Research Article

FACTORS AFFECTING OUTCOME IN DECEASED DONOR RENAL TRANSPLANTATION: A COHORT STUDY -A SINGLE CENTRE EXPERIENCE

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ARTICLE INFO

ABSTRACT

Introduction: Deceased donor renal transplantation (DDRT) is still infrequent in India, constituting less than 5% of the total renal transplants of about 3500 per year. Renal transplantation, the best RRT modality, is increasing in popularity, due to improvements made in public education and deceased donor transplantation (DDT) programme.

Aims and Objectives: The aim of this study is to identify factors affecting graft function in deceased renal transplantation. For this data of recipient and donor parameters were collected and analysed, its effects on graft function and development of delayed graft function (DGF) were evaluated.

Materials and Methods: A Retrospective and prospective analysis of 11 deceased donor renal transplants performed between March 2016 and March 2019 at Government Kilpauk Medical College and Government Royapettah Hospital, Chennai were done. All the transplants were blood group compatible. Various recipient and donor factors were evaluated and its relation to graft function was studied.

Results: Mean age of the recipients was 35.5 years (male: female ratio 5:6), and that of the donors was 33.6 years (male: female ratio 11:1). The mean cold ischemia time (CIT) was 7.4 hrs. Four had CIT <6hrs. Shortest CIT was 5.15hrs and the longest was 13.4hrs. Delayed graft function (DGF) was noted in 7 recipients and immediate graft function was noted in 4 patients. Cold ischemia time and development of DGF were important predictors of graft survival.

Conclusion: The two most important factors determining graft and patient survival in our study were cold ischemia time and attainment of graft functions immediately after transplant. The incidence of DGF was 64%, and acute rejection was 27.2%. DGF also noted in recipients with pre-existing combined medical illness,increasing donor age and decreased urine output in early postop period.

INTRODUCTION

Deceased donor renal transplantation (DDRT) is still infrequent in India, constituting less than 5% of the total renal transplants of about 3500 per year. [1] Renal replacement therapy (RRT) resources are scarce in India, with wide urban-rural and interstate disparities. Renal transplantation, the best RRT modality, is increasing in popularity, due to improvements made in public education, the deceased donor transplantation (DDT) programme and the availability of free and affordable transplant services in government hospitals and certain non-governmental philanthropic organizations. The DDT rate in India is now 0.34 per million populations, among the lowest in the world. An efficient renal transplant improves the quality of life [2], corrects metabolic consequences of chronic kidney disease (CKD) and reduces the mortality risk with most patients compared with maintenance dialysis [3,4].

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Aims and Objectives

The aim of this study is to identify factors affecting graft function in deceased renal transplantation. For this data of recipient and donor parameters were collected and analysed, its effects on graft function and development of delayed graft function (DGF) were evaluated.

MATERIALS AND METHODS

A Retrospective and prospective analysis of 11 deceased donor renal transplants performed between March 2016 and March 2019 at Government Kilpauk Medical College and Government Royapettah Hospital, Chennai were done. All the transplants were blood group compatible. Recipient data analysis included age, sex, native kidney disease, cold ischemia time, delayed graft function (DGF), dialysis requirement, rejection episodes and infective episode. Donor characteristics viz. age, sex, history of hypertension and serum Creatinine level before procurement were studied. Donor renal vessel characters were also studied. Cross match test was

carried out by complement-dependent microlymphocytotoxicity test. Outcome of these factors affecting graft function was studied. Graft survival was estimated within 12 months of transplantation. Cases of ABO incompatibility and positive cross matches were excluded. The study was approved by local ethical and transplant committee.

Immunosuppressive Regimen

Immunosuppressive regimen consisted of steroids, tacrolimus, and mycophenolate mofetil. The induction agent protocol was single dose of anti-thymocyte globulin at the dose of 1.5 mg/kg and two doses of basiliximab on day 1 and day 4. The acute cellular rejection was treated with 3 doses of intravenous methylprednisolone (500 mg each and antibody-mediated rejection was treated with plasmapheresis (1 plasma volume removal per session over 4–8 sessions) and intravenous immunoglobulin (100 mg/kg/day over 5–10 doses).

Outcome definitions

Delayed graft function (DGF) was defined as need for dialysis support within a week of transplant. [5] Immediate graft function (IGF) was defined as non-requirement of dialysis after transplantation.

Post Operative Follow Up

- Daily RFT monitoring.
- USG KUB with Doppler study were done on POD 3
- CT angiogram reserved for those with abnormal Doppler study with raising serum Creatinine.
- Biopsy done on POD 7 or when S.creatinine is raising.
- HD done in 1st wk for those with reduced urine output.
- ACMR managed with pulsed steroid+ ↑ tacrolimus dose
- ABMR managed with Rituximab and plasmapheresis.

RESULTS

Analysis of 11 deceased donor renal transplants performed between March 2016 and March 2019 at Government Kilpauk Medical College and Government Royapettah Hospital, Chennai was done. Mean follow up period was 12 months.

Donor and recipient Characteristics

Mean age of the recipients was 35.5 years (male: female ratio 5:6), and that of the donors was 33.6 years (male: female ratio 11:1).Youngest donor was 19yrs, eldest donor 50yrs.Youngest recipient was 26yrs, eldest recipient was 44yrs.

Donor and Recipient Parameters

The mean cold ischemia time (CIT) was 7.4 hrs. Four had CIT <6hrs. Shortest CIT was 5.15hrs and the longest was 13.4hrs. Double renal arteries, double renal veins and triple renal veins were found in 3, 2 and 1 cases of graft respectively. Laterality of graft-Right kidney in 7 cases (64%). All donors had no co morbid illnesses, where as all recipients had hypertension. In addition 2 recipients had hypothyroidism and 3 had IgA nephropathy. Average post op serum Creatinine on 1st day was 3.4mg/dl, with lowest and highest values noted were 2.2mg/dl and 5mg/dl respectively. Average urine output on 1st day was 2.1L, with lowest and highest values noted were 200ml and 7L respectively.

Graft Function

Delayed graft function (DGF) was noted in 7 recipients and immediate graft function was noted in 4 patients. Cold ischemia time and development of DGF were important predictors of graft survival.6 out of 7 with CIT >6hrs were associated with dialysis requirement in 1st wk. Biopsy revealed acute rejection in 3 cases and ATN in 7 cases and were managed as mentioned earlier. Effect of various variables was studied in both DGF and IGF groups. There was no statistically significant difference in donor age, recipient age and recipient gender between IGF (n = 4) and DGF (n = 7) groups. Mean cold ischemic time was shorter in patients with IGF group than in DGF group (5.8hrs vs. 8.4 hrs). Two patients (50%) in the IGF group developed ACMR and one patient (14.2%) in DGF group developed ABMR on follow-up. There was no statistically significant difference between IGF and DGF groups in the incidence of acute rejection.

The mean urine output in the first post operative day was 2.7L and 0.6L in the IGF and DGF groups respectively. Mean Serum Creatinine in the first post operative day were 2.8mg/dl and 3.7mg/dl in the IGF and DGF groups respectively. All patients in the recipient group had hypertension as pre-existing co morbid illness. In addition Ig A nephropathy and hypothyroidism were noted in 3 and 2 patients in DGF group respectively. Infection episode (pelvic abscess) was noted in one patient in DGF group, requiring emergency laparotomy and drainage of collection following which patient expired due to septicemia with multi organ failure. At mean follow up of 12 months, no graft loss were noted in IGF group while 2 patients in DGF group required graft nephrectomy for complications like external iliac artery aneurysm and expanding perirenal hematoma due to anastomosis site leak respectively.

Table 1 Donor and recipient characteristics

Donor Characteristics	Value
Age (years)	33.6
Gender (male/female),%	100/0
Cause of death (%)	
RTA with intracranial haemorrhage	100
Co morbid illnesses (%)	0
Terminal serum Creatinine (mg/dl)	1.1
Cold ischemia time (hr)	7.4
Renal vessel characteristics (%)	
Single renal artery and vein	54.5
Double renal arteries and single renal vein	27.5
Single renal artery and double renal veins	9
Single renal artery and triple renal veins	9
Laterality (%)	
Right kidney	64
Left kidney	36

Table 2 Recipient characteristics

Characteristics	Value
Age (years)	35.5
Gender (male/female),%	45.5/54.5
Co morbid illnesses (%)	
Hypertension	54.5
Hypertension Hypothyroidism	18.2
Hypertension+IgA Nephropathy	27.3
First post operative day serum Creatinine (mg/dl)	3.4
First post operative day urine output(L/24hr)	2.1
Delayed Graft Function/Immediate graft function (%)	63.6/36.4
Biopsy (%)	
Rejection	27.3
Acute tubular necrosis	63.6
Infection (%)	11

Table 3 Comparison of variables between immediate graft function and delayed graft function groups

Characteristics	DGF	IGF
Recipient Age (years)	36.8	33.3
Donor age (years)	37.3	27.3
Cold ischemia time(hrs)	8.4	5.8
Comorbid illnesses (%)		
Hypertension	28.6	100
Hypertension Hypothyroidism	28.6	0
Hypertension+IgA Nephropathy	42.8	0
First post operative day serum Creatinine (mg/dl)	3.7	2.8
First post operative day urine output(L/24hr)	2.7	0.6
Biopsy (%)		
Rejection	14.3	50
Acute tubular necrosis	85.7	25
Infection (%)	14.3	0
Graft loss (%)	28.6	0
Death (%)	14.3	0
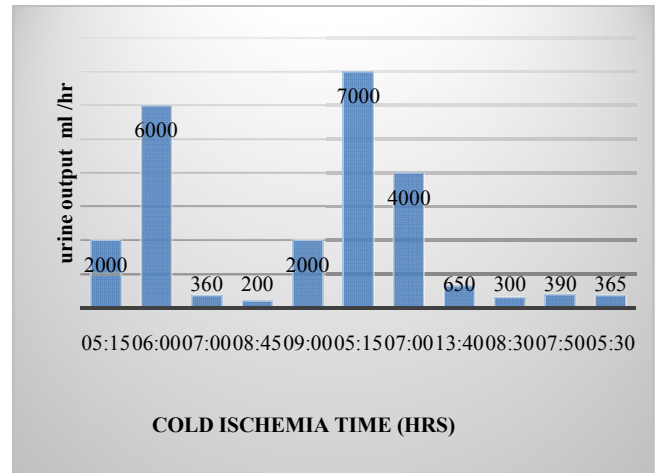
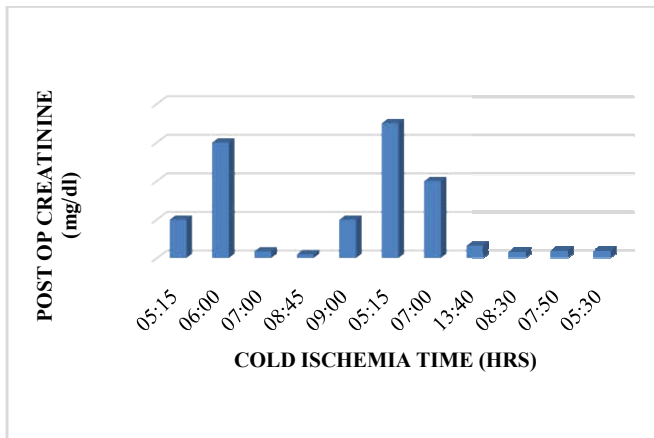**Graph 3** Cold ischemia time vs Urine output
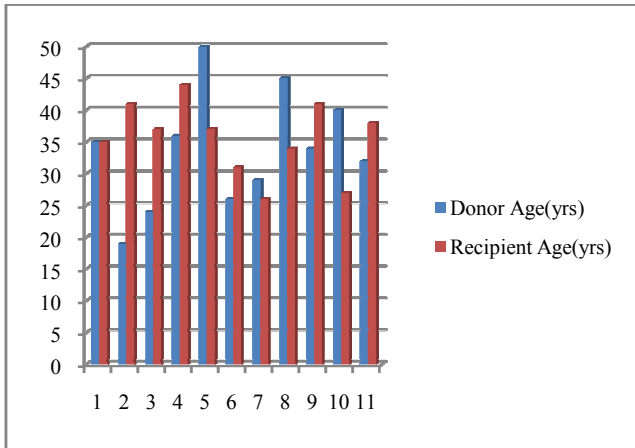
Graph 1: Donor age and Recipient age
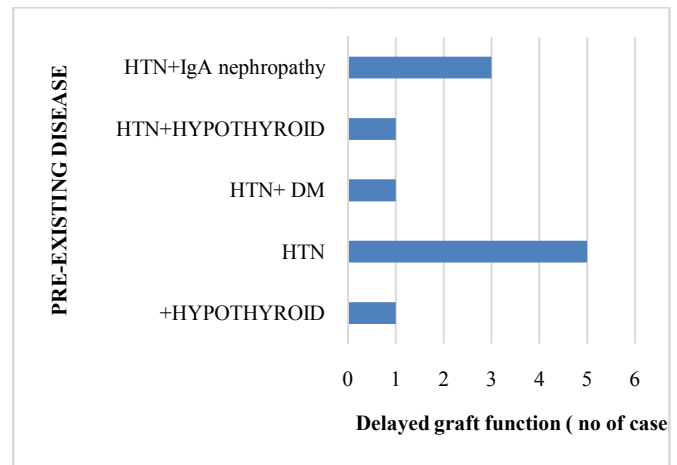
Graph 4 Relation of DGF with pre-existing recipient disease

Table 4 Overall Outcome

ATN	Delayed Graft Function	Acute rejection	Graft Nephrectomy	Death
6	7	3	2	1

DISCUSSION

In our study, 54.5% of the recipients were females and all donors were male (100%) in contrary to Gopalkrishnan et al study [5] where 14.9% of donors and 28.9% of recipients were females. In Ruta et al [6] study 61.1% of donors and 38.9% of recipients were females. These are in contrast to the gender disparity noted in living related donor transplant scenario in India in which majority of the donors are women. The mean donor age in our study was 33.6yrs (range 19-50) and that of recipient was 35.5yrs (range 26-44). In Ruta et al [6] study the mean donor and recipient ages were 44yrs and 45.42yrs respectively as compared to 34yrs for donors in Gopalkrishnan et al[5] study.

No gender association was noted with development of DGF or graft failure in our study contrary to other studies where female transplant recipients had better survival than male recipients. [7]

Cold ischemia time and development of DGF were important predictors of graft survival.6 out of 7 with CIT >6hrs were associated with dialysis requirement in 1st wk. Mean CIT in our study was 7.4hrs when compared to 340±170 mins in Gopalkrishnan et al[5] and 19.6±4.57 hrs in Ruta et al[6] study. Prolonged CIT was found to be a risk factor for DGF. DGF

Graph 2 Post operative S.creatinine vs Cold Ischemia Time

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had significant impact on graft survival. This finding is in concordance with studies by Boom et al[8] Gopalkrishnan et al[5], Ruta et al[6], Helfer et al[9]and Cheung CY.[10]

The incidence of DGF in our study was 64% compared to 48.5% in Gopalkrishnan et al[5], 54.8% in Surazee[11], and 31.7% in Ruta et al[6] studies. 3 cases (27.2%) with donor age >40yrs were associated with DGF compared to 28% in Ruta et al [6] study. This finding is in concordance with other studies where increasing donor age is associated with increased risk of DGF[12]. DGF also seen in 3 pts (27.2%) with pre-existing combined HTN and IgA nephropathy compared to 32% in Gopalkrishnan et al[5]and 40% in Surazee[11] study. Recipients with multiple co morbidities are associated with increased risk of developing DGF[13].

Post op S.creatinine and cause of death in donors had no role in predicting graft survival in our study contrary to other studies where some association was found[14,15]. In our study those with reduced urine output in first post operative day was associated with increased risk of DGF with mean urine output in DGF group was 600ml.

No association was noted with laterality of donor kidney and renal vessel characters in our study, while some association was noted between vascular complications causing reduced graft function in grafts with multiple renal arteries in Edurado et al [16]and other studies[17].Incidence of acute rejection was 27.2% in our study compared to 24% in Surazee[11] study, 36% in Ruta et al[6] study. This finding is in concordance with other studies[18,19].

Table 5 Comparison of various studies

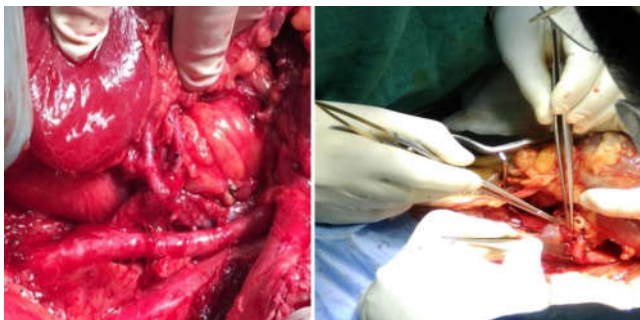|	Our Study	Gopalakrishnan et al	Surazee et al	Ruta et al
Recipient sex (Females)	54.5%	28.9%	NA	38.9%
Donor Age>40yrs	27.2%	NA	NA	28%
DGF	64%	48.5%	54.8%	31.7%
Acute Rejection	27.2%	NA	24%	36%
Pre-existing combined HTN and IgA nephropathy	27.2%	32%	40%	NA

Figure 1 Case of Double renal arteries and single renal artery respectively
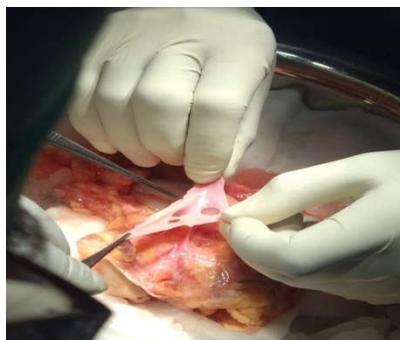

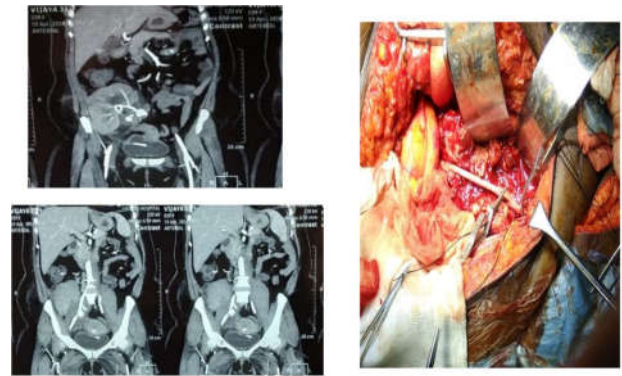**Figure 2** Case of triple renal veins cadaver graft

Figure 3-Post cadaver transplantation CT image showing EIA aneurysm, managed by graft nephrectomy with saphenous vein graft reconstruction of EIA

Figure 4 CT showing expanding perirenal hematoma managed by Graft Nephrectomy due to anastomotic site leak.

Limitations of our study

The differences in this study outcomes are presumable due to methodology of the research, number of study population, categorization of the variables and a shorter follow up period. Moreover, the course of post transplantation care and adverse events can overshadow the impact of donor and recipient factors on graft outcomes.

CONCLUSION

The two most important factors determining graft and patient survival in our study were

- Cold ischemia time- Increased CIT associated with increased risk of developing DGF
- Attainment of graft functions immediately after transplant i.e, DGF associated with reduced graft function.

The incidence of DGF was 64%, and acute rejection was 27.2%. DGF also noted in

- Recipients with pre-existing combined medical illness.
- Increasing donor age.
- Decreased urine output in early postoperative period.

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