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Simultaneous bilateral native nephrectomy and renal transplantation in autosomal dominant polycystic kidney disease

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Abstract
Background: End-stage renal failure patients benefit most from kidney transplantation. Due to big kidneys and organ compression, autosomal dominant polycystic kidney disease patients have high morbidity. Symptomatic polycystic kidney disease patients have many native nephrectomies timing options. The aim of study is to reduce surgery, hospitalization, and anesthetic exposure and assess postoperative morbidity and death.
Method: An analysis was conducted on data acquired retrospectively from 30 patients at a private international hospital in Zheen. An analysis of the results with respect to the following factors was conducted: surgical time, complications, hospital stay duration, perioperative morbidity and mortality, and transplant kidney status.
Results: Twenty patients diagnosed with autosomal dominant polycystic kidney disease underwent simultaneous bilateral native nephrectomy and renal transplantation (Group 1) between January 2014 and January 2019. Ten patients underwent pre-transplant nephrectomy (Group 2). There was no statistically significant variation observed in the duration of hospital stays or operating times. 100% of patients and grafts survived in both categories.
Conclusion: The duration of hospital stays and duration of operations for renal transplantation did not differ significantly between the two groups, according to the findings of our study. Furthermore, we provided evidence that the operation was executed without any or minimal postoperative complications, which resolved without incident.

Keywords: Simultaneous, bilateral, nephrectomy, transplantation, autosomal, dominant, polycystic kidney disease

Introduction
Renal replacement therapy, including kidney transplantation, has significantly advanced medical care in the 20th century. However, selecting the right therapy varies per individual, based on patient priorities and risk assessment. Native nephrectomy, the surgical removal of native kidneys, is sometimes necessary in end-stage renal disease (ESRD) patients undergoing transplantation. Indications for this procedure include symptomatic renal stones resistant to less invasive treatments, high-grade solid renal tumors, symptomatic or infected polycystic kidneys, persistent anti-glomerular basement membrane antibody levels, uncontrolled significant proteinuria, recurrent pyelonephritis, and severe vesicoureteral reflux with infections [1]. Autosomal dominant polycystic kidney disease (ADPKD) is the most common inherited renal disorder, affecting about 1 in 1,000 people globally. It arises from mutations in PKD1 or PKD2 genes, leading to dysfunctional protein products, polycystin 1 and 2, and resulting in abnormal cell growth and fluid accumulation in cysts [2]. ADPKD accounts for up to 10% of ESRD cases, with around 50% of patients requiring renal replacement or transplantation by age 70 [3]. The disease is characterized by multiple bilateral cysts in the kidneys, which gradually diminish renal function, leading to renal failure or ESRD in about 70% of patients [4]. Clinically, most ADPKD patients are asymptomatic, but some experience symptoms like abdominal or flank pain, hematuria, or urinary tract infections [5]. Hypertension is the most common complication, leading to further renal and cardiovascular issues. First-line treatment for hypertension in these patients includes angiotensin-converting enzyme inhibitors, with angiotensin receptor blockers as an alternative [6].

Pain, often due to cyst rupture or nephrolithiasis, is another common symptom [7]. Approximately 30-50% of ADPKD patients will experience a urinary tract infection, and about 9% will have cyst infections requiring hospitalization [8]. Nephrolithiasis, or kidney stones, is another complication, with stones typically composed of uric acid or calcium oxalate [9]. Over 40% of individuals with ADPKD develop gross hematuria, a risk factor for rapid kidney function decline, especially if occurring before age 30 [10]. Other manifestations include extrarenal cysts, commonly seen in the liver, and intracranial aneurysms, which are more prevalent in ADPKD patients than in the general population, particularly in those with a family history of such aneurysms [11]. ESRD occurs in approximately 70% of ADPKD patients by the age of 58, ranking as the fourth leading cause of ESRD in the US and globally [12]. ADPKD is inherited in an autosomal dominant manner, meaning a 50% chance of transmission to offspring of either sex if one parent is affected. About 90% of cases are inherited, while 10% result from new mutations [13]. Diagnosis primarily relies on kidney imaging, such as ultrasound, CT scans, or MRI, with specific criteria based on age and family history [14]. Management of ADPKD focuses on symptom relief, with treatments targeting hypertension, chronic pain, and cyst infections. Recent therapies aim at the underlying pathophysiological mechanisms of the disease, including key signaling pathways [15]. Surgical interventions, like nephrectomy, are considered for refractory hematuria, recurrent infection, chronic pain, or tumor suspicion [16]. The aim of the present study was to show the results of patients who had underwent renal transplantation concurrent with bilateral native nephrectomies in ADPKD.

Method

The study was conducted as a retrospective analysis, focusing on adult patients diagnosed with Autosomal Dominant Polycystic Kidney Disease (ADPKD) who underwent renal transplantation (RT) at our institution. The review spanned from January 2014 to January 2019, examining the institution's kidney transplant database to identify relevant medical records. Patients were categorized into two groups based on their nephrectomy procedures: Group 1 comprised 20 ADPKD patients who underwent simultaneous bilateral native nephrectomy (SBNN) and RT, while Group 2 consisted of 10 ADPKD patients who had a unilateral nephrectomy prior to transplantation. Data regarding operative time, blood transfusion requirements, hospital stay duration, timing of nephrectomy, reasons for nephrectomy, ICU duration, and any complications were extracted from patient records. For Group 1, all patients received bilateral native nephrectomies through an open midline laparotomy. The surgeries utilized the harmonic scalpel Ultracision to reduce postoperative bleeding and lymphatic spread. After nephrectomy, the posterior peritoneal flap was reconstructed to prevent visceral adhesions. During these procedures, a urological team conducted the bilateral nephrectomies, while transplant surgeons performed donor nephrectomies in a nearby operating room. A rotating nurse facilitated communication between the teams, ensuring timely progress and confirming nephrectomy completion before proceeding to critical stages of the donor allograft implantation. The donor kidney was implanted in the recipient's iliac fossa, connecting the donor renal vein to the recipient's external iliac vein and the donor renal artery to the recipient's internal iliac artery. The cold ischemia time was kept under 40 minutes. In all cases, the donor's ureter was reimplanted into the recipient's bladder using the Lich-Gregoire technique, with a Double-J stent placement. In contrast, Group 2 patients underwent unilateral nephrectomy via a retroperitoneal loin incision, followed by renal transplantation through a retroperitoneal Gibson incision. Statistical analysis of the collected data was performed using Microsoft Excel. Descriptive statistics including mean, standard deviation, range, and percentages were calculated for various variables. To determine the relationships between these variables, multivariate analysis was conducted using paired T-tests, considering a p-value of less than 0.05 as statistically significant.

Results

A total of 30 patients of ADPKD involved in this study underwent RT. of these 30 patients, 20 patients had their kidney nephrectomies at the same session with LDRT (group 1). The remaining 10 patients underwent native nephrectomy before renal transplantation (Group 2).

Patient characteristics are listed in Table 1. In Group 1; (12 patients of a total 20) were males, and 8 patients were females, while in group 2; male to female ratio was the same, consisting of 5 female patients and 5 male patients. The mean age in group 1 was found to be (40.45) years, ranging from (19 -53) years. In group2 the mean age was (42.2) years ranging from (33-58) years. The mean BMI in group1 was 31.04, ranging from (29.6-34.6), mean BMI in group2 was 30.38, ranging from (32-29.5).

Table 1: Patient characteristic.

Characteristic	Group 1	Group 2	p -Value
Number of patients	**20 patients**	**10 patients**	
Gender	60% (12/20) Male	50% (5/10) male	0.24032
	40% (8/20) Female	50% (5/10) female	
Mean age	40.45 (19-53)	42.2 (33-58)	
Mean BMI	31.04	30.38	0.0308
Minimum	29.6	32	
Maximum	34.6	29.5	

Indications for nephrectomy were usually several for each patient. Incidences of indications as summarized in Table 2.are pain (25%), UTI (15%), creating space for graft (10%) and hematuria (10%) for group1. Multiple indications were found in 40% of patients. In group 2, multiple indications was found in 50% of patients, creating space (40%), pain (20%), UTI (20%), and hematuria (10%).

Table 2: Indication of nephrectomy

Indications of Nephrectomy	Group 1	Group 2
Hematuria	10% (2/20)	10% (1/10)
Intractable pain	25% (5/20)	20% (2/10)
Tumor suspicion	None	None
UTI	15% (3/20)	20% (2/10)
Creating space	10%(2/20)	40% (4/10)
combination	40% (8/20)	50% (5/10)

Duration of operation of the two groups is listed in Table 3 and figure 4; Total operative time was significantly longer in group 2 than in groups 1. The mean overall duration of operation of group1 was 265.75 (± 14.8 minutes) (95 min. for NN+170.75min. for RT), ranging (295-240) min. The mean overall duration of operation of group2 was 298.5 (±17.48 min.) (110 min. for NN+188.5min for RT), ranging (330-275) min.

Table 3: Duration of operation

Duration of operation (min.)	Group1	Group 2	P value
Mean overall duration (min.)	265.75±14.8	298.5±17.48	0.00043
Mean duration for NN (min.)	95	110	0.23
Mean duration for RT (min.)	170.75	188.5	0.07

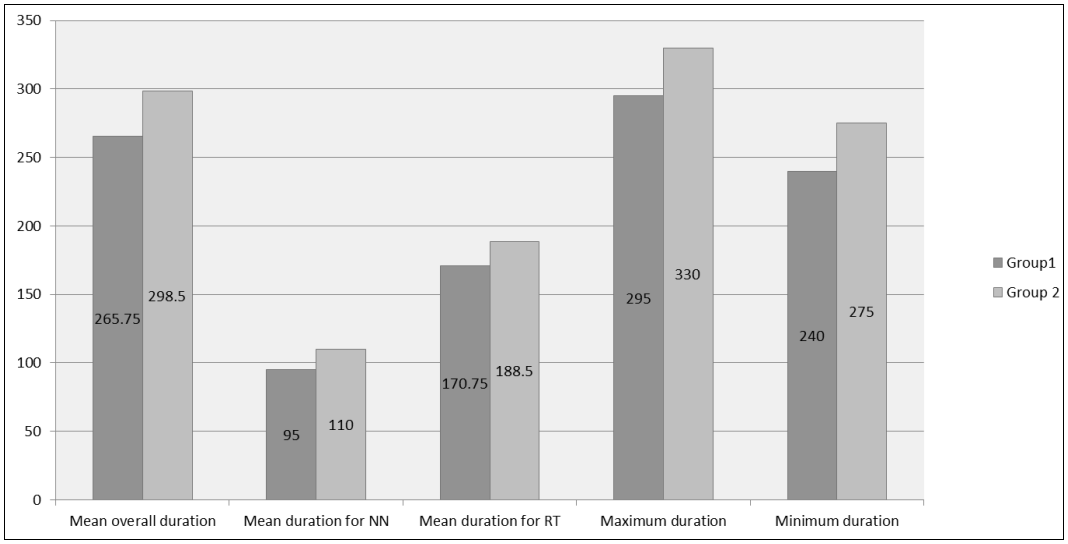

Fig 4: Duration of operation

Table 4 show the difference of length of hospital stay between the groups; Median postoperative length of hospital stay was 6.9 days ± 0.78 (6-8) days for group1. For group2 the average for both procedures was 9.4 days ± 3.9 (8-10) days, that is 3.2 days for NN and 6.2 days for RT.

Table 4: Length of hospital stay

Length of hospital stay in days	Group 1	Group 2		P value
Mean overall Length of hospital stay	6.9 ± 0.78	9.4 ± 3.9		0.000148
		3.2 for NN	6.2 for RT	
Maximum hospital stay	8	10		
Minimum hospital stay	6	8		

Perioperative data is listed in table 5; Mean pre-operative serum creatinine was (5.91mg/dl) in group1 & (6.32 mg/dl) in group 2 and was decreased postoperatively to 0.8 mg/dl & 0.9 mg/dl respectively. Mean pre- operative hemoglobin level was decreased from 10.98 mg/dl to 9.1mg/dl for group1 & from 10.1 mg/dl to 9.22 mg/dl for group 2. Nineteen patients from a total of 20 in group 1 required blood transfusion during perioperative period. In group 2 all the patients required blood transfusion during perioperative period.

Table 5: Patient variables

Patient Variables	Group 1	Group 2	P value
Mean pre op creatinine	5.9 (mg/dl)	6.32 (mg/dl)	
Mean creatinine on discharge	0.8 (mg/dl)	0.9 (mg/dl)	0.09578
Mean pre transplant hemoglobin	10.98 (mg/dl)	10.1 (mg/dl)	0.0128
Mean post transplants hemoglobin	9.1 (mg/dl)	9.22 (mg/dl)	0.2
Number of patients receiving PRBC	95% (19/20)	100% (10/10)	0.123
Number of patients receiving >1PRBC	40% (8/20)	80% (8/10)	

Table 6 summarize complication rate; Complication rate were categorized into surgical and non- surgical complications. Surgical complications were found in 20% of group1, & in 40% of Group 2, while non-surgical complications were found in 20% of Group 1, & in 30% of group 2. One patient in group1 was re operated on the same day because of bleeding and hematoma collection.

There were neither episodes of rejection nor delayed graft function in both groups

Table 6: Complication

Complication	Group 1	Group 2
Surgical complication	20% (4/20)	40% (4/10)
Lymphocele	1/20	2/10
Wound dehiscence/hernia	1/20	0/10
Post-operative haematoma/bleeding	1/20	1/10
Superficial wound site infection	1/20	1/10
Non-surgical complications	20% (4/20)	30% (3/10)
Acute rejection episode	0/20	0/10
Delayed graft function	0/20	0/10
Sepsis	1/20	0/10
Pneumonia	1/20	1/10
UTI	1/20	2/10
ICU admission	1/20	0/10

Graft and patients' survival rates after one month were 100% in both groups. The specimens revealed typical characteristics of ADPKD in all cases, with replacement of renal tissue by multiple cysts.

Discussion

This single-center, retrospective study investigated the outcomes of renal transplantation (RT) in patients with Autosomal Dominant Polycystic Kidney Disease (ADPKD) who underwent native nephrectomy (NN) and RT. The study aimed to identify significant factors influencing transplant outcomes, amidst ongoing debates about the indications, timing, and approach to NN in ADPKD patients. Approximately 20-30% of the ADPKD population require surgery due to their condition [17], but there's controversy over the optimal timing and method for NN [18]. Some advocate for the 'sandwich' technique, involving unilateral nephrectomy before and removal of the remaining kidney after transplantation [19]. Two primary approaches are discussed: the retroperitoneal staged technique, involving ipsilateral concurrent nephrectomy and contralateral nephrectomy at a later date alongside RT [20], and the concurrent bilateral approach for NN and RT via an intra-peritoneal access [21]. However, pre-transplant nephrectomy has been linked with increased morbidity and mortality, leading to the recommendation against routine pre-transplant nephrectomy [22]. The 'sandwich' technique, removing the more severely affected kidney first, then the second post-transplantation, is considered safer [23], but requires three surgical procedures. Our study's methodology involved a midline trans-peritoneal approach, as adopted by Kramer *et al.* [24], to limit the procedure to a single incision, as opposed to multiple incisions which could exacerbate postoperative pain. In our study, patients undergoing concurrent bilateral nephrectomy required less operation time and had shorter hospital stays compared to those in the staged NN and RT group, as the latter involved two separate procedures. Additionally, the need for blood transfusion was higher in the staged group. Complications were categorized into surgical and non-surgical, with a slightly higher rate in the pre-transplant group. All complications were effectively managed without adverse consequences [24]. Our results aligned with studies by Glassman *et al.* [21], Fuller *et al.* [25], Turner *et al.* [26], Kramer *et al.* [24], Nunes *et al.* [27], and Neeff *et al.* [28]. Fuller *et al.* reported that concomitant native nephrectomy could be performed safely, without adversely affecting early graft function [25]. Kramer *et al.* found that simultaneous bilateral nephrectomy combined with living donor transplantation was successful with acceptable complications [24]. This contrasts with Ismail *et al.* findings, which showed a higher rate of surgical complications and graft loss in their patient series [29]. Wu *et al.* research supported our findings that synchronous nephrectomy decreases operation time and the need for separate operations [30], while Wagner *et al.* noted shorter hospital stays in the SBNN+RT group, consistent with our results [31].

Conclusion

In our study, synchronous bilateral native nephrectomy and renal transplantation for ADPKD patients significantly reduced overall operation time and hospital stay, while effectively alleviating all symptoms in a single operation. This combined approach demonstrated minimal postoperative complications, suggesting it as a viable option for end-stage ADPKD patients at transplant centers equipped for such simultaneous procedures.

Conflict of Interest

Not available

Financial Support

Not available

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