Evaluation of Nephrolithiasis in Autosomal Dominant Polycystic Kidney Disease Patients

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Background and objectives: Nephrolithiasis (LIT) is more prevalent in patients with autosomal dominant polycystic kidney disease (ADPKD) than in the general population. Renal ultrasonography may underdetect renal stones because of difficulties imposed by parenchymal and/or cyst wall calcifications.

Design, setting, participants, & measurements: A total of 125 patients with ADPKD underwent ultrasonography and unenhanced computed tomography (CT) scan, routine blood chemistry, and spot and 24-h urine collections.

Results: CT scan detected calculi in 32 patients, including 20 whose previous ultrasonography revealed no calculi. The percentage of hypocitraturia was high but not statistically different between patients with ADPKD+LIT or ADPKD. Hyperuricosuria and distal renal tubular acidosis were less prevalent but also did not differ between groups, whereas hyperoxaluria was significantly higher in the former. Hypercalciuria was not detected. Renal volume was significantly higher in patients with ADPKD+LIT *versus* ADPKD, and a stepwise multivariate logistic regression analysis showed that a renal volume ≥500 ml was a significant predictor of LIT in patients with ADPKD and normal renal function, after adjustments for age and hypertension.

Conclusions: CT scan was better than ultrasonography to detect LIT in patients with ADPKD. Larger kidneys from patients with ADPKD were more prone to develop stones, irrespective of the presence of metabolic disturbances.

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Autosomal dominant polycystic kidney disease (ADPKD) is one of the most common inherited diseases in humans, affecting 4 to 6 million people worldwide, and accounts for ESRD in 7 to 10% of hemodialysis and renal transplant patients (1). A frequent association of nephrolithiasis with ADPKD has been reported (2,3) to be responsible for significant morbidity because of flank pain, hematuria, and urinary tract infection. Patients with ADPKD may be predisposed to stone formation because of a structural abnormality secondary to cyst growth, renal tubular stasis, metabolic disorders, or a combination of these factors (4,5).

Renal ultrasound may underdetect nephrolithiasis in patients with ADPKD because of the frequent occurrence of renal calcifications. Unenhanced helical computed tomography (CT) provides an excellent technique for detecting calcifications and for distinguishing renal calculi from cyst calcifications in patients with ADPKD (3).

Considering the diagnostic difficulties and the increased morbidity of nephrolithiasis associated with ADPKD, as well as the limited knowledge of the metabolic and/or anatomic factors that contribute to stone formation, the aim of this study was to seek the presence of renal stones in patients with ADPKD through both renal ultrasound and unenhanced helical CT scan and to evaluate the metabolic profile of such patients.

Materials and Methods

A total of 312 patients were referred to the Polycystic Kidney Disease Unit of the Nephrology Division, Universidade Federal de São Paulo (São Paulo, Brazil), because of the presence of an affected progenitor or sibling with ADPKD. Abdominal and renal ultrasound were performed in the Radiology Department of the same institution in all cases by a single consultant radiologist using a Siemens Antares ultrasound system (Erlangen, Germany) and a 3- to 5-MHz convex-array transducer. The sonographic diagnosis of ADPKD was confirmed in 125 patients, based on criteria established by Ravine *et al.* (6). All 125 patients who were recruited on the basis of the ultrasound findings were submitted to a clinical evaluation and to an unenhanced CT scan (Picker PQ 5000, Cleveland, OH), by which hepatic cysts could be also identified. On CT scans, renal cyst calcifications were diagnosed by their relationship to cysts, location outside the renal collecting system, and morphology (*e.g.*, curvilinear calcification), and the presence of associated nephrolithiasis (ADPKD+LIT) was defined by images of calculi within the urinary collecting system. Patients were considered to present LIT only when ultrasound images of calculi were further confirmed by CT scan. The maximum time lapse between performance of ultrasound and CT scan was 30 d. On ultrasound, the number of cysts was determined, and the size of the largest cyst in each kidney was measured. Kidney length, width, and anteroposterior diameter were also determined. Renal volume was then calculated using a standard formula of a modified ellipsoid for each kidney as follows: Renal volume = $4/3\ \pi \times (\text{anteroposterior diameter} + \text{width}/4)^2 \times \text{length}/2$ (7). To compare renal volume between ADPKD groups with or without associated nephroli-

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thiasis, we considered the volume of the kidney(s) containing the stone(s) in the former group and the highest kidney volume among the two kidneys in the latter. Written consent was obtained from all patients, and the local ethics committee approved the study.

Hypertension was considered on the basis of a history of hypertension, present BP measurements, or actual/past use of antihypertensive medications. Serum parameters included routine blood chemistry (creatinine, sodium, potassium, calcium, uric acid, and chloride). A blood sample for venous blood gases was drawn anaerobically into an heparinized tube and analyzed immediately after collection whenever possible or kept on ice for no longer than 30 min for plasma bicarbonate (HCO_3) determination, through venous blood gas analysis. A 24-h urine sample was delivered for determination of urine volume, calcium, uric acid, citrate, oxalate, sodium, potassium, creatinine, urea, magnesium, and phosphate, and the determined creatinine clearance was adjusted for body surface area. Thiazides were withdrawn at least 72 h before urine collection. A morning 12-h fasting spot urine sample (under conditions of water restriction) was collected for urinary pH (upH), osmolality, microalbuminuria, and culture. In the presence of a positive urine culture ($>10^5$ colony-forming units/ml), the results of upH and albumin were not considered and the spot urine analysis was repeated in a further occasion, after the treatment of the urinary tract infection. upH was measured by a pHmeter. Distal renal tubular acidosis (dRTA) was considered in cases of fasting upH >5.5 in the presence of systemic acidosis, defined by a plasma HCO_3 <22 mEq/L (complete form). In the absence of spontaneous acidosis, patients were further submitted to an ammonium chloride (NH_4Cl) loading test to detect incomplete forms of dRTA, as described previously (8). Briefly, urine was collected for a period of 3 h, after 2 h of NH_4Cl ingestion (0.1 g/kg body wt), and pH and net acid excretion were determined. A reduction of urinary pH <5.5 coupled with a two-fold increase in ammonium excretion and a three-fold increase in titratable acidity were considered to be an adequate response to the acid load. Ammonium excretion was also determined in 10 healthy subjects (one female and nine male) from the laboratory staff for comparisons with patients with ADPKD. Decreased renal concentrating capacity was defined by urine osmolality <800 mOsm/kg after 12 h of water restriction, and normal ranges for microalbuminuria were <15 μg/min. Hypercalciuria was defined as calcium ≥4 mg/kg body wt, hyperuricosuria as uric acid >750 or 800 mg/24 h (for female or male, respectively), hypocitraturia as citrate <320 mg/24 h, hyperoxaluria as urine oxalate >45 mg/24 h, and hypomagnesuria as urinary magnesium <70 mg/24 h as described previously (9). Metabolic disturbances and urinary acidification tests were evaluated only in patients who had normal renal function and a creatinine clearance >60 ml/min per 1.73 m^2 (10). Ion activity product (AP) with respect to calcium oxalate (Tiselius Index) was calculated as follows: $AP(CaOx) = 1.9 \times calcium^{0.84} \times oxalate \times citrate^{-0.22} \times magnesium^{-0.12} \times volume^{-1.03}$ (11).

Urinary oxalate was measured by an enzymatic method using the Sigma Oxalate Diagnostic kit (Sigma, St. Louis, MO). Calcium was determined by atomic absorption spectrophotometry (Perkin-Elmer Atomic Spectrophotometer 290B, Norwalk, CT). Serum creatinine was determined according to a modified Jaffé reaction (12) in Hitachi 912 (Roche Diagnostic System, Basel, Switzerland) by an isotope dilution mass spectrometry traceable method. Uric acid was determined by the uricase method (Hitachi 912; Roche) (13), urinary citrate by a citrate-lyase enzymatic reaction (14), and sodium and potassium by ion selective electrodes.

Statistical analyses were conducted with SPSS 12.0 (SPSS, Chicago, IL). Categorical variables were compared between groups using χ^2 analysis or Fisher exact test when appropriate. The proportion of positive findings obtained by ultrasound or CT scan were compared by McNemar test. Continuous variables were compared between groups using Mann-Whitney test. $P < 0.05$ was considered statistically significant. A univariate logistic regression analysis was used to estimate the odds ratio for the occurrence of nephrolithiasis with the variables age, gender, hypertension, renal volume, number and size of cysts, and creatinine clearance. A stepwise multiple regression analysis was performed to determine the independent variable(s) related to nephrolithiasis. Receiver operator characteristic curve analysis was used to determine the cutoff value of a significant renal volume with respect to the risk for nephrolithiasis occurrence.

Results

ADPKD was identified in 125 patients (80 female/45 male) aged 15 to 80 yr, being distributed among 69 families. Nephrolithiasis was disclosed in 35 of these 125 patients, with 32 cases detected on CT scan including 20 that were not visible at ultrasound. Figure 1 illustrates a case of a barely visible calculus at ultrasound, clearly shown in a CT scan. Three patients did not present calculi on CT scan, but one of them had been previously submitted to extracorporeal shock wave lithotripsy and the other two had passed calculi. As shown in Table 1, the proportion of calculi detected by CT scan in the whole sample was statistically higher than the one detected by ultrasound (25 *versus* 15%; $P < 0.021$). A higher percentage of patients with

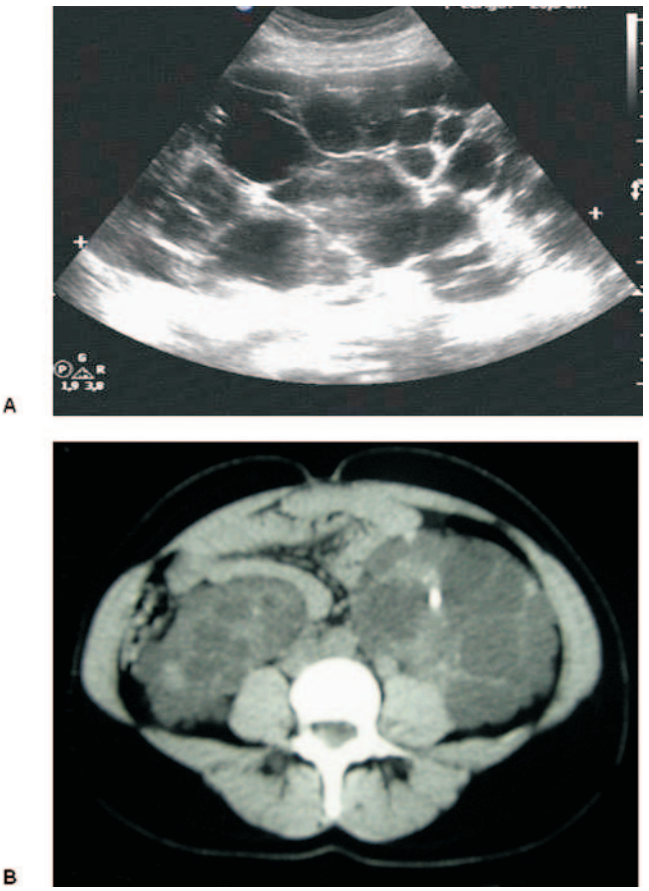

Figure 1. (A and B) Ultrasound of left kidney with multiple cysts without calculus (A) and unenhanced computed tomography scan showing the image of the calculus in the left kidney in the same patient (B).

Table 1. Presence of urinary calculi on renal ultrasound and CT scan[a]

Urinary Calculi on Ultrasound	Urinary Calculi on CT		Total
	+	−	
+	12	7	19 (15%)
−	20	86	106
Total	32 (25%)	93	125

[a]McNemar test: $P = 0.021$. CT, computed tomography.

ADPKD+LIT reported low back pain than patients with ADPKD, almost reaching statistical significance (57 *versus* 36%; $P = 0.052$). Cyst calcifications were detected in 55 (44%) of 125 patients. Eighteen (56%) of 32 patients with ADPKD+LIT had both cyst calcifications and calculi.

Table 2 shows clinical and laboratory characteristics of patients with ADPKD associated with nephrolithiasis or not. Gender distribution was similar, but patients with ADPKD+LIT were significantly older than patients with ADPKD and presented a higher percentage of hypertension, although without statistical significance. The percentage of patients with decreased renal function (stages 3 through 5 chronic kidney disease [CKD]) and median values of creatinine clearance were not different between groups. A higher percentage of patients with ADPKD+LIT presented hepatic cysts and impairment in submaximal urinary osmolality than patients with ADPKD, albeit not reaching statistical significance. The presence of urinary tract infection (two past and two recent episodes) was evidenced only in patients with ADPKD+LIT. Microalbuminuria was detected in 10 of 35 patients with ADPKD+LIT (four with normotension and six with hypertension) and in 30 of 90 patients with ADPKD (16 with normotension and 14 with hypertension), but the percentage of microalbuminuria did not differ between groups (29 *versus* 24%) or among patients with hypertension and normotension. The presence of microscopic hematuria on urinalysis was not statistically different between patients ADPKD+LIT and ADPKD (28 *versus* 16%; $P = 0.21$, data not shown).

As shown in Table 3, median values of serum biochemistries were not statistically different between patients with ADPKD+LIT and ADPKD. Median values of urinary parameters also did not differ between them, except for urinary oxalate, which was significantly higher in patients with ADPKD+LIT *versus* ADPKD. The risk for urinary crystallization (AP_{CaOx} index) was also not different between groups. Despite a median NH_4 excretion (after NH_4Cl load) that was not significantly different between groups (Table 3), this parameter was significantly lower in patients with ADPKD+LIT when compared with 10 healthy control subjects (31 *versus* 50 μEq/min; $P = 0.015$, data not shown).

The percentage of metabolic disturbances in both groups is presented in Table 4. Hypercalciuria was absent, and hyperuricosuria, hypomagnesiuria, and hypocitraturia were not different between ADPKD+LIT and ADPKD groups. The percentage of hypocitraturia was very high in both (54 and 48%, respectively), and the percentage of hyperoxaluria was significantly higher in the former group (18 *versus* 4%; $P < 0.05$). Table 5 summarizes the results of the urinary acidification assessment test. The percentage of fasting upH <5.5 was high in ADPKD+LIT and ADPKD groups, both under normal conditions (52 and 64%, respectively) and after the NH_4Cl load (37 and 27%, respectively) without significant differences between groups; therefore, the percentage of dRTA was low in both ADPKD+LIT and ADPKD groups, in either complete (7%) or incomplete forms (4 and 2%, respectively).

As shown in Table 6, patients with ADPKD+LIT presented a significantly higher median renal volume than patients with ADPKD. The size of the largest cyst and the number of cysts were not statistically different between groups. When we divided the patients into groups with normal renal function or with stages 3 through 5 CKD, only the ADPKD+LIT group with normal renal function presented a significantly higher renal volume when compared with patients with ADPKD (319 *versus* 203 ml; $P < 0.01$).

A receiver operator characteristic curve analysis showed a cutoff value for a significant renal volume as a predictor of nephrolithiasis to be 502 ml (this value was then approximated to 500 ml for categorization in the model of regression

Table 2. Clinical and laboratory characteristics[a]

Characteristic	ADPKD + LIT ($n = 35$)	ADPKD ($n = 90$)	P
Gender (male/female)	14/21	31/59	0.700
Age (yr; median [range])	37 (15 to 80)[a]	27 (15 to 60)	0.040
Hypertension (n [%])	21 (60)	38 (42)	0.110
Stages 3 through 5 CKD (n [%])	7 (20)	20 (22)	0.970
Creatinine clearance (median [range])	78 (6 to 121)[a]	84 (18 to 135)	0.740
Hepatic cysts (n [%])	21 (60)	40 (44)	0.170
Urinary tract infection (n [%])	4 (12)	0 (0)	0.007
Microalbuminuria (n [%])	10 (29)	22 (24)	0.800
Urinary osmolality (<800 mOsm/kg; n [%])	16 (46)	37 (41)	0.790

[a]ADPKD, autosomal dominant polycystic kidney disease; CKD, chronic kidney disease; LIT, nephrolithiasis.

Table 3. Median values of serum and urinary parameters[a]

Parameter	ADPKD + LIT (n = 35; Median [Range])	ADPKD (n = 90; Median [Range])	P
Serum			
creatinine (mg/dl)	1.1 (0.7 to 6.6)	1.1 (0.7 to 4.4)	0.31
sodium (mEq/L)	140 (134 to 146)	141 (135 to 148)	0.19
potassium (mEq/L)	4.2 (3.3 to 5.9)	4.3 (3.3 to 5.2)	0.10
calcium (mg/dl)	9.1 (8.4 to 9.9)	9.3 (8.1 to 10.4)	0.13
uric acid (mg/dl)	5.2 (2.4 to 9.5)	4.9 (1.5 to 8.6)	0.37
chloride (mmol/L)	105 (102 to 113)	106 (61 to 117)	0.77
HCO_3, plasma (mEq/L)	25 (20 to 30)	26 (20 to 32)	0.34
Urine			
volume (ml/d)	1840 (590 to 3560)	1510 (430 to 4300)	0.64
calcium (mg/d)	112 (39 to 274)	102 (6 to 285)	0.39
uric acid (mg/d)	469 (134 to 1047)	497 (171 to 1141)	0.92
citrate (mg/d)	295 (89 to 922)	301 (78 to 923)	0.97
oxalate (mg/d)	31 (19 to 66)	25 (10 to 65)	0.03
sodium (mEq/d)	172 (76 to 388)	202 (52 to 410)	0.51
potassium (mEq/d)	52 (18 to 94)	44 (13 to 130)	0.28
creatinine (mg/d)	1203 (682 to 2226)	1241 (525 to 2964)	0.40
urea (g/d)	16.0 (1.3 to 44.0)	14.0 (12.0 to 42.0)	0.46
magnesium (mg/d)	79 (41 to 163)	79 (18 to 149)	0.29
phosphate (mg/d)	771 (368 to 1621)	629 (123 to 1614)	0.08
AP_{CaOx} index	0.9 (0.4 to 2.6)	0.8 (0.2 to 3.7)	0.22
fasting upH	5.7 (4.9 to 6.8)	5.6 (4.7 to 8.0)	0.63
NH_4 (μEq/min) after NH_4Cl load	31 (23 to 74)	42 (20 to 59)	0.24

[a]AP, activity product; upH, urinary pH.

Table 4. Percentage of metabolic disturbances[a]

Parameter	ADPKD+LIT (n = 28; n [%])	ADPKD (n = 70; n [%])	P
Hypercalciuria	0 (0.0)	0 (0.0)	
Hyperuricosuria	3 (11.0)	6 (8.5)	0.71
Hypomagnesiuria	8 (29.0)	24 (34.0)	0.76
Hypocitraturia	15 (54.0)	34 (48.0)	0.82
associated with incomplete dRTA	1	1	
associated with complete dRTA	2	4	
Hyperoxaluria	5 (18.0)	3 (4.0)	0.041

[a]dRTA, distal renal tubular acidosis.

analysis). A univariate logistic regression analysis that included all patients showed that age (odds ratio [OR] 1.03; 95% confidence interval [CI] 1.01 to 1.06; $P = 0.041$) and renal volume ≥500 ml (OR 3.96; 95% CI 1.72 to 9.11; $P < 0.01$) were significant variables but not gender, hypertension, creatinine clearance, the number of cysts, or the size of the higher cyst. The stepwise multiple regression analysis performed on patients who were categorized into normal renal function or with stages 3 through 5 CKD groups showed that renal volume ≥500 ml was the only significant predictor of nephrolithiasis in patients with ADPKD and normal renal function (OR 6.30; 95% CI 1.62 to 24.46; $P = 0.008$) but not in the subgroup of patients with stages 3 through 5 CKD (OR 3.30; 95% CI 0.31 to 35.32; $P = 0.32$).

Discussion

ADPKD is associated with an increased incidence of nephrolithiasis, occurring in 20 to 36% of patients (2,3); however, the diagnosis of nephrolithiasis in ADPKD by ultrasonography might be impaired as a result of the frequent occurrence of parenchymal or cyst wall calcifications (4). In the general population, CT has superior sensitivity (95%) and specificity (98%) over all other modalities to detect kidney stones (15). When CT scan is used as the reference standard, the ultrasound sensitiv-

Table 5. Urinary acidification assessment[a]

Parameter	ADPKD+LIT (n = 27; n [%])	ADPKD (n = 58; n [%])	Total
UpH <5.5			
spontaneous	14 (52)	37 (64)	51
after NH_4Cl	10 (37)	16 (27)	28
UpH >5.5			
complete dRTA	2 (7)	4 (7)	6
incomplete dRTA (after NH_4Cl)	1 (4)	1 (2)	2

[a]dRTA, distal renal tubular acidosis.

Table 6. Renal volume, size of largest cyst, and number of cysts[a]

largest renal cyst size (cm; median [range]) Parameter	ADPKD+LIT (n = 35)	ADPKD (n = 90)	P
Renal volume (ml; median [range])	508 (86 to 1449)	220 (72 to 4970)	0.04
Largest renal cyst size (cm; median [range])	3.7 (0.7 to 9.0)	3.3 (0.5 to 10.6)	0.66
Cysts (n [%])			0.40
0 to 6	7 (20)	15 (23)	
7 to 14	2 (06)	18 (18)	
≥15	26 (74)	57 (59)	
CrCl ≥60 ml/min	(n = 28)	(n = 70)	
renal volume (ml; median [range])	319 (86 to 1449)	203 (72 to 4970)	0.04
largest renal cyst size (cm; median [range])	3.6 (0.7 to 7.9)	2.8 (0.5 to 10.6)	0.40
Stages 3 through 5 CKD	(n = 7)	(n = 20)	
renal volume (ml; median [range])	723 (296 to 1216)	651 (106 to 3336)	0.76
largest renal cyst size (cm; median [range])	4.2 (3.0 to 10.5)	5.0 (0.8 to 9.4)	0.34

[a]CrCl, creatinine clearance.

ity can be as low as 24%, despite a specificity of 90% (16); therefore, it has been suggested that CT scan could be more efficient in detecting stones that had been missed by sonography, as well as in separating stones from renal calcifications in ADPKD (3,17).

In this study, to diagnose renal stones, all patients with ADPKD were submitted to a CT scan, which showed 32 of 125 patients with nephrolithiasis. Our findings showed that CT was indeed better than ultrasound to detect urinary calculi, because 20 patients whose calculi were not visible on ultrasound presented evident images on CT scan. Present figures of sensitivity and specificity for CT were 63 and 81%, respectively. In addition to the 32 patients, three patients were considered as stone formers because despite not presenting stones on CT scan, they had either passed calculi or been submitted to extracorporeal shock wave lithotripsy; therefore, the overall prevalence of nephrolithiasis in this sample was 28%.

Low back pain as a result of cyst enlargement, rupture or infection, or nephrolithiasis is commonly reported by patients with ADPKD during the course of their disease (18). In this series, low back pain was much more frequent in patients with ADPKD+LIT than in patients with ADPKD, almost reaching statistical significance (P = 0.052). Torres *et al.* (4) also observed that 49% of patients with ADPKD and nephrolithiasis had symptoms. Urinary tract infection was also seen only in ADPKD associated with LIT in this sample.

The second aim of this study was to investigate whether anatomic abnormalities and/or metabolic disturbances might have contributed to the development of nephrolithiasis in this series of patients with ADPKD. The analysis of metabolic disturbances encompassed only patients with normal renal function because the presence of stages 3 through 5 CKD compromises the results of the lithogenic parameters (9). We found a high percentage of hypocitraturia in both ADPKD+LIT or ADPKD groups, without statistical difference between them. Hyperuricosuria and dRTA were less prevalent but also did not differ between groups, whereas hyperoxaluria was significantly higher in the former. Hypercalciuria was not detected. A previous evaluation of 444 patients with nephrolithiasis and without ADPKD in our service (19) revealed 58% of hypercalciuria, 53% of hypocitraturia, 23% of hyperuricosuria, and <1% of hyperoxaluria; therefore, this sample of patients with ADPKD+LIT presented a unique metabolic profile showing no hypercalciuria, 18% of hyperoxaluria, and the same figures of hypocitraturia (approximately 50%) when compared with patients with nephrolithiasis and without ADPKD. The reasons for a higher percentage of hyperoxaluria and the lack of hypercalciuria in this sample, as in other series (2) as well, are not

clear. The high percentage of hypocitraturia in ADPKD here depicted was described by other authors (2,20) and also remains unexplained. It was not related to dRTA, because only 9.5% of all patients with ADPKD in this series had incomplete or complete forms of dRTA. Moreover, most patients with ADPKD and with or without associated nephrolithiasis had urinary pH <5.5, either spontaneously (62% of them) or after NH_4Cl load (30% of them), indicating that a low rather than a high upH was the rule in these patients, which is consistent with previous reports (2,4,21,22). In addition, patients with ADPKD+LIT exhibited lower ammonium excretion after NH_4Cl load when compared with healthy subjects, suggesting a possible defect in ammonium excretion (23,24), similar to the one observed in uric acid stone formers (23). Although such a finding could predispose to the formation of uric acid stones, as suggested in other series (4), only three patients from this sample had voided calculi in the past, but such stones were no longer available for analysis. Anyway, because the occurrence of hypocitraturia is undeniable in the ADPKD setting (2,20), alkalinization with potassium citrate might be useful in the prevention of uric acid stones and to reduce calcium oxalate supersaturation.

Forty percent of patients with ADPKD and with or without associated nephrolithiasis in this series presented decreased urinary osmolality, which may be accounted for by the disruption of the renal architecture by the cysts, interfering with the countercurrent exchange and multiplication mechanisms, confirming previous reports of submaximal urinary concentration capacity (25). With respect to anatomic abnormalities, this study disclosed a significantly higher kidney volume in patients with ADPKD and nephrolithiasis than in patients with ADPKD. Such difference was evident only in patients with normal renal function, disappearing in the subgroup with stages 3 through 5 CKD. Because polycystic kidneys' progressive enlargement is inversely correlated with creatinine clearance and presumably directly related with distorted anatomy favoring stone formation, the reasons for such findings remain unclear. The higher renal volume of patients with ADPKD+LIT might have been ascribed to a higher number of cysts, because the percentage of patients in this group who presented ≥15 cysts per kidney had been greater (74%) than in the ADPKD group (59%), although not reaching statistical significance. Grampsas *et al.* (20) also observed a significantly higher number of cysts and larger predominant cyst size in 15 individual stone-forming ADPKD kidneys compared with kidneys without stones, suggesting intrarenal anatomic obstruction as a cause for nephrolithiasis; however, renal volume was not assessed in their study. It is noteworthy that the differences of renal volume between groups currently identified could have been even greater had we considered the mean volume of two kidneys in the ADPKD group rather than the greater kidney volume among the two kidneys when we compared with the renal volume of the individual stone-forming kidney.

Finally, the stepwise multiple regression analysis showed that a renal volume >500 ml was a significant predictor of nephrolithiasis in patients with ADPKD and with normal renal function even after adjustments for age and hypertension. We are aware that the renal volume measured by magnetic resonance imaging is more appropriate, as recently shown by the Consortium for Radiologic Imaging Studies of PKD (CRISP) study (26), especially when the goal is to determine renal blood flow and progression. Nevertheless, magnetic resonance imaging is not routinely available, and reimbursement cannot always be obtained in most clinical radiology departments. In a recent review by Grantham *et al.* (27), renal volume, often determined by ultrasound or CT scan, was shown to be directly associated with many variables such as proteinuria, microalbuminuria, hypertension, hematuria, and progressive loss of renal function. Our findings strongly support that greater kidney volumes are also associated with nephrolithiasis.

Conclusions

Our data suggested that nephrolithiasis is highly prevalent in ADPKD (28%) and that CT scan was important to detect renal calculi, eventually missed by ultrasound. The percentage of metabolic disturbances was not higher in ADPKD+LIT, except for urinary oxalate, which was marginally elevated in a higher proportion of patients in this group. Larger kidney volumes have been shown to be prone to developing stones, irrespective of the presence of metabolic disturbances. Upcoming therapies aimed at reducing the size of the cysts and, consequently, renal volume not only may affect progression but also may help to reduce the occurrence of renal stones.

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Disclosures

None.

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