant recipients from the time of anesthetic induction until
the third day after transplantation; thereafter, norfloxacin, 400
mg per day, was prescribed until discharge. (Patients who re-
ceived heart transplants were administered ceftazidime instead
of cefotaxime.) All patients received cotrimoxazole prophylaxis
during the first 6 months after transplantation. Upon reception
of donor blood cultures (usually 48–72 h after transplantation),
recipient samples from blood or other sites were obtained, and
thereafter, specific antimicrobial therapy was administered for
7–10 days.

Statistical analysis was performed by use of the SPSS software
package. Actuarial rates of graft and recipient survival were
calculated by means of the Kaplan-Meier method. Comparisons
between actuarial survival rates were made by means of the log
rank test. An unpaired Student’s t test or Wilcoxon rank sum
test were used to compare quantitative values, and the \(\chi^2\) or
Fisher’s exact test was used to analyze nominal values.

Results. Twenty-nine (5%) of 569 donors (18 liver donors
and 11 heart donors) had bacteremia at the time of organ do-
nation. The control group comprised 145 patients who had ran-
domly been chosen among patients who did not receive a trans-
plant from a donor with bacteremia. As is shown in table 1, donors
with bacteremia did not differ from those without bacteremia
with regard to patient age, duration of stay in the ICU, mean
dose of dopamine, use of dobutamine or noradrenaline, and use
of antibiotics during the 24 h before harvesting. Donors
with bacteremia were febrile more often than were donors with-
out bacteremia, although >60% of donors with bacteremia were
afebrile during the 24 h before organ retrieval.

Table 2 summarizes demographic and pretransplantation
characteristics of both groups of recipients. As expected, the 2
groups did not differ with regard to age, sex, severity of un-
derlying liver or heart disease, or the need for an urgent trans-
plant. As is shown in table 3, gram-positive bacteria were found
in 22 patients and gram-negative microorganisms were isolated
from 7 patients. Four patients had polymicrobial bacteremia
(Staphylococcus aureus and Streptococcus viridans in 2 patients;
Enterococcus faecalis and Acinetobacter baumannii in 1 patient;
and Pantoea agglomerans and Pantoea agglomerans in 1 patient).
Transmission of the bacteria that was isolated in the culture of
the blood sample obtained from the donor was not documented
in any of the recipients. On the basis of the results of the anti-
biotic susceptibility patterns of the bacteria isolated in blood
cultures, it was determined that the antibiotic combination used
in the prophylaxis of transplant recipients was not appropriate
for these isolates in 6 patients (4 patients with A. baumannii,
1 patient with Pseudomonas aeruginosa, and 1 patient with S.
marscenses and Enterobacter agglomerans).

Table 4 shows the comparison of the outcome of grafts and
patients according to the presence of unrecognized bacteremia
in the donor at the time of organ procurement. The incidence
of infectious complications and episodes of acute rejection was
also similar in both groups of patients. In an attempt to find

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Table 1. Comparison of the baseline characteristics of solid-organ donors who had bacteremia
with those of donors who did not have bacteremia.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Had bacteremia (n = 29)</th>
<th>Did not have bacteremia (n = 145)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean years ± SD</td>
<td>31.2 ± 16.5</td>
<td>30.4 ± 15.0</td>
<td>.79</td>
</tr>
<tr>
<td>Duration of stay at the intensive care unit, mean days ± SD</td>
<td>2.6 ± 2.3</td>
<td>1.9 ± 1.0</td>
<td>.11</td>
</tr>
<tr>
<td>Dose of dopamine used, mean µg/mL ± SD</td>
<td>8.2 ± 6.0</td>
<td>7.2 ± 5.8</td>
<td>.39</td>
</tr>
<tr>
<td>Dobutamine use, %a</td>
<td>6</td>
<td>11</td>
<td>.31</td>
</tr>
<tr>
<td>Noradrenaline use, %a</td>
<td>5</td>
<td>6</td>
<td>1.0</td>
</tr>
<tr>
<td>Fever in the 24 h before harvesting, %a</td>
<td>32</td>
<td>14</td>
<td>.004</td>
</tr>
<tr>
<td>Use of antibiotics before harvesting, %a</td>
<td>23</td>
<td>14</td>
<td>.14</td>
</tr>
</tbody>
</table>

*a These figures denote the percentage of donors in whom dobutamine or noradrenaline was used to maintain
hemodynamics and in those who developed fever or received antibiotics before harvesting.
more subtle differences in the outcome of patients and organs transplanted from donors with bacteremia and those without bacteremia, we compared the duration of hospitalization with either the mean level of creatinine (in heart transplant recipients) or AST/alanine aminotransferase (ALT; in liver transplant recipients) during the first 2 weeks after transplantation. No significant differences were found between the groups of patients with regard to these parameters, either.

Donors who had bacteremia did not differ from those who did not have bacteremia with regard to actuarial 60-day patient survival ($P = .9$). The percentage of recipients who required >1 transplant and the actuarial 60-day graft survival were also similar in both groups ($P = .88$).

Five recipients of organs transplanted from donors with bacteremia died within 60 days after transplantation. Two patients died of respiratory failure that was unrelated to infection (adult respiratory distress syndrome due to severe pancreatitis in a liver transplant recipient and massive pulmonary embolism in a heart transplant recipient), and 1 patient died of a myocardial infarction without any evidence of infection. One patient died as a result of graft failure after a second heart transplant. One liver transplant recipient died of multiorgan failure due to bacterial sepsis with Enterobacter cloacae (the donor was colonized with E. faecalis).

Discussion. The increasingly unbalanced ratio of organ supply to potential recipients has led most transplant centers to change to a less restrictive organ donor policy to increase the number of donors [11]. In this context, older patient age, a prolonged stay in the ICU, and hemodynamic instability are no longer considered contraindications for organ donation [1]. Several reports and some animal studies have alerted clinicians about the risks of bacterial transmission from donor to recipient, which has led to disastrous consequences, including sepsis, invasive arterial infection, and poor initial graft function [12–14]. On the basis of these reports, many transplant centers are reluctant to consider patients with bacteremia as potential donors, and only recently have some authorities begun to consider organ donations from patients with documented bacteremia if a sufficient course of antibiotic therapy has been administered to the potential donor [15].

The present study shows the absence of transmission of bacteremia from the donor to the recipient. Moreover, in our study, we have shown that the use of organs from donors with bacteremia is not associated with a higher incidence of poor graft function or with immunologic or surgical problems in the recipients. This finding contrasts with the findings presented in several case reports [4–7] that describe transmission of bacterial agents through organ transplantation that are associated with an unfavorable outcome in the recipient.

### Table 3. Microorganisms isolated from 29 solid-organ donors with bacteremia.

<table>
<thead>
<tr>
<th>Isolate</th>
<th>No. of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Staphylococcus aureus</td>
<td>8</td>
</tr>
<tr>
<td>Enterococcus faecalis</td>
<td>8</td>
</tr>
<tr>
<td>Acinetobacter baumannii</td>
<td>5</td>
</tr>
<tr>
<td>Streptococcus viridans</td>
<td>4</td>
</tr>
<tr>
<td>Streptococcus agalactiae</td>
<td>2</td>
</tr>
<tr>
<td>Coagulase-negative Staphylococcus</td>
<td>2</td>
</tr>
<tr>
<td>Enterococcus faecium</td>
<td>1</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>1</td>
</tr>
<tr>
<td>Serratia marcescens</td>
<td>1</td>
</tr>
<tr>
<td>Pantoea agglomerans</td>
<td>1</td>
</tr>
</tbody>
</table>

* Four patients had polymicrobial bacteremia.
Table 4. Clinical outcome of recipients of solid organs obtained from donors with bacteremia and donors without bacteremia.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Recipients of transplants obtained from donors</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>With bacteremia (n = 29)</td>
</tr>
<tr>
<td>Mortality</td>
<td>5 (17)</td>
</tr>
<tr>
<td>Graft thrombosis</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Graft primary nonfunction</td>
<td>2 (7)</td>
</tr>
<tr>
<td>Patients with surgical reintervention</td>
<td>5 (18)</td>
</tr>
<tr>
<td>Duration of hospitalization, mean ± SD</td>
<td>30.1 ± 16.2</td>
</tr>
<tr>
<td>Duration of intensive care unit stay, mean ± SD</td>
<td>11.2 ± 13.4</td>
</tr>
<tr>
<td>Patients who developed severe infection</td>
<td>11 (38)</td>
</tr>
<tr>
<td>Retransplantation</td>
<td>1 (4)</td>
</tr>
<tr>
<td>Acute rejection episodes, mean ± SD</td>
<td>1.07 ± 0.98</td>
</tr>
<tr>
<td>Serum creatinine, mean mg/dL ± SD</td>
<td></td>
</tr>
<tr>
<td>Day 3</td>
<td>1.2 ± 0.8</td>
</tr>
<tr>
<td>Day 7</td>
<td>1.03 ± 0.44</td>
</tr>
<tr>
<td>Day 14</td>
<td>1.01 ± 0.43</td>
</tr>
<tr>
<td>Serum alanine aminotransferase, mean IU/L ± SD</td>
<td></td>
</tr>
<tr>
<td>Day 3</td>
<td>120 ± 124</td>
</tr>
<tr>
<td>Day 7</td>
<td>238 ± 267</td>
</tr>
<tr>
<td>Day 14</td>
<td>178 ± 205</td>
</tr>
</tbody>
</table>

**NOTE.** Data are no. (%) of patients, unless otherwise indicated.

* No statistically significant differences were found for any of these variables.

Nevertheless, the design of our study does not warrant the assertion that organs from donors with bacteremia are safe in all circumstances. In fact, some degree of selection bias might have been present in our experience. Presumably, patients with positive results of blood culture and evident signs of sepsis were never considered as potential donors. Therefore, our selection criteria included stable patients with unrecognized bacteremia at the time of organ retrieval, which probably represents the subgroup of patients with positive results of cultures of blood samples with the most favorable profile. Recognition of these donors is not always easy in a clinical setting because, in our experience, >60% of the patients were afebrile during the 24 h before organ donation, and they did not require the use of additional drugs to maintain hemodynamics.

All of the recipients included in the study received wide-spectrum perioperative antimicrobial prophylaxis, and when it was learned that the donor had bacteremia, the recipients received 7–10 days of pathogen-specific antimicrobial therapy. The design of the study did not allow us to determine whether antibiotics effectively prevented the transmission of bacterial organisms from organ donors to recipients, but some authors have suggested that antimicrobial treatment of the recipient could prevent bacterial transmission from the donor [16]. In fact, Freeman et al. [17] recently reported a lack of transmission of bacterial and fungal microorganisms from donor to recipient owing to use of antimicrobial therapy, although in their experience, most donors were also treated with antibiotics because most organs were procured after the date of the positive blood culture result. Our results confirm this experience, although in the present study, only 20% of donors with bacteremia received antibiotics before organ donation, and 6 recipients were not treated with appropriate antimicrobial therapy during the first 72 h after transplantation.

Vascular and graft function problems have also been found to be related to bacteremia in the donor [6, 7, 13]. We did not find that the incidence of graft thrombosis, primary nonfunction, number of repeated laparotomies (most of them due to bleeding), and the need for retransplantation in recipients of transplants obtained from donors with bacteremia differed from those in the rest of recipients. Moreover, the possibility of major deleterious effects of unrecognized bacteremia in the donor in graft function was not likely, because mean levels of creatinine and AST/ALT (in liver transplant recipients) during the first weeks after transplantation and the total duration of stay in the hospital were similar in both groups.

Eighteen percent of the recipients of transplants obtained from donors with bacteremia died during the follow-up period, and in no case could the cause of the death be related to the presence of a positive result of blood culture in the donor. Actuarial survival rates were similar in both group of recipients.
Our study shows the absence of transmission of unrecognized bacteremia in the donor to the organ recipient, and it illustrates the lack of a deleterious effect that this has in graft function and survival, thus implying that these organs are perfectly adequate for transplantation. We do not know what kind of influence antimicrobial therapy had on this favorable outcome, but we think it is prudent to administer pathogen-specific antimicrobial therapy to organ recipients for several days. Our data do not support the use of organs obtained from donors with bacteremia and signs of sepsis, but it is possible that the decision of reject potential organ donations from patients with bacteremia should be reconsidered, because some of these organs could possibly be used. This approach can help increase the supply of organs that are available for transplantation.

Acknowledgments

We thank Paz Cebrián, Soledad Vereda, and Sofía Vázquez, from the Local Organ Procurement Office, for technical assistance. We also thank Dr. Rafael Delgado, for his critical review of the article in manuscript.

References