Medicon Medical Sciences
Volume 5 Issue 5 November 2023
Article Type: Research Article
ISSN: 2972-2721

Impact of Anastomosis Time on Early Renal Graft Function: Slow Can Be Better

Qaisar Iqbal[1], Taqi F Toufeeq Khan[1]*, Muneeb Hassan[1], Irfan Mirza[2], Tahir Rashid[2] and Nisar Anwar[2]

[1]*Kidney Transplant Unit, department of transplant surgery, Rehman Medical Institute Peshawar*

[2]*Kidney Transplant Unit, Department of nephrology, Rehman Medical Institute Peshawar*

***Corresponding Author:** Taqi F Toufeeq Khan, Head of department. Kidney transplant unit, Rehman Medical Institute Peshawar, Pakistan.

Received: September 25, 2023; **Published:** October 28, 2023

Abstract

Introduction: Prolonged recipient warm ischemia can cause delayed graft function (DGF), resulting in poor graft outcomes. Short Anastomosis times (AT) are considered beneficial for prompt early graft function (EGF).

Objective: We examined the impact of prolonged AT on EGF.

Materials and Methods: A retrospective cohort study of 120 living donor renal transplants (LDRT) performed between January 2019 and March 2022 at the Renal Transplant Unit of Rehman Medical Institute, Peshawar. The study population was divided into two groups based on AT; GI with AT less than 40 minutes, GII with AT more than 40 minutes. Cold saline irrigation was used to maintain low graft temperature during implantation.

Results: Four patients had poor EGF (3.33%), two DGF (1.67%) and two SGF (1.67%). Mean AT in GI was 37.23±1.93 vs mean AT in GII 47.07±6.90 (p value .00001). Time taken for 50% reduction in serum creatinine (SC) (SC50), SC at discharge, and last SC in both groups were comparable. No significant difference was found in incidence of poor EGF in the 2 groups (OR 0.19, 95% CI, P=0.355).

Conclusion: In the presence of low graft temperatures, prolonged AT did not adversely affect EGF.

Keywords: recipient warm ischemia; anastomosis time; early graft function

Introduction

Renal transplantation is the best treatment modality for patients with chronic renal failure and offers an enhanced and cost effective quality of life and life expectancy [1]. Although high rates of early graft function (EGF) have been achieved in living donor kidney transplantation, acute kidney injury remains a problem. Ischemia reperfusion injury is the principal mechanism of graft injury, which causes delayed graft function (DGF) that is an independent risk factor for poor graft and patient survival [2, 3]. Cold and warm ischemia are the primary causes of DGF in renal transplant patients, and prolonged cold ischemia is more relevant in deceased donor transplants [4]. There are 2 types of warm ischemia (WI), and it is now established that both donor and recipient warm ischemia (RWI) contribute to DGF and poor graft outcomes [5]. Prolonged RWI is an independent risk factor for DGF, the rise in graft temperature during implantation increases metabolic activity, causing warm ischemic injury [6]. Traditionally, transplant teams strive to keep RWI to a minimum, and cooling the graft during implantation can slow this rise in graft temperature, removing the pressure of the clock to enable an unrushed anastomoses. We examined the impact of anastomosis time (AT) on EGF.

Material and Methods

After approval from our institutional review board, we conducted a retrospective cohort study of all living donor renal transplants (LDRT) performed between January 2019 and March 2022 at the Renal Transplant Unit of Rehman Medical Institute, Peshawar. The study population was divided into two groups based on AT; GI with AT less than 40 minutes, GII with AT more than 40 minutes. All living donors and recipients underwent a rigorous medical, ethical and psychological evaluation based on our protocols. The side of donor nephrectomy was decided based on renal vascular anatomy and differential renal function. Renal vascular anatomy was visualized by computerized tomographic angiography and no donors were rejected because of arterial anatomy. Recipient WI (RWI) is calculated from the time the graft is removed from cold storage to the time of re-perfusion after removal of clamps.

Surgical procedure

The surgical unit comprised of a single surgeon performing all recipient procedures and general surgeon performing the donor surgery. The donor and recipient operations were carried out concurrently in adjoining operating rooms. Histidine-tryptophan-ketogluterate (HTK) solution was used in all back-table graft flushing and storage. Vascular anastomoses were carried out end to side to the external iliac vessels with a running 6/0 polypropylene suture. In cases with two arteries, a single lumen was created where feasible, or implanted separately. In cases with 3 arteries also, a single lumen was created when possible and the third artery was either implanted separately or connected to the inferior epigastric artery. If a polar artery was deemed too small, it was ligated. The ureterovesical anastomosis was an extravesical neoureterocystostomy over a 4Fr JJ stent using a running 6/0 PDS suture. Doppler imaging of the graft was performed within the first 2 days of transplant or as indicated.

Immunosuppression

All recipients received induction with anti thymocyte globulin (ATG, Sanofi), and ATG (Fresenius) since September 2021. The dosage depended on HLA mismatches, a maximum of 6mg/kg in divided doses, and 2mg/kg for zero mismatches. Additionally, methyl prednisolone 500mg was given intra-operatively and 250mg administered daily for another 3 days. Maintenance triple immunosuppression was tacrolimus, mycophenolate and prednisolone, oral steroid were not given in cases with zero mismatches, diabetes mellitus, and recipients with cardiac and bone disease. Universal CMV prophylaxis with Valgancyclovir was prescribed for a minimum of 3 months and 6 months for high risk recipients.

Follow up protocol

All transplant recipients were followed up by the surgery and nephrology teams. Doppler imaging of all grafts was done when clinically required. All recipients were followed up with monthly labs including tacrolimus levels.

Definitions

Delayed graft function was the need for dialysis within the first week after transplant. Slow graft function (SGF) was serum creatinine (SC) more than 3mg/dl after 5 days, without dialysis. Immediate Graft Function (IGF) was production of urine with a decrease in SC. Donor WI was the time from clamping of renal artery to immersion of graft in cold preservation solution. Cold ischemia was time from immersion of graft in cold preservation solution to its removal from storage. Anastomosis time was time from start of vascular anastomosis to reperfusion of the graft.

Data collection and statistical analysis

Kidney transplant data was retrieved from hospital database after approval by hospital ethical committee. We used IBM SPSS statistics 20 for data analysis.

Results

There were 120 patients in this cohort, mean age (years) was 36.05±10.40 range (9-57) for GI and 37.61±10.87 range (13-55) for GII, recipient male to female ratio was 7.6:1. Donor mean age was 32.67±10.31 range (19-58) for GI and 33.98±10.58 range (18-62) for GII, donor male to female ratio was 1.14:1. One recipient had a prior transplant, 0.83% (n=1). Multiple donor arteries were present in 15% (n=18). Four patients had poor EGF (3.33%), two DGF (1.67%) and two SGF (1.67%). Five recipients (4.17%) received a steroid sparing immune suppression regime. Detailed demographics are given in table 1. Mean AT in GI was 37.23±1.93 vs mean AT in GII 47.07±6.90(p value .00001). Time taken for 50% reduction in SC (SC50), SC at discharge, and last SC in both groups were comparable. A statistically insignificant number had poor EGF in GII (OR 0.19, 95% CI, P=0.355).

Number of patients in each group		***GI***	***GII***	***Significance of difference between means & percentages***
		Up to 40(%)	***>40(%)***	
Recipient age (years)		36.05±10.40 range(9-57)	37.61±10.87 range(13-55)	
Recipient age (years)	5-20	4(10.3)	4(4.9)	0.589
	21-35	16(41.0%)	32(39.5)	
	36-50	16(41.0)	34(42)	
	51-65	3(7.7)	11(13.6)	
Recipient gender	Male	35(89.7)	71(87.7)	0.738
	Female	4(10.3)	10(12.3)	
HLA Typing	Zero Mismatches	4(10)	4(5)	0.413
	Zero Matches	2(5)	5(6.2)	
	Up to 5 mismatches	13(32.5)	37(46.2)	
	5-10 mismatches	21(52.5)	34(42.5)	
Donor arteries	Single	37(92.5)	65(81.2)	0.104
	Multiple	3(7.5)	15(18.8)	
Panel reactive antibody	Positive	7(17.5)	14(17.5)	1.000
	Negative	33(82.5)	66(82.5)	
Donor Specific Antibodies	Positive	0(0)	2(2.5)	0.313
	Negative	40(100)	78(97.5)	
Donor Type	LRD	25(62.5)	52(65)	0.788
	LURD	15(37.5)	28(35)	
Donor Age (years)		32.67±10.31 range(19-58)	33.98±10.58 range(18-62)	
Donor Gender	Male	20(20)	44(55)	0.605
	Female	20(50)	36(45)	
Donor Kidney Side	Right	9(22.5)	32(40)	0.057
	Left	31(77.5)	48(60)	
Graft Function	DGF	0(0)	2(2.5)	0.335
	SGF	0(0)	2(2.5)	

Table 1: Baseline characteristics of two groups.

Discussion

Recipient warm ischemia is from the time the graft is removed from cold storage to re-perfusion, while AT is time from start of venous anastomosis to re-perfusion, and is the subject of this study. Donor warm ischemia in open donor nephrectomy is generally minimal, unless complicated by arterial injury, as in one each of our DGF and SGF cases. One of the SGF occurred in recipient whose 50 % artery supplying the kidney was damaged during kidney recovery and resulted in prolonged donor warm ischemia, the artery was repaired during bench surgery with interrupted 7/0 Prolene sutures. DGF in another patient also occurred because of prolonged warm ischemia time in the donor.

One of our recipients who's AT was 72 minutes had two arteries, the smaller artery was recovered very short, making anastomosis difficult, prolonging AT, but had immediate function with normal SC on 4th post-operative day, and at last follow-up. There is consensus within the transplant fraternity that AT must be minimized, but without agreement on its safe upper limit [7, 8] Group II with 81 patients had AT>40 minutes, and expected to have poorer EGF, but this was not statistically significant different between the two groups in all SC parameters. The previously reported safe upper limit of AT in a study by one of the current authors was 60 minutes and we found similar results in this study [9]. Cooling the graft throughout implantation by continuous cold irrigation is, we feel why prolonged AT was better tolerated, as lower temperatures reduce metabolism and negate the deleterious effects of the extra AT and explain the good EGF despite longer ATs.

	IT (mintutes)	***IT (mintutes)***
	Upto 40 mins	***>40 mins***
No. of cases	39	81
DGF	0	2(2.5%)
SGF	0	2(2.5%)
Graft dysfunction (SGF+DGF)	0	4(5%)
Odd ratio for graft dysfunction	0.19 95% confidence interval (Cl)	Significance P=0.355*

*Fisher exact test.

Table 2: Association between IT duration and graft dysfunction.

We feel that lower graft temperatures, and not time that resulted in the high rate of IGF, despite prolonged ATs. The second assistant irrigates the graft and uses suction to ensure visibility of the anastomotic site. It is surprising that lower graft temperature during anastomosis that makes longer AT safer, is not given due importance. Graft temperatures rise at 0.5C/min when removed from ice and can reach 34C in 60 min [10]. We placed ice filled packs on both sides of graft and irrigated with ice cold saline throughout implantation. Good graft perfusion is the primary goal and requires an unrushed vascular anastomosis. The reasons for our longer AT include multiple arteries, recipients with high BMI, left sided implantation, and right donor kidneys. Ours is a fellowship program, and trainees get hands on experience which increases AT. Others have also shown the benefits of lower graft temperatures, Pupka et al compared graft outcomes from same cadaveric donor using crushed ice filled bag for one, and standard technique for the other [11]. Their mean AT was 23.6±8.1 min, they found lower incidence of DGF (26% vs. 61%, p=0.015), and a 40% higher eGFR (p=0.026) after 2 weeks in the cooled kidney, and they concluded that keeping kidney cool during anastomosis had better results. In our cohort, even an AT of over 70 minutes was found to be safe with immediate function, the only plausible reason is lower graft temperatures. Other variables can also affect early graft function, such as type of donor, quality of graft and peri-operative hemodynamics. Ours is a living donor transplant program with short DWI and CIT, and may have contributed to good EGF despite longer ATs. In assessing impact of AT on graft function we have not relied solely on SGF and DGF but also examined SC50,SCD7 and SC at follow up after 6 months (Table 3) which showed no significant difference between the two arms. The study has the limitations of single center retrospective study and relatively smaller number of patients in GI. Selection bias was low because we included all consecutive cases. Since the main aim

of the study was to measure impact of AT on EGF, our short follow up may not be time enough to document longer term consequences. Our results should encourage young surgeons not to perform the vascular anastomosis under the pressure of the clock, but to focus primarily on fashioning a meticulous anastomosis, while maintaining low graft temperatures by cooling the graft.

		Rewarming Ischemia Time (in minutes)				*p-value*
		GI<= 40		*GII> 40*		
		Count	*%*	*Count*	*%*	
Anastomosis time (AT) (Mean)		39 37.23±1.93	32.5%	81 47.07±6.90	67.5%	0.00001
Pre-operative SC (mg/dl)	3-6	26	66.7%	46	56.8%	0.456
SC50 (hours)	7-10	12	30.8%	34	42.0%	0.225
	11& above	1	2.6%	1	1.2%	
	6 -12	13	33.3%	35	43.2%	
	13-18	13	33.3%	29	35.8%	
	19-24	3	7.7%	9	11.1%	
	25-30	5	12.8%	3	3.7%	
	31 & above	5	12.8%	5	6.2%	
SC at Discharge (mg/dl)	< 1.5	31	79.5%	75	92.6%	0.103
	1.5-3	6	15.4%	5	6.2%	
	>3	2	5.1%	1	1.2%	
Last SC (mg/dl)(minimum 6 months after transplant)	< 1.5mg/dl	36	92.3%	68	84.0%	0.271
	1.5-3	2	5.1%	12	14.8%	
	> 3	1	2.6%	1	1.2%	

SC-serum creatinine, SC 50-time taken for 50% reduction from preoperative SC.

Table 3: Pre-operative SC, time for 50% reduction in SC, SC at discharge and SC at 6 month onward was insignificant in both the groups.

References

1. Merrill JP, et al. "Successful homo-transplantation of the human kidney between identical twins". J Am Med Assoc 160 (1956): 277-282.
2. Yarlagadda SG, et al. "Association between delayed graft function and allograft and patient survival: a systematic review and meta-analysis". Nephrol Dial Transplant 24 (2009): 1039-1047.
3. Tapiawala SN, et al. "Delayed graft function and the risk for death with a functioning graft". J Am Soc Nephrol 21 (2010): 153-161.
4. Salahudeen AK, Haider N and May W. "Cold ischemia and the reduced long-term survival of cadaveric renal allografts". KidneyInt 65.2 (2004): 713-718.
5. Rod X, et al. "Impact of ischemia time on renal function after partial nephrectomy: a systematic review". BJUInt 118.5 (2016): 692-705.
6. Kuipers TG, et al. "Kidney temperature course during living organ procurement and transplantation". Transpl Int 30.2 (2017): 162-169.

7. Heylen L, et al. "The impact of anastomosis time during kidney transplantation on graft loss: A Eurotransplant cohort study". Am J Transplant 17.3 (2017): 724-32.
8. Hellegering J, et al. "Deleterious influence of prolonged warm ischemia in living donor kidney transplantation". Transplant Proc 44 (2012): 1222-26.
9. Khan TFT, et al. "Implantatation warm ischemia time in kidney transplant recipients; Defining its limits and impact on early graft function". Ann Transplantation 24 (2019): 432-38.
10. Feuillu B, et al. "Kidney warming during transplantation". Transpl Int 165 (2003): 307-12.
11. Pupka A, et al. "The modification of renal transplantation with the usage of own polythene receptacle". Polim Med 33 (2003): 33-37.

Volume 5 Issue 5 November 2023