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Renal Transplantation in the Rat – A New Simple, Non-Suture Technique

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Summary. Renal transplantation in the rat can be performed by a simple technique utilising cuff anastomosis. This method is quick and reliable, and the results compare well with those achieved by standard microsurgical techniques.

Key Words: Renal transplantation, Cuff anastomosis, Rat kidney.

Introduction

Experimental transplantation in a small animal such as the rat has considerable advantages over that in larger animals. Multiple controlled experiments can be carried out. The rat is relatively cheap, easy to handle and house, and the existence of inbred strains allows for either iso- or allotransplantation. However, techniques of organ grafting in the rat require skills in microsurgery which take a considerable time to acquire.

We describe a simple new technique for renal transplantation which requires no sutures for vascular and ureteric anastomoses and can be performed successfully after minimal practice.

Materials and Methods

Renal isotransplantation was performed using 200–300 g Agus strain rats. Anaesthesia was achieved with Sodium Pentobarbitone at a dose of 4 mg/100 g body weight given intraperitoneally and supplemented by ether inhalation.

Donor Nephrectomy. The abdomen was opened through a midline incision and the left kidney, was exposed. The posterior peritoneum was incised and the left renal vessels were mobilised. A length of approximately 1.5 cm of abdominal aorta carrying the left renal artery was mobilised after the superior mesenteric, right renal and lumbar arteries had been ligated and divided. Haemostatic clips were applied to the aorta which was then transected approximately 0.75 cm proximal and distal to the renal artery. The left renal vein was then divided at its junction with the inferior vena cava. The ureter was divided near the bladder, leaving the kidney free with an intact arterial supply and venous drainage. The graft was immediately cooled and placed in Collin's solution at 4 °C. The aorta was cannulated and the graft flushed with 2 ml of cold Collin's solution. A 3 mm polyethylene cuff of 2.1 mm outside diameter (O.D.) was then slipped over the renal vein the end of which was then everted over the cuff and secured with a 7/0 silk ligature. The graft was stored in Collin's solution at 4 °C until transplantation.

Recipient Operation. The left kidney was exposed transperitoneally and the left renal vein was completely mobilised. A 1.5 cm segment of infrarenal aorta was dissected free. An approximating clamp was applied to the aorta which was then bisected and the two ends were washed out with heparinised saline. A 3 mm long polyethylene cuff (O.D. 1.6 mm) was slipped over both ends of the aorta which were then everted over the cuffs and secured with 7/0 silk ligatures. The graft was removed from the Collin's solution and orientated so that the aorta was parallel to the recipient aorta. The proximal end of the donor aorta was drawn over the proximal cuff and secured with a circumferential 7/0 ligature. The distal aortic anastomosis was performed in the same way. A haemostatic clamp was applied to the renal artery of the graft and the approximating clamp removed restoring the blood supply to the pelvis and hind legs of the animal. The recipient left renal artery was ligated and divided and the renal vein ligated as near to the hilum as possible. A clip was placed on the vein at its junction with the inferior vena cava. The venous anastomosis was achieved by placing the cuff of the donor vein into the recipient renal vein through a venotomy, and securing it with a circumferential 7/0 silk ligature. The vascular clamps were removed from the renal vein and artery thus restoring the blood supply to the graft (Fig. 1). The recipient's left kidney was then removed.

The donor ureter was initially anastomosed end-to-end to the recipient left ureter with approximately 10 interrupted 11/0 monofilament nylon sutures. Although we found this method quite satisfactory, we felt we could reduce the operating time and make the procedure simpler by using a 5 mm long polyethylene stent for the ureteric anastomosis (O.D. 0.63 mm). This was then inserted into the donor ureter and secured with a 7/0 silk ligature near the divided end at the time of donor nephrectomy. The distal end of the stent was then inserted into the recipient ureter and secured in the same way. An immediate contralateral nephrectomy was then performed.

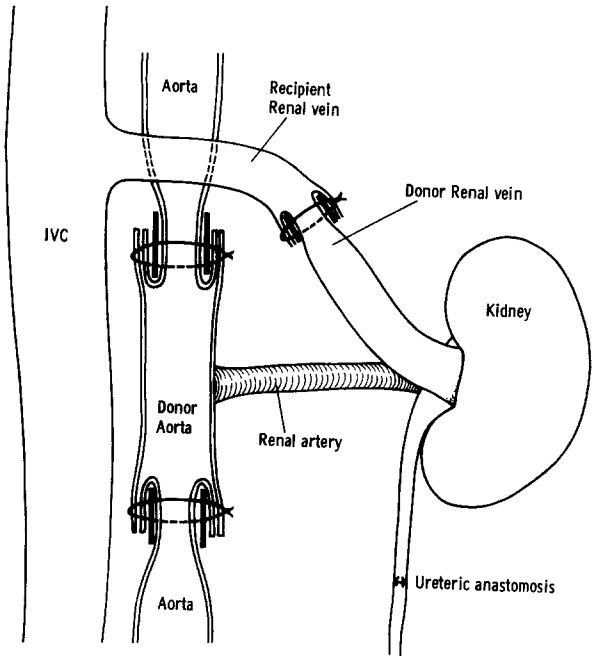

Fig. 1

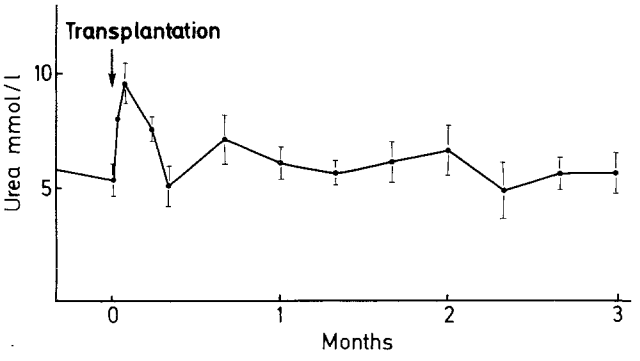

Fig. 2

Animals were sampled by tail vein bleeding for blood urea nitrogen (B.U.N.) prior to and post-transplant. All animals were followed-up for 3 months post-transplant, then sacrificed, and the grafts examined histologically.

Results

Forty isografts were performed using this technique, the average operative time being 40 min. Aortic clamping was always less than 10 min and the mean warm ischaemic interval was 12 min. Out of a total of 40 transplants, there were 8 deaths 6 of which were after the first 10 operations. The cause of death included haemorrage and peritonitis. In the surviving animals there was only one instance of graft failure, due to thrombosis at the site of the anastomosis. All grafts showed evidence of immediate function as shown by the production of urine. However, there was a transient rise in the B.U.N. which had returned to normal by 2 weeks post-transplant and remained normal up to 3 months post-operation (Fig. 2). Histological findings showed normal kidneys and ureters with only a minimal degree of intimal proliferation in the vascular anastomosis. There was no evidence of ureteric obstruction.

Discussion

Non-suture methods have been utilised clinically, particularly in transplantation of organs and plastic surgery and the mechanical stapling of 1–4 mm diameter vessels has been evaluated [1, 3, 5, 6]. Cuff anastomotic techniques were first described by Nitze [4] and have been criticised with some justification because they may cause some narrowing of the lumen at the anastomotic site.

In our experience, although some mechanical narrowing was inevitable, this resulted in only one vessel thrombosis. Renal function was not impaired in the remaining animals. The use of intraluminal stents for ureteric anastomoses was well tolerated which confirms the findings of others [2]. The polyethylene stents did not interfere with urine flow and remained in place for the 3 months study period.

During the preliminary 10 operations the mortality rate was high. However, with relatively minimal practice, the subsequent survival rate compared well with those achieved by standard microsurgical techniques. This method of transplantation was safe and rapid in the rat and replaced the more lengthy and more complicated microsurgical suture techniques.

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Invited Commentary

Cuff techniques have been empolyed for some time, and very successfully too – Kamada in Cambridge uses cuffs for all his orthotopic rat liver transplants –, but it seems that the main advantage of this technique for rat renal transplants is the fact that it permits operation by personel, who are only minimally trained. However, there would appear to be no great difference in operation time between this and a conventional suture technique, employed by someone more practised.

The inevitable narrowing of the vessel lumen when using a cuff, must be considered. The aortic cuff is quoted as having an outside diameter of 1.6 mm, and the renal vein 2.1 mm. Allowing for the thickness of the aortic wall, there will probably be a moderate to severe compromise of aortic flow. Even so, the animals seem to tolerate this well.

Advantages of the technique are:

- may be employed after basic microsurgical training;
- no possibility of renal vessel stenosis;
- stent connection of the ureter prevents possible leakage from a ureteric suture line, which is a major factor in post-operative technical failures.

Possible disadvantages may be:

- longer donor and recipient preparation;
- recipient aorta cross-clamped;
- limit of one donor kidney per donor rat;
- no re-use of recipient animal in the event of vascular anastomosis failure:
- use of ureteric stent decreases ureteric lumen.

In the hands of a well trained microsurgeon, the conventional more elegant techniques with near-normal post-operative haemodynamics, may remain preferable, although there is no doubt that the cuff technique will be useful for those with limited time for research.

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Reply

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We would agree with most of the comments. However, we wish to make some points about them. First, although the operative time is no longer than conventional suture techniques, the warm ischaemic interval is shorter. This, we feel, is a significant advantage allowing immediate contralateral nephrectomy and monitoring of graft function. Second, although the lumen of the aorta is narrowed, but not by as much as the figures seem to suggest, we have found very few complications. We have now performed over 500 kidney and pancreas grafts using aortic interposition and have seen only 5 aortic thromboses and no cases of hind leg paralysis. This indicates that the blood flow to the lower limbs is sufficient. Furthermore, it would also suggest that the cross clamping of the recipient aorta is a safe experimental procedure.

The technique does require longer donor preparation, the procedure taking us about 20 min but this is not a practical disadvantage. The longer recipient preparation is really insignificant if the total operative time is about the same.

We feel that the conditions where re-use of an animal after an anastomotic failure is practical are rare, and in any case we have rarely seen graft failure owing to a breakdown of the anastomosis.

Finally we have experienced no problems of ureteric obstruction as long as an immediate contralateral nephrectomy is performed.