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EFFECT OF DONOR KIDNEY WEIGHT/ RECIPIENT BODY WEIGHT (DKW/RBW) MISMATCH ON PATIENT AND GRAFT OUTCOME IN LIVE DONOR RENAL TRANSPLANTATION

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ABSTRACT

Background: Live donor renal transplantation offers excellent outcomes, but matching donor organ size to recipient metabolic demand may be critical. The precise impact of the DKW/RBW ratio on graft function and specific post-operative complications remains poorly defined in live donor cohorts. This study evaluated the "Effect of DKW/RBW mismatch on patient and graft outcome in live donor renal transplantation".

Materials and Methods: The Study Design is Prospective Cohort Study. 102 consecutive live donor renal transplant patients were included in the study. We measured DKW intra operatively and calculated the DKW to RBW ratio and then the patients were divided into three groups; those with ratio less than 2.5(<2.5), 2.5 to less than 3.5 (2.5-<3.5) and the third group with ratio more than/equal to 3.5 (>/=3.5). Recipients were followed for 12 months to evaluate short and medium term graft survival and clinical complications.

Results: Significant positive correlation between DKW and donor body weight (DBW). Insignificant effect of DKW/RBW mismatch on patient and graft outcome in live donor renal transplantation.

Conclusion: During donor and recipient matching, the effect of DKW/RBW should not be over emphasized until a method to measure renal parenchymal volume and nephron number more precisely has been developed. Large group studies with rationale selection of donor and recipient males and females are needed to accurately compute the effect of graft size on patient and graft outcome in live donor renal transplantation.

Keywords: Kidney transplantation, living donors, graft survival, body weight, organ size.

INTRODUCTION

Renal transplantation is the treatment of choice in end stage renal failure.[1] The hyper filtration theory (originally proposed by Brenner and Milford),[2] predicts that renal function gradually decreases with time, and that this process may be accelerated by reduced nephron mass. In fact, chronic hyper filtration together with reduced functioning kidney mass might damage the graft, initiating the vicious cycle of a further reduction in renal mass which in turn causes more significant hyper filtration leading to progressive decline in the glomerular filtration rate (GFR), proteinuria, hypertension (HTN) and eventually chronic graft failure.[3] This mechanism may be particularly important in a transplanted kidney; the initial nephron mass being provided by a single kidney which may then lose nephrons as a result of episodes of acute rejection and use of nephrotoxic immunosuppressive drugs.[4] In other words nephron under dosing may lead to shortened graft survival.

There are observations which suggest that graft survival is shorter when the complement of donor nephrons is low as described ahead. Kidney transplants from female donors to male recipients fare worse than the male donor to female recipient combination (kidneys in women weigh 10-20% less than those in men and have proportionately fewer glomeruli). In recent years, an increasing amount of

experimental and clinical evidence supports the view that transplanted renal mass as well as recipient metabolic demand are important predictors of graft survival. For example, transplanted kidneys from old and very young donors have a poorer outcome than transplanted kidneys from adults, and very large recipients fare less well than normal size recipients.[5]
To demonstrate the impact of functioning renal mass, a number of surrogates have been proposed [6]:

1. DBW- Kidney weight and body weight correlate directly.[7,8]
2. Preoperative kidney graft size as measured by ultrasound (USG).[9]
3. Preoperatively Kidney graft volume as measured by Helical Computerized Tomography (CT) scan.[10]
4. Preoperative kidney graft volume as measured by Magnetic Resonance Imaging (MRI)
5. Measurement of Donor kidney Volume (DKV) intra operatively by measuring glass.
6. Direct measurement of DKW intra operatively and the calculation of DKW/RBW ratio.

Direct weighing of the graft intra operatively (DKW) seems to be the best surrogate index of nephron number available.[11] The only measure that comes close is the renal volume as measured by MRI, but that too is less accurate than weighing kidney directly and also not cost effective. Isolated reports have shown that small donor kidney in a large recipient could be a major risk factor also for post transplant complications such as HTN and New Onset Diabetes After Transplantation (NODAT).
However, the parameters such as the total number of patent glomeruli or total filtration area of the donor kidney are thought to precisely represent the performance of the transplanted kidney than any other surrogate mentioned above.
The aim of present study was to analyze the effect of DKW/RBW mismatch on patient and graft outcome in live donor renal transplantation.

MATERIALS AND METHODS

Study Population
102 patients with renal failure, planned for live donor renal transplantation in a Tertiary Care Centre were chosen for study and followed up.
Inclusion Criteria
Live kidney transplant recipients who were:

- Having first transplant
- More than 15yr to less than 61yr of age
- With BMI less than 35.
- Giving consent for the study and available for follow up

were included in this study.
Procedure
Baseline demographic information was collected for donors and recipients, which included age, sex, preoperative donor GFR and HLA antigen mismatch between donor and recipient. Since the body weights of dialyzed patients vary with time with the differences amounting to even many kilograms, all live kidney transplant recipients giving consent for this study were weighed on the morning of transplant (dry body weight) and also their heights were measured. The heights and weights of the corresponding live kidney donors were also measured. Intra operatively DKW was measured after perfusing it with a cold perfusing solution.
As per usual protocol, all patients received methylprednisolone as component of immunosuppressive therapy started preoperatively, with or without induction therapy (Basiliximab/Daclizumab).
Post transplant, all recipients were put on standard triple drug therapy with Tacrolimus/cyclosporine, mycophenolate mofetil/azathioprine and steroids. The patients were then followed up at 3, 6, 9 and 12 months post transplant and following criteria were measured during each follow up –

- Serum creatinine (SrCr)
- Creatinine clearance (CrCl) as derived from Cockcroft and Gault formula [12].
- 24 hr urinary protein excretion
- Any post transplant complications, especially HTN and NODAT

The number and severity of Acute Cellular Rejection (ACR) episodes were recorded.
The collected data was analyzed by measuring:

1. DKW/RBW) ratio as gm/kg.
2. Correlation between DKW and Donor GFR.
3. Graft function in terms of SrCr & CrCl.
4. Patient outcome in terms of post transplant complications such as HTN & NODAT.
5. Correlation between DBW and DKW.
6. Correlation between DKW/RBW ratio and short and medium term patient & graft outcome.

Statistical Methods
ANOVA with post-hoc analysis was applied for comparison of DKW/RBW ratio with continuous variables and Chi- square test applied for comparison of DKW/RBW ratio with discrete variables. SPSS software was used for analysis of data.

RESULTS

102 consecutive Renal transplant patients for the period from 09/07/2007 to 02/06/2008 were included in the study. DKW/RBW was calculated for each Donor-Recipient pair and then the patients were divided into three groups; those with ratio less than 2.5 (<2.5), 2.5 to less than 3.5 (2.5-<3.5) and the third group with ratio more than/equal to 3.5 (>/=3.5). Group-1 consisted of 22 patients, group-2 of 61 patients and group-3 of 19 patients. There was no difference in the pre-operative work-up, immunosuppression protocol and postoperative management between the three groups. DKW/RBW ratio (as three groups) was compared with the baseline characteristics such as Donor age, donor pre donation GFR, donor sex, donor kidney size, recipient age, recipient sex and RBW (TABLE-1).

The results were as follows: Donor age, Donor CrCl and Donor kidney size, all the three variables did not vary significantly between the three DKW/RBW ratio groups. The proportion of donor males and females varied significantly between the three DKW/RBW ratio groups. Proportion of males were 9.1%, 19.7% and 57.9% in the 3 consecutive groups, respectively and that of females were 90.9%, 80.3% and 42.1%, respectively. Recipient age varied significantly between the three DKW/RBW ratio groups. Recipient age was 37.2+/-12.5, 32.4+/-10 and 26.4+/-8.3 in the 3 groups, respectively, indicating a significant difference in the recipient age between groups 1 and 3.

Recipient weight also varied significantly between the three ratio groups, and it was 62.6+/-9.8, 54.3+/-5.8 and 43.3+/-7.5 in the three groups, respectively. Recipient sex did not vary significantly between the three DKW/RBW ratio groups.

Table 1: Showing the correlation of DKW/RBW ratio with the baseline characteristics as mentioned above

Baseline Characteristics	DKW/RBW ratio (gm/kg) groups			P value
	1.5-2.499 (n=22)	2.5-3.499 (n=61)	>/=3.5 (n=19)	
Donor age	42.8+/-10.3	45+/-10.8	43.9+/-10.7	.705
Donor CrCl (ml/min)	93.3+/-13.8	87.3+/-13.4	89.5+/-17.3	.250
Donor Kidney size	9.73+/-.53	9.79+/-.56	9.89+/-.58	.630
Recipient age	37.2+/-12.5	32.4+/-10	26.4+/-8.3	.005
Donor females	20/22	49/61	8/19	.001
Donor males	2/22	12/61	11/19	.001
Recipient females	3/22	6/61	5/19	.190
Recipient males	19/22	55/61	14/19	.190
Recipient weight	62.6+/-9.8	54.3+/-5.8	43.3+/-7.5	.000
Post Transplant HTN	15/22	50/61	17/19	.205
NODAT	6/22	6/61	2/18	.119
Post Transplant Cr_12m	1.17+/-.28	1.35+/-.49	1.18+/-.26	.125
Post Transplant CrCl_12m	79+/-16.2	65.2+/-19.2	59.8+/-12.4	.002

The same ratio, that is DKW/RBW (as 3 groups) was also compared with post transplant variables such as SrCr and CrCl, each at 6 and 12 month post transplant (TABLE-2). DKW/RBW ratio was also compared with post transplant HTN, NODAT and other complications group (TABLE-2), thereby indicating the effect of DKW/RBW ratio on graft and patient outcome post transplant.

Table 2: Showing the correlation of DKW/RBW ratio with post Transplant variables

Baseline Characteristics	DKW/RBW ratio(gm/kg) groups			P value
	1.5-2.499 (n=22)	2.5-3.499 (n=61)	>/=3.5 (n=19)	
Post Transplant SrCr_6m	1.16+/-.28	1.28+/-.36	1.18+/-.39	.329
Post Transplant SrCr_12m	1.17+/-.28	1.35+/-.49	1.18+/-.26	.125
Post Transplant CrCl_6m	79+/-15.9	66.9+/-16.2	61.9+/-17.3	.003
Post Transplant CrCl_12m	79+/-16.2	65.2+/-19.2	59.8+/-12.4	.002
Post Transplant HTN	15/22	50/61	17/19	.205
NODAT	6/22	6/61	2/18	.119
ACR(no group)	20/22	57/61	19/19	.439
ACR(yes group)	2/22	4/61	0/19	.439

The results were as follows: Varying DKW/RBW ratios had an insignificant effect on Post transplant SrCr at both 6 month and 12 month post transplant that is the Serum creatinine did not vary significantly between the three ratio groups. The ratio (DKW/RBW) had a significant effect on post transplant CrCl at both 6 month and 12 month, between the three ratio groups, that is creatinine clearance varied significantly between groups 1 and 3 and also between groups 1 and 2. CrCl was 79+/-15.9, 66.9+/-15.2 and 61.9+/-15.3 in the three consecutive groups at 6 month post transplant and it was 79+/-16.2, 65.2+/-19.2 and 59.8+/-12.4 in the three consecutive groups at 12 month post transplant, thereby indicating a significant difference in the CrCl between groups 1 and 3 and also between groups 1 and 2 at 6 months and 12 months post transplant. However, DKW/RBW ratio had an insignificant effect on CrCl between groups 2 and 3 at both 6 and 12 month post transplant. Varying DKW/RBW ratios had an insignificant effect on post transplant HTN, NODAT, other complications and ACR between the three groups, that is the risk of post transplant complications was not different between the three ratio groups.

On computing the correlation between DBW and DKW (TABLE-3), it was found that there was a significant positive correlation between the two.

Table 3: Showing the correlation between DBW and DKW

Correlations

		D_WT	DKW
D_WT	Pearson Correlation	1	.636**
	Sig. (2-tailed)		.000
	N	102	102
DKW	Pearson Correlation	.636**	1
	Sig. (2-tailed)	.000	
	N	102	102

**. Correlation is significant at the 0.01 level

DISCUSSION

Renal transplantation offers the best treatment option for patients with end stage renal disease. Besides immunological factors, non-immunological factors contribute to the appearance and progression of Interstitial fibrosis and tubular atrophy (IFTA) and consequently to late graft failure after renal transplantation. One such non-immunologic hypothesis linking chronic decline of graft function to hyper filtration due to nephron under dosing is very attractive. Hyper filtration injuries secondary to an inadequate nephron mass are likely to have an additive effect on the damage caused by immune mediated injuries, and the final pathway of glomerulosclerosis is likely to be initiated when a critically low level of functioning nephron mass is reached. However, the hyper filtration hypothesis has been difficult to prove in clinical transplantation, because the measures of functioning renal mass are currently unavailable, and there may be substantial variability in the baseline nephron numbers across otherwise healthy populations. Compared with deceased donor transplantation, living donor kidney transplantation is the superior setting in which to examine non-immunologic causes of IFTA.

In the present study, DKW was used as the surrogate of nephron number and the aim of present study was to to see if in future proper matching between DKW and RBW can lead to improved outcome after renal transplantation. The present study also showed that the DKW/RBW ratio had an insignificant effect on post transplant SrCr, ACR and also on post transplant complications such as HTN and NODAT.

The study done by Tanveer Iqbal Dar et al,[13] showed that the ratio of DKW to RBW does not have a significant effect on long-term graft function inspite of an early improvement in the function with increased DKW to RBW ratio.

The study done by Yang Qiu et al,[14] measured Donor kidney morphology parameters, esp. DKW using electronic weighing scale and DKV using measuring glass and it concluded that nephron dosing to the recipient's metabolic demands mismatch combined with the age of the donor has a significant impact on the early post-transplant renal function in renal transplant recipients

The study done by Migali Giral et al,[15] concluded that incompatibility between graft and recipient weight (DKW to RBW) is an independent predictor of long-term graft survival, suggesting that avoiding kidney and recipient weight incompatibility may improve late clinical outcome after kidney transplantation.

The study done by Amgad E. El-Agroudy et al. (retrospective study) showed that a low DBW/RBW ratio may lead to inferior long term renal allograft survival.

The study done by Masoud Khosravi et al,[16] demonstrated that 12-month CrCl is influenced by ratio of DKV/RBW. However USG imaging used here provide indirect measure of renal size as USG provides only 2-dimensional measurement.

The study done by Arash Mahdavi et al,[17] cocluded that Renal transplant recipients' volume indices, such as Renal Parenchymal Volume/RBW had strong correlations with eGFR at different points in time, and renal transplant recipients with the volume ratios higher than their cut-off points had a good chance of having a 4-year post-transplantation eGFR higher than 60 mL/min. Here the renal volume was estimated from CT angiography.

The study done by Anjali B. Saxena et al,[18] concluded that transplantation of donor-recipient pairs with a ratio of DKV (as measured by MRI) to RBW of less than 2 cm^3/kg was associated with significantly worse graft function.

Thus, the differences seen in our study with some other studies may be explained in part by the disparity between the number of donor and recipient males and females in this study (Indian study) as compared with other studies, with the fact that there is large predominance of recipient males as compared to recipient females and a large predominance of donor females as compared to donor males. A significant degree of under nutrition and consequent underweight seen among Indian recipients may be responsible for a good RBW being associated with a better prognosis, thereby influencing the effect of DKW/RBW ratio on post transplant CrCl. Also in the present study, Cockcroft-Gault formula was used for measurement of GFR. It must be mentioned that the validity of equations to predict GFR in the setting of a solitary functioning allograft has not been fully confirmed and a comparison of DKW/RBW ratio to true GFR (e.g.:inulin clearance) should be undertaken to more rigorously confirm the relationship between DKW/RBW ratio and allograft GFR. The follow –up period of 1 yr does not predict long term patient and graft outcome. Even the correlation between kidney weight and total number of glomeruli is not particularly satisfying.

All in all, our data suggest that the importance of DKW/RBW ratio should not be overemphasized

when matching kidney graft donors and recipients, at least with regard to graft outcome in the short to medium term and some large group studies with rationale selection of donor and recipient males and females are needed to accurately compute the effect of DKW/RBW ratio on patient and graft outcome in live donor renal transplantation.

Limitations of the Study

More number of patients can be recruited in future studies. As recipients were followed up for a period of 1 year only, long term patient and graft outcome cannot be commented upon. This study did not correlate DKW with some other modality like Donor MRI done preoperatively and so appropriate donor as per graft size cannot be selected preoperatively.

CONCLUSION

Till recently among the available parameters, DKW appears to be the best surrogate of nephron number available. As kidney weight and body weight correlate directly the ratio between the weight of the kidney and that of the recipient may be roughly expressed by the ratio between the body weights of the donor and the recipient. The effect of DKW/RBW should not be over emphasized until a method to measure renal parenchymal volume and nephron number more precisely has been developed. As routine weighing of the graft intra operatively is not always practicable and this surrogate index of nephron number is available only when the transplant is already underway, an additional investigational modality to estimate the graph size preoperatively should be planned so that the DKV/size available preoperatively can be correlated with the DKW and donor selection can be done prior to the transplant. More direct 3 dimensional measurements such as by CT scan and MRI or even better modalities are likely to provide more accurate information regarding kidney volume and/or nephron number.

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