Different Effect of IgA Nephropathy and Polycystic Kidney Disease on Arterial Stiffness

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Key Words

Arterial stiffness • Chronic kidney disease • IgA nephropathy • Polycystic kidney disease • Renal function

Abstract

Background: Renal function is a major predictor of vascular function and cardiovascular diseases. Little information exists about the effect of specific renal diseases on vascular function in chronic kidney diseases (CKD). **Methods:** One hundred and twenty patients (60 with IgA nephropathy, IgAN, and 60 with polycystic kidney disease, PKD) with CKD stages 1–4 were studied and compared. Pulse-wave velocity was measured by the digital volume pulse (DVP) method and stiffness index (SI_{DVP}) was derived. **Results:** All CKD (IgAN and PKD) patients had increased SI_{DVP} compared to controls (10.39 vs. 8.87 ± 1.79 m/s, $p = 0.008$). PKD patients had increased SI_{DVP} compared to IgAN and controls (11.14 ± 2.19 , 9.66 ± 2.02 and 8.87 ± 1.79 m/s, respectively, $p < 0.001$). An inverse correlation was found between SI_{DVP} and glomerular filtration rate in all CKD (IgAN and PKD) patients ($p = 0.001$) and in IgAN alone ($p < 0.01$), but not in PKD. With multivariate regression analysis, only age and 24-hour systolic blood pressure exerted independent effects on SI_{DVP} . **Conclusions:** Compared to controls, arterial stiffness was increased in CKD

patients. However, arterial stiffening was more pronounced in PKD than in IgAN, suggesting that vascular function is not similarly altered in etiologically different CKD groups. The fact that blood pressure was an independent risk factor underscores a therapeutic opportunity.

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Introduction

Patients with chronic kidney disease (CKD) often die of cardiovascular (CV) disease before even requiring renal replacement therapy [1, 2]. Although we know that any degree of decreased renal function or any proteinuria increases the risk for CV disease, the mechanisms linking CKD and CV diseases are not fully explained and likely involve both traditional and nontraditional CV risk factors. We focused our attention on damaged vascular function as one of the nontraditional mechanisms responsible for the disproportionate CV disease burden in CKD patients. Noninvasive assessment of vascular function with a well-documented bearing on CV mortality risk is now available by the determination of arterial stiffness [3].

Along with atherosclerosis (mainly affecting the intima of the arteries), arteriosclerosis (affecting mainly the

media of large and middle-sized arteries) is the most important arterial disease also in CKD patients. Arteriosclerosis characterized by reduced arterial elasticity or compliance is closely related to arterial stiffness. Longitudinal epidemiologic studies have demonstrated the independent predictive value of arterial stiffness on CV outcome in different populations [4–7]. It is generally accepted that arterial stiffness is increased in patients with end-stage renal disease (ESRD) [8–13]. Novel data suggest pronounced arterial stiffening in CKD patients with microalbuminuria or mild-to-moderately decreased renal function [14–17]. The mechanisms of increased arterial stiffening in CKD patients are not entirely defined, but may include chronic volume overload, chronic microinflammation, lipid peroxidation, abnormalities of the nitric oxide system, sympathetic overactivity, activation of the renin-angiotensin-aldosterone system (RAAS), increased mechanical stress by hypertension, and calcification of the arterial wall [18, 19].

The population of CKD patients in the stiffness studies was not homogenous according to the etiology of the renal disease. No comprehensive study has yet been conducted in patients with uniform types of CKD. Therefore, we wanted to examine and compare the arterial stiffness in two homogenous forms of CKD with different etiology: in immune-mediated IgA nephropathy (IgAN) and in inherited polycystic kidney disease (PKD). It was supposed that the arterial stiffness is increased in both CKD groups but on the basis of the different pathogenesis of the two renal diseases (immune-mediated vs. inherited) arterial stiffening is not equally altered in the two CKD populations.

IgAN is the most common immunologically mediated glomerular renal disease in the world [20]. Longer observation in many countries has shown that IgAN commonly causes ESRD in as many as 40% of patients within 20 years after diagnosis [21–23]. For this reason, the disease is very suitable for longitudinal CV disease and CV risk assessment of blood pressure, lipid value, and glucose metabolic disorders. For instance, Finnish IgAN patients were shown to develop much more premature CV disease than the general Finnish population [23].

PKD is the most common inherited renal disease and occurs in 1 of 400–1,000 individuals [24]. In most of the cases, it shows an autosomal-dominant inheritance. Two genes (polycystin genes 1 and 2) are implicated in its development. The clinical picture is characterized by cystic involvement of the kidneys with slow progression to ESRD and by some extrarenal CV manifestations, e.g. intra- and extracranial aneurysms, cardiac valvular de-

fect and increased carotid intima-media thickness [25, 26]. It is accepted that CV complications are the main cause of death also in PKD [27, 28].

We studied cohorts of well-characterized IgAN and PKD patients matched for age, kidney function, the most important CV risk factors and treatments, and focused our attention on their vascular function (arterial stiffness). Our purpose was 2-fold. We wanted to identify the effect of kidney diseases per se on arterial stiffness of these nonuremic patients clarifying whether the two homogenous forms of kidney diseases with different etiology have the same effect on arterial stiffness or not. Furthermore, we wanted to identify the CV risk factors with the strongest determinants on arterial stiffness in our CKD patients.

Patients and Methods

A cross-sectional study was performed in 120 CKD patients (60 IgAN and 60 PKD patients) with normal or mild-to-moderately decreased renal function (CKD stage 1–4). All of the CKD patients were followed up in the Outpatient Department of the Nephrological Center, University of Pécs, Hungary. The diagnosis was verified by renal biopsy in IgAN patients, and was based on typical abdominal ultrasound picture in PKD. Patients with confounding acute disorders including infections, unstable coronary heart disease, uncontrolled diabetes, or not yet adequately controlled high blood pressure (BP >180/110 mm Hg) were excluded from the study. Patients with supraventricular arrhythmias were also excluded. The patients were advised to consume a low-sodium- (maximum 5 g sodium chloride/day) and protein-restricted diet (0.6–0.8 g/kg ideal body weight/day) depending on their renal function [29]. The internal review board approved the study and written informed consent was obtained.

Risk Factor Assessment

The classic CV risk factors were analyzed in all groups. The patients underwent a 75-gram glucose tolerance test. Impaired glucose tolerance (IGT) was defined as a 2-hour glucose level between 7.8 and 11.1 mmol/l. If it was above 11.1 mmol/l, diabetes mellitus (DM) was diagnosed. Impaired fasting glucose was established if the fasting glucose value was between 6.1 and 6.9 mmol/l and the 2-hour glucose level was less than 7.8 mmol/l [30]. If any of them was detected, glucose metabolic disorder was diagnosed. Dyslipidemia was defined as a triglyceride level >1.7 mmol/l or high-density cholesterol (HDL) <1.0 mmol/l for men or <1.3 mmol/l for women. Twenty-four-hour ambulatory blood pressure monitoring (ABPM) was performed in every patient (ABPM-IV, Meditech, Hungary). Twenty-four-hour systolic and diastolic blood pressure, pulse pressure, diurnal index and heart rate were evaluated. Patients were termed hypertensive if their 24-hour average blood pressure on ABPM exceeded 130/80 mm Hg, or if they required antihypertensive treatment. Glomerular filtration rate was estimated (eGFR) according to the Cockcroft-Gault formula adjusted for body surface (ml/min/1.73 m²). The degree

Fig. 1. The Pulse Trace system. A finger clip containing an infrared light-emitting diode and a receiver is applied to the index finger of the dominant hand (adapted from the users' manual of Micro Medical Co., Rochester, UK). The curve on the left side is derived from the volume change of the digital artery. DVP comprises two distinct waves within one cardiac cycle. The time between the first peak and the inflection point in the waveforms is determined. SI_{DVP} can be calculated by the following equation: SI_{DVP} (m/s) = body height/ Δt_{DVP} .

of renal insufficiency of the patients was classified according to the Clinical Practice Guidelines for Chronic Kidney Diseases from the National Kidney Foundation – Kidney Disease Outcomes Quality Initiative Group for CKD [31] as follows: CKD 1–2 group (eGFR ≥ 60 ml/min), CKD 3–4 group (eGFR: 15–59 ml/min). Patients with ESRD (CKD5, eGFR < 15 ml/min) or those receiving renal replacement therapy were not included in this study.

Fifty subjects with normal renal function and with no history of renal disease formed the control group. These persons had variable elements of CV risk factors. They exhibited a similar age range as the patients and were recruited from amongst the general community. Their data including the parameters of ABPM were analyzed similarly to IgAN and PKD patients.

Vascular Stiffness Determinations

Finger photoplethysmographic method with the Pulse Trace system, Micro Medical Ltd., Rochester, UK) was used for the estimation of pulse-wave velocity (PWV) [32, 33]. The method enables to determine the stiffness index (SI) which can be derived from the digital volume pulse (DVP) and is reflected as SI_{DVP} [34]. A finger clip containing an infrared light-emitting diode and a receiver was applied to the index finger of the dominant hand to get the DVP (fig. 1). The DVP comprises two distinct waves within one cardiac cycle, i.e. an early systolic peak arising from pressure wave propagating from the heart along the arterial tree to the finger followed by a delayed second peak caused by pressure wave reflected backward mainly from the aortic bifurcation. The time between the first peak and the inflection point in the waveforms was determined (Δt_{DVP}). SI_{DVP} was calculated by the following equation: SI_{DVP} (m/s) = body height/ Δt_{DVP} [35]. Because the timing of the diastolic component relative to the systolic component depends on the PWV of pressure waves in the aorta and large arteries, the increased SI_{DVP} mirrors the propagation of the arterial stiffening [36, 37]. More details of the validity of the method can be seen in the Discussion section.

Patients and controls had taken their regular medicines as necessary. The participants were asked not to smoke and not to drink coffee on the day of the examination. All subjects were examined in the supine position after at least 10 min rest. A single waveform was obtained by averaging DVP contours during a period of 30 s.

To enhance the accuracy of the investigation of SI_{DVP} , five period samples were taken and the upper and lower merit of DVP was deleted. The remaining three merits were averaged and used in further analysis. A variability test was performed with the remaining three merits. All measurements were performed in the morning hours between 9 and 11 a.m., thereby eliminating confounding effects of circadian variability. The person analyzing the data was not aware of any clinical information regarding the subjects.

Statistical Analysis

All results are presented as mean value $\pm$ SD for variables with normal distribution, unless otherwise indicated. The difference between the clinical parameters of IgAN, PKD and the control groups was investigated by one-way ANOVA. Pearson χ^2 or Fisher's exact test were applied to analyze categorical variables. Correlation analyses were performed to determine association between renal function as well as blood pressure and SI_{DVP} . Multinomial logit was used to assess the difference between the CKD and control groups during ageing. Univariate and multivariate linear regression analyses were performed to identify independent risk factors associates with SI_{DVP} . Nine risk factors were analyzed: age, gender, 24-hour systolic blood pressure, 24-hour diastolic blood pressure, glucose metabolic disorders (DM, IGT and IFG), dyslipidemia, BMI, hyperuricemia and eGFR. $p < 0.05$ was considered statistically significant. Data analysis was performed using the SPSS software program version 13.0 (SPSS Inc., Chicago, Ill., USA).

Results

Clinical and Demographic Characteristics of CKD Patients and Controls

Clinical and demographic population variables are summarized in table 1. The incidence of classic CV risk factors (hypertension, glucose metabolic disorders, dyslipidaemia, obesity, age, smoking habit) was similar across the different groups, including systolic, diastolic,

Table 1. Baseline characteristics of the patients

	PKD group (n = 60)	IgAN group (n = 60)	Control group (n = 50)	p
Male, n (%) [*]	21 (35)	36 (60)	30 (60)	<0.05
Age, years	45 ± 11	46 ± 13	45 ± 13	NS
Hypertension, n (%)	49 (82)	49 (82)	31 (62)	NS
Systolic BP, mm Hg ^a	131 ± 18	126 ± 15	127 ± 14	NS
Diastolic BP, mm Hg ^a	80 ± 10	76 ± 8	76 ± 10	NS
Pulse pressure, mm Hg ^a	51 ± 11	50 ± 12	51 ± 9	NS
Heart rate, beats/min ^a	74 ± 10	76 ± 11	73 ± 6	NS
Obesity, n (%)	23 (38)	19 (32)	19 (38)	NS
Obesity BMI	28.0 ± 6.2	27.4 ± 5.1	27.9 ± 5.1	NS
Dyslipidemia, n (%)	27 (45)	30 (50)	27 (54)	NS
Glucose metabolic disorders, n (%)	13 (22)	19 (32)	17 (34)	NS
Current smokers, n (%)	22 (37)	17 (28)	14 (28)	NS
eGFR, ml/min ^{**}	70 ± 37	72 ± 35	108 ± 19	<0.05
Treatment				
ACEI/ARB, n (%)	46 (77)	50 (83)	31 (62)	NS
Calcium antagonists, n (%) [*]	31 (52)	12 (20)	18 (36)	<0.05
β-Blockers, n (%)	21 (35)	16 (27)	19 (38)	NS
α-Receptor blockers, n (%)	5 (8)	3 (5)	3 (6)	NS
Imidazolin receptor agonist, n (%)	2 (3)	2 (3)	3 (6)	NS
Diuretics, n (%)	7 (12)	5 (8)	5 (10)	NS
Statins, n (%)	22 (37)	21 (35)	23 (46)	NS

^a At ABPM. ^{*} p < 0.05 PKD group vs. IgAN and control groups, ^{**} p < 0.05 PKD group and IgAN group vs. control group. NS = Nonsignificant.

and pulse pressure measured by 24-hour ABPM. There was a gender difference, because the PKD group contained significantly more female patients. Most of the patients were receiving antihypertensive drugs. The use of calcium antagonists was more frequent in the PKD group, but the other antihypertensive and lipid-lowering therapy (angiotensin-converting enzyme inhibitors, ACEI, angiotensin-II receptor blockers, ARB, β-blockers, α-receptor blockers, imidazolin receptor agonists, diuretics and statins) was similar in the two CKD groups. The eGFR of the control group was normal, but the eGFR of the PKD and IgAN groups was significantly lower than in controls. The eGFR of the two CKD groups was statistically similar (table 1).

A variability testing was performed with the three SI_{DVP} merits, as outlined earlier. The result of this analysis was 0.52 ± 0.63 m/s, indicating quite low variability of our data.

Comparison of SI_{DVP} in CKD Patients and Controls

SI_{DVP} was increased in the group of all CKD (IgAN and PKD) patients compared to controls (10.39 vs. 8.87 ± 1.79

m/s, $p = 0.008$). Separately examining the two CKD groups, the SI_{DVP} of the PKD group (11.14 ± 2.19 m/s) was significantly higher than the SI_{DVP} of the IgAN (9.66 ± 2.02 m/s) and control groups (8.87 ± 1.79 m/s) ($p < 0.001$ in both relations) while there was no significant difference in the SI_{DVP} values between the IgAN group and the controls (fig. 2a). Because of the gender difference between the PKD and IgAN groups, to exclude its effect on arterial stiffness, the SI_{DVP} of men and women was analyzed separately in both groups. No significant difference was found in SI_{DVP} either among PKD patients (SI_{DVP} of men: 11.19 ± 1.88 m/s vs. SI_{DVP} of women: 11.11 ± 2.36 m/s, p was nonsignificant) or among IgAN patients (SI_{DVP} of men: 9.57 ± 2.16 m/s vs. SI_{DVP} of women: 9.80 ± 1.85 m/s, p was nonsignificant) on the basis of gender.

SI_{DVP} and Renal Function in CKD Patients

The two groups of CKD patients were matched according to their eGFR. There were 24 patients in CKD stage 3–4 and 36 patients in CKD stage 1–2 both in the IgAN and the PKD groups. The SI_{DVP} of the CKD 3–4 IgAN patients was significantly higher than that of the controls

Fig. 2. a SI_{DVP} in the CKD groups. SI_{DVP} of the PKD group was significantly higher than SI_{DVP} of IgAN patients and controls: 11.14 ± 2.19 , 9.66 ± 2.02 and 8.87 ± 1.79 m/s, respectively ($p < 0.001$ in both relations). There was no significant difference in SI_{DVP} values between the IgAN group and controls. **b** SI_{DVP} in the IgAN subgroups (CKD 3–4, CKD 1–2) and in controls. SI_{DVP} of CKD 3–4 IgAN patients was significantly higher than of controls (10.43 ± 2.30 vs. 8.87 ± 1.79 m/s, $p < 0.05$) while SI_{DVP} of CKD 1–2 IgAN patients (9.15 ± 1.72 m/s) did not differ significantly from controls. Arterial stiffness of the CKD 3–4 patients was slightly, but not significantly higher than of CKD 1–2 patients in IgAN. **c** SI_{DVP} in the PKD subgroups (CKD 3–4, CKD 1–2) and in controls. The SI_{DVP} in both groups (CKD 3–4 and of CKD 1–2 patients) was significantly higher than in controls (11.41 ± 2.23 and 10.95 ± 2.17 m/s vs. 8.87 ± 1.79 m/s, $p < 0.001$, respectively).

(10.43 ± 2.30 vs. 8.87 ± 1.79 m/s, $p < 0.05$), while the SI_{DVP} of CKD 1–2 IgAN patients (9.15 ± 1.72 m/s) was not significantly different from the controls (fig. 2b). There was no significant difference in stiffening of the CKD 3–4 patients compared to the CKD 1–2 patients in the IgAN group. In the PKD patients, the SI_{DVP} in both groups (CKD 3–4 and of CKD 1–2 patients) was significantly higher than in controls (11.41 ± 2.23 and 10.95 ± 2.17 m/s vs. 8.87 ± 1.79 m/s, $p < 0.001$, respectively (fig. 2c). There was a significant negative correlation between SI_{DVP} and eGFR in the group comprising all (IgAN and PKD) CKD patients ($r = -0.288$, $p = 0.001$) (fig. 3a) and in the IgAN patients ($r = -0.368$, $p < 0.01$, fig 3b), but not in the PKD patients ($r = -0.229$, p was nonsignificant; fig 3c).

Assessment of Risk Factors

Univariate linear regression analyses were performed in both renal groups to assess the confounding factors affecting SI_{DVP}: age, gender, 24-hour systolic blood pres-

sure, 24-hour diastolic blood pressure, glucose metabolic disorders (diabetes, IGT or IFG), dyslipidemia, BMI, hyperuricemia, and eGFR. In this model, age, 24-hour systolic blood pressure and 24-hour diastolic blood pressure as well as eGFR had a significant impact on SI_{DVP} when analyzing all renal patients together (IgAN and PKD). With multivariate regression analysis, examining all renal patients' age and 24-hour systolic blood pressure together exerted independent effects on SI_{DVP}. Furthermore, there was a significant correlation between SI_{DVP} and 24-hour systolic blood pressure as well as 24-hour diastolic blood pressure in the group of all CKD (IgAN and PKD) patients ($r = 0.252$, $p = 0.02$ and $r = 0.301$, $p = 0.007$, respectively).

Age Dependency of SI_{DVP}

Using an estimated regression model to compare the increase of SI_{DVP} during aging in the three groups, it was demonstrated that the SI_{DVP} of PKD and IgAN patients

Fig. 3. a Correlation between eGFR and SI_{DVP} in all CKD patients. There was a significant correlation between eGFR and SI_{DVP} : $y = -0.0178x + 11.663$; $r = -0.288$, $p = 0.001$. **b** Correlation between eGFR and SI_{DVP} in IgAN. The relation is significant: $y = -0.021x + 11.179$; $r = -0.368$, $p < 0.01$. **c** Correlation between eGFR and SI_{DVP} in PKD. There was no significant correlation between eGFR and arterial stiffness in this group: $y = -0.0162x + 12.355$; $r = -0.229$, p was nonsignificant.

increased significantly faster than the SI_{DVP} of controls in all the age groups (PKD vs. controls $0.091-0.073 > 0$, beta 0.814, 95% CI 1.682–3.028, $p < 0.001$; IgAN vs. controls $0.089-0.073 > 0$, beta 0.313, 95% CI 1.059–1.764, $p < 0.005$) (fig. 4).

Discussion

The novel findings of this study are that in two homogenous CKD populations (IgAN and PKD) a rather marked but not similar increase of arterial stiffness exists as compared to controls. Arterial stiffness (SI_{DVP}) was significantly higher in PKD patients than in IgAN as well as in controls. Furthermore, an inverse significant correlation was found between SI_{DVP} and eGFR in the group of all CKD (IgAN and PKD) patients, as well as in IgAN patients but not in PKD. There was a significant correlation between SI_{DVP} and systolic and diastolic blood pressure in the group of all CKD (IgAN and PKD) patients.

Fig. 4. Estimated regression model. The three lines representing the three examined groups demonstrate that the SI_{DVP} of the CKD patients was increased in both groups (PKD > IgA) and in all age groups compared to controls.

The fact that blood pressure was also an independent risk factor underscores a more aggressive therapeutic opportunity.

Previous studies have reported increased stiffness in renal patients with ESRD before or during renal replacement therapy [6, 9]. However, in most studies dealing with CKD patients, the etiology of the CKD is rarely mentioned and stiffness of renal patients with different etiology have not been compared yet. Furthermore, there are only a few publications on arterial stiffening in renal patients with preserved or only slightly reduced renal function. Our purpose was the routine, pre-symptomatic screening of IgAN and PKD patients to obtain the arterial stiffness. We aimed to find those CKD patients who have an increased risk of developing further CV disease. We selected patients with relatively preserved glomerular function to specifically minimize the influence of uremia-related factors such as volume overload, disorders of calcium and phosphate metabolism, and other confounders on arterial stiffness.

We identified an increased vascular stiffness in both CKD groups (IgA and PKD) compared to controls. SI_{DVP} of IgAN patients was significantly lower than SI_{DVP} of PKD patients. Looking for the connection between SI_{DVP} and renal function there was a stepwise (but not significant) increase of arterial stiffness corresponding to the stages of the CKD and a significant correlation between arterial stiffness and the degree of impairment of renal function (eGFR) in the IgAN patients. Wang et al. [38] reported similar findings in 102 CKD patients with various renal diseases from Taiwan. They found that SI was independently associated with renal function, a finding we could not corroborate here. However, the patients described by Wang et al. [38] may have been different. Ethnic and environmental (for instance dietary) differences could be responsible, as well as methodology. The increase of arterial stiffness associated with the parallel decline of renal function in smaller groups of etiologically non-homogenous CKD patients from France, UK and the Netherlands [39–41]. These patients generally had more advanced renal disease than those reported here.

At the same time, vascular stiffness of PKD patients was significantly increased in the early stages (CKD 1–2) of the disease (fig. 2c) and in already juvenile patients (fig. 4). The stiffness did not correlate with the degree of renal function. Our finding confirms the results of Borresen et al. [42] who found that pulse-wave reflection was amplified even in young PKD patients with normal renal function. As Ecker and Schrier [25] summarized recently, CV abnormalities are common in PKD. Cardiac diastol-

ic dysfunction, endothelial dysfunction, increased intima-media thickness, impaired coronary flow velocity reserve and cardiac valvular abnormalities may present in young patients with PKD who have well-preserved renal function. The etiology of early CV abnormality in PKD is not clear. Polycystins 1 and 2 are strongly expressed in the endothelium as well as in human adult vascular smooth cells and the vascular abnormalities in PKD patients may be related to altered expressions of polycystin with primary disruption of polycystin functions [43]. Further observations demonstrated an early exaggerated activation of the RAAS both in adults and in children with PKD even before the onset of hypertension [44–47]. A possible explanation can be cyst expansion causing a local renal ischemia [24]. Immunohistochemical studies of nephrectomy specimens from PKD patients have shown hyperplasia of renin-secreting cells of the juxtaglomerular apparatus, suggesting that chronic stimulation of the RAAS is present [48].

Some investigators suggest that the RAAS is very important in the development of arterial stiffness not only in PKD patients [49]. ACEI or ARB treatment significantly improved the parameters of stiffness in the general population, hypertensive patients and renal patients on dialysis, as reviewed by Gusbeth-Tatomir [50]. Hypertension is also very common in IgAN and PKD [51]. However, there are no data about the stiffness-decreasing effect of ACEI and/or ARB treatment in IgAN and PKD patients. The beneficial impact of RAAS inhibition may be limited to some but not all CKD patients, since most of our patients received ACEI and/or ARB therapy. Possibly, our treatment was begun too late or was not aggressive enough or should have been combined with renin inhibition or mineralocorticoid receptor blockade.

Arterial stiffness can be measured by several methods. Aortic pulse wave velocity (PWV) is the indirect measurement of large arterial stiffness most often used. SI_{DVP} derived by the contour analysis of DVP is an alternative simple method to analyze arterial stiffness. However, as Sollinger et al. [9] discussed, the two methods do not provide identical information. Aortic PWV, measured over the carotid-femoral region, determines the velocity of pressure transmission between both detection sites and is related inversely to aortal compliance. SI_{DVP} is a composite parameter influenced by flexibility of the large central arteries as well as reflective properties of the peripheral arterial bed. In addition to the velocity of pressure wave reflection along the large central conduit arteries, the DVP waveform is affected by characteristics of ventricular ejection and the exact distribution of aortic and more

peripheral sites of pressure wave reflection [52]. Despite these differences, a significant correlation was found between SI_{DVP} and PWV in healthy individuals, patients with ESRD and patients with coronary artery disease [34, 47, 53]. The usefulness of the SI_{DVP} as a noninvasive alternative to detect arterial stiffness was also successfully tested in patients with hypertension, diabetes mellitus and children [36, 54, 55]. Furthermore, SI_{DVP} can help in the risk stratification of both hypertensive and apparently healthy people with different CV risk factors [56, 57].

The technique of finger photoplethysmography has the advantages of being relatively simple, easily portable and also avoids some difficulties during the detection of pressure waveform encountered with other methods. Such confounders include the accurate recording of femoral pressure waveforms in patients with obesity and severe atherosclerosis or the psychological discomfort of the inguinal location [58, 59].

Limitations

We are aware of limitations in our study. Because of the cross-sectional design, we cannot say for certain that the association between increased arterial stiffness and decreased renal function is causal in our CKD patients. Since the course of both diseases exceeds often more than

20–30 years, the authors will not be in a position to answer longitudinal questions. Not all of the patients had 24-hour creatinine clearance values determined and, for this reason, we used the estimated renal function (Cockcroft-Gault formula) for mathematical analysis. Finally, we examined a relatively small number of patients to get well-matched homogenous renal populations.

In conclusion, the present study suggests that various types of kidney diseases may act differently on arterial stiffness. Studies investigating the arterial stiffness in CKD patients should take this possibility into consideration. Further longitudinal well-conducted clinical investigations are warranted to clear the impact of reduced arterial elasticity on the progression of different renal diseases. Future longitudinal research studies should focus on the better understanding of the complex interplay between arterial function, CV risk factors and treatments, CV diseases and CKD.

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