ORIGINAL ARTICLE

Positive Cultures of Organ Preservation Fluid Predict Postoperative Infections in Solid Organ Transplantation Recipients

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OBJECTIVE. The significance of positive cultures of organ preservation fluid (OPF) in solid organ transplantation is not known. We sought to describe the microbiology and define the clinical impact of positive OPF cultures.

DESIGN. Retrospective cohort study.

SETTING. Tertiary care hospital.

PATIENTS. A consecutive sample of all solid organ transplantations at our center between July 2006 and January 2009 was reviewed. A total of 331 allografts (185 kidneys, 104 livers, 31 pancreases, and 11 hearts) met the inclusion criterion of having OPF cultures taken from the transplanted allograft.

METHODS. Organisms recovered from OPF were classified as high or low risk according to their virulence. Clinical outcomes were compared between recipients of organs with positive OPF cultures and recipients of organs with negative OPF cultures.

RESULTS. OPF cultures were positive in 62.2% of allografts and yielded high-risk organisms in 17.8%. Normal skin flora constituted the majority of positive OPF cultures, while Enterobacteriaceae spp. and *Staphylococcus aureus* made up the majority of high-risk organisms. Recipients of allografts with positive OPF cultures developed more frequent bacterial infections, regardless of allograft type (relative risk, 2.39; 95% confidence interval [CI], 1.61–3.54). Moreover, isolation of a given organism in OPF samples was associated with the development of a clinical infection with the same organism, regardless of allograft type.

CONCLUSIONS. Positive cultures of OPF are common events in solid organ transplantation, frequently involve high-risk organisms, and are associated with the development of postoperative clinical bacterial infections. Further study is required to determine the optimal strategies for their prevention and management.

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Transmission of infection via the implantation of a contaminated organ is a potentially serious complication of solid organ transplantation (SOT). Many transplant centers perform routine intraoperative cultures of organ preservation fluid (OPF) in order to detect allograft contamination and prevent or treat infection in the recipient. However, neither the prognostic significance nor the optimal management of positive OPF cultures is known. As a result, recommendations for the management of positive OPF cultures rely on expert opinion and case series rather than comprehensive epidemiologic evidence.[1]

Several studies have described the microbiology of OPF, including more than 10 descriptive studies of renal allografts in the 1970s and 1980s.[2] In these series, cultures of OPF were positive in up to 23% of organs, with skin flora constituting approximately half of isolates and yeasts and Enterobacteriaceae together accounting for approximately 30% of isolates. A more recent study of 610 transplanted livers found that 48% of OPF cultures were positive, with a similar distribution of isolates.[3]

In these and other studies of hepatic and renal allografts, individual cases of donor-to-host microbial transmission have been described.[3,4] Nearly all of these cases involved either gram-negative bacteria or fungi. However, there has been no large, systematic study evaluating the clinical outcomes of SOT patients with or without positive OPF cultures. We therefore performed a retrospective cohort study with the aims of (1) describing the microbiologic features of modern-day OPF

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cultures and (2) determining whether positive OPF cultures are associated with an increased risk of postoperative adverse events in SOT.

METHODS

Study Design

In this retrospective cohort study, we evaluated infectious outcomes, long-term graft survival, and mortality in a cohort of patients who underwent SOT at our center. All SOT events taking place at the McGill University Health Centre between July 2006 and January 2009 were reviewed using the transplantation program database. This database includes prospectively collected clinical data and limited laboratory data for all SOT patients at our center. Transplantation events were included in the analysis if OPF samples from the transplanted allograft were collected for culture. Available donor information included age, cause of death, organ recovery center, and noninfectious comorbidities, as well as cytomegalovirus and human immunodeficiency virus status. Length of donor intensive care unit (ICU) stays and need for vasopressor drugs were unavailable. Recipient information included all relevant demographic and operative data, all drugs used in hospital, including antimicrobials and immunosuppressants, and all positive microbiologic results for the duration of patients' follow-up at our center. Clinical outcomes, including infections, graft survival, and time to ICU discharge, were prospectively abstracted from recipients' medical records by a medical archivist using standardized definitions. Surgical site infections (SSIs) were not recorded as a distinct entity in the transplant database. We therefore retrospectively abstracted the diagnosis of SSI via a chart review of all SOT patients, using current Centers for Disease Control and Prevention/National Healthcare Safety Network (CDC/NHSN) definitions.[5] No standardized protocol specifying the management of positive OPF cultures was in place during the study period.

Microbiologic Evaluation

The OPF used for all organs was unsupplemented Viaspan Cold Storage Solution (Barr Laboratories), which contained no antimicrobial additives. OPF samples were collected at the time of organ removal, inoculated directly into aerobic, anaerobic, and Myco/F lytic BACTEC liquid-media bottles (Becton, Dickinson), and incubated for a total of 5 (aerobic and anaerobic samples) or 21 days (myco/F samples). The volume of OPF aliquotted for culture was 10 mL. Cultures were classified as "high risk" if they yielded *Staphylococcus aureus*, β-hemolytic *Streptococcus* species, *Streptococcus pneumoniae*, *Enterococcus* species, gram-negative bacteria, any spore-forming anaerobic gram-positive bacteria, or fungi. All other positive cultures were defined as "low risk," including normal skin flora such as coagulase-negative *Staphylococcus* species and *Corynebacterium* species.

Perioperative Antimicrobial Prophylaxis

Clinical protocols in our institution during the study period called for the following perioperative prophylactic systemic antimicrobial regimens. Heart and kidney recipients received cefazolin 2 g intravenously (IV) 20–60 minutes before incision and 2 more doses at 8-hour intervals. Recipients of livers or combined kidney-pancreas transplantation received either cefazolin as above, plus ciprofloxacin 400 mg IV 60–120 minutes before incision, or ticarcillin-clavulanate 3.1 g IV 20–60 minutes before incision, with 3 more doses at 6-hour intervals. Fluconazole 200 mg IV was administered daily for 7 days to all liver and kidney-pancreas recipients during this time. Alternative regimens were used for patients with allergies to β-lactam antibiotics, according to their creatinine clearance.

Statistical Analysis

Baseline characteristics of recipients of allografts with positive OPF cultures were compared to those of recipients of allografts with negative OPF cultures by means of descriptive statistics (difference in means or proportions and the associated 95% confidence interval [CI]). For recipients of multiple sequential transplantations, these variables were averaged across time. Simultaneous transplantation of multiple organs was considered a single event, and OPF culture results were considered in aggregate. The percentage of cultures positive for each organism was determined for all organs as well as within subgroups defined by the type of organ. We estimated the risk ratios by measuring the association between any positive OPF cultures associated with a transplantation event and any postoperative clinical infection, as assessed by the treating physician within 90 days of surgery. A postoperative period of 90 days was chosen on the basis of the timing of postoperative infections in previous reports.[6] For SSIs, events occurring within a postoperative period of 30 days were analyzed, in accordance with current CDC/NHSN definitions. We also estimated risk ratios of the association between positive OPF cultures and a subsequent clinical infection within a 90-day period with the same organism as that identified in the OPF culture. Given the predominance of kidney and liver transplantations in our database, we also estimated the above risk ratios separately among patients receiving these organs.

Among kidney and liver transplantation recipients, a Kaplan-Meier approach was used to examine the change in probability of recipient survival and graft survival over time within groups of recipients of allografts with positive OPF cultures, compared to that in recipients of allografts with negative OPF cultures. Patients surviving beyond February 25, 2009, were censored. Hazard ratios were estimated with a Cox proportional-hazards model. We calculated the median number of days that recipients of allografts received at least 1 antimicrobial (defining an "antimicrobial-day") in the first 90 post-

TABLE 1. Baseline Characteristics of Organ Transplant Recipients at Time of Transplantation

Group and characteristics	OPF−	OPF+	Difference[a] (95% CI)
All organs			
N	108	182	
Age, mean, years (SD)	52.35 (12.41)	53.47 (12.22)	1.12 (−1.83, 4.08)
Male sex	73 (67.59)	118 (64.84)	−2.76 (−14.72, 9.21)
Simultaneous multiple organ transplant	9 (8.33)	20 (10.99)	2.65 (−5.00, 10.31)
Previous organ transplants	4 (3.70)	13 (7.14)	3.45 (−2.73, 8.65)
Diabetes	39 (36.11)	73 (40.10)	3.99 (−8.26, 16.26)
CMV D+/R−	18 (16.67)	19 (10.44)	−6.23 (−15.28, 2.83)
Kidney			
N[b]	78	105	
Age, mean, years (SD)	51.99 (12.81)	52.74 (12.90)	0.75 (−3.04, 4.54)
Male sex	51 (65.38)	67 (63.81)	−1.76 (−16.69, 13.54)
Simultaneous multiple organ transplant	7 (8.97)	19 (18.10)	9.12 (−1.72, 19.96)
Previous organ transplants	2 (2.56)	4 (3.81)	1.25 (−5.48, 7.13)
Diabetes	27 (34.62)	47 (44.76)	10.15 (−5.18, 25.47)
CMV D+/R−	13 (16.67)	12 (11.43)	−5.24 (−16.62, 6.15)
Deceased donor	57 (73.08)	92 (87.62)	14.54 (1.74, 27.35)
Liver			
N	25	69	
Age, mean, years (SD)	55.91 (9.69)	56.12 (10.69)	0.20 (−4.48, 4.89)
Male sex	19 (76.00)	46 (66.67)	−9.33 (−32.16, 13.49)
Simultaneous multiple organ transplant	2 (8.00)	3 (4.35)	−3.66 (−5.95, 20.86)
Previous organ transplants	2 (8.00)	8 (11.59)	3.59 (−14.27, 14.84)
Diabetes	9 (36.00)	22 (31.88)	−4.12 (−28.63, 20.40)
CMV D+/R−	4 (16.00)	7 (10.14)	−5.86 (−25.2, 7.54)
Pancreas			
N	9	22	
Age, mean, years (SD)	41.67 (9.39)	43.73 (9.86)	2.06 (−5.95, 10.07)
Male sex	7 (77.78)	17 (77.27)	−0.51 (−33.33, 32.32)
Simultaneous multiple organ transplant	6 (66.67)	16 (72.73)	6.06 (−23.75, 40.35)
Previous organ transplants	0 (0)	0 (0)	...
Diabetes	8 (88.89)	21 (95.45)	6.57 (−22.30, 35.43)
CMV D+/R−	2 (22.22)	3 (13.64)	−8.59 (−42.30, 16.73)
Heart			
N	5	6	
Age, mean, years (SD)	50.37 (8.28)	43.64 (12.03)	−6.73 (−20.71, 7.24)
Male sex	4 (80.0)	4 (66.67)	−13.33 (−78.16, 51.50)
Simultaneous multiple organ transplant	3 (60.0)	2 (33.33)	−26.67 (−100, 48.82)
Previous organ transplants	0 (0)	1 (16.67)	16.67 (−29.82, 63.15)
Diabetes	5 (20.0)	6 (33.33)	13.33 (−51.50, 78.16)
CMV D+/R−	1 (20.0)	0 (0)	−20.0 (−73.39, 33.39)

NOTE. OPF−, no. recipients (%) of allografts with negative OPF (organ preservation fluid) culture; OPF+, no. recipients (%) of allografts with positive OPF culture; CMV D+/R−, cytomegalovirus serostatus: donor positive, recipient negative.

[a] Difference in proportions of each variable between OPF− and OPF+, except for the age, where the difference is between the means.

[b] Two patients received multiple kidney transplantations during the study period, resulting in 185 kidneys for 183 recipients.

operative days. The Wilcoxon rank-sum test was used to compare the median duration of antibiotic therapy between patients receiving allografts with positive OPF cultures and those receiving allografts with negative OPF cultures. For recipients of multiple sequential transplantations, only the first transplantation event was included in the survival analysis and the analysis of antimicrobial use.

RESULTS

Baseline Characteristics

Between July 2006 and January 2009, 394 organs were transplanted. OPF culture results were available for 331 (84%) organs transplanted to a total of 290 recipients at 301 transplantation events (Table 1). There were no significant differ-

TABLE 2. Descriptive Microbiology of Organ Preservation Fluid (OPF) Samples

Culture result	Total organs	Kidney	Liver	Pancreas	Heart
Total	331 (100)	185 (100)[a]	104 (100)	31 (100)	11 (100)
High-risk organisms	59 (17.8)	31 (16.8)	17 (16.4)	9 (29.03)	2 (18.2)
Staphylococcus aureus	17 (5.14)	7 (3.78)	5 (4.81)	3 (9.68)	2 (18.18)
β-hemolytic *Streptococcus* spp.	12 (3.63)	5 (2.70)	5 (4.81)	1 (3.23)	1 (9.09)
Enterococcus spp.	13 (3.93)	7 (3.78)	6 (5.77)	0 (0)	0 (0)
Enterobacteriaceae	32 (9.67)	19 (10.27)	10 (9.62)	3 (9.68)	0 (0)
Other aerobic gram-negative bacilli	2 (0.60)	0 (0)	2 (1.92)	0 (0)	0 (0)
Anaerobic gram-negative bacilli	6 (1.81)	5 (2.70)	1 (0.96)	0 (0)	0 (0)
Clostridium spp.	5 (1.51)	3 (1.62)	1 (0.96)	1 (3.23)	0 (0)
Candida spp.	8 (2.42)	4 (2.16)	1 (0.96)	0 (0)	0 (0)
Other fungi	1 (0)	0 (0)	0 (0)	1 (3.2)	0 (0)
Low-risk organisms	147 (44.4)	75 (40.6)	55 (52.9)	14 (41.9)	4 (36)
Coagulase-negative *Staphylococcus* spp.	138 (41.69)	72 (38.92)	49 (47.12)	14 (45.16)	3 (27.27)
Other α-hemolytic *Streptococcus* spp.	5 (1.51)	2 (1.08)	3 (2.88)	0 (0)	0 (0)
Corynebacterium spp.	22 (6.65)	13 (7.03)	4 (3.85)	4 (12.90)	1 (9.09)
Propionibacterium spp.	22 (6.65)	12 (6.49)	6 (5.77)	3 (9.68)	1 (9.09)
Other	21 (6.34)	11 (5.95)	7 (6.73)	2 (6.45)	1 (9.09)
Negative	125 (37.76)	79 (42.70)	32 (30.77)	9 (29.03)	4 (45.45)

NOTE. Data are no. (%) of allografts. Totals may exceed 100% because some samples of OPF grew more than one organism.

[a] Two patients received multiple kidney transplantations during the study period, resulting in 185 kidney allografts for 183 recipients.

ences in baseline characteristics between patients in whom OPF culture was obtained and those for whom a culture was not obtained. Forty of the 290 patients underwent sequential transplantations of the same organ, simultaneous transplantation of multiple organs, or both.

Descriptive Microbiology of OPF Samples

Of 331 allografts from which OPF was analyzed, 125 (37.8%) were OPF culture negative, 147 (44.4%) yielded low-risk pathogens, and 59 (17.8%) grew high-risk pathogens (Table 2). Renal and cardiac allografts had lower proportions of positive OPF cultures (57.3% and 54.5%, respectively) than did hepatic and pancreatic allografts (69.2% and 71.0%, respectively). The proportion of allografts with OPF yielding high-risk organisms was similar for renal, cardiac, and hepatic allografts (16.8%, 18.2%, and 16.4%, respectively) but was higher for pancreatic allografts (29.0%; Fisher's exact test, $P = .42$). Enterobacteriaceae were the most commonly identified high-risk organisms for all organ types, except for cardiac allografts, for which *S. aureus* was most common. *Candida* species were recovered more frequently from the OPF of renal allografts (2.16%) than from that of other organs. Coagulase-negative *Staphylococcus* species were the most common low-risk organisms identified from OPF all organ types.

Outcomes

Patients were followed for a median of 417 days (range, 36–918). The risk of clinical bacterial infections occurring within 90 days after transplantation was 25% (28 of 114 allografts) among recipients of allografts with negative OPF. These infections were more frequent among recipients of allografts with positive OPF cultures, regardless of allograft type (relative risk, 2.39; 95% CI, 1.61–3.54; Figure 1). Positive OPF cultures remained a significant predictor of infections after adjustment for potential confounders, including age, prolonged use of antithymocyte globulin, and ICU admission (Table 3). This trend was similar for recipients of allografts harboring either low- or high-risk organisms. Moreover, for all recipients in aggregate, we found an association between isolation of a given organism in OPF samples and the development of a clinical infection with the same organism within 90 days of transplantation. The occurrence of such infections in recipients of renal and hepatic allografts is shown in Figure 1. Infection rates did not differ significantly when calculated over 30 or 90 days after transplantation.

Similarly, there was a consistent trend toward more SSIs among recipients of allografts with positive OPF cultures, compared to recipients of allografts with negative OPF cultures (all organ recipients combined: relative risk, 2.06; 95% CI, 0.97–4.37), although this association did not reach the $P = .05$ significance level (Table 4). Specific organisms isolated in OPF also appeared to be potentially predictive of increased risk of an SSI with the same organism when it was possible to calculate the relative risk (*Pseudomonas* species: relative risk, 8.01; 95% CI, 4.39–14.62; *Enterococcus* species: relative risk, 3.76; 95% CI, 0.95–14.98; coagulase-negative *Staphylococcus* species: relative risk, 1.68; 95% CI, 0.52–5.39).

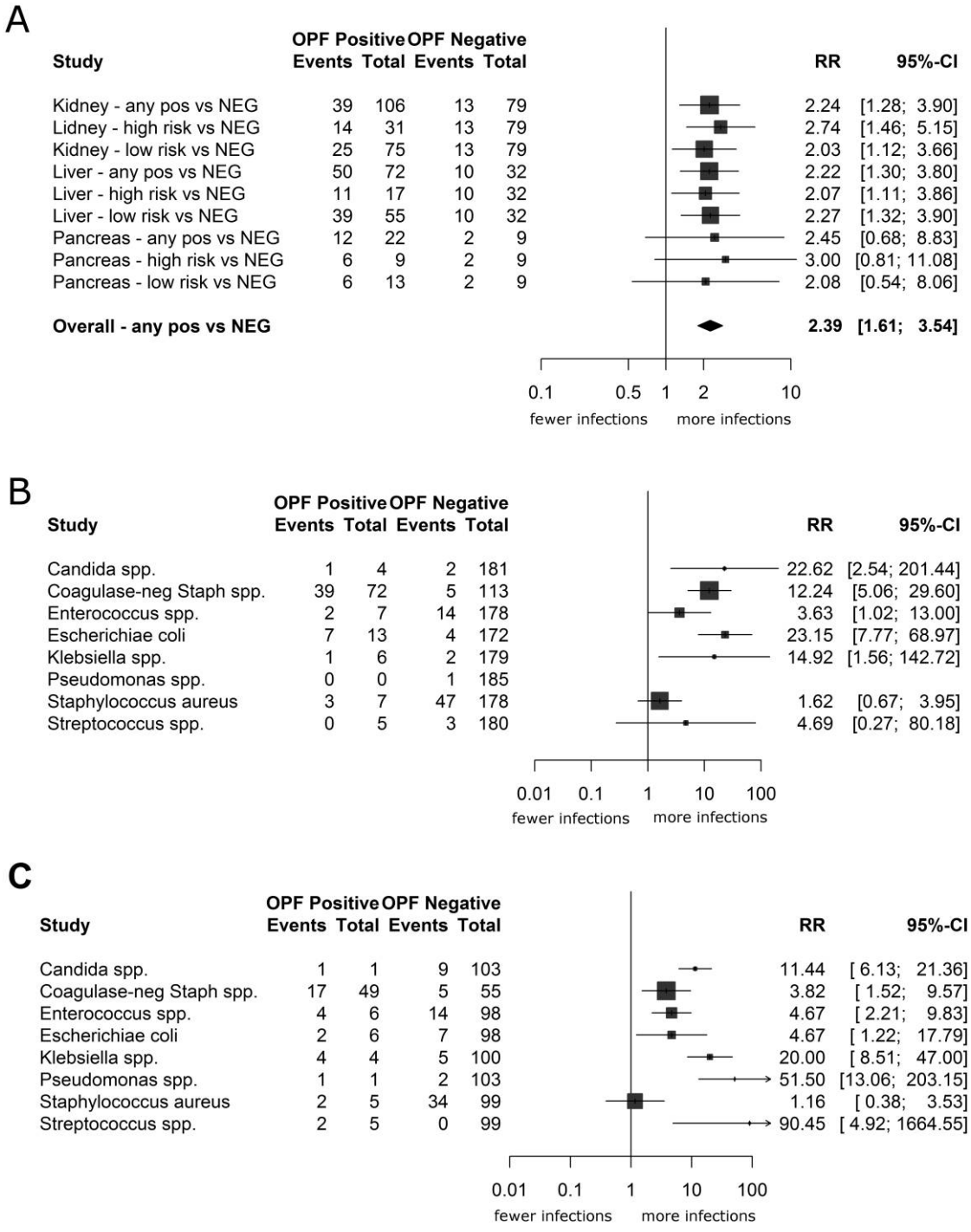

FIGURE 1. Relative risk of postoperative bacterial infection. *A*, Risk of postoperative bacterial infection within 90 days in recipients of transplants with positive OPF cultures, compared to that in recipients of transplants with negative OPF cultures was assessed according to the type of organ transplanted and whether OPF cultures yielded any growth, low-risk organisms only, or any high-risk organisms. *B*, *C*, The risk of a clinical postoperative infection with the same organism as that found in OPF (renal allografts, *B*; hepatic allografts, *C*) was also assessed. OPF, organ preservation fluid; events, number of postoperative infections; total, number of transplantations; RR, relative risk; CI, confidence interval; NEG, negative OPF cultures.

TABLE 3. Relation between the Development of Bacterial Infections within 90 Days of Transplantation and Selected Variables

Clinical variable	Crude OR (95% CI)	Adjusted OR (95% CI)
Positive OPF cultures	2.13 (1.51, 3.02)	1.72 (1.18–2.51)
Recipient age (as a continuous variable)		1.01 (0.98–1.03)
Any ICU admission		3.00 (1.77–5.10)
Use of ATG for >6 days		1.49 (0.61–3.63)

NOTE. From a multivariate logistic regression model. Odds ratios (OR) are reported here instead of relative risk because of the modeling technique used. ATG antithymocyte globulin; CI, confidence interval; ICU, intensive care unit; OPF, organ preservation fluid.

Bloodstream infections were analyzed separately, but it was not possible to demonstrate a significant association with OPF status (all organ recipients combined: relative risk 1.97; 95% CI, 0.66–5.92; Tables 4, 5, and 6).

Graft survival did not differ between recipients of allografts with positive OPF cultures and recipients of allografts with negative OPF cultures (all recipients combined: hazard ratio, 1.06; 95% CI, 0.62–1.79). Mortality did not differ between recipients of renal allografts with positive OPF cultures and recipients of renal allografts with negative OPF cultures (hazard ratio, 1.17; 95% CI, 0.25–2.97), but there was a trend toward increased mortality in recipients of hepatic allografts with positive OPF cultures relative to recipients of hepatic allografts with negative OPF cultures (hazard ratio, 1.69; 95% CI, 0.65–4.44; Figure 2). Liver and kidney-pancreas recipients were admitted to ICU per protocol, and time to ICU discharge did not differ by OPF status (hazard ratio, 0.86; 95% CI, 0.56–1.33).

Antimicrobial Use

Overall, the median number of antimicrobial-days (treatment and prophylactic) was similar between recipients of allografts with positive OPF cultures and recipients of allografts with negative OPF cultures (16 and 21 antimicrobial-days, respectively; Wilcoxon rank sum test, $P = .43$).

Predictors of Positive OPF Cultures

Although available donor information was limited, we observed that deceased kidney donors were more likely to yield positive OPF cultures than were living donors (relative risk, 1.61, 95% CI, 1.03–2.52). No other association was identified

TABLE 4. Number and Relative Risk (RR) of Surgical Site Infections (SSI) and Bloodstream Infections (BSI)

	OPF+		OPF−		
Outcomes comparison	No. infections (%)	No. recipients	No. infections (%)	No. recipients	RR (95% CI)
Risk of SSI within 30 days					
Renal allografts					
Any positive vs NEG	12 (11.32)	106	4 (5.06)	79	2.24 (0.75–6.67)
High-risk vs NEG	3 (9.67)	31	4 (5.06)	79	1.91 (0.45–8.05)
Low-risk vs NEG	9 (12.0)	75	4 (5.06)	79	2.37 (0.76–7.37)
Hepatic allografts					
Any positive vs NEG	18 (25.0)	72	4 (12.5)	32	2.00 (0.74–5.44)
High-risk vs NEG	3 (17.64)	17	4 (12.5)	32	1.41 (0.36–5.59)
Low-risk vs NEG	15 (27.27)	55	4 (12.5)	32	2.18 (0.79–6.01)
Risk of BSI within 90 days					
Renal allografts					
Any positive vs NEG	5 (4.71)	106	2 (2.53)	79	1.86 (0.37–9.36)
High-risk vs NEG	2 (6.45)	31	2 (2.53)	79	2.55 (0.38–17.30)
Low-risk vs NEG	3 (4.00)	75	2 (2.53)	79	1.58 (0.27–9.19)
Hepatic allografts					
Any positive vs NEG	7 (9.72)	72	1 (3.13)	32	3.11 (0.40–24.25)
High-risk vs NEG	1 (5.88)	17	1 (3.13)	32	1.88 (0.13–28.25)
Low-risk vs NEG	6 (10.90)	55	1 (3.13)	32	3.49 (0.44–27.71)

NOTE. Risk of postoperative SSI within 30 days and of postoperative BSI within 90 days in recipients of transplants with positive OPF cultures (OPF+) compared to recipients of transplants with negative OPF cultures (OPF−), according to the type of organ transplanted and whether OPF cultures yielded any growth, low-risk organisms only, or any high-risk organisms. OPF, organ preservation fluid; CI, confidence interval; NEG, negative OPF cultures.

TABLE 5. Timing of Infections

Infection type	OPF+	OPF−
Any bacterial infection	4 (0–59)	6.5 (1–29)
Surgical site infection	15 (0–29)	17 (5–27)
Bloodstream infection	7 (2–83)	18 (5–35)

NOTE. Data are median no. of days (range) to diagnosis of infection, within 90 days of transplantation, among 290 recipients of 331 organs.

between OPF culture positivity and donor characteristics, including cold or warm ischemia time, cause of donor death, donor diabetes status, or the factors detailed in Table 1.

DISCUSSION

Our study indicates that positive cultures of OPF are common events in SOT, frequently involve high-risk organisms, and are associated with the development of postoperative clinical bacterial infections. The percentage of positive OPF cultures in our cohort was higher than that in previous case series,[2-4,7] although the distribution of microorganisms was consistent with recent reports.[3,8] This higher-than-expected rate of OPF culture positivity may be attributable to the increased sensitivity of modern culture techniques, compared to that of older protocols relying on solid culture media only. Another consequence of liquid-culture use was the inability to quantitate microbial burden, precluding the correlation of outcomes with the level of contamination. The possibility also exists that OPF was contaminated after sample collection. However, the association between isolation of a given organism in OPF and the development of a postoperative clinical infection with the same organism argues that these culture results do not represent contamination after sample collection and supports a direct etiologic role of positive OPF cultures in subsequent clinical infections. These data suggest that organ procurement procedures are a potentially important risk factor for contamination of organs.

Previous studies have not established whether postoperative complications occur more frequently in the setting of positive OPF cultures. However, an emerging body of evidence among recipients of *Candida*-contaminated renal allografts has added to our knowledge of the significance of such cultures. Albano et al[6] linked the genotypes of *Candida* isolates recovered from graft site infections in 18 kidney recipients to those in either donor tissues or OPF, establishing a causal relationship between OPF cultures and subsequent infections. Prophylactic antifungal therapy may modify this risk, as 16 recipients of *Candida*-contaminated allografts who received prophylactic antifungal therapy did not develop infection during 1 year of follow-up.[8,9] Our study provides further evidence that positive OPF cultures for *Candida* sp. are associated with an increased risk of postoperative *Candida* infection in recipients of allografts, compared to that of negative OPF cultures. In addition, we found that this association between postoperative infection and OPF culture positivity extends to bacterial pathogens and argues strongly that implantation of contaminated organs can lead to significant infection after transplantation.

SSIs were also more frequent in recipients of allografts with positive OPF cultures than in recipients of OPF-culture-negative allografts, although the result was not statistically significant. The retrospective assessment of SSIs may have underestimated this outcome, and the small number of SSIs in each subgroup was a limiting factor in our ability to substantiate a true association. However, such an association would be plausible and is supported by the fact that specific organisms isolated in OPF also appeared to be predictive of increased risk of an SSI with the same organism when it was possible to calculate the relative risk. For bloodstream infections, the small number of infections limited our ability to demonstrate an association with OPF status, if one was present. Neither subgroup showed increased adverse outcomes of any kind in recipients of allografts harboring high-risk organisms compared to recipients of allografts harboring low-risk organisms. This may be related to the size of our cohort, or it may mean that low-risk organisms are as likely to cause postoperative complications as organisms designated high risk on the basis of previous studies.[2-4,6,8]

Despite the association of positive OPF cultures with postoperative infections, neither all-cause mortality nor graft survival differed by OPF status. Our cohort may have been insufficiently powered to demonstrate a difference between the two groups. However, other reports have indicated that infections in the early posttransplant period have serious consequences. Infection was the second-leading cause of mortality among a cohort of 1,218 kidney recipients,[10] and bloodstream infections in the first posttransplant month have been found to be a significant predictor of 1-year survival in liver transplant recipients.[11] This argues strongly for prevention of risk factors underlying such infections.

Surprisingly, postoperative infections caused by *S. aureus* did not seem to be associated with OPF culture status. This was the case for both overall postoperative infections (Figure 1*B*, 1*C*) and SSIs (0 *S. aureus* infections in 17 recipients of

TABLE 6. Site of Infections

Source of infection	Episodes (%)
Central venous catheter	13 (28.3)
Intra-abdominal	12 (26.1)
Surgical site infection	7 (15.2)
Primary	6 (13.0)
Urinary tract infection	2 (4.3)
Hemodialysis-associated	1 (2.2)
Pneumonia	1 (2.2)
Other	3 (6.5)
Total	46 (100)

NOTE. Sites of infections leading to bloodstream infections within 90 days of transplantation, among 290 recipients of 331 organs.

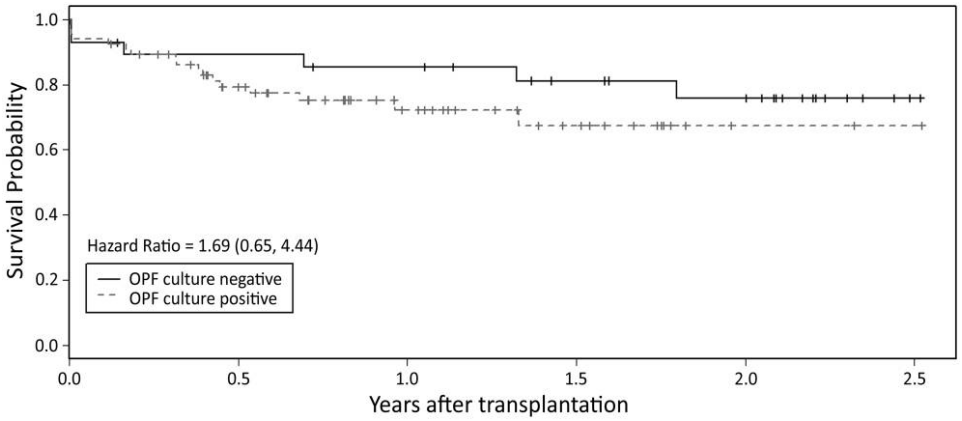

FIGURE 2. Kaplan-Meier estimate of recipient survival. Overall survival among recipients of hepatic allografts, comparing those receiving allografts with positive organ preservation fluid (OPF) cultures to those receiving allografts with negative OPF cultures. Hazard ratio includes 95% confidence interval in parentheses.

S. aureus–contaminated allografts vs 5 *S. aureus* infections in 309 recipients with negative OPF cultures; 1-sided Fisher's exact test, $P = .76$). This observation may reflect that oxacillin-resistant *S. aureus* is uncommon in our center's transplant population and that most isolates would be susceptible to the prophylactic antimicrobials in use during the study period.

We sought to assess whether differences in antimicrobial use could have affected infectious outcomes. Our results did not demonstrate a difference in antimicrobial use between recipients of allografts with positive OPF cultures and recipients of allografts with negative OPF cultures. This likely reflects that, in the absence of evidence-based strategies to guide therapy aimed at preventing the excess bacterial infections we observed, individualized physician responses to OPF culture results were heterogeneous. This comparison could have been confounded by the per-protocol use of some form of prophylactic postoperative antimicrobials in nearly all SOT recipients, depending on allograft type.

The regimens used during the study period were not designed to be active against *Enterococcus* species or oxacillin-resistant *Staphylococcus* species. Given the prevalence of such species in both OPF and postoperative infections in our study, it may be reasonable to target these organisms in all recipients, pending OPF culture results. Using this approach would result in an approximate increase of 1%–2% in vancomycin use, based on the volume of transplantations in our center and the mean vancomycin use in 130 hospitals in the United States.[12] Since the intensity of vancomycin use has been associated with increased prevalence of vancomycin-resistant organisms,[13] prophylactic regimens should be considered with care. Alternately, incorporating antibiotics into OPF may prove a useful strategy to limit transfer of viable organisms. In the setting of confirmed positive OPF bacterial cultures, further study is needed to define prophylactic antimicrobial regimens that prevent the development of overt infections, such as has been done with transplantation of organs obtained from bacteremic donors.[14]

In conclusion, positive cultures of OPF predict postoperative infections in SOT recipients. Further, the correlation between organisms recovered from OPF cultures and those from postoperative infections suggests that these infections stem directly from contamination at implantation. Future studies that will have to be performed include determining the predictors of positive OPF cultures, identifying strategies to prevent allograft contamination, and the optimal antimicrobial management of recipients of allografts with positive OPF cultures.

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REFERENCES

1. Fischer SA, Avery RK. Screening of donor and recipient prior to solid organ transplantation. *Am J Transplant* 2009;9(suppl 4): S7–S18.
2. Gottesdiener KM. Transplanted infections: donor-to-host transmission with the allograft. *Ann Intern Med* 1989;110(12): 1001–1016.
3. Cerutti E, Stratta C, Romagnoli R, et al. Bacterial- and fungal-

positive cultures in organ donors: clinical impact in liver transplantation. *Liver Transplant* 2006;12(8):1253–1259.
4. Calviño J, Romero R, Pintos E, et al. Renal artery rupture secondary to pretransplantation *Candida* contamination of the graft in two different recipients. *Am J Kidney Dis* 1999;33(1): E3.
5. Horan TC, Andrus M, Dudeck MA. CDC/NHSN surveillance definition of health care-associated infection and criteria for specific types of infections in the acute care setting. *Am J Infect Control* 2008;36(5):309–332.
6. Albano L, Bretagne S, Mamzer-Bruneel MF, et al. Evidence that graft-site candidiasis after kidney transplantation is acquired during organ recovery: a multicenter study in France. *Clin Infect Dis* 2009;48(2):194–202.
7. Sharma AK, Smith G, Smith D, et al. Clinical outcome of cadaveric renal allografts contaminated before transplantation. *Transplant Int* 2005;18(7):824–827.
8. Matignon M, Botterel F, Audard V, et al. Outcome of renal transplantation in eight patients with *Candida* sp. contamination of preservation fluid. *Am J Transplant* 2008;8(3):697–700.
9. Canaud G, Timsit MO, Zuber J, et al. Early conservative intervention for *Candida* contamination of preservative fluid without allograft nephrectomy. *Nephrol Dial Transplant* 2009;24(4): 1325–1327.
10. Linares L, Cofan F, Cervera C, et al. Infection-related mortality in a large cohort of renal transplant recipients. *Transplant Proc* 2007;39(7):2225–2227.
11. Bert F, Larroque B, Paugam-Burtz C, et al. Microbial epidemiology and outcome of bloodstream infections in liver transplant recipients: an analysis of 259 episodes. *Liver Transplant* 2010;16(3):393–401.
12. Polk RE, Fox C, Mahoney A, Letcavage J, MacDougall C. Measurement of adult antibacterial drug use in 130 US hospitals: comparison of defined daily dose and days of therapy. *Clin Infect Dis* 2007;44(5):664–670.
13. Fridkin SK, Edwards JR, Courval JM, et al. The effect of vancomycin and third-generation cephalosporins on prevalence of vancomycin-resistant enterococci in 126 U.S. adult intensive care units. *Ann Intern Med* 2001;135(3):175–183.
14. Freeman RB, Giatras I, Falagas ME, et al. Outcome of transplantation of organs procured from bacteremic donors. *Transplantation* 1999;68(8):1107–1111.