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Impact of Onset of Graft Function on Outcome Following a Deceased Renal Transplant - A Comparitive Retrospective

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Abstract

Introduction: Deceased Donor Renal Transplantation (DDRT) constitutes less than 5% of the total renal transplants of about 3500 per year in India. Tamil Nadu has an active DDRT program through Transplant Authority of Tamil Nadu (TRANSTAN), with donation rate of is 0.3 per million populations against the national rate of only 0.08 per million. The first deceased donor renal transplant in our institute was performed in 1994 and since then 122-deceased, donor transplantations have been performed.

Aims: i) To analyse incidence of primary non-graft function, immediate graft function and delayed graft function. ii) To analyse impact of onset of graft function on patient and graft survival after deceased donor renal transplantation.

Materials and Method: We performed a retrospective analysis of all deceased donor renal transplants from January 1994 to July 2018. All the transplants done during this period were included which accounted for a total of 122 cases. Data was collected by accessing the old medical records which were maintained prospectively. The data were analysed in SPSS 17 software. P value of <0.05 was considered statistically significant. Suitable statistics test was applied as necessary. Kaplan-Meier analysis was used to evaluate survival rates of graft and recipients at 1 year and 3 years.

Results: The average donor age was 31.8 years. The most common cause of brain death was MVA (Motor vehicle accidents). The Recipients were aged between 17 and 57 years, with a mean of 34 years. 27 (22.67%) were females. Idiopathic ESRD was the major aetiology for ESRD, followed by Chronic Glomerulonephritis (CGN). Average Cold ischemia time was 7.60 hours. 71.6% cases had standard renal anatomy with single renal artery and renal vein. 23.5% (28 cases) kidneys had double renal arteries 12.29% (5 cases) had triple arteries and one case had double renal vein. Postoperatively 35 (29.1%) cases had Delayed Graft Function. 12 (10%) patients developed sepsis of which 9 (7.5%) had chest infections. Two cases of anast0motic dehiscence and one case of graft artery thrombosis occurred which were managed accordingly. One Year survival rate was 89.33 % and 73 % for patient and graft respectively. Three years' survival rate was 56.4 % and 44% for patient and graft respectively.

Conclusion: Deceased donor renal transplantation increases the donor pool significantly. Meticulous harvesting, good bench dissection and planning to reduce cold ischemia time will improve the outcome of deceased donor renal transplantation.

Keywords: Cold ischemia time; Deceased donor renal transplantation; Delayed graft function; Renal vessel anatomy

Introduction

ESRD (End Stage Renal Disease) has an incidence of around 151 per million populations in India, contributing to a major disease burden. However, the rate of renal transplantation is only 3.20 per million populations per year, in India [1,2]. Two percent of kidneys transplanted are from deceased donors. Deceased Donor Transplantation (DDT) in the state of Tamil Nadu has made major strides since 2008 and has a deceased donor rate of 2 per million populations. This is as a result of public–private partnership spearheaded by the efforts of the state transplant coordinator and the participating team [3,4]. This partnership has provided DDT to the underprivileged sections of the society through the participating teaching hospitals in Tamil Nadu, especially in Chennai. Deceased donor transplantation was started in our institute in 1994 and so far 122 cases have been performed. The cadaver transplant program was started by G.O. No. 296 dated 16/09/2008, since then it was properly streamlined and number of cases in our centres has been drastically increased. Then Transplant Authority of Tamil Nadu (TRANSTAN) was formed by G.O. 396 dated 12/12/2014

under the chairmanship of the Honourable Chief Minister of Tamil Nadu. It is an autonomous government body which governs all the aspects of the programme viz. brain death certification, organ retrieval, and allocation [5]. The online transplant registry maintains records of patients on waiting list for Kidney, Liver or Heart transplants in the state of Tamil Nadu. The convenor, Tamil Nadu Cadaver Transplant Program has a pivotal role in TRANSTAN [6]. This study was done to measure the outcomes of DDRT in a public-funded tertiary care hospital. We performed a retrospective analysis of all the 122 deceased donor renal transplantations in our institute.

Aims

Primary objective

To analyse incidence of primary non graft function, immediate graft function and delayed graft function.

Secondary objective

To analyse impact of onset of graft function on early outcome and @ 1 year and 3 years

Methodology

We performed a retrospective analysis of all deceased donor renal transplants from January 1994 to July 2018. All the transplants were blood group compatible. Data analysis included donor and recipient age, donor kidney laterality, etiology of ESRD, duration of haemodialysis, cold ischemia time, graft vessel anatomy, Delayed Graft Function (DGF), rejection episodes and mortality. Human Leukocyte Antigen (HLA) matching could not be done due to logistic reasons. Cross match test was carried out by complement-dependent micro-lymphocytotoxicity test. In total 122 cases of deceased donor transplantation were included in the study. The data were analysed in SPSS 17 software. P value of <0.05 was considered statistically significant.

Surgical procedure

Kidney harvesting from the deceased donor was done by the same transplant team taking great care to preserve adequate periureteric tissue and to avoid dissection in the "golden triangle" defined by the gonadal vein stump, renal hilum, and lower pole of the kidney. The recipient surgery was performed through Modified Gibsons incision. The peritoneum was medialised and iliac vessels were exposed and dissected. The renal artery was anastamosed to recipient internal iliac artery using 6-0 prolene continuous sutures. Similarly, the vein was anastamosed end to side to recipient external iliac vein using 6-0 prolene continuous sutures. The ureter was fashioned to create a non-redundant, tension free anastomosis, and all recipients underwent extravesical refluxing ureteroneocystostomy. The ureter-to-mucosa anastomosis was performed using running 4-0 vicryl. All patients received 5F/16 cm Polyurethane double J stents. A 20 Fr Foley's catheter was routinely inserted intraoperatively and removed on the sixth postoperative day. Surgical drains were used in all patients and were removed when drainage was less than 30 ml/day of serous fluid.

Antibiotics, immunosuppression, and other drugs

All patients received prophylactic antibiotics (Injection Ceftriaxone 1 gm every 12 h) for 48 h after surgery. A standard triple immunosuppressive regimen using Tacrolimus, Mycophenolate Mofetil (35 mg/kg/day) and Prednisolone (0.5 mg/kg/day) were given to all patients. Anti thymocyte globulin induction was done. Episodes of biopsy proven rejection were treated with three intravenous doses of Methylprednisolone (500 mg/day).

Graft preservation

HTK (Histidine-Tryptophan-Alpha Ketoglutarate) was the perfusion fluid used in all the deceased donor transplantations included in the study. The standard sterile three bag technique was used for packing and transportation of the harvested kidney.

Induction agent

A single dose of Rabbit Anti-Thymocyte Globulin (rATG) 1.5 mg/kg was given as intravenous infusion in the preoperative and intraoperative period. An alternate induction agent used was Interleukin-2 receptor blocker (Basiliximab) which is given as 20 mg two doses - first dose just before surgery followed by second dose 4 days later.

Post-operative care protocol

- Input/ output charting
- Renal function test
- Immunosuppression
- Tacrolimus
- Mycophenolate mofetil
- Prednisolone.
- Doppler ultrasound – when necessary
- Renal biopsy – rarely
- Tacrolimus levels at day 4 and day 10

Outcome definitions

Immediate Graft Function (IGF) was defined as non-requirement of dialysis after transplantation; Delayed Graft Function (DGF) as need for dialytic support within a week of transplant, Primary Non-Function (PNF) as patients whose graft never functioned.

Results

Donor characteristics

The average donor age was 31.8 years. 109 donors (89.34%) were standard criteria donors (SCD) and the remaining 13 (10.65%) were extended criteria donors (ECD). The most common cause of brain death was MVA (Motor vehicle accidents) (Table 1).

Kidney laterality	Number	%
Right side	54	44.26
Left side	68	55.73
Total	122	100

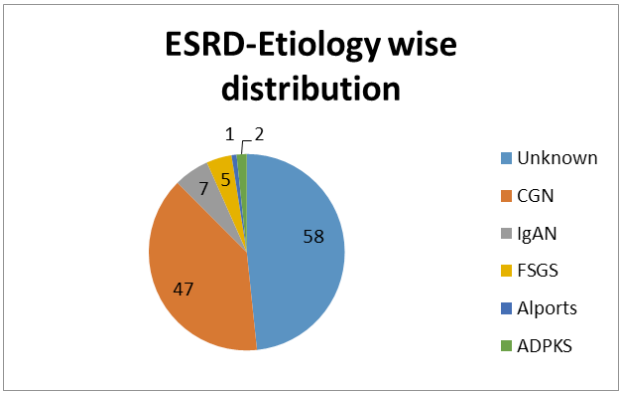
Table 1: Distribution of kidneys based on side.

Recipient characteristics

Recipients were aged between 17 and 57 years, with a mean of 34 years. The mean duration of haemodialysis was 20.1 months with minimum duration of 1 month and maximum of 60 months.

Aetiology for ESRD

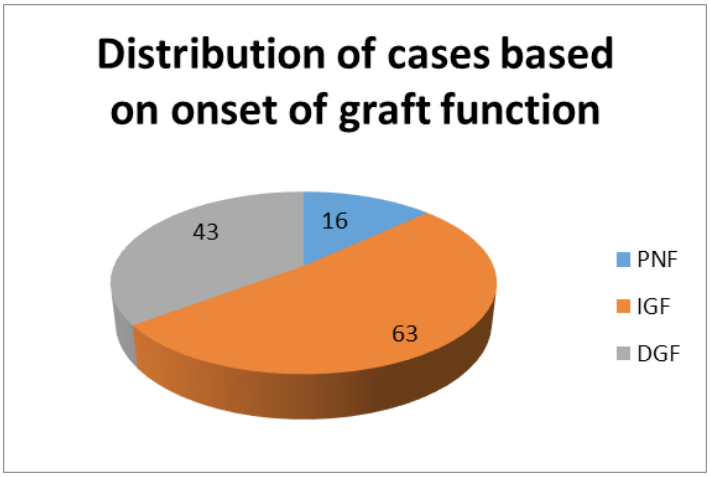
In majority of cases, the aetiology was unknown, followed by CGN was the most common cause (Graph 1).



Graph 1: Etiology of ESRD.

Graft function

Incidence of primary non graft function 13.11% (16 cases), immediate graft function 51.63% (63 cases) and delayed graft function 35.24% (43 cases) (Graph 2).



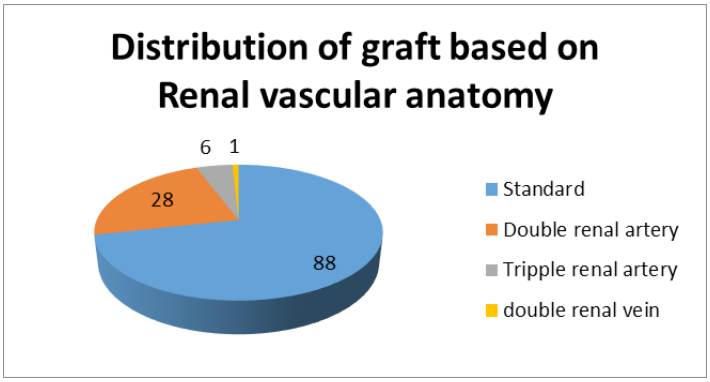
Graph 2: Distribution of cases based on onset of graft function.

Factors affecting onset of graft function

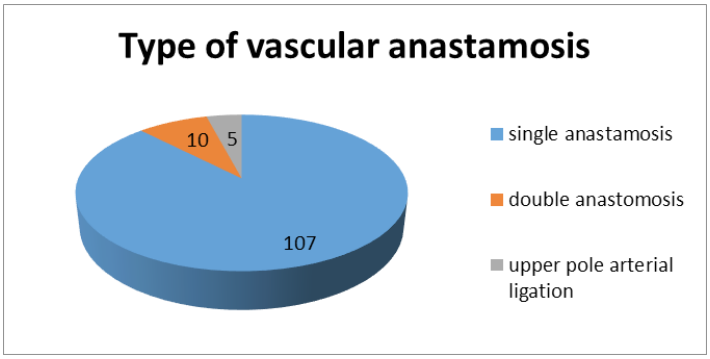
There was no statistically significant difference in **donor age,** recipient age and recipient gender between IGF and DGF groups. ($p>0.05$).

Impact of vascular anastamosis on graft fuction

Out of 122 cases, 88 (72.13%) kidneys had standard anatomy with single renal artery and single renal vein. 33 (27.04%) kidneys had multiple renal arteries and one patient had double renal vein. Out of these 33cases of anomalous renal artery anatomy, 28 cases (84.84%, n- 33) had double renal artery and 6 cases (18.18%, n- 33) had triple renal arteries. Among these 28 cases of anomalous double renal artery, 15 cases were harvested along with an aortic patch and had a single arterial anastamosis. Double anastomosis to External Iliac artery and Internal iliac artery was done in 8 cases and in other 5 cases the upper pole artery was safely ligated. Out of six kidneys having triple renal arteries, four were harvested with common aortic patch and anastamosed. In the remaining two patients, two arteries in common cuff and third artery was directly anastomosed (with one vessel being anastomosed end to end). In our study, out of 33 anomalous renal artery anatomy,10 cases had double arterial anastamosis and 5 had safe ligation of upper pole artery ligation. Among these 15 cases, 5 cases had DGF and 9 had IGF (Graphs 3,4 and Table 2).



Graft 3: Distribution of grafts based renal vascular anatomy.



Graph 4: Types of vascular anastomosis.

Type of anastomosis	IGF	DGF	P value
Upper pole artery ligation	3	2	0.93
Double anastomosis	6	4	0.96
P = >0.5			

Table 2: Impact of type of graft vascular anastomosis on onset of graft function.

Cold ischemic time

The average cold ischemia time in the present study is 7.6 hours. The CIT was prolonged when organs were procured in other centres and transported (Table 3).

CIT	IGF	DGF
<6 hrs	17	16
>6 hrs	46	27
P=0.5		

Table 3: Impact of duration of CIT on onset of graft function.

Effect of onset of graft function on outcome

There was no difference in the incidence of new onset of diabetes after transplant (NODAT) [p-0.83] and infection episodes due to virus and bacteria among the two groups (p-0.8). The incidence of acute rejection was 16.03 % (n = 17) (Table 4).

Variables	IGF (63)	DGF (43)	P value
Acute Rejection episodes	9	8	0.55
NODAT	15	11	0.83
Infections	16	10	0.8
Functional graft @12 months	57	30	**0.006**
Mortality @ 12 months	2	3	0.36
Mortality @ 36 months	14	25	**0.001**

Table 4: Effect of onset of graft function on outcome.

There was no statistically significant difference between IGF (n = 9/63) and DGF (08/43) groups in the incidence of acute rejection (P = 0.55). Number of deaths in the IGF and DGF groups was 2 and 3 @ 12 months respectively (P = 0.36). Overall mortality @ 3years was 36.79 %. It was also noted that patient with DGF had higher mortality rates compared to IGF patients (p-0.001).

Biopsies in DGF cases

All patients with DGF who remained dialysis dependent at 2 weeks underwent biopsy. Out of 43 cases 28 patients (65.11%) needed graft biopsy. 18 (64.28 %) showed acute tubular injury; 7 patients (25%) had acute rejections; 2 patients (7.14%) had pyelonephritis and 1 was found to have interstitial nephritis (Table 5).

Death @ 12 months	Late death @ 36 months
Sepsis - 3- (fungal-1, Gram negative-2)-	Sepsis – 30 (fungal-8, Gram negative-12, Gram positive 10)
Surgical complications - 2	Cerebrovascular accident – 5 Acute Myocardial infarction – 1 Unexplained -3

Table 5: Cause of death in our study.

The average duration of follow up was 3 years. The mean serum creatinine level was 1.43±0.42 mg/dl on follow up.

Discussion

We present a series of deceased donor renal transplantation done at our institution from 1994 to 2018. Our Centre caters to patients of poor socio-economic group who live in poor living conditions. The donors were mainly from victims of road traffic accidents and are mostly standard criteria donors (SCD).

The impact of cold ischemia times and graft vascular anatomy on outcome of deceased donor renal transplantation has been analysed. The table below shows the comparison of graft outcomes with cold ischemia times in other Indian studies (Table 6).

Study	CIT (hours)	DGF (%)
Moyers.C, et al. [7]	15	26.5
Swami YK, et al. [8]	6.25 ± 2.5	34
Gumber MR, et al. [9]	5.56 ± 2.04	30.6
Mehta TR, et al. [10]	10.3 ± 4	42.4
Our data	7.6	29.1

Table 6: CIT and DGF in different Indian studies.

Our series had comparable incidence of delayed graft function with other series in India, whereas Moyers et al had reported a better graft outcome in spite of prolonged cold ischemia times. This probably resulted from post-operative factors like higher doses of immunosuppression given in their study. In the present study, immediate outcome was almost the same when cold ischemia time was below or above 6 hours (Table 3). The use of grafts with multiple renal arteries has been associated with increased incidence of vascular and urologic complications. In the present study, 28 kidneys had double renal arteries and 6 had triple renal arteries. Five cases of them required either upper polar artery ligation and 10 cases had more than one arterial anastomosis. Six of these 15 patients developed DGF postoperatively but it was not statistically significant when compared to DGF in patients who underwent single arterial anastomosis (P=0.5) [10-12].

Although we had good graft function in up to 1 year in comparison with other Indian series the graft outcomes and patient outcome at the end of 3 years was inferior. Out of 122 patients, 39 patients died. The most important and commonest cause of mortality was sepsis. Almost one third of patients with infective complications developed graft failure and subsequently poor overall patient survival. In cadaveric transplant recipients there is also a false perception that their treatment got over once transplant surgery was done. The infection rates are higher probably due to poor socioeconomic status of our patient groups and poor hygiene and sanitary condition of our patients. With adequate counselling we have been able to educate patient about basic sanitation. Though renal transplantation in Tamil Nadu is funded by the government through chief minister's insurance scheme, which is a boon to the people of low socioeconomic strata, it is difficult for the common person to withstand the cost incurred in the post-transplant period. In spite of free medications offered by the government, the cost incurred in travel, need for repeated hospitalization, regular follow up, compliance to medications are some issues which come in the way of long term success in deceased donor renal transplantation. This study has limitations inherent for a retrospective study. Recipients of ECD organs were not studied as a separate cohort in view of small number, HLA matching could not be done due to logistic reasons, and the impact of donor renal dysfunction and potential donor sepsis on the graft outcome could not be analysed. Despite these limitations, DDRT model of Tamil Nadu has proved that DDRT program catering to underprivileged patients is feasible in a government funded hospital and has evinced interest among other Indian states to emulate the program [13-15].

Conclusion

Deceased donor renal transplantation increases the donor pool significantly. This can be sustained by early identification of brain death, improving hospital infrastructure, covering long term costs post-transplant for poor patients and educating public about organ donation.

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