



Outcome of Live Related Kidney Transplants with Multiple Renal Arteries

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Abstract

Introduction: The use of grafts with multiple renal arteries has been considered a relative contraindication because of the increased incidence of vascular and urological complications. The aim of the study is to determine whether the kidney grafts with multiple arteries have an adverse effect on the post transplant graft function and survival.

Methods: A total of 107 kidney transplants done in our centre till december 2015 were reviewed. These were divided in two groups; group A- kidney grafts with single renal artery. Group B- kidney grafts with multiple renal arteries. Eighty nine grafts had single renal artery and eighteen had grafts with multiple renal arteries and hence required multiple vascular anastomoses. Anastomoses time, average blood loss, warm ischemia time(WIT), cold ischemia time(CIT), serum creatinine at 3,6 and 12 months, delayed graft function(DGF), renal artery stenosis (RAS), urological complications, graft survival at one year were studied in each group.

Results: No significant differences were seen in the two groups regarding serum creatinine (p value of 0.224, 0.248, 0.458 at 3, 6 and 12 months respectively), DGF (7:2, p value 0.645), RAS (2:1, p value of 0.428), urological complications (10:3, p value of 0.645). Significant differences are seen in anastomoses time (29.83: 44.72 mins, p value <0.001), WIT (17.1 : 18.4 sec, p value of <0.001), CIT (50.9: 77.5 min, p value <0.001), blood loss (157:219 ml, p value of <0.001) and lymphocele formation (4:4, p value of 0.026). However this did not seem to have any effect in the graft survival at one year. The difference in graft survival between the two groups was insignificant (8:2, p value of 0.674)

Conclusions: kidney transplantation using grafts with multiple renal arteries may be associated with higher rates of lymphocele formation along with increased blood loss, CIT, WIT and anastomoses time. However it is equally safe as using grafts with single renal artery regarding vascular, urological complications as well as the graft survival.

Introduction

Chronic kidney disease is a major global problem and growing at the rate of more than 5 percent worldwide^[1]. The prevalence of CKD has been estimated at between 10-15% in industrialized countries and is increasing, possibly as a result of ageing population and the increasing incidence of diabetes, vascular disease and obesity. The approximate prevalence of CKD is 800 per million populations (pmp), and the incidence of end-stage renal disease (ESRD) is 150-200 pmp^[2].

The treatment of choice for stage IV CKD is kidney transplantation. Significant improvement both in patient and graft survival has happened in recent decades due to improvement in both surgical techniques and introduction of more potent immunosuppressive regimens.

According to several autopsy series, the incidence of multiple renal arteries ranges between 18 to 30%^[3]. Multiple renal arteries are unilaterally found in 25% of the population and bilaterally in 10%, and may represent a challenge to the surgeon^[4,5]. Novick et al.^[6] reported that the incidence of unilateral MRAs was 23% and that of bilateral MRAs was 10%.

Vascular complications in renal grafts with a single artery, including thrombosis and arterial stenosis, range from 1 to 16%^[7,8]. Urologic complications occur in 2% to 10% of transplanted patients^[9,10]. The incidence of urological complications ranges from 3% to 34%^[10,11]. Lymphocele occurs in 1% to 12% of all kidney transplants^[12]. Transplantation of kidneys from living donors with multiple renal arteries has been discouraged in past due to higher rates of vascular or urologic complications, and decrease graft function^[13]. Incidence of vascular complications like arterial thrombosis and renal artery stenosis are reported more frequently when kidneys with multiple renal arteries are implanted^[14]. In particular, thrombosis and stenosis of polar arteries can cause infarction, infection, and urologic complications, such as calyceal or ureteral fistulas and ureteral necrosis, increasing morbidity and graft loss^[3].

Successful allografts with multiple renal arteries (MRAs) have been made possible by improved techniques. Results of renal artery reconstruction improved with the introduction of extracorporeal microsurgical repair of arterial injuries. Bench reconstruction of multiple arteries has become common place in the major transplant centers around the world^[3]. These technical refinements have significantly expanded the pool of cadaveric, living related and living unrelated donors. The smaller artery usually is anastomosed in an end to-side fashion to the main artery. If both renal arteries are of similar size, the ends of the two vessels can be sutured together side to side. With polar arteries, approach has been to aggressively revascularize arterial vessels directed to the lower pole of the kidney, regardless of the size because these vessels potentially supply the ureter.

Recent studies have demonstrated that laparoscopic donor nephrectomy of kidneys with multiple renal vessels is safe and effective, providing kidney donor and allograft outcomes comparable to those of open surgery^[15, 16].

In this study we analysed complications and outcome of recipients of living donor kidney transplantation using allografts with multiple renal arteries in comparison to single renal artery.

Material & Methods

A total of 107 patients who underwent renal transplants at our centre upto December 2015 were included in the study. Eighty nine (83.2%) donor kidneys had single renal artery (SRA) and eighteen (16.8%) had multiple renal arteries (MRA). During pre operative donor evaluation, medical and surgical suitability for live donation were assessed. The arterial anatomy was delineated by selective renal angiography and/or CT Angiogram in all cases. All donor recipient pairs were T cell cross matched and ABO blood type compatible.

An informed consent was taken from each patient before he/she was made a part of the study. All patients were divided into two groups, group A and group B. Group A included recipients with

single renal artery allografts anastomosed to the external iliac artery. Group B included two sets of patients

- i. Recipients with multiple renal artery allografts with a single anastomoses. (multiple renal arteries are converted to single artery by ex-vivo bench reconstruction surgery)
- ii. Recipients with multiple renal artery allografts, implanted with multiple arterial anastomosis.

The harvesting and transplant procedures were done according to conventional technique in the twin urology operation theatres simultaneously by two surgical teams working together in a co-ordinated manner. Allograft was harvested and perfused using a renal perfusate. Various perfusates were used from time to time like the ringer lactate, Renograf solution and now the HTK solution is used as a perfusate in most of the cases. The kidney is perfused for almost 8 minutes. Ex-vivo bench surgery was performed where ever required. Post surgery patients were shifted to transplant ICU and put on immunosuppressive therapies based on the transplant recipient's immunological risk and donor factors. All patients received triple drug immunosuppression consisting of steroids, CNI (cyclosporine or tacrolimus) and antimetabolite (MMF or azathioprine). Some selected patients (immunological high risk) in addition received induction with either ATG or IL-2 receptor

blocker (basiliximab). Doppler ultrasound was performed on 5th pod and repeated at the time of discharge from hospital. data was collected and analysed for various variables

All recipients were instructed to follow up in the outpatient clinic on regular basis. The frequency of visits depended upon the duration of the post operative period and clinical course of the patient. All suspected acute and chronic kidney rejection episodes were confirmed with a transplant biopsy, performed under ultrasound guidance. The ultrasound is important prior to the biopsy to rule out obstruction or any alternate reason for the elevated creatinine. Biopsies were usually performed by the nephrologist.

Results and Discussion

A total of 107 patients who underwent renal transplants at our centre were included in the study. In all cases an open donor nephrectomy was performed. All these patients were made part of our study.

Eighty nine (83.2%) donor kidneys had single renal artery (SRA) and eighteen (16.8%) had multiple renal arteries (MRA).

Majority of the recipients belonged to the age group of 31-40 yrs both in males as well as females. The second most common age group in both, included 21-30 and 41-50 with nearly equal frequency. The youngest recipient being a 13 years old boy who received a kidney from his mother and the oldest being a 60 yrs old male who received a kidney from his wife.

Age & Gender distribution						
Age group	Male		Female		Total	
	N	%	N	%	N	%
≤ 20	3	3.5 %	1	4.5%	4	3.73%
21-30	21	24.7%	7	31.8%	28	26.16%
31-40	35	41.1%	9	40.9%	44	41.12%
41-50	20	23.5%	5	22.7%	25	23.36%
51-60	4	4.7%	0	-	4	3.73%
61-70	2	2.3%	0	-	2	1.86%
Total	85		22		107	

In patients with MRA, there is an increased risk of injury from more extensive dissection^[17]. There is

a requirement for complicated vascular reconstruction and more difficult anastomosis at

the time of implantation. This is very well the reason for increased average bleeding at the time of surgery in the MRA group. In our series the average blood loss in the MRA group was 219.44 ± 21.27 ml which was significantly higher than in the SRA group with average blood loss of 157.08 ± 17.20 (p value of <0.001). Paramesh et al. ^[17] reported almost similar amounts of average blood loss in both groups but there study was based on

LDN while as our study takes into account the open donor nephrectomy. They reported an average blood loss of 98 ± 104 ml in donors of SRA and 90 ± 68 ml in donors of MRA which was statistically insignificant. The reason for increased blood loss in our series is mainly because we have calculated the blood loss of both the donors as well as the recipients. Also all our donor nephrectomy were performed by open method.

Variable		single vessel \pm Mean S.D	Multiple vessel \pm Mean S.D	Mean difference	P. value
Blood loss (ml)		157.08 +/- 17.20	219.44 +/- 21.275	62.366	<0.001
Anastomosis time (min)		29.83 +/- 1.59	44.72 +/- 4.68	14.891	<0.001
Serum creatinine (mg/dl)	3 Month	1.0733 +/-0.36978	1.1944 +/-0.44520	0.12119	0.224
	6 months	1.2963 +/- 0.32189	1.3938 +/-0.20807	0.09745	0.248
	12 months	1.5580 +/-0.22297	1.6062 +/-0.29993	0.04823	0.458
WIT (sec)		17.10 \pm 1.477	18.44 \pm 1.199	1.343	<0.001
CIT (min)		50.93 \pm 2.632	77.50 \pm 4.287	26.567	<0.001

Prolonged warm and cold ischemia times have been shown to be associated with worst allograft outcomes ^[18,19]. Our study involved 18 patients with multiple renal arteries. While mean warm ischemia time in SRA group was 17.10 ± 1.47 sec it was 18.44 ± 1.19 sec in MRA group. Cold ischemia time was significantly higher in the MRA group (50.93 ± 2.632 mins in SRA and 77.50 ± 4.287 in MRA) with a p value= <0.001 . Similarly anastomosis time was significantly higher in the MRA group (29.83 ± 1.59 mints in SRA and 44.72 ± 4.68 mints in MRA) with a p value of <0.001 . R saidi et al. studied 350 patients who underwent living donor kidney transplantation from January 2000 to March 2007. 319 allografts (91.1%) had a single artery (group 1) and 31 (8.9%) had multiple arteries (group 2). The operative time was shorter in group 1 compared with group 2 (mean [SD], 173 ^[35] vs. 259 ^[48] minutes; $P < .001$). Ashraf et.al^[20] reported

similar findings in their study. They studied 105 patients in total with 33 MRA and 72 SRA group. They concluded that the two groups had almost similar WIT but an increased CIT in MRA group. Meyer, et al.^[21] studied 130 patients with 108 SRA donors and 22 MRA donors. They reported higher WIT and CIT in MRA group. However this prolonged CIT and anastomosis time did not seem to negatively influence the graft function in their series which is quiet consistent with other studies.

As a measure of functioning of the graft kidney in the recipient we measured the serum creatinine values in each group at 3 month, 6 month and 12 month intervals respectively. Average S.creatinine values in SRA group at 3 month were 1.07 ± 0.369 mg/dl and in the MRA group was 1.194 ± 0.445 mg/dl at 6 months the values were 1.29 ± 0.321 and 1.39 ± 0.208 mg/dl respectively. Similarly at 12 months the values were 1.55 ± 0.222 and 1.60

± 0.299 mg/dl in SRA and MRA group respectively. No significant difference was seen between the two groups at any of the 3 month, 6 month or the 12 month interval. The p values for each interval stood at 0.224, 0.248 and 0.458 respectively. E benediiti, et al.^[22] as a measure of graft function, compared mean creatinine values among the three groups, i.e., the values at 1, 3, and 5 years post-transplant; they did not differ significantly ($p = 0.45$). Bedeir, et al.^[23] included 1,087 with single (group 1) and 113 with multiple (group 2) arteries. Mean serum creatinine \pm SD at 1 year was 1.4 ± 0.5 and 1.5 ± 0.6 mg/dl, and at 5 years it was 1.8 ± 1 and 2.1 ± 1.4 mg/dl for the 2 groups respectively. No significant difference was seen between the two groups. Gawish, et al.^[24] retrospectively studied about 35 grafts with MRA. The mean serum creatinine levels were 122, 139 and 156 $\mu\text{mol/L}$ at 1 month, 1 year and 5 years, respectively. In the SRA group, the mean serum creatinine levels were 115, 121, and 141 $\mu\text{mol/L}$ at 1 month, 1 year, and 5 years, respectively. Again no significant difference was seen in the serum creatinine values between the two groups at any time.

In most studies DGF is defined as the need of dialysis treatment in the first week after renal transplantation. This is a criterion that is easy to register and to obtain from large databases^[25]. The effect of DGF on short and long term patient and graft survival is unclear. Some authors reported an effect of DGF on graft survival^[26] while others did not or only found this effect when it coincided with the occurrence of acute rejection episodes^[27]. In our SRA group of 89 patients about 7 (7.9%) developed delayed graft function. Among 18 of the MRA group 2 (11.1%) developed DGF. The difference between the two groups was insignificant with a p value of 0.645. E Benedetti, et al.^[22] also in 1995, in their series of patients didn't find any significant difference between the two groups for DGF. Basaran. O, et al.^[28] studied 1095 patients who underwent renal transplantation at their center, between November 1975 and March 2003. Seventy-nine (7.2%) cases required multiple-artery anastomoses (group I) and 1016 (92.8%) a single-artery anastomosis (group II). There was no significant differences between the groups with respect to rate of post transplantation hypertension ($P = 0.67$), acute tubular necrosis ($P = 0.55$), or number of acute rejection episodes ($P = 0.34$).

Variable		Single vessel	Multiple vessel	P value
DGF	Normal	82 (92.1%)	16 (88.9%)	0.645
	Delayed	7 (7.9%)	2 (11.1%)	
Lymphocele	No	85 (95.5%)	14 (77.8%)	0.026
	Yes	4 (4.5%)	4 (22.2%)	
Renal artery stenosis	Absent	87 (97.8%)	17 (94.4%)	0.428
	Present	2 (2.2%)	1 (5.6%)	
Urological complications	Absent	79 (88.8%)	15 (83.4%)	0.645
	Present	10 (11.2%)	3 (16.6%)	
Graft survival	Yes	81 (91%)	16 (88.9%)	0.674
	No	8 (9%)	2 (11.1%)	

Lymphocele is a lymphatic collection around a transplanted kidney. Diagnosis is made when there is a pelvic collection with similar properties to the plasma. This is confirmed with biochemical analysis of the fluid that shows similar electrolyte content compared with the plasma with low protein level. The incidence of clinically significant lymphocele is about 20%, but it may develop in 12% to 40% of transplant recipients^[29, 30]. E. mazzucchi, et al.^[31] studied the data of 64 renal transplants with multiple arteries performed between January 1995 and December 1999 and compared to 292 transplants with single renal artery. The incidence of lymphoceles was 3.1% in grafts with a single artery and 12.5% in grafts with more than 1 artery which was significantly higher ($p = 0.0015$). R. Saidi, et al.^[32] included 350 patients who underwent living donor kidney transplantation from January 2000 to March 2007. 319 allografts (91.1%) had a single artery (group 1) and 31 (8.9%) had multiple arteries (group 2), including 2 arteries in 21 grafts (67.8%), 3 arteries in 6 (19.3%) and 4 arteries in 4 grafts (12.9%). The incidence of symptomatic lymphocele in the two groups was 2.8% vs. 3.2% (SRA VS MRA) respectively. In our series among the 89 SRA transplants only 4(4.5%) developed a clinically significant lymphocele. In the MRA group 4 patients (22.2%) developed lymphocele. This was significantly higher with a p value of 0.026. The higher rates of lymphocele are explained due to more extensive and complicated tissue dissection in these cases^[33].

Transplant renal artery stenosis (TRAS) is an increasingly recognized, potentially reversible complication of kidney transplantation. It has become an important curable cause of hypertension, graft dysfunction and graft loss in kidney recipients. The incidence varies from 1% to 23%^[34]. The usual presentation is worsening or new onset hypertension and /or graft dysfunction in the absence of rejection, drug toxicity, ureteric obstruction and infection. Several etiologic mechanisms have been proposed for TRAS, acute rejection, suture technique, atherosclerotic arterial

disease in the donor or recipient, arterial trauma during organ procurement or transplant, cytomegalovirus (CMV)^[35,36], deceased donor transplants, prolonged cold ischemia and arterial kinking because of a longer renal artery^[37]. Roza et al. analyzed 42 living donor open nephrectomies with multiple arteries and observed 8 patients (19%) with urological complications and 3 (7%) with vascular complications^[13]. Carter et al. also showed a higher rate of ureteral complications in patients with multiple arteries (17% vs. 3%) when analyzing 361 LDN. The authors concluded that this higher rate could be a result of insufficient perfusion in the kidney's lower pole, probably related to excessive traction or cautery lesion during dissection^[38]. However, other papers analyzing LDN did not show a higher incidence of vascular and ureteral complications when harvesting kidneys with multiple arteries^[39,40]. In our study, the rate of vascular and ureteral complications was almost similar in both groups. At our institution, the ureteral dissection is performed carefully to maintain an adequate vascular supply to the lower pole and distal ureter. The back-table reconstruction and vascular anastomosis are meticulously performed to ensure an adequate lumen in the anastomosis in order to prevent thrombosis or minimize technical errors. Among the 89 SRA patients only two developed RAS. This was about 2.2% of the whole group. Similarly only one (5.6%) among 18 MRA group developed RAS. the difference was statistically insignificant with a p value of 0.428. One patient in SRA group developed anastomotic site leak and had to be explored on 3rd pod. Graft kidney was lost to ischemic injury and graft kidney nephrectomy had to be done. Another patient in the MRA group developed the same problem. Patient was reexplored on 2nd pod and augmentation of anastomosis was done and the graft continues to function normally till date. E. Beneditti, et al.^[22] studied 835 SRA patients and 163 MRA patients. Their percentage of vascular complications 4.6% (2.2% early and 2.4% late) compares very favorable with our

results. Another study by E. Mazzucchi, et al.^[31] concluded no significant difference between SRA and MRA group in terms of vascular complications and graft outcome

Renal artery thrombosis was seen in one patient of SRA group. The patient had atherosclerotic iliac vessels which were detected at the time of making anastomosis, renal artery thrombosis was diagnosed clinically by sudden onset of oliguria or anuria and confirmed by color Doppler flow studies. Transplant nephrectomy was performed within 1 day after establishing the diagnosis. Similarly one among the MRA developed renal artery thrombosis leading to graft loss. E Benedetti et al.^[22] reported renal artery thrombosis in 4 patients (0.4%). This complication occurred exclusively in SRA group in 1 of the 132 (0.7%) grafts with end-to-end anastomoses to the internal and in 3 of 703 (0.4%) grafts with end-to-side anastomoses to the external iliac artery ($p = 0.9864$). Among the SRA group 10 developed various urological complications. This is about 11.23% of the total group. Three (3) recipients in the MRA group developed urological complications. It is about 16.66% of the total group. The difference is insignificant with a p value of 0.645. Most common urological problem in both groups proved to be UTI (5 among SRA and 2 among MRA). Ureteric stenosis at the ureteric anastomotic site was seen in 2 recipients of SRA and 1 recipient of MRA group. ureteric anastomotic site leak was seen in 2 recipients in the SRA group and none among the MRA group. Both patients required re exploration for repair. One patient in the SRA developed clot retention. R. saidi, et al.^[32] in their study involving 319 SRA and 31 MRA observed the rate of urological complications at 1.6% vs. 3.2% respectively. Hwang, et al.^[41] found no significant difference in the urological complications of the two groups (p value of 0.371). Ashraf, et al.^[20] recently studied 105 kidney transplants over a period of 4 years. The data of 33 renal transplants with multiple arteries were compared with 72 transplants with single artery. They concluded

almost similar results, with no major difference in urological complications of two groups.

Urological complication	SRA	MRA
UTI	5	2
Ureteric stenosis	2	1
Ureteric anastomotic leak	2	0
Clot retention	1	0
Total	10	3

Graft survival was studied at 1 year for each of the two groups. In the SRA group 8 grafts were lost out of the 89 SRA transplants. This is about 9% of the total group. Similarly two grafts were lost out of the 18 in the MRA group. This was about 11.1% of the total group. Here again the difference between the two groups was statistically insignificant with a p value of 0.674. In the SRA group 4 grafts were lost to acute rejection and had to be reverted back to dialysis. Two grafts were lost to hyperacute rejection. One among them was being operated for a 2nd transplant (the first transplant was lost to acute rejection). Another patient who developed hyperacute rejection had received kidney from an unrelated donor (brother in law). One graft was lost to vascular anastomotic leak and the patient had to undergo re exploration for donor kidney nephrectomy. Another kidney was lost to renal artery thrombosis. The patient was a chronic hypertensive and had atherosclerotic iliac vessels which were detected on table, which might have been the reason for this complication. Similarly among the MRA artery group one graft was lost to acute rejection that was confirmed by kidney biopsy. The other graft was lost to renal artery thrombosis. One yr graft survival in our series is 91% and 88.9% in SRA and MRA groups respectively.

E beneditti et al.^[22] reported graft survival rates at 1 and 5 years post-transplant at 88.3% and 71.7% in Group A, 94.4% and 72.8% in Group B, and 82.8% and 77.4% in Group C ($p = 0.9013$) respectively. Gawish, et al.^[24] reported graft

survival rates at 94.3%, 88.6%, and 83% at 1, 5, and 10 years, respectively. In the SRA group, the actuarial graft survival rates were 93.7%, 88.1%, and 84.4% at 1, 5, and 10 years. R saidi et al.^[32] reported that the actuarial 1- and 5-year allograft survival rates were comparable in both groups (98.4% and 91.5% in group 1 and 96.8% and 87.1% in group 2). Gazanfer, et al.^[42] who studied 205 transplants with multiple renal arteries reported that the Graft and patient survival at 1 year were 93% and 97% respectively.

Conclusions

Kidney transplantation using MRA grafts was associated with higher rates of (MRA VS SRA): Blood loss(219.44 vs. 157.08 ml, p value<0.001), Anastomosis time(44.72 vs. 29.83 min, p value<0.001), WIT(18.44 vs. 17.10 sec, p value<0.001, CIT(77.50 vs. 50.93 min, p value<0.001), Lymphocele formation(22.2% vs. 4.5%, p value= 0.026).

Reasons may very well be:

- More extensive dissection in MRA group.
- Technically more difficult procedure.
- Multiple Anastomosis.

Kidney transplants with multiple renal arteries were found to be equally safe in terms of: Delayed graft function(11.1% vs. 7.9%, p value= 0.645), S. Creatinine at 3, 6, and 12 months(p values of 0.224, 0.248, 0.458 respectively), Renal artery stenosis(5.6% vs. 2.2%, p value= 0.428), Urological complications(16.6% vs. 11.2%, p value= 0.645), Graft survival(88.9% vs. 91%, p value= 0.674)

In conclusion

- Multiple renal arteries are not a contraindication for renal transplants and can be used as effectively as single renal artery grafts.
- Kidney grafts with multiple arteries have no adverse effect on the post transplant graft function and survival.

However our study has few limitations that deserve to be mentioned. First, this study is a

single centre retrospective as well as a prospective study with a relatively smaller number of patients, especially in the MA group. Secondly our study lacks information on long term results and the renal function analysis was based only on early graft function. Although this is suboptimal, previous reports have shown that poor early function results are associated with worst long-term outcomes.

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