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Prior dialysis does not affect the outcome of pediatric renal transplantation

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Abstract. The effect of pretransplantation dialysis treatment was examined retrospectively in 70 children less than 6 years old receiving a primary renal transplant at the University of Minnesota. Patient and graft survivals were compared at 1, 2 and 3 years and there were no significant differences between patients who received only hemodialysis (group 1), only peritoneal dialysis (group 2), or no prior dialysis (group 3). All patients received deliberate blood transfusions before transplantation and children at risk for recurrent diseases were excluded from the analyses. No grafts were lost due to perioperative thrombosis. Also, treatment with cyclosporine A did not significantly influence the outcomes. In this series, the choice to proceed directly to renal transplantation without an interposed interval of dialysis imposes no penalty in terms of patient or graft survival. Likewise, when dialysis was required, the dialysis mode selected exerted no clear effect on the outcome of transplantation.

Key words: Transplantation – Dialysis – Uremia

Introduction

At present, the therapies available for young children with end-stage renal disease (ESRD) mirror those for the adult patient. However, the child's intellectual development, physical size, underlying renal disease and family constellation are additional variables which may modify the selection of renal replacement therapy. So the task confronting the child's physician is to develop a therapeutic plan which recognizes the available treatment choices and seeks to optimize the child's health, rehabilitation, growth and development. At present, the practical experience needed to guide such critical choices is limited.

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For the uremic child, successful renal transplantation is usually viewed as the final therapeutic goal, but the effects of various dialysis modalities as well as the duration and severity of uremia on transplant outcome are unclear. Theoretically, there has been speculation that the improved immune reactivity seen during peritoneal dialysis might compromise the success of transplantation [1].

Since children frequently have congenital renal disease, significant improvement or recovery from ESRD [2] is unlikely; rather slowly advancing uremia is the norm. This offers the opportunity of "early" or preemptive transplantation, without prior dialysis, as a primary ESRD therapy. However, little is known about the potential adverse effects of such an approach. In a review of over 1700 transplant recipients, Migliori et al. [3] found that most did well even if they never received dialysis treatment. However, some authors have proposed that transplantation without antecedent dialysis may be less successful [4] and a recent multicenter survey also suggested that preemptive transplantation in children might be associated with an increase in graft thrombosis [5].

Earlier studies [6–8] have presented important data on renal transplantation in pediatric patients, but the total numbers of younger children were small and comparisons are further complicated by differieng dialysis techniques, noncontemporaneous eras, multiple centers, etc. In a single center, we retrospectively examined the impact of prior dialysis therapy on the outcome of subsequent renal transplantation, in an attempt to reveal any hidden costs in certain approaches to ESRD treatment in our youngest children.

Patients and methods

Between July 1979 and October 1987, 92 children less than 6 years old received their first renal transplant at the University of Minnesota Variety Club Children's Hospital. From this group, 13 children at risk for recurrent disease (either oxalosis, focal sclerosing glomerulonephritis, or hemolytic-uremic syndrome) in the allograft were excluded from further consideration. An additional 9 patients who received a combination of dialysis therapies were also excluded. The remaining 70 children re-

Table 1. Clinical patient characteristics

Patients	Group 1 (hemodialysis)	Group 2 (peritoneal dialysis)	Group 3 (none)
Sex	8 girls, 13 boys	6 girls, 10 boys	8 girls, 25 boys
Age (range)	2.4 years (0.5–5.3)	2.2 years (0.9–5.5)	2.4 years (0.5–5.7)
Donor source			
Living	15	9	31*
Cadaver	6	7	2
Cyclosporine use			
Yes	11	9	11
No	10	7	22

* By chi-square analysis, there are more living donors ($P < 0.02$) in group 3; no other comparisons are significantly different

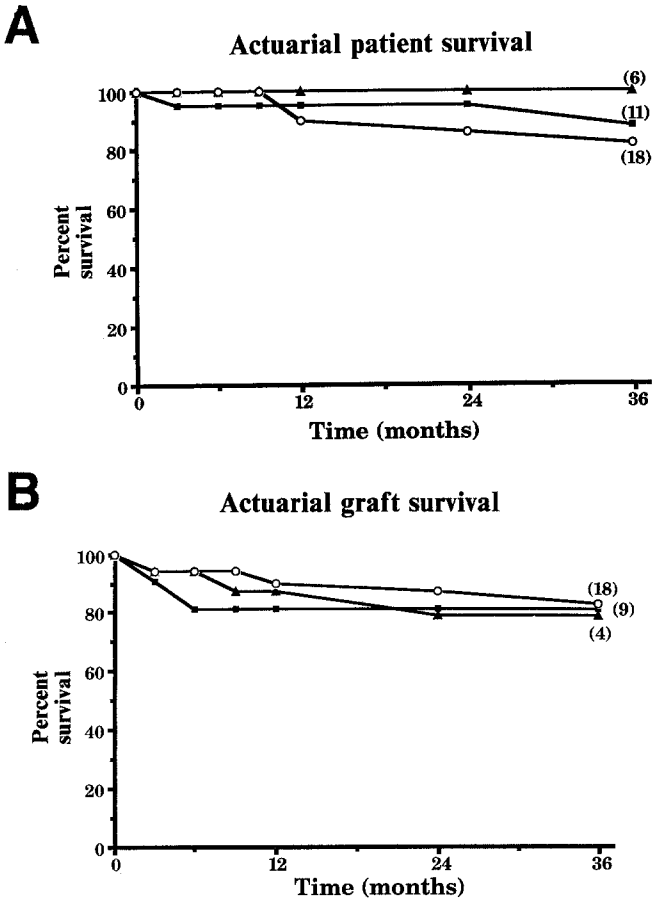

Fig. 1. Actuarial patient (**A**) and allograft (**B**) survivals for 70 primary renal transplant patients who were less than 6 years old at transplantation. The patients and allografts are grouped by preoperative dialysis therapy. The *numbers in parentheses* indicate those at risk in each group. There are no significant differences between any of the groups. —■— Hemodialysis ($n = 21$); —▲— peritoneal dialysis ($n = 16$); —○— no dialysis ($n = 33$)

ceived only a single mode of dialysis (peritoneal or hemodialysis) or no chronic dialysis and are the subjects of this report.

Following the convention of Migliori et al. [3], the patients were classified exclusively, according to the dialysis therapy they received for a minimum of 30 days prior to renal transplantation. Group 1 ($n = 21$) received only hemodialysis (HD) and group 2 ($n = 16$) were treated only by peritoneal dialysis (PD). Group 3 included 28 children who were never dialyzed, as well as 5 patients who received brief (an average of only four treatments) hemodialysis immediately before their surgery.

All the patients in this study received deliberate blood transfusions from at least three separate donors, a minimum of 4 weeks prior to transplantation. The standard immunosuppression protocol included Minnesota antilymphoblast globulin, azathioprine and prednisone [9, 10]. In 1984, cyclosporine A (CSA) was added (5 mg/kg per day) to this protocol and routine splenectomy was discontinued [9].

Statistics. For the purpose of analysis, functioning renal grafts lost due to a patient's death are also considered to be graft losses. Clinical patient characteristics were compared by the chi-square test, with the Yates correction for continuity and the Bonferroni correction for multiple comparisons. Group actuarial outcomes were calculated by life table analyses and compared by the Gehan test [11]. Values are considered significant when P is below 0.05.

Results

The characteristics of patients in each of the three groups are compared in Table 1. None of the groups differ significantly in sex, age, or treatment with CSA, but more patients in group 3 did receive grafts from living related donors ($P < 0.02$).

Patient and allograft survival are shown in the Fig. 1. At 3 years, the actuarial patient survival was 88%, 100% and 82% for groups 1, 2 and 3, respectively. These values do not differ statistically. Only the comparison of overall patient survival between groups 2 and 3 approached significance ($P = 0.09$). At 5-year followup, though patient numbers are smaller, no significant differences were detected (data not shown). Similarly, the transplanted kidneys functioned at 3 years in 81%, 79% and 83% for groups 1, 2 and 3, respectively. Again no significant differences were found between groups at any time up to 5 years.

Examination of the 9 children excluded because they received combinations of dialysis before transplantation revealed 100% patient and graft survival. However, due to the small numbers, there were no statistical differences between these children and any of the three study groups. Reanalysis of the groups with these 9 patients included does not change any intergroup comparison of patient or graft survival.

When patients are divided according to the donor source, although the number of cadaver kidney recipients is small (only 15 of 70), there are no significant outcome

Table 2. Cause of graft losses by group

	Time after transplant	Cause	Other Data
Group 1 (HD)			
Patient no.			
1	4 days	Death	Unintentional enterotomy at surgery, sepsis, death
2	3 months	Rejection	Cardiac arrest at home, after 31 months on CAPD
3	4 months	Rejection	Alive with second graft
Group 2 (PD)			
Patient no.			
4	3 months	Infarction	Embolization/graft infarction after dilatation of arterial stenosis, alive on PD
5	18 months	Rejection	Alive with second graft
6	8 months	Rejection	Alive on CAPD
Group 3 (none)			
Patient no.			
7	69 months	Death	Pneumococcal sepsis, functioning graft at death
8	3 months	Rejection	Died, *Haemophilus influenza* sepsis after 9 months on CAPD
9	50 months	Death	Pneumococcal sepsis, functioning graft at death
10	1 month	Rejection	Died, after failed second allograft
11	26 months	Death	Arrhythmia, functioning graft at death
12	11 months	Death	Pneumococcal sepsis, functioning graft at death
13	48 months	Death	De novo neuroblastoma
14	18 months	Death	Died with intractable seizures after surgery for bowel obstruction, functioning graft at death
15	64 months	Rejection	Alive after second graft

CAPD, Continuous ambulatory peritoned dialysis; HD, hemodialysis; PD, peritoneal dialysis

differences between groups 1, 2 and 3. When patients are grouped according to their immunosuppressive therapy, that is, all those receiving CSA versus all who never received CSA, there are again no significant differences between patient groups 1, 2 and 3. Finally, when the results are analyzed by the duration of dialysis (i.e. more or less than 90 days), no outcome differences emerged.

The specific causes of all graft losses and deaths are listed in Table 2. In total, 10 deaths occurred, 2 in group 1 and 8 in group 3. The septic deaths (5 cases) all occurred in splenectomized patients. Six of the children who died had functioning renal allografts at the time of death. Indeed, in group 3 all graft loses after the 1st year were due to patient death, and no allografts were lost due to rejection.

Discussion

Pediatric nephrologists generally agree that the optimal therapy for a child with ESRD is a functioning renal allograft. Less clear are the best strategies to attain this goal [12]. Growing children with chronic renal insufficiency often experience a gradual decline in renal function accompanied by increasing impairment of growth and development. When the need for renal replacement therapy is imminent, a choice to proceed with either transplantation or dialysis must be made. These two therapies should be viewed as complementary rather than competitive, the overreaching goal being an intact child with a functioning renal allograft.

Despite earlier concerns [1], renal transplantation in both adults [13, 14] and children [15–17] on PD has been demonstrated to be safe and successful. Still it seems that preemptive transplantation (i.e. without prior chronic dialysis) offers the opportunity to avoid dialysis, with its complications and costs, while capturing the benefits of renal transplantation earlier.

To better define the effect exerted by prior dialysis therapy on patient or graft survival, we selected a recent era (since 1979) when all patients received deliberate, preoperative blood transfusions. The analysis is limited to first transplants, regardless of donor source, but excludes patients in whom recurrent disease might potentially confuse the picture. On the other hand, we included all the remaining children from 6 months to 6 years of age, since repeated analyses of our data have consistently failed to find any survival differences related to recipient age, including infants [9, 10, 18].

In their original study of renal transplantation in children on dialysis, Stefanidis et al. [19] noted no overall differences in graft survival between children never dialyzed and those treated with HD or PD. But in the important subset of children less than 6 years old ($n = 20$), patients receiving PD had better graft survival. These authors also noted that since none of the nondialyzed patients had received transfusions, the effects of dialysis and transfusion could not be separated. The present study focuses on this same age group, but since all the patients were deliberately transfused, the impact of dialysis therapy can be examined separately. Our comparisons detect no difference in either patient or allograft survival associated with prior dialysis therapy. These results remain consistent, even when the groups are stratified by donor source or CSA administration. The failure to demonstrate differences based on donor source probably results from the small number of cadaver kidneys in this study, since the effect of donor source was clearly seen in our overall experience [9].

Although patients on PD are thought to have more normal cellular immune function [20], there is no suggestion in our series or the larger series of Stefanidis et al. [19] that this results in increased graft losses. Similarly, although a recent survey [5] suggested that allograft thrombosis was more frequent in nondialyzed children, our series found no such effect. In fact, no perioperative thrombosis was detected in any child and the only perioperative graft loss (and death) occurred in an HD patient (no. 1).

In conclusion, preemptive transplantation in younger children is not associated with differences in either patient or graft survival. Based on these data, it should be possible to completely avoid dialysis, the associated complications and expense, in selected children. Additionally, when dialysis is necessary, the specific choice of dialysis modality itself does not affect transplantation outcome. These observations should allow greater latitude to the pediatric nephrologist when planning ESRD treatment for the individual child.

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