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Early Arterial Stiffness and Inflammatory Bio-Markers in Normotensive Polycystic Kidney Disease Patients

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Key Words
Inflammation · Hypertension · Polycystic kidney disease

Abstract

Background/Aims: Cardiovascular disease is the main cause of morbidity and mortality in autosomal-dominant polycystic kidney disease (ADPKD) patients. To clarify temporal relationship between ADPKD, hypertension and the loss of renal function, we examined these factors in patients with early-stage ADPKD who did not yet have hypertension. ***Methods:*** Fifty patients with ADPKD (42% males, 36.6 ± 9.9 years, no blood pressure medication) and 50 healthy controls (44% males, 35.4 ± 6.4 years) were studied cross-sectionally. Pulse wave velocity (PWV), cardiac morphology and function, aortic elastic indexes, estimated glomerular filtration rate (eGFR), 24-hour ambulatory blood pressure, interleukin-6 (IL-6), tumor necrosis factor-α (TNF-α) and highly sensitive C-reactive protein (hs-CRP) were measured in all participants, using conventional methods. ***Results:*** Despite a normal blood pressure, aortic stiffness index and pulse wave velocity values were increased in patients compared to controls (6.8 ± 4.7 vs. 5.1 ± 3.3, p = 0.043 and 9.6 ± 1.3 vs. 5.8 ± 1.1 m/s, $p < 0.001$). In univariate analysis, IL-6, TNF-α, hs-CRP and eGFR were all significantly correlated with PWV. The independence of these correlations were analyzed in a regression model, and showed PWV to be significantly predicted by IL-6, TNF-α and hs-CRP. ***Conclusion:*** Increased arterial stiffness and pulse wave velocity are early manifestations of ADPKD appearing before hypertension or reduced eGFR. However, these vascular abnormalities are related to signs of systemic low grade inflammation, suggesting a common pathophysiological mechanism apparently present also in other vascular diseases but yet to be elucidated.

Introduction

Autosomal-dominant polycystic kidney disease (ADPKD) is the most common hereditary cause of chronic kidney disease (CKD), being present in approximately 8–10% of patients with end-stage renal disease (ESRD) [1]. Furthermore, ADPKD is associated with highly prevalent hypertension, which is often difficult to treat [2]. Like in other types of CKD, ADPKD also markedly increases the

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risk of cardiovascular disease (CVD) and death. It has been postulated that a reduced nephron perfusion in ADPKD is responsible for triggering hypertension in these patients, and indeed they often respond well to angiotensin converting enzyme inhibitors (ACEI) and angiotensin receptor blockers (ARBs) [3, 4]. However, these medications have not been able to drastically reduce the very high prevalence of CVD in this patient group [3], meaning that other pathophysiological pathways may also be involved.

Arterial stiffness is an important determinant of hypertension in other patient populations, for example diabetes mellitus, atherosclerosis and non-ADPKD ESRD [5]. Several studies show that increased arterial stiffness parameters are an independent predictor of the prognosis in hypertension, stroke, myocardial infarction, congestive heart failure and atherosclerosis [6–9].

However, the putative role of impaired arterial elasticity has not been well studied in the high-risk ADPKD population. With the hypothesis that mechanisms other than hypoperfusion (reduced GFR) and subsequent fluid retention contribute to hypertension in ADPKD, we examined the relationship of renal function and inflammatory biomarkers with the prevalence of arterial stiffness in normotensive ADPKD patients with a normal renal function.

Subjects and Methods

Study Population

Between February 2011 and October 2011, 50 patients were enrolled in the study from the Turkish Society of Nephrology Polycystic Kidney Disease Working Group Registry in Kayseri, Turkey. The diagnosis of ADPKD was confirmed by a positive family history and the presence of 5 or more renal cysts on renal ultrasound, distributed to both kidneys. Demographic characteristics (e.g. gender, age, education status and smoking history), renal manifestations (e.g. hematuria, urinary system infection, urinary tract stones and renal replacement therapy) and cardiovascular manifestations (e.g. hypertension and mitral valve prolapse) were recorded on the web-based data recruitment forms. Extrarenal manifestations, including the presence of hernias, liver cysts and colonic diverticuli, were also registered. After the study group was assembled, patients were asked to participate after receiving informed consent. Enrolled patients were reevaluated in terms of systemic inflammation, urinary tract stones and infection. A urinary infection was defined as an infection only if confirmed by one or more positive urinary cultures. None of the patients showed any signs of either stones or infection. The following participants were excluded from the study: those under 17 years of age or above 60 years of age (n = 16), those with a history of myocardial infarction and stroke (n = 7), and those with known high systemic blood pressure or prescribed antihypertensive drugs (n = 21). Finally, a total of 50 patients were enrolled in the study. Based on these, we recruited a matched control group (n = 50) from people who were admitted to our family medicine center for routine check-ups. Inclusion criteria were no known diseases and not currently taking any drugs.

Estimated glomerular filtration rate (eGFR) was calculated using the Modification of Diet in Renal Disease (MDRD) formula: MDRD = 186 × (serum creatinine (mg/dl)) – 1.154 × age – 0.203. A correction factor of 0.742 was used for women [10]. The study was approved by the University Ethics Committee and Local Hospital Review Committee. All participants provided written informed consent.

Biochemical Measurements

Blood samples were taken from the veins in the antecubital fossa with subjects in a seated position and following a 20-min rest and after 12 h of fasting. Glucose, creatinine, and lipid profile were determined by standard methods. Tripotassium EDTA based anticoagulated blood samples were drawn to measure complete blood count stored at 4°C and assessed by a Sysmex K-1000 (Block Scientific, USA) auto-analyzer within 30 min of sampling. hs-CRP was measured using a BN2 model nephelometer (Dade-Behring, Germany). The expected values for hs-CRP in our laboratory ranged from 0 to 3 mg/l. IL-6 and TNF-α were measured in serum using ELISA kits from R&D Systems Inc. (Minneapolis, Minn., USA).Reported intra-and inter assay coefficients of variation (Cvs) were 3.2 and 2.9% for IL-6, and 7.9 and 10.1% for TNF-α, respectively.

Echocardiography

All participants were examined at inclusion using a Vivid 7 instruments (GE Medical Systems, Milwaukee, Wisc., USA), with a 2.5-MHz transducer and harmonic imaging. The echocardiographies were performed in the echocardiography laboratory at baseline by a cardiology specialist and according to the recommendations of the American Society of Echocardiography. Echocardiographic examinations were conducted in the left lateral decubitus position using parasternal long-short axis and apical views. At least 3 consecutive beats in sinus rhythm were recorded, and the average values were taken. The LV end-diastolic and end-systolic dimensions (LVEDD and LVESD), interventricular septal and posterior wall thicknesses (IVSd and LPWd) were measured from M-mode images of the left ventricle generated in the long-axis view with the cursor at the tip of the mitral valve leaflets. The LV ejection fraction was calculated using the formula: LVEF % = (LVEDV – LVESV)/LVEDV × 100. The left ventricular mass (LVM) was calculated using the formula: LVM = 0.8 × (1.04 [(IVSd + LVEDD + LPWd)^3 – (LVEDD)^3]) + 0.6 g [11].

Aortic Stiffness

M-mode echocardiography was carried out in all participants to evaluate aortic elasticity indexes including aortic strain, aortic distensibility and aortic stiffness index using a GE-Vingmed Vivid 7 system (GE-Vingmed Ultrasound AS, Horten, Norway) with a 2.5-MHz transducer.

Aortic stiffness was calculated based on the relationship between changes in aortic diameter and pressure during 3 consecutive heart beats. The aortic diameter was recorded at a level 3 cm above the aortic valve in the parasternal long-axis view. The internal aortic diameters were measured in systole and diastole using the distance between the trailing edge of the anterior aortic

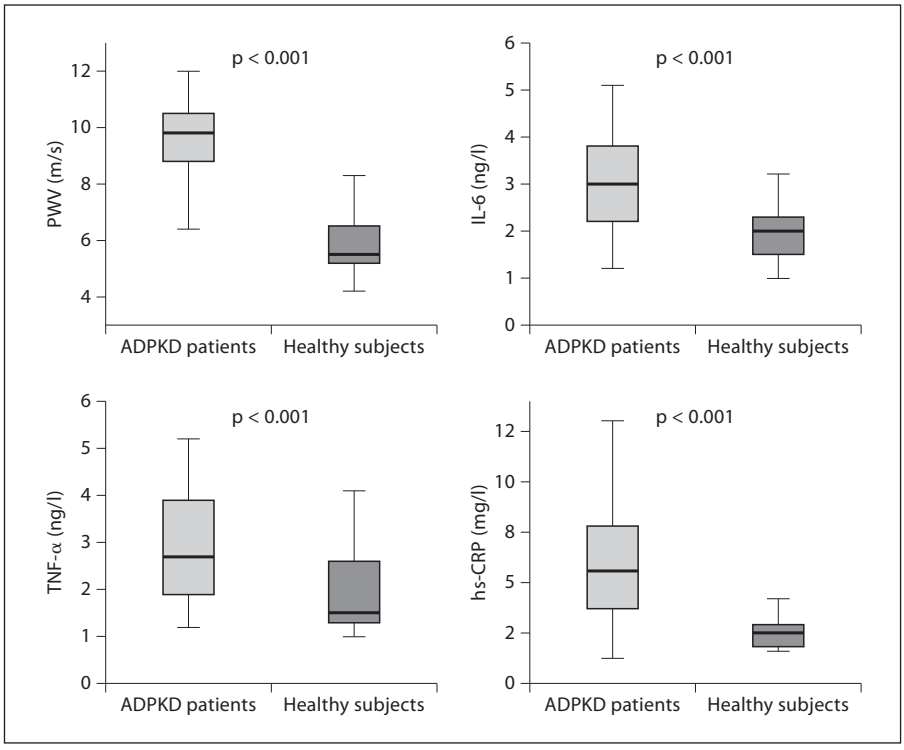

Fig. 1. Comparison of pulse wave velocity, hs-CRP, IL-6 and TNF-α between ADPKD patients and control group.

wall and the leading edge of the posterior aortic wall. The diastolic diameter (DD) was measured at the peak of the QRS complex on a simultaneously recorded electrocardiogram, while systolic aortic diameter (SD) was recorded at the maximum anterior position of the aorta. Simultaneously, blood pressure (BP) was measured by an oscillometric method using the MEC-1000 patient monitor (Mindray, Shenzhen, PR China). The following aortic elasticity indices were calculated [12]:

Aortic strain = (SD – DD)/DD, where SD and DD are the aortic systolic and diastolic diameters.

Aortic stiffness index = Ln (SBP/DBP)/((SD – DD)/DD), where SBP and DBP are the systolic and diastolic blood pressures, and 'Ln' is the natural logarithm.

Aortic distensibility = 2 × (SD – DD)/((SBP – DBP) × DD).

Pulse Wave Velocity

Vascular studies were performed in a quiet, temperature-controlled room with subjects resting in a supine position. Systolic and diastolic blood pressures were measured in duplicate using a semi-automated, noninvasive oscillometric sphygmomanometer, following a 10-min rest period. Pulse-wave analysis measured in the carotid and femoral arteries using a pulse wave velocity (PWV) machine (Micro Medical Pulse Trace, Rochester, UK) in accordance with the manufacturer's recommendations. Briefly, the transducers were positioned over the carotid and femoral arteries, always on the right side of the body. PWV was automatically calculated by measuring the time for the pulse wave to travel between the carotid and femoral arteries. All measurements were performed over 15 heart beats by a single operator blinded to the patient's grouping exposure.

Ambulatory Blood Pressure Measurements

The 24-hour blood pressure monitoring was performed using a Del Mar Medical Pressurometer Model P6 (Del Mar Reynolds, Irvine, Calif., USA) and the results were assessed using the manufacturer's computer software. Ambulatory measurements were conducted once every 15 min from 7 a.m. until 11 p.m., and once every 30 min from 11 p.m. until 7 a.m. Evaluation was performed taking the mean values of day and night blood pressures into account. Hypertension was considered to be present if the systolic pressure was >140 mm Hg and/or diastolic pressure was >90 mm Hg, or if the individual was taking antihypertensive medication.

Statistical Analysis

Continuous variables were tested for normal distribution by the Kolmogorov-Smirnov test. We report continuous data as mean and standard deviation or median. We compared continuous variables using Student's t test. Categorical variables were summarized as percentages and compared with the χ^2 test. Pearson correlation coefficients were calculated to examine the degree of association between variables. $p < 0.05$ was considered significant. In multivariate analysis variables for which the unadjusted univariate p value was <0.10 in linear regression analysis were included. We reduced the model by using backward elimination multivariate linear regression analysis and compared remaining risk markers using likelihood ratio tests. $p < 0.05$ was considered significant, and the confidence interval (CI) was set to 95%. All statistical analyses were performed using SPSS version 15 (SPSS, Inc., Chicago, Ill., USA).

Table 1. Clinical, echocardiographic features and blood pressure monitoring of ADPKD patients and healthy controls

Variables	ADPKD patients (n = 50)	Healthy controls (n = 50)	p
Age, years	36.6 ± 9.9	35.4 ± 6.4	n.s.
Males, %	42	44	n.s.
Systolic BP, mm Hg	116.7 ± 9.1	113.8 ± 8.0	n.s.
Diastolic BP, mm Hg	76.8 ± 6.0	75.3 ± 4.6	n.s.
Smoking status, %	16	22	n.s.
eGFR[a], ml/min/1.73 m^2	83.9 ± 5.8	85.4 ± 3.6	n.s.
BMI	26.2 ± 4.3	25.3 ± 3.5	n.s.
Hemoglobin, g/l	13.1 ± 1.9	13.3 ± 1.9	n.s.
Platelet count, × 1,000/mm^3	243 ± 62	249 ± 65	n.s.
White blood cell count, $10^3/\mu l$	8.6 ± 3.1	8.3 ± 2.8	n.s.
Biochemical parameters			
Plasma fasting glucose, mg/dl	91.0 ± 10.1	92.2 ± 11.0	n.s.
Creatinine, mg/dl	0.93 ± 0.30	0.84 ± 0.11	n.s.
Fasting total cholesterol, mg/dl	178.6 ± 31.5	173.3 ± 29.9	n.s.
Fasting HDL-C, mg/dl	44.1 ± 11.3	42.9 ± 7.1	n.s.
Fasting LDL-C, mg/dl	108.5 ± 26.2	111.6 ± 22.7	n.s.
Fasting triglyceride, mg/dl	141.2 ± 97.7	134.7 ± 75.2	n.s.
hs-CRP, mg/l	6.1 ± 3.1	2.8 ± 1.0	<0.001
IL-6, ng/l	3.0 ± 1.0	2.0 ± 0.7	<0.001
TNF-α, ng/l	2.8 ± 1.1	1.9 ± 0.8	<0.001
24-Hour BP monitoring, mm Hg			
Average 24-hour systolic BP	113.9 ± 8.6	111.1 ± 8.3	n.s.
Average daytime systolic BP	116.7 ± 9.1	113.8 ± 8.0	n.s.
Average nighttime systolic BP	108.2 ± 9.4	107.4 ± 8.7	n.s.
Average 24-hour diastolic BP	74.6 ± 5.5	72.7 ± 4.1	n.s.
Average daytime diastolic BP	76.8 ± 6.0	75.3 ± 4.6	n.s.
Average nighttime diastolic BP	70.3 ± 6.5	69.7 ± 4.3	n.s.
Average 24-hour mean BP	94.1 ± 6.6	91.6 ± 4.8	n.s.
Average daytime mean BP	90.1 ± 6.6	87.5 ± 3.9	n.s.
Average nighttime mean BP	83.1 ± 7.3	81.6 ± 4.2	n.s.
Pulse wave measurements			
AoS, mm	29.0 ± 4.1	28.3 ± 3.1	n.s.
AoD, mm	28.2 ± 3.1	25.6 ± 3.3	0.002
Aortic strain	0.07 ± 0.04	0.12 ± 0.05	<0.001
Aortic distensibility ($cm^2 \cdot dyn^{-1} \cdot 10^{-3}$)	3.9 ± 2.8	5.8 ± 3.0	0.030
Aortic stiffness index	6.8 ± 4.7	5.0 ± 3.2	0.041
PWV, m/s	9.6 ± 1.3	5.8 ± 1.2	<0.001
Cardiac measurements			
Left ventricular end-diastolic diameter, mm	47.0 ± 3.4	46.5 ± 7.6	n.s.
Left ventricular end-systolic diameter, mm	30.9 ± 3.9	30.2 ± 4.0	n.s.
Inter ventricular septum diameter, mm	9.5 ± 1.5	9.4 ± 1.1	n.s.
Left ventricular posterior wall diameter, mm	9.3 ± 1.2	8.7 ± 1.3	n.s.
Left ventricular ejection fraction, %	65.1 ± 5.8	64.4 ± 5.0	n.s.
Left ventricular mass, g	153.3 ± 46.5	149.4 ± 37.3	n.s.
Systolic pulmonary artery pressure, mm Hg	27.0 ± 3.1	25.1 ± 5.3	n.s.
Right ventricular end-diastolic diameter, mm	30.6 ± 3.1	30.4 ± 2.7	n.s.

[a] Calculated formula by MDRD.

Data are expressed as mean ± SD for normally distributed data.

BMI = Body mass index; BP = blood pressure; HDL-C = high-density lipoprotein cholesterol; LDL-C = low-density lipoprotein cholesterol; AoS = aortic systolic diameter; AoD = aortic diastolic diameter; PWV = pulse wave velocity.

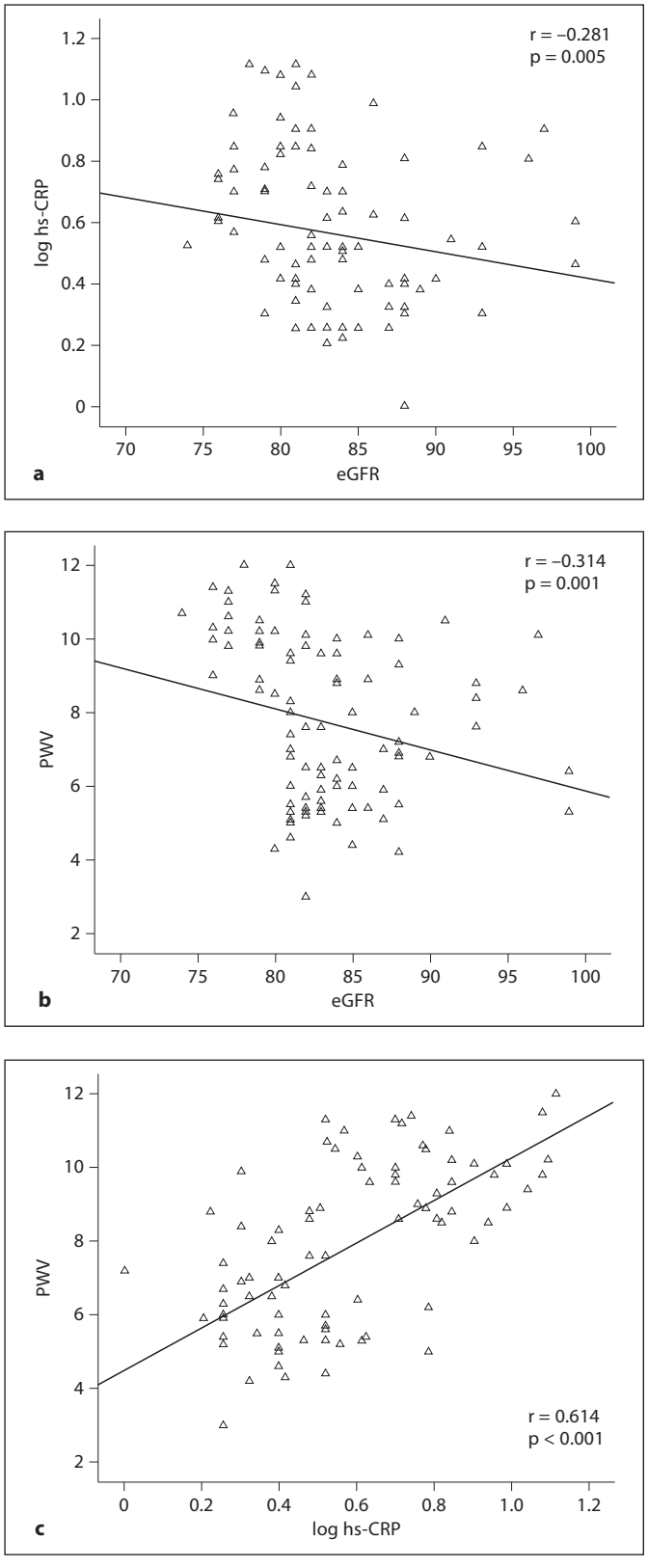

Fig. 2. The correlation analyses of pulse wave velocity, hs-CRP and eGFR in all study patients.

Results

The baseline characteristics for ultrasonographic pulse wave data of patients and controls are summarized in table 1. Briefly, of the 50 patients, 42% were male with mean age 36.6 ± 9.9 years. The 50 controls had a mean age of 35.4 ± 6.4 years and 44% were male. There were no significant differences in blood pressures or glomerular filtration rate between the groups. However, there were significant differences in serum levels of IL-6 (3.0 ± 1.0 vs. 2.0 ± 0.7, $p < 0.001$), TNF-α (2.8 ± 1.1 vs. 1.9 ± 0.8, $p < 0.001$), and hs-CRP (6.1 ± 3.1 vs. 2.8 ± 1.0, $p < 0.001$) between the two groups (fig. 1).

While most echocardiographic measurements were similar between the groups, patients with ADPKD showed a significantly lower aortic strain and distensibility than did the controls (0.07 ± 0.04 vs. 0.12 ± 0.05, $p < 0.001$ and 3.9 ± 2.8 vs. 5.8 ± 3.0 $cm^2 \cdot dyn^{-1} \cdot 10^{-3}$; $p = 0.032$, respectively). Blood pressure monitoring confirmed all patients as normotensive (table 1).

Measuring pulse wave velocity, the aortic stiffness index and pulse wave velocity values were increased in patients with ADPKD compared with controls (6.8 ± 4.7 vs. 5.1 ± 3.3, $p = 0.041$, 9.6 ± 1.3 vs. 5.8 ± 1.2 m/s, $p < 0.001$, respectively) (fig. 1). In univariate analysis of all patients and controls (table 2) hs-CRP correlated with aortic distensibility, hs-CRP and IL-6 with aortic stiffness index, and hs-CRP, IL-6, TNF-α and eGFR all correlated with PWV. The results very similar when analyzing only ADPKD patients (table 3).

Figure 2 shows univariate plots of eGFR versus hs-CRP (log-transformed) (a), eGFR versus PWV (b), and PWV versus hs-CRP (log-transformed) (c) in the whole study population (n = 100).

The independence of multiple correlations was analyzed with multivariate linear regression analyses. In all subjects, PWV was independently predicted by IL-6 ($\beta = 0.231$, $p = 0.017$), TNF-α ($\beta = 0.283$, $p = 0.001$) and hs-CRP ($\beta = 0.317$, $p = 0.001$).Only hs-CRP ($\beta = –0.310$, $p = 0.002$) was independently associated with aortic strain (table 4).

Discussion

This study proposes two major findings in patients with normotensive ADPKD and preserved renal function. First, early stage normotensive ADPKD patients already show signs of larger artery dysfunction (a decreased aortic distensibility) with systemic consequences (an in-

Table 2. Univariate correlates of selected markers in all 100 study participants

Variables	SBP		DBP		Aortic strain		Aortic index		Aortic distensibility		PWV	
	r	p	r	p	r	p	r	p	r	p	r	p
hs-CRP	0.164	n.s.	0.233	0.020	–0.310	0.002	0.280	0.005	–0.280	0.007	0.623	<0.001
IL-6	0.307	0.002	0.316	0.001	–0.264	0.008	0.224	0.025	–0.190	0.059	0.603	<0.001
TNF-α	0.149	n.s.	0.267	0.007	–0.045	n.s.	–0.073	n.s.	0.026	n.s.	0.612	<0.001
eGFR	–0.079	n.s.	–0.096	n.s.	0.020	n.s.	0.047	n.s.	–0.026	n.s.	–0.270	0.007
Age	0.248	0.013	0.096	n.s.	0.054	n.s.	0.178	0.077	–0.045	n.s.	0.110	n.s.

SBP = Systolic blood pressure; DBP = diastolic blood pressure; PWV = pulse wave velocity.
Values expressed as n.s. (not significant) if p ≥ 0.10.

Table 3. Univariate correlates of selected markers in 50 ADPKD patients

Variables	SBP		DBP		Aortic strain		Aortic index		Aortic distensibility		PWV	
	r	p	r	p	r	p	r	p	r	p	r	p
hs-CRP	–0.063	n.s.	0.051	n.s.	–0.059	n.s.	0.424	0.002	–0.277	0.051	0.522	<0.001
IL-6	0.266	0.062	0.171	n.s.	–0.280	0.049	0.374	0.007	–0.164	n.s.	0.476	<0.001
TNF-α	0.072	n.s.	0.243	0.089	0.115	n.s.	–0.187	n.s.	0.118	n.s.	0.566	<0.001
eGFR	–0.083	n.s.	–0.082	n.s.	–0.086	n.s.	0.115	n.s.	–0.086	n.s.	–0.472	0.001
Age	0.468	0.001	0.188	n.s.	–0.267	0.061	0.458	0.001	–0.397	0.004	–0.001	n.s

SBP = Systolic blood pressure; DBP = diastolic blood pressure; PWV = pulse wave velocity.
Values expressed as n.s. (not significant) if p ≥ 0.10.

Table 4. Multiple regression model predicting of pulse wave velocity (PWV) and aortic strain in all study subjects (n = 100)

Variables	β	SE	p
PWV			
hs-CRP	0.317	0.071	0.001
IL-6	0.231	0.226	0.017
TNF-α	0.283	0.177	0.001
SBP	0.171	0.014	0.022
Aortic strain			
hs-CRP	–0.310	0.002	0.002

The original model included age, IL-6, TNF-a, hs-CRP, eGFR, SBP, DBP, glucose, total cholesterol, and plasma triglyceride.
SBP = Systolic blood pressure; SE = standard error.
Adjusted $r^2 = 0.533$ for PWV and for aortic strain $r^2 = 0.087$.

creased PWV). These changes appear before echocardiographic verifiable cardiac hypertrophy. Secondly, there are independent correlations these changes in artery function and increased circulating levels of hs-CRP, IL-6 and TNF-α, a sign of inflammatory activity that may be linked to the observed changes.

Aortic stiffness is thought to reflect artery dysfunction [13] common in CKD patients, but of unknown etiology [14]. Aortic stiffness measurements (aortic strain, distensibility, stiffness index and pulse wave velocity), which are calculated from pulsatile changes in the aorta, are used practically for measuring large arterial stiffness; this approach has recently been recognized as an independent predictor of future cardiovascular risk [15]. Carotid-femoral PWV is used for global measure of aortic stiffness, and most validated method to noninvasively measure of arterial stiffness. It is considered as the gold standard index of aortic stiffness, given its simplicity, accuracy, reproducibility, and strong prediction of adverse outcomes [16, 17]. PWV has been shown to be an independent pre-

dictor of coronary heart disease and stroke in healthy subjects and an independent predictor of mortality in the general population. Carotid-femoral PWV is also a predictor of future changes in SBP and future development of hypertension in healthy volunteers [18]. Several studies demonstrate increased arterial stiffness and a link to adverse outcomes in patients with congestive heart failure, hypertension, myocardial infarction, as well as to atherosclerotic changes of the arterial wall and endothelial dysfunction. Indeed, arterial stiffness has been reported to be the best predictor of cardiovascular morbidity and mortality in several CVD populations [19–21]. Thus, PWV in chronic kidney disease is an eligible marker for to vigilance for future cardiovascular risks and could be therapeutic goals for prevention in the early stage of ADPKD.

In the ADPKD population, Borresen et al. [22] showed that arterial stiffness is increased in young normotensive ADPKD patients with a normal GFR, a finding supported by our data. They proposed this finding to result from endothelial dysfunction mediated by impaired nitric oxide synthesis and have followed-up this hypothesis by demonstrating endothelial dysfunction in vitro together with impaired acetylcholine mediated the vasodilatation of the small subcutaneous resistance arteries in a group of young normotensive ADPKD patients [23]. In another study [24], arterial stiffness more pronounced in ADPKD than in IgA nephropathy patients. Likewise, Menon et al. [25] have demonstrated that inflammation is evident in the circulation early in ADPKD, even when kidney function is preserved.

While our study design precludes the inference of causality, it is interested that only inflammation predicted arterial stiffness. Inflammation may exert its adverse vascular effects by either structural changes in the artery wall or through impaired cell signaling effects linked to endothelial dysfunction [26, 27]. Indeed, pro-inflammatory signaling has been shown to increase vascular stiffness contribute to endothelial dysfunction, elevate vascular smooth muscle tone, depress endothelial flow mediated dilation, worsens the response to vascular wall injury, impair neo-angiogenesis, and promote atherosclerotic plaque formation [28]. In CKD, inflammation is one of the strongest predictor of CVD and mortality [29], also in ADPKD patients [3, 25].

In these patients, inflammation generally rises as kidney function drops. Inflammation also plays a role in the pathogenesis of ADPKD [25, 30–32]. Cowley et al. [30] have reported that proinflammatory chemoattractants have a role in the development of interstitial inflammation and renal failure in ADPKD. Li et al. [31] demonstrated high levels of TNF-α in the cyst fluid of patients with ADPKD.

Based on these earlier reports and on our own data, we thus proposed that large artery dysfunction is an early characteristic of ADPKD linked to an unknown inflammatory process. The arterial dysfunction furthermore leads to increased aortic stiffness and PWV, but not (yet) systemic blood pressure, consequences that may well be important in mediating the overt hypertension, cardiac hypertrophy and increased incidence of vascular diseases seen in later stage ADPKD.

The major limitations of the current study are the small sample size and a cross-sectional design. Also, we did not perform invasive procedures to assess aortic elasticity and pulse pressure, which is important as these are generally considered more accurate than PWV [33].

In conclusion, we show that artery dysfunction predates hypertension and reduced GFR in ADPKD, but is predicted by signs of systemic or local inflammation. These findings may contribute to increased vigilance in these patients and help to elucidate pathways and therapeutic goals to decrease the risk of CVD and adverse outcomes in ADPKD patients.

Disclosure Statement

None.

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