Outcome of Patients Initiating Chronic Peritoneal Dialysis During the First Year of Life

William A. Carey, MD, Karen L. Martz, MS, Bradley A. Warady, MD

BACKGROUND AND OBJECTIVE: Among children with end-stage renal disease (ESRD), those who initiated chronic dialysis during the first year of life historically were less likely to survive or receive a kidney transplant compared with those who initiated dialysis later in childhood. We hypothesized that recently treated infants have experienced improved outcomes.

METHODS: We queried the North American Pediatric Renal Trials and Collaborative Studies database, obtaining information on 628 children who initiated maintenance peritoneal dialysis for treatment of ESRD at <1 year of age. We further subcategorized these children by age (neonates, ≤31 days and infants, 32–365 days) and date of dialysis initiation (past, 1992–1999, and recent, 2000–2012).

RESULTS: Survival while on dialysis and overall survival were significantly better among neonates and infants in the recent cohort. Overall survival at 3 years after dialysis initiation was 78.6% and 84.6% among the recently treated neonates and infants, respectively. Neonates and infants in the recent cohort also were more likely to terminate dialysis for transplantation, and graft survival was improved among recently transplanted infants (3-year graft survival 92.1%).

CONCLUSIONS: Among children who initiate chronic peritoneal dialysis for treatment of ESRD in the first year of life, survival has improved in recent years. Graft survival also has improved for the subset of these patients who received a kidney transplant.

WHAT'S KNOWN ON THIS SUBJECT: Historically, children with end-stage renal disease who initiated chronic dialysis during the first year of life were far less likely to survive or successfully receive a kidney transplant compared with those who initiated chronic dialysis at older ages.

WHAT THIS STUDY ADDS: In recent years, survival has improved markedly among children who initiate chronic peritoneal dialysis at <1 year of age. Among those infants who initiate dialysis after the neonatal period and later undergo kidney transplantation, graft survival has improved as well.
End-stage renal disease (ESRD) occurs rarely among children <1 year of age, but for these children its consequences are profound.1–5 Even with the early initiation of maintenance dialysis therapy, these patients are at high risk for a variety of morbidities and mortality.6–8 This is especially true for those who initiate dialysis during the neonatal period.1,4,5,8,9 Despite advances in the medical and surgical management of all infants <1 year with ESRD, it is unclear whether the outcome of those who receive chronic dialysis therapy has improved over time.

Our inability to compare temporal changes in the outcomes of infants with ESRD and receiving chronic dialysis relates to limitations inherent to the 2 main types of data published on the subject. Registry reports, such as those from the Australia and New Zealand Dialysis and Transplant Registry and the North American Pediatric Renal Trials and Collaborative Studies (NAPRTCS), include large numbers of patients from a variety of centers, but are hampered by referral and selection biases.2,4,5 Single-center studies presumably reflect the outcomes of consistent management practices, but their patient volumes and/or follow-up periods tend to be quite limited.6–8 Given the discrepancies between registry and single-center outcomes and the limitations of each type of study, there is good reason that many physicians find it difficult to counsel families with confidence about the long-term prognosis of these patients, and in turn, some physicians who care for infants with ESRD (eg, neonatologists and nephrologists) remain hesitant to offer maintenance dialysis or initiate the transplant process.10–12

We therefore conducted the following study to provide some additional data on the issue of the outcome of infants who initiate chronic dialysis during the first year of life, hypothesizing that patient survival and transplantation outcomes have improved in recent years among patients registered in the NAPRTCS database.

METHODS

Since 1992, NAPRTCS has maintained a voluntary registry database that includes clinical information on children who initiated maintenance dialysis before 21 years of age.13 The NAPRTCS kidney transplant registry was initiated in 1987. More than 100 pediatric nephrology centers from throughout North America have contributed data to the NAPRTCS, making it one of the largest pediatric nephrology collaboratives worldwide, and a source of data that is deemed representative of the pediatric nephrology population at large.

Subsequent to entry into the NAPRTCS registry, patient follow-up data are voluntarily entered every 6 months. For this study, we queried the NAPRTCS dialysis database to obtain information about all children with ESRD who initiated maintenance dialysis during the calendar years 1992 to 2012. Specifically, we analyzed patient survival while on dialysis and overall survival, as well as the causes of patient death; the likelihood and reason for termination of dialysis; and the time to transplantation. We also queried the NAPRTCS transplant database to assess graft survival after the index kidney transplant.13

To compare the outcomes of these children on the basis of age at initiation of dialysis, we categorized them into the following age groups: 0 to 365 days, 12 to 24 months, 2 to 5 years, 6 to 12 years, and 13+ years. Among the infants aged <1 year, we further categorized patients as neonates (≤31 days of age) and infants (32–365 days of age).

To determine whether outcomes had improved in recent years for all these children, we stratified them by the calendar year in which dialysis was initiated or the index kidney transplant occurred. Specifically, we compared children who either initiated dialysis or received their first kidney transplant during the calendar years 1992 to 1999 (past cohort) with those who did so during the calendar years 2000 to 2012 (recent cohort). Dividing the cohorts in this manner enabled us to describe how dialysis care evolved over the course of 2 decades, the latter of which began with publication of the first pediatric-specific guidelines for the prevention and treatment of peritonitis in children receiving peritoneal dialysis (PD).14

Product limit estimates of the time to death, time to dialysis termination for transplantation, and graft survival were compared using the Log-rank test. Plots depicting patient survival, graft survival and time to dialysis termination were created using Kaplan-Meier methods. Overall survival was calculated from the date of the first registry-reported initiation of dialysis until the date of death or last NAPRTCS follow-up for censored patients. Survival while on dialysis was calculated from the date of the first registry-reported initiation of dialysis until the date of death, with patients censored at dialysis termination. The Cox proportional hazards model was used to test multivariate associations with patient overall survival. Factors considered included dialysis initiation era, patient age, gender, primary disease status, and need to switch to hemodialysis during first course of dialysis. We compared termination characteristics using the χ² test. All tests of significance were 2-sided with α = 0.05. All analyses were conducted by using SAS version 9.2 or higher (SAS Institute, Inc, Cary, NC).

RESULTS

NAPRTCS data were available for 6522 children who initiated maintenance dialysis (PD and hemodialysis) for treatment of ESRD
at <21 years of age between 1992 and 2012. Among patients who initiated dialysis during the first year of life, the vast majority (628 of 670, 94%) initiated PD, whereas only 40 (6%) initiated hemodialysis (the dialysis modality was unknown for 2 patients). Given that PD was the predominant modality in our population of interest, we limited our subsequent analyses only to those patients who received PD for their initial course of maintenance dialysis.

A total of 4060 children in the NAPRTCS database initiated PD for treatment of ESRD between 1992 and 2012. Among all age groups, children 0 to 365 days of age at dialysis initiation (n = 348) from 1992 to 1999 had the lowest survival during the initial course of dialysis and lowest overall survival with values of 73.4% and 73.0%, respectively, at 3 years after dialysis initiation (Fig 1 A and C). However, among the 280 children of the same age who initiated PD from 2000 to 2012, the discrepancy in these survival metrics narrowed considerably, with 3-year survival during the initial course of dialysis and overall survival improving to 88.1% and 82.5%, respectively (Fig 1 B and D).

Of the 628 children who initiated PD during the first year of life, 241 were neonates and 387 were infants at dialysis initiation. As shown in Table 1, the patient characteristics, primary renal diagnoses, and dialysis characteristics were similar between the temporal cohorts, with the exception of the weight of the infant group 30 days after dialysis initiation which was significantly greater in the recent cohort. Obstructive uropathy and renal dysplasia were the most common known diagnoses in both age groups. As shown in Fig 2 A and B, both the neonates (n = 98) and infants (n = 182) who initiated dialysis during 2000 to 2012 had significantly better survival while on dialysis (Log-rank P = .0002) and better overall survival (Log-rank P = .0031) than similarly aged patients from the past (1992–1999) cohort. Among the neonatal cohorts, 3-year survival during the initial course of dialysis increased from 70.0% to 91.0%, whereas overall survival at 3 years increased from 68.7% to 78.6%. Among the infant group, 3-year survival during the initial course of dialysis increased from 75.4% to 86.4% and overall survival increased from 75.8% to 84.6% at 3 years after dialysis initiation.

Multivariate analysis revealed that initiation of PD in the more distant era or during the neonatal period was associated with an increased risk of mortality, although there was no
disparity in risk due to gender or ethnicity (Table 2). The primary renal diagnosis also influenced the risk of mortality, with polycystic kidney disease conferring the greatest risk of death. Infection and cardiopulmonary disease were the leading causes of death among all children in this study (data not shown).

This improvement in survival was accompanied by a simultaneous shift in termination characteristics (Table 3). Among neonates, 205 (85%) of the 241 neonates are known to have terminated their initial course of PD, 92% of the past cohort and 76% of the recent cohort. Thirty-nine percent (51/131) of the neonates starting dialysis in the 1992 to 1999 era terminated for transplant compared with 68% (50/74) of the 2000 to 2012 neonatal cohort ($\chi^2 P < .001$). In infants 32 to 365 days old at dialysis initiation, 83% overall are known to have terminated their initial course of PD, with 93% and 72% terminating in the 1992 to 1999 and 2000 to 2012 eras, respectively. Of the 321 terminated patients, 53% (101/190) from the 1992 to 1999 cohort terminated for transplant versus 65% (85/131) from the 2000 to 2012 cohort ($\chi^2 P = .036$). Time to dialysis termination for transplant is shown in Fig 3A.

Of the 628 neonates and infants who initiated chronic PD, 310 (49%) received a renal transplant that was recorded in the NAPRTCS transplant registry. The patient characteristics, primary renal diagnoses, and dialysis characteristics were similar to those of the entire neonatal and infant PD cohort (data not shown). Among neonates who received a kidney transplant, graft survival was similar in the past and recent cohorts (3-year graft survival 86.3% and 84.2%, respectively) However, infants in the recent cohort had better graft survival in comparison with infants in the past cohort ($P = .05$), with 3-year graft survival of 92.1% (Fig 3B).

**DISCUSSION**

When deciding whether to initiate maintenance dialysis therapy for an infant <1 year of age with ESRD, physicians and parents must grapple with complex medical, social, and ethical issues. Mortality rates as high as 48% have been recorded in neonates initiating chronic dialysis and <50% of pediatric dialysis health care providers would choose to provide dialysis to all children <1 year, as reported in an international survey. This decision-making process is made all the more challenging by the absence of clear, consistent evidence on the
present-day outcomes of these patients. To address this challenge, we compared the survival and transplantation outcomes of 2 temporal cohorts of children registered in the NAPRTCS dialysis and transplant databases.

The age at which children initiated maintenance dialysis had an effect on actuarial survival. In both temporal cohorts, patients who initiated PD during the first year of life had worse survival during the initial course of dialysis and worse overall survival than children in the 4 older age groups. However, what is most impressive is the finding that in recent years, the survival of children who have initiated chronic dialysis before 1 year of age has improved markedly, and now closely approximates that of older children receiving maintenance dialysis. These findings suggest that the overwhelming majority of the youngest children who initiate chronic dialysis can survive in the long-term and to an age at which body size does not pose substantial technical challenges for kidney transplantation. Similar findings of improved outcomes were previously published by Mitsnefes et al17 when describing the outcomes of children who initiated chronic dialysis at 0 to 5 years of age. Although the reasons for this improvement were not investigated in the current analysis, previous publications have emphasized the positive impact that greater attention to dialysis technology, nutrition, infection prevention and management, and dialysis adequacy have had on patient outcome.18–21 It is conceivable that the greater mean weight and mean weight z score observed in the recent temporal cohort of the infant group likewise reflect the combined benefit of all these improvements and also may have contributed to the improved patient survival.

A closer look at patients in the youngest age group within the NAPRTCS dialysis database suggests that survival has improved over time for those who initiated chronic dialysis as neonates and throughout the first year of life. Similar data were previously published on a smaller

TABLE 2 Hazard Ratios for Death Among Neonates and Older Infants Who Initiated PD for Treatment of ESRD

<table>
<thead>
<tr>
<th>Baseline Factor</th>
<th>Comparison Group</th>
<th>Reference Group</th>
<th>Hazard Ratio</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0–31 d</td>
<td>1–12 mo</td>
<td>1.45</td>
<td>1.02–2.05</td>
<td>.0395</td>
</tr>
<tr>
<td>Gender</td>
<td>Girls</td>
<td>Boys</td>
<td>1.16</td>
<td>0.80–1.69</td>
<td>0.4302</td>
</tr>
<tr>
<td>Race (overall P = .8076)</td>
<td>Black</td>
<td>White</td>
<td>1.26</td>
<td>0.79–2.00</td>
<td>0.3410</td>
</tr>
<tr>
<td></td>
<td>Hispanic</td>
<td></td>
<td>1.00</td>
<td>0.60–1.65</td>
<td>0.9846</td>
</tr>
<tr>
<td></td>
<td>Other</td>
<td></td>
<td>1.10</td>
<td>0.53–2.29</td>
<td>0.7968</td>
</tr>
<tr>
<td>Primary disease status (overall P = .0006)</td>
<td>A/hypo/dysplastic</td>
<td>Obstructive uropathy</td>
<td>1.94</td>
<td>1.01–3.73</td>
<td>0.0468</td>
</tr>
<tr>
<td></td>
<td>Congenital nephrotic</td>
<td></td>
<td>3.83</td>
<td>1.68–8.71</td>
<td>0.0014</td>
</tr>
<tr>
<td></td>
<td>Polycystic disease</td>
<td></td>
<td>4.28</td>
<td>2.08–8.80</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td></td>
<td>Other/Unknown</td>
<td></td>
<td>2.44</td>
<td>1.24–4.64</td>
<td>.0065</td>
</tr>
<tr>
<td>Switch dialysis modality</td>
<td>No</td>
<td>Yes</td>
<td>1.67</td>
<td>0.95–2.95</td>
<td>0.0753</td>
</tr>
</tbody>
</table>

Ratios were derived using a multivariate Cox regression model with overall survival as the response variable.

Cl, confidence interval.
comparably aged NAPRTCS cohort\textsuperscript{4} and more recently by van Stralen et al\textsuperscript{5} on a combined cohort of 264 children who initiated dialysis as neonates and who were enrolled into 1 of 4 contributing dialysis registries. Three-year survival during the initial course of PD increased by approximately 15% to 20% for neonates and infants in the more recent NAPRTCS cohort, and overall 3-year survival increased by ~10%. Our multivariate analysis did reveal an increased mortality risk for neonates compared with the infant group. This is a finding previously documented by others and is potentially related to an increased frequency of comorbidities in the neonatal group, a well-recognized risk factor.\textsuperscript{5,8,20,22} The substantial mortality risk associated with the diagnosis of autosomal recessive polycystic kidney disease is well characterized and reflects the previous findings of Guay-Woodford and Desmond, and others who found an exceedingly high mortality rate in neonates with autosomal recessive polycystic kidney disease who required surgery for relief of abdominal pressure or to initiate PD.\textsuperscript{23–25}

Consistent with recent single-center reports\textsuperscript{8,9} and the report by van Stralen et al\textsuperscript{5} based on patient experiences between 2000 and 2011, most of the mortality seen in the past cohort of neonates and infants occurred during the first year after dialysis initiation. In contrast, the course of overall mortality for the more recently treated neonates and infants in the NAPRTCS dialysis database appears to be more gradual over the first 3 years of maintenance dialysis. This new temporal pattern of mortality may reflect improvements in surgical and medical management at the time of dialysis initiation, or it may be a reflection of a more select patient population with less frequent use of chronic dialysis in those neonates/infants with significant potentially life-threatening comorbidities.\textsuperscript{22,26}

Termination characteristics also improved among infants who initiated chronic PD during 2000 to


<table>
<thead>
<tr>
<th>Peritoneal Dialysis Status</th>
<th>≤31 d</th>
<th>≥31 d</th>
<th>32–365 d</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dialysis status (n = 143)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>On initial course at follow-up</td>
<td>12</td>
<td>8.4</td>
<td>24</td>
<td>24.5</td>
</tr>
<tr>
<td>Terminated dialysis mode (n = 131)</td>
<td>131</td>
<td>91.6</td>
<td>74</td>
<td>75.5</td>
</tr>
<tr>
<td>Reason for termination (n = 131)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death reported in nonterminated patient</td>
<td>9</td>
<td>6.9</td>
<td>3</td>
<td>4.1</td>
</tr>
<tr>
<td>Patient transplanted</td>
<td>51</td>
<td>38.9</td>
<td>50</td>
<td>67.6</td>
</tr>
<tr>
<td>Change of modality</td>
<td>18</td>
<td>13.7</td>
<td>2</td>
<td>2.7</td>
</tr>
<tr>
<td>Death (as reason for termination)</td>
<td>28</td>
<td>21.4</td>
<td>6</td>
<td>8.1</td>
</tr>
<tr>
<td>Native kidney function returned</td>
<td>20</td>
<td>15.3</td>
<td>10</td>
<td>13.5</td>
</tr>
<tr>
<td>Other/Unknown</td>
<td>5</td>
<td>3.8</td>
<td>3</td>
<td>4.1</td>
</tr>
</tbody>
</table>

### FIGURE 3

Time to termination due to transplant (A) and renal graft survival (B) among neonates (≤31 days) and older infants (32–365 days) who initiated chronic PD for treatment of ESRD.

![Image of Time to termination due to transplant and Graft survival graphs](image-url)
2012 compared with the previous era. A large majority of infants in the recent cohort terminated their course of dialysis to receive a kidney transplant. After this transition from maintenance dialysis to renal transplantation, graft survival among the recently transplanted infants was better than that of infants in the past cohort and is consistent with the results of recent single-center reports and those published by the Scientific Registry of Transplant Recipients.6–8,27 Because graft survival has consistently improved among all pediatric age groups over the past few decades as a result of a variety of factors, including improved immunosuppression and surgical technique and a better understanding of transplant-related immunology,28 there is every reason to expect that transplant outcomes will continue to improve overall and among the youngest patients.

There are several limitations to our study. NAPRTCS maintains 3 databases: chronic kidney disease, children who have initiated dialysis for treatment of ESRD (dialysis), and children who have received a kidney transplant (transplant).13 None of these databases necessarily captures the whole of a registered patient’s experience; for example, a patient may have received predialysis and dialysis care at a non-NAPRTCS center before transferring to a NAPRTCS center where kidney transplantation was performed, in which case data would be available only for posttransplant outcomes. As a result, the patients in our dialysis cohorts were not necessarily included in our transplant cohorts and, conversely, not all patients in our transplant cohort were members of our dialysis cohorts. Thus, we were unable to compare the outcomes of 2 distinct groups of patients as they progressed from the initiation of dialysis therapy through the course of their first kidney transplant.

NAPRTCS maintains a voluntary registry; thus, it is conceivable that selection bias played a role in our results as well, with some participating centers reporting only those cases with favorable outcomes. It is also likely that only those children who progressed to home dialysis were entered into the registry (versus those neonates, for example, who died during their original hospitalization while receiving PD). Although this may have been the case, such reporting bias likely would have spuriously inflated the clinical outcomes for patients of a given age to a similar extent in each temporal cohort. In addition, the approach to patient entry and the results obtained are comparable to that of other pediatric dialysis registries, such as the registry of the International Pediatric Peritoneal Dialysis Network. Of course, future initiatives designed to capture information on all infants who initiate chronic dialysis, irrespective of comorbidities and patient outcome, are imperative if all risk factors for poor outcomes are to be identified and valid prediction models are to be developed.

CONCLUSIONS

We have demonstrated that the likelihood of patient survival and successful kidney transplantation has increased for children who initiate dialysis during the first year of life for the treatment of ESRD. We believe that these data are important additions to the limited information available on this patient population and because of the prognostic information it provides, will prove valuable to health care providers and affected families alike.

ABBREVIATIONS

ESRD: end-stage renal disease
NAPRTCS: North American Pediatric Renal Trials and Collaborative Studies
PD: peritoneal dialysis

REFERENCES

11. Teh JC, Frieling ML, Sienna JL, Geary DF. Attitudes of caregivers to management
of end-stage renal disease in infants.


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