ORIGINAL ARTICLE

Long-Term Survival of Children with End-Stage Renal Disease

Stephen P. McDonald, Ph.D., and Jonathan C. Craig, Ph.D.,
for the Australian and New Zealand Paediatric Nephrology Association

ABSTRACT

BACKGROUND

Although renal-replacement therapy for children with end-stage renal disease has been used for several decades, data on patients' long-term survival are sparse.

METHODS

We examined the long-term survival of all children and adolescents who were under 20 years of age when renal-replacement therapy commenced (study period, April 1963 through March 2002), using data from the Australia and New Zealand Dialysis and Transplant Registry. Survival was analyzed with the use of Kaplan–Meier methods and age-standardized mortality rates. Risk factors for death were analyzed with the use of Cox regression analysis with time-dependent covariates.

RESULTS

A total of 1634 children and adolescents were followed for a median of 9.7 years. The long-term survival rate among children requiring renal-replacement therapy was 79 percent at 10 years and 66 percent at 20 years. Mortality rates were 30 times as high as for children without end-stage renal disease. Risk factors for death were a young age at the time renal-replacement therapy was initiated (especially for children under 1 year of age, among whom the risk was four times as high as for children 15 to 19 years of age) and treatment with dialysis (which was associated with a risk more than four times as high as for renal transplantation). Overall, a trend toward improved survival was observed over the four decades of the study.

CONCLUSIONS

Despite improvement in long-term survival, mortality rates among children requiring renal-replacement therapy remain substantially higher than those among children without end-stage renal disease. Increasing the proportion of children treated with renal transplantation rather than with dialysis can improve survival further.

From the Australia and New Zealand Dialysis and Transplant (ANZDATA) Registry, Queen Elizabeth Hospital, Adelaide, Australia (S.P.M.); and the Centre for Kidney Research and the National Health and Medical Research Council Centre for Clinical Research Excellence in Renal Medicine, Children's Hospital at Westmead, and the School of Public Health, University of Sydney — all in Sydney (J.C.C.). Address reprint requests to Dr. McDonald at the ANZDATA Registry, Queen Elizabeth Hospital, 28 Woodville Rd., Woodville South SA 5011, Australia, or at stephenm@anzdata.org.au.

N Engl J Med 2004;350:2654-62.

End-stage renal disease, which is a rare but important health problem among children, occurs in about 5 to 10 children per million each year.[1] The disease is a chronic condition; even renal transplantation does not mean lifelong cure. Quality-of-life studies have shown that life without native kidney function is very difficult for children and their families.[2]

Forty years ago, children with end-stage renal disease died. Now, almost all such children are treated with dialysis or renal transplantation. Treatment typically involves multiple therapies, depending upon the availability of kidneys for transplantation and the long-term survival of the transplants. Long-term survival rates among children with end-stage renal disease are uncertain, and there are few data to inform patients, families, clinicians, and policymakers about survival. The available studies are generally short-term,[3-6] are based on single-center experiences,[7] and include only information with regard to patients receiving dialysis, patients undergoing transplantation, or patients in specific age groups.[8]

The Australia and New Zealand Dialysis and Transplant (ANZDATA) Registry has prospectively collected data on all children in whom renal-replacement therapy was started in Australia or New Zealand beginning in 1963. Using data from this registry, we examined long-term survival among children treated for end-stage renal disease and identified modifiable and unmodifiable risk factors for death.

METHODS

STUDY DESIGN

We performed a prospective inception-cohort study from the time renal-replacement therapy was initiated for all children and adolescents younger than 20 years of age in Australia and New Zealand who were registered in the ANZDATA Registry. The registry collects information every six months from all the renal units in Australia and New Zealand about all patients receiving renal-replacement therapy who have a diagnosis of chronic renal failure and for whom indefinite renal-replacement therapy is intended. Details regarding the registry have been reported elsewhere.[9]

The data collection is complete from the first use of renal-replacement therapy in Australia and New Zealand and includes information on the cause of end-stage renal disease, demographic characteristics of the patients, a limited range of coexisting conditions (which since 1991 have included coronary artery disease, peripheral vascular disease, cerebrovascular disease, chronic lung disease, hypertension, and smoking), and details of dialysis treatment and renal transplantation. Nephrologists are asked to provide a cause of death for children who have died, but death certificates are not directly reviewed by the ANZDATA Registry.

The consent and privacy provisions of the ANZDATA Registry have evolved over time and currently require informed consent from patients or a parent or legal guardian and include a right of access to personal information.[9] The registry is conducted in accordance with the Australian Commonwealth Privacy Act and associated state legislation governing health data collection. The anonymity of patient information is maintained by the coding of data during compilation; only information with personal identifiers removed is released by the registry.

All patients who were younger than 20 years of age when renal-replacement therapy commenced and whose first treatment occurred before April 1, 2002, were included in our analysis. Patients were followed until death or until March 31, 2002, whichever occurred first. Children who regained native renal function permanently despite their initial assessment were excluded; data on those lost to follow-up were censored as of the date of the last follow-up visit. The sole outcome examined was death, ascertained with the use of the registry data.

STATISTICAL ANALYSIS

The time from the start of renal-replacement therapy to death or the date on which the data were censored was analyzed with the use of the Kaplan–Meier method and Cox proportional-hazards models. Standardized mortality rate ratios and age-specific mortality rate ratios were calculated for Australian children only, with the use of contemporary life-expectancy values derived from life tables of the Australian Bureau of Statistics.

A multivariate Cox proportional-hazards model was constructed with age, sex, the decade in which renal-replacement therapy was initiated, primary renal disease, and type of dialysis (hemodialysis or peritoneal dialysis) as predictive variables. A categorical, time-dependent covariate was used for the type of renal-replacement therapy (hemodialysis, peritoneal dialysis, or transplantation) to allow for changes in type of therapy over time. Age and the year in which renal-replacement therapy was start-

ed were considered as categories in order to avoid the assumption of linear relationships with outcome. Age was analyzed in five-year categories, except for children younger than one year of age, who were considered as a separate group because they have a worse prognosis.[3,4,6,10] Inclusion in the final model was determined by a backward stepwise process with the use of the likelihood ratio to evaluate the effect of omitting variables. Stata statistical software (version 7.0, Stata) was used for the analysis; a P value of 0.05 was considered to indicate statistical significance, and 95 percent confidence intervals are provided when relevant.

RESULTS

DEMOGRAPHIC CHARACTERISTICS

Between April 1, 1963, and March 31, 2002, 1634 children and adolescents under 20 years of age commenced renal-replacement therapy in Australia or New Zealand (Table 1). Of these patients, 917 were boys (56 percent). A total of 18,392 person-years of follow-up were available. Of these, 4072 person-years took place during hemodialysis treatment (including 1435 person-years, or 35 percent, in the form of hemodialysis at home), 1633 person-years of peritoneal dialysis (including 1473 person-years, or 90 percent, in the form of of peritoneal dialysis at home), and 12,686 person-years with a functioning renal transplant. Data on 32 children (2 percent) were censored as of the date of the last follow-up visit, owing to loss to follow-up (primarily as a result of relocation overseas). The median period of follow-up was 9.7 years (range, 1 month to 35 years; interquartile range, 4.1 to 17.6 years).

The number of children over five years of age when renal-replacement therapy is initiated has been constant since the mid-1980s, but the number under five years of age at the start of therapy has increased. Reported causes of end-stage renal disease were consistent with those in other studies and varied with age. Congenital problems predominated among younger children, and reflux nephropathy and glomerulonephritis among older children. Twenty-six percent of children who were younger than 5 years of age when renal-replacement therapy commenced had renal hypoplasia and dysplasia, as compared with 5 percent of those who were 10 to 19 years of age when the therapy was initiated. In children younger than five years of age at the initiation of renal-replacement therapy, only 11 percent had glomerulonephritis and 3 percent had reflux nephropathy. In contrast, 44 percent of children 10 to 19 years of age had glomerulonephritis and 25 percent had reflux nephropathy.

Table 1. Number of Children Treated for End-Stage Renal Disease in Australia and New Zealand in the Period from 1963 to 2002, According to Age and Decade of Initial Treatment.

Decade of Initial Treatment	Age					
	<1 Yr	1–4 Yr	5–9 Yr	10–14 Yr	15–19 Yr	Total
1963–1972	0	4	6	31	86	127
1973–1982	0	12	57	120	262	451
1983–1992	9	38	75	156	267	545
1993–2002	26	64	85	121	215	511
Total	35	118	223	428	830	1634

MODE OF TREATMENT

Among the 1634 children, 1398 (86 percent) received 1 or more renal transplants (of 1939 transplantations, 136 were of grafts that were transplanted into patients who had not previously received dialysis treatment, or preemptive grafts, and 3 were performed outside Australia or New Zealand). Overall, the median waiting time from the initiation of renal-replacement therapy among the 515 children whose first allograft was from a living donor was 137 days (interquartile range, 10 to 382), and the median waiting time was 402 days (interquartile range, 192 to 785) among those whose first graft was a cadaveric allograft. The proportion of allografts from living donors has steadily increased over time — from 5 percent to 21 percent, 35 percent, and 64 percent among children commencing renal-replacement therapy in the decades 1963 to 1972, 1973 to 1982, 1983 to 1992, and 1993 to 2002, respectively. Median times from the initiation of renal-replacement therapy to the first transplantation among patients who received dialysis for a period were 161, 334, 324, and 296 days among children who commenced renal-replacement therapy in the decades 1963 to 1972, 1973 to 1982, 1983 to 1992, and 1993 to 2002, respectively. Monoclonal- or polyclonal-antibody therapy for prophylaxis against rejection was used after transplantation of 319 allografts (16 percent).

The proportion of children receiving renal transplantation as renal-replacement therapy has remained steady over time. More older children tended to be treated with dialysis than with renal

transplantation. Among children in our study, the median duration of hemodialysis was 1.7 years (interquartile range, 0.5 to 4.3), that of peritoneal dialysis 1.1 years (interquartile range, 0.4 to 2.5), and that of a functioning transplant 7.4 years (interquartile range, 2.7 to 14.3).

OVERALL SURVIVAL AND CAUSES OF DEATH

During the study period there were 436 deaths: 142 deaths occurred in patients with a functioning renal transplant, 97 in patients who were receiving peritoneal dialysis, and 197 in patients who were receiving hemodialysis. The most common cause of death was cardiovascular disease (45 percent), and the second most common cause was infection (21 percent). Of the deaths due to cardiovascular causes, 25 percent were attributed to cardiac arrest (cause uncertain), 16 percent to cerebrovascular accident, 14 percent to myocardial ischemia, 12 percent to pulmonary edema, 11 percent to hyperkalemia, and 22 percent to other cardiovascular causes.

The cause of death varied with the type of renal-replacement therapy — cardiovascular causes accounted for 57 percent of deaths among children receiving hemodialysis, 43 percent among those receiving peritoneal dialysis, and only 30 percent among those with a functioning renal transplant. In contrast, malignant diseases were responsible for 14 percent of deaths among children who had a functioning transplant, but only 1 percent of deaths among patients receiving hemodialysis and 2 percent among those receiving peritoneal dialysis. Death from malignant disease generally occurred late, accounting for only 1 percent of deaths in the first four years after renal-replacement therapy was initiated and 2 percent five to nine years after the start of renal-replacement therapy. In contrast, malignant disease accounted for 13 percent of deaths that occurred 10 to 14 years after the start of renal-replacement therapy and 17 percent of deaths 15 or more years after its start.

The proportion of deaths attributed to infection has declined over time, from 39 percent (12 of 31 deaths) between 1963 and 1972 to 16 percent (26 of 163) between 1993 and 2002. Across age groups, cardiovascular death accounted for 20 percent of deaths (2 of 10) among children younger than 1 year of age at the start of renal-replacement therapy, 24 percent (6 of 25) among those 1 to 4 years of age at its start, but 47 percent among those 5 to 9 years of age at the start of renal-replacement therapy (23 of 49), 44 percent among those 10 to 14 years of age at its start (48 of 110), and 48 percent among those 15 to 19 years of age at its start (117 of 242).

Rates of survival after 5, 10, 15, and 20 years of renal-replacement therapy are shown in Table 2. Contemporary Australian population data indicate that the expected 20-year survival among children is greater than 97 percent at all ages[11]; however, for this cohort with end-stage renal disease, mortality greatly exceeded the population rates in all age groups (Table 3).

Rates of long-term survival among infants as compared with older children with end-stage renal disease appear worse, particularly in the first five years after the initiation of renal-replacement therapy (Table 2). After a substantial improvement in survival occurred in most age groups in the years from 1963 to 1973, and further improvement from 1973 to 1983, less change occurred from 1983 on-

Table 2. Unadjusted Long-Term Survival among Children with End-Stage Renal Disease in Australia and New Zealand, According to Age at the Start of Renal-Replacement Therapy.

Age (Yr)	Survival			
	5 Yr	10 Yr	15 Yr	20 Yr
	percentage (95 percent confidence interval)			
<1	73 (54–85)	67 (46–81)	67 (46–81)	—
1–4	79 (70–86)	78 (68–85)	74 (16–83)	74 (61–83)
5–9	87 (81–91)	79 (73–85)	73 (66–80)	72 (64–79)
10–14	88 (85–91)	79 (74–83)	70 (65–75)	68 (62–73)
15–19	86 (83–88)	79 (76–82)	72 (68–75)	65 (60–69)
0–19	86 (84–88)	78 (76–80)	71 (69–74)	66 (63–69)

Table 3. Age-Specific Rate Ratios for Death within 10 Years among Children Who Started Renal-Replacement Therapy in Australia in the Period from 1963 to 2002, as Compared with Age-Specific Mortality among the General Australian Population.*

Decade Therapy Started	Rate Ratio for Death			
	0–4 Yr	5–9 Yr	10–14 Yr	15–19 Yr
1963–1972	116 (37–358)	236 (98–566)	111 (64–198)	52 (36–75)
1973–1982	63 (26–151)	122 (75–199)	71 (49–104)	20 (14–28)
1983–1992	30 (16–57)	30 (13–73)	37 (23–59)	19 (13–27)
1993–2002	32 (17–59)	94 (39–226)	35 (16–78)	30 (18–49)

* Numbers in parentheses are 95 percent confidence intervals.

ward (Fig. 1). In data categorized by calendar year, the death rates were 11.0 (95 percent confidence interval, 7.9 to 15.4) per 100 patient-years between 1963 and 1972, 4.4 (95 percent confidence interval, 3.7 to 5.3) per 100 patient-years between 1973 and 1982, 2.0 (95 percent confidence interval, 1.7 to 2.4) per 100 patient-years between 1983 and 1992, and 1.8 (95 percent confidence interval, 1.5 to 2.1) per 100 patient-years since 1993.

Rates of survival also varied with the type of renal-replacement therapy. Overall mortality rates were 4.8 (95 percent confidence interval, 4.2 to 5.6) per 100 patient-years among patients receiving hemodialysis, 5.9 (95 percent confidence interval, 4.9 to 7.2) per 100 patient-years among those receiving peritoneal dialysis, and 1.1 (95 percent confidence interval, 0.9 to 1.3) per 100 patient-years among those with a functioning renal transplant.

Multivariate analysis suggested that a younger age at the start of renal-replacement therapy, receiving dialysis rather than renal transplantation, and commencing renal-replacement therapy before 1983 were associated with an increased risk of death. There was a weak interaction between transplantation and the decade in which renal-replacement therapy was started (P=0.07), but the benefit associated with transplantation at all times was similar (Fig. 2).

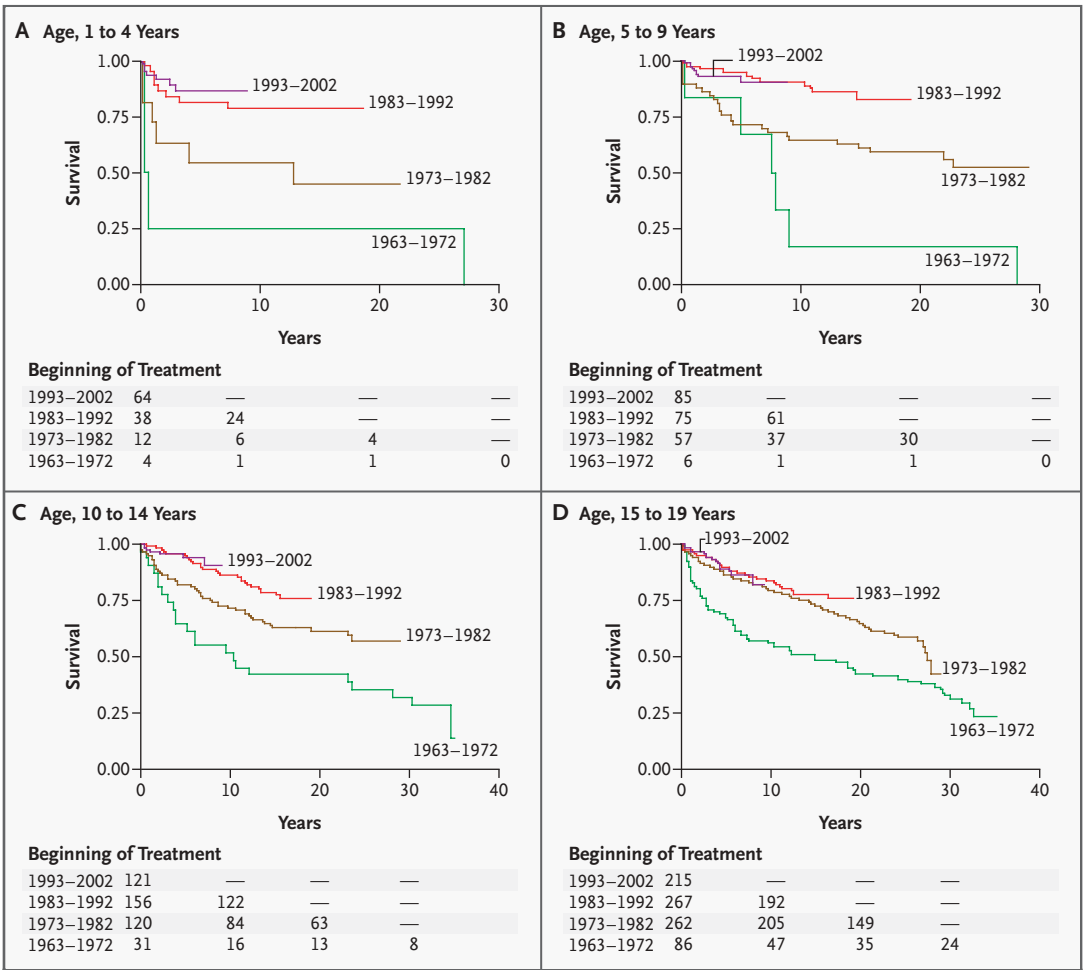


Figure 1. Kaplan–Meier Graphs of Overall Rates of Survival among Children and Adolescents with End-Stage Renal Disease in Australia and New Zealand from 1963 to 2002, According to Age and Decade during Which Treatment Began.

The number of patients at risk at each time point is shown below each graph. Dashes indicate that follow-up data are not yet available.

DELAY BEFORE TRANSPLANTATION

Delay in kidney transplantation as a potential risk factor for early death was analyzed by comparing mortality among groups with different lengths of time until transplantation. To account for survival bias, delay as a predictor of early death was analyzed beginning two years after the initiation of renal-replacement therapy. There was no significant difference in mortality observed among those who survived to two years among groups with different lengths of time until transplantation (Fig. 3).

DISCUSSION

Our data indicate that a substantial improvement in the long-term survival of children and adolescents with end-stage renal disease occurred over the past 40 years. The experimental nature of the use of dialysis and transplantation among children during the decade from 1963 to 1972 provides a partial explanation, given that the improvement in mortality subsequently slowed. Ten-year survival remains about 80 percent, and age-specific mortality is about 30 times as high as among children without end-stage renal disease.

These mortality rates are similar to those reported in a U.S. study for the period from 1990 to 1996[12] but are slightly higher than those reported in a Dutch study of a smaller cohort[13] that did not include adolescents. The distribution of primary renal disease and the mortality rates among patients receiving dialysis in our study are similar to those in recent reports from the North American Pediatric Renal Transplant Collaborative Study (NAPRTCS), in which the duration of follow-up was shorter for a cohort of pediatric dialysis patients.[6] The causes of death reflect the excess risk of cardiac disease and vascular disease and the high prevalence of left ventricular hypertrophy and dyslipidemia among children treated with renal-replacement therapy.[14-16] The number of deaths from cardiovascular disease among the patients who received dialysis in our study was higher than that reported by the U.S. Renal Data System (37 percent)[17] and by the NAPRTCS (21 percent).[18] Detailed comparisons, however, are hindered by the different coding systems used in the various studies, especially the different definitions of diagnoses coded "unknown" and "other."

The trend toward improvement in the rates of survival among patients in our study has also been observed since 1987 among patients in the NAPRTCS Registry who have undergone renal transplantation.[18] The 2003 NAPRTCS report[18] noted that the overall rate of survival to 36 months was 96.6 percent among recipients of kidney transplants from living donors and 94.8 percent among those receiving cadaveric kidneys — values similar to the 1.1 percent annual mortality rate we observed among transplant recipients. The strengths of our study — the large number of children in the study, prospective data collection, the

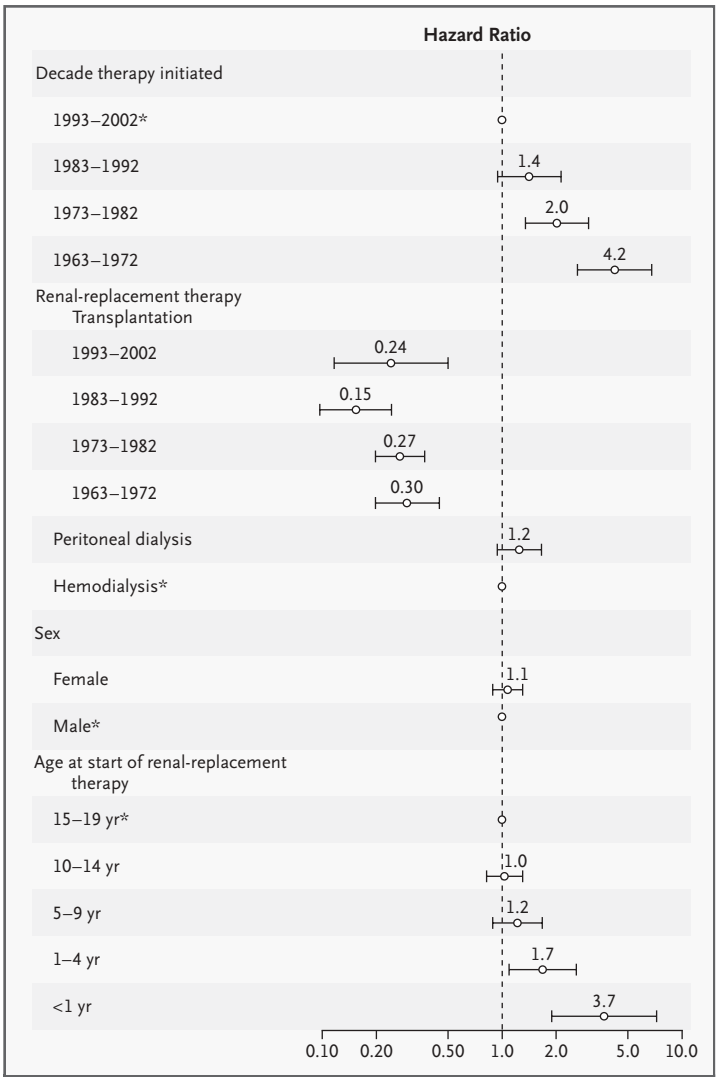
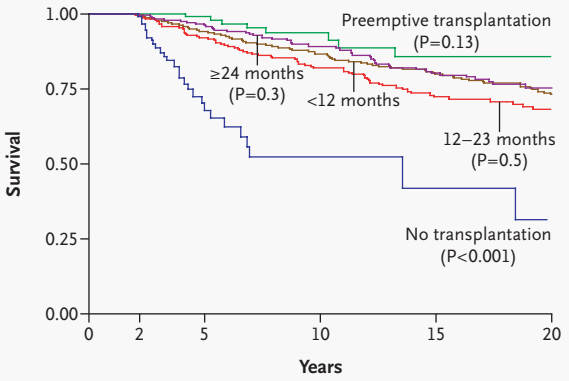


Figure 2. Hazard Ratios for Death among Children and Adolescents with End-Stage Renal Disease in Australia and New Zealand, According to Selected Predictive Variables.

Hazard ratios were derived in a multivariate Cox proportional-hazards model. The asterisks indicate the reference categories. Horizontal bars indicate 95 percent confidence intervals.



Period of Dialysis before Transplantation

Preemptive transplantation	118	88	43	22	10
<12 months	593	525	395	272	155
12–23 months	310	275	186	124	64
≥24 months	279	233	169	108	65
No transplantation	95	30	7	4	2

Figure 3. Kaplan–Meier Graph of Survival Rates among Children and Adolescents in Australia and New Zealand Who Survived at Least Two Years after the Start of Renal-Replacement Therapy, According to the Length of Time to Transplantation.

The numbers at the bottom are patients at risk grouped by period of dialysis treatment before transplantation. P values are for the comparison with patients who underwent transplantation within 12 months after renal-replacement therapy was started. Preemptive transplantation refers to renal transplantation in patients who had not previously received peritoneal dialysis or hemodialysis.

availability of accurate data on the type of renal-replacement therapy, and the long duration of follow-up with minimal loss to follow-up — enabled us to provide valid and reasonably precise estimates of long-term survival and to identify modifiable and unmodifiable risk factors for death.

The year in which renal-replacement therapy was initiated, the age of patients at the start of renal-replacement therapy, and the type of dialysis used were associated with the risk of death. Our data suggest that the older a child is when renal-replacement therapy is required, the better his or her chances for long-term survival. This improved survival may be due to the less aggressive nature of the underlying renal disease process, to the fact that associated coexisting conditions are more likely to occur in infants and young children, or to the greater technical challenges of delivering renal-replacement therapy to young and small children.

Perhaps more important is our finding that dialysis is associated with a risk of death that is four times the risk associated with renal transplantation. The improvement in survival after renal transplantation is substantial and sustained. This finding is consistent with the relative survival advantage among adults who have undergone transplantation, as shown in studies conducted in Australia and New Zealand[19] and in the United States.[20] The proportion of children with end-stage renal disease who are treated with transplantation can be increased by increasing the number of kidneys available for transplantation (that is, by increasing rates of donation from living donors or by preferentially allocating cadaveric kidneys to children) and by means of improvements in the preservation of the renal function of allografts. These interventions are being attempted widely, with some variation among and within countries. Others have shown a survival advantage in the short term among children who receive "preemptive" transplants from living donors before the need for dialysis arises.[5]

We did not find that a longer period of dialysis before transplantation was detrimental to survival after transplantation. However, there was limited statistical power in the present study for this comparison. Although we looked at survival only among children who survived longer than two years after the onset of end-stage renal disease, some residual survival bias may account for this lack of difference; the ANZDATA Registry does not collect enough details about coexisting conditions for us to adjust fully for this potential effect. Nevertheless, patients who have a longer wait for renal transplantation will have worse overall outcomes, because they are exposed for a longer period to the increased risk of death that is associated with dialysis treatment. This fact is a clear incentive to increase the rates of transplantation among children with end-stage renal disease.

There was a low rate of loss to follow-up in the cohort. Informally, the ANZDATA Registry data are believed to be accurate: information is checked against available data from tissue-typing and organ-donation sources, but formal audit mechanisms were not in place during the period we studied. Data on deaths were not checked against death certificates; a previous study that matched the registry's data on deaths with national death-certificate reports[21] has confirmed that mortality (though not necessarily cause) was accurately ascertained.

The current study has weaknesses. The ANZDATA Registry does not record details of patients with end-stage renal disease who are not

treated, and treatment thresholds have clearly been lowered over time, particularly among children. These changing thresholds are likely to be reflected in both referral and selection biases — that is, sicker children were less likely to be referred for renal-replacement therapy and, after they are referred, are less likely to be offered such treatment. These biases would lead to the underestimation of improvements in outcome over time, with an increasing tendency toward treating sicker children. Attitudes among nephrologists toward offering renal-replacement therapy to very young children vary considerably.[22] Although the qualifications of treating physicians are not specifically collected by the registry, patients under 20 years of age in Australia and New Zealand are treated almost exclusively by pediatric nephrologists in specialist pediatric centers. Other information about details of treatment in the registry are limited. Data on hemoglobin concentrations and the use of erythropoietic agents have been collected only since 2000, and data on lipid levels and blood pressure are not collected. The use of growth hormone has been sparse; approximately one third of children in Australia and less than 10 percent in New Zealand have received growth hormone.[1]

Any misclassifications of data with regard to exposure or outcome are likely to be nondifferential with respect to study periods and types of treatment; thus, our findings regarding associations between the type of treatment and outcomes are conservative. The time-dependent covariates used in our model result in the attribution of death to the type of renal-replacement therapy in use immediately before death. This method may result in an overestimation of the benefit of transplantation, since deaths that occurred among patients receiving dialysis but that were related to the recent failure of a renal transplant were attributed to the use of dialysis. Another obvious source of bias in the comparison of outcomes between dialysis and transplantation is the selection of the healthier patients to undergo transplantation, although the high proportion of patients in our study cohort who received a renal transplant suggests this effect is relatively minor.

Our data indicate that long-term survival can be expected for most children with end-stage renal disease. Transplantation remains the major modifiable factor in improving the long-term survival of children and adults with this disease. Early transplantation appears indicated to prevent exposure to the increased risks associated with dialysis therapy. Yet mortality rates among children who undergo transplantation remain in excess of those in the normal population. The challenge ahead is to reduce the incidence of the cardiovascular and malignant diseases that account for the bulk of long-term mortality among children with end-stage renal disease.

Supported by the Australian Government Department of Health and Ageing, the New Zealand Department of Health, and Kidney Health Australia (formerly the Australian Kidney Foundation).

Dr. McDonald reports having received lecture fees from Amgen Australia and Janssen-Cilag Australia; he is employed by ANZDATA, and although he receives no direct industrial support, part of his salary is funded by a grant from Amgen Australia to the ANZDATA Registry, which also receives grant support from Janssen-Cilag Australia, Novartis, Wyeth Australia, and Fresenius. Dr. Craig reports having received grants from Janssen-Cilag Australia, Novartis, Amgen Australia, Wyeth Australia, and Fresenius.

We are indebted to the staff of all Australian and New Zealand renal units for their efforts in data collection (the ANZDATA Registry exists because of their dedicated efforts), and to Steven Morrell of the School of Public Health at the University of Sydney for help with the age-specific mortality rates.

REFERENCES

1. Walker RG. Paediatric report. In: Disney APS, ed. The twenty-second report: Australia and New Zealand Dialysis and Transplant Registry 1999. Adelaide, Australia: ANZDATA Registry, 1999:90-97.
2. Henning P, Tomlinson L, Rigden SP, Haycock GB, Chantler C. Long term outcome of treatment of end stage renal failure. Arch Dis Child 1988;63:35-40.
3. Ehrich JH, Rizzoni G, Brunner FP, et al. Renal replacement therapy for end-stage renal failure before 2 years of age. Nephrol Dial Transplant 1992;7:1171-7.
4. Wood EG, Hand M, Briscoe DM, et al. Risk factors for mortality in infants and young children on dialysis. Am J Kidney Dis 2001;37:573-9.
5. Vats AN, Donaldson L, Fine RN, Chavers BM. Pretransplant dialysis status and outcome of renal transplantation in North American children: a NAPRTCS study. Transplantation 2000;69:1414-9.
6. Leonard MB, Donaldson LA, Ho M, Geary DF. A prospective cohort study of incident maintenance dialysis in children: an NAPRTC study. Kidney Int 2003;63:744-55.
7. Ledermann SE, Scanes ME, Fernando ON, Duffy PG, Madden SJ, Trompeter RS. Long-term outcome of peritoneal dialysis in infants. J Pediatr 2000;136:24-9.
8. Coulthard MG, Crosier J. Outcome of reaching end stage renal failure in children under 2 years of age. Arch Dis Child 2002;87:511-7.
9. Russ GR. Australia and New Zealand Dialysis and Transplant Registry Report 2002. Adelaide, Australia: Australia and New Zealand Dialysis and Transplant Registry, 2002.
10. Held PJ, Turenne MN, Liska DW, et al. Treatment modality patterns and transplantation among the United States pediatric end-stage renal disease population: a longitudinal study. In: Terasaki P, ed. Clinical transplants 1991. Los Angeles: UCLA Tissue Typing Laboratory, 1992:71-85.
11. Deaths: Australia, 2000. Canberra, Australia: Australian Bureau of Statistics, 2001. (ABS catalogue no. 3302.0.)
12. Parekh RS, Carroll CE, Wolfe RA, Port FK. Cardiovascular mortality in children

and young adults with end-stage kidney disease. J Pediatr 2002;141:191-7.
13. Groothoff JW, Gruppen MP, Offringa M, et al. Mortality and causes of death of end-stage renal disease in children: a Dutch cohort study. Kidney Int 2002;61:621-9.
14. Mitsnefes MM, Daniels SR, Schwartz SM, Meyer RA, Khoury P, Strife CF. Severe left ventricular hypertrophy in pediatric dialysis: prevalence and predictors. Pediatr Nephrol 2000;14:898-902.
15. Bakkaloglu SA, Ekim M, Tumer N, Soylu K. The effect of CAPD on the lipid profile of pediatric patients. Perit Dial Int 2000;20:568-71.
16. Silverstein DM, Palmer J, Polinsky MS, Braas C, Conley SB, Baluarte HJ. Risk factors for hyperlipidemia in long-term pediatric renal transplant recipients. Pediatr Nephrol 2000;14:105-10.
17. Renal Data System. USRDS 2003 annual data report: atlas of end-stage renal disease in the United States. Bethesda, Md.: National Institute of Diabetes and Digestive and Kidney Diseases, 2003.
18. North American Pediatric Renal Transplant Cooperative Study (NAPRTCS). 2003 Annual report: renal transplantation, dialysis, chronic renal insufficiency. Rockville, Md.: EMMES, 2003.
19. McDonald SP, Russ GR. Survival of recipients of cadaveric kidney transplants compared with those receiving dialysis treatment in Australia and New Zealand, 1991-2001. Nephrol Dial Transplant 2002;17:2212-9.
20. Wolfe RA, Ashby VB, Milford EL, et al. Comparison of mortality in all patients on dialysis, patients on dialysis awaiting transplantation, and recipients of a first cadaveric transplant. N Engl J Med 1999;341:1725-30.
21. Li SQ, Cass A, Cunningham J. Cause of death in patients with end-stage renal disease: assessing concordance of death certificates with registry reports. Aust N Z J Public Health 2003;27:419-24.
22. Geary DF. Attitudes of pediatric nephrologists to management of end-stage renal disease in infants. J Pediatr 1998;133:154-6.