IS IT REALLY WORTH RE-TRANSPLANTING PATIENTS?

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Summary

Increasingly patients whose first renal transplant fails are being re-transplanted. A study of patients in one unit was undertaken to assess whether second kidney grafts were as successful as first allografts and whether certain factors determined the outcome of secondary transplants.

Second and subsequent grafting can be performed with confidence of a successful outcome provided a careful selection of patients is made. The outcome of subsequent grafts should show no significant difference from the overall results of first renal allografts.

Introduction

Renal transplantation with immunosuppression in the treatment of end stage renal failure is associated with a significant morbidity and mortality. Yet in Europe 20% of all renal allografts are second transplants [1] and an increasing number of previously transplanted patients are now returning to dialysis programmes. Is it really justified after the failure of their first transplant to subject these patients to further risk by re-transplantation?

Some centres believe that provided careful immunological screening is performed, a successful outcome of subsequent renal allografts can be anticipated [2,3], whilst others report very limited success [4]. However a number of factors may be important in determining the outcome of secondary allografts [5,6] and it has been suggested that the time interval between first and second allograft may be significant or the mode of failure of the first allograft, with the duration of the first kidney transplant being critical [7,8].

We undertook a review of patients undergoing treatment in one unit over a ten year period to assess the value of re-transplantation in our programme of treatment of renal failure and to assess the importance of the previously cited factors.
Patients

In our series of 418 kidney transplants performed between 1966 and 1976, 77 patients had had second allografts, 6 a third, and one patient received a fourth, fifth and sixth allograft.

Three of the patients who had second allografts from a cadaveric donor had received their first graft from a live related donor.

The following factors were assessed:

(a) The survival of patients and outcome of allograft in secondary transplantation.

(b) The influence of the aetiology of the first allograft failure on the outcome of secondary renal transplants.

(c) The influence of the duration of survival of the first allograft on subsequent grafts.

(d) The time interval between first and second renal allografts.

Surgical Technique

Second renal transplants were usually performed by using the opposite iliac vessels. However in patients undergoing third or subsequent allografts no 'virgin' site in the iliac-fossa was available; the graft was then either placed extraperitoneally in the site already used for the first allograft or situated intraperitoneally.

In patients with grafts placed intraperitoneally in the pelvis, an end to side anastomosis to the external iliac vessels was carried out after vessel identification via the peritoneal cavity. These grafts were left within the peritoneal cavity and supported in position by capsular sutures to the pelvic peritoneal wall. The ureter was anastomosed intraperitoneally to the bladder using a ureteroneocystostomy and a small Tizard ureteric catheter inserted up the ureter from the bladder to allow monitoring of urine output, and permit radiological studies of the kidney. However the assessment of anuria post-operatively in the intraperitoneal kidney may be difficult as percutaneous renal biopsy is not possible because of the real danger of damage to the intestine.

Results

A statistically significant improvement in patient survival was seen during the study in patients undergoing multiple transplants \( p = <0.01 \) at 1 and 10 years. Forty-nine per cent of patients survived with multiple renal grafts, whereas only 30% of first renal allograft patients were alive at 10 years (Figure 1).

However, no significant difference was observed between allograft survival of first or subsequent allografts (Figure 2).

Third allografts may be performed with an expectation of reasonable graft survival, even after two preceding graft failures; although the results are not statistically significant because of the small numbers.

Figure 3 shows the percentage of grafts surviving following re-transplantation related to the cause of first allograft failure. Patients fared better in terms of graft survival for the first two years provided that the failure of their first graft
was due to non-immunological causes. However by three years there was no significant difference. Nor was there any clear difference in the outcome of subsequent allografts between patients rejecting the first allografted kidney acutely when compared with those undergoing more delayed rejection.

The percentage of second graft survival when correlated with the time interval between first allograft failure and re-transplantation showed no significant difference within the first twelve months. However subsequently at second and
third years, poorer overall graft survival was obtained in those in whom transplantation had not been performed for over a year after failure of the first allograft, but this was not associated with a significant change in overall patient survival. In this one centre prolonged first renal graft survival did not infer any improvement in overall subsequent graft survival.

Comments

The failure of a renal allograft with return to dialysis is a frequent occurrence. For some of these patients the experience of transplantation and immunosuppression will have been unfortunate, with the development of cushingoid facies, gastrointestinal disturbance and diabetes. Some of these patients will re-adjust well to the return to the restrictions of dialysis. Many others are anxious to be reconsidered for transplantation and it appears from this study that, in spite of technical surgical problems, many will achieve a successful re-transplant, although the outcome for second grafts is not significantly different from first time allografts.

The mode of failure of the first graft is clearly important in assessing second graft outcome, with patients initially having technical failures doing well subsequently.

In our study no difference in second graft function was found for an increased time interval between grafts or between acute or chronically rejected kidneys; however, the selection of patients for re-transplantation is clearly critical as is reflected by an improved patient survival following the natural selection process of the fittest coming forward for re-transplantation.
References

2 Opelz, G, Mickey, MR and Terasaki, PI (1972) Science, 178, 617
3 Opelz, G and Terasaki, PI (1976) Transplantation, 21, 483

Open Discussion

VAN ROOD (Leiden) I think the problem is a very important one, and I would just like to call your attention to recently published work by Paul et al from Leiden, in which he pointed out that early graft loss is often due to antibody directed against the endothelium of the arteries in the donor kidney. I don’t think that you did present any data on this point and my question is whether after these publications appeared you re-analysed your data as to whether you could pick up such antibodies, and in this context it is perhaps worth mentioning that you can also pick them up by testing for them on monocytes. Antigens are shared by the endothelium and the monocytes which is of course an easy thing to look at, and my question is whether you have also looked at sera, especially of the patients who rejected the second graft in the presence of such antibodies.

SLOOFF No, we didn’t look specifically at that kind of antibody. In patients with cytotoxic antibodies before the second transplantation it appeared that one third of these patients had cytotoxic antibodies against their first donor kidney and two thirds had cytotoxic antibodies against blood which was given at the time of the first transplantation. The interesting thing was that the graft survival in these two groups was different.

GELIN Did you do any such analysis in Cambridge?

McMASTER No we have not done so in these patients but I am aware of the work which is referred to and we are currently re-evaluating the whole question of transplantation.

WOOD (Leicester) Among the factors which may account for lower graft survival rate in second transplants are firstly that you may be retransplanting a group of so called ‘immunological responders’ and secondly you may be giving a second graft to a group of patients who were sensitive to azathioprine the first time with persistently low white counts in response to the drug. Have either of you looked at those two factors in your patients?

McMASTER We have looked at the question of ‘responders’ and there was no clear data that we found that determined the outcome in terms of cytotoxic
antibody response. We have not looked specifically at white cell counts.

SLOOFF We did not look into this data.

VRIESMAN Could I ask Professor Van Rood about the incidence of positive anti monocyte antibodies cross reacting with the endothelium in terms of typing before grafting.

VAN ROOD I don't think this data is yet available. The studies of Paul were done on first transplants mainly, but there is now data coming along which indicates that also in retransplantations you would expect these antibodies to be very important and it is also clear that these antibodies can be induced by blood transfusions and pregnancy alone but also and perhaps especially by rejection as you would expect.

VRIESMAN Does it account for all the factors?

VAN ROOD I never think that one single factor will account for everything but I think it will be a very important thing.

BRYNGER I ask about the surgical way of placing a third kidney graft abdominally. We have now performed around 77 third or more grafts in Gothenburg and we have not been forced to place one of these kidneys intraperitoneally so far. I admit that there might be some technical problems preparing the vessels but the problems can always be overcome, and I think that it is not necessary to go intraperitoneally.

McMASTER I think that it is not always necessary, but if your first kidney has failed with infection or urinary leakage that side may be difficult to re-explore and there may be other reasons why the other side may not be desirable – for example the use of shunts on that side. We found not infrequently that we have had to place it intraperitoneally. The outcome is usually satisfactory. The monitoring may be more difficult.

MAMOS (London) May I ask both speakers whether they analysed their results with regard to the pre-existing renal disease? In other words did they find any significance with diseases like mesangio-capillary nephritis recurring in the renal allograft?

McMASTER I am not sure that I can answer that question completely. I have no data to support the relationship between pre-existing disease and rejection episodes.

GELIN Even if there is an actual shortage of organs the patient who fails his first graft should not be neglected. He is still a very good candidate for full rehabilitation if we pick the proper situation and condition for him. The shortage of organs must be overcome by closer cooperation with the neighbouring hospitals and we can all work to enhance that ambition.

Secondly, if rejection is a main reason for the outcome of the re-graft it depends on what kind of rejection episode made the graft fail; whether it is an acute severe rejection or if it is a chronic rejection. The slow chronic rejecting
kidney does not decrease the chances of success for the second or third graft. Finally, it should be preferable to keep the retransplanted organ in an extraperitoneal location even in third and fourth retransplants. I think that retransplantation must be a necessary part of the policy in an active transplant centre.