Membranoproliferative glomerulonephritis type II (MPGN II) is an uncommon form of complement-dependent acquired renal disease. Although it has been recognized since the 1970s that MPGN II recurs almost universally in renal transplants, data regarding the long-term consequences of disease recurrence are limited. Therefore, a retrospective comparative analysis of 75 patients with MPGN II contained in the North American Pediatric Renal Transplant Cooperative Study transplantation database was performed. Five-year graft survival for patients with MPGN II was significantly worse (50.0 ± 7.5%) compared with the database as a whole (74.3 ± 0.6%; \( P < 0.001 \)). Living related donor organs had a significantly better 5-yr survival (65.9 ± 10.7%) compared with cadaveric donor organs (34.1 ± 9.8%; \( P = 0.004 \)). The primary cause of graft failure in 11 (14.7%) patients was recurrent disease. Supplemental surveys were obtained on 29 (38%) of 75 patients. Analysis of these data indicated that recurrent disease occurred in 12 (67%) of the 18 patients with posttransplantation biopsies. Although there was no correlation between pretransplantation presentation, pre- or posttransplantation C3 levels, and either disease recurrence or graft failure, there was a strong association between heavy proteinuria and disease recurrence. The presence of glomerular crescents in allograft biopsies had a significant negative correlation with graft survival. At last follow-up, patients with recurrent disease had significantly higher serum creatinine and qualitatively more proteinuria than patients without biopsy-proven disease. These data indicate that recurrent MPGN II has a significant negative impact on renal allograft function and survival.


Membranoproliferative glomerulonephritis type II (MPGN II) is an uncommon form of chronic renal disease characterized by persistent systemic hypocomplementemia, glomerular C3 deposition, and abundant dense deposits within the lamina densa of the glomerular basement membrane (GBM) (1). Since the original characterization of this disease by Habib in 1975, little progress has been achieved with respect to the pathogenesis and the treatment of this disorder (2). Results of therapeutic trials using corticosteroids, immunosuppressive agents, or antiplatelet therapy have been disappointing (1,3). Despite major advances in our ability to slow the progression of many forms of chronic renal injury, the clinical course of MPGN II remains one of slow deterioration, with 50% of patients developing ESRD within 10 yr of diagnosis (1,4). Renal transplantation remains the final therapeutic option for the majority of patients with MPGN II. However, MPGN II has been reported to recur in 18 to 100% of renal allografts, depending on the criteria used to define recurrence, and rates of graft failure as a result of disease recurrence have ranged from 0 to 100% (5,6). Currently, there are fewer than 170 reported cases of renal transplants in adults and children with MPGN II (2,4–27). Most reports are limited in terms of sample size, with the most recent case series in 1999 containing fewer than one dozen patients (26). Detailed information is available on fewer than half of the reported patients, and long-term follow-up data are surprisingly sparse. Although the almost invariable recurrence of dense deposits in renal allografts is not disputed, the impact of the recurrence of these deposits on graft survival is uncertain. To investigate the impact of disease re-
currence in a large population of pediatric renal transplant patients, we analyzed the North American Pediatric Renal Transplant Cooperative Study (NAPRTCS) database with respect to overall graft survival and obtained supplemental data surveys to identify potential predictors of disease recurrence.

Materials and Methods

The NAPRTCS database (1985 to 2002) was queried for individuals who had biopsy-proven MPGN II. Data including age, gender, ethnicity, age at transplantation, cadaveric (CAD) versus living-related donor (LRD) source, type of immunosuppression, graft survival, duration of dialysis, and cause of graft failure were analyzed in comparison with the NAPRTCS database as a whole.

Supplemental questionnaires were sent to all centers that were identified as having a patient with MPGN II contained within the NAPRTCS database. The centers were asked to provide additional information regarding (1) original presentation, (2) immediate pre-transplantation features, (3) posttransplantation course, (4) and status at most recent follow-up. The information requested included age, height, weight, serum albumin, creatinine, C3 concentrations, nephritic factor, degree of hematuria and proteinuria, clinical features (asymptomatic hematuria or proteinuria, acute glomerulonephritis, nephrotic syndrome, or rapidly progressive glomerulonephritis), the presence of hypertension, treatment and/or immunosuppression, and biopsy findings. For the purposes of this study, disease recurrence was defined solely on the basis of electron dense deposits within the GBM. In addition, a comprehensive search of electronic databases as well as manual reviews of references from published manuscripts, review articles, and textbooks were performed to identify reports of individuals who had MPGN II and underwent renal transplantation. Data regarding graft survival and length of follow-up were abstracted and collated.

Statistical Analyses

Data were analyzed using SAS and SPSS software. Survival analysis was performed using log-rank analysis. Distribution and frequency of variables was analyzed by either $\chi^2$ analysis or Fisher exact test when appropriate. Comparisons between groups were performed using the $t$ test, Pearson correlation statistics, and the log-rank test. $P < 0.05$ was assumed to be statistically significant. The studies contained in this report were approved by the Children’s Hospital Medical Center Institutional Review Board.

Results

Seventy-five primary renal allografts in patients with MPGN II were identified within the NAPRTCS database. Demographic data are presented in Table 1. As a group, MPGN II patients did not differ from the database as a whole with respect to gender, ethnicity, or donor source. They were, as expected, older, with 58% being older than 12 yr compared with 45% of the database ($P = 0.03$). There was no significant difference in donor source. Supplemental surveys were received on 29 patients (response rate of 39%). There were no significant differences in terms of demographic data comparing the responding group with the entire MPGN II population contained in the database (Table 1). That a significant number of patients had been transferred to adult transplant centers for care, and medical records dating back several decades were no longer accessible had a negative impact on the overall response rate.

Initial Presentation and Management (Survey Population)

The clinical features of the survey population at the initial pretransplantation diagnosis of MPGN II are presented in Table 1.

<table>
<thead>
<tr>
<th>Table 1. Demographic data for primary renal allografts from the NAPRTCS database, MPGN II patients contained within the database, and MPGN II patients with supplemental survey informationa</th>
</tr>
</thead>
<tbody>
<tr>
<td>NAPRTCS (Database)</td>
</tr>
<tr>
<td>-------------------</td>
</tr>
<tr>
<td>N</td>
</tr>
<tr>
<td>Gender</td>
</tr>
<tr>
<td>male</td>
</tr>
<tr>
<td>female</td>
</tr>
<tr>
<td>Race</td>
</tr>
<tr>
<td>white</td>
</tr>
<tr>
<td>black</td>
</tr>
<tr>
<td>Hispanic</td>
</tr>
<tr>
<td>other</td>
</tr>
<tr>
<td>Calcinurin inhibitors</td>
</tr>
<tr>
<td>Age at transplant</td>
</tr>
<tr>
<td>0 to 1 yr</td>
</tr>
<tr>
<td>2 to 5 yr</td>
</tr>
<tr>
<td>6 to 12 yr</td>
</tr>
<tr>
<td>&gt;12 yr</td>
</tr>
<tr>
<td>Transplant source</td>
</tr>
<tr>
<td>living donors</td>
</tr>
<tr>
<td>cadaver donors</td>
</tr>
</tbody>
</table>

aNAPRTCS, North American Pediatric Renal Transplant Cooperative Study; MPGN II, membranoproliferative glomerulonephritis type II.

b$p < 0.05.$
2. Mean age at initial presentation was 10.4 ± 0.6 yr. Most patients had a significant reduction in renal function with a mean serum creatinine of 2.7 ± 0.5 mg/dl and an estimated GFR of 62.4 ± 10.7 ml/min uncorrected. Serum albumin concentrations were also reduced, with a mean of 2.6 ± 0.2 g/dl. Hypocomplementemia was present at the time of diagnosis in 95% of patients with a mean serum C3 level of 50.4 ± 9.0 mg/dl. Severe depression of C3 levels (<20 mg/dl) was present in 20% of patients. Renal biopsies at the time of initial diagnosis were indicative of severe renal injury. Glomerular injury was particularly pronounced. Moderate to severe mesangial proliferation was noted in 65% of biopsies. Some degree of global sclerosis was present in half of the biopsies, with 20% having >20% global sclerosis. Most prominent, however, was the severity of crescentic disease, which was noted in 70% of biopsies, with >50% of patients having >50% glomerular crescents. Interstitial fibrosis was unusual, with <15% having more than moderate fibrosis; however, 45% had moderate to severe interstitial infiltrates.

The disease in these patients’ native kidneys was treated by a variety of therapeutic regimens. Steroids were given to 92% of patients in a number of different modalities: 62.5% received pulse methylprednisolone (mean number of pulses 3.9 ± 0.7; range 2 to 10) in combination with either daily or alternate-day oral prednisone, cyclophosphamide was given to 17% of patients, two patients were treated with alternate-day prednisone alone, two patients were treated with antihypertensive therapy alone, and a single patient was treated with daily prednisone. Choice of therapy had little impact on renal survival, with a mean time from diagnosis to transplantation of 3.4 ± 0.6 yr.

Graft Survival

On the basis of the NAPRTCS database, the number of primary transplants for MPGN II was evenly distributed during the 16-yr study period, with an average of 2.7 patients per year. The proportion of CAD or LRD renal transplants did not vary significantly within 5-yr cohorts during the study period (Figure 1). The mean follow-up times for the 5-yr cohorts 1987 to 1992, 1993 to 1997, and 1998 to 2003 were 56, 42, and 23 mo, respectively. There were no statistically significant intracohort differences for duration of follow-up between LRD and CAD organ recipients. With regard to graft survival, differences in 10-yr survival were difficult to analyze given the limited number of patients available for analysis; only one patient had follow-up >9 yr. However, there was a significant difference in graft survival at 5 yr (Figure 2A). In comparison with the database as a whole, renal allografts in patients with MPGN II had significantly worse survival at 5 yr: 74.3 ± 0.6% compared with 50.0 ± 7.5%, respectively (P < 0.001). Allograft survival of patients with MPGN II was significantly worse than that of other patients with a primary diagnosis of glomerulonephritis contained in the NAPRTCS database (Figure 2B). The 5-yr survival of non–MPGN II glomerulonephritis transplants (n = 852) was 80.8% for LRD and 71.1% for CAD donors (P = 0.003). Of the 165 renal transplants performed in individuals with MPGN II reported in the literature, data on graft survival and length of follow-up were available on 78 (4,5,8,9,11–15,17–26). The 45 ± 2.0% 5-yr graft survival in this population was not significantly different from that seen in the MPGN II patients contained in the NAPRTCS database (Figure 3).

When graft survival of the NAPRTCS database was analyzed by donor source, there was a clear difference in survival (Figure 4). Patients who had MPGN II and received CAD allografts had a 5-yr graft survival of 34.1 ± 9.8% compared with 65.9 ± 10.7% graft survival of LRD allografts (P = 0.004). Comparison of LRD graft survival in MPGN II patients and the database as a whole indicates that that there was little difference in LRD survival (65.9 ± 10.7% versus 81.0 ± 0.7%, respectively; P > 0.05).

During the study period, 29 of the 75 primary MPGN II allografts contained in the database failed (Table 3). In comparison with the database as a whole, there were no significant differences in causes of graft loss with the exception of disease recurrence (P < 0.05). Disease recurrences exceeded chronic allograft nephropathy by three-fold as a cause of graft failure. Of the 75 primary transplants, 11 (14.7%) were lost as a result of disease recurrence, with a mean time to graft failure of 823 ± 188 d (range 6 to 2170 d). When analyzed by donor source, 82% (9 of 11) of the failures caused by recurrence occurred in CAD

Table 2. Clinical features at initial pretransplantation presentation of MPGN II patients in the survey group (data available on 25 of 29 patients)

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Frequency (n of 25)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rapidly progressive glomerulonephritis</td>
<td>40% (10 of 25)</td>
</tr>
<tr>
<td>Nephrotic syndrome</td>
<td>24% (6 of 25)</td>
</tr>
<tr>
<td>Acute glomerular nephritis</td>
<td>12% (3 of 25)</td>
</tr>
<tr>
<td>Asymptomatic hematuria/proteinuria</td>
<td>20% (5 of 25)</td>
</tr>
<tr>
<td>Hypertension and renal failure</td>
<td>4% (1 of 25)</td>
</tr>
</tbody>
</table>
allografts compared with 18% (2 of 11) in the LRD group (\( P < 0.01 \)). There was no difference in frequency of recurrence with respect to ethnicity, gender, or age. Although the mean duration of pretransplantation dialysis was shorter in the LRD population than the CAD recipients, 14 and 24 mo, respectively, this difference was not statistically significant. Duration of pretransplantation dialysis did not correlate with graft survival (\( P = 0.6 \)).

One living unrelated donor transplant was performed and was still functioning 21 mo later at the time of last follow-up. Seven preemptive transplants were performed; three have failed as a result of posttransplant lymphoproliferative disorder, chronic rejection, and unknown reasons. The four remaining grafts were functioning at the time of last follow-up, 11, 11, 85, and 108 mo posttransplantation.

Five repeat renal transplants were identified in five individuals. The causes of initial graft failure were primary nonfunction, graft thrombosis, hemolytic uremic syndrome, recurrent disease, and recurrent urinary tract infections. Three of the five grafts were functioning at last follow-up. The recipients of the
Table 3. Comparison of causes of primary graft failures between NAPRTCS database as a whole and the MPGN II patients within the database

<table>
<thead>
<tr>
<th>Cause of graft failure</th>
<th>NAPRTCS Database (n = 7851)</th>
<th>MPGN II (n = 75)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total grafts lost</td>
<td>1924 (24%)</td>
<td>29 (38.7%)a</td>
</tr>
<tr>
<td>Disease recurrence</td>
<td>6.3% (121)</td>
<td>38.0% (11)a</td>
</tr>
<tr>
<td>Acute rejection</td>
<td>14% (267)</td>
<td>3.5% (1)</td>
</tr>
<tr>
<td>Chronic rejection</td>
<td>33% (628)</td>
<td>10.4% (3)</td>
</tr>
<tr>
<td>Vascular thrombosis</td>
<td>11% (206)</td>
<td>7.0% (2)</td>
</tr>
<tr>
<td>Primary nonfunction</td>
<td>2.5% (48)</td>
<td>3.5% (1)</td>
</tr>
<tr>
<td>Malignancy</td>
<td>1.4% (27)</td>
<td>3.5% (1)</td>
</tr>
<tr>
<td>Death with function</td>
<td>9.5% (183)</td>
<td>13.7% (4)</td>
</tr>
<tr>
<td>Other</td>
<td>17.4% (336)</td>
<td>20.1% (6)</td>
</tr>
</tbody>
</table>

Note: aP < 0.05.

Two remaining grafts had died; one individual with hemolytic uremic syndrome–related initial graft failure had significant graft dysfunction from recurrent MPGN II in the second graft at the time of his death, and the other individual died with a functional graft.

Analysis of MPGN II Recurrence in the Survey Population

Recurrence data for the survey population are presented in Table 4. Graft loss was attributed directly to disease recurrence in four patients—30.7% of the patients with biopsy-proven recurrence, or slightly less than 14% of the survey population. Although the presence of biopsy-proven recurrence had a negative impact on graft survival, with a median graft survival in the recurrence group of 5.4 yr compared with 9.7 yr in patients without biopsy-proven disease, this did not reach the level of statistical significance (P = 0.09).

Reported indications for biopsy at the time of recurrence were possible acute rejection in 55% of patients, suspected recurrence in 22%, and scheduled surveillance biopsies in 11%. The remainder had no indication reported. Biopsy findings at the time of recurrence did not correlate with biopsy findings at the time of initial pretransplantation diagnosis. The severity of mesangial proliferation was typically less than that seen at pretransplantation diagnosis in all patients with disease recurrence. Only three patients were noted to have moderate to severe mesangial proliferation. One patient had marked glomerular sclerosis (60%), and one patient had severe crescentic disease (40% glomerular crescents). No patient had significant evidence of tubulointerstitial disease. Concurrent pathology was noted in three patients: two had evidence of acute rejection, and one patient had evidence of chronic rejection. Multiple biopsies were available on five patients with recurrent disease ranging from 3 mo to 4 yr after the initial biopsy. Glomerular sclerosis was found in four of the five patients with serial biopsies with from 10 to 50% of the glomeruli affected. This did not differ significantly from the severity of glomerular sclerosis noted in biopsies of patients without evidence of disease recurrence (data not shown). Serial biopsies from three patients were found to have crescentic glomerular lesions, two with >40% affected glomeruli. The presence of glomerular crescents in the allograft biopsy had a negative correlation with graft survival and were never seen in biopsies of patients without evidence of MPGN II recurrence (R = −0.541, P = 0.03).

At the time of biopsy, patients with biopsy-proven disease recurrence had evidence of significant renal dysfunction: mean serum creatinine concentration 2.8 ± 0.7 mg/dl and heavy proteinuria with a median value of 3+ by urine dipstick. Whereas microscopic hematuria was equally common in those with or without biopsy-proven recurrent disease, heavy proteinuria was exceedingly uncommon in patients without biopsy-proven recurrence. Worsening of hypertension was reported in <30% of patients with recurrence, and serum albumin levels were almost universally normal (mean serum albumin 3.5 ± 0.2 g/dl). Serum C3 levels were reported as normal in 37.5% of patients at the time of biopsy-proven disease recurrence. There was no correlation between the severity of hypocomplementemia either at initial presentation or at the time of transplantation and disease recurrence (Table 5). Nephritic factor assays were not routinely performed either pre or posttransplantation, except in two instances in which they were reported as negative.

Treatment for disease recurrence varied substantially. At the time of recurrence, all patients were on calcineurin inhibitors as part of their immunosuppression regimen. Cyclosporine was stopped in one patient, three patients were switched from cyclosporine to tacrolimus, and two patients had tacrolimus discontinued. The remainder had the dose of calcineurin inhibitor reduced. Oral prednisone was increased in six patients, two were changed to alternate-day prednisone, and four patients were treated with pulse methylprednisolone. Two of the four patients who were treated with pulse methylprednisolone experienced graft failure as a result of disease recurrence. Two patients were treated with plasmapheresis; in both cases, the grafts eventually failed as a result of disease recurrence. Overall, patients with biopsy-proven MPGN II recurrence had significantly worse renal function at the time of last follow-up than patients without evidence of disease recurrence; they had heavier proteinuria, with 75% having 3+ compared with 92% of

Table 4. MPGN II disease recurrence within the survey population (n = 29)

<table>
<thead>
<tr>
<th>Disease Category</th>
<th>Recurrent MPGN II</th>
<th>Nonrecurrent MPGN II</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biopsy-proven recurrence</td>
<td>13/29 (44.8%)</td>
<td>16/29 (54.2%)</td>
</tr>
<tr>
<td>Clinically suspected, not biopsied</td>
<td>12 (41.4%)</td>
<td>6 (20.6%)</td>
</tr>
<tr>
<td>Graft failure as a result of recurrence</td>
<td>4/29 (13.8%)</td>
<td>10 (34.6%)</td>
</tr>
</tbody>
</table>
those without recurrence with trace or less ($P < 0.001$). Patients with biopsy-proven recurrence also had more severe renal insufficiency, with a mean serum creatinine of 4.8 ± 1.3 mg/dl compared with 1.9 ± 0.4 mg/dl in those without recurrence ($P = 0.025$).

**Discussion**

This study represents the largest single case series of renal transplantation in patients with MPGN II and serves to highlight the difficulties that the transplant physician who cares for these patients faces. Although the data provided by the survey population represents the largest and most detailed analysis available to date on renal transplantation in MPGN II, because of the small sample size and the possibility of confounding effects from unmeasured variables, these data must be viewed with caution. Findings contained in this report indicate that the overall allograft survival in patients with MPGN II is significantly worse compared with a well-defined contemporaneous control group of pediatric renal transplant recipients, with a 5-yr allograft survival rate of only 50% compared with nearly 75% in the control population. There has been considerable debate over the use of LRD as an organ source for transplantation in MPGN II, and it has been suggested that cadaveric sources be used preferentially. However, in this study, fewer than 40% of cadaveric organs were functioning 5 yr posttransplantation compared with 65% in the database as a whole, whereas there was no statistical difference in graft survival for LRD organs. These data strongly suggest that LRD organs have a significant long-term survival advantage compared with CAD organs. The basis for this is uncertain; however, it is possible that abnormalities in the recipient’s complement system, which initiate the primary disease, are accelerated by the increased immunoreactivity of a cadaveric renal allograft. Activation of the complement system has been well described in both acute and chronic allograft rejection, and recent studies linking low levels of chronic complement activation to the development of chronic allograft nephropathy support this hypothesis, although this remains speculative at best (28–30). It is important to recognize that this study does not address the impact of genetic deficiencies in complement proteins on disease recurrence. This is particularly relevant with respect to Factor H deficiency and MPGN II. The use of LRD in this subset of MPGN II patients is still of major concern, and further studies are required to address this critical question (31–33).

Supplemental survey data indicate that patients who had MPGN II and underwent renal transplantation as children had a much more rapid progression to ESRD than that typically cited in the literature (1). Historically, 50% of patients with MPGN II will progress to ESRD within 10 yr of diagnosis (4). However, within the current study population, the mean interval from diagnosis to transplantation was <4 yr. The biopsy findings at the time of initial pretransplant presentation suggest that most, if not all, of the patients contained in this study had evidence of severe renal injury, with >70% of the patients having crescentic lesions at the time of initial diagnosis. Given that the mean age at presentation was slightly less than 11 yr, patients who presented with milder disease likely progressed to ESRD in early adulthood and thus are not contained in the NAPRTCS database. Although it could be argued that this represents an inherent selection bias toward patients who are at increased risk for graft loss as a result of recurrence, several lines of evidence suggest that this is not true. First, there was no correlation between biopsy findings at the time of initial diagnosis and either graft loss as a result of disease recurrence or graft survival. Second, the graft survival data derived from previous published reports of MPGN II allografts, which represent a largely adult population, are almost identical to those seen in the pediatric population contained in this study. This suggests that the poor outcome seen in the NAPRTCS population is representative of the MPGN II population as a whole and not limited to pediatric transplantation alone. In distinction to these data is the report by Briganti et al. (27). In a comprehensive analysis of recurrent glomerulonephritis in the ANZDATA transplantation database, they reported no graft losses as a result of recurrent MPGN II in a cohort of 18 patients. However, because of the small sample size, details regarding

### Table 5. Relative frequencies of clinical parameters in the survey population for patients with biopsy-proven recurrence compared with those without evidence of disease recurrence

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Recurrent MPGN II ($n = 13/29$)</th>
<th>No Recurrence ($n = 16/29$)</th>
<th>$P$ Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>RPGN at initial diagnosis</td>
<td>18%</td>
<td>57%</td>
<td>0.10</td>
</tr>
<tr>
<td>Nephrotic syndrome at initial diagnosis</td>
<td>18%</td>
<td>29%</td>
<td>0.66</td>
</tr>
<tr>
<td>Asymptomatic hematuria and proteinuria at initial diagnosis</td>
<td>36%</td>
<td>7%</td>
<td>0.13</td>
</tr>
<tr>
<td>C3 &lt; 20 mg/dl at initial diagnosis</td>
<td>42%</td>
<td>12%</td>
<td>0.09</td>
</tr>
<tr>
<td>Low C3 at time of transplantation</td>
<td>50%</td>
<td>18%</td>
<td>0.10</td>
</tr>
<tr>
<td>Low C3 at time of biopsy</td>
<td>63%</td>
<td>25%</td>
<td>0.26</td>
</tr>
<tr>
<td>C3 &lt; 20 mg/dl at initial diagnosis</td>
<td>42%</td>
<td>12%</td>
<td>0.09</td>
</tr>
<tr>
<td>&gt;3+ proteinuria at biopsy</td>
<td>70%</td>
<td>16%</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Serum creatinine &gt; 2.5 at biopsy</td>
<td>45%</td>
<td>16%</td>
<td>0.11</td>
</tr>
<tr>
<td>Hematuria at biopsy</td>
<td>85%</td>
<td>50%</td>
<td>0.19</td>
</tr>
</tbody>
</table>
donor source and length of follow-up were not described. Overall, in this report, recurrent disease was the third most common cause of graft failure after chronic rejection and death, with a 10-yr incidence of failure as a result of recurrent disease of 8.4%.

In this study, the frequency of graft failure directly attributable to disease recurrence was 15% at 5 yr. This indicates that graft failure as a result of recurrent disease is a much greater problem in the MPGN II population than in other forms of glomerulonephritis. The higher failure rate is in agreement with previous reports by Andresdottir and others (24,26). Consistent with previous reports, the histologic findings at the time of biopsy-proven recurrence were variable, ranging from isolated dense deposits within the GBM to marked mesangial proliferation to crescentic glomerular lesions. There was no clear correlation between biopsy findings and graft survival with the exception of glomerular crescents, which had a significant negative correlation with graft survival. The data obtained from serial biopsies indicate that there is progression from isolated GBM deposits to severe glomerular injury in some patients. The lack of correlation between isolated recurrence of the defining lesion of MPGN II, dense deposits, and graft survival is one of the critical findings contained in this study. This suggests that there is a subset of patients with MPGN II in whom the finding of isolated recurrence of dense deposits does not herald impending graft failure.

Analysis of clinical variables failed to identify clinically useful predictors of disease recurrence or graft loss. It had been suggested that patients who presented initially with rapidly progressive glomerulonephritis or nephrotic syndrome were at an increased risk for graft failure as a result of disease recurrence. However, analysis of these clinical features at initial presentation as well as the severity of renal insufficiency and degree of hypocomplementemia failed to predict graft failure as a result of disease recurrence or graft survival. In fact, patients who presented with asymptomatic disease were more likely to have biopsy-proven recurrence than those whose initial presentation included rapidly progressive glomerulonephritis or nephrotic syndrome. The utility of serum complement levels to predict or reflect disease, it was impossible to determine whether any of these interventions had any impact on graft survival.

Taken together, the data contained in this report indicate that renal transplantation in patients with MPGN II should be undertaken with caution. Patients and families should be counseled regarding the poor overall graft survival, regardless of whether disease recurs, and that there seems to be an advantage with respect to graft survival for LRD allografts compared with CAD organs. At present, there do not seem to be any clear predictors of disease recurrence or prognostic markers for graft survival, save for the presence of persistent heavy proteinuria. Finally, should MPGN II recur in the allograft, there are few data to suggest that any therapeutic interventions will have a positive impact on graft survival save for isolated reports of plasmapheresis, for which there are few long-term outcome data.

Acknowledgments

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Access to UpToDate on-line is available for additional clinical information at http://www.jasn.org/