PERITONEAL DIALYSIS CAN BE AN OPTION FOR DOMINANT POLYCYSTIC KIDNEY DISEASE: AN OBSERVATIONAL STUDY

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◆ **Background:** Autosomal dominant polycystic kidney disease (ADPKD) has been considered a relative contraindication for peritoneal dialysis (PD), although there are few specific studies available.

◆ **Methods:** A multicenter historical prospective matched-cohort study was conducted to describe the outcome of ADPKD patients who have chosen PD. All ADPKD patients starting PD ($n = 106$) between January 2003 and December 2010 and a control group (2 consecutive patients without ADPKD) were studied. Mortality, PD-technique failure, peritonitis, abdominal wall leaks and cyst infections were compared.

◆ **Results:** Patients with ADPKD had similar age but less comorbidity at PD inclusion: Charlson comorbidity index (CCI) 4.3 (standard deviation [SD] 1.6) vs 5.3 (SD 2.5) $p < 0.001$, diabetes mellitus 5.7% vs 29.2%, $p < 0.001$ and previous cardiovascular events 10.4% vs 27.8%, $p < 0.001$. No differences were observed in clinical events that required transient transfer to hemodialysis, nor in peritoneal leakage episodes or delivered dialysis dose. The cyst infection rate was low (0.09 episodes per patient-year) and cyst infections were not associated to peritonitis episodes. Overall technique survival was similar in both groups. Permanent transfer to hemodialysis because of surgery or peritoneal leakage was more frequent in ADPKD. More ADPKD patients were included in the transplant waiting list (69.8 vs 58%,

$p = 0.04$) but mean time to transplantation was similar (2.08 [1.69 – 2.47] years). The mortality rate was lower (2.5 vs 7.6 deaths/100 patient-year, $p = 0.02$) and the median patient survival was longer in ADPKD patients (6.04 [5.39 – 6.69] vs 5.57 [4.95 – 6.18] years, $p = 0.024$).

◆ **Conclusion:** Peritoneal dialysis is a suitable renal replacement therapy option for ADPKD patients.

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KEY WORDS: Peritoneal dialysis outcomes; technique failure; dialysis modality; mortality; abdominal wall complications; kidney transplant; comorbidity; peritonitis.

Autosomal dominant polycystic kidney disease (ADPKD) is the most common hereditary disease requiring renal replacement therapy (RRT) (1). In Europe, the annual incidence rate of RRT due to ADPKD is 7.8 cases per million in men and 6.9 in women (2). In the Madrid regional registry (REMER) 6.73% of incident RRT patients in 2011 suffered from ADPKD (3). The Spanish public healthcare system pays for any RRT-related costs. Most ADPKD patients can choose between hemodialysis (HD), peritoneal dialysis (PD) and, if feasible, preemptive renal transplantation. However, some nephrologists do not consider PD a suitable method for ADPKD patients, because of a perceived increased risk of complications and technique failures. The high kidney

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volume may reduce the effective peritoneal surface and increase intraperitoneal pressure, resulting in poor dialysis efficacy and pressure-driven complications. Additionally, cyst infection or abdominal wall complications may impact negatively on patient or technique survival (4,5).

On the other hand, patients with ADPKD tend to be younger with less comorbid conditions and more likely to get a transplant. Thus, they may benefit from a PD-first model, considered for some authors as the most appropriate initial dialysis technique (6).

This study aims to describe the clinical outcomes and polycystic-related PD complications in a clinical practice setting. This will help clinicians to provide reliable information about technique outcomes to ADPKD patients requiring RRT.

MATERIALS AND METHODS

This is a prospective study including every patient starting PD in 19 public hospitals in the central region of Spain. Patients were asked to provide informed consent at initiation of PD. Data collected at data base include: demographic parameters, cause of nephropathy, previous RRT (transfer from HD, graft failure or naïve), reason for choosing PD, comorbidity (Charlson comorbidity index [CCI]) (7) and pre-PD cardiovascular events (stroke, acute myocardial infarction, peripheral arteriopathy). Clinical data were recorded every 6 months from PD program inclusion until the end of the technique for any reason (8). Those data included: dialysis dose (weekly Kt/V) (9), residual renal function, peritoneal transport characteristics (Peritoneal Equilibrium Test), hemoglobin, and blood pressure (BP). Clinical events such as: abdominal wall problems (hernias or leakage), peritonitis (10), and hospitalization events, were also recorded. Patient withdrawal from PD was classified into: recovery of renal function, death, transfer to HD, transplantation, and follow-up loss (transferred to a non-Grupo Centro de Diálisis Peritoneal [GCDP] center) (11). Our central office data manager collected, audited, and debugged the data by ranks and logical routines.

Between January 2003 and December 2010, a systematic sampling identified all ADPKD patients starting PD. The control group was formed by the 2 consecutive patients without ADPKD that initiated PD in the same center (ratio 1:2). This method provided a balanced distribution for both groups in each center.

The first aim of this study was to compare the clinical outcomes of ADPKD and non-ADPKD patients starting PD. The secondary objective was to describe the specific polycystic-related PD complications and their impact on

PD outcomes (cyst infections, abdominal wall problems and required pre-transplantation surgery).

STATISTICAL ANALYSIS

Numerical variables are shown as mean and standard deviation (SD). Comparisons were made by Student t-test or χ^2 test according to the nature of the variables. Survival analysis was assessed by the Kaplan-Meier method until event or December 2010 (censored date). For patient survival analysis, death was the event and for PD technique survival, transfer to HD was the event, considering any other outcome as censored data. For the estimation of time to transplantation, only patients on the transplantation waiting list were included. In all cases, data are shown as mean probability or median of survival and 95% confidence interval (CI). All rates obtained (mortality, hospitalization, and peritonitis) refer to the real PD time for each patient.

RESULTS

A total of 318 patients were included, of whom 61.0% were male, with a mean age of 53.7 years (SD 15.1) (Table 1). The Charlson comorbidity index (CCI) was 4.9 (SD 2.3) and 21.4% were previously diagnosed with diabetes mellitus (DM), while 22% had suffered a cardiovascular (CV) event prior to the start of PD. Patients came from outpatient predialysis chronic kidney disease (CKD) clinics (75.8%), from HD (16.6%) or started PD after a failed transplantation (7.6%). A majority (63.2%) of patients began continuous ambulatory peritoneal dialysis (CAPD) and the rest, automated peritoneal dialysis (APD). The cumulative follow-up time was 557.5 patient-years. Figure 1 shows the patient flow-chart.

The ADPKD group included 106 patients (11.3% of all patients that started PD in this period) and 212 patients were non-ADPKD. Table 1 lists the most relevant clinical data at the time of starting PD for both groups. The total follow-up time of ADPKD patients was 202.1 patient-years with a mean of 1.92 years per patient (range: 1.49 to 6.79 years) and 355.4 patient-years and mean 1.70 years per patient (range: 0.03 to 7.47 years) in non-ADPKD patients. Patients with ADPKD were of similar age to the control group, but had less comorbidity, based on lower CCI [4.3 (SD 1.6) vs 5.3 (SD 2.5) $p < 0.001$], prevalence of DM (5.7% vs 29.2%, $p < 0.001$), and CV events before the start of PD (10.4% vs 27.8%, $p < 0.001$). The percentage of patients with prior HD was also lower in the ADPKD group (7.6% vs 21.1%, $p = 0.004$). There were not significant differences in mean body surface or infusion volumes (data not shown).

TABLE 1
Baseline Data^a

	Total	No ADPKD	ADPKD	<i>p</i> value
N	318	212	106	
Follow-up (patient-years)	557.52	355.43	202.09	
Age (years)	53.71 (15.14)	53.43 (16.53)	54.28 (11.92)	0.6
Male (%)	61	61.4	60	0.8
CV (%)	22.0	27.8	10.4	<0.001
DM (%)	21.4	29.2	5.7	<0.001
Charlson index	4.93 (2.29)	5.27 (2.50)	4.27 (1.58)	<0.001
No patient choice of PD (%)	5.2	6.3	2.9	0.2
Prior HD (%)	16.6	21.1	7.6	
Prior transplantation (%)	7.6	8.6	5.7	0.004
No prior RRT (%)	75.8	70.3	86.7	
APD (%)	36.8	33.7	43.4	0.1
BMI (kg/m ²)	26.37 (4.20)	26.49 (4.34)	26.12 (3.92)	0.47

ADPKD = autosomal dominant polycystic kidney disease; CV = cardiovascular events; DM = diabetes mellitus; PD = peritoneal dialysis; HD = hemodialysis; RRT = renal replacement therapy; APD = automated peritoneal dialysis, BMI = body mass index.

^a Data shown as mean (standard deviation) or percentage.

Figure 1 — Patient flow chart. GCDP = Grupo Centro de Diálisis Peritoneal; ADPKD = autosomal dominant polycystic kidney disease; HD = hemodialysis; TX = transplant; RF = renal function; PD = peritoneal dialysis.

Table 2 presents the most relevant follow-up clinical-target data. Patients with ADPKD had lower systolic blood pressure but higher hemoglobin and baseline Kt/V. There were no significant differences in other parameters, including hospital admissions or peritonitis rates (0.54 vs 0.56 episodes/year). Peritonitis etiology was

similar, including the percentage of enterobacteria (ADPKD 12.8% vs control 11.6%, $p = 0.9$).

A total of 62 abdominal surgical procedures were recorded, including 42 (67.7%) herniorrhaphies, 11 (17.7%) pre-transplant nephrectomies, 7 (11.3%) catheter repositioning and 2 (3.2%) other interventions. Patients with ADPKD needed more pre-transplant nephrectomies (9.4% vs 0.5%, $p < 0.001$) and fewer catheter repositioning interventions (2.8% vs 23.1%, $p = 0.015$) than non-ADPKD. There were no differences in the surgical intervention rates that required temporary use of HD. Only 4 cases required a permanent transfer to HD, all of them ADPKD ($p = 0.22$ with Yates correction).

There were a total of 40 peritoneal leakage episodes with a similar incidence in both groups (ADPKD: 14.2% vs non-ADPKD: 11.8%, $p = 0.55$), mostly pericatheter leaks. Seven out of 106 (6.6%) ADPKD patients were permanently transferred to HD for this reason versus 3 out of 212 (1.4%) patients in the non-ADPKD group ($p = 0.01$).

Ultrasound or CT scan diagnosed 18 cyst infections in 12 different patients. Seventeen episodes required hospital admission for an average of 17.5 days (2 – 96 days). Four nephrectomies were performed for this reason with a definitive transfer to HD in 2 of them.

The mortality rate was lower in ADPKD patients (2.5 vs 7.6 deaths/100 patient-years, $p = 0.02$), without any difference in causes of death (data not shown). The median time to death was higher in ADPKD patients (ADPKD: 6.04 [5.39 – 6.69] vs non-ADPKD: 5.57 [4.95 – 6.18] years, $p = 0.024$) (Figure 2A).

TABLE 2
Baseline Clinical Indicators^a

	Total	No ADPKD	ADPKD	<i>p</i> value
N	318	212	106	
SBP (mmHg)	133.89 (19.65)	136.46 (20.38)	128.62 (16.97)	<0.001
DBP (mmHg)	80.26 (12.26)	80.23 (12.51)	80.31 (11.78)	0.9
BP controlled (%)	50.2	49.3	52	
High SBP (%)	20.3	23	14.7	0.21
BP uncontrolled (%)	29.6	27.8	33.3	
Hb (g/dl)	12.18 (1.50)	11.96 (1.49)	12.63 (1.44)	0.001
Hb >11 g/dl (%)	80.3	75.8	89.2	0.005
D/P Cr4h>0.81 (%)	6.7	7.5	5.1	0.5
Weekly Kt / Vurea basal	2.58 (0.76)	2.52 (0.80)	2.68 (0.65)	0.10
RRF basal (mL/min)	7.4 (4.1)	7.1 (4.4)	7.9 (3.4)	0.10
Total CrCl basal (L/week)	103.0 (128.1)	105.6 (155.5)	97.8 (33.5)	0.64
RRF at 6 months (mL/min)	6.3 (4.3)	6.3 (4.7)	6.3 (3.5)	0.9
Weekly Kt / Vurea at 6 months	2.48 (0.66)	2.51 (0.7)	2.42 (0.59)	0.37
Total CrCl at 6 months (L/week)	88.7 (32.54)	90.48 (34.04)	85.51 (29.57)	0.28
Weekly Kt/V / >1.8 at 6 months (%)	87	84.3	92.4	0.06
Peritonitis rate (episodes/year)	0.55	0.56	0.54	0.78
Hospitalization rate (episodes/year)	0.69	0.72	0.63	0.22

ADPKD = autosomal dominant polycystic kidney disease; SBP = systolic BP; DBP = diastolic BP; Hb = hemoglobin; D/P Cr4h = dialysate/plasma creatinine ratio at 4h in the standard peritoneal equilibrium test; RRF = residual renal function; CrCl = creatinine clearance.

^a Data shown as mean (standard deviation) or percentage. BP controlled ≤135/85; BP uncontrolled >135/85. High SBP >135 mmHg.

The overall rates of PD technique failure (ADPKD: 17.1% vs control: 20.6%) and median time to event were similar for both groups (ADPKD: 6.2 [4.81 – 7.66] years vs non-ADPKD: 6.5 [2.88 – 10.08], $p = 0.255$, Figure 2B). After 3 years, the probability of remaining in PD was 0.74 for ADPKD vs 0.67 for non-ADPKD patients. The most frequent cause of transfer to HD in the ADPKD group was abdominal wall problems (47.1%) vs peritonitis in non-ADPKD patients (37.1%).

The proportion of patients in the transplant waiting list was higher in ADPKD (69.8%) than in the non-ADPKD group (58%) ($p = 0.04$). The mean time to receive a graft was 2.08 [1.69 – 2.47] years, being similar in both groups (ADPKD: 2.14 [1.77 – 2.52] vs non-ADPKD: 2.08 [1.28 – 2.88] years) (Figure 2C).

DISCUSSION

Clinical outcomes of ADPKD patients on PD were at least as good as those of non-ADPKD PD patients. No differences were observed between groups regarding abdominal wall complications or achievement of clinical targets (Kt/V, hemoglobin, BP). This contrasts with former reports (4,12) and with the assumption that ADPKD might be a partial contraindication for PD (13). Indeed, patient survival was higher in ADPKD patients.

Therefore, PD can be an acceptable treatment option for ADPKD patients who choose this home therapy technique.

Renal replacement therapy in Spain is completely paid by the public healthcare system. Patients can choose the dialysis modality (unless there is a clinical contraindication), similar to many Western countries and in contrast with others that use a PD-first strategy (14,15). According to the data from 2011 Madrid RRT registry, end-stage renal disease patients chose HD more often as initial RRT than PD with a ratio of 6 to 1 (3). However, the prevalence of PKD among patients starting HD (14%) is lower than those starting PD (28%) (3).

In our cohort there was no age difference between ADPKD patients and controls, unlike in other reports (15). Some common complications of PD might be more frequent or severe in ADPKD patients. These include abdominal wall complications, the need for pre-transplant nephrectomy because of space constraints (16) and peritonitis (14). However, in the GCDP the temporary transfer to HD due to abdominal complications or the incidence of peritoneal leakage did not differ between ADPKD patients and controls. Furthermore, the incidence, outcome, and etiology of peritonitis were similar in ADPKD and controls. Several reports suggest that enterobacterial peritonitis may have worse outcomes and lead to early technique failure (17) but we did not find differences between groups. Overall

Figure 2 — Kaplan-Meier curves for ADPKD (PKD) and control patients (no PKD). A) Patient survival. B) PD technique survival. C) Transplantation. Only patients on the transplant waiting list were considered for assessment of transplantation. ADPKD = autosomal dominant polycystic kidney disease; PKD = polycystic kidney disease; HD = hemodialysis; PD = peritoneal dialysis.

technique failure rates were similar, whereas a higher rate of transfer to HD because of the specific abdominal wall causes (surgery or leakage) was noted in ADPKD patients. It has been suggested that volume and pressure problems may lead to a lower effective peritoneal surface, worse tolerance and even low dose of dialysis (9,18). However, we found no differences in infusion volume or dialysis dose. The use of cyclers in ADPKD patients could help to avoid these problems.

Kidney transplantation was the leading discontinuation cause of PD in our study and in other GCDP reports. Median PD time before transplantation was around 2 years for patients who were on the transplantation waiting list

(19). The renal transplant rate was higher in the ADPKD group. This may be related to their lower comorbidity.

Several studies have identified younger age and lower comorbidity as factors that could explain a better outcome of ADPKD patients (20). In the present cohort, there was no age difference between ADPKD patients and controls, unlike in other reports (15). For this reason, both groups were more homogeneous and could be properly compared. However, similar to the French Language Peritoneal Dialysis Registry (15), this is especially noteworthy in the prevalence of DM, a poor prognostic factor in PD patients (21), and the number of prior CV events. Kumar *et al.* excluded diabetic

patients and found no difference in survival between ADPKD and non-ADPKD patients (11,20). Patients with ADPKD were more frequently monitored in predialysis CKD-clinics allowing better care and a planned access to PD in optimized conditions. They probably also had improved control of hypertension and anemia, as well as early inclusion on the transplantation waiting list. This is more relevant under an integrated RRT model promoting planned homecare RRT and early transplantation (19).

There are certain limitations to this study that should be discussed and we cannot exclude biases inherent to registry data collection. First, the lower comorbidity and frequent predialysis follow-up of ADPKD patients can positively impact outcomes, thus acting as confounders. Autosomal dominant polycystic kidney disease patients with bigger kidneys may not be offered PD. In this regard, total kidney volume data were not available (22). However, the sample size, similar age of the 2 groups and long follow-up ensure a valuable contribution to our current understanding of PD in ADPKD.

CONCLUSIONS

Peritoneal dialysis in ADPKD patients was associated with a similar overall rate of technique failure as in non-ADPKD patients. Despite this, most technique failures are directly related to ADPKD itself (such as nephrectomy and leakage). Patient survival and transplantation rates for ADPKD compared favorably with non-ADPKD patients. Thus, PD can be an excellent technique to provide RRT to those ADPKD patients who choose it.

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DISCLOSURES

A scientific committee oversees the database, data management, and analyses. Supporters do not have access to the database or analysis before publication. The authors have no financial conflicts of interest to declare.

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