Risk Factors Predicting Urological Complications Of Living-Donor Renal Transplantation-A Single Center Experience

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ABSTRACT

Background: Urological complications following kidney transplantation are not unusual and can be associated with risk of graft failure.

Aim of The Work: to estimate occurrence of urological complications following living donor kidney transplantation and correlation with relevant risk factors related to complications development.

Patients and Methods: The current trial was achieved at urology department in the national institute of urology and nephrology and included 240 patients who underwent renal transplantation, data was collected from patient files and recorded, complications were correlated with pertinent risk factors and the influence of complications on graft survival was assessed.

Results: Urological complications occurred in 26.3% of patients. Bacterial infection was the most common early complication (in the first postoperative month) (8.8%), followed by perinephric hematoma urinary leakage, ureteral obstruction and urinary retention. Lymphocele was demonstrated to be the most common late complication (7.9%), followed by erectile dysfunction, vesicoureteral reflux and ureteral stricture. Regarding predictors of occurrence of urological complications, age of the recipient/ donor, gender of the recipient/ donor, diabetes, hypertension, chronic interstitial nephritis, lupus nephritis, double graft artery/ vein and operative duration were non-significant predictors. However, there was statistically significant correlation between occurrence of urological complications and graft survival (P-value<0.05).

Conclusion: Study concludes that urological complications of renal transplantation were common (26%). Bacterial infection was the most common early complication, while lymphocele was the most common late complication. None of the potential risk factors could significantly predict the occurrence of urological complications. However, occurrence of urological complications significantly affects graft survival.

Keywords: Urological complications; living-donor renal transplantation; Single center experience.

INTRODUCTION

A kidney transplant remains the preferable way to replace a kidney for the majority of cases in end-stage renal failure. However, it is not without risks. Individuals who underwent renal transplantation face a steady fight to survive for a long time. The large plurality of transplantation failure is referred to allogeneic immune-mediated injury, recurrent infections or glomerulonephritis, cardiovascular diseases and tumors. However, a number of kidney transplants are lost because of urological complications, especially in the early post-transplant period[1,2].

In spite of large improvement in the field of transplantation, a little minority of renal transplants are still lost because of urological complications. Some of these problems can be traced back to the period of retrieval and implantation. Serial ultrasound screening of the transplanted kidney in the early post-operative period has essential role in early detection. The prognosis is commonly excellent if the complications are early detected and managed[2].

Therefore, recognizing these complications is extremely important for the multidisciplinary management of these patients[3].

The occurrence of urologic complications of renal transplantation varies vastly in the review. The gross occurrence ranges from 3.4–11.2%. intricacies like ureteral stricture, urine leak, symptomatic vesicoureteral reflux (VUR), urolithiasis, bladder outlet obstruction, and urinary tract obstruction from lymphocele are common . Complications are often known as early or late [4,5].

The last decades have seen a considerable lowering in complication rates because of better realization of the biological behavior, development in the techniques of vascular and ureteric anastomosis, and

the availability of effective regimens for immunosupression[2].

The purpose of the current study was to determine the incidence of urological complications after living donor renal transplantation, complications were correlated with pertinent risk factors and the influence of complications on graft survival was assessed.

PATIENTS AND METHODS

This is a retrospective case control study and was carried out at urology department in the national institute of urology and nephrology and included 240 patients who underwent renal transplantation in the period from 2011 to 2019, patients were followed up for at least two years.

Detailed history was taken from all patients included in the study, patients underwent full physical examination and laboratory investigations in the form of urine analysis, blood group, complete blood count , blood glucose, multiscreen panel (calcium, phosphate, AST, urea, creatinine, uric acid), electrolytes (sodium, potassium, chloride, CO2), total and direct bilirubin, albumin and total protein, lipid profile, serology (Hepatitis B, Hepatitis C, CMV, HIV) and human leukocyte antigen (HLA) typing.

Radiological studies included chest X-ray, kidneys, ureters, bladder (KUB) radiography, pelvi-abdominal ultrasound, electrocardiogram, echocardiography, aorto-iliac doppler and ascending cystogram.

Patients underwent Triple Immunosuppression protocol (calcinurin inhibitor, mycophenolate and steroids).

The harvested kidney was immediately immersed in iced saline and perfused with crystalloid solution.

Regarding operative technique: patients were explored via para-rectal, extraperitoneal approach, the right side was preferred as the accessibility of the iliac vein made the operation easier than with the left side.

The peritoneum was withdrawn medially and the retroperitoneal space covering the iliac vessels was advanced. An autologous retractor was placed and the iliac vessels were exposed. Lymphatic tissue overlying the vessels was attached or closed off using electrocautery.

The renal vein was anastomosed to the external iliac vein using proline 5/0 sutures in an end to side fashion, if there were multiple renal veins, the largest might be used, the others were ligated safely due to internal collateralization of the renal venous drainage.

The renal artery was anastomosed using proline 6/0 sutures to the external iliac artery (in 221 cases) or the common iliac artery (in 19 cases) in an end to side way. Multiple donor arteries were encountered in 32 cases. In these cases the donor arteries were anastomosed individually or anastomosed to each other before being anastomosed to the recipient vessels. In most of our cases, the anastomosis ischaemia time ranged between 30 to 60 minutes with a mean duration of 43 +_12.2 minutes.

Immediate diuresis within 10 minutes after release of the vascular clamp was observed in most cases but in 23 cases the start of diuresis was delayed ranging from few minutes to few days.

The ureter was implanted in the bladder via an anti-reflux technique (extra-vesical Lich Gregoire technique) as it is simple, has low incidence of haematuria, requires a lower length of the ureter and is mostly faster than intravesical techniques, and the creation of an anti-flow tunnel inhibits reflux of infected urine into the allograft. Ureteral stents were inserted. A closed suction drain was placed, Foley catheter was left for drainage of the bladder for 5-7 days.

In the first Post-operative day, investigations included CBC, creatinine, urea, sodium, potassium, renal duplex and pelviabdominal ultrasound.Urine output and CVP were evaluated.

Urine output and CVP were followed up every day, while CBC, creatinine, urea, sodium and potassium were followed up every other day for at least 5 days.

Renal duplex was repeated in the fifth postoperative day. Ultrasound CBC, creatinine, urea, sodium and potassium were repeated after 1 month and every 6 months, patients were followed up for at least two years.

Additional investigations were done for complicated cases in the form of urinalysis, urine culture and sensitivity for bacterial infection (UTI), ultrasound and CT for perinephric heamatoma, ultrasound and ascending cystogram for urinary leakage (urinoma), ultrasound for ureteral obstruction, ultrasound and CT for lymphocele, ascending cystogram for vesicoureteric reflux, and penile duplex for erectile dysfunction.

Statistical analysis: Data have been analyzed statistically by univariate and multivariate analysis utilizing SPSS (Statistical Package for Social Sciences) program version 22. To characterize the trial sample, quantitative results e.g. age have been summarized as minimum, maximum, mean and standard deviation. Qualitative results e.g. sex, was tabulated as count and percentage. Student's t-test have been applied to compare continuous multivariate and the chi-squared test for categorical multivariate. In all tests, $P < 0.05$ have been considered to indicate significant differences, the survival of the graft and patients was calculated by using Kaplan-Meier technique with variations in survival computed with the long- rank test, Stepwise logestic regression was used for the multivariate analysis

RESULTS

This study included 240 patients that were subjected to renal transplantation.

Regarding the general characteristics of the patients, the mean age of the recipient was 41.62 years, while the mean age of the donor was 44.33 years. The male to female (M.F) ratio in the recipient was approximately 2:1, while in the donor was approximately 1.5:1. The Incidence of double graft

artery was 13.3%, while the incidence of double graft vein was 8.3% (Table 1).

Urological complications occurred in 26.3% of patients. Bacterial infection was demonstrated to be the most common early complication (in the first postoperative month) (8.8%), followed by perinephric hematoma (1.7%), urinary leakage (1.7%), ureteral obstruction (1.7%) and urinary retention (1.3%). Lymphocele was demonstrated to be the most common late complication(7.9%), followed by erectile dysfunction (2.1%), vesicoureteral reflux (1.7%) and ureteral stricture (1.3%).

As regards the Graft function at the end of follow-up period in the studied sample, the majority of cases had functioning grafts (60.8%), while 33.3% and 4.5% of cases developed chronic kidney disease (CKD) and end stage kidney disease (ESKD) respectively (Table 2).

The mean Graft survival period in the current study was 37.05 ± 17.448 (median was 37 months) and ranging from 6 months to 70 months (Table 3).

Complication free cases demonstrated significant increase in survival in comparison with complicated ones (P<0.05) (Table 4).

The Kaplan Meier assessment of graft survival in the current study showed that the median complete success was 57 months and the median qualified success was more than 60 months (Table 5 and figure.)

The Univariate analysis for predictors of occurrence of urological complications showed that age of the recipient/ donor, gender of the recipient/ donor, diabetes, hypertension, chronic interstitial nephritis (CIN), lupus nephritis, double graft artery, double graft vein and operative duration were non-significant predictors (P>0.05) (Table 6).

Regarding the correlation between occurrence of urological complications and graft survival it was demonstrated that occurrence of urological complications significantly affects graft survival (P<0.05) (Table 7).

Recipient age (years)		Mean 41.62 ± 7.842	Range 22.00- 60.00
Donor age (years)		Mean 44.33 ± 6.249	Range 33.00-55.00
Reciepient sex	Male N (%)	162 (67.5%)	
	Female N (%)	78 (32.5%)	
Donor sex	Male N (%)	142 (59.2%)	
	Female N (%)	98 (40.8%)	
Double graft artery N (%)		32 (13.3%)	
Double graft vein N (%)		20 (8.3%)	

Table (1): General characteristics of the patients.

	All patients (n= 240)
All urological complications	26.3% (63)
Early onset	15.0% (36)
Late onset	12.9% (31)
Early onset complications	
Bacterial infection (UTI)	8.8% (21)
Perinephric hematoma	1.7% (4)
Urinary retention	1.3% (3)
Urinary leakage (urinoma)	1.7% (4)
Ureteral obstruction	1.7% (4)
Late onset complications	
Lymphocele	7.9% (27)
Vesicoureteral reflux (VUR)	1.7% (4)
Erectile dysfunction (ED)	2.1% (5)
Ureteral stricture	1.3% (3)
Graft function at the end of follow-up	
Functioning	60.8% (146)
CKD	33.3% (80)
ESKD	5.4% (13)

12 patients experienced multiple complications

Table 2: Incidence of urological complications, its onset and graft function at the end of follow-up period.

All patients (n= 240)	Mean	Median	Range
Survival (months)	37.05 ± 17.448	37.00	6.00, 70.00

Table 3: Graft survival in the current study.

	Absent complications (n= 165)	Complications (n= 75)	95% CI	P
Survival (months)	38.69 ± 17.301	33.43 ± 17.337	0.51, 10.01	**0.030**

Data is expressed as mean and standard deviation. 95% CI: 95% confidence interval of the mean difference between both groups. P is significant when < 0.05.

Table 4: Comparison of graft survival between patients with and without complications.

	Median	95% CI
Complete success	57.00	52.46, 61.54
Qualified success	More than 60 months	-

Data is expressed as, median and 95% confidence interval.

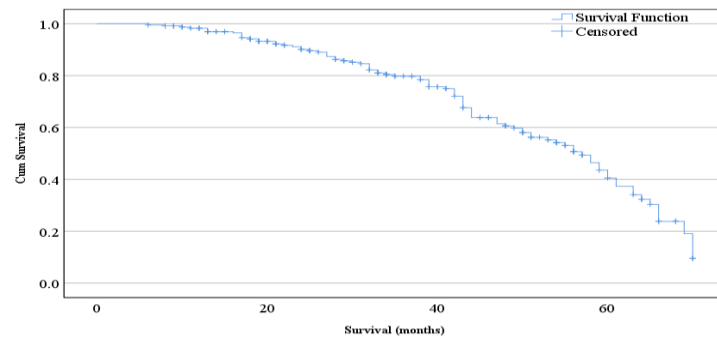**Table 5:** Kaplan Meier assessment of graft survival in the current study.

Fig. 1: a-Kaplan Meier assessment of graft survival with complete success in the current study:
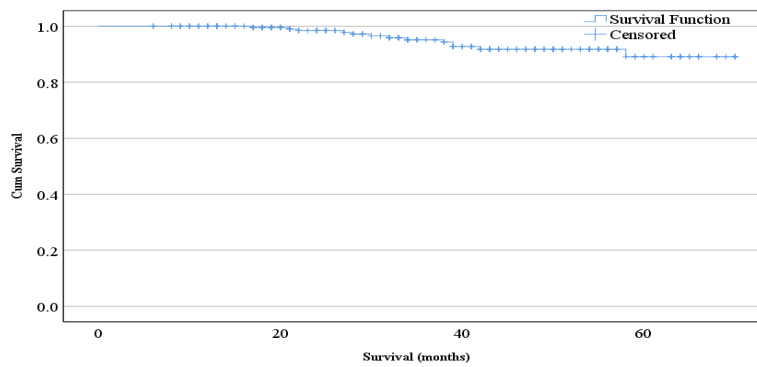

Fig. 1: b-Kaplan Meier assessment of graft survival with qualified success.

Potential risk factor	P	Exp(B)
Recipient age (years)	0.198	0.976
Donor age (years)	0.088	0.959
Female Recipient	0.158	1.539
Female donor	0.829	0.937
DM	0.398	1.306
HTN	0.420	0.694
CIN	0.999	0
Lupus nephritis	0.222	2.094
Double graft artery	0.796	1.116
Double graft vein	0.151	2.000
Duration	0.440	1.373

Exp(B): exponentiation of the B coefficient.

Table 6: Univariate analysis for predictors of occurrence of urological complications .

Variable	Correlation coefficient	P
Occurrence of urological complications	-0.152	**0.019**

Table 7: Correlation between occurrence of urological complications and graft survival.

DISCUSSION

As regards recipient and donor characteristics, the mean age of the recipient was 41.62 ± 7.842, while the mean age of the donor was 44.33 ± 6.249. In addition, M.F ratio was approximately 2:1 in the recipient and approximately1.5:1 in the donor.

While, El- Mekresh et al.[6] conducted their study on 1200 successive living-donor kidney transplants, 892 man and 308 women (mean age 29.8 years, range 5 ± 62; donors 34.9 years, range 17 ± 69).

Urological complications occurred in 26.3% of cases (15% with early onset and 12.9% with late onset).As regards early onset complications: Bacterial infection occurred in 21 patients (8.8% of cases) , all improved on antibiotics, perinephric hematoma occurred in 4 patients (1.7% of cases),all improved on conservative treatment in the form of antibiotics and bed rest, Urinary retention occurred in 3 patients (1.3% of cases), two of them were due to clot retention that was evacuated by catheter irrigation, in one patient while needed cystoscopic evacuation in the other, in the third patient retention was caused by BPH and the patient needed later TURP. Urinary leakage occurred in 4 patients , all improved by prolonged catheter drainage. Ureteric obstruction occurred in 4 patients (1.7%) caused by edema or clot retention and resolved spontaneously in few days.

As regards late onset complications: Lymphocele occurred in 27 patients (7.9% of cases), 19 cases were asymptomatic and resolved spontaneously within 6 weak, 8 patients had hydronephrosis by ultrasound that was confirmed by CT, 5 of them improved by US guided drainage, while 3 patients needed open marcipulization. Vesicoureteric reflux occurred in 4 patients(1.7%) all were stable on conservative treatment in the form of antibiotics with mentainance therapy. ED occurred in 5 patients 2 patients improved on type 5 phosphodiesterase inhibitors while 3 patients discontinued treatment. Ureteric stricture occurred in 3 patients, nephrostomy tube was fixed, in 2 patients antegrade pyelogram showed vesicoureteric junction stricture that needed ureteroneocystostomy, while in the third patient antegrade pyelogram showed pelviureteric junction obstruction that needed endoscopic dilatation.

Slagt et al.[7] demonstrated that, urological complications included, urinary tract infections (23%), surgical site infections (8.8%) Primary non-function (9%) and lymphoceles (3%) .

In addition, Alberts et al.[10] demonstrated that urological complications happened in 12.3% of cases. In 5.2% of cases surgical revision was vital. Surgical intervention included ureteroneocystostomy(71.7%), ureteropyelostomy reconstruction (16.7%) and other techniques.(11.7%)

Moreover, El- Mekresh et al.[6] revealed that complications were detected in 8% of cases, urinary leaks happened in 3.1% of cases, ureteric strictures in 1.9% and lymphoceles leading to ureteric obstruction in 1.4%, Percutaneous needle biopsy was intricated by haematuria and clot anuria in 0.5% of cases. Late problems involved stones (0.9%), bladder tumors (0.3%) and haemorrhagic cystitis (0.17%).

Furthermore, Shokeir et al.[11] displayed that 14% cases encountered urological problems. These problems involved ureteric stricture (4.4%), urinary leakage (4%), intricated lymphocele (3.2%), hematoma requiring surgical intervention (0.8%), wound dehiscence (0.4%) and stone ureter (0.4%).

In terms of lymphoceles, Presser et al.[12] reported symptomatic lymphoceles needing intervention in 2.7% of cases.

Such wide variation in the incidence of urological complications among studies could be explained by several reasons. The first cause was the method of reporting; some authors did not include lymphoceles as a urological complication which was reported to be the most common late complication in the current study and others ignored the UTI which was reported to be the most common early complication in the current study.

Furthermore, the complication rate was slightly higher in patients who received kidneys from living donors than in those who received organs from cadavers; this is presumably a result of more extensive hilar dissection required during harvesting from the living donor, with the attendant risks of injury to the blood supply of the ureter. This may another cause for higher frequency in the current study compared to the other researches.

The current study revealed that, the mean Graft survival period was 37.05 ± 17.448 (median was 37 months) and ranging from 6 months to 70 months.

This came in accordance with Slagt et al.[7] who demonstrated that, the mean graft survival was 4.02 years with a standard deviation of 3.47. Minimum graft survival was 0 day due to primary non function and maximum was 12.1 years. .

As regards graft survival, the current study demonstrated that there was a statistically significant difference among complicated and non-complicated cases ($P<0.05$).

This came in agreement with Choate et al.[3] who demonstrated that, urological complications can have considerable effect on graft function and survival. Another research by Arpali et al[5] found that ureteral stenosis was the only urological complication to have a potent passive association with long-term graft survival. On the other hand, Slagt et al.[7] demonstrated no variation in long term graft survival among the inhabitants with and without urological complications which is confirmed by another investigations van Roijen et al., Dinckan et al., and Alberts et al.. [8,9,10]

Moreover, Shokeir et al.[11] demonstrated that graft survival was not influenced by the incidence of operating complications.

The current study demonstrated that recipient age, donor age, female Recipient, female donor, DM, HTN, CIN, lupus nephritis, double graft artery, double graft vein and duration were non-significant predictors for occurrence of urological complications($P>0.05$).

In agreement Streeter et al.[13] and Dinckan et al.[9] demonstrated that, potent risk factors for urological problems involving age, extended cold ischemia and Diabetes Mellitus were recorded not to perform an essential function in the incidence of urological problems.

On the contrary, Slagt et al.[7] demonstrated in their Univariate analysis that, there was an increase in the number of man donors (p=0.041), man beneficiaries (p=0.002), pre-emptively transplanted beneficiaries (p=0.007), and arterial reconstructions (p=0.004) in the group with urological problems. In addition, low urological problems existed in beneficiaries on hemodialysis (p=0.005). Further total operative interventions (p<0.001), surgical site infections (p=0.042), urinary tract infections (p<0.001) and lymphoceles (p<0.001) existed in the group with urological problems. Variables analysis cleared that man beneficiaries (p=0.010) and arterial rebuilding (p=0.019) were independent risk factors.

In addition, El- Mekresh et al.[6] revealed that, the age of the beneficiaries (< 10 years), procedure of establishing urinary continuity and a high dose of steroids had an independent effective influence on the occurrence of urological problems. Nevertheless, their improvement did not affect graft or patient survival.

Moreover, Shokeir et al.[11] reported in their univariate analysis that, factors which significantly influenced the existence of operative problems were beneficiarie's age, lower urinary tract abnormalities, the type of primary urinary continuity, the time to diuresis, and height and weight of the client. On multivariate analysis, the type of primary urinary continuity was the only factor that assisted statistical significance.

Limitations of the current study included retrospective analysis of data and constant technique of ureteroneocystostomy (extravesical lich gregoire technique with placement of ureteric stents)

CONCLUSION

The current study demonstrated that urological complications of living-donor renal transplantation were common (26%). Bacterial infection was the most common early complication, while lymphocele was the most common late complication.. None of the potential risk factors could significantly predict the occurrence of urological complications. However, occurrence of urological complications significantly affects graft survival.

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