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ORIGINAL ARTICLE

Outcome of autosomal dominant polycystic kidney disease patients on peritoneal dialysis: a national retrospective study based on two French registries (the French Language Peritoneal Dialysis Registry and the French Renal Epidemiology and Information Network)

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ABSTRACT

Background. Pathological features of autosomal dominant polycystic kidney disease (ADPKD) include enlarged kidney volume, higher frequency of digestive diverticulitis and abdominal wall hernias. Therefore, many nephrologists have concerns about the use of peritoneal dialysis (PD) in ADPKD patients. We aimed to analyse survival and technique failure in ADPKD patients treated with PD.

Methods. We conducted two retrospective studies on patients starting dialysis between 2000 and 2010. We used two French registries: the French Renal Epidemiology and Information Network (REIN) and the French language Peritoneal Dialysis Registry (RDPLF). Using the REIN registry, we compared the clinical features and outcomes of ADPKD patients on PD ($n = 638$) with those of ADPKD patients on haemodialysis (HD) ($n = 4653$); with the RDPLF registry, those same parameters were determined for ADPKD patients on PD ($n = 797$) and compared with those of non-ADPKD patients on PD ($n = 12\,059$).

Results. A total of 5291 ADPKD patients and 12 059 non-ADPKD patients were included. Analysis of the REIN registry found that ADPKD patients treated with PD represented 10.91% of the ADPKD population. During the study period, PD was used for 11.2% of the non-ADPKD population. Compared with ADPKD patients on HD, ADPKD patients on PD had higher serum albumin levels (38.8 ± 5.3 versus 36.8 ± 5.7 g/dL, $P < 0.0001$) and were less frequently diabetic (5.31 versus 7.71%, $P < 0.03$). The use of PD in ADPKD patients was positively associated with the occurrence of a kidney transplantation but not with death [hazard ratio 1.15 (95% confidence interval 0.84–1.58)]. Analysis of the RDPLF registry found that compared with non-ADPKD patients on PD, ADPKD patients on PD were younger and had fewer comorbidities and better survival. ADPKD status was not associated with an increased risk of technique failure or an increased risk of peritonitis.

Conclusions. According to our results, PD is proposed to a selected population of ADPKD patients, PD does not have a negative impact on ADPKD patients' overall survival and PD technique failure is not influenced by ADPKD status. Therefore PD is a reasonable option for ADPKD patients.

Keywords: ADPKD, chronic hemodialysis, patient survival, peritoneal dialysis, technical survival

INTRODUCTION

Autosomal dominant polycystic kidney disease (ADPKD) is an inherited disorder that accounts for 6–10% of all patients treated by renal replacement therapy (RRT) each year [1, 2]. The pathological feature of this disease is an increased kidney volume secondary to cyst formation, leading to reduced

intraperitoneal space [3, 4]. In addition, diverticulitis and abdominal wall hernias are also more frequently reported in ADPKD patients [5]. For these reasons, many nephrologists harbour concerns about the use of peritoneal dialysis (PD) in ADPKD patients, thinking that it will be associated with increased complications, more frequent technique failure and possibly increased mortality. However, available data supporting or refuting these fears are limited.

In France, two national nephrology registries coexist, namely the Renal Epidemiology and Information Network (REIN) registry, which aims to collect information on the epidemiology of end-stage renal disease (ESRD) patients as well as their treatment modalities and survival; and second, the French language Peritoneal Dialysis Registry (RDPLF), which collects similar information but specifically for patients treated by PD.

We took advantage of these registries and designed a retrospective study to analyse survival and technique failure among ADPKD patients treated with PD.

MATERIALS AND METHODS

Registries

The REIN was founded in 2001 as a tool to provide support, evaluation and research on public health. It has progressively covered the French territory between 2002 and 2011, with a 100% uptake of patients starting RRT in each participating region. Data are collected prospectively at the initiation of RRT [i.e. haemodialysis (HD), PD or transplantation] for all patients in France with renal failure considered irreversible. Clinical and demographic information are updated annually by a team of 36 clinical research assistants dedicated to the REIN [6].

The RDPLF has recorded PD patients' data since 1986 [7] for patients from metropolitan France, the French departments and territories and also from Algeria, Argentina, Belgium, Switzerland, Tunisia and Uruguay. Data are collected prospectively in real time. However, for the purposes of the present study, only PD patients undergoing treatment in metropolitan France were selected.

Patients

Patients starting dialysis between January 2000 and December 2010 (RDPLF) and between January 2002 and December 2014 (REIN) were included. The follow-up was extended up to December 2015 for both registries. We excluded patients without a diagnosis of nephropathy. We compared clinical features and outcomes of ADPKD patients on PD with those of ADPKD patients on HD (REIN registry). Similarly, clinical features and outcomes of ADPKD patients on PD were compared with those of non-ADPKD patients on PD (RDPLF registry).

Data collection

Baseline parameters collected for each population were age, sex and modified Charlson comorbidity index (CCI) score for the RDPLF registry and age, sex, serum albumin, body mass index (BMI) and a history of diabetes, hypertension, heart failure, coronary heart disease or stroke for the REIN registry.

Overall survival was defined as the time from the start of dialysis to death and technique survival was defined as the time from the start of dialysis to a change of dialysis technique (death and transplantation were considered as competing risk). For transplantation access, transplantation was considered as an outcome and death as the competing risk. Patients who were lost to follow-up and who did not experience an event at the endpoint were censored for the event. Episodes of peritonitis (all micro-organisms and Gram-negative *Bacillus*) were recorded.

Statistical analysis

Continuous data were expressed as mean and standard deviation, qualitative variables as number and percentage. Clinical and biological characteristics of ADPKD patients and non-ADPKD patients were compared (RDPLF registry). A comparison according to the method of dialysis (PD versus HD) was performed (REIN registry). Bivariate analysis was done to compare populations' characteristics using chi-square, Fisher's exact tests, Student or Mann–Whitney tests as appropriate. Variables with a P-value <0.05 by bivariate analysis were used for adjustment in multivariable analysis for technical survival, global survival at 3 and 5 years and transplantation access.

For technical survival and transplantation access, analyses were realized with the Fine and Gray model and results were expressed as the subdistribution hazard ratio (SHR) with 95% confidence interval (CI). The Fine and Gray model was used to take into account competing risks. For global survival, analyses were realized with the Cox regression model and results were expressed as the hazard ratio (HR) with 95% CI.

Statistical analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC, USA).

RESULTS

In France, between 2002 and 2014, 5848 ADPKD patients started RRT and were therefore included in the REIN registry. Among them, 638 patients were on PD, 4653 patients were on HD and 557 patients received pre-emptive kidney transplantation (Figure 1).

During the same period, a total of 12 856 patients started RRT with PD for ESRD. Those patients were therefore included in the RDPLF registry. Among them, 797 patients (6.2%) had ADPKD and 12 059 (93.8%) were non-ADPKD patients.

Baseline characteristics of the patients

Analysis of the general characteristics of the two registries showed that only a minority of ADPKD patients (10.91%) were treated with PD, whereas HD was more frequently used. The prevalence of PD in the non-ADPKD population and during the study period was 11.5%. The median follow-up in each group was 47.9 months (95% CI 0–162.6) for the HD group and 47.9 months (95% CI 0–165.6) for the PD group. In addition, compared with non-ADPKD patients on PD, ADPKD patients were younger (57.7 ± 14.1 versus 63.6 ± 19.1 years; $P < 0.0001$) and had fewer comorbidities as assessed by the modified CCI (2.7 ± 1.2 versus 4.0 ± 2.0; $P < 0.0001$). The baseline

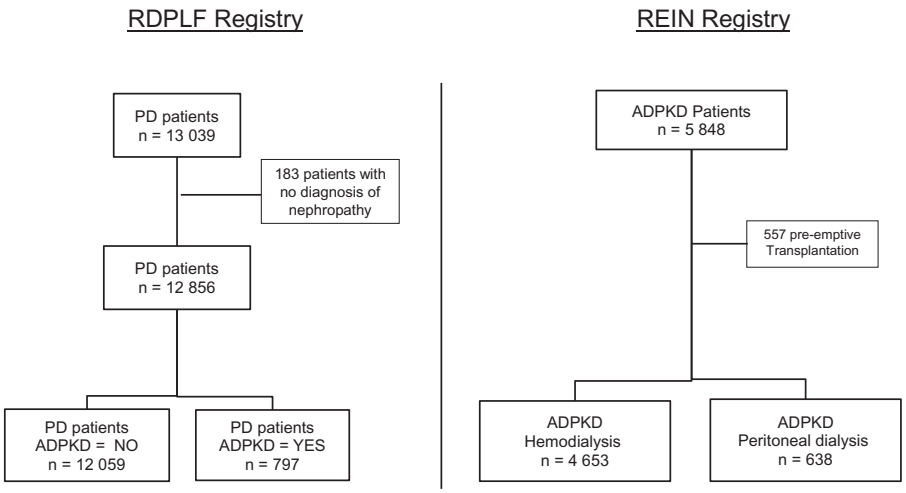

FIGURE 1: Flow chart of the RDPLF and REIN registries.

Table 1. Baseline characteristics of the study population REIN and RDPLF registry

Clincal or Biological Parameter	RDPLF registry—PD patients			REIN registry		
	PD yes, ADPKD no ($n = 12\,059$)	PD yes, ADPKD yes ($n = 797$)	P-value	APKD yes, HD yes ($n = 4353$)	ADPKD yes, PD yes ($n = 638$)	P-value
Gender (male), %	57.6	50.6	0.0001	55.8	51.9	0.002
Age (years), mean ± SD	63.6 ± 19.1	57.7 ± 14.1	<0.0001	59.5 ± 12.9	58.3 ± 13.2	0.02
MCCI, mean ± SD	4.0 ± 2.0	2.7 ± 1.2	<0.0001			
Albumin (g/dL), mean ± SD				36.8 ± 5.7	38.8 ± 5.4	<0.0001
BMI (kg/m^2), mean ± SD				25.2 ± 4.8	25.0 ± 4.0	NS
Diabetes, %				7.7	5.3	0.03
History of hypertension, %				77.1	74.8	0.20
Heart failure, %				9.2	8.0	0.32
Coronary heart disease, %				10.4	7.7	0.04
Stroke, %				5.6	4.6	0.312

MCCI, modified CCI.

characteristics of the patients included in both registries are shown in Table 1.

Outcome of ADPKD patients according to type of dialysis

Patient's survival. We used data from the REIN registry to compare the clinical characteristics and mortality of ADPKD patients on PD with those of ADPKD patients on HD. ADPKD patients on PD were younger (58.3 ±13.2 versus 59.5 ± 12.9; P = 0.02) with slightly higher serum albumin levels (38.8 ± 5.4 versus 36.8 ± 5.7 g/dL; P < 0.0001) and they were less frequently diabetic (5.3 versus 7.7%; P = 0.03).

Mortality rates (at 3 and 5 years) were not different between ADPKD patients on PD and those on HD. Indeed, after 5 years of treatment there was 77 deaths in the PD group (12.1%) versus 635 deaths in the HD group (13.7%) (P = 0.86).

By univariate comparison with HD, PD as the first treatment modality was not associated with an increased risk of death (Table 2). By multivariable analysis, PD was still not significantly associated with an increased risk of death, whereas the presence of diabetes and older age were found to be significant risk factors for death. Conversely, higher albumin level, higher BMI, female sex and access to kidney transplantation were found to have a significant protective effect (Table 2 and Figure 2). Taken together, these results suggest that for ADPKD patients, the use of PD is not associated with an increased mortality risk.

Transplantation. Over the study period, 51.08% of the ADPKD population (PD and HD) underwent transplant. We studied the baseline characteristics of ADPKD patients according to whether or not they underwent transplant. Transplanted ADPKD patients were more often treated by PD rather than HD (59.72% versus 49.89%; P < 0.0001). Furthermore, at the initiation of RRT they had higher levels of albumin (38.3 ± 5.4 versus 35.9 ± 5.8 g/dL; P < 0.0001) and less diabetes (3.7 versus 11.3%; P < 0.0001) (Table 3).

We found that ADPKD patients on PD had greater chances of transplantation compared with ADPKD patients on HD. Indeed, the use of PD was significantly associated with the chance of occurrence of a transplantation event. These results were found using a competitive risk model with death as a competitive event [SHR 1.367 (95% CI 1.227–1.523), P < 0.0001 (univariate) and 1.226 (1.064–1.413), P < 0.005

(multivariable)]. In addition, by multivariable analysis, a higher albumin level was significantly associated with the likelihood of transplantation, while older age was significantly associated with a lower likelihood of a transplantation event.

In agreement with this latter result, the time between the start of dialysis and the transplantation event was shorter for ADPKD patients on PD [27 (95% CI 25–30) months versus 38 (36–40) compared with ADPKD patients on HD; $P < 0.0001$].

Duration of PD use

Switches between types of dialysis were recorded in the REIN registry. Therefore we analysed the frequency of changes in the type of dialysis in ADPKD patients and found that after 3 years of treatment, 23.2% of the ADPKD patients initially treated with PD where switched to HD, whereas only 1.44% of ADPKD patients initially treated with HD had changed their dialysis modality. Similarly, after 5 years of treatment the proportion of patients with a switch was 26.8% among patients initially treated with PD as the first-line modality. We then analysed the factors associated with technique survival. By multivariable analysis using a competitive risk model with death or transplantation as competitive events, we found that, compared with HD, the use of PD in the ADPKD population was significantly associated with an increased risk of a change in the type of dialysis after 3 and 5 years. However, it is noteworthy that the overall proportion of switching in the entire PD population was 29.9% and was not statistically different from that of ADPKD patients. These results suggest that common causes of PD technical failure, such as alteration of the peritoneal membrane, infections, or psychosocial problems, are more likely responsible of these changes in dialysis modality rather than factors related to the ADPKD condition *per se*.

Table 2. Five-year survival of ADPKD patients: multivariable analysis

Parameter	HR (95% CI)	P-value
Dialysis modality (PD)	1.19 (0.87–1.63)	0.27
Serum albumin	0.95 (0.93–0.96)	<0.0001
Female	0.7 (0.58–0.9)	0.003
Age	1.06 (1.05–1.07)	<0.0001
BMI	0.97 (0.94–0.99)	0.04
Diabetes (yes)	1.61 (1.17–2.20)	0.003
Coronaropathy	1.38 (1.06–1.80)	0.01
Transplantation	0.39 (0.27–0.57)	<0.0001

Outcome of ADPKD patients treated by PD

We used the RDPLF registry to compare the outcome of ADPKD patients on PD with that of non-ADPKD patients on PD.

Patient survival. Among PD patients, ADPKD patients had better survival than non-ADPKD patients. Indeed, 3 years after starting PD the number of deaths was 80 (10%) in ADPKD patients versus 3735 (31%) in non-ADPKD patients ($P < 0.0001$). A similar trend was observed after 5 years. ADPKD status was significantly associated with better survival by univariate analysis. This was confirmed by multivariate analysis where ageing and modified CCI were significantly associated with an increased risk of death, while ADPKD status had a significant protective effect (Figure 3A and Table 4).

Transplantation events occurred more frequently in ADPKD patients compared with non-ADPKD patients (42.91 versus 17.35%; $P < 0.0001$).

Duration of PD use. We analysed the risk of technique failure with a Fine and Gray model, considering transplantation and death as a competitive risk for PD failure. We found that ADPKD status was not associated with an increased risk of failure of the PD technique after 3 or 5 years (Figure 3B). Conversely, male patients had a significantly increased risk of technique failure (1.03–1.17; $P = 0.0032$). Interestingly, older age was associated with a small, albeit significant, improvement in technique survival (0.98–0.99; $P < 0.0001$).

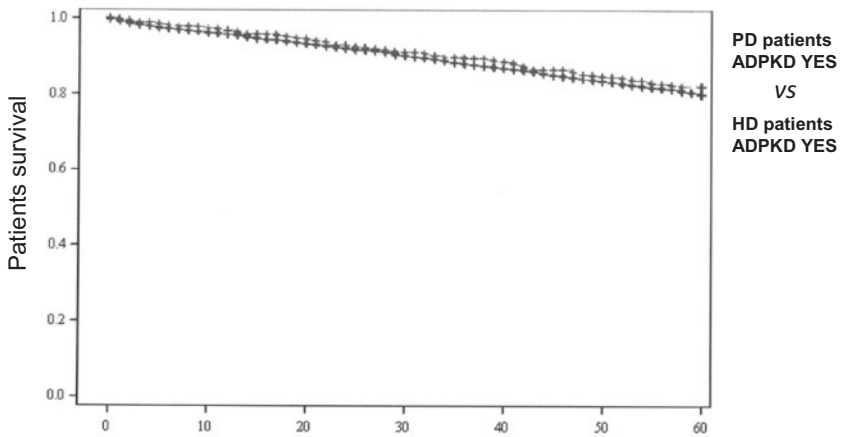

FIGURE 2: Overall survival of ADPKD patients according to dialysis modality. Data analysis from the REIN registry.

Table 3. Clinical and biological features of ADPKD patients (at initiation of dialysis) according to the occurrence of a transplantation event

Parameter	ADPKD patients		P-value
	Transplantation event ($n = 2702$)	No transplantation event ($n = 2588$)	
Age (years), mean ± SD	53.3 ± 9.4	65.7 ± 13.1	<0.0001
Gender (male), %	48.8	55.4	0.003
Albumin (g/dL), mean ± SD	38.3 ± 5.4	35.9 ± 5.8	<0.0001
BMI (kg/m^2), mean ± SD	25.0 ± 4.1	25.4 ± 5.2	0.02
Diabetes, %	3.7	11.3	<0.0001
Peritoneal dialysis, %	9.9	14.1	<0.0001
History of HTA, %	75.9	77.8	NS
Coronaropathy, %	5.0	15.2	<0.0001
Heart failure, %	3.9	14.4	<0.0001
Stroke, %	3.5	7.4	<0.0001

BMI, Body mass index; HTA, history of hypertension; ERA-EDTA, European Renal Association & European Dialysis and Transplant Association

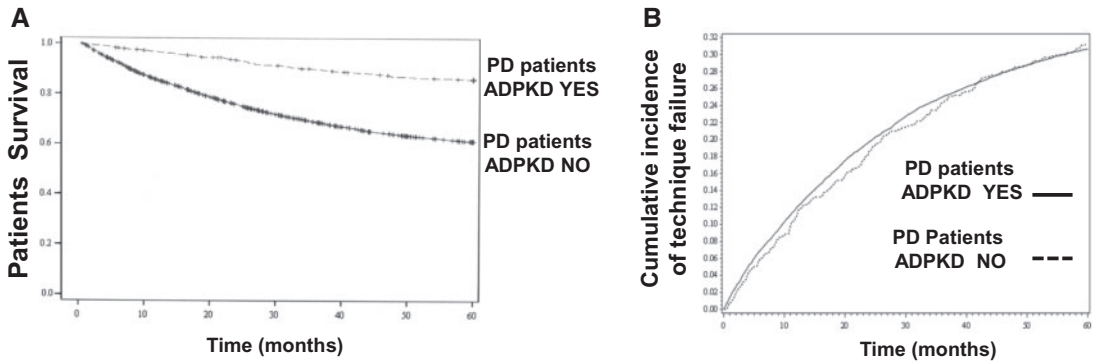

FIGURE 3: **(A)** Overall survival of ADPKD patients on PD compared with non-ADPKD patients on PD. Data analysis from the RDPLF registry. **(B)** Cumulative incidence of technique failure between ADPKD patients and non-ADPKD patients treated with PD (after 5 years). Kidney transplantation and death were considered as competitive risks with a Fine and Gray model. Data analysis from the RDPLF registry.

Table 4. Five-year mortality in patients on PD: multivariable analysis

Parameter	HR (95% CI)	P-value
ADPKD	0.56 (0.45–0.69)	<0.0001
Sex (male)	0.96 (0.90–1.02)	0.72
Age	1.06 (1.05–1.06)	<0.0001
Modified CCI	1.18 (1.16–1.19)	<0.0001

Peritonitis. We analysed the percentage of patients who had at least one episode of peritonitis during the study period and found that 32.4% of ADPKD patients had at least one peritonitis episode ($n = 258/797$) compared with 34.7% of non-ADPKD patients ($n = 4184/12\,059$) ($P = 0.18$) (Figure 5). The average number of peritonitis episodes per patient was 1.9 ± 1.4 in the non-ADPKD group and 2.1 ± 1.5 in the ADPKD group ($P = 0.912$). Furthermore, the median time between initiation of PD and occurrence of the first peritonitis episode was 3.5 years (95% CI 3.3–3.6) for non-ADPKD patients versus 3.6 years (95% CI 3.0–4.4) in the ADPKD group. These findings suggest that ADPKD status is not associated with more peritoneal infection.

Finally, we analysed the frequency of Gram-negative *Bacillus* infections. There was no statistical difference in the occurrence of Gram-negative peritonitis between the two groups (6.9% in ADPKD patients versus 6.1% in non-ADPKD patients; $P = 0.21$) (Figure 4).

DISCUSSION

Peritoneal dialysis is an efficient dialysis modality [8–10]. However, despite its numerous advantages, only 7–10% of patients on RRT are treated with PD [2]. Among the limiting factors that contribute to the underuse of PD, the fear of technique failure is often reported [11].

ADPKD is the leading cause of genetic disorder–related ESRD [1]. In this disease, the progressive increase in the volume of the kidneys secondary to cyst formation is responsible for the progression of chronic renal failure [3, 12]. In addition, the size of the peritoneal cavity is progressively reduced by the increasing kidney and hepatic volumes. Because this reduced peritoneal space could have an impact on the efficiency of PD, we analysed the outcome of ADPKD patients treated with PD compared with ADPKD patients on HD and to non-ADPKD patients treated with PD.

In the first part of the study we used the REIN registry to compare survival and access to transplantation among ADPKD patients according to their type of dialysis (PD versus HD). We

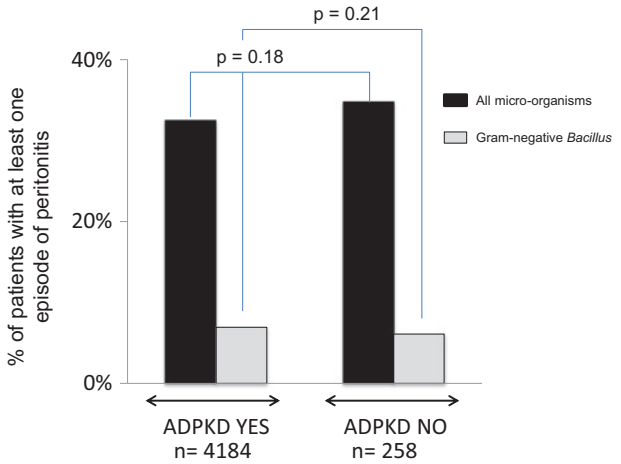

FIGURE 4: Percentage of patients having at least one episode of peritonitis (ADPKD versus non-ADPKD) according to all micro-organisms and Gram-negative *Bacillus*.

found that PD was used in only 10.9% of the ADPKD population. This rate was similar to the prevalence of PD in the general ESRD population of France [13], but still remains low. The prevalence of PD among the ADPKD population is in line with a recent analysis from the European Renal Association & European Dialysis and Transplant Association (ERA-EDTA) registry on the trends in RRT for ADPKD patients over the last 20 years in several European countries [14]. This study reports a decrease in the use of PD as an RRT over the last two decades ranging from 7.1 to 5.8%. This decrease was in agreement with the general trend in the use of PD in other causes of ESRD. In addition, the ERA-EDTA analysis reported a decrease in the use of haemodialysis as an RRT in the ADPKD population (49.1–35.1%) in favour of transplantation, with this latter increasing from 43.5 to 59.1%. Taken together, these results show that PD is underused in the French ADPKD population, as in other European countries.

We then analysed the general characteristics of the French ADPKD population treated with PD. We found that ADPKD patients on PD were younger, had higher serum albumin levels and less diabetes and were more frequently transplanted than ADPKD patients on HD. Our results show that ADPKD patients on PD had fewer comorbidities, suggesting that these patients were probably selected for treatment with PD. To the best of our knowledge, our study is the first to compare the clinical and biological characteristics of ADPKD patients on PD with those of ADPKD patients on HD. Our results indicate that PD treatment is not proposed to all ADPKD patients, but rather to a selected subpopulation with fewer comorbidities. This confirms that nephrologists have an important role in the patient's choice of dialysis modality. Strategies to increase PD prevalence should include information targeting physicians.

Interestingly, we found that the survival of ADPKD patients was not influenced by the type of dialysis. This is an important point confirming that PD had no deleterious impact on the survival of ADPKD patients. Conversely, we did observe that among the ADPKD population, older age and diabetes were associated with an increased risk of death.

To the best of our knowledge, the only report to date reporting the survival of ADPKD patients according to the type of dialysis is a publication from the ERA-EDTA registry [14]. Indeed, Spithoven *et al.* [14] found that the general trend in 2 years survival among ADPKD patients on RRT was towards an increase over the last 20 years, ranging from 88.3% in 1991 to 90.8% in 2006. Analysis according to the type of RRT found a significant reduction in mortality in all RRT modalities. However, the reduction was more pronounced for patients starting on PD (−45%) compared with those who started on HD (−25%), whereas mortality was reduced by 48% in transplanted ADPKD patients. In this same report, the reduction in mortality was mainly in cardiovascular deaths, suggesting that in recent years, significant progress has been made in reducing cardiovascular-related mortality in PD patients. Taken together, these results suggest that the use of PD as RRT for ADPKD patients does not have a negative impact on survival in these patients. Therefore PD is a reasonable option for RRT of ADPKD patients.

In the second part of this study we compared the outcomes of ADPKD patients on PD to those of other (non-ADPKD) patients on PD. We found that ADPKD patients were younger than the general PD population, with fewer comorbidities, leading to better survival. The duration of PD use was similar in both groups, suggesting that a reduction in the peritoneal space and a related increase in intraperitoneal pressure was not associated with increased technique failure for ADPKD patients. Additionally, we did not find any significant difference in the rate of peritonitis in ADPKD patients compared with the general PD population, despite the fact that some reports indicate that ADPKD is associated with an increased risk of diverticulitis, leading to a greater risk of infection with PD. Furthermore, there were no differences in the number of total peritonitis events for each patient presenting a peritonitis complication.

These results are in agreement with previous reports from other national registries, confirming that PD is a reasonable therapeutic option for polycystic kidney disease [15–23]. In the present study, we did not analyse the frequency of occurrence or the impact of abdominal hernias on PD technical outcomes. Indeed, previous reports have suggested an increased frequency of hernias with PD use in ADPKD patients [5, 22]. However, the same studies concluded that abdominal hernias were not associated with an increase in technique failure. Taken together, the results of our study confirm that the use of PD is safe for ADPKD patients.

One of the limitations of our present study is the lack of information on the kidney volume of ADPKD patients on PD. This limitation is related to the design of the study (registry-based study). Indeed, ADPKD is associated with an increase in total kidney volume, but there is substantial heterogeneity between individuals [24, 25]. We did not have the kidney volume data for the patients included in our study and therefore our conclusions may not be generalizable to all ADPKD patients. A recent publication suggests that the outcome of PD in ADPKD patients may be influenced by kidney volume [26]. Hamanoue *et al.* [26] recently reported an increased incidence of abdominal hernia and a higher frequency of reduced volume infusion due to a higher prevalence of abdominal fullness in ADPKD patients with large total kidney volumes. However, this study concerned a limited number of patients and PD adequacy was not evaluated. Hence the impact of reduced volume infusion on PD efficiency was not analysed. Large prospective studies

should be designed to assess the impact of kidney volume on PD outcome.

In summary, in this study we report for the first time a comparison of the clinical and biological features of ADPKD patients according to their dialysis modality. We report that ADPKD patients treated with PD are selected and correspond to those with fewer comorbidities and higher chances of being transplanted. Nevertheless, PD had no negative impact on the survival of ADPKD patients. Additionally, we confirmed that, in comparison with other causes of ESRD, ADPKD patients treated with PD are not exposed to an increased risk of infection or technique failure. Our results plead in favour of wider use of PD in ADPKD patients.

CONFLICT OF INTEREST STATEMENT

None declared.

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