Does nephrectomy of failed allograft influence graft survival after re-transplantation?

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Abstract

Background. The aim of the study was to determine the effect of removal of a failed kidney allograft on the outcome of subsequent transplant.

Methods. Retrospective analytical study comparing graft survival for patients (1993–2005) who had previous graft nephrectomy with those who had not.

Results. Of 89 patients with kidney re-transplants, 68 had a transplant nephrectomy (Group I) while 21 had retained failed grafts (Group II). There was no significant difference in the two groups in the PRA level at the time of re-transplantation (37% versus 29%). Mean follow-up was 47 months. Acute rejections in Group I were 49.1% and in Group II, 31.2% (P = 0.20). Twenty (29%) grafts failed in Group I and four (19%) in Group II. One, three and five years’ actuarial graft survival in Group I was 83.8%, 76% and 66.2%, while in Group II, it was 94.7%, 86.8% and 69.5%, respectively (P = 0.66). Five-year actuarial patient survival in Groups I and II was 94.1% and 87.5%, respectively (P = 0.69). Multivariate analysis showed that PRA level significantly influenced graft survival independent of nephrectomy (P = 0.04).

Conclusion. Nephrectomy of a failed allograft does not seem to significantly influence the survival of a subsequent graft.

Keywords: graft nephrectomy; kidney transplant; nephrectomy; renal re-transplantation

Introduction

As recipients of kidney transplants are growing in number, so are the patients with failed transplants and the number of potential candidates for re-transplantation. The outcome of re-transplants, as with those of primary transplants, has significantly improved in recent times, but still lags behind that of primary transplant [1]. Sensitization due to previous transplant is documented to be the main reason for this difference [2].

A failed transplant is a continuous source of antigenic stimulation for anti-HLA antibodies and its presence in the recipient may promote continued sensitization [3]. While this in turn decreases the probability of a cross-match-negative donor kidney, it might also influence the outcome of the subsequent transplant.

The failed allograft may also induce a chronic inflammatory response due to its immunoreactivity, as reflected by elevated C-reactive protein, erythrocyte sedimentation rate, erythropoietin resistance, hypoalbuminaemia and malnutrition [4,5]. This response not only leads to increased morbidity of patients on haemodialysis but also could compromise recipient fitness for re-transplantation. Studies have shown that the removal of a failed allograft improves the well-being of patients on dialysis [6]. However, its effect on the outcome of subsequent transplants has not been well studied, particularly in the modern era of immunosuppression.

The aim of this study was to compare the outcome of transplant recipients who retained a previous transplant with those who had undergone a prior transplant nephrectomy.

Patients and methods

Patients undergoing kidney re-transplantation in our unit during the period January 1993 to April 2005 were included in the study. Data were collected from the hospital records. Patients who had previous graft nephrectomy (Group I) were compared with those who did not have it (Group II) for graft survival, patient survival and rate of acute rejections. Recipient and donor demographics, number of re-transplants, HLA matching and panel reactive antibodies (PRA) were also studied for their effect on the transplant outcome. The rate of acute rejection was that of treated rejections.

The graft survival and patient survival of the two groups calculated by the Kaplan–Meier method were compared with a log rank test. For graft survival, patients dying with functional grafts were censored as failed grafts.
Multivariate analysis was done by the Cox regression hazard model. Nominal variables were analysed by the chi-square test and numeric variables by the Mann–Whitney U-test. A value of \( P < 0.05 \) was considered statistically significant.

### Results

Of 89 patients with kidney re-transplants, 68 had a nephrectomy (Group I) while 21 had retained failed grafts (Group II). The indication for graft nephrectomy in the majority was to treat symptoms, including tenderness and anaemia related to a retained failed allograft (78%, \( n = 53 \)), while in the rest it was to create space for the new graft. Mean follow-up was 47 months. The baseline characteristics of each group are shown in the Table 1. Of note, there was no significant difference in the PRA level, measured before the most recent transplant, at the time of re-transplantation (37% versus 29%). All patients received prednisolone in the immunosuppression regime. Cyclosporine was used in 65% and 59%, tacrolimus in 35% and 45%, azathioprine in 61% and 65%, mycophenolate in 39% and 46% and Basiliximab induction in 36% and 41%, respectively in Groups I and II.

In Group I, of the total of 89 previous grafts, 33.7% (\( n = 30 \)) survived >5 years, 36% (\( n = 32 \)) survived 1–5 years and 30.3% (\( n = 27 \)) survived <1 year. The respective figures for Group II, with a total of 22 previous failed grafts, were 36.4% (\( n = 8 \)); 36.4% (\( n = 8 \)) and 27.2% (\( n = 6 \)). Causes of graft failure in Groups I and II were acute rejection in 48.3% (\( n = 43 \)) and 45.4% (\( n = 10 \)), chronic allograft nephropathy in 31.6% (\( n = 28 \)) and 32% (\( n = 7 \)), recurrent original disease in 13.3% (\( n = 12 \)) and 13.6% (\( n = 3 \)) and surgical complications in 6.8% (\( n = 6 \)) and 9% (\( n = 2 \)). Acute rejections in Group I were 49.1% (\( n = 33 \)) and in Group II, 31.2% (\( n = 7 \)). The difference was not statistically significant (\( P = 0.20 \)). Eighty-three percent (\( n = 27 \)) of the rejections in Group I and 85% (\( n = 6 \)) in Group II were steroid responsive. Twenty (29%) grafts failed in Group I and four (19%) in Group II.

One, three and five years’ actuarial graft survival (Figure 1) in Group I was 83.8%, 76% and 66.2% while in Group II, it was 94.7%, 86.8% and 69.5%, respectively (\( P = 0.66 \)). Five patients died in Group I and two in Group II. Five-year actuarial patient survival (Figure 2) in the two groups was 94.1% and 87.5%, respectively (\( P = 0.69 \)).

Multivariate analysis showed that the above results were not influenced by demographics of donor/recipient, HLA mismatches and donor type and number of re-transplants (Table 1). However, PRA level had a statistically significant influence on patient and graft survival, irrespective of whether the patient had nephrectomy or not (\( P = 0.04 \)).

Also by using Cox regression, no statistically significant difference was found in patient and graft survival in the two groups by having no pre-transplant dialysis, dialysis for <1 year or dialysis for >1 year (\( P = 0.27 \)).

### Discussion

In the absence of universally accepted indications for removal of a failed graft, the rate of transplant nephrectomy varies widely from 0.5 to 43%, depending on the policy of an individual centre [7,8]. In our unit, a failed transplant is removed either in symptomatic patients or if space is required for the new transplant.

In most of the transplant units, transplant nephrectomy is undertaken only in patients suffering from ‘graft intolerance syndrome’. This approach has been challenged by some authors, as even apparently asymptomatic patients have been found to suffer from manifestations of chronic inflammatory response and thus are at risk of facing its consequences [9]. A case for removal of all failed allografts is thus made [5,6]. A major concern with this approach is the high morbidity and mortality of transplant nephrectomy [10]. Its alternative could be transcatheter intra-arterial embolization of the graft, which is reported to be less complicating [9].

Studies have shown that the timing of the nephrectomy in relation to re-transplantation is an important determinant for the new graft outcome [7]. Despite the issue of sensitization, an interval between the removal of the failed allograft and re-transplantation may allow time for the effects of immunosuppression and chronic inflammatory state to settle in the recipient. Compared with primary transplantation, pre-emptive re-transplantation has been found to have an inferior graft outcome [7]. A certain period of dialysis before re-transplantation is reported to be thus beneficial. Our study, however, did not show a significant difference in graft and patient survival between patients with or without dialysis prior to re-transplant.
Literature from the post-cyclosporine era exploring the effects of transplant nephrectomy on a subsequent transplant has shown contradictory results. Abouljoud et al. observed a negative influence of primary allograft nephrectomy on the second transplant outcome [8]. They further found that a lower donor age, delayed re-transplantation after nephrectomy and antibody induction might improve the results. Sumrani et al. also reported that primary allograft nephrectomy, by increasing PRA level, could be detrimental to the new transplant [11].
In contrast, an analysis of 127 re-transplant patients, by Douzdjian et al., observed that despite the association of primary allograft nephrectomy with higher preformed antibody levels, re-graft survival was not influenced by nephrectomy [12]. In their study, however, the rate of acute rejections was significantly higher in the nephrectomy group than in groups without it (73% versus 42%, P = 0.03). These findings are similar to ours as our transplant nephrectomy patients had a higher PRA level and a trend towards increased acute rejections. Yagmurur et al. have also reported similar findings based on retrospective analysis of 53 recipients of a second allograft, 21 of which had primary allograft nephrectomy. One, three and five years’ graft survival rates were 83%, 89% and 64% in patients with allograft nephrectomy versus 79%, 68% and 45%, respectively in patients without it. However, acute rejections were not significantly different in the two groups (43% versus 38%). They thus concluded that graft nephrectomy before re-transplantation does not make any difference. Further, they found a negative correlation of second graft survival with the time interval between the nephrectomy and re-transplant [13]. Recently, Lair et al. analyzed the effect of the presence of a first graft on the outcome of a second graft in a rodent allograft model and in a cohort of 240 human second kidney allograft recipients. The study could not find any significant difference in the graft outcome after second transplants with or without primary allograft nephrectomy [14]. The results of our study are thus more consistent with those of recently reported studies.

Our study, like others reported in the literature, showed rejection as the leading cause of previous graft failure in re-transplant patients, indicating sensitization to be a major concern in these patients. In our analysis, PRA levels, measured before the most recent transplant, had a significant influence over re-transplant survival, irrespective of whether nephrectomy was done or not. One way of knowing the effect of graft nephrectomy on the degree of sensitization could be to measure PRA serially before and after nephrectomy. In both groups, the PRA level was quite high, with little difference in the two groups in this respect. PRA level was not a factor in decision making for nephrectomy in our patients. In both groups, graft survival was relatively lower possibly because we were dealing with the group of patients who were highly sensitized and had poor transplant history. Reported graft survival in such patients was also low as evident from the quoted studies.

Despite some theoretical advantages of failed allograft nephrectomy, the studies carried out including this one have not shown it to have a positive effect on re-transplant survival. It is probable that the current immunosuppression regimens balance any immunological discrepancies. Furthermore, the retained graft might fix the circulating anti-HLA antibodies thereby sparing the new transplant.

In conclusion, nephrectomy of a failed allograft does not seem to significantly influence the survival of a subsequent graft. The decision to remove or retain a failed graft in the context of re-transplantation should thus be based on known clinical indications for the procedure.

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References


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