Original Articles

Impact of graft loss among kidney diseases with a high risk of post-transplant recurrence in the paediatric population

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ABSTRACT

Background. Some kidney diseases tend to recur in the renal allograft after transplantation. We studied the risk of graft loss among primary renal diseases known for their high risk of recurrence and compared it with that of patients with hypoplasia and/or dysplasia.
Methods. Within the European Society of Paediatric Nephrology and European Renal Association and European Dialysis and Transplant Association (ESPN/ERA-EDTA) registry, we studied children from 33 countries who received a kidney transplant before the age of 20 between 1990 and 2009. Patients were censored after 5 years of follow-up and cumulative incidence competing risk analysis was used to calculate survival curves.
Results. Patients with focal and segmental glomerulosclerosis (FSGS), haemolytic uraemic syndrome (HUS), membranoproliferative glomerulonephritis Type I or II (MPGN), IgA nephropathy or Henoch Schönlein Purpura (HSP/IgA) or systemic lupus erythomatosus (SLE) underwent pre-emptive transplantation significantly less often than patients with hypoplasia and/or dysplasia. The rate of living donation was lower among patients with FSGS and SLE than in patients

with hypoplasia and/or dysplasia. In comparison with hypoplasia and/or dysplasia patients with a risk of 14.4%, the 5-year risk of graft loss was significantly increased in patients with FSGS (25.7%) and MPGN (32.4%) while it was not significantly increased in children with HUS (18.9%), HSP/IgA (16.3%) or SLE (20.3%). One-year graft survival strongly improved among HUS patients from 17.1% in 1995–1999 to 3.6% in 2005–2009 and was not accompanied by a decrease in the number of transplantations.

Conclusion. The risk of graft loss is increased among specific causes of renal failure with a high risk of post-transplant recurrence. It seems likely that, due to anticipation of such risk, physicians perform less pre-emptive transplantation and provide fewer grafts from living related donors in patients with these conditions. Improved risk stratification by physicians, resulting in the identification of patients with HUS at higher or lower risk of recurrence, might explain the much improved graft survival rates.

INTRODUCTION

Renal transplantation is the treatment of choice for children and adults with end-stage renal disease. However, it is not always an ultimate solution, as some kidney diseases tend to recur in the renal allograft and disease recurrence is more frequent in children than in adults [1]. One could make a distinction between kidney diseases that tend to have a 'full blown' recurrence leading to graft loss, and kidney diseases that recur without apparent increased risk of graft loss [1]. Although several studies reported an increased risk of graft loss among very rare specific kidney diseases, they were usually based on a very limited number of patients and were compared with the general risk of graft loss.

In the present paper we describe the real-life risk of graft loss among kidney diseases known to be associated with a high risk of disease recurrence and subsequent graft loss [idiopathic focal and segmental glomerulosclerosis (FSGS), haemolytic uraemic syndrome (HUS), membranoproliferative glomerulonephritis (MPGN) and mesangiocapillary glomerulonephritis Type I and II (dense deposit disease)] together with those kidney diseases with a high risk of disease recurrence but in which the risk of graft loss is expected to be low(er), namely IgA nephropathy and Henoch Schönlein Purpura (HSP/IgA) and systemic lupus erythomatosus (SLE). We compared these risks with those of patients with hypoplasia or dysplasia (excluding patients with obstructive uropathy or reflux), who do not suffer from disease recurrence. We wanted to determine (i) patient characteristics at the time of transplantation for individuals with specific kidney diseases; (ii) the risk of graft loss for these kidney diseases and (iii) subgroups that were at higher or lower risk and any recent time trend in the risk of graft loss.

MATERIALS AND METHODS

Within the framework of the European Society of Paediatric Nephrology and European Renal Association and European Dialysis and Transplant Association (ESPN/ERA-EDTA) Registry, countries collected individual patient data on the date of birth, gender, treatment modality at the start of renal replacement therapy (RRT) and changes in RRT modality [2]. Patients aged 20 years or less who received a transplant between 1 January 1990 and 31 December 2009 were included in the analysis. Austria, Belgium, Belarus, Bulgaria, Croatia, Czech Republic, Denmark, Estonia, Finland, France, FYR of Macedonia, Greece, Hungary, Iceland, Italy, Latvia, Lithuania, Montenegro, the Netherlands, Norway, Poland, Portugal, Romania, Russia, Serbia, Slovakia, Slovenia, Spain, Sweden, Switzerland, Turkey, Ukraine and the UK all contributed to the study. To avoid a selection bias among patients, we limited our analyses to time periods for which countries contributed complete data. The kidney diseases were coded according to the ERA-EDTA coding system [3]: FSGS (Code 11), HUS (Code 88), MPGN Type I (Code 15), MPGN Type II (Code 13), HSP/IgA (Code 12 and 85), SLE (Code 84), hypoplasia and/or dysplasia (Codes 60, 61, 63, and 66). In the ESPN/ERA-EDTA registry, insufficient data were available on the recurrence of the disease as the cause of graft loss. We assumed that any additional risk of graft loss among diseases known for their increased risk of disease recurrence, when compared with that among patients with hypoplasia and/or dysplasia would be due to disease recurrence. Patients were censored after living with a transplant at the end of the observation period, reaching 31 December 2009, being transferred to a centre for treatment of adult patients without information on the follow-up or after death without prior dialysis (assumed with a functioning graft).

Analyses

Analyses were performed using SAS 9.2. Differences between categorical variables were calculated using the χ^2 test, whereas differences between continuous variables were calculated using a t-test. The associations between patient characteristics at the time of transplantation and the likelihood of transplantation were calculated using logistic regression analyses, resulting in odds ratios (ORs) and 95% confidence intervals (95% CIs). To study 1- and 5-year graft survival and to determine the percentage of graft survival, survival curves were calculated taking the competing event death into account by using cumulative incidence competing risk analysis [4]. In this analysis, significance was determined using P-values calculated according to Pepe and Mori [5]. Trends over time were only calculated among those countries providing complete follow-up data between 1995 and 2009 and only those causes of renal failure were selected in whom at least 20 patients per era received a renal allograft. Cox-regression models were used to calculate the risk of graft loss at 1 and 5 years. The obtained hazard ratios (HRs) were adjusted for age at the start of RRT, age at transplantation, gender and era of transplantation. For different subgroups, the Cox-regression analyses were repeated. A sensitivity analyses was performed including adjustment for living versus deceased donation. P-values of <0.05 were considered as statistically significant.

K.J. Van Stralen *et al.*

RESULTS

In the ESPN/ERA-EDTA registry between 1 January 1990 and 31 December 2009, 5892 patients with end-stage renal failure received a renal transplant. The 3937 patients who suffered from other causes of renal failure than the ones under study were excluded. Therefore, 1955 patients were included in the present analyses. Patient characteristics are shown in Table 1.

Characteristics at time of transplantation

Patients with a high risk of recurrence of their underlying condition underwent pre-emptive transplantation significantly less frequently than those with hypoplasia and/or dysplasia, even after adjustment for age, gender and time period (Table 2). Compared with children with hypoplasia and/or dysplasia, patients with FSGS were 74% less likely, those with HUS 52% less likely, those with MPGN 80% less likely and those with HSP/IgA 68% less likely to receive a transplant pre-emptively when compared with receiving a transplant while being on dialysis for more than a year. However, when a patient started on dialysis, there were no differences between the different causes of renal failure with respect to receiving a transplant after short-term dialysis or dialysis for more or less than 1 year, except among patients with SLE. In addition, patients with FSGS and SLE received a transplant from a deceased donor significantly more often than from a living donor (OR 1.65, 95% CI 1.16–2.34, respectively, 3.50 95% CI 1.14–10.8) when compared with children with hypoplasia and/or dysplasia.

Risk of graft loss

Patients with FSGS had the highest risk of graft loss in the first year after transplantation namely 14.7%, Table 3. Patients with other kidney diseases lost their graft in 6.8% (HSP/IgA) and 10.1% (MPGN) of the cases, which was not significantly different from those with hypoplasia and/or dysplasia (6.4%), Figure 1.

After 5 years, 32.4% of the patients with MPGN had suffered from a graft loss, which was considerably higher than among those with hypoplasia and/or dysplasia (14.4%), Table 4, while the risk among patients with FSGS was 25.7%. The patterns of graft loss differed between the different causes of renal failure, while the risks of graft loss for example due to FSGS (Figure 1A) was very high in the first year and were more stable thereafter, the risk of graft loss in MPGN was consistently high over time (Figure 1C).

Focal and segmental glomerulosclerosis

Patients with FSGS who started RRT during puberty (>12) had a significantly higher 5-year risk of graft loss (32.4%) when compared with those who started RRT before the age of 6 (17.1%), Figure 1A. Patients with FSGS who started RRT between the ages of 6 and 12 had an intermediate, but significantly increased risk of graft loss (27.7%). Relative risks for the different age groups when compared with their peers of the same age with hypoplasia and/or dysplasia resulted in

HRs of 1.4 for the youngest, 1.7 for those between 6–12 and 3.2 for the oldest age group (Table 4). Among patients with FSGS who received a pre-emptive transplantation the risks of graft loss were very similar (5.8% at 1 year and 22% at 5 years) when compared with the overall FSGS group; however, numbers were small.

Haemolytic uraemic syndrome

The 5-year risk of graft loss among patients with HUS was 18.9%. Patients with HUS who started RRT before the age of 6 had a higher risk (21.9%) of graft loss at 5 years than those who had started thereafter (16.5%), Figure 1B. The risk of 1-year graft loss significantly decreased among patients over time (17.1% in 1995–1999 to 3.6% in 2005–2009, P = 0.03). This decrease was not associated with a change in the number of transplanted patients in absolute terms or relative to the number of patients with hypoplasia and/or dysplasia.

Membranoproliferative glomerulonephritis

When studying MPGN Type I and Type II separately, we found that the risk of 5-year graft loss was 23.5% for MPGN Type I and 67.5% among patients with Type II, Figure 1C. Although the rates between both types were significantly different from patients with hypoplasia and/or dysplasia, they were not significantly different from each other.

Systemic lupus erythomatosus

Patients with SLE had a slightly but not significantly increased risk of graft loss (20.3% at 5 years). However, after adjustment for the lower rate of living donation and pre-emptive transplantation, surprisingly the differences between SLE and hypoplasia and/or dysplasia patients were significant, showing a 3-fold increased risk of graft loss for SLE patients when compared with those with hypoplasia and/or dysplasia (Table 4).

HSP/IgA nephropathy

Patients with HSP/IgA had no increased risk of graft loss when compared with patients with hypoplasia and/or dysplasia. There were no differences between patients with HSP alone when compared with those with IgA nephropathy.

DISCUSSION

Patients with FSGS and MPGN had a significantly higher risk of graft loss when compared with patients with hypoplasia and/or dysplasia. There were large differences in the pattern of graft loss; while patients with FSGS mainly suffered from graft loss shortly after transplantation, patients with MPGN had a consistently high rate of graft loss independent from time since transplantation. The risk of graft loss was not increased for patients with HSP/IgA nephropathy. All patients received a pre-emptive transplant less often than patients with hypoplasia and/or dysplasia, and patients with FSGS or SLE received an organ from a living donor less often in comparison with patients with hypoplasia and/or dysplasia. We will discuss the results separately for each disease.

Table 1. Baseline characteristics

	Number of patients	Age at start RRT Mean (p5–p95)	Age at transplant Mean (p5–p95)	% females
FSGS	407	**9.7 (2.4–16.8)**	**11.4 (3.5–18.4)**	47.7
HUS	197	8.2 (0.8–17.5)	10.1 (2.5–18.5)	**54.8**
SLE	40	**13.8 (7.6–18.8)**	**15.9 (8.6–19.6)**	77.5
MPGN	93	**12.0 (3.6–18.8)**	**13.7 (4.9–19.2)**	**45.2**
HSP/IgA	122	**14.0 (6.7–18.9)**	**15.3 (9.5–19.4)**	40.2
Hypoplasia and/or dysplasia	1048	8.6 (0.14–17.1)	10.3 (1.9–18.1)	33.0

Bold values denote significant difference from hypoplasia and/or dysplasia (P < 0.05).
FSGS, focal and segmental glomerulosclerosis; HUS, haemolytic uraemic syndrome; SLE, systemic lupus erythomatosus; MPGN, membranoproliferative glomerulonephritis type I or II; HSP/IgA, IgA nephropathy or Henoch Schönlein Purpura.

Table 2. Transplant characteristics for patients with different causes of renal failure, and odds ratios for (i) receiving a transplant from a deceased versus a living donor; (ii) receiving a transplant pre-emptively compared with >1 year on dialysis or (iii) within a year on dialysis compared with >1 year on dialysis, adjusted for age at start of RRT, gender and period

	Percentages		Odds ratios		
	% Living donor[a]	% Pre-emptive Tx	Deceased versus living donor[a,b]	Pre-emptive tx[b]	Tx after dialysis <1 year[b]
FSGS	29.3	**9.1**	**1.65 (1.16–2.34)**	**0.26 (0.18–0.39)**	0.99 (0.76–1.33)
HUS	34.7	**12.2**	1.22 (0.80–1.86)	**0.48 (0.29–0.77)**	1.17 (0.81–1.68)
SLE	**16.7**	**10.0**	**3.50 (1.14–10.8)**	**0.20 (0.07–0.60)**	**0.36 (0.16–0.82)**
MPGN	45.7	**8.6**	0.82 (0.44–1.53)	**0.22 (0.10–0.48)**	0.89 (0.55–1.45)
HSP/IgA	43.8	**13.1**	1.00 (0.60–1.66)	**0.32 (0.18–0.59)**	1.04 (0.68–1.62)
Hypoplasia and/or dysplasia	41.0	26.1	1	1	1

Bold values denote significant difference from hypoplasia and/or dysplasia (P < 0.05).
OR, odds ratio; FSGS, focal and segmental glomerulosclerosis; HUS, haemolytic uraemic syndrome; SLE, systemic lupus erythomatosus; MPGN, membranoproliferative glomerulonephritis Type I or II; HSP/IgA, IgA nephropathy or Henoch Schönlein Purpura.
[a]Information on living versus deceased donation was available for 55.6% of the patients.
[b]Adjusted for age, gender and time period.

Focal and segmental glomerulosclerosis

After 5 years, over a quarter of the patients with FSGS had lost their renal allograft, which is equal to the fraction reported in previous studies, and very close to that reported also among adult patients [6, 7]. There was a strong difference in graft survival between patients who were below the age of 6 at the start of RRT and those who started during puberty. Very young patients with FSGS more often have genetic or congenital forms of FSGS, which might less often lead to a recurrence. Unfortunately, no information on the genetic background of the patients was available. Other studies have also suggested higher risks of graft loss among adolescents than among younger patients, with a lower risk again among the adult population [1, 8].

Haemolytic uraemic syndrome

Patients with HUS had an increased risk of graft failure. However, this increased risk only reached significance in the 1994–1999 period. Since then there has been a big improvement in graft survival. Recommendations not to perform transplantations (from living related donors) in patients with atypical HUS [9] may have resulted in a selection towards more patients with typical HUS. Furthermore, genetic screening of patients with atypical HUS for abnormalities in specific

Table 3. One-year risk of graft loss for specific causes of renal failure

	Number at risk at 1 year	1-year graft loss (%)	HR—1-year graft loss	HR—1-year graft loss[a]	HR—1-year loss[a,b]
FSGS	304	**14.7**	**2.44 (1.71–3.48)**	**2.46 (1.72–3.55)**	1.75 (0.98–3.13)
≤6 years at the start of RRT	84	11.7	1.71 (0.86–3.40)	1.79 (0.84–3.82)	1.37 (0.42–4.45)
6–12 years at the start of RRT	121	**14.2**	**1.93 (1.08–3.40)**	**1.88 (1.04–3.40)**	2.03 (0.74–5.58)
>12 years at the start of RRT	101	**17.4**	**4.38 (2.28–8.43)**	**4.61 (2.35–9.04)**	2.18 (0.80–5.94)
HUS	149	7.5	1.17 (0.66–2.09)	1.18 (0.66–2.11)	1.17 (0.52–2.60)
≤6 years at the start of RRT	71	9.4	1.33 (0.60–2.96)	1.47 (0.62–3.48)	2.05 (0.63–6.68)
>6 years at the start of RRT	79	5.9	0.97 (0.41–2.28)	1.00 (0.42–2.38)	0.64 (0.15–2.77)
SLE	31	10.2	1.74 (0.64–4.79)	1.94 (0.59–5.48)	1.80 (0.51–6.42)
MPGN	74	10.1	1.61 (0.80–3.24)	1.70 (0.84–3.46)	1.01 (0.30–3.41)
MPGN Type I	48	**13.3**	**2.15 (1.03–3.87)**	**2.64 (1.23–5.66)**	2.05 (0.60–7.07)
MPGN Type II	26	4.7	0.54 (0.07–3.87)	0.60 (0.08–4.33)	Not possible to estimate
HSP/IgA	97	6.8	1.10 (0.59–2.29)	1.22 (0.57–2.59)	0.71 (0.21–2.12)
Hypoplasia and/or dysplasia	869	6.4	1	1	1

Bold values denote significant difference from hypoplasia and/or dysplasia (P < 0.05).
HR, Hazard Ratio; FSGS, focal and segmental glomerulosclerosis; RRT, renal replacement therapy; HUS, haemolytic uraemic syndrome; SLE, systemic lupus erythomatosus; MPGN, membranoproliferative glomerulonephritis Type I or II; HSP/IgA, IgA nephropathy or Henoch Schönlein Purpura.
[a]Adjusted for age at start of RRT, age at transplantation, gender and era of transplantation.
[b]Additionally adjusted for living versus deceased donation, information on living versus deceased donation was available for 55.6% of the patients.

complement regulating proteins is increasingly performed and a genetic disease cause can now be identified in 50–70% of cases [10, 11]. Since the number of patients with HUS receiving a transplantation did not change, current practice will have most likely led to a improved risk stratification, resulting in a lower number of patients with a high-risk profile receiving a transplant and an increased number of transplants in those with a low-risk profile.

Unfortunately, our data did not allow the distinction between patients with typical and atypical HUS. We tried to distinguish between these groups by studying two different age groups as traditionally young age at onset was an indicator for typical HUS. However, we found a higher risk of graft loss among patients who started RRT before the age of 6, while the risk among those who were above 6 years was very similar to that among patients with hypo- or dysplasia. Recently, Geerdink et al. also showed that nearly half of the patients with atypical HUS first manifest before the age of 5, questioning age as a valuable marker for the type of HUS

[12]. Early onset atypical HUS might be an even more aggressive form, explaining the high risk of graft loss.

Systemic lupus erythomatosus

There was a tendency towards increased graft loss among patients with SLE, although it was not significantly different from that of patients with hypoplasia and/or dysplasia. Our results were similar to those found in adults, but these varied widely as 5-year graft survival has been shown to be between 69 and 91% [13–15]. Nevertheless, the tendency towards an increased risk of graft loss was worse than expected given the potential for current immunosuppressive regimens to maintain remission [1].

Membranoproliferative glomerulonephritis

MPGN is usually divided into Type I and II on the basis of ultrastructural features [16, 17]. It has been suggested, however, that differences in recurrence rates may be more related to the severity of the disease than to the underlying
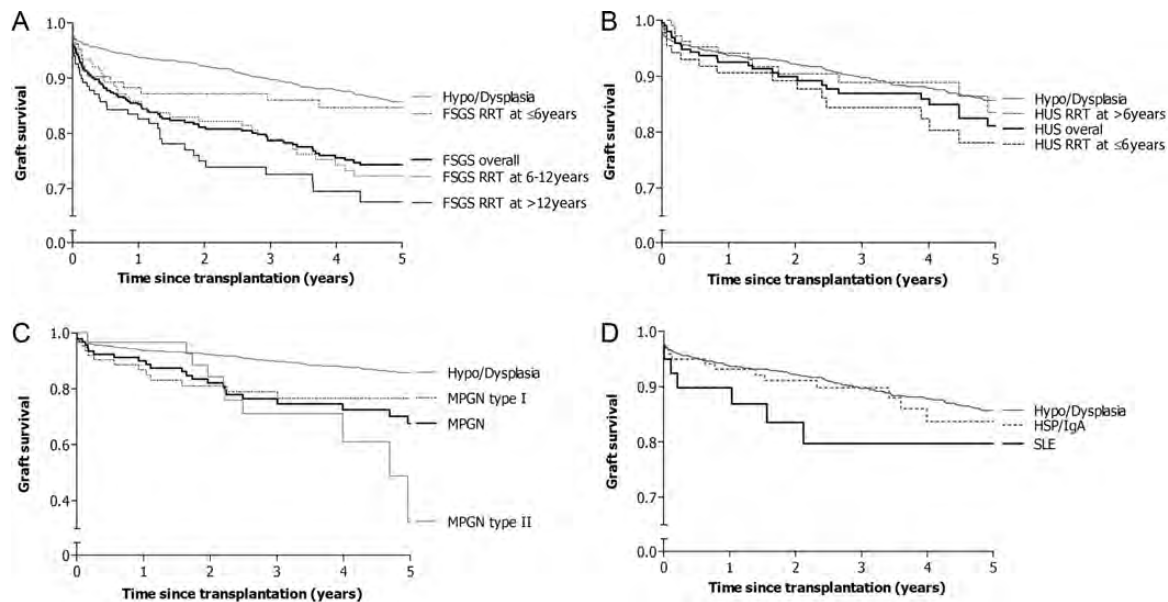
FIGURE 1: Graft survival among specific causes of end-stage renal disease compared with patients with hypoplasia and/or dysplasia. The curves have been adjusted for competing risks, namely death. (**A** and **B**) Separate curves for those children starting on RRT according to different age groups for patients with FSGS (A) and HUS (B). (**C**) Separate curves for patients with MPGN Type I and II (dense deposit disease). (**D**) Curves for patients with HSP/IgA and SLE. FSGS, focal and segmental glomerulosclerosis; RRT, renal replacement therapy; HUS, haemolytic uraemic syndrome; SLE, systemic lupus erythomatosus; MPGN, membranoproliferative glomerulonephritis Type I or II; HSP/IgA, IgA nephropathy or Henoch Schönlein Purpura.

ultrastructural features [17]. We found a higher risk of graft loss at 5 years among patients with dense deposit disease which was similar to that found in previous studies performed in the 1980s [18]. The low graft loss among patients with MPGN Type I was similar to that reported in other studies among adult patients [6, 19]. Differences between MPGN Type I and II did not reach statistical significance due to the small number of patients with MPGN Type II. Unlike the other causes of renal failure, the rate of graft loss did not improve over time in the years since transplantation. Previous studies suggested a 50% reduced risk of graft loss among patients with an organ from a living-related donor [18], which possibly also explains the slightly higher proportion of patients who received an organ from a living donor. However, adjustment for living versus deceased donation did not affect the risk estimates suggesting a very low advantage of a living donation among patients with MPGN when compared with that among patients with hypoplasia and/or dysplasia.

IgA nephropathy or Henoch Schönlein Purpura

Even though previous studies have reported recurrence rates of around 33% (range 9–61%) for patients with HSP/IgA nephropathy [16], many studies, among adult patients, have shown that this does not affect graft survival [6, 20]. Our data also show that the risk of graft loss (16.3%) was very similar to that among patients with hypoplasia and/or dysplasia. Little is known about the rate of actual graft loss in these children, but in adults 5-year graft loss rates have been reported of 16–30% [20–23].

LIMITATIONS

In this study, we investigated whether the risk of graft loss was increased among children suffering from causes of renal failure with a high rate of recurrence of the primary disease in the transplantations. We compared those risks with the risk among patients with hypoplasia and/or dysplasia. Although patients with hypoplasia and/or dysplasia do not have higher risks of graft loss due to disease recurrence, there might be other factors affecting the risk of graft loss. Many patients with hypoplasia and/or dysplasia are diagnosed antenatally and disease progression is typically slower and more predictable than patients with glomerulopathy, making these conditions more amenable to pre-emptive transplantation. There was quite a large group of patients in whom information on whether the received kidney was from a living or a deceased donor was missing. This might have affected the results of the sensitivity analyses.

In this study, we cannot say whether an increased risk of graft loss is actually related to a recurrence of the disease or whether other factors are involved. Conversely, we do not have information on disease recurrence without graft loss. Nevertheless, we believe that most of the additional risk when compared with hypoplasia and/or dysplasia will have been caused by a recurrence of the disease.

Finally, children become adults. Although for some of the patients we had follow-up data into adulthood, this information was not available for all. There has been debate on the presence of an increased graft loss after transfer to adulthood [23, 24], although opposed by others [25], and if this

K.J. Van Stralen *et al.*

Table 4. 5-year risk of graft loss for specific causes of renal failure

	Number atrisk at 5 years	5-year graftloss (%)	HR—5-yeargraft loss	HR—5-yeargraft loss[a]	HR—5-yeargraft loss[a,b]
FSGS	138	**25.7**	**2.09 (1.59–2.75)**	**2.04 (1.54–2.70)**	**2.20 (1.37–3.52)**
≤6 years at the start of RRT	51	17.1	1.46 (0.80–2.67)	1.36 (0.70–2.64)	1.01 (0.34–3.02)
6–12 years at the start of RRT	65	**27.7**	**1.58 (1.04–2.40)**	**1.72 (1.13–2.64)**	**2.43 (1.11–5.29)**
>12 years at the start of RRT	22	**32.4**	**3.51 (2.15–5.72)**	**3.17 (1.92–5.24)**	**3.75 (1.61–8.75)**
HUS	55	18.9	1.28 (0.84–1.94)	1.39 (0.91–2.12)	1.90 (1.05–3.44)
≤6 years at the start of RRT	29	21.9	**1.83 (1.00–3.34)**	**1.96 (1.01–3.83)**	**3.43 (1.33–8.89)**
>6 years at the start of RRT	26	16.5	0.96 (0.53–1.77)	1.08 (0.58–1.98)	0.88 (0.31–2.56)
SLE	9	20.3	1.84 (0.86–3.94)	1.58 (0.72–3.44)	**3.21 (1.19–8.69)**
MPGN	27	**32.4**	**2.36 (1.51–3.70)**	**2.15 (1.36–3.40)**	**2.73 (1.31–5.71)**
MPGN Type I	25	**23.5**	**1.95 (1.10–3.46)**	**1.91 (1.06–3.44)**	**2.76 (1.14–6.67)**
MPGN Type II	2	**67.5**	**3.34 (1.75–6.38)**	**2.68 (1.38–5.23)**	2.70 (0.91–7.98)
HSP/IgA	28	16.3	1.12 (0.64–1.94)	1.08 (0.61–1.91)	0.90 (0.34–2.37)
Hypoplasia and / or dysplasia	401	14.4	1	1	1

Bold values denote significant difference from hypoplasia and/or dysplasia (P < 0.05).
HR, hazard ratio; FSGS, focal and segmental glomerulosclerosis; RRT, renal replacement therapy; HUS, haemolytic uraemic syndrome; SLE, systemic lupus erythematosus; MPGN, membranoproliferative glomerulonephritis Type I or II; HSP/IgA, IgA nephropathy or Henoch Schönlein Purpura.
[a]Adjusted for age at start of RRT, age at transplantation, gender, and era of transplantation.
[b]Additionally adjusted for living versus deceased donation, information on living versus deceased donation was available for 55.6% of the patients.

were the case we might have underestimated the actual risk of graft loss for all causes of renal failure.

CONCLUSION

Graft loss remains a major problem in children living with a renal allograft. This large study was able to determine the actual rate of graft loss for many of the rare diseases in whom graft loss is feared to be high. In dense deposit disease, MPGN Type I and FSGS requiring RRT after the age of 6 the risk of graft loss is extremely high. Conversely, we were able to show that among some of these causes of renal failure the rate of graft loss is not increased.

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CONFLICT OF INTEREST STATEMENT

None declared.

REFERENCES

1. Cochat P, Fargue S, Mestrallet G et al. Disease recurrence in paediatric renal transplantation. Pediatr Nephrol 2009; 24: 2097–2108
2. Tizard EJ, Verrina E, van Stralen KJ et al. Progress with the European Society for Paediatric Nephrology (ESPN)/ERA-EDTA Registry for children with established renal failure (ERF). Nephrol Dial Transplant 2009; 24: 2615–2617
3. van Dijk PC, Jager KJ, de Charro F et al. Renal replacement therapy in Europe: the results of a collaborative effort by the ERA-EDTA registry and six national or regional registries. Nephrol Dial Transplant 2001; 16: 1120–1129
4. Verduijn M, Grootendorst DC, Dekker FW et al. The analysis of competing events like cause-specific mortality—beware of the Kaplan–Meier method. Nephrol Dial Transplant 2011; 26: 56–61
5. Pepe MS, Mori M. Kaplan–Meier, marginal or conditional probability curves in summarizing competing risk failure time data? Stat Med 1993; 12: 737–751
6. Briganti EM, Russ GR, McNeil JJ et al. Risk of renal allograft loss from recurrent glomerulonephritis. N Engl J Med 2002; 347: 103–109
7. Vinai M, Waber P, Seikaly MG. Recurrence of focal segmental glomerulosclerosis in renal allograft: an in-depth review. Pediatr Transplant 2010; 14: 314–325
8. Moroni G, Gallelli B, Quaglini S et al. Long-term outcome of renal transplantation in adults with focal segmental glomerulosclerosis. Transpl Int 2010; 23: 208–216
9. Zimmerhackl LB, Besbas N, Jungraithmayr T et al. Epidemiology, clinical presentation, and pathophysiology of atypical and recurrent hemolytic uremic syndrome. Semin Thromb Hemost 2006; 32: 113–120
10. Malina M, Roumenina LT, Seeman T et al. Genetics of hemolytic uremic syndromes. Presse Med 2012; 41: e105–e114
11. Loirat C, Fremeaux-Bacchi V. Hemolytic uremic syndrome recurrence after renal transplantation. Pediatr Transplant 2008; 12: 619–629
12. Geerdink LM, Westra D, van Wijk JA et al. Atypical hemolytic uremic syndrome in children: complement mutations and clinical characteristics. Pediatr Nephrol 2012; 27: 1283–1291
13. Oliveira CS, Oliveira I, Bacchiega AB et al. Renal transplantation in lupus nephritis: a Brazilian cohort. Lupus 2012; 21: 570–574
14. Azevedo LS, Romao JE, Jr, Malheiros D et al. Renal transplantation in systemic lupus erythematosus. A case control study of 45 patients. Nephrol Dial Transplant 1998; 13: 2894–2898
15. Ghafari A, Etemadi J, Ardalan MR. Renal transplantation in patients with lupus nephritis: a single-center experience. Transplant Proc 2008; 40: 143–144
16. Ponticelli C, Glassock RJ. Posttransplant recurrence of primary glomerulonephritis. Clin J Am Soc Nephrol 2010; 5: 2363–2372
17. Little MA, Dupont P, Campbell E et al. Severity of primary MPGN, rather than MPGN type, determines renal survival and post-transplantation recurrence risk. Kidney Int 2006; 69: 504–511
18. Braun MC, Stablein DM, Hamiwka LA et al. Recurrence of membranoproliferative glomerulonephritis type II in renal allografts: The North American Pediatric Renal Transplant Cooperative Study experience. J Am Soc Nephrol 2005; 16: 2225–2233
19. Lorenz EC, Sethi S, Leung N et al. Recurrent membranoproliferative glomerulonephritis after kidney transplantation. Kidney Int 2010; 77: 721–728
20. Andresdottir MB, Haasnoot GW, Persijn GG et al. HLA-B8, DR3: a new risk factor for graft failure after renal transplantation in patients with underlying immunoglobulin A nephropathy. Clin Transplant 2009; 23: 660–665
21. Kanaan N, Mourad G, Thervet E et al. Recurrence and graft loss after kidney transplantation for Henoch-Schönlein Purpura nephritis: a multicenter analysis. Clin J Am Soc Nephrol 2011; 6: 1768–1772
22. Samuel JP, Bell CS, Molony DA et al. Long-term outcome of renal transplantation patients with Henoch-Schönlein Purpura. Clin J Am Soc Nephrol 2011; 6: 2034–2040
23. Samuel SM, Nettel-Aguirre A, Hemmelgarn BR et al. Graft failure and adaptation period to adult healthcare centers in pediatric renal transplant patients. Transplantation 2011; 91: 1380–1385
24. van den Heuvel ME, van der Lee JH, Cornelissen EA et al. Transition to the adult nephrologist does not induce acute renal transplant rejection. Nephrol Dial Transplant 2010; 25: 1662–1667
25. Kramer A, Stel VS, Tizard J et al. Characteristics and survival of young adults who started renal replacement therapy during childhood. Nephrol Dial Transplant 2009; 24: 926–933

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K.J. Van Stralen et al.