Original Article

Rejection rates in kidney transplant patients with and without IgA nephropathy

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Abstract

**Background.** Based on graft survival rates it has been claimed that patients with IgA nephropathy have a reduced risk of rejection after kidney transplantation. We wanted to evaluate this hypothesis.

**Methods.** Certified IgA nephropathy was the original disease in 70 of 874 consecutive kidney transplant patients (8.0%). Eighty per cent of the patients were men. Median age was 37 years, range 9–64. Fifty-three per cent had living donors and 20% of the transplantations were pre-emptive. Non-diabetic patients matched for age, sex, type of donor, and transplant number served as controls. Median follow-up time was 68 months. Duration of treatment for rejection during the first year post-transplant and graft loss due to rejection was recorded.

**Results.** The fraction of patients treated for rejection during the first year was 53% versus 54% of controls and the number of days when any antirejection treatment was given was 5.0 ± 7.5 versus 5.5 ± 7.4. Actual 3-year graft survival was 81% versus 80% and the number of grafts lost due to rejection was 9 versus 11.

**Conclusions.** Rejection rates were not reduced in patients with IgA nephropathy and survival of grafts and patients not better than for matched controls.

**Key words:** IgA nephropathy; kidney transplantation; rejection; graft survival; patient survival; antirejection treatment

Introduction

IgA nephropathy was first described in 1968 [1] and is the most common form of chronic glomerulonephritis (CGN) [2–5]. Only a minority of patients ever develop end-stage renal disease but IgA nephropathy has been reported to be the original disease in about 10% of kidney transplant patients [4]. A reduced risk of rejection, graft loss and mortality after transplantation to patients with IgA nephropathy has been proposed [6], and the view seems to have gained acceptance [7]. A mechanism of action for such an effect has also been hypothesized, namely that IgA HLA antibodies might protect from the effects of IgG antibodies [8]. We have used the registry of kidney transplants performed in Göteborg 1985–1993 to test the notion on our well-characterized and closely followed population.

Subjects and methods

The Transplant Unit in Sahlgrenska University Hospital, Göteborg, Sweden, serves 40% of Sweden’s 8.7 million inhabitants. From January 1985 to January 1993, 1000 consecutive patients received 1095 kidney transplants in the unit. In a retrospective analysis, the patients’ renal diagnoses were analysed and re-evaluated. Renal biopsies had been obtained from 345 patients. The original protocols from the histopathological investigations were obtained for all but eight patients. Basic information on this work has been published previously [9]. In the cohort of 1000 kidney transplant patients, 874 received first transplants, 160 due to biopsy-proven CGN (18.3%), 70 of whom had certified IgA nephropathy. Patients with systemic disease, i.e. Henoch–Schönlein disease, are not included in this presentation.

Contemporary non-diabetic controls were picked from the consecutive file of patients, matched for age ± 5 years, sex, and kidney source—cadaveric or living donor—all first transplants. Transplantation from a living donor was accomplished in 27% of the total cohort, predominantly from parents and siblings. Cadaveric organs were allocated mainly according to time on the waiting list, without attempts at HLA matching. The proportion of patients with cadaveric donors who received grafts without foreign HLA DR antigens was 19%.

In the period, the waiting time has ranged from 18 to 24 months, including any time before initiation of dialysis. Preemptive transplantation was performed in 23% of all patients.

During the entire period, immunosuppression was based on cyclosporin A and prednisolone. For the first 2 years, patients took part in a randomized study evaluating the effect of adding azathioprine. After that, triple drug therapy has been the standard. Induction therapy with ATG for 5–10 days was given only to PRA-positive patients and those with

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delayed onset of graft function, when cyclosporin was withheld. Antirejection therapy consisted of methylprednisolone in bolus doses on 4 consecutive days, followed by a second course, ATG or OKT 3 in resistant cases.

Patients living in the Göteborg area were followed at our out-patient clinic. For the other patients, reports were sent at least once a year from the local renal units. In addition, patients were seen in the unit at regular follow-up visits 6 months and 1, 3, 5 and 10 years after transplantation. The report was based on information available in November 1996. No patient or control was lost to follow-up except by death. Patients alive had been followed for 36 months to 11 years, median 68 months.

Statistical methods

Unless otherwise stated, values are mean ± SD. Survival was calculated as cumulative survival according to Kaplan–Meier, the significance of differences tested by log-rank test (Mantel–Cox). The $\chi^2$-test was used to compare frequencies and the Mann–Whitney U test to test non-normally distributed values. $P$ values above 0.05 were considered non-significant.

Results

Table 1 shows demographic data for IgA nephropathy patients, the matched controls, and the entire cohort of transplant patients in the time period. IgA nephropathy patients were significantly younger at the time of transplantation than the rest of the patients in the entire cohort, $n = 874$, $P < 0.0001$. There was also a higher proportion of men ($P = 0.003$) and of transplantations from living donors ($P < 0.0001$). Thirty-seven of 70 IgA nephropathy patients had living donors; 23 were parents, 11 siblings, 2 spouses, and one was an uncle.

For patients with cadaveric donors, there was no difference from the total cohort in the degree of HLA DR mismatching. The proportion of transplantations performed before initiation of dialysis did not differ from the total cohort. Control patients were matched for all factors except pre-emptive transplantation and degree of DR mismatching, which turned out to be similar.

There was no significant difference in patient survival between IgA nephropathy patients and their matched controls, $P = 0.51$. Seven patients with IgA nephropathy died, one within the first year with pancreatitis, perforations of the colon, and a never-functioning graft, the others later due to infections (2), malignant disease (2) or coronary heart disease (2). Nine control patients died, four within the first year of pneumonitis (3) or pancreatitis (1), five later of coronary heart disease (4) or peripheral vascular disease (1).

There was no difference in graft survival between patients with and without IgA nephropathy, $P = 0.96$. Although there was a trend for better survival with living donors, this difference was not significant, $P = 0.38$. Figure 1 shows results for IgA nephropathy patients and matched controls, both groups split according to kidney source. There is no indication of improved graft survival in IgA nephropathy in either subgroup.

In total, 20 of 70 grafts transplanted to patients with certified IgA nephropathy were lost during follow-up.
Table 2. Rejection and antirejection treatment first year after transplantation for kidney transplant patients with IgA nephropathy and their matched controls

<table>
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<tr>
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<th>IgA nephropathy (n = 70)</th>
<th>Matched controls (n = 70)</th>
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</thead>
<tbody>
<tr>
<td>Fraction treated for rejection</td>
<td>53%</td>
<td>54%</td>
</tr>
<tr>
<td>Number of days (of all) (mean ± SD)</td>
<td>5.0 ± 7.5</td>
<td>5.5 ± 7.4</td>
</tr>
<tr>
<td>Number of days (if treated) (mean ± SD)</td>
<td>9.4 ± 8.1</td>
<td>10.0 ± 7.4</td>
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<tr>
<td>Grafts lost due to rejection within 6 months</td>
<td>6</td>
<td>3</td>
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<td>3</td>
<td>8</td>
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and 20 of the controls’ grafts. In the IgA nephropathy group, 7 graft losses occurred early (within 6 months), caused by never-functioning graft (1), acute biopsy-verified rejection (5), or chronic vascular rejection (1). Recurrence of IgA nephropathy was the major cause of late graft loss (5). The total number of graft loss caused by rejection was similar in IgA nephropathy patients and controls, as shown in Table 2. The Table also shows that the rejection rates during the first year and the mean number of days when any antirejection treatment were given was not different.

**Discussion**

Our study confirms previous reports of good overall results of transplantation to patients with IgA nephropathy [6,7,10]. This is true especially for patient survival, which was superior to that in the contemporary cohort (data not shown), probably related to the fact that IgA patients were significantly younger. In contrast, there was no significant difference from the controls matched for age. The UCLA Registry also reported reduced mortality in patients with IgA nephropathy [6]. Their control group, however, was not matched and, like our main group, may have differed from the study patients in several respects other than underlying renal disorder.

Graft survival rates were almost identical with those in the closely matched controls. Even when split according to type of donor, graft survival curves for IgA nephropathy patients and controls remained very similar. In contrast to our finding, superior survival of first grafts from cadaveric donors was reported in IgA nephropathy patients compared with the rest of the patients in the UCLA Registry [6]. This difference was also seen when only patients aged 20–50 years were compared. However, the average age in each group was not published and may have differed considerably within this range.

The possibility that IgA nephropathy patients reported to the UCLA Registry represented a positive selection, for instance were more often from excellent centres, was not, in our opinion, ruled out. In particular, the prevalence of IgA nephropathy was lower than expected, about 3% to be compared with our 8.0%. Only 128 of more than 200 centres had reported any patient at all with this diagnosis. This probably reflects policies for obtaining kidney biopsies in the USA. If a renal biopsy is not a regular procedure, a young patient in a good general physical condition is probably more likely to be subjected than a weaker candidate. Furthermore, it is possible that the diagnosis has not been confirmed by biopsy in each case, as in our series, but was sometimes based on inconclusive clinical indications such as a history of episodes of haematuria triggered by infections. In another published study, the diagnosis was set on clinical grounds in the majority of patients [11].

Another possible uncertainty is the way survival was calculated: not more than half of the patients would actually have been followed for 3 years when the results of transplantations performed in 1985–1990 were calculated in early 1991. If there is a true difference in the experience from our centre and the accumulated data of the UCLA Registry, this might be connected with different policies for HLA matching. In such a case, HLA matching would be more favourable in IgA nephropathy patients than in patients with other diagnoses. We find this hypothesis somewhat far-fetched.

A recent French study of kidney transplantation to patients with IgA nephropathy reports excellent graft survival, 75.2% at 5 years, but with no control group for comparison [7]. Another study including about the same numbers as in our study reports no advantage of IgA nephropathy with respect to graft survival [12], yet with data presented in a condensed form which precludes detailed comparison with the UCLA data or our data.

Survival of kidney transplants is most often presumed to depend on acute or chronic rejection. We have in fact investigated and analysed reasons for graft loss and found that the incidence of graft loss due to rejection was not reduced in IgA nephropathy patients. Finally, the incidence and severity of rejection episodes was not reduced. No corresponding data have been published previously.

In summary, there was no indication of a reduced risk of rejection in IgA nephropathy patients.

**References**


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