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RENAL/TRANSPLANTATION

ORIGINAL ARTICLE

Vascular and haemorrhagic complications of adult and paediatric live-donor renal transplantation: A single-centre study with a long-term follow-up

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Abstract *Objectives:* To compare the haemorrhagic and vascular complications between paediatric and adult renal transplant recipients with a long-term follow-up.

Patients and methods: Between March 1976 and December 2006, in all, 1865 live-donor renal transplants were carried out. Patients were stratified according to their ages into two groups; paediatric ($\leqslant$18 years; 259) and adult ($>$18 years; 1606). Variables assessed included incidence, risk factors, management and sequelae of vascular and haemorrhagic complications. The effect of these complications on patient and graft survival was compared.

Results: Haemorrhage requiring active intervention (percutaneous drainage or surgical exploration) was reported in seven children (2.7%) and 29 adults (1.8%), while thrombotic or stenotic complications were recorded in two children (0.77%) and 19 adults (1.18%; $P < 0.05$). Female gender, delayed onset of diuresis and acute tubular necrosis were significant predictors of vascular complications on univariate analysis, but none remained significant on multivariate analysis. In adults, vascular complications had a significant negative effect on mean (SD) 10-year graft survival compared to patients with no complications, at 19.8 (7.63)% vs. 55.7 (1.66)%

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($P = 0.01$). Children who developed vascular complications had a significantly higher 5- and 10-year graft survival rate than adults ($P = 0.01$).

Conclusion: The incidence of vascular complications is comparable in paediatric and adult transplants. Vascular complications had a significant negative influence on graft survival in adult recipients. Children who developed vascular complications appear to tolerate its effects and have a better graft survival than have adults.

Introduction

Renal transplantation is the treatment of choice for patients with end-stage renal disease. It has been shown that vascular complications have compromised patient and graft survival [1–3]. To ensure better results, patients should be continuously monitored clinically, biochemically and radiologically for the early detection and management of any vascular complication.

Live-donor paediatric transplants are expected to be more liable to vascular complications because of the marked discrepancy between the size of the adult kidney (usually from one of the parents) and the small body mass index of the child. This discrepancy will induce major changes in the haemodynamics of the child that might precipitate the occurrence of adverse vascular events. Nevertheless, a reported comparison of vascular complications between adult and paediatric renal transplants with a long-term follow-up remains lacking. To the best of our knowledge, there is no single-centre study with a long-term follow-up addressing this issue.

Thus the aim of the present study was to compare haemorrhagic and vascular complications in paediatric and adult live-donor renal transplants in one tertiary centre and analyse their effect on graft and patient survival.

Patients and methods

After obtaining approval from the institutional review board and medical ethical committee, we retrospectively reviewed the charts of 1865 renal transplant recipients who were transplanted between March 1976 and December 2006. Recipients were stratified into adults (> 18 years) and children (≤18 years). Delayed onset of diuresis after completing the vascular anastomosis was reported if it occurred > 5 min after release of the vascular anastomosis. Acute tubular necrosis (ATN) was considered only when confirmed by a biopsy. Vascular complications were defined as haemorrhagic only if they required active intervention. Thrombotic and stenotic complications included renal vascular thrombosis and renal arterial stenosis (RAS) when confirmed symptomatically and radiologically.

Surgical technique

The kidneys were harvested by open flank incision. For paediatric transplants, we used a right pararectal incision with an extraperitoneal approach. In small children, the aorta and inferior vena cava were usually dissected up to the level of the inferior mesenteric artery. Ureteric anastomosis was established through uretero-vesical reimplantation in the vast majority of patients. Vascular and ureteric anastomoses are shown in Table 1. We followed our policy of heparinisation at 1 week after surgery in the vast majority of cases. Most patients were treated with cyclosporine-based immunosuppression, including methyl prednisolone and azathioprine, while mycophenolate mofetil, tacrolimus and sirolimus were used in a few patients in both groups (Table 1).

Diagnosis of complications and follow-up

When cases of renal artery thrombosis or stenosis were suspected clinically, Doppler ultrasonography (US), MR angiography and/or conventional angiography were used to confirm the diagnosis. Cases of haemorrhage were diagnosed by clinical observation and grey-scale US. The diagnosis was confirmed by CT or MRI, with or without aspiration of peri-graft collections.

After surgery, all patients had a life-long follow-up with a pre-set regimen [4]. The mean (SD, range) follow-up was 7.6 (5.4, 3–27) years. During the follow-up, transplant RAS (TRAS) was diagnosed clinically by observation of severe persistent hypertension, and radiologically by Doppler US and MR angiography and/or conventional angiography.

Data were stored in an electronic database. The Pearson and chi-square tests were used to determine the statistical significance of differences. Survival of grafts and patients was calculated using the Kaplan–Meier technique. Differences in survival were calculated by the log-rank test, with $P < 0.05$ taken to indicate significance. The incidence of haemorrhagic and vascular complications was correlated with several pre-transplant, technical and post-transplant risk factors by univariate analysis. Significant factors on univariate analysis were further investigated by multivariate analysis using the Cox proportional-hazards analysis.

Table 1 Characteristics of the patients in the two study groups.

Variables, n (%)	Adult (1606)	Children (259)
Pre-transplant		
Recipient age (year)		
⩽10	0	43 (16.6)
10–18	0	216 (83.4)
19–30	767 (47.8)	0
31–40	536 (33.3)	0
41–50	256 (16.0)	0
>50	47 (2.9)	0
Recipient sex		
Male	1223 (76.1)	166 (64.1)
Female	383 (23.9)	93 (35.9)
Donor age (years)		
<30	683 (42.5)	55 (21.3)
30–	482 (30.0)	114 (44.0)
40–	292 (18.2)	71 (27.4)
50–	148 (9.3)	19 (7.3)
Donor sex		
Male	811 (50.5)	89 (34.4)
Female	795 (49.5)	170 (65.6)
Human leukocyte antigen mismatch		
Zero match	121 (7.5)	4 (1.6)
One	273 (17)	27 (10.4)
Two	868 (54.1)	188 (72.6)
Three	200 (12.5)	34 (13.1)
Four	142 (8.9)	6 (2.3)
Transplant received		
First	1537 (95.7)	139 (53.7)
Second	67 (4.2)	120 (46.3)
Third	2 (0.1)	0
Technical		
No of renal arteries		
Single	1434 (89.3)	230 (88.8)
Multiple	172 (10.7)	29 (11.2)
Main renal artery to:		
Internal iliac	1472 (91.64)	165 (63.7)
External iliac	111 (6.9)	4 (1.5)
Common iliac	22 (1.4)	75 (29)
Aorta	1 (0.06)	15 (5.8)
Renal vein to:		
External Iliac	1576 (98.14)	141 (54.4)
Common iliac	20 (1.24)	8 (3.1)
IVC	10 (0. 62)	110 (42.5)
Primary urinary recontinuity		
Politano Leadbetter	156 (9.7)	19 (7.3)
Lich Grigoir	1426 (88.8)	228 (88)
Uretero-ureteric	19 (1.2)	10 (3.9)
Pelvi-ureteric	2 (0.12)	1 (0.4)
Ileal conduit	3 (0.18)	1 (0.4)
Ischaemia time (min)		
⩽30	198 (12.3)	25 (9.7)
31–60	1243 (77.4)	183 (70.6)
>60	165 (10.3)	51 (19.7)
Start of diuresis		
Immediate	1489 (92.7)	224 (86.5)
Delayed	117 (7.3)	35 (13.5)
Post-transplant		
ATN		
No	1527 (95.1)	243 (93.8)
Yes	79 (4.9)	16 (6.2)
Acute rejection		
No	898 (55.9)	139 (53.7)
Yes	708 (44.1)	120 (46.3)

Table 1 (continued)

Variables, n (%)	Adult (1606)	Children (259)
Immunosuppression		
Steroid + Aza	279 (17.4)	22 (8.5)
Steroid + CsA	143 (8.9)	30 (11.6)
Steroid + CsA + Aza	780 (48.6)	143 (55.2)
Steroid + sirolimus + (MMF or FK)	207 (12.9)	43 (16.6)
Others	197 (12.3)	21 (8.1)

IVC, inferior vena cava; Aza, azathioprine; CsA, cyclosporine A; MMF, mycophenolate mofetil; FK, tacrolimus.

Results

The adult and paediatric groups included 1606 and 259 recipients, respectively. Of the adult group, there were 1223 men and 383 women, with a mean (SD, range) of 32.4 (8.84, 19–62) years. There were 1537 first, 67 second and two third transplants. In all, 1554 recipients were treated with dialysis before transplantation, while the remaining 52 had a pre-emptive renal transplantation.

In the paediatric group, there were 166 boys and 93 girls with a mean (SD, range) age of 14.0 (3.48, 5–18) years. The mean body weight at transplantation was 34 (12, 15–72) kg, and 24 patients weighed ⩽20 kg, while the remaining 235 weighed > 20 kg. Four children had a re-transplantation. In all, 241 recipients were treated with dialysis before transplantation, while the remaining 18 had a pre-emptive renal transplantation. A summary of the demographic characteristics of recipients and donors of both groups is given in Table 1.

Haemorrhage occurred in 29 adult transplants (1.8%) and in seven children (2.7%), with no significant difference. Table 2 summarises the causes of haemorrhage in

Table 2 Haemorrhagic and thrombotic or stenotic vascular complications in adult and child renal transplants.

Complications, n (%)	Adults (1606)	Children (259)
Haemorrhagic	29 (1.8)	7 (2.7)
Initial management		
Percutaneous drainage	4 (0.3)	0
Surgical exploration	25 (1.5)	7 (2.7)
Source of haemorrhage (explored patients)		
Rupture graft	9 (0.5)	2 (0.77)
Site of vascular anastomosis	5 (0.31)	2 (0.77)
Slipped ligature over inferior epigastric artery	1 (0.06)	0
Tunnel of ureterovesical anastomosis	1 (0.06)	0
Graft biopsy	3 (0.18)	0
Nonspecific bleeding	6 (0.37)	3 (1.15)
Thrombotic or stenotic vascular	19 (1.18)	2 (0.77)
Types		
Renal artery thrombosis	13 (0.8)	1 (0.39)
Renal vein thrombosis	1 (0.06)	0
RAS	5 (0.32)	1 (0.39)
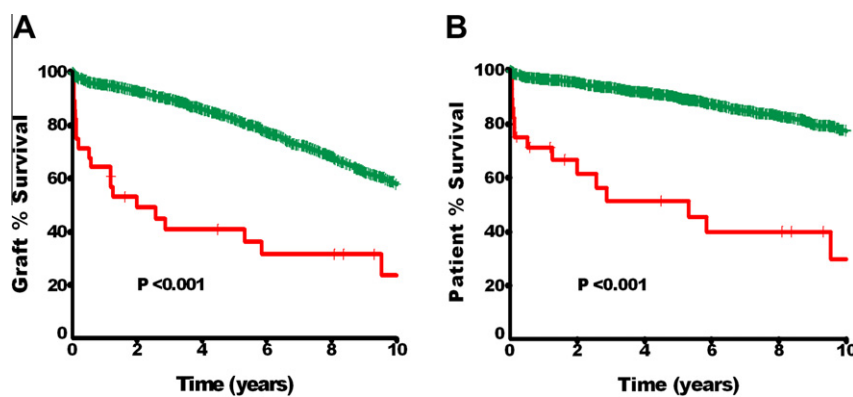
Figure 1 (A) 10-year graft survival and (B) 10-year patient survival of adults with and without vascular complications.

patients of both groups. In the adult group, haemorrhagic complications occurred at a mean (SD, range) postoperative interval of 12 (11, 1–60) days. Surgical exploration was carried out in 25 patients, while the remaining four were treated by percutaneous drainage of the haematoma. Rupture of the graft was the cause of bleeding in nine patients; in four of them the graft was salvaged after evacuating the haematoma and capsulotomy, while the damage was so severe in the remaining five kidneys that graft nephrectomy was required. The source of haemorrhage could be identified and secured in 10 patients, while no specific site of bleeding could be recognised in the remaining six. One patient died due to rupture of the arterial anastomotic site leading to irreversible haemorrhagic shock.

In the paediatric group, haemorrhagic complications were recorded at a mean (SD, range) postoperative interval of 13.5 (6.0, 6–19) days. All seven children with haemorrhagic complications were treated by surgical exploration. Rupture of the graft was the cause of bleeding in two patients in whom the injury was beyond repair, and required graft nephrectomy. In two other patients the site of bleeding could be identified and secured, while in the remaining three the cause of bleeding could not be specifically identified (Table 2). One child died because of irreversible haemorrhagic shock due to bleeding from the arterial anastomotic site.

Thrombotic or stenotic vascular complications were recorded in 19 adult recipients (1.18%) and in only two children (0.77%) (no significant difference). Table 2 summarises the types of thrombotic and stenotic vascular complications in patients of both groups.

In the adult group, renal artery thrombosis was diagnosed in 13 patients (0.8%) at a mean (SD, range) postoperative period of 2.9 (3.1, 1–10) days. Early exploration and thrombectomy saved six grafts, while graft nephrectomy was the result in the remaining seven patients. Renal vein thrombosis was diagnosed in one adult transplant 4 days after surgery and was treated by graft nephrectomy. Only one case of renal artery thrombosis occurred in the paediatric group and required graft nephrectomy.

RAS was diagnosed in five adult transplants at a mean (SD, range) duration of 46.8 (65.3, 6–156) months. Two grafts were lost at the time of diagnosis, while percutaneous transluminal angioplasty (PTA) was carried out in the remaining three patients; there was an improvement in two and re-stenosis occurred in one. Only one child had RAS, diagnosed 12 months after transplantation, and was successfully treated by PTA.

On testing various pre-transplant, technical and post-transplant risk factors (Table 1) the univariate analysis showed that female gender, delayed diuresis and ATN were predictors of the occurrence of haemorrhagic complications. Nevertheless, none remained significant on multivariable analysis.

Haemorrhagic and thrombotic or stenotic vascular complications had a significant negative effect on both patients and graft survival at 5 and 10 years in adults (Fig. 1).

Table 3 Long-term graft and patient survival in paediatric and adult renal transplants with and without vascular complications.

Mean (SD) variable	With vascular complications			No vascular complications		
	Adults	Children	P	Adults	Children	P
Graft survival, %						
5-year	36.72 (7.5)	37.5 (17.12)	0.43	80.07 (1.12)	77.71 (2.96)	0.82
10-year	19.78 (7.63)	37.5 (17.12)	0.08	55.68 (1.66)	48.18 (4.33)	0.74
Patient survival						
5-year	55.9 (9.32)	71.43 (17.07)	0.01	89.32 (0.86)	90.61 (2.13)	0.90
10-year	30.11 (11.03)	71.43 (17.07)	0.01	76.34 (1.49)	77.75 (4.81)	0.49
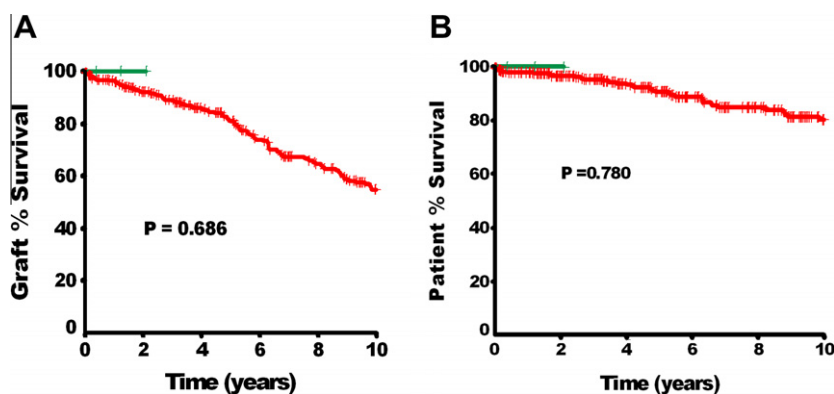
Figure 2 (A) 10-year graft survival and (B) 10-year patient survival of children with and without vascular complications.

In recipients with vascular complications, there was an insignificant trend towards a higher 10-year patient survival rate in children rather than adults ($P = 0.08$). However, paediatric recipients had a significantly higher 5-year ($P = 0.01$) and 10-year ($P = 0.01$) graft survival than had adults (Fig. 2; Table 3). In recipients with no vascular complication, the 5- and 10-year graft ($P = 0.82$ and 0.74) and patient survival ($P = 0.9$ and 0.49) were comparable in adults and children with no vascular and haemorrhagic complications (Table 3).

Discussion

Over the past three decades, the rate of complications after kidney transplantation has decreased due to improvements in surgical and diagnostic techniques, as well as to the greater safety of the immunosuppressive regimens. The incidence of vascular complications was reportedly as high as 30% during the early stages of development of the transplant procedure [5]. Currently the incidence rate is 0.8–6% [1–3].

Several mechanisms causing vascular thrombosis have been addressed. Causes include a faulty suture technique producing incomplete intimal re-approximation with secondary intraluminal fibrosis [6]. Furthermore, postoperative hypotension, hypercoagulable state, atherosclerosis of the donor or recipient vessels, trauma to the donor artery during perfusion, wide disparity in vessel size, torsion of the graft while making the anastomosis, kinking of artery and angulation of the vein due to improper location of the graft or to the anastomosis, were all reported [6].

In the present series, the overall incidence of renal artery thrombosis was 0.5%, it was 0.6% in adults, which is similar to that in our previous report [3], and 0.7% in the children. This might be explained by meticulous vascular anastomosis by well-trained highly specialised urologists, and our routine policy of heparinisation at 1 week after transplantation.

The issue of postoperative heparinisation in renal transplantation remains controversial. Heparin was found to decrease thromboembolic complications with no effect on lymph drainage or bleeding sequelae [7]. Two different groups of investigators showed that low molecular weight heparin can reduce or even abolish the thrombotic sequelae with no increase in the postoperative surgical bleeding [8,9]. Humar et al. [10] denied the need for anticoagulation for 'non-risky' renal transplants, and advised restricting a short course of heparinisation only for 'risky' patients.

In our institute, we conducted a prospective randomised study and concluded that postoperative heparin administration in 'non-risky' live-donor renal transplantation was associated with a significant decrease in haemoglobin level, as well as prolonged and excessive lymph drainage, with no improvement in graft outcome, and should not be a routine in such live-donor renal transplants [11].

TRAS is a potentially serious complication that ultimately leads to hypertension and/or graft dysfunction. Among 41,867 transplant patients in the USA, risk factors of TRAS were extended-criteria donors, older recipient and donor age, induction immunosuppression, delayed graft function, and ischaemic heart disease [12]. The incidence of TRAS varies, depending on the definition and diagnostic techniques used, from 1% to 23% [13], with a greater incidence in cadaveric transplantations (2–7.1%) than for live donors (0.3–2.2%) [14,15]. We reported a relatively low incidence of TRAS of 0.3% and 0.4% in our adult and paediatric transplant recipients, respectively. This might be attributed to the wide spatulation, interrupted sutures and delicate handling of both the graft and iliac vessels.

PTA is the initial treatment of choice, with an initial success rate of 60–90% [16]. Henning et al. [16] reported an immediate success rate for PTA of 92.3% that was maintained over the follow-up of 33.15 months. PTA with stent placement at a mean follow-up of 7.1 years showed long-term patency [17]. Open surgery is indicated only when PTA fails, or is inaccessible or shows severe stenosis, with a success rate of 63–92%, but with 12% recurrence of stenosis [18].

In the current study we found that vascular complications have a negative effect on patients and graft survival in adults; this is similar to other reports. In a single-centre study involving 1367 patients, graft loss was reported in 2.8% of cases that were affected by major vascular complications [19]. The mean time to these vascular complications was 1.8 months after transplantation. Fechner et al. [20] reported significant impairment of kidney function and graft survival in patients who were re-operated for vascular complications.

Vascular complications are more common in children and more severe. Losses of graft function as a result of vascular complications preceded up to 35% of deaths in children, especially in those aged < 6 years at transplantation [21]. In the present study, vascular complication had a negative effect on graft survival in children from a clinical perspective. Graft nephrectomy was carried out in two of seven cases with haemorrhagic complications. Moreover, one patient died because of irreversible haemorrhagic shock. However, with so few patients the study was not powered to show a significant difference on statistical assessment. Similarly, Irtan et al. [22] reported vascular complications in 27 of 193 children (13.9%), leading to graft loss in seven.

An interesting finding in the present study was that in recipients with vascular complications, there was a trend towards a higher 10-year patient survival rate in favour of children. Moreover, children had a significantly higher 5- ($P = 0.01$) and 10-year ($P = 0.01$) graft survival rate than adults. This might be attributed to better healing power and higher capacity of tissue regeneration in children than in adults. Thus it seems that child donor grafts are better able to increase their function with the growth of the child than are adult grafts [22–24]. This advantage might give children the privilege of a better reaction to vascular complications and subsequently higher survival than in adults.

This study has drawbacks that are inherent to its retrospective design. In addition, the comparison between groups of different ages might affect the results because of the heterogeneity of both groups and the difference in pathophysiological responses and vascular volume effects after haemorrhagic complications.

In conclusion, there is no greater incidence of vascular complications in children than in adult transplants. The vascular complications have significant adverse effects on patient and graft survival in adult renal transplants. Paediatric transplant recipients showed better graft survival than adult transplant recipients, highlighting their ability to tolerate the negative effect of vascular complications.

Conflict of interest

The authors have no conflict of interest to declare.

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