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[< Previous](#) | [Next >](#)

ARTICLE LINKS:

[Abstract](#) | [References \(21\)](#) | [View full size inline images](#)

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INCREASED INCIDENCE OF POSTOPERATIVE INFECTIONS ASSOCIATED WITH PERITONEAL DIALYSIS IN RENAL TRANSPLANT RECIPIENTS

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Abstract [TOP](#)

Background. Infection is a frequent postoperative complication in renal transplant recipients. However, little information is available concerning the effect of pretransplantation dialysis modality on posttransplantation complications including infection. We therefore evaluated the effect of hemodialysis (HD) versus peritoneal dialysis (PD) on the incidence of postoperative infection as well as several other posttransplantation outcomes.

Methods. A retrospective analysis was performed using medical records covering the period 30 days after transplantation of 156 dialysis patients who underwent renal transplantation at a single center during a 22-month period. Of these patients, 103 received only HD, 32 received only PD, 13 received PD in the past and HD immediately before transplantation (PH/HD), and 8 received HD in the past and PD immediately before transplantation (HD/PD). The presence of culture-proven infection, types of infecting organisms, length of initial hospital stay, and incidence of rejection during the first 30 days after transplantation were determined for each patient.

Results. All groups were similar with regard to age, race, gender, underlying disease, donor type, incidence of delayed graft function, and perioperative antibiotic prophylaxis. There were more infectious complications within 30 days after transplantation in patients on PD just prior to transplantation (PD and HD/PD) than in HD patients (67.5% vs. 25.9%, $P<0.00001$). When types of infectious organisms were assessed, PD patients were found to have a greater incidence of infections with microorganisms that colonize human skin ($P<0.0001$). The median length of hospital stay was 3 days longer for PD patients and 6.5 days longer for HD/PD patients than for patients receiving HD ($P=0.01$ and 0.04), and PD and HD/PD patients were more likely to have an episode of rejection than HD patients ($P=0.02$).

Conclusions. Renal replacement therapy with PD immediately before transplantation negatively affects outcome as compared with HD, predisposing patients to a greater incidence of postoperative infections and rejection and a longer hospital stay. Further study in a randomized controlled trial may help determine how adjustment of the dialysis method can optimize transplantation outcome.

Since the first human renal transplant in 1936 by the Soviet surgeon Voronoy (1), the number of renal transplantations performed yearly in the United States has grown to 9004 in 1995 (2). As discussed in Gokal's article (3), multiple studies have shown that the quality of life is significantly better for patients with functional renal transplants as compared with those receiving dialysis. In the United States, hemodialysis (HD*) is the major modality used for renal replacement therapy (58% of patients versus 9% with peritoneal dialysis [PD] and 25% with functional renal allografts) (4). Although renal transplantation is a viable alternative to dialysis, the usual time on the waiting list for a cadaveric organ remains greater than a year, and most recipients require dialysis before transplantation.

Many have sought to achieve better transplantation outcomes through improved surgical techniques and technological innovations, but limited and controversial data exist regarding the effect of pretransplantation dialysis method on posttransplantation outcomes (5-16). Forty-five percent of chronic ambulatory PD patients develop peritonitis during their first 6 months of PD, and 60% during their first year (17-18). Gram-positive bacteria colonizing human skin, primarily *Staphylococcus epidermidis*, *Staphylococcus aureus*, and Streptococci account for 60-80% of cases of peritonitis in PD recipients; enteric bacteria account for another 15-30% (19). The transplanted organ and its surrounding structures have been said to represent the most frequent and important sites of infection in transplant recipients (20). Renal allograft survival as well as patient survival is decreased in patients whose postoperative course is complicated by infection (21). Whether subclinical peritonitis exists in patients receiving PD and whether placement of the renal graft in the neighboring iliac fossa increases the risk for infection in the postoperative period are unknown.

The objective of our study was to compare the postoperative outcome of patients receiving HD or PD before transplantation, including the incidence of infectious complications, median length of hospital stay, and incidence of rejection.

METHODS TOP

Patients. We performed a retrospective review of 156 patients who underwent renal transplantation at the University of Maryland between January 1, 1994 and November 1, 1995. All dialysis patients whose complete inpatient and outpatient medical records were available (including daily progress notes as inpatients or weekly clinic notes as outpatients, culture

Article Outline

- [Abstract](#)
- [METHODS](#)
- [RESULTS](#)
- [DISCUSSION](#)
- [REFERENCES](#)

Figures/Tables

- [Table 1](#)
- [Figure 1](#)
- [Figure 2](#)
- [Figure 3](#)

reports, and pharmacy records detailing events from the time of transplantation through the 30-day study period) were included for analysis. Patients not yet receiving dialysis were excluded from the study. Based on these criteria, 70.3% of all dialysis patients who underwent renal transplantation during this period of time were evaluable for this analysis. Patients were classified into four groups according to the method of dialysis: those who received only HD, those who received only PD, and those who received both forms of dialysis (HD first and PD just before transplantation [HD/PD], or PD first and HD just before transplantation [PD/HD]).

All renal transplant patients during this time period received immunosuppressive therapy according to a protocol that consisted of antithymocyte globulin induction plus daily azathioprine (1 mg/kg) and corticosteroids (methylprednisolone 500 mg i.v. followed by a prednisone taper). In addition, cyclosporine was added to the regimen when serum creatinine level decreased below 2.5 mg/dl. Although perioperative antibiotic prophylaxis varied considerably during this time period (as documented in *Results* below), all transplant recipients received a standard postoperative antimicrobial prophylactic regimen beginning when patients were capable of oral intake (generally within 72 hr of surgery). This regimen consisted of nystatin (200,000-400,000 U swish and swallow five times daily) or Mycelex (10 mg of troche t.i.d.) oral antifungal agent plus oral trimethoprim/sulfamethoxazole (80 mg of trimethoprim once daily) for a minimum of 26 weeks (patients known to be allergic to sulfa agents received either ampicillin or ciprofloxacin antibacterial prophylaxis). No systemic antifungal therapy was given. In addition, any patient at risk for cytomegalovirus infection (seropositive donor or recipient) received intravenous ganciclovir prophylaxis for 2-4 weeks after transplantation (5 mg/kg b.i.d. adjusted for renal function).

The diagnosis of infection at a specific site required that a culture obtained from that site was positive for bacteria or yeast. In addition, the presence of Tenkhoff site or wound infection required that the presence of cellulitis and/or exudate was documented, and the diagnosis of urinary tract infection required the presence of pyuria plus $>10^3$ organisms/milliliter; the diagnosis of infection at any other site required evidence for systemic infection (two of the following three parameters: oral temperature greater than 99.9°F or rectal temperature greater than 100.9°F, hypotension, and/or abnormally elevated total white blood cell count) in the setting of a positive culture.

Statistical analysis. The primary exposure variable in the study was the type of dialysis before transplantation. The primary outcome was culture-proven infection during the first 30 days after transplantation, with secondary outcomes including: acute rejection during the first 30 days and length of hospital stay associated with transplantation. Risk estimates for categorical variables were determined using contingency tables with associated relative risks and the Pearson chi-square statistic to determine statistical significance. Comparison of means for continuous variables were made with the Student's *t* test. All odds ratios (OR) are reported with 95% confidence intervals, and means were expressed as \pm the standard error. Logistic regression was used to analyze the association between dialysis modality with culture-proven infection and rejection, adjusting for multiple covariates. Linear regression was used to evaluate the relationship between type of dialysis and length of hospital stay. Computations were performed with the Statistical Package for the Social Sciences (SPSS, Inc., Chicago, IL).

RESULTS TOP

Patient characteristics. Overall, the four dialysis groups were well balanced with regard to all baseline demographic and clinical characteristics. No significant differences in age, race, gender, transplant type, underlying disease, or incidence of delayed graft function were found between patients receiving HD or PD just before transplantation ([Table 1](#)). Renal failure was most commonly due to hypertension, diabetes mellitus, glomerulonephritis, and polycystic kidney disease in the population studied.

Table 1. Patient demographics

During the time period that these patients underwent transplantation, nine antibiotic regimens were used for perioperative prophylaxis. These included (number of patients in parentheses): vancomycin/gentamicin (5), vancomycin/aztreonam (2), vancomycin/ciprofloxacin (2), vancomycin/ceftriaxone (39), cefotetan (2), cefazolin (96), cefazolin/gentamicin (6), nafcillin/aztreonam (2), and ampicillin/aztreonam (1). The regimen used for one patient was unknown. Because coagulase-

negative *Staphylococcus* and *Enterococcus* are common pathogens on the transplantation service, the patients were categorized as having a regimen that did or did not include vancomycin. Statistical analysis revealed no significant difference in antibiotic prophylaxis between the four patient groups ($P=0.92$). Similarly, there was no significant difference in postoperative antibiotic prophylaxis, with 142 of the 156 patients receiving oral trimethoprim/sulfamethoxazole ($P=0.95$ between the four groups), and all patients receiving either Mycelex or nystatin antifungal prophylaxis.

Infectious complications. Patients receiving PD at the time of transplantation (PD and HD/PD groups) had higher rates of infection compared with patients on HD (67.5% vs. 25.9% $P<0.00001$) (Fig. 1). Patients previously on PD who were changed to HD before transplantation were similar to patients on HD alone, suggesting that the increased risk associated with PD is reversible once PD is discontinued. There was also an increased risk of infection associated with PD after adjustments for age, gender, race, transplant type, underlying disease, presence of delayed graft function, and type of antibiotic prophylaxis (OR=6.7, $P<0.00001$).

Figure 1. Infection rates during the first 30 days after renal transplantation. The percent of patients with culture-proven infection in the PD, PD/HD, and HD/PD groups was compared with the percent of patients with culture-proven infection in the HD group, and the relative risk (RR) was calculated for each group. P values were determined using the Pearson chi-square statistic.

When the incidence of infection by site was analyzed, patients receiving PD were more likely to have infection in the abdomen, bloodstream, surgical wound, or Tenkhoff catheter site than patients receiving HD (Fig. 2). In contrast, the incidence of intra-arterial or intravenous line-related infection, urinary tract infection, or infection at other sites did not differ significantly between the four groups.

Figure 2. Sites of culture-proven infection in renal transplant recipients. Infections were categorized as occurring intra-abdominally, superficially at the surgical wound or Tenkhoff catheter site, in the bloodstream, at an arterial/venous line tip (A/V line), in the urinary tract (UTI), or at a site distinct from these categories. The relative risk (RR) for PD, PD/HD, or HD/PD patients developing an infection at each site was calculated compared with HD patients developing an infection at the same site. Groups with significantly increased risk of infection at a particular site are indicated by an asterisk and the corresponding RR value.

The types of organisms involved in these infections were grouped into four categories: skin flora (coagulase-positive Staphylococci, coagulase-negative Staphylococci, *Corynebacterium* and non-group D Streptococci), enteric flora (*Escherichia coli*, *Enterobacter*, *Enterococcus*, and *Clostridium difficile*), other Gram-negative rods (*Pseudomonas*, *Xanthomonas*, *Klebsiella*, *Serratia*, and *Providencia*), and yeast. When the incidence of infection by organism was analyzed, there were greater numbers of infections caused by skin flora for both the PD and the HD/PD patients as compared with the HD patients (Fig. 3), and infections caused by enteric organisms were also more common for HD/PD patients and approached significance for PD patients as compared with HD patients.

Figure 3. Type of organisms causing culture-proven infection in renal transplant recipients. Organisms were categorized as skin flora (coagulase-positive Staphylococci, coagulase-negative Staphylococci, *Corynebacterium*, and non-group D Streptococci), enteric flora (*Escherichia coli*, *Enterobacter*, *Enterococcus*, and *Clostridium difficile*), other Gram-negative rods (*Pseudomonas*, *Xanthomonas*, *Klebsiella*, *Serratia*, and *Providencia*), or yeast. The relative risk (RR) for PD, PD/HD, or HD/PD patients developing an infection with each type of organism is calculated compared with HD patients developing an infection with the same type of organism. Groups with significantly increased risk of infection with a particular type of organism are indicated by an asterisk and the corresponding RR value.

Data regarding the time to removal of the Tenkhoff catheter was available for 77.5% of the PD and HD/PD patients studied. The median time to removal was 9 days after transplantation, with a range of 0 to 35 days. PD patients who did

not have their Tenckhoff catheters removed within 6 days of transplantation were nine times more likely to develop infection within the 30-day posttransplantation period (OR=9.0, $P=0.009$).

Secondary outcomes. PD before transplantation was associated with longer length of stay and a greater incidence of rejection during the first 30 days after transplantation. The median length of stay was 3 days longer for PD patients and 6.5 days longer for HD/PD patients than HD patients ($P=0.01$ and $P=0.04$). However, the length of hospital stay was similar in the HD and PD/HD groups. This finding again suggests the risk associated with PD may be reversible. After adjusting for age, gender, race, transplant type, underlying disease, presence of delayed graft function, and type of antibiotic prophylaxis, the length of stay was 4.6 days longer for PD patients than for HD patients ($P=0.006$). PD patients and HD/PD patients were also significantly more likely to have an episode of rejection (34% and 37.5%, respectively, vs. 16.5% in the HD patients) during the first 30 days after transplantation ($P=0.02$), even when adjustments for age, gender, race, transplant type, underlying disease, presence of delayed graft function, and type of antibiotic prophylaxis were made (OR=3.3, $P=0.007$).

DISCUSSION TOP

Our study supports the hypothesis that the use of PD just before transplantation is associated with a significant increase in intra-abdominal, bloodstream, and wound site infections with specific types of infecting organisms, particularly skin and enteric flora. The University of Maryland Transplant Program is in a somewhat unique position to evaluate the influence of various parameters on the rate of infectious complications during the early posttransplantation period, because during the time period studied each patient was followed daily by a designated Transplant Infectious Disease specialist from the time of transplantation until hospital discharge. This very active participation by the Infectious Disease service, combined with daily surveillance laboratory tests including urinalysis on each patient, allowed for rapid and culture-proven diagnosis of many infectious complications. However, culture-proven infection was not the only outcome measure to differ between the two groups. Patients receiving PD before transplantation were also more likely to experience rejection within the first 30 days after transplantation and have a significantly increased length of initial hospital stay, parameters that may be influenced by the presence of postoperative infection but should not have been influenced by our intensive Infectious Disease follow-up.

Whether the mode of dialysis after transplantation affects outcome has been controversial. A few smaller studies have reported no significant difference in graft survival between PD and HD patients (6, 7, 12). However, these studies failed to closely examine parameters such as overall infection rates, rejection rates, or length of hospital stay. Moreover, reports by Guillou et al. and Gelfand et al. (8, 9) support a better overall outcome for patients receiving pretransplantation HD. In a small study, Gelfand et al. (8) reported a 50% higher rejection rate for 17 transplants in PD patients compared with 13 transplants in HD patients; and contrary to the other small studies noted above, a report by Guillou et al. (9) noted improved graft survival reaching significance at 1 year for HD patients versus PD patients (63.5% vs. 35.5%). Most recently, however, a much larger study found that pretransplantation HD was associated with a modest (approximately 1.5-fold) increased risk of delayed graft function in over 9000 recipients of cadaveric renal transplants (13), although that study noted no difference in acute rejection between HD and PD patients. It is possible that a similar difference in the presence of delayed graft function was not detected in our study because we included patients with living-related transplants, and because of the much smaller number of patients involved; indeed, three other smaller studies, one of which included a cohort of 662 patients, also reported no significant difference in delayed graft function between HD and PD patients (14-16). However, we may have been able to detect a difference in acute rejection between HD and PD patients that was undetectable in the study by Bleyer et al. (13) because this diagnosis required biopsy-proven evidence in our patients, whereas their study relied only on the response of health care providers as to whether or not the patient received antirejection therapy during the initial hospitalization.

It is unlikely that the increase in infectious complications in our patients on PD resulted from a decreased function of the immune system in PD as compared with HD patients. Several authors utilizing various immunologic markers have reported greater suppression of immune function in HD patients (4), which suggests a greater risk for infectious complications in HD patients than PD patients postoperatively. Moreover, the organism type together with the sites of increased incidence of infection, and the failure to show a significant increase in urinary tract infection, suggests that a global difference in susceptibility to infection does not exist in these PD patients. However, it is possible that the increased risk of infection associated with PD results from a subclinical peritonitis present at the time of transplantation or developed

during the postoperative period (although it should be noted that none of the PD catheters left in place was ever used or flushed in any of our patients after transplantation). Posttransplantation bacterial infections occur primarily in the first month after transplantation (21), with the sites most commonly affected including wounds, vascular access devices, the bloodstream, and the urinary tract. Skin flora and enteric organisms are the primary pathogens in peritonitis in PD recipients (5). These same organisms were also responsible for a greater incidence of infections in our PD patients after transplantation.

Our data from a large diverse adult patient population receiving care at a single center strongly suggest an advantage for patients receiving HD just before transplantation with significant decreases in rates of infection, rates of rejection, and length of hospital stay. Factors such as total length of time on dialysis, patient compliance, or other unknown factors that may have influenced the type of dialysis used in each case are unknown and could be relevant for the outcomes analyzed. It is also possible that the presence of specific underlying diseases such as diabetes mellitus may influence susceptibility to infectious complications. Prospective controlled trials in which patients are randomized to receive HD or PD before transplantation, or in which PD patients are randomized to have their Tenckhoff catheters removed or left in place at the time of transplantation, may help determine the means for optimizing transplantation outcome.

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* Abbreviations: HD, hemodialysis; OR, odds ratio; PD, peritoneal dialysis. [\[Context Link\]](#)

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