

RISK OF RENAL ALLOGRAFT LOSS FROM RECURRENT GLOMERULONEPHRITIS

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ABSTRACT

Background Recurrent glomerulonephritis is a known cause of renal allograft loss; however, the incidence of this complication is poorly defined. We determined the incidence, timing, and relative importance of allograft loss due to the recurrence of glomerulonephritis.

Methods A total of 1505 patients with biopsy-proved glomerulonephritis received a primary renal transplant in Australia from 1988 through 1997. Recurrence was confirmed by renal biopsy. The Kaplan–Meier method was used to estimate the 10-year incidence of allograft failure due to recurrent glomerulonephritis, and this incidence was compared with the incidence of acute rejection, chronic rejection, and death with a functioning allograft. Characteristics of the recipients and donors were examined as potential predictors of recurrence.

Results Allograft loss due to the recurrence of glomerulonephritis occurred in 52 recipients, with a 10-year incidence of 8.4 percent (95 percent confidence interval, 5.9 to 12.0). The type of glomerulonephritis, the sex of the recipient, and the peak level of panel-reactive antibodies were independent predictors of the risk of recurrence. Recurrence was the third most frequent cause of allograft loss at 10 years, after chronic rejection and death with a functioning allograft. Despite the effect of recurrence, the overall 10-year incidence of allograft loss was similar among transplant recipients with biopsy-proved glomerulonephritis and among those with other causes of renal failure (45.4 percent [95 percent confidence interval, 40.9 to 50.2] vs. 45.8 percent [95 percent confidence interval, 42.3 to 49.3], $P=0.09$).

Conclusions Recurrence is an important cause of allograft loss for those with renal failure due to glomerulonephritis. No risk factors for recurrence were identified that warrant altering the approach to transplantation. However, accurate estimates of risk can now be provided to potential recipients of renal allografts. (N Engl J Med 2002;347:103-9.)

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GLOMERULONEPHRITIS is the primary cause of end-stage renal disease in up to 50 percent of those who go on to receive a renal transplant.¹ Recurrence has been reported in 6.0 to 19.4 percent of renal-allograft recipients, and the prevalence increases with the duration of follow-up.²⁻⁵ Those who have recurrence have a higher risk of allograft loss, with recurrence being reported

as the cause of loss in 1.1 to 4.4 percent of transplant recipients.^{2-4,6} As the rates of allograft survival improve, largely because of the prevention of loss due to acute rejection, the incidence of allograft loss due to recurrent glomerulonephritis will become more important.^{6,7}

The expected outcome for patients with end-stage renal failure due to glomerulonephritis, and hence their decision whether to proceed with transplantation, may be affected by their risk of allograft loss due to the recurrence of glomerulonephritis. However, current data provide variable estimates of this risk for such patients. We examined the incidence and timing of risk factors for allograft loss due to biopsy-proved recurrences of glomerulonephritis and compared these data with the data on allograft loss due to acute rejection, chronic rejection, or death with a functioning allograft.

METHODS**Data Collection**

Since 1963, information regarding all renal transplantations performed in Australia has been compiled by the Australia and New Zealand Dialysis and Transplant Registry (ANZDATA), a nonprofit, government-sponsored organization, for purposes of quality assurance and auditing. Base-line clinical information and follow-up information collected every six months regarding outcomes in all recipients of renal transplants, as well as clinical information about the donors, are submitted to ANZDATA by all transplantation centers. All transplant recipients are advised that selective clinical information will be collected and submitted to the registry. The anonymity of patients' information is maintained by coding of data during compilation, and anonymous data are issued by the registry for purposes of analysis.

Study Population

Relevant data were retrieved from ANZDATA for renal transplantations performed from 1988 through 1997, with follow-up to the end of September 1998, to determine the 10-year actuarial incidence of allograft loss due to the recurrence of glomerulonephritis. A total of 3998 primary renal transplantations were performed in Australia from January 1, 1988, through December 31, 1997. The underlying primary disease was glomerulonephritis in 1839 of the cases (46.0 percent). Of these, 1505 cases (81.8 percent) were biopsy proved and were included in our analysis. Characteristics of the patients are summarized in Table 1.

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TABLE 1. CHARACTERISTICS OF THE PATIENTS ACCORDING TO THE TYPE OF BIOPSY-PROVED GLOMERULONEPHRITIS.

CHARACTERISTIC	MESANGIOCAPILLARY GLOMERULONEPHRITIS TYPE I (N=88)	FOCAL SEGMENTAL GLOMERULOSCLEROSIS (N=221)	MEMBRANOUS NEPHROPATHY (N=81)	IgA NEPHROPATHY (N=532)	PAUCI-IMMUNE CRESCENTIC GLOMERULO- NEPHRITIS (N=102)	OTHER TYPES OF GLOMERULO- NEPHRITIS (N=481)	ALL BIOPSY- PROVED CASES OF GLOMERULO- NEPHRITIS (N=1505)
Recipients							
Recurrence (no.)	9	16	5	15	2	5	52
Age (yr)*							
Median	45	46	53	48	51	42	46
Interquartile range	34–55	34–58	42–62	39–56	34–63	33–57	36–57
Male sex (%)*	56	69	77	77	64	59	68
Peak panel-reactive antibody titer (%)†							
Median	10	4	3	6	6	7	6
Interquartile range	0–30	0–18	0–17	0–22	2–24	0–33	0–25
Duration of dialysis before transplantation (yr)							
Median	1.5	1.4	1.3	1.3	1.6	1.5	1.4
Interquartile range	0.7–3.2	0.8–2.5	0.4–3.0	0.7–2.7	0.8–3.0	0.7–3.1	0.7–2.9
Donors							
Age (yr)							
Median	35	36	37	38	38	38	37
Interquartile range	23–46	20–49	26–49	24–49	21–48	24–50	23–49
Male sex (%)	67	59	68	62	60	56	60
Cadaveric donor (%)	83	82	78	76	74	79	79
Cold-ischemia time (hr)‡							
Median	19	14	16	14	15	15	15
Interquartile range	12–22	10–19	5–20	4–19	9–19	8–19	8–20
0–3 HLA mismatches (%)	73	77	65	72	75	72	73

*P<0.001 for the comparison among the six types of glomerulonephritis.

†P=0.003 for the comparison among the six types of glomerulonephritis.

‡P=0.005 for the comparison among the six types of glomerulonephritis.

Statistical Analysis

Outcome Variables

The primary outcome was the 10-year actuarial incidence of allograft loss due to the recurrence of glomerulonephritis. Allograft loss due to recurrence was defined as the loss of allograft function, resulting in the need to restart dialysis, the need for retransplantation, or death and attributed to a recurrence of the original glomerulonephritis, as demonstrated by a biopsy of the transplant. The incidence of allograft loss due to recurrent glomerulonephritis was compared with the incidence of allograft loss from other major causes — acute rejection, chronic rejection, and death with a functioning allograft — at 1, 5, and 10 years after transplantation. We also performed subgroup analyses of the 10-year incidence of allograft loss due to recurrent glomerulonephritis among patients with specific types of glomerulonephritis that accounted for the cases of at least 50 recipients and for which at least one case of recurrence was documented; these types included mesangiocapillary glomerulonephritis type I, focal segmental glomerulosclerosis, membranous nephropathy, IgA nephropathy, and pauci-immune crescentic glomerulonephritis. The risk of recurrence for each specific category of glomerulonephritis was compared with the average risk of recurrence for all categories of glomerulonephritis combined, with the use of deviation-from-means coding. In addition, transplant recipients with biopsy-proved glomerulonephritis were compared with recipients with other causes of renal failure with respect to the 10-year incidence of allograft loss due to acute rejection, chronic rejection, death with a functioning allograft, and all causes combined. Primary and recurrent glomerulonephritis was proved by

biopsy in all cases. The timing of the biopsies was not captured in the registry data base, but results of the biopsies were available at the time of transplantation and at the time allograft loss was reported.

Predictive Factors

Ten characteristics of recipients and donors that were known at the time of transplantation were examined as potential predictors of the 10-year actuarial incidence of allograft loss due to recurrent glomerulonephritis. The recipient-related characteristics included age, sex, peak levels of panel-reactive antibodies, duration of dialysis before transplantation, and type of glomerulonephritis. Types of glomerulonephritis were classified into six major categories: mesangiocapillary glomerulonephritis type I (in 88 patients), focal segmental glomerulosclerosis (in 221 patients), membranous nephropathy (in 81 patients), IgA nephropathy (in 532 patients), pauci-immune crescentic glomerulonephritis (in 102 patients: extracapillary and intracapillary glomerulonephritis in 70 patients, microscopic polyarteritis in 17 patients, and Wegener's granulomatosis in 15 patients), and other types of glomerulonephritis (in 481 patients: Henoch–Schönlein purpura in 24 patients, IgA-negative mesangioproliferative glomerulonephritis in 40 patients, mesangioproliferative glomerulonephritis with no immunofluorescence performed in 19 patients, mesangiocapillary glomerulonephritis type II in 18 patients, mesangiocapillary glomerulonephritis type III in 2 patients, anti-glomerular basement membrane antibody disease in 44 patients, lupus nephritis in 81 patients, scleroderma in 7 patients, proliferative glomerulonephritis in 65 patients, familial glomerulonephritis including Alport's syndrome in 70 patients, glomerulonephritis with systemic disease in 4 patients, postinfective

glomerulonephritis in 4 patients, fibrillary glomerulonephritis in 1 patient, IgM glomerulonephritis in 1 patient, advanced glomerulonephritis in 92 patients, and unknown types in 9 patients). Donor-related characteristics included age, sex, source of the allograft (cadaveric or living donor), cold-ischemia time, and number of HLA mismatches.

The Kruskal–Wallis rank test for the equality of populations and Pearson’s chi-square test were used to evaluate differences in terms of recipient-related and donor-related characteristics at base line among groups defined according to the type of glomerulonephritis. Rates of allograft loss caused by recurrent glomerulonephritis, death with a functioning graft, chronic rejection, or acute rejection were computed by the Kaplan–Meier method,⁸ with an assumption of independence of the different causes of allograft loss. For each of the four cause-specific analyses, data on allograft loss from causes other than the one of interest were censored at the time of loss. The univariable association between each of these factors and the 10-year actuarial incidence of allograft loss due to recurrent glomerulonephritis was determined by log-rank tests for the equality of survivor functions.

In determining which risk factors were independently predictive of recurrent glomerulonephritis, we included all 10 recipient-related and donor-related characteristics in the initial multivariable Cox regression model. Factors were removed from the multivariable model in a stepwise fashion, beginning with the risk factor with the highest P value; the likelihood-ratio test was used to confirm that each deleted factor did not contribute significantly to the multivariable model. In analyses of patients with mesangiocapillary glomerulonephritis type I, focal segmental glomerulosclerosis, IgA nephropathy, or pauci-immune crescentic glomerulonephritis, predictors specific to the type of glomerulonephritis were also examined in a similar fashion. For the survival analysis, the assumption of proportional hazards for the final models was confirmed with

the use of scaled Schoenfeld residuals.⁹ All P values are two-sided, and a P value of 0.05 or less was considered to indicate statistical significance. All statistical analyses were performed with Stata statistical software (version 6.0). No sponsorship funding was received for this study.

RESULTS

Allograft loss due to recurrent glomerulonephritis occurred in 52 of the recipients of renal allografts; of these, 16 had focal segmental glomerulosclerosis, 9 had mesangiocapillary glomerulonephritis type I, 1 had mesangiocapillary glomerulonephritis type III, 15 had IgA nephropathy, 4 had Henoch–Schönlein purpura, 5 had membranous nephropathy, and 2 had pauci-immune crescentic glomerulonephritis. No grafts were lost due to the recurrence of non-IgA mesangioproliferative glomerulonephritis, mesangiocapillary glomerulonephritis type II, anti-glomerular basement membrane antibody disease, lupus nephritis, scleroderma, proliferative glomerulonephritis, familial glomerulonephritis including Alport’s syndrome, glomerulonephritis with systemic disease, postinfectious glomerulonephritis, fibrillary glomerulonephritis, or IgM glomerulonephritis. The incidence of allograft loss due to recurrence of any type of glomerulonephritis at 10 years was 8.4 percent (95 percent confidence interval, 5.9 to 12.0) and increased over time (Fig. 1).

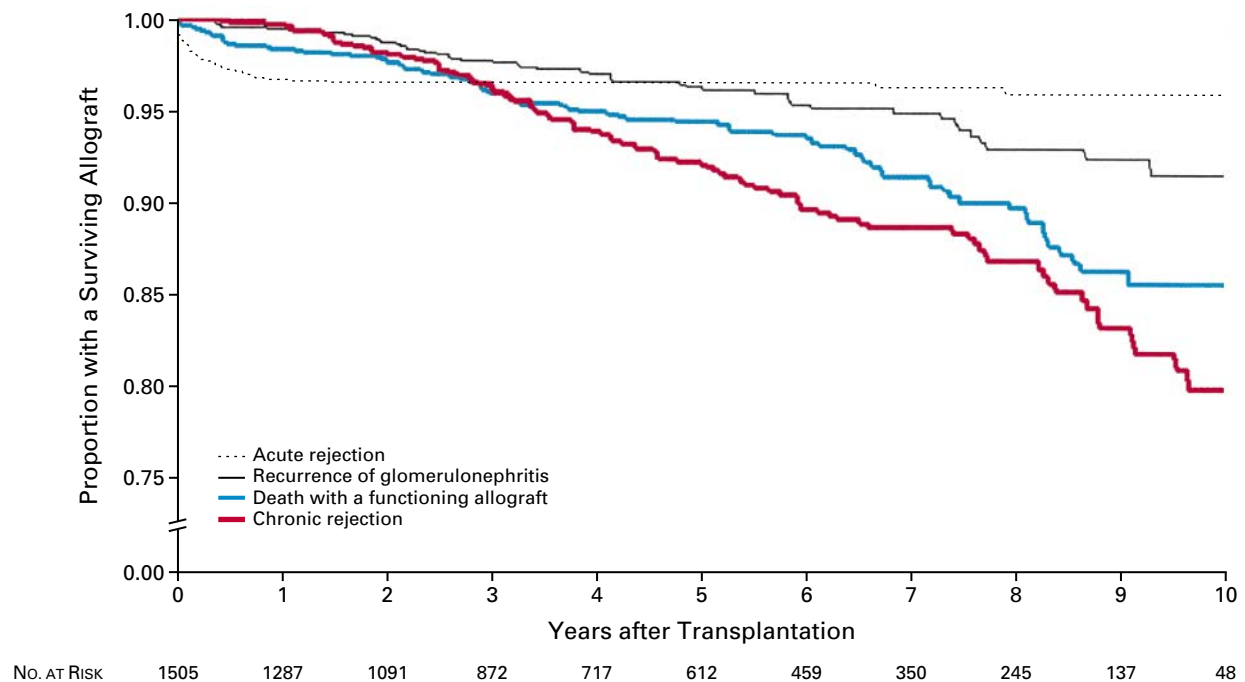


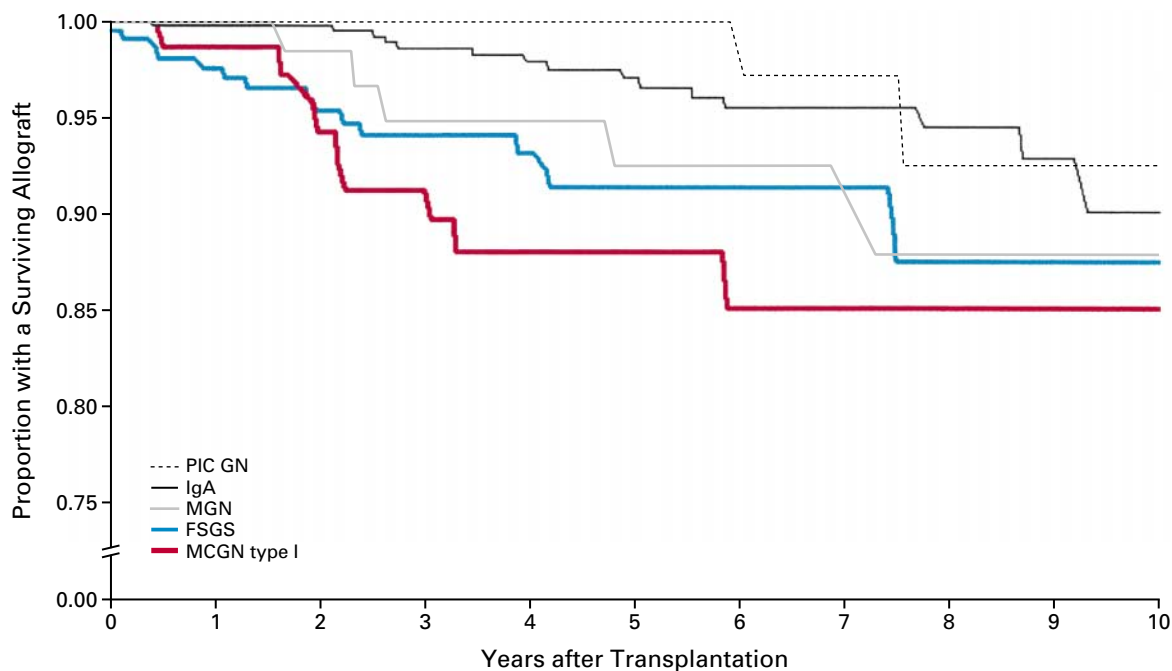
Figure 1. Kaplan–Meier Analysis of Allograft Loss Due to Recurrence of Glomerulonephritis, Acute Rejection, Chronic Rejection, and Death with a Functioning Allograft.

At one year, the incidence of allograft loss due to acute rejection was the highest, at 3.3 percent (95 percent confidence interval, 2.5 to 4.4), followed by loss due to death with a functioning allograft, at 1.7 percent (95 percent confidence interval, 1.1 to 2.5), loss due to recurrent glomerulonephritis, at 0.6 percent (95 percent confidence interval, 0.3 to 1.1), and loss due to chronic rejection, at 0.3 percent (95 percent confidence interval, 0.1 to 0.8). The roles of acute and chronic rejection were reversed by five years, at which point the cause of the highest incidence of allograft loss was chronic rejection, at 7.8 percent (95 percent confidence interval, 6.2 to 9.7), followed by death with a functioning allograft, at 5.6 percent (95 percent confidence interval, 4.4 to 7.2), recurrent glomerulonephritis, at 3.7 percent (95 percent confidence interval, 2.7 to 5.1), and acute rejection, at 3.5 percent (95 percent confidence interval, 2.7 to 4.7). At 10 years, the incidence of allograft loss due to recur-

rent glomerulonephritis was 8.4 percent (95 percent confidence interval, 5.9 to 12.0), as compared with 4.1 percent (95 percent confidence interval, 3.0 to 5.6) for loss due to acute rejection, 15.0 percent (95 percent confidence interval, 11.6 to 19.4) for loss due to death with a functioning allograft, and 20.3 percent (95 percent confidence interval, 16.0 to 25.5) for loss due to chronic rejection (Fig. 1).

Differences in the incidence and timing of allograft loss were evident among groups defined according to the type of glomerulonephritis. The greatest incidence of allograft loss occurred among patients with focal segmental glomerulosclerosis or mesangiocapillary glomerulonephritis type I. Allograft loss also tended to occur earlier in patients with these types of glomerulonephritis than in those with recurrent IgA nephropathy, membranous glomerulonephropathy, or pauci-immune crescentic glomerulonephritis (Fig. 2).

The 10-year incidence of allograft loss from any



No. AT Risk	0	1	2	3	4	5	6	7	8	9	10
PIC GN	102	90	74	62	56	48	36	26	16	5	2
IgA	532	462	398	312	253	217	153	119	87	47	15
MGN	81	70	60	49	44	40	31	20	15	9	5
FSGS	221	189	156	124	103	91	65	54	36	19	5
MCGN type I	88	75	64	57	48	40	28	25	16	12	4

Figure 2. Kaplan–Meier Analysis of Allograft Loss Due to Recurrence of Glomerulonephritis, According to the Type of Glomerulonephritis.

PIC GN denotes pauci-immune crescentic glomerulonephritis, IgA IgA nephropathy, MGN membranous glomerulonephropathy, FSGS focal segmental glomerulosclerosis, and MCGN mesangiocapillary glomerulonephritis.

cause was similar among recipients with biopsy-proved glomerulonephritis and among those with renal failure from other causes (45.4 percent [95 percent confidence interval, 40.9 to 50.2] vs. 45.8 percent [95 percent confidence interval, 42.3 to 49.3], $P=0.09$) (Table 2). Although the incidence of chronic rejection was similar in the two groups (20.3 percent [95 percent confidence interval, 16.0 to 25.5] among recipients with biopsy-proved glomerulonephritis vs. 16.1 percent [95 percent confidence interval, 13.2 to 19.6] among those with renal failure from other causes, $P=0.24$), there was a lower incidence of death with a functioning allograft in the group with glomerulonephritis (14.1 percent [95 percent confidence interval, 11.0 to 18.0] vs. 25.2 percent [95 percent confidence interval, 21.8 to 29.0], $P<0.001$) (Table 2). Acute rejection was a major cause of allograft loss within the first year after transplantation, but over the 10-year period, it became less important among both recipients with glomerulonephritis and those with other causes of renal disease (Fig. 1).

The type of glomerulonephritis was predictive of the 10-year actuarial incidence of allograft loss due to recurrent glomerulonephritis according to univariable analysis, and it remained independently predictive in multivariable analysis, as did the sex of the recipient and the peak level of panel-reactive antibodies (Table 3). As compared with the average for all recipients with a primary diagnosis of glomerulonephritis, the incidence of allograft loss due to recurrence was significantly higher among recipients with focal segmental glomerulosclerosis (adjusted hazard ratio, 2.03 [95 percent confidence interval, 1.19 to 3.44]; $P=0.009$) or mesangiocapillary glomerulonephritis type I (adjusted hazard ratio, 2.91 [95 percent confidence interval, 1.53 to 5.55]; $P=0.001$), as well as among male recipients (adjusted hazard ratio, 2.24 [95 percent

confidence interval, 1.10 to 4.53]; $P=0.03$) and among recipients with higher peak panel-reactive antibody titers (adjusted hazard ratio for each increment of 10 percent, 1.10 [95 percent confidence interval, 1.00 to 1.21]; $P=0.05$) (Table 3). No predictive factors were identified for allograft loss due to recurrences of specific types of glomerulonephritis.

DISCUSSION

Our study demonstrates the importance of recurrent glomerulonephritis as a cause of allograft loss after renal transplantation. Previous studies have reported varying rates of allograft loss due to recurrence because of inconsistencies in diagnostic criteria, duration of follow-up, populations of patients, and study design.⁶ Recurrences can be differentiated from new cases of glomerulonephritis, chronic rejection, and toxic effects of drugs only on the basis of a renal biopsy. We therefore undertook a comprehensive, long-term analysis of allograft loss due to recurrent glomerulonephritis of all types, in which both the primary lesion and the recurrence were confirmed by biopsy in all cases. This analysis of all patients who received a renal allograft in Australia during the 10-year period from 1988 through 1997 found recurrent glomerulonephritis to be the third most frequent cause of allograft loss among patients with a primary diagnosis of biopsy-proved glomerulonephritis, after chronic rejection and death with a functioning allograft.

The major causes of allograft loss have been identified as death with a functioning allograft, acute rejection during the first year after transplantation, and chronic rejection after that point.¹⁰ The effect of acute rejection on allograft survival has decreased markedly during the past 20 years,⁷ and in fact, in Australia, the 10-year incidence of allograft loss due to acute rejection was only 4.1 percent between 1988 and

TABLE 2. 10-YEAR CAUSE-SPECIFIC INCIDENCE OF ALLOGRAFT LOSS AMONG PATIENTS WITH BIOPSY-PROVED GLOMERULONEPHRITIS AND THOSE WITH ALL OTHER TYPES OF RENAL DISEASE.

TYPE OF RENAL DISEASE	RECURRENT GLOMERULONEPHRITIS				ALL CAUSES
	RECURRENT GLOMERULONEPHRITIS	CHRONIC REJECTION	ACUTE REJECTION	DEATH WITH A FUNCTIONING ALLOGRAFT	
	percent (95 percent confidence interval)				
Biopsy-proved glomerulonephritis					
Mesangiocapillary glomerulonephritis type I	14.4 (7.6–26.4)	23.0 (13.1–38.5)	5.0 (1.9–12.3)	2.6 (0.7–10.1)	44.3 (33.3–57.2)
Focal segmental glomerulosclerosis	12.7 (7.3–21.6)	18.4 (11.6–28.4)	1.4 (0.5–4.4)	20.2 (11.5–36.6)	51.0 (40.7–62.3)
Membranous nephropathy	12.5 (4.7–30.7)	15.3 (5.3–39.5)	2.6 (0.7–10.0)	8.5 (3.0–23.1)	40.1 (26.5–57.4)
IgA nephropathy	9.7 (4.7–19.5)	22.5 (14.1–34.8)	3.5 (2.0–6.2)	12.0 (6.5–21.7)	43.3 (34.0–53.9)
Pauci-immune crescentic glomerulonephritis	7.7 (1.9–27.9)	13.3 (6.4–26.7)	7.6 (2.2–24.4)	29.4 (15.8–50.5)	53.7 (39.5–69.2)
Other types of glomerulonephritis	3.1 (1.2–8.0)	20.4 (13.6–29.9)	5.3 (3.6–7.8)	16.3 (11.4–23.1)	44.7 (37.7–52.4)
Any type	8.4 (5.9–12.0)	20.3 (16.0–25.5)	4.1 (3.0–5.6)	14.1 (11.0–18.0)	45.4 (40.9–50.2)
Other types of renal disease	—	16.1 (13.2–19.6)	5.4 (4.0–7.1)	25.2 (21.8–29.0)	45.8 (42.3–49.3)

TABLE 3. RISK OF ALLOGRAFT LOSS SECONDARY TO RECURRENT GLOMERULONEPHRITIS, ACCORDING TO CHARACTERISTICS OF RECIPIENTS AND DONORS.*

CHARACTERISTIC	UNADJUSTED HAZARD RATIO FOR ALLOGRAFT LOSS (95% CI)	P VALUE	ADJUSTED HAZARD RATIO FOR ALLOGRAFT LOSS (95% CI)†	P VALUE
Cause of disease in recipient				
Mesangiocapillary glomerulonephritis type I	2.63 (1.39–4.98)	0.003	2.91 (1.53–5.55)	0.001
Focal segmental glomerulosclerosis	2.00 (1.18–3.41)	0.01	2.03 (1.19–3.44)	0.009
Membranous nephropathy	1.58 (0.71–3.50)	0.26		
IgA nephropathy	0.78 (0.45–1.34)	0.36		
Pauci-immune crescentic glomerulonephritis	0.52 (0.16–1.69)	0.28		
Other types of glomerulonephritis	0.30 (0.13–0.66)	0.003	0.30 (0.13–0.66)	0.003
Age of recipient (per 10-yr increment)	0.92 (0.75–1.13)	0.42		
Male recipient (as compared with female)	1.76 (0.91–3.43)	0.10	2.24 (1.10–4.53)	0.03
Peak panel-reactive antibody titer (per 10% increment)	1.06 (0.96–1.16)	0.25	1.10 (1.00–1.21)	0.05
Duration of dialysis before transplantation (per 1-yr increment)	0.97 (0.84–1.12)	0.71		
Age of donor (per 10-yr increment)	0.92 (0.77–1.10)	0.38		
Male donor (as compared with female)	0.70 (0.41–1.21)	0.20		
Living donor (as compared with cadaveric donor)	1.47 (0.77–2.81)	0.24		
Cold-ischemia time (per 1-hr increment)	0.99 (0.96–1.03)	0.62		
No. of HLA mismatches (per additional mismatch)	0.97 (0.79–1.20)	0.81		

*Hazard ratios for specific types of glomerulonephritis are for the comparison with the mean risk of recurrence for all categories of glomerulonephritis. CI denotes confidence interval.

†Hazard ratios for factors that remained independently predictive in multivariable analysis were adjusted for all other independently predictive factors.

1997. Our study shows that for those with a primary diagnosis of biopsy-proved glomerulonephritis, recurrence is more frequent than acute rejection as a cause of allograft loss during the first 10 years after transplantation. In contrast, the study documents that, for specific types of glomerulonephritis, the frequency of allograft loss due to chronic rejection or death with a functioning allograft is as great as or greater than the frequency of loss due to recurrence (Table 2).

Rates of renal-allograft survival have improved during the past 20 years, so that the average cadaveric allograft transplanted in the United States is currently predicted to function for more than 10 years after transplantation.⁷ The present study has confirmed previous reports that the effect of recurrence of glomerulonephritis increases over time.^{2,4,11} Thus, as allografts last longer,⁷ the relative importance of recurrent glomerulonephritis as a cause of allograft loss is likely to increase, and patients as well as transplantation teams will need to consider this risk in their planning before transplantation.

In order to provide meaningful information for patients with various types of glomerulonephritis, we examined disease-specific rates of recurrence. Reported recurrence rates vary widely according to diagnostic criteria, duration of follow-up, and study size.¹¹⁻²⁰ Recurrence does not always result in allograft loss.⁴ In our

study, recurrence was detected only when it caused allograft loss, and therefore the recurrence rates we report underestimate the overall risk of recurrence. Allograft loss due to recurrence was observed only in those with focal segmental glomerulosclerosis, mesangiocapillary glomerulonephritis type I or type III, IgA nephropathy, Henoch–Schönlein purpura, membranous nephropathy, or pauci-immune crescentic glomerulonephritis. The rates of allograft loss that we observed are similar to published rates.¹¹⁻²⁰ Our study also confirmed trends toward increases over time in the rates of allograft loss due to recurrent IgA nephropathy,^{11,12} mesangiocapillary glomerulonephritis type I,¹⁸ membranous nephropathy,¹⁷ and focal segmental glomerulosclerosis.^{14,16}

Allograft loss due to recurrence was not observed in those with anti-glomerular basement membrane antibody disease, lupus nephritis, scleroderma, mesangiocapillary glomerulonephritis type II, Alport's syndrome and other types of familial glomerulonephritis, postinfectious glomerulonephritis, IgA-negative mesangioproliferative glomerulonephritis, or fibrillary glomerulonephritis. This finding suggests that the risk of allograft loss due to recurrence within the first 10 years after transplantation is low for patients with these diagnoses. However, caution is warranted in interpreting these data. First, the number of study patients with

some diagnoses was small, and the absence of allograft loss due to recurrence may reflect the small sample size. Second, it is likely that some proportion of patients had a recurrence without progression to allograft loss within the 10-year follow-up period. This possibility is most pertinent for patients with lupus nephritis,²¹ scleroderma,²² mesangiocapillary glomerulonephritis type II,¹⁹ or fibrillary glomerulonephritis,²³ all of which have been reported to recur, with late allograft loss occurring in some cases. Third, current transplantation practices in Australia, such as deferring transplantation for 12 months after the completion of treatment in cases of anti-glomerular basement membrane antibody disease, may reduce the risk of recurrence of specific types of glomerulopathy.

Overall, our study suggests that the risk of allograft loss due to recurrence of glomerulonephritis is not attributable to factors examined in our analysis that can be modified. Male sex of the recipient and high peak panel-reactive antibody titers were found to be associated with an increased risk of allograft loss due to recurrence. The presence of certain types of glomerulonephritis represented the strongest risk factor for recurrence leading to allograft loss. However, for specific types of glomerulonephritis, the incidence of allograft loss due to recurrence was lower than or similar to the incidence of loss due to chronic rejection, the incidence of loss due to death with a functioning allograft, or both. Given this finding in conjunction with the finding that the overall incidence of allograft loss among patients with biopsy-proved glomerulonephritis was similar to the incidence among those with other causes of renal failure, we conclude that it is not logical to discriminate against potential recipients with glomerulonephritis in selecting patients for renal transplantation. The selection of recipients and donors should be no different for patients with glomerulonephritis from that for other candidates for renal transplantation. Potential recipients should, however, be informed of the risk of recurrence.

In summary, the results of this survival analysis should enable transplantation teams to provide potential recipients with an accurate estimate of the risk of allograft loss due to recurrent glomerulonephritis within the first 10 years after transplantation. Since recurrence is the third most common cause of allograft loss among those with primary glomerulonephritis, these data are clearly important for patients planning to pursue transplantation. Since our study and others have shown that the incidence of allograft loss due to recurrence increases over time, we predict that recurrent glomerulonephritis will be an increasingly important cause of allograft loss as overall allograft-survival rates continue to improve.

We are indebted to the renal-transplant recipients of Australia, to their clinicians, and to ANZDATA for providing the data for this analysis.

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