Research Article



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Simultaneous bilateral nephrectomy and living donor kidney transplantation for autosomal dominant polycystic kidney disease, a single center experience

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Abstract

To report the outcome of simultaneous bilateral nephrectomy (SBN) and living donor renal transplantation (LDRT) for Autosomal Dominant Polycystic Kidney Disease (ADPKD) in our center.

Methods: retrospective comparative chart review study between ADPKD patients who underwent SBN and LDRT (group A) and ADPKD patient who underwent LDRT only (group B) at our center.

Results: From May 2010 to August 2017, 7 patients in group A and 15 patients group B were included. Males represented 86% of both groups. Mean patient age (years) and body mass index (BMI) were 46.4 ± 7.6 , 27.2 ± 6.9 vs. 43.1 ± 6.9 , 25.6 ± 4.2 in groups A and B, respectively. Most common indications of SBN were abdominal discomfort and pain (100%); surgeons indicated loss of abdominal domain (57%), early satiety (28%) and hematuria (28%). All patients received kidney from living donors. Mean operative time and estimated blood loss were 379.8 ± 24 min, 130.7 ± 15 vs. 464 ± 30 ml, 170 ± 10 in groups A and B respectively. Average length of stay(days) was 9.4 ± 1 and 7.8 ± 1.1 in groups A and B respectively. All patients had immediate graft function with average serum creatinine(mmol/l) on discharge, one month and last follow up were 85.6, 78.6, 81 vs. 77 ± 17 , 84 ± 12 , 93 ± 8 in groups A and B, respectively. There was no mortality, rejections, wound complications, collections or reoperation in both groups. One year graft and patient survival in both groups was 100%.

Conclusion: SBN and LDRT is an acceptable alternative to a conventional two stage procedure without added morbidity and without significant negative impact on patient and graft survival, obviating the need for a separate procedure.

Abbreviations: SBN: Simultaneous bilateral nephrectomy; LDRT: Living donor renal transplantation; ADPKD: Autosomal dominant polycystic kidney disease; EBL: Estimated blood loss; LOS: Length of stay; BMI: Body mass index; ESRD: End stage renal disease

Introduction

Autosomal dominant polycystic kidney disease (ADPKD) is the most prevalent, potentially lethal, monogenic human disorder [1]. ADPKD is estimated to affect at least 1 in every 1000 individuals worldwide, making this disease the most common inherited kidney disorder with a diagnosed prevalence of 1:2000 and incidence of 1:3000-1:8000 in a global scale [2-4]. It accounts for up to 10% of End Stage Renal Disease (ESRD)cases, and up to 50% of these patients progress to needing renal replacement therapy or transplantation by 70 years of age [5]. ADPKD can cause a range of clinical symptoms related to cyst burden and renal failure, including flank or abdominal pain, bleeding, infection, loss of abdominal domain, nephrolithiasis, anemia, and hypertension [5,6].

The necessity and timing of nephrectomy are debatable [7-11]. Historic treatment for ADPKD and ESRD required nephrectomy to be performed weeks or months before a scheduled transplant, necessitatinga dialysis bridge [6,12]. Otherwise the kidneys were removed months or years following transplantation if symptoms of pain, infection or hematuria persisted [6,13]. In this study, we present our initial experience of SBN and LDRT and review the literature.

Material and methods

Study design

This is a retrospective comparative chart review study between ADPKD patients who underwent simultaneous uni/bilateral native nephrectomies and LDRT (group A) and ADPKD patient who underwent LDRT only (group B) at our center. Standardized donor and recipient selection and management were followed. Donor and recipient records were reviewed, after approval from the Institutional Review Board.

Definitions

DGF was defined as the need for dialysis for any reason in the first week following transplantation [14].

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Donors and recipients evaluation and management

All donors underwent in-depth preoperative pre-transplant medical, psychosocial, and financial evaluation and testing by a multidisciplinary team before the decision was made to proceed with the donation and transplantation respectively. Donors underwent computed tomographic angiography, to evaluate hilar vascularity, as well as the presence of any abnormalities.

Symptomatic recipients were screened with abdominal imaging and computerized tomography of the brain to assess concomitant berry aneurysm. Parameters chosen for examination were age, sex, body mass index (BMI), American Society of Anesthesiology (ASA) class, presence of diabetes mellitus, hypertension, coronary artery disease, congestive heart failure, or other comorbidities, dialysis status, operative time, operative blood loss, transfusion requirement, weight of the removed kidneys, hospital stay, indications for nephrectomy, specimen mass, ICU stay, intra/post-operative complications, and readmissions [6,15].

Post-transplant management

All patients received surgical site prophylaxis with a first-generation cephalosporin for 24 hours, anti-fungal prophylaxis with nystatin or fluconazole for 1 month, and anti-Pneumocystis prophylaxis with sulfamethoxazole-trimethoprim (dapsone if allergic to sulfa) for at least 12 months. Antiviral prophylaxis consisted of oral valganciclovir for 3-6 months, depending on donor and recipient cytomegalovirus serologic status. Post-transplant renal allograft function was evaluated by measuring SCr levels as well as estimating glomerular filtration rate (eGFR) using the abbreviated Modification of Diet in Renal Disease formula to determine the viability of the combined technique [14].

Immunosuppression

Kidney transplant patients received induction immunosuppression with either Basiliximab20 mg infused over 20-30 minutes intravenous as a single intra-operative dose or rabbit antithymocyte globulin at a dose of 1.5 mg/kg (maximum dose, 150 mg based on actual body weight) for 3-7 doses depending on initial graft function. Maintenance immunosuppression consisted of tacrolimus, mycophenolate mofetil (MMF), and steroids.

Post-transplant follow up; recipients are seen weekly for a month, monthly for 6 months, then annually. At each visit we perform a complete physical examination and check vitals, weight, renal profile and eGFR using the Modification of Diet in Renal Disease equation.

Statistical analysis

Endpoints included patient survival as well as uncensored and death-censored graft survival. Other study endpoints included DGF and renal allograft function. Data were placed on an SPSS 15.0(SPSS inc., Chicago, IL) spreadsheet for analysis. We used Chi-Squared and Student's *t* test to compare categorical and continuous variables, respectively. Statistical significance was set at P less than 0.05, and all reported P values are two sided [15]. Categorical data were summarized as proportions and percentages and continuous data were summarized as means and standard deviations [14].

Surgical technique

All patients received a kidney from a live donor. For the first two cases we started with the recipient operation and if the nephrectomies were uncomplicated, we asked the other team to start the donor surgery. Donor and recipient operations began concurrently to minimize anesthetic exposure and ischemic time of the kidney allograft. Following the recipient nephrectomy, the transplant team prepared the target vessels for transplantation. Cold ischemia time rarely exceeds 45 minutes. In the first 3 patients, after finishing the nephrectomies, we closed the laparotomy wound and then performed a classic retroperitoneal kidney transplantation through a separate incision. In the remaining 3 patients the allograft were placed intraperitoneally. Attempts were made to remove the kidneys atraumatically with minimal cyst rupture. The renal hilar vessels were divided and secured by double suture ligation and over sewing. All efforts aimed to spare the adrenal gland in every case. In intraperitoneal allograft transplantation, allograft fixation is essential in the recipient to avoid graft torsion, given the intraperitoneal approach, and the vast amount of space following native nephrectomy [6,16].

Results

During the period between May 2015 and August 2017, 7 patients underwent native nephrectomy and LDRT (group A) and 15 patients with ADPKD underwent LDRT without nephrectomy (group B). Males represented 86% of both groups (6 and 13 in groups A and B respectively). Mean patient age (years) and BMI were 46.4 \pm 7.6, 27.2 \pm 6.9 vs. 43.1 \pm 6.9, 25.6 \pm 4.2 in groups A and B respectively. 5 vs. 10 patients were on hemodialysis while 2 vs. 3 were preemptive transplantation in groups A and B respectively (Tables 1 and 2). In our series, indications for nephrectomy were often multiple for each case with, most commonly, patients reporting abdominal discomfort and pain (100%) and early satiety (28%), hematuria (28%) and surgeons indicated loss of abdominal domain (57%) (Table 1).

All received a kidney from living donors and 4 of the donor nephrectomies were performed laparoscopically. The average donors age (years) and BMI were 30.5 ± 7.6 and 25.75 ± 4.6 vs. 32.6 ± 7.1 and 29.12 ± 2.4 in groups A and B, respectively (Table 3).

4 patients have well controlled hypertension. 6 patients underwent SBN and LDRT while one patient underwent right native nephrectomy and LDRT. One patient underwent cholecystectomy for gallstones (Table 1).

Mean operative time and estimated blood loss were 379.8 ± 24 min, 130.7 ± 15 vs. 464 ± 30 ml, 170 ± 10 in groups A and B respectively. In group A, one patient required blood transfusion, one patient had postoperative lower limb weakness and numbness on the same side of transplantation, andthere was one readmission with picture of intestinal obstruction that improved conservatively (Table 4). Average length of stay(days) was 9.4 ± 1 and 7.8 ± 1.1 in groups A and B respectively. All patients had immediate graft function with an average serum creatinine(mmol/l) on discharge, one month and last follow up were 85.6,78.6,81 vs. $77 \pm 17,84 \pm 12,93 \pm 8$ in groups A and B, respectively (Table 5). Average follow up period in both groups was 54 months (8-71 months). There wasno mortality, rejections, wound complications, collections or reoperation in either group. One year graft and patient survival in both groups was 100% (Tables 6 and 7).

Discussion

The current agreement on the indications for SBN and LDRT is symptomatic ADPKD patients with early satiety, recurrent fever episodes caused by urinary tract infections, cyst rupture, nephrolithiasis, life limiting abdominal/back pain, hematuria or suspected malignancy and the need for space for the allograft [6,10,13,17-21]. In our cohort,

Table 1. Group A patient demographics

Patient	Age	Sex	BMI	Dialysis type	Procedure	Indication	Specimen mass
1	35	F	25.3	PREEMPTIVE	SBN + LDRT (extraperitoneal)	Abdominal discomfort, weight loss, early satity	Right kidney 27x17 cm. Weight 2.52 Kg Left kidney 31x18cm. Weight 2.68 Kg
2	51	М	28.7	HD	SBN + LDRT (extraperitoneal) + cholecystectomy for gall stones	Recurrent pain and hematuria, lack of space	Right kidney 21x14 cm. Weight 1.29 kg left kidney 21x12 cm. weight 1.2 Kg
3	43	М	24	HD	SBN + LDRT (extraperitoneal)	Abdominal discomfort, lack of space	Right kidney 27x11 cm. Weight 1.6 kg left kidney 21x14 cm. weight 1.7 Kg
4	58	М	31	PREEMPTIVE	Rt. Nephrectomy + LDRT	Recurrent pain and hematuria	30X16 Cm. weight 3.6 kg
5	45	М	27.2	HD	SBN + LDRT	Abdominal discomfort, Lack of space	Right kidney 26x13 cm. Weight 2.2 kg left kidney 21x11 cm. weight 1.6 Kg
6	33	М	28	HD	SBN + LDRT	Abdominal discomfort, early satity, hematuria	Right kidney 22x13 cm. Weight 1.6 kg left kidney 22x11 cm. weight 1.3 Kg
7	54	М	23.9	HD	SBN + LDRT	Abdominal discomfort, lack of space	Right kidney 19x13 cm. Weight 1.1 kg left kidney 23x11 cm. weight 1.8 Kg

Table 2. Recipients demographics of both groups

Mean ± SD	Group A	Group B	P Value
Number	7	15	
Age(year)	46.4 ± 7.6	43.1 ± 6.9	0.824
Sex			
М	5	13	
F	1	2	
BMI	27.2 ± 4.6	25.6 ± 4.2	0.084
Dialysis Type			
Preemptive	2	3	
HD	5	10	
PD	0	2	

Table 3. Donors' demographics of both groups

Mean ± SD	Group A	Group B	P value
Age(year)	30.5 ± 7.6	32.6 ± 7.1	0.364
Sex	·		
М	5	11	
F	2	4	
BMI	25.75 ± 4.6	29.12 ± 2.4	0.019
Nephrectomy	·		
- Open	3	3	
- Laparoscopic	4	12	
OR Time(mins)	208.21 ± 71.33	215 ± 42.16	0.041
WIT(mins)	3.2 ± 1.58	4.99 ± 1.02	0.0043

Table 4. Group A recipients' perioperative parameters

Patient	Operative Time(min)	Estimated blood loss(ml)	Transfusion units	Hospital Stay(days)	COMPLICATIONS
1	410	300	0	9	No
2	390	400	0	10	No
3	370	500	0	8	No
4	379	720	2	8	Blood loss required 2 units blood tx
5	350	400	1	12	Left lower limb weakness, improved with PT, the patient has left LL poliomyelitis
6	360	250	0	11	Readmission with picture of intestinal obstruction, improved conservatively
7	410	390	0	9	No

Mean ± SD	Group A	Group B	P Value
Operative Time (min)	379.8 ± 24	130.7 ± 15	< 0.0001
Estimated blood loss (ml)	464 ± 30	170 ± 10	< 0.0001
Transfusion units	2	0	
Hospital Stay (days)	9.4 ± 3	7.8 ± 1.1	0.0783
Complications	-Left lower limb weakness -Blood transfusion	0	
Readmissions	1	0	
Reoperation	0	0	
Mortality	0	0	

Table 5. Recipients' perioperative parameters in both groups

Table 6. Group A Allograft Outcome

Deffered	Mean creatinine (mmol/l) after				
ratient	On discharge	1 month	Last follow up		
1	85	87	85		
2	77	73	68		
3	101	95	92		
4	77	67	73		
5	88	71	87		
6	68	73	71		
7	90	85	97		

Table 7. Allograft outcome in both groups

	Group A	Group B	P Value		
Mean creatinine (mmol/l) ± SD after					
• 7 days	85.6 ± 12	77 ± 17	0.2445		
• 1 month	78.6 ± 14	84 ± 12	0.3615		
Last follow up	81 ± 9	93 ± 8	0.0050		
Immediate graft function	100%	100%			
One year graft survival	100%	100%			
One year patient survival	100%	100%			
Rejections	no	no			

abdominal discomfort and pain was the main indication for SBN followed bythe surgeons indicated loss of abdominal domain, early satiety, then hematuria.

SBN and LDRT have been debated for some time with some authors reporting favorable outcomes for a procedure [6,13,18-23]. The advantages of performing nephrectomy before transplantation include the reduced risk of bleeding, infectious complications, and the risk for tumor development. It also relieves the patient's subjective complaints. In addition, most importantly, it reduces the risk of perioperative complications related to the nephrectomy itself; moreover, prevention of an extra anesthetic/surgical procedure and the anephric/anuric state. SBN also avoids the possibility of sensitization to HLA occurring due to blood transfusion at the time of pre-transplant nephrectomy [7].

Kramer A, *et al.* believed that an interval on dialysis is worth avoiding because neither peritoneal dialysis nor hemodialysis offers the same degree of improvement to quality of life as a functioning renal allograft, since dialysis has been associated with multiple adverse effects such as accelerated atherosclerosis and elaboration of proinflammatory factors that may compromise both patient and graft survival post-transplantation. Furthermore, vascular or peritoneal access for dialysis entails additional risk [6,24-26]. In our study, 5 group A patientswere on dialysis.

Several authors reported that post-operative complications and reoperation rates were not different for SBN versus LRT alone. There wereno adverse effects on graft function and no increased incidence of delayed graft function. Patient and graft survival for groups LRT+SBN were excellent up to the 12-month follow up, commensurate with other reports [7,19,20,27]. Similarly, in our study we have had a few complications that did not lead to mortality or graft loss. The degree of patient satisfaction is another parameter that should be considered. SBN and LDRT are more desirable to patients [8,23]. In the current cohort, 6 of group A patients were very satisfied by the procedure, and only one, who has left lower limb poliomyelitis, was unsatisfied as he developed immediate postoperative motor weakness and numbness on right lower limb that subsequently improved with physical therapy.

In contrast, there are many authors who hold that it is wise to avoid any pre-transplant or simultaneous procedures except in symptomatic cases [10,12,28]. The disadvantage of pretransplantation nephrectomy is that it renders the patient in an anephric and anuric state with all related problems [7,29]. Additionally, pretransplantation nephrectomy adds an operative risk to transplantation, including transplant cancellation due to an unexpected reason, complication in the native nephrectomy, delayed graft function from recipient, sepsis due to the rupture of infectious cysts, graft torsion in the intraabdominal space, significant fluid shifts, hypotension with ensuing allograft hypoperfusion from a significantly larger operation, prolonged anesthetic exposure and side effects of induction immunosuppression [6,7,30]. Furthermore, pretransplantation nephrectomy increases the need for intraoperative and postoperative blood and plasma products associated with adverse effects, such as allergic reactions, infection, immunosuppression, transmission of pro-inflammatory mediators, transfusion related acute lung injury, increased mortality in patients undergoing cardiac surgery and allosensitization, placing the transplant patient at increased risk for acute kidney injury, acute rejection and graft loss [7,16,31]. Interestingly, Ahmad SB, et al. reported that despite SBN and LDRT patients receiving more blood transfusions had a lower rate of total acute rejection episodes than those who received LDRT alone [16].

Ahmad SB, *et al.* indicated that the extensive dissection required during removal of the large, cystic kidneys, some with scarring due to chronic infection or inflammation, was associated with more intraoperative complications such as damage to major vessels, liver, and spleen. Other disadvantages of nephrectomy include increases in hospital length of stay, postoperative pain, delay in return to ambulation, and prolonged ileus. The intra-abdominal portion of BN commonly causes a post-operative ileus [16]. In this study there was moderate bleeding during the right native nephrectomy, due to a slipped renal vein ligature, that required blood transfusion, however there were no visceral injuries.

Kramer A, *et al.* reserved staged nephrectomy for cadaveric kidney recipients with ADPKD while performing SNB and LDRT for living donor kidney recipients; they believed that the simultaneous approach would be unsuitable in cadaveric kidney recipients because the success of transplant depends in part on the prompt function of the renal allograft [6].

In one study, the average length of stay for SBN and LDRT, LDRT alone and staged nephrectomy were 6.9, 4.8 and11.8 days respectively [16,20] Despite longer hospital stays, SBN and LDRT not only reduces overall hospital costs incurred by multiple hospital admissions, but also avoids the cost of interim dialysis sessions [16]. In our cohort the mean length of stay was 9.4 \pm 3 and 7.8 \pm 1.1 days in groups A and B respectively.

Ahmad SB, *et al.* reported that readmission rates were slightly higher at 53% and 55% for LDRT alone and SBN + LDRT, respectively,

within 1 year [16]. In our study, one group A patient was readmitted with a picture of intestinal obstruction that responded to conservative management.

The approach to native nephrectomy with APCKD patients has been variable. Nephrectomy can be performed open versus laparoscopically; uni- or bi-laterally; and before, after, or simultaneous with renal transplant [16]. Kramer A, et al. stated that, despite the midline transperitoneal approach, it carries an increased risk of visceral injury, scanning such as the liver laceration. This approach was chosen because it limits the entire procedure to one incision, and the nephrectomies and transplantation can be done through this approach [6]. In our study, for the first 3 patients, after finishing nephrectomies, we closed the midline laparotomy wound and then performed a classic retroperitoneal kidney transplantation through a separate incision. In the remaining 3 patients the allograft were placed intraperitoneally. Despite the large midline incision and dissection, ventral hernia or small bowel obstruction occurrence was not significantly increased in this group compared to LDRT alone [16]. In our study, the mean operative time and estimated blood loss were significantly lower in group B than group A.

The continuing emergence of minimally invasive technology presents new opportunities for ADPKD management. Several studies have reported that laparoscopic BN is safe, feasible, and reduces hospital stay, blood loss, and recovery time in the hands of experienced surgeons [22,32-36]. Ismail, *et al.* compared pretransplant laparoscopic vs concomitant open nephrectomy series of 11 patients, finding they had more major complications, including one graft loss, in addition to a predictable increase in operative time and blood loss [37]. Lipke MC, *et al.* stated that large polycystic kidneys with a volume of greater than 3,500 ml are a major risk factor for conversion to open surgery [33].

Study limitations

This study has inherent limitations, mainly due to the small number of patients, which make the extraction of solid conclusions rather challenging; the decision of the appropriate timing and procedure should be individualized.

Conclusion

Simultaneous bilateral nephrectomy and kidney transplantation can be successfully performed in selected patients in experienced centerswithout significant impact on graft outcomeand should be considered especially in patients who are not on dialysis yet and undergoing preemptive transplantation.

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