

Identification of the Factors Associated With Intraperitoneal Pressure in ADPKD Patients Treated With Peritoneal Dialysis



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Introduction: Peritoneal dialysis (PD) is reported to be underused in the autosomal dominant polycystic kidney disease (ADPKD) population because doctors fear technical failure caused by reduced abdominal space and high intraperitoneal pressure (IPP).

Methods: We designed a multicenter retrospective study to be carried out in 15 French centers recruiting 60 patients with ADPKD treated with PD to identify factors associated with IPP. Inclusion criteria were start of PD between 2010 and 2017, available tomodensitometry, and IPP measurement in the first year of dialysis. The clinical and radiological data for each patient were reviewed by the same operator. Total kidney volume (TKV), liver volume, and the volume of the abdominal cavity were measured using contouring.

Results: TKV and the volume of the abdominal cavity in women and men were, respectively, 2397 ml versus 3758 ml and 9402 ml versus 12,920 ml. In the univariate analysis, IPP was significantly and positively associated with body surface area ($P = 0.0024$), body mass index (BMI) ($P < 0.0001$), the volume of the abdominal cavity ($P = 0.0005$), and the volume of the dialysate infused in the peritoneal cavity (IPV) ($P = 0.0108$). In the multivariate analysis, only BMI was still significantly associated with IPP ($P = 0.0004$).

Conclusions: Our results identified BMI as the main factor linked to IPP in patients with ADPKD. Despite a reliable assessment of the volume of their organs we did not find any correlation between liver and kidney volumes and IPP. To our knowledge, this is the first study designed to identify factors associated with IPP in patients with ADPKD on PD.

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KEYWORDS: ADPKD; intraperitoneal pressure; peritoneal dialysis

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ADPKD is the most widespread genetic kidney disease leading to end-stage renal disease in Europe and worldwide.^{1–3} PD is underused in this population.^{4,5} In a recent study by our group, we used the French registry REIN (Renal Epidemiology and Information Network) to analyze the characteristics of patients with ADPKD treated with PD compared with those treated with hemodialysis.⁶ We confirmed that only 10.9% of the ADPKD population was treated

with PD. Furthermore, patients with ADPKD on PD had lower comorbidity, suggesting that PD had been proposed to a selected ADPKD population. This selection could at least partially account for the underuse of PD in the ADPKD population.

Recent studies have shown a similar global survival rate for patients with ADPKD treated with PD and those treated with hemodialysis. In addition, the PD technical survival rate is similar in ADPKD compared with patients without ADPKD.^{7–18} Therefore, identification of unbiased criteria for selecting patients with ADPKD for PD treatment could reassure nephrologists and increase the use of PD in this population.

In patients with end-stage renal disease and ADPKD, the presence of enlarged kidneys and enlarged liver is

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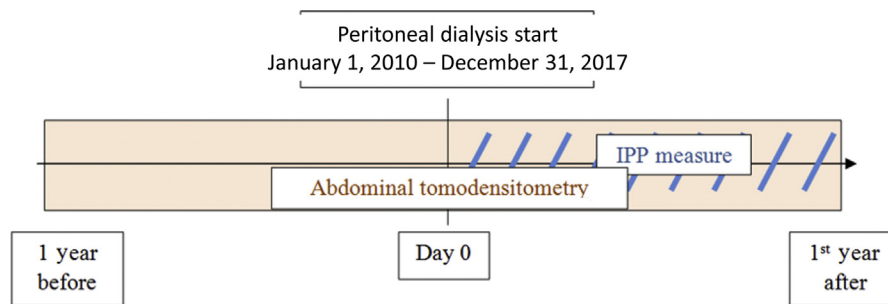


Figure 1. Inclusion criteria for patients with autosomal dominant polycystic kidney disease. IPP, intraperitoneal pressure.

thought to be associated with technical failure, because of reduced abdominal space and high IPP. IPP measurement is routinely used with PD patients for prescription of their dialysis exchange volume management. IPP has been reported to be associated with technical outcomes in the PD population.^{19–23} However, to our knowledge, no study has been addressed to analyzing IPP specifically in patients with ADPKD treated with PD, whereas the present study sought to establish the factors associated with IPP in patients with ADPKD to make it possible to identify those patients who could benefit from PD. We therefore designed a multicenter retrospective study in 15 French centers recruiting 60 patients with ADPKD treated with PD. Our aims were to identify factors associated with IPP in patients with ADPKD on PD, and to test the possibility of creating a score to predict IPP in this population.

METHODS

Study Design

We carried out a national, multicenter, retrospective, cohort study in which 15 French centers participated.

Those included in the study were patients with ADPKD who started PD between January 1, 2010, and December 31, 2017, with (i) available tomography and (ii) IPP measurement in the first year of therapy. A further inclusion criterion was a tomography performed from 1 year before to 1 year after the start of PD (Figure 1).

IPP is a simple, noninvasive technique. It was measured in the supine position as previously described by Durand *et al.*²⁴ Before drainage, the height of the dialysis fluid in the PD line was measured under atmospheric pressure, taking the axillary line as the reference point of the resting subject.²⁴

Patients with a history of nephrectomy or radio-embolization before the start of PD were excluded.

Data Collected

The following clinical data were collected from each patient's medical records: date PD was started, age, sex,

height, weight, BMI, body surface area, history of pregnancy, urinary volume, comorbidities, Charlson Comorbidity Index, IPP value, date of assessment, and IPV.

Centralized reading of all the abdominal tomographies was done in the hospital in Reims by an operator blinded to the clinical data. TKV, liver volume, and the volume of the abdominal cavity were measured by contouring using OxiriX software. The kidneys, liver, and abdominal cavity were manually outlined. The area of each region of interest was calculated and then multiplied by the slice thickness. Finally, all slice volumes were added together to calculate the volume of each 3-dimensional structure (Figure 2).

The volume of the abdominal cavity was defined as the sections located between the bottom of the heart and the top of the bladder. The organ-free volume was defined as the volume of the abdominal cavity without TKV and liver volume.

For the 3 patients who had a history of previous kidney transplantation without transplantectomy, measurement of the organ-free volume excluded the transplantation area.

Statistical Analysis

Quantitative variables were described as mean and SD and qualitative variables were defined as numbers and percentages. Comparisons between clinical and radiological data were investigated with the χ^2 , Fisher's exact, Student's, or Mann-Whitney test, as appropriate. For the correlation of tests of 2 measured parameters, a Pearson's test was performed. A *P* value <0.05 was considered statistically significant.

Linear regression was performed to investigate the relationship between IPP and individual clinical and radiological variables.

Multiple linear regression was performed to identify factors associated with IPP.

We also tried to create a score that would enable us to estimate IPP: for this analysis, the dependent variable was IPP, and the independent variables were the

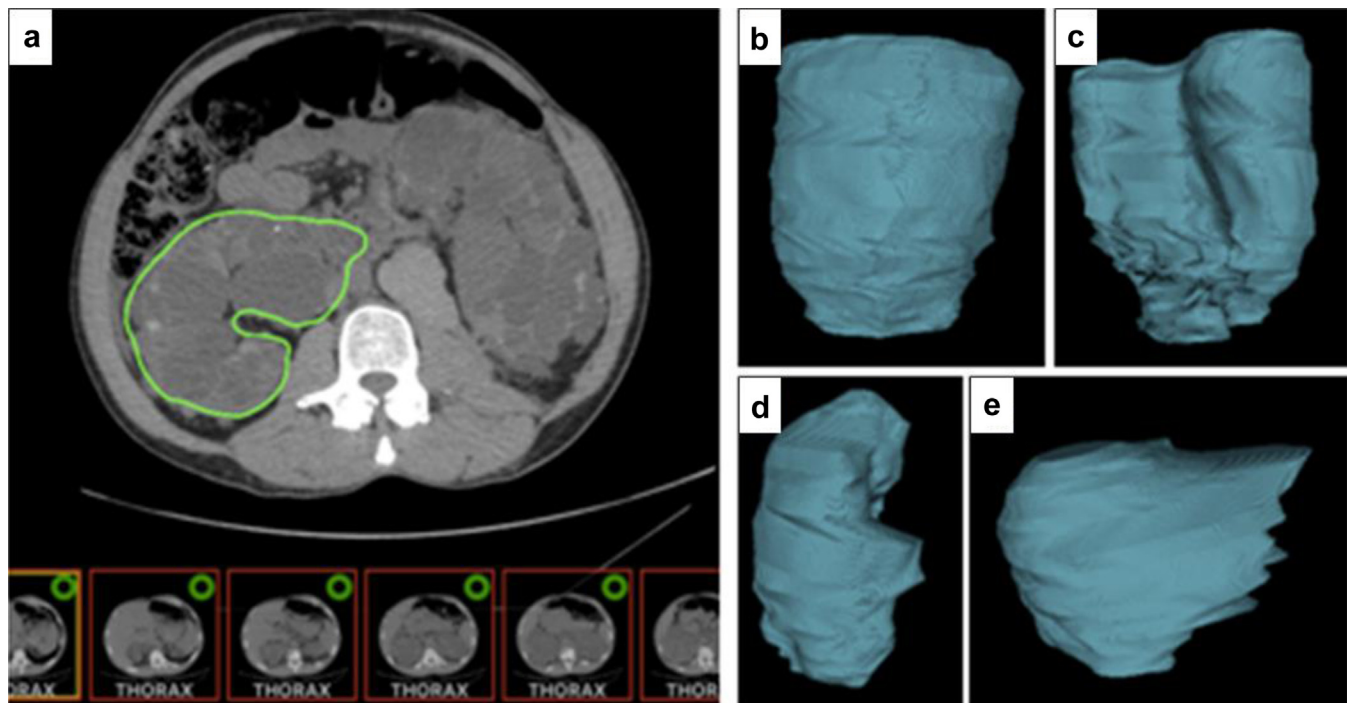


Figure 2. Volume measurement with contouring (OsiriX software, OsiriX Lite, Geneva, Switzerland). (a) Axial section for reconstruction. (b) Abdomen reconstruction and volume measurement: front. (c) Abdomen construction: post. (d) Kidney reconstruction and volume measurement. (e) Liver reconstruction and volume measurement.

clinical and radiological variables with a P value < 0.20 by univariate analysis. Backward selection was used to define the final model (the stay significance level was 0.20).

Concordance between calculated and measured IPP was assessed using an intraclass correlation coefficient.

Analysis was performed using SAS version 9.4 (SAS Institute, Cary, NC).

RESULTS

Baseline Characteristics

Sixty patients with ADPKD from 15 French centers were included in this study.

Table 1. Baseline characteristics of the study population with volume measurements: total kidney volume, liver volume, volume of the abdominal cavity

Baseline data	Total ($n = 60$)	Men ($n = 28$)	Women ($n = 32$)	P
Clinical characteristics				
Age	57 ± 10.7	55 ± 9.9	59 ± 11.1	0.110
Height (m)	1.70 ± 0.1	1.78 ± 0.1	1.63 ± 0.1	<0.0001
Weight (kg)	75 ± 16.1	85 ± 15.3	66 ± 10.9	<0.0001
Body mass index (kg/m ²)	26 ± 4.2	27 ± 4.0	25 ± 4.3	0.077
Body surface area (m ²)	1.87 ± 0.23	2.03 ± 0.20	1.72 ± 0.14	<0.0001
Residual diuresis (ml)	1698 ± 564	1844 ± 538	1570 ± 564	0.060
Comorbidities				
Pregnancy			1.5 ± 1.5	
Charlson score (mean)	3.67 ± 1.54	3.43 ± 1.69	3.9 ± 1.39	0.066
Diabetes (%)	7	11	3	0.331
Coronaryopathy (%)	5	7	3	0.594
Stroke (%)	13	4	22	0.057
History of transplantation (n)	3	2	1	0.594
Dialysis parameters				
IPP (cmH ₂ O)	14.6 ± 3.5	14.9 ± 3.9	14.3 ± 3.3	0.528
IPV (ml)	1793 ± 327	1885 ± 234	1712 ± 377	0.070
Total kidney volume (ml)	3032 ± 1622	3758 ± 1747	2397 ± 1207	0.002
Liver volume (ml)	1936 ± 602	1990 ± 608	1888 ± 602	0.517
Volume of abdominal cavity (ml)	11,044 ± 3164	12,920 ± 3111	9402 ± 2160	<0.0001

IPP, intraperitoneal pressure; IPV, volume of dialysate infused in the peritoneal cavity.

Table 2. Pearson correlation coefficient with *P* of clinical and radiological data

Data	IPP	IPV	BMI	BSA	Pregnancy	Organ volume	Liver volume	Total kidney volume	Volume of abdominal cavity
IPP (cmH ₂ O)	1.000	0.327 0.0108	0.500 <0.0001	0.384 0.0024	-0.201 0.1239	0.094 0.4741	0.109 0.4064	0.059 0.6562	0.436 0.0005
IPV (ml)		1.000	0.301 0.0196	0.368 0.0038	-0.136 0.3000	0.192 0.1422	0.130 0.3217	0.154 0.2414	0.332 0.0096
BMI (kg/m ²)			1.000	0.689 <0.0001	-0.055 0.6750	0.345 0.0069	0.208 0.1112	0.287 0.0264	0.718 <0.0001
BSA (m ²)				1.000	-0.336 0.0086	0.413 0.0010	0.285 0.0273	0.329 0.0101	0.783 <0.0001
Pregnancy					1.000	-0.421 0.0008	-0.068 0.6032	-0.418 0.0009	-0.372 0.0034
Organ volume (ml)						1.000	0.315 0.0142	0.936 <0.0001	0.682 <0.0001
Liver volume (ml)							1.000	-0.039 0.7655	0.275 0.0338
Total kidney volume (ml)								1.000	0.616 <0.0001
Volume of abdominal cavity (ml)									1.000

BMI, body mass index; BSA, body surface area; IPP, intraperitoneal pressure; IPV, volume of dialysate infused in the peritoneal cavity. Bold values are significant.

The main characteristics of the population are described in Table 1. The cohort consisted of 28 men and 32 women. Mean age was 57 ± 11 years. Height, weight, and body surface area were significantly lower in women than in men. The median Charlson's index was 3. Mean IPP was 14.6 ± 3.5 cmH₂O with a median of 14.3 cmH₂O and 17 % ($n = 10$) of the patients had an IPP above the normal range > 18 cmH₂O. Mean IPV was 1793 ml (2000 ml + -100 ml for 40 patients, 1500 ml for 15 patients and 1000 ml for 5 patients) (Table 1).

Mean organ volumes measured using tomodensitometry are reported in Table 1. TKV and the volume of the abdominal cavity were statistically lower in women compared with men, respectively, 2397 ± 1207 ml versus 3758 ± 1747 ml ($P < 0.002$); and 9402 ± 2160 ml versus 12920 ± 3111 ml ($P < 0.0001$). The mean abdominal organ-free volume was 6076 ± 2358 ml.

One year after the start of PD, 45 patients (75%) were still on PD, 2 (3%) had been switched to hemodialysis, and 13 (22%) had received transplantation. No death was recorded during the study period.

Correlation Study

Our next step was to analyze the correlations between clinical and radiological data (Table 2). TKV, liver volume, and the volume of the abdominal cavity were significantly and positively correlated with BMI and body surface area.

Conversely, we did not find a correlation between IPP and the volume of patients' organs, although IPP was significantly correlated with the volume of the abdominal cavity, BMI, body surface area, and IPV (Table 2).

Linear Regression Analysis

IPP was significantly and positively correlated with body surface area ($\beta = 5.86$, $R^2 = 0.148$, $P = 0.0024$), BMI ($\beta = 0.42$, $R^2 = 0.251$, $P < 0.0001$), volume of the abdominal cavity ($\beta = 0.0005$, $R^2 = 0.191$, $P = 0.0005$), and IPV ($\beta = 0.0035$, $R^2 = 0.107$, $P = 0.0108$). The best linear correlation was found between IPP and BMI (Figure 3); however, TKV, ratio of TKV over body surface area, and liver volume were not significantly associated with IPP (Table 3).

In the multiple regression analysis, only BMI was still significantly correlated with IPP ($P = 0.0004$), whereas IPV and abdominal volume no longer were (Table 4)

We then tested the possibility of using this multivariate analysis to create a score to predict IPP. The score was the following: $IPP = 1.226 + (BMI * 0.372) + (IPV * 0.0021)$, where 1.226 is the value of the intercept. However, the intraclass correlation coefficient of this score was only 0.44 (0.22–0.63).

DISCUSSION

PD is underused in the ADPKD population.⁴ This is in part related to the fear of technical failure in these patients, because of presence of enlarged organs and increased IPP. However, the link between IPP and organ volume has never been evaluated in patients with ADPKD on DP.

Elevated IPP has been associated with PD complications, such as hydrothorax, abdominal wall hernias, and gastroesophageal reflux.^{25,26} In studies in patients with kidney diseases other than ADPKD, mean IPP ranged from 13 to 17 cmH₂O.^{25–28} In our study of a cohort of 60 patients with ADPKD, mean IPP was 14.6 cmH₂O and the incidence of elevated IPP (defined as

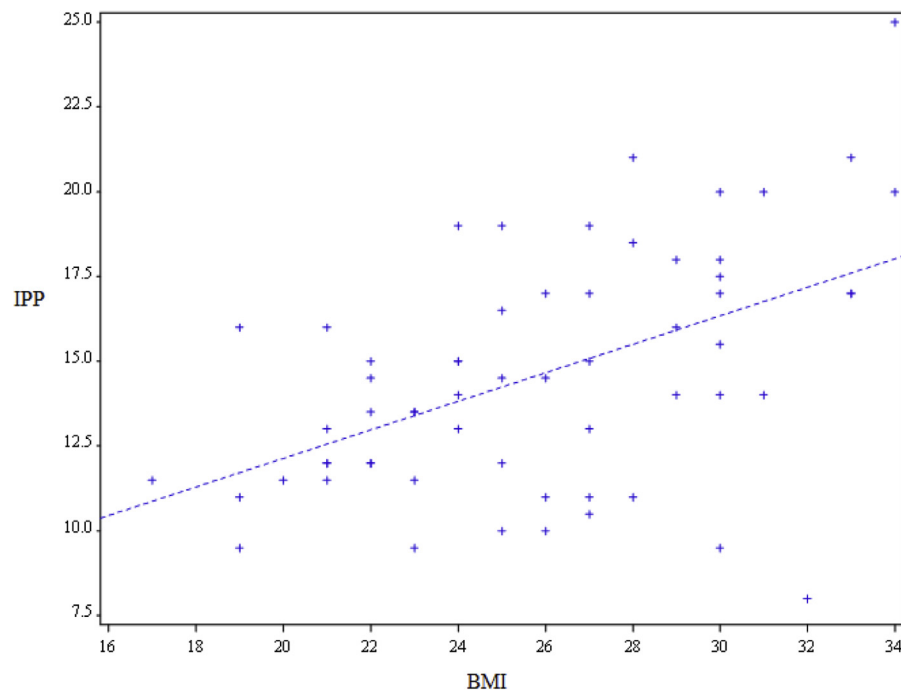


Figure 3. Positive correlation between intraperitoneal pressure (IPP) and body mass index (BMI) in patients with autosomal dominant polycystic kidney disease.

>18 cmH₂O) was 17%, which is comparable to the results found in the non-ADPKD population.^{25–28}

Our results identify BMI as the main factor associated with IPP. Interestingly, we did not find any correlation between IPP and kidney and liver volume.

We measured the liver and kidney volume with OsiriX software (OsiriX Lite, Geneva, Switzerland) and a contouring technique on serial sections of computed tomography scan, a technique that is routinely used by radiologists.^{29–32} Our results are in agreement with a previous report by Hamanoue *et al.*³³ in which the authors calculated the organ volume of patients with ADPKD at time of dialysis start by summing the areas of kidneys and liver outlined precisely on 1-cm computed tomography slices. This method is similar to the one we used, and our results were concordant: TKV = 2787 ± 1945 ml versus 3032 ± 1622 ml, liver

volume = 2198 ± 1139 ml versus 1936 ± 602 ml. These findings support the use of computed tomography scan to assess liver and kidney volumes in patients with ADPKD.

Quite unexpectedly, we did not find any correlation between organ volume and IPP. This finding may be related to the small number of patients included in the study. However, the size of our population is comparable to the populations studied by Dejardin *et al.*²⁶ and Castellanos *et al.*,²⁷ 2 attempts to assess IPP in an unselected population on PD.

Within these limits, our study suggests that IPP may be unrelated to organ volume, at least in our selected population. This finding suggests that PD should be more frequently proposed to patients with ADPKD. The role of a preselection process focusing on patients with relatively smaller kidneys needs to be assessed in larger studies.

To our knowledge, this is the first study identifying factors associated with IPP in patients with ADPKD on PD. We found a significant correlation between IPP and BMI. IPV was significant only in the univariate analysis. These same parameters were previously

Table 3. Univariate analysis

Data	Estimated value β	R^2	P
Age	0.03	0.009	0.461
Body mass index	0.42	0.251	<0.0001
Height	5.73	0.024	0.2354
Sex	0.58	0.007	0.5279
Body surface area	5.86	0.148	0.0024
Pregnancy	-0.54	0.040	0.1239
Liver volume	0.0006	0.012	0.4064
Total kidney volume	0.0001	0.003	0.6562
Abdominal volume	0.0005	0.191	0.0005
IPV	0.0035	0.107	0.0108

IPV, volume of dialysate infused in the peritoneal cavity. Factors are associated with intraperitoneal pressure.

Table 4. Multivariate analysis of intraperitoneal pressure and clinical and radiological data

Data	Estimated value β	P
Body mass index	0.372	0.0004
IPV	0.002	0.1043

IPV, volume of dialysate infused in the peritoneal cavity.

reported to be associated with IPP in the general PD population.^{26,34–37} For instance, Dejardin *et al.*²⁶ reported a positive correlation between IPP and BMI or IPV, together with a high risk of enteric peritonitis in patients with elevated IPP. Furthermore, Castellanos *et al.*²⁷ showed a positive correlation between IPP and BMI or comorbidity. We confirmed these findings, specifically in patients with ADPKD. In addition, our results raise the question of the significance of BMI in patients with ADPKD. In fact, in these patients, BMI can reflect obesity as well as the weight of the enlarged organs. Several equations have been proposed to distinguish obesity from organ enlargement³⁸; however, to our knowledge, none of these equations had been validated. Hence, the significance of BMI in our ADPKD population is due to a cumulative effect of obesity and organ weight.

By extension, our results suggest that BMI could be a surrogate marker for organ weight. BMI is more easily calculated than the volume of organs. Based on the results of our multivariate analysis, we created a score relying on BMI and IPV; the intraclass correlation coefficient was only moderate: 0.44 (0.22–0.63). Therefore, validation and improvement of the score is mandatory. If validated, this score would make it possible to identify patients with ADPKD who could benefit from PD.

In summary, this study suggests that the prevalence of high IPP is similar in patients with ADPKD and in the overall PD population. Furthermore, in this study we report, to our knowledge for the first time, the identification of factors associated with IPP in 60 patients with ADPKD on PD. We found that IPP was positively associated with BMI and IPV in the univariate analysis. Interestingly, we did not find a correlation between IPP and kidney and liver volume.

This study has some limitations: (i) BMI was not corrected for the volume of patients' organs, (ii) the proposed score for estimating IPP based on our findings has a moderate intraclass correlation coefficient, (iii) 20 patients received less than 1900 ml of IPV (1500 ml for 15 patients and 1000 ml for 5), and (iv) a pre-selection of patients with ADPKD with small organs cannot be excluded. Large prospective studies are therefore warranted to confirm our findings and validate the score we have proposed. The results of the study presented here provide a strong rationale for such future studies.

DISCLOSURE

All the authors declared no competing interests.

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