



Safety and feasibility of synchronous unilateral nephrectomy and contralateral heminephrectomy for extremely severe autosomal dominant polycystic kidney disease: Techniques and outcome

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Purpose: To demonstrate the safety and feasibility of synchronous unilateral nephrectomy and contralateral heminephrectomy in extremely severe autosomal dominant polycystic kidney disease (ADPKD), which corresponds to the Mayo imaging classification classes 1D and 1E.

Materials and Methods: We retrospectively reviewed patients who underwent unilateral nephrectomy and contralateral heminephrectomy at the Seoul National University Hospital (Seoul, Korea) between May 1, 2016 and August 1, 2021. The preoperative kidney volume was calculated using the ellipsoid equation (length×width×thickness× $\pi/6$). The Mayo imaging classification was determined by height-adjusted total kidney volume and age. Using a midline vertical incision, heminephrectomy was performed first by horizontal transection, followed by contralateral nephrectomy. Hilar vessel clamping or resection-bed suturing was not required.

Results: In all, nine patients with ADPKD of the highest severity (Mayo class 1D/1E) underwent unilateral heminephrectomy and contralateral nephrectomy for the most common cause of severe abdominal discomfort and malnutrition. All nine patients had end-stage renal disease with hypertension and anemia. The median preoperative total kidney volume was 10,905.8 mL (interquartile range [IQR], 8,170.4–16,227.6 mL). The median operation time was 140 minutes (IQR, 125–185 min) and the median estimated blood loss was 250 mL (IQR, 200–425 mL). Eight of the nine patients were discharged without ICU care or any complications. Delayed pseudoaneurysm occurred in one case and was successfully managed by embolization. All patients were symptom-free for a median follow-up period of 2 years.

Conclusions: Synchronous unilateral nephrectomy and contralateral heminephrectomy are safe and feasible treatment options for severe bilateral ADPKD.

Keywords: ADPKD; Feasibility study; Heminephrectomy; Safety

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INTRODUCTION

Autosomal dominant polycystic kidney disease (ADPKD) is a progressive, genetic, and systemic disorder associated with both extrarenal and renal complications [1]. Extrarenal complications occur due to the enlarged mass on the affected kidneys compressing the surrounding tissues, causing abdominal distension, pain, chronic back pain, and malnutrition. Renal complications, on the other hand are directly related to disease etiology. Cystic fluid accumulation causes recurrent infection or hemorrhagic rupture, and gradual loss of renal parenchyma, which is replaced by multiple cysts, causes gross hematuria, and decreases the glomerular filtration rate (GFR), leading to end-stage renal disease (ESRD). Moreover, activation of the renin-angiotensin-aldosterone system causes hypertension and affects multiple organs systemically [2]. An additional problem is that there is no space for kidney transplantation because the kidneys occupy the entire abdominal cavity [3].

Considering that the disease course varies from indolent to rapid growing type and the affected kidney volume shows wide distribution, disease classification is strongly required in making a proper treatment plan [4]. Irazabal et al. [5] recently classified ADPKD patients (from the Mayo Clinic Translational Polycystic Kidney Disease Center) into five different categories according to the image-based measurement of height-adjusted total kidney volume (HtTKV) ranges for age. The classification was validated for its utility in diagnosis, treatment, and prediction of prognosis with regard to renal function deterioration and kidney growth rate [5,6]. Using this imaging classification, Bae et al. [7] further classified the ADPKD disease group into three grades: class 1A, lowest severity; 1B and 1C, intermediate severity; 1D and 1E, highest severity, which was associated with clinical complications.

Accumulating case-based evidence shows that both laparoscopic and open bilateral nephrectomy are feasible and safe treatment options for ADPKD patients [1,8-12]. However, most of the studies demonstrating minimally invasive approaches are limited to the lowest (class 1A) and intermediate (class 1B and 1C) severity groups of patients with a relatively small size of affected kidney and with low morbidity. The highest severity group (class 1D and 1E) tended to have a higher risk of hypertension, low GFR, hematuria, and greater morbidity and mortality during surgical resection [13,14]. In fact, Seoul National University Hospital (Seoul, Korea) previously experienced a 20% rate of immediate or delayed mortality due to acute hypotension in this group of patients. Thus, there are a couple of factors to consider

in surgical treatment planning for these patients. First, the laparoscopic approach is not feasible because of the extremely large kidney volume [13,14]. Second, these patients require a surgical approach that satisfies the conditions of maximal resection of the kidney while at the same time safely preserving a portion of the kidney. The volume reduction method, which is the primary goal of this treatment, is used to eliminate future complications, whereas the volume maintenance method is used to reduce the morbidity and mortality rates driven by an abruptly changed renin-angiotensin-aldosterone axis-induced hemodynamic instability [15].

In this study, we would like to introduce our initial experience with a novel surgical approach for extremely severe ADPKD, which corresponds to the Mayo imaging classification classes 1D and 1E. Unilateral nephrectomy and contralateral heminephrectomy could successfully eradicate disease-associated complications while, at the same time, reducing morbidity by renal volume partial preservation. We believe that this safe and effective surgical approach could be the treatment of choice for extremely severe ADPKD, which harbors different disease courses unlike relatively less severe ADPKDs (lowest to intermediate severity).

MATERIALS AND METHODS

1. Ethics statement

This study was approved by the Institutional Review Board (IRB) of Seoul National University Hospital (approval number: 2108-147-1246). Informed consent was waived owing to the retrospective nature of the study design. The study was performed in accordance with applicable laws and regulations, good clinical practices, and ethical principles, as described in the Declaration of Helsinki.

2. Patient population

We retrospectively reviewed patients who underwent unilateral nephrectomy and contralateral heminephrectomy at the Seoul National University Hospital between May 1, 2016 and August 1, 2021. During this period, nine patients were registered in the database.

3. Kidney volume measurement

The formula for kidney volume calculation is based on the ellipsoid equation ($\text{length} \times \text{width} \times \text{thickness} \times \pi/6$). The parameters were obtained from four measurements with respect to the anterior-posterior, medial-lateral, superior-inferior, and transverse axes, using the axial, coronal, and sagittal sequences in preoperative abdominopelvic computed tomography (APCT). Once the right, left, and total kidney

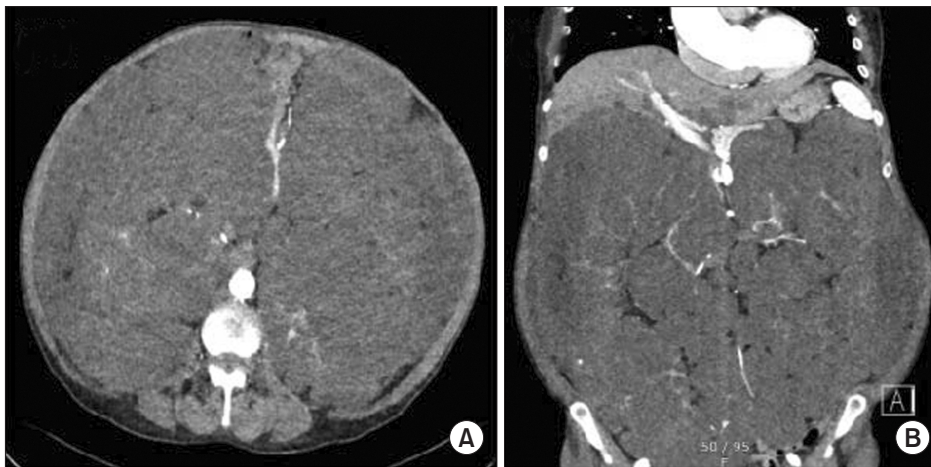


Fig. 1. The representative preoperative abdominopelvic computed tomography of Mayo imaging classification 1E. (A) Axial view. (B) Coronal view.

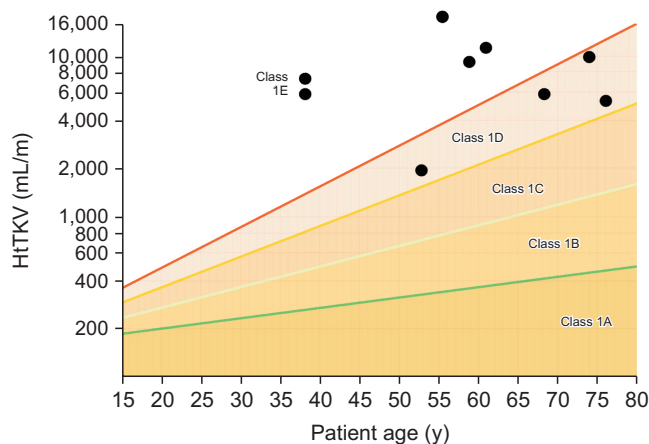


Fig. 2. The distribution of nine patients according to the Mayo classification diagram. Four patients are grouped as class 1D, while the other five are grouped as class 1E. HtTKV, height-adjusted total kidney volume.

volumes (TKVs) were calculated, HtTKV was estimated using the patient's height. Using two parameters, HtTKV and age, the Mayo imaging classification grade was estimated using the following website: <https://www.mayo.edu/research/documents/pkd-center-adpkd-classification/doc-20094754>.

Fig. 1 shows representative APCT images of class 1E, and the distribution of all patients enrolled in this study is shown in Fig. 2.

4. Surgical technique

The patient was first positioned supine on the operating table. A Foley urethral catheter was placed to drain the bladder only if the patient had measurable urine output. Using a single midline vertical incision, heminephrectomy was performed first by horizontal transection to safely preserve the renal volume. In this way, we could cope with the conversion to total nephrectomy due to major vessel injury or collecting system injury by performing contralateral

heminephrectomy instead afterwards. Heminephrectomy is usually performed on the left side if there is no significant difference between right and left kidney size because total nephrectomy on the right side provides more space for the enlarged liver, which is frequently involved as an extrarenal manifestation. Second, it also provides sufficient space for kidney transplantation, which is usually anastomosed to the right iliac fossa. Due to huge volume-induced anatomical disarrangement, ureter identification is the top priority to find the right plane for heminephrectomy. Following the ureter in the cephalic direction, the renal hilum and renal pelvis can be encountered. Heminephrectomy is then performed using electrocauterization through the surgical plane and by concomitantly suturing opened calyces, vessels, or bleeding parenchyma with 5–6 barbed sutures. Patients with ADPKD of the highest severity have very thin renal parenchyma, making this procedure possible with only minimal bleeding without clamping the hilar vessels. For elaborate heminephrectomy completion, the lower major calyces encountered during the plane dissection were completely ligated or sutured. Indeed, large cyst having high risk of rupture, infected cyst, or cyst filled with hemorrhagic fluid were removed. However, small sized cysts were preserved as much as possible to reduce acute complications, such as ileus and peritonitis induced by insufficiently drained remnant cystic fluids [16]. Finally, at the heminephrectomy resection bed, commercial absorbable hemostats, such as Surgicel (Ethicon, Raritan, NJ, USA), Tachosil (Baxter, Deerfield, IL, USA), and Floseal (Baxter), which are sufficient for bleeding control, were applied (Fig. 3).

5. Collected parameters

Patient demographics and clinical data, including reasons for surgery, age at surgery, follow-up period after surgery, preoperative anemia, GFR, bilateral kidney volume, TKV,

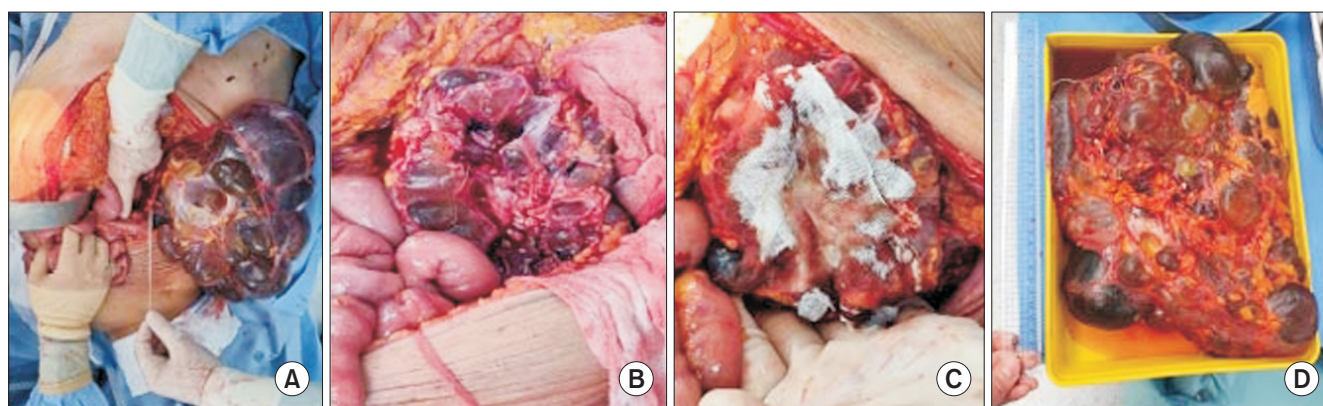


Fig. 3. The operative findings of unilateral nephrectomy and contralateral heminephrectomy. (A) For heminephrectomy, a retroperitoneal dissection was performed to deliver high volume of kidney to secure the surgical field, and ureter identification was primarily performed (ureter retraction with nylon tape). (B) The cross section view of the kidney after heminephrectomy, which shows very thin renal parenchyma and no active bleeding. (C) Floseal and Surgicel were applied on the resection plane. (D) Huge contralateral nephrectomy specimen with preserved cysts after heminephrectomy.

Table 1. Baseline characteristics of patients and indications for surgery

Characteristic	Value
Number of patients	9
Age (y)	62.0 (49.3–73.7)
Sex (male:female)	4:5 (44.4:55.6)
Body mass index (kg/m ²)	25.8 (23.8–29.3)
Systemic effects of kidney failure	
Hypertension	9 (100.0)
Anemia	9 (100.0)
End-stage renal disease	9 (100.0)
Hemodialysis	9 (100.0)
Hemodialysis duration (mo)	11.8 (2.9–73.3)
Scheduled for kidney transplantation	4 (44.4)
Indications for surgery	
Recurrent infection	5 (55.6)
Hemorrhagic rupture	2 (22.2)
Severe abdominal discomfort	6 (66.7)
Malnutrition	5 (55.6)
Uncontrolled pain	5 (55.6)
Postoperative follow-up period (mo)	28.3 (5.9–46.8)

Values are presented as number only, median (interquartile range), or number (%).

largest cystic size, Mayo imaging classification, HtTKV, operation time, estimated blood loss, operation findings, intensive care unit (ICU) care event, drain removal date, and the type and severity of complications, were collected.

RESULTS

Nine patients (4 males and 5 females) with ADPKD of the highest severity (Mayo class 1D or 1E) underwent unilateral nephrectomy and contralateral heminephrectomy

during the study period (Table 1). The median age of the patients was 62.0 years (interquartile range [IQR], 49.3–73.7 y). The patients' median body mass index was 25.8 kg/m² (IQR, 23.8–29.3 kg/m²), which is considered overweight according to the World Health Organization (WHO) Asian classification [17]. All nine patients had ESRD, with hypertension and anemia. All patients received regular hemodialysis for a median duration of 11.8 months (IQR, 2.9–73.3 mo), but no patient underwent peritoneal dialysis. Only four of the nine patients were scheduled for elective kidney transplantation. Severe abdominal discomfort (n=6, 66.7%), malnutrition (n=5, 55.6%), uncontrolled pain (n=5, 55.6%), and recurrent infection (n=5, 55.6%) were the most common reasons for deciding to undergo surgery. The median postoperative follow-up period was 28.3 months (IQR, 5.9–46.8 mo).

Regarding the preoperative computed tomography findings, the median preoperative right kidney volume was 4,387.2 mL (IQR, 3,576.4–9,624.2 mL) and that of the left kidney was 5,601.2 mL (IQR, 4,366.9–7,325.4 mL) (Table 2). The TKV was 10,905.8 mL (IQR, 8,170.4–16,227.6 mL), which was approximately more than two-fold larger than the previous case-series reports [8,9,13,18–20], and the median HtTKV was 6,963.8 mL/m (IQR, 4,992.6–9,971.3 mL/m). Five patients were in class 1E, and the other four patients were in class 1D. The median size of the largest kidney cyst was 6.6 and 6.5 cm for right and left kidneys, respectively. As regards laterality, right-side nephrectomy and left-side heminephrectomy were more common (n=7, 77.8%). For heminephrectomy, all cases preserved the upper half of the parenchyma, including the renal pelvis and hilum, while resecting the lower half.

In terms of perioperative findings, the median operation time was 140 minutes (IQR, 125–185 min) and the median

Table 2. Preoperative Mayo imaging classification and laterality

Patient	RK volume (mL)	LK volume (mL)	TK volume (mL)	HtTKV (mL/m)	Mayo class	Largest RK cyst (cm)	Largest LK cyst (cm)	Nephrectomy laterality	Heminephrectomy laterality
1	1,499.8	1,467.5	2,967.3	1,752.1	1D	6.6	6.5	Right	Left lower
2	4,387.2	5,432.0	9,819.2	5,789.6	1E	5.9	6.5	Right	Left lower
3	9,180.9	5,146.9	14,327.8	8,982.9	1E	8.6	5.2	Right	Left lower
4	5,126.7	6,224.3	11,351.0	6,963.8	1E	6.4	6.9	Right	Left lower
5	3,222.5	3,586.8	6,809.3	4,288.0	1D	3.7	4.2	Right	Left lower
6	4,315.1	6,590.7	10,905.8	7,403.8	1D	5.1	6.1	Left	Right lower
7	3,930.2	5,601.2	9,531.4	5,697.2	1D	6.7	7.2	Left	Right lower
8	10,067.4	8,060.0	18,127.4	10,959.7	1E	11.0	13.4	Right	Left lower
9	15,740.0	14,156.0	29,896.0	17,493.3	1E	11.9	11.9	Right	Left lower
Median (IQR)	4,387.2 (3,576.4–9,624.2)	5,601.2 (4,366.9–7,325.4)	10,905.8 (8,170.4–16,227.6)	6,963.8 (4,992.6–9,971.3)		6.6 (5.5–9.8)	6.5 (5.7–9.6)		

Renal volume is calculated by using the ellipsoid formula: volume=length×width×thickness×π/6.
RK, right kidney; LK, left kidney; TK, total kidney; HtTKV, height-adjusted total kidney volume; IQR, interquartile range.

estimated blood loss was 250 mL (IQR, 200–425 mL) (Table 3). Each patient required intraoperative or postoperative transfusion, except for one patient (class 1D), who had the smallest TKV and HtTKV among the nine patients. Eight patients (88.9%) were discharged without significant complications (\geq grade 3 Clavien–Dindo complications) and did not require ICU care. However, in one case, renal artery branch pseudoaneurysm occurred afterward. The patient underwent embolization and received ICU care for 3 days. The median postoperative hospital stay was 7.0 days (IQR, 6.0–10.5 d), which was mainly determined by the surgical drain tube maintenance (period median, 6.0 d; IQR, 4.0–7.0 d). Surgicel was the most common hemostat used in the heminephrectomy resection bed.

The most severe case had a TKV of 29,896.0 mL and an HtTKV of 17,493.3 mL/m (Mayo class 1E), which is about three times larger than that reported in previous studies [1,9]. Preoperative inspection showed huge abdominal distention, and right total nephrectomy with left heminephrectomy was performed (Fig. 4). The operation time was 125 minutes, with an estimated blood loss of 500 mL; however, no intraoperative transfusion was needed. The patient was discharged 6 days postoperatively without complications.

DISCUSSION

Historically, open bilateral nephrectomies for huge ADPKD kidneys have been associated with significant morbidity and mortality rates of up to 38% and 5%, respectively, because they require extensive procedures with significant tissue manipulation and prolonged convalescence [21–24]. Moreover, simultaneous bilateral nephrectomy for particularly large bilateral ADPKD kidneys could cause severe hemodynamic instability in the postoperative period because of the abrupt reduction in renin and angiotensin [15]. According to the previous studies, 50% to 70% of patients experienced postoperative hypotension, requiring inotropic agents and ICU care [18,25,26], which is sometimes refractory and persistent [27,28]. Moreover, considering these patients require dialysis, pre-dialysis hypotension poses a major threat to survival. With this regard, our surgical technique has great advantage in that by preserving approximately 25% of TKV, no patients showed clinically meaningful hypotension.

As a new era of minimally invasive surgery emerges, several groups have been reported to treat ADPKD patients via the laparoscopic approach. Guo et al. [29] reported a systematic review and meta-analysis comparing laparoscopic versus open nephrectomy, which showed superiority of the laparoscopic approach in reducing complication rates, shorter

Table 3. Perioperative findings and complications

Patient	Operative time (min)	EBL (mL)	Intraoperative transfusion (pack)	Postoperative transfusion (pack)	Clavien–Dindo grade ≥3 complication	ICU care	Drain tube maintenance days	Postoperative hospital days	Hemostat material on heminephrectomy resection bed
1	190	250	0	0	0	0	4	6	Surgicel, Tissel
2	180	200	1	1	0	0	4	12	Surgicel, Tissel, Floseal
3	125	300	2	0	0	0	6	8	Surgicel, Greenplast
4	195	500	1	1	0	0	4	6	Surgicel, Greenplast, Floseal
5	175	200	0	2	0	0	8	14	Surgicel, Veriplast
6	140	200	0	8	Lt. RA injury	1	8	9	Surgicel, Tissel, Tachosil
7	130	150	0	2	0	0	6	7	Surgicel, Tissel, Hemopatch
8	125	350	2	2	0	0	6	7	Surgicel, Floseal
9	125	500	0	2	0	0	5	6	Surgicel, Floseal, Greenplast
Median (IQR)	140 (125–185)	250 (200–425)	0 (0–1.5)	2.0 (0.5–2.0)			6.0 (4.0–7.0)	7.0 (6.0–10.5)	

EBL, estimated blood loss; ICU, intensive care unit; Lt., left; RA, renal artery; IQR, interquartile range.

length of hospital stay, and less estimated blood loss, while having a longer operative time. They also found that cases of the laparoscopic approach had significantly lower kidney weights compared to open cases. In this context, Lipke et al. [13] reported that kidneys with a volume larger than 3,500 mL are hardly manageable with the laparoscopic approach. In fact, TKV of previous laparoscopic approach cases was approximately 5,000 mL, which is relatively small compared with that of our study, which is 10,905.8 mL (Table 2).

This is the first study performing synchronous unilateral nephrectomy and contralateral heminephrectomy for extremely large kidneys in bilateral ADPKD (class 1D and 1E) for the purpose of both renal volume reduction and preservation. It is encouraging that partial renal volume preservation maintained hemodynamic stability during the post-operative period, and thus no patient required immediate ICU care. Although one patient showed delayed grade 3 complications due to heminephrectomy side renal artery branch pseudoaneurysm followed by embolization, other cases had no complications and no postoperative bleeding. Due to extreme parenchymal thinning, it paradoxically made it easy to perform heminephrectomy by covering the resection bed with commercial hemostats, such as Surgicel, Tissel, and Floseal without additional hilar vessel clamping or bed suturing. Additionally, several surgical considerations or techniques are important to achieve successful morbidity-free surgery. Owing to the possibility of major vessel or collecting system injury, heminephrectomy should be initially performed, followed by total nephrectomy on the contralateral side. Suturing of vessels, major and minor calyces, or bleeding parenchyma with barbed suture while dissecting the plane for heminephrectomy is important to decrease the risk of unpredicted bleeding or urine leakage. For the choice of laterality, total nephrectomy on the right side with heminephrectomy on the left side should be initially considered to secure space for enlarged liver and kidney transplantation. We performed right-side heminephrectomy and left-side total nephrectomy in two cases. The first case had the smallest TKV among the nine cases, offering sufficient space for possible kidney transplantation and had left-side dominant complications with renal cyst infection and hemorrhagic cyst rupture. The second case also had a relatively small TKV (class 1D) and an unusual asymmetrical enlargement of ADPKD with a 1.5-fold larger left kidney. However, all the class 1E cases with extremely large kidneys underwent right nephrectomy with left heminephrectomy.

Although eight of the nine patients received intraoperative or postoperative transfusion, we think this was primarily due to basal preoperative anemia (median preoperative

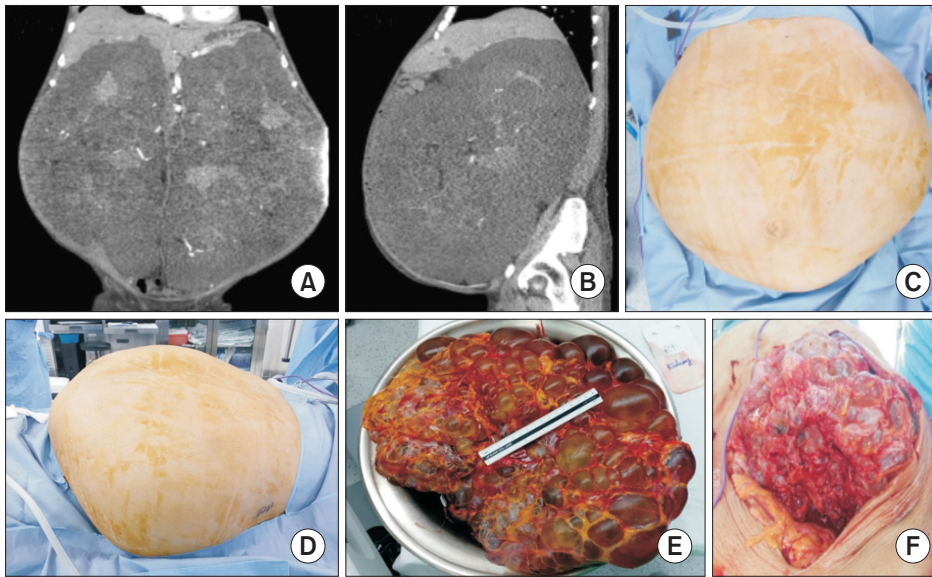


Fig. 4. Demonstration of the most severe of the nine cases. (A, B) Coronal and sagittal view of pre-operative APCT. (C, D) Abdominal distention confirmed by pre-operative inspection. (E) Specimen of right side kidney after total nephrectomy, weighing 13 kg. (F) The cross section view of the left kidney after heminephrectomy.

hemoglobin, 9.5 g/dL; IQR, 8.6–10.8 g/dL) resulting from decreased kidney function. Moreover, transfusion was a prophylactic procedure to prevent further drop of blood pressure, based on the fact that intraoperative blood loss (median 250 mL) was comparable to previous laparoscopic approaches in other studies [1,8,9,12,13,18,19,29,30]. Meanwhile, the median postoperative hospital stay was 7 days, which was slightly longer than that in the previous laparoscopic approaches. This difference might be due to the longer duration of convalescence in open surgery. However, we believe that the major reason for this is the necessity for longer maintenance of the surgical drain tube due to the surgery being performed on approximately more than two-fold larger kidneys than those in previous studies, as mentioned above. Moreover, postoperative hospital days were adjusted for 1 to 2 days longer, according to the patient's dialysis schedule for the patient's convenience.

A limitation of this study is its retrospective nature and the fact that no statistical analysis could be performed due to the small sample size. Furthermore, although perioperative safety and feasibility were confirmed in all nine patients, not all patients were followed up sufficiently to monitor recurrence of complications (four patients with less than 2 years of follow-up). However, we could evaluate the safety and feasibility of a novel surgical approach for class 1D and 1E ADPKD patients. Although the follow-up period varied, no patients showed recurrence of complications originating from the remnant kidney. Prospective and larger cohort studies with longer follow-up periods should be conducted to validate this novel surgical approach as a widely applicable treatment option.

CONCLUSIONS

We demonstrated the safety and feasibility of unilateral nephrectomy and contralateral heminephrectomy for extremely severe ADPKD. Renal volume reduction and partial preservation are both important surgical factors that reduce morbidity and mortality, and eradicate ADPKD-induced medical problems. No patients showed postoperative complication recurrence within a median follow-up period of 2 years.

CONFLICTS OF INTEREST

The authors have nothing to disclose.

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None.

AUTHORS' CONTRIBUTIONS

Research conception and design: Chang Wook Jeong. Data acquisition: Jang Hee Han, Seung-hwan Jeong, and Chang Wook Jeong. Statistical analysis: Jang Hee Han, Seung-hwan Jeong, and Hyeong Dong Yuk. Data analysis and interpretation: Jang Hee Han, Seung-hwan Jeong, and Chang Wook Jeong. Drafting of the manuscript: Jang Hee Han and Chang Wook Jeong. Critical revision of the manuscript: Hyeon Hoe Kim, Curie Ahn, and Chang Wook Jeong. Obtaining funding: Chang Wook Jeong. Administrative, technical, or material support: Curie Ahn and Chang Wook Jeong. Supervision: Curie Ahn and Chang Wook Jeong. Ap-

proval of the final manuscript: Hyeong Dong Yuk, Ja Hyeon Ku, Cheol Kwak, Hyeon Hoe Kim, Curie Ahn, and Chang Wook Jeong.

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