Nosocomial Infections with Vancomycin-Resistant *Enterococcus faecium* in Liver Transplant Recipients: Risk Factors for Acquisition and Mortality


The risk factors for acquisition of and mortality due to nosocomial infection with vancomycin-resistant *Enterococcus faecium* (VREF) in orthotopic liver transplant (OLT) recipients were studied at a tertiary care hospital; 32 VREF-infected OLT patients (cases) were compared with 33 randomly selected OLT recipients (controls). More antibiotics were administered preoperatively to cases (mean, 4 antibiotics per patient for 474 antibiotic-days) than to controls (mean, 1.8 antibiotics per patient for 131 antibiotic-days). Cases were more likely than controls to have received vancomycin therapy preoperatively and to have been hospitalized in the intensive care unit (ICU) preoperatively. Logistic regression revealed that the risk factors for acquisition of VREF infection were surgical reexploration and a prolonged stay in the surgical ICU postoperatively. In the cases, the risk factors for mortality were admission to the ICU preoperatively and hemodialysis. The mortality rate associated with polymicrobial bloodstream infections was 100% despite appropriate therapy. Sixteen and 18 cases received parenteral chloramphenicol and doxycycline, respectively, for treatment of VREF infection. There were no hematologic adverse effects attributed to chloramphenicol treatment. DNA analysis of selected *E. faecium* isolates suggested that infections were due to multiple clones. In summary, the source of VREF infection in OLT patients is the gastrointestinal tract. Antibiotic selective pressure may contribute to colonization. Infection with VREF is a predictor of morbidity and mortality in OLT patients.

Enterococci currently account for 12% of nosocomial infections and 8% of all nosocomial bacteremias [1]. Since 1988, vancomycin-resistant enterococci have caused clusters of nosocomial infections, and presently, these infection clusters are occurring with increased frequency [2-4]. In 1993, 14% of enterococcal isolates from critical care units were resistant to vancomycin [5]. While *Enterococcus faecium* accounts for only 10%-15% of all enterococcal isolates, *E. faecium* strains account for a great proportion of vancomycin resistance in intensive care units (ICUs) [6, 7]. In addition, the proportion of *E. faecium* causing bloodstream infections is increasing [8]. Nosocomial infections with vancomycin-resistant *E. faecium* (VREF) have been associated with increased mortality in some series [9-13], although this finding could not be demonstrated for patients with bloodstream infections in one series [14].

At Mount Sinai Hospital, a 1,200-bed acute tertiary care hospital in New York City, the frequency of enterococcal infectious episodes per the number of orthotopic liver transplants (OLTs) performed was 64 of 347 (18.4%) during 1990-1992 vs. 25 of 155 (16.1%) during 1993 (P = .5). In contrast, the proportion of VREF causing enterococcal infectious episodes increased from 15 of 64 (23.4%) during 1990-1992 to 15 of 25 (60%) during 1993 (P < .001). In 1994, we began an investigation to define the independent risk factors for acquisition of nosocomial VREF-associated infections, to identify the risk factors for mortality, and to review therapeutic strategies for the management of nosocomial VREF infections in liver transplant patients.

Materials and Methods

Epidemiologic Investigation

To examine the rate of enterococcal infections in liver transplants at Mount Sinai Hospital, we reviewed the microbiology records of all liver transplant recipients from January 1988 through July 1994 for enterococcal isolates from blood, wound specimens, peritoneal specimens, bile, and catheter tips.

Case Definition

A case was defined as any OLT patient for whom VREF was isolated from sterile body fluid or pus from a surgical wound during the study period (January 1993 through July 1994) and who met the Centers for Disease Control and Prevention (CDC) definition for nosocomial infection [15]. VREF infection was defined as hospital-acquired if the first positive culture for VREF was ascertained at least 48 hours after admis-
sion. Bacteremia secondary to wound infection required that the same organisms were isolated from the surgical wound and bloodstream. Polymicrobial bacteremia was defined as recovery of more than one organism from a single blood culture; different organisms from cultures of blood drawn within 24 hours were attributed to the original infectious process. Cases were identified by reviewing microbiology and medical records.

Analytic Epidemiologic Studies

Cases were compared with controls (33 randomly selected OLT patients without evidence of infection or colonization with VREF). Random numbers were used to select controls from a computer-generated list of all patients who had received OLTs during the study period. The medical records of cases and controls were reviewed for demographics, United Network Organ Sharing classification, indication and date of transplantation, immunosuppression, length of stay in the surgical ICU, date of VREF infection, body sites from which VREF was isolated, postoperative complications, and outcome. Death was attributed to infection in cases if the death certificate listed sepsis as the cause of death, the patient was receiving intravenous antibiotic therapy for VREF infection at the time of death, and the clinical course was consistent with sepsis.

Antibiotic Use

During 1993, perioperative bacterial prophylaxis consisted of intravenous cefotaxime (1 g every 8 hours) and vancomycin (1 g every 12 hours) for a total of 48 hours. On 1 January 1994, the use of vancomycin in the prophylactic regimen was discontinued. The regimen for small bowel decontamination consisted of SDD ointment (2% polymyxin E, 2% gentamicin, and 100,000 U of nystatin/g in an oral base) four times a day while the patient was intubated and 10 mL of SDD suspension (polymyxin E, 100 mg; gentamicin, 80 mg; and nystatin, 2 million U/10 mL) four times a day thereafter. The medical records were reviewed for administration of antibiotics before transplantation, treatment of VREF infection, and side effects of treatment. To assess the impact of preoperative antibiotic therapy, the numbers of antibiotics and antibiotic-days (the sum of the number of days each antibiotic was administered) during hospitalization were evaluated.

Microbiological Identification Tests

Isolates recovered from clinical specimens were identified as E. faecium by the automated system MicroScan (Baxter Diagnostics, Deerfield, IL). MICs of vancomycin, penicillin, and ampicillin were measured by a microbroth dilution test with use of the MicroScan according to the manufacturer’s directions. Resistance to vancomycin was defined as an MIC of >16 µg/mL [16]. Standardized disk diffusion tests with Mueller-Hinton agar were performed on all VREF isolates to confirm resistance to vancomycin and to determine susceptibility to chloramphenicol, doxycycline, ciprofloxacin, rifampin, imipenem, and trimethoprim-sulfamethoxazole (TMP-SMZ) [17].

DNA Analysis

Pulsed-field gel electrophoresis of a Smal digest of genomic DNA was performed as previously described [18]. Southern blot hybridization with a vanA specific DNA probe was performed according to standard techniques [19].

Statistical Analysis

Data were abstracted by means of a standardized form and were analyzed with use of Epi-Info Version 5.01 software (CDC, Atlanta). Proportions were compared by using the Fisher’s exact or χ² test; odds ratios and 95% confidence intervals were also calculated. Continuous variables were compared by the Student’s t or Wilcoxon rank-sum test. Multivariate analysis was done with use of PC SAS Proc Logistic (SAS Institute, Cary, NC). A stepwise procedure was used in the development of preliminary logistic regression models, and first-order interaction terms were evaluated. Final models included variables significant at a P value of <.1 in stepwise analysis. All probabilities were two-tailed.

Results

From 1 January 1993 through 31 July 1994, 228 patients received 279 OLTs. The monthly distribution of new patients with VREF infection during the study period is shown in figure 1. Nosocomial infection with VREF was documented in 36 OLT patients. VREF was the most common organism recovered from infected OLT patients during the study period.

Thirty-two OLT patients in whom VREF infection developed during hospitalization for OLT surgery (cases) were ana-
lyzed. Four patients were excluded from the analysis as VREF infection developed 104–568 days (mean, 301 days) after transplantation. Three of the four patients died of septic shock secondary to perforated vissus, peritonitis, and polymicrobial bacteremia, respectively. The fourth patient had biliary peritonitis secondary to T tube removal.

All VREF infections were nosocomially acquired. When the first VREF-positive culture was ascertained, 25 cases (78%) were in the surgical ICU. The length of stay to the first VREF-positive culture was 7–92 days (mean, 34.9 ± 20.3 days). Infection was acquired 2–54 days (mean, 18.8 ± 12 days) after the operation. VREF was isolated from multiple specimens from 27 cases (84.4%), including blood (12), peritoneal fluid (23), surgical wound specimens (17), abscess cavity specimens (8), liver tissue specimens (4), hematoma specimens (5), bile (3), and pleural fluid (3). Twenty-six cases (81.3%) had polymicrobial infections, including 10 fungal infections. VREF was the only organism isolated from six cases.

Twelve cases (37.5%) had bloodstream infections with VREF. In 10 cases, VREF bloodstream infections were related to intraabdominal infections; two cases had catheter-related VREF bloodstream infections. Copathogens were isolated from the VREF-positive cultures of blood from nine cases; these pathogens included *Pseudomonas aeruginosa*, 4; *Enterobacter cloacae*, 2; *Klebsiella pneumoniae*, 1; Acinetobacter species, 1; *Cryptococcus neoformans*, 1. In addition, five cases had non-VREF bloodstream infections associated with intraabdominal infections due to multiple pathogens (*K. pneumoniae*, 2; *P. aeruginosa*, 1; *E. cloacae*, 1; and *Acinetobacter* species, 1).

**Analytic Epidemiology**

**Cases vs. controls.** To assess the risk factors associated with acquisition of VREF infection, 32 cases were compared with 33 controls (VREF-negative OLT recipients). The demographics and baseline clinical characteristics of the two groups were similar. Cases were significantly more likely than controls to have been hospitalized in the medical ICU before transplantation (table 1).

The postoperative complications of cases and controls were compared (table 2). In the postoperative period, 29 cases (91%) required reexploration: 13 underwent reexploration once; 8, twice; and 8, three or more times. Fourteen cases (44%) had disruption of the continuity of the gastrointestinal tract: biliary leak, 9; intestinal perforation, 2; anastomotic dehiscence, 2; and esophageal rupture, 1. Thirteen cases (41%) required retransplantation because of primary nonfunction (5), rejection (3), hepatic artery thrombosis (1), portal vein thrombosis (2), and recurrent hepatitis (2). Four cases required a third OLT because of primary nonfunction (2) and rejection (2). VREF infections were associated with an increased length of total hospital stay and an increased number of days in the surgical ICU (table 2).

Twelve controls (36.4%) had postoperative infections. Five controls required reexploration: four underwent reexploration once, and one underwent reexploration three times. Sites of infection in the controls included catheter, 3; abscess, 4; peritoneum, 5; deep surgical wound, 2; and superficial wound, 2. The infection was caused by a single pathogen in nine controls, and one had a mixed infection; cultures were negative for two controls. There were three catheter-related bloodstream infections caused by *Staphylococcus aureus*. In addition, there were three bloodstream infections related to intraabdominal infections (*P. aeruginosa*, 1; *E. cloacae*, 3; and *K. pneumoniae*, 1). Fungal infections were not observed in the controls. Two (6%) of the controls died of septic shock related to bloodstream infections (*P. aeruginosa*, 1; and *K. pneumoniae*, 1).

Multivariate analysis revealed that the significant independent risk factors for acquisition of VREF infection were increased number of reexplorations and length of stay in the surgical ICU (table 3).

**Mortality due to VREF infection.** Sixteen cases (50%) died; eight died of infection as the primary cause, and seven died of infection as a contributing cause. One patient died of brain death secondary to graft failure. When we considered the entire group of cases and controls, VREF infection itself was a strong predictor of mortality (*P* < .0001). Fifteen (58%) of 26 cases with polymicrobial infections died compared with one (17%) of six cases with monoinfection (*P* = .08). Of the 12 cases with VREF bacteremia, nine (100%) of nine with polymicrobial bacteremia died compared with none of three with bacteremia due to VREF alone (*P* = .04). Multivariate analysis revealed that the significant independent risk factors for mortality were hospitalization in the ICU preoperatively and hemodialysis (table 3). The number of reexplorations, although an independent risk factor for acquisition of VREF infection, was not statistically significant in the logistic regression of risk factors for mortality.

**Antibiotic use.** Fifteen cases and 11 controls had received antibiotic therapy (including quinolones, β-lactam agents, and vancomycin) preoperatively (*P* value was not significant). Five cases and no controls received vancomycin treatment before surgery (*P* = .02). Overall, more antibiotics were administered preoperatively to cases (mean, 4 antibiotics per patient for 474 antibiotic-days) than to controls (mean, 1.8 antibiotics per patient for 131 antibiotic-days) (*P* = .04). There were no differences in perioperative antibiotic prophylaxis or use of small bowel decontamination between the two groups.

After the diagnosis of VREF infection, 18 cases were treated with doxycycline for a total of 228 days (mean, 12.6 days per patient; range, 1–34 days); 16 cases were treated with chloramphenicol (12.5 mg/kg every 6 hours) for a total of 214 days (mean, 14.2 days per patient; range, 2–25 days). Six (37.5%) of the cases who received chloramphenicol therapy died (five had polymicrobial bacteremia, and one had disseminated aspergillosis). Cases were monitored for neutropenia and thrombocytopenia or elevated values of liver function.
tests as adverse effects of chloramphenicol or doxycycline therapy. Reversible neutropenia (absolute neutrophil count, <1,000/mm³) developed in five cases. There was no statistical difference in the incidence of neutropenia in patients who were treated with chloramphenicol vs. those who did not receive chloramphenicol treatment.

Elevated values of liver function tests were attributed to rejection if there was a pathological diagnosis consistent with rejection. There were no instances of hepatotoxicity attributed to administration of doxycycline. After the first VREF-positive culture, 17 cases received vancomycin therapy (total, 259.93 g; mean, 16 g per patient). Additional antibiotics used for treatment of VREF infections included ampicillin/sulbactam (5 cases), TMP-SMZ (3), amikacin (2), imipenem (2), and rifampin (2).

**Characteristics of VREF isolates.** All isolates were resistant to ampicillin. Susceptibilities to additional antibiotics were

<table>
<thead>
<tr>
<th>Variable</th>
<th>Cases (n = 32)</th>
<th>Controls (n = 33)</th>
<th>OR (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reexploration</td>
<td>29 (91)</td>
<td>5 (15)</td>
<td>54.133 (11.808–248.164)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Retransplantation</td>
<td>13 (41)</td>
<td>2 (6)</td>
<td>10.605 (2.153–52.238)</td>
<td>.001</td>
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<tr>
<td>Hepatic artery thrombosis</td>
<td>7 (22)</td>
<td>0</td>
<td>19.706 (1.075–361.260)</td>
<td>.004</td>
</tr>
<tr>
<td>Biliary leak</td>
<td>9 (28)</td>
<td>0</td>
<td>27.085 (1.502–488.475)</td>
<td>.001</td>
</tr>
<tr>
<td>Hemodialysis</td>
<td>20 (63)</td>
<td>8 (24)</td>
<td>5.208 (1.502–488.475)</td>
<td>.002</td>
</tr>
<tr>
<td>Rejection</td>
<td>19 (59)</td>
<td>14 (42)</td>
<td>2.779 (1.075–361.260)</td>
<td>.004</td>
</tr>
<tr>
<td>Neutropenia</td>
<td>5 (16)</td>
<td>1 (3)</td>
<td>1.984 (0.739–5.322)</td>
<td>.17</td>
</tr>
<tr>
<td>Death</td>
<td>16 (50)</td>
<td>2 (6)</td>
<td>5.926 (0.652–53.872)</td>
<td>.08</td>
</tr>
</tbody>
</table>

**NOTE.** OLT = orthotopic liver transplant; VREF = vancomycin-resistant *Enterococcus faecium.*

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<table>
<thead>
<tr>
<th>Variable</th>
<th>Cases (n = 32)</th>
<th>Controls (n = 33)</th>
<th>OR (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of reexplorations</td>
<td>2.59 ± 1.94</td>
<td>0.5 ± 0.79</td>
<td>5.208 (1.502–488.475)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Hospital days</td>
<td>75.5 ± 35.4</td>
<td>32.2 ± 17.2</td>
<td>2.779 (1.075–361.260)</td>
<td>.001</td>
</tr>
<tr>
<td>Days in surgical intensive care unit after transplantation</td>
<td>27.9 ± 20.5</td>
<td>7.1 ± 8.08</td>
<td>1.984 (0.739–5.322)</td>
<td>.17</td>
</tr>
</tbody>
</table>

**NOTE.** OLT = orthotopic liver transplant; VREF = vancomycin-resistant *Enterococcus faecium.*
Table 3. Results of logistic regression of the risk factors for acquisition of vancomycin-resistant Enterococcus faecium infection and mortality in orthotopic liver transplant patients.

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Adjusted OR (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acquisition</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Repeated exploratory laparotomy</td>
<td>3.2596 (1.5204–6.9883)</td>
<td>.0024</td>
</tr>
<tr>
<td>Days in surgical intensive care</td>
<td>1.1003 (1.0205–1.1863)</td>
<td>.0128</td>
</tr>
<tr>
<td>Hemodialysis</td>
<td>3.4415 (0.7560–15.6672)</td>
<td>.1100</td>
</tr>
<tr>
<td>Mortality</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Days in intensive care unit before transplantation</td>
<td>24.4566 (2.7899–214.3898)</td>
<td>.0039</td>
</tr>
<tr>
<td>Hemodialysis</td>
<td>10.1706 (1.1293–91.5958)</td>
<td>.0560</td>
</tr>
<tr>
<td>Repeated exploratory laparotomy</td>
<td>1.5812 (0.9052–2.7622)</td>
<td>.1074</td>
</tr>
</tbody>
</table>

available for 29 VREF isolates. Of these isolates, 93% were susceptible to chloramphenicol; 64%, to doxycycline; 20%, to TMP-SMZ; 7%, to ciprofloxacin; and 7%, to rifampin. Twenty-six clinical VREF isolates from 26 cases were tested for molecular relatedness by using pulsed-field gel electrophoresis; 17 distinct patterns were found. Twenty (77%) of 26 isolates hybridized to the vanA-specific DNA probe.

Discussion

Vancomycin-resistant enterococci have caused clusters of nosocomial infections since 1988 [2]. In 1991, outbreaks of these enterococci were reported in 38 hospitals in New York, and these outbreaks are currently occurring with increased frequency [8, 9, 14, 19]. At our institution, we noted that the number of infectious episodes caused by VREF in OLT patients in 1993 was significantly higher than that in the years 1988–1992. The genetic heterogeneity of the VREF isolates analyzed suggests that the infections were due to multiple clones and not to the dissemination of one epidemic strain [20]. The stable number of new patients with VREF infection per month throughout the study period further supports the hypothesis that these isolates have become endemic in our institution.

Resistance to vancomycin in 77% of the isolates analyzed was due to the vanA gene; this finding is in agreement with other reports from hospitals in the United States [7, 14]. The vanA gene is known to be located on transposons [7, 19, 21]. Dissemination of specific strains of VREF within a hospital has been documented [13, 22, 23]; in many cases, however, multiple strains are distributed in the hospital environment, and the mode of transmission is unproven [8, 24, 25].

In our institution, the rates of VREF infection during the study period were highest among liver transplant patients. Twenty-two percent of all VREF isolates were recovered from these patients. Severe underlying disease, prolonged hospitalization, therapy with multiple antibiotics (including vancomycin), renal failure, and general immunosuppression have been previously associated with nosocomial infections due to VREF [12, 14, 19, 25]. In liver transplant recipients, additional risk factors coexist, including exogenous immunosuppression, liver failure, and surgery.

The most common site of infection in our patient population was the abdomen. Fifteen cases underwent surgical intervention of the gastrointestinal tract following orthotopic liver transplantation. Supportive evidence from surveillance stool cultures has implicated the patients’ gastrointestinal flora as the source of VREF infections in pediatric recipients of liver transplants [26]. In another report [27], VREF colonization before orthotopic liver transplantation increased the rates of intra-abdominal infection and was highly associated with mortality.

Cases were more likely than controls to have been admitted to the ICU before transplantation. Only the most debilitated patients, including those with variceal bleeding or stage 4 encephalopathy, were admitted to the ICU. Such patients are likely to have multiple intravascular devices for monitoring and support and are more likely to be treated empirically with vancomycin. An increased number of reexplorations and length of stay in the surgical ICU postoperatively were independent risk factors for acquisition of VREF infection. Compared with controls, cases had increased numbers of postoperative complications, including retransplantation, hepatic artery thrombosis, biliary leak, and hemodialysis.

VREF infections were associated with increased morbidity; this increased morbidity was shown by significantly increased hospital stays and longer hospitalizations in the surgical ICU. Cases also had increased mortality compared with controls. Independent risk factors for mortality were admission to the ICU before transplantation and hemodialysis. Both factors reflect an increased severity of illness. Multiple reexplorations, although a risk factor for acquisition of infection, were not a risk factor for mortality. When we considered the entire group of liver transplant patients, both cases and controls, the presence of a VREF infection was a strong predictor of mortality. Of the cases, 81.3% had polymicrobial infections, thus making it difficult to attribute mortality exclusively to VREF infection. Only one of the six cases for whom VREF was the only organism causing infection died. The cause of this patient’s death was graft failure.

The mortality rate among the cases with VREF bacteremia was 75%. Enterococcal bacteremia was known to be associated with a crude mortality rate of 33%–68% before the emergence of vancomycin-resistant enterococci [28, 29]. Two previous studies [30, 31] have shown that the mortality rate associated with Enterococcus faecalis bloodstream infection is higher than that associated with Enterococcus faecalis bloodstream infection. In another study [14], however, the mortality rate associated with vancomycin-resistant enterococcus bacteremia was not significantly higher than that associated with vancomycin-susceptible enterococcus bacteremia after controlling for severity of illness.

Enterococcal bacteremia is often preceded by septic shock and polymicrobial bacteremia; thus, it may be more often a
marker of a severe underlying disease than the immediate cause of death [32]. Nine (75%) of the VREF bloodstream infections were mixed with gram-negative bacilli, while the mortality rate associated with polymicrobial bloodstream infection was 100%. Bloodstream infection due to gram-negative organisms remains a leading cause of morbidity and mortality after surgery and in critically ill patients [33].

In one study [34], appropriate antibiotic therapy was shown to reduce mortality due to enterococcal infection even when adjustments were made for polymicrobial etiology, prior surgery, and nosocomial acquisition. Therapeutic options for VREF infection are limited and usually include chloramphenicol or doxycycline [35,36]. Ninety-three percent of our isolates were susceptible to chloramphenicol. Administration of chloramphenicol as monotherapy for VREF infection in 16 cases did not have an impact on reducing mortality, but only the most severely ill patients, including those with bacteremia, received chloramphenicol therapy.

All patients with polymicrobial infections were treated with multiple antibiotics. We did not use chloramphenicol in combination with other agents with in vitro activity against VREF, such as doxycycline and rifampin. Chloramphenicol was not associated with hematologic side effects. Resistance to the administered agents did not occur in recurrent VREF isolates from the same patient.

In one report on the use of chloramphenicol for the treatment of VREF infections [35], the mortality rate remained high among patients with VREF bacteremia. In that report, seven of 16 patients treated with chloramphenicol had VREF bacteremia; six patients died. Two of the 16 patients were solid organ transplant recipients; both survived, but neither of them had VREF bacteremia. Further evaluation of the use of chloramphenicol in solid organ transplant recipients may be needed in a multicenter prospective study.

The impact of infection control measures on reducing the risk for colonization and infection with VREF has been controversial. Use of gloves and gowns has been shown to control transmission of glycopeptide-resistant enterococci from U.S. hospitals. Am J Med 1991;91(3B):72S–5S. Ninety-three percent of our isolates received chloramphenicol therapy.

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Guidelines on reduced antimicrobial use and, in particular, vancomycin use in tertiary care hospitals may need reevaluation. As the number of VREF infections increase, chloramphenicol and doxycycline will receive increased usage. Clinical trials of a new synthetic streptogramin derivative—quinupristin/dalfopristin (Synercid, Rhone-Poulenc-Rorer Pharmaceuticals, Collegeville, PA)—with in vitro activity against VREF are under way, and this agent may prove of value in treating VREF infections [37].

In summary, because of the nature of their disease and extensive surgery, liver transplant patients are at increased risk for postoperative infections with pathogens of the gastrointestinal tract. The presence of multiple VREF clones in OLT patients suggests that the antibiotic selective pressure and especially the use of vancomycin may account for colonization. We would discourage the use of vancomycin as perioperative prophylaxis in institutions that still employ this regimen. VREF infection may be an indicator of a generalized debilitated state associated with increased morbidity and mortality. In this setting, hospitalization in the ICU before surgery, hemodialysis, and polymicrobial bacteremia further increase mortality. The prognosis for transplant patients with established infections is poor, especially for those with polymicrobial bacteremia.

References


