J Nephrol (2014) 27:173–179
DOI 10.1007/s40620-013-0021-4

ORIGINAL ARTICLE

Abdominal aortic calcification and renal resistive index in patients with chronic kidney disease: is there a connection?

Gabriel Stefan · Cristina Capusa · Simona Stancu · Ligia Petrescu · Elena Dana Nedelcu · Iuliana Andreiana · Gabriel Mircescu

Received: 16 April 2013 / Accepted: 12 August 2013 / Published online: 15 January 2014

Abstract
Background We aimed to evaluate the relationship between abdominal aortic calcification (AAC) and renal resistive index (RRI), parameters associated with cardiovascular outcome, in non-dialysis chronic kidney disease (CKD) patients.
Methods Seventy-seven stable patients mainly in CKD stages 3B and 4 (44 and 28 %), median age 69 years, with a positive history of systemic atherosclerosis were prospectively enrolled. RRI, carotid intima-media thickness (IMT), Kauppila score for AAC (AACs), cardio-ankle vascular index (CAVI) and ankle-brachial index (ABI) were assessed. Traditional and non-traditional atherosclerosis risk factors were also evaluated.
Results Vascular (50 %), diabetic (26 %) and primary glomerular nephropathies (8 %) were the main causes of CKD. AAC was highly prevalent (77 %). In the whole cohort, RRI was directly related to AACs ($rs = 0.35$, $p < 0.001$). AACs correctly identified patients with RRI >0.7 in 69 % (56–81 %) of cases, a cut-off of 5 resulting the best combination of sensitivity (65 %) and specificity (68 %). Compared to those with AACs <5, patients with AACs >5 were older, had higher serum cholesterol, C-reactive protein and IMT, lower ABI, but similar CAVI, estimated glomerular filtration rate, serum calcium and phosphate. In the whole cohort, AACs was negatively correlated with ABI ($rs = -0.51$, $p < 0.001$) and positively with IMT ($rs = 0.27$, $p = 0.01$), supporting a role for Kauppila score in integrating information on both intra- and extrarenal atherosclerosis.
Conclusions As Kauppila score correlates with RRI in non-dialysis CKD patients, it could be a fast, convenient and relatively inexpensive tool for estimating RRI, and consequently the intrarenal vascular status, but further research is warranted.

Keywords Abdominal aortic calcification · Atherosclerosis · Chronic kidney disease · Kauppila score · Renal resistive index

G. Stefan · C. Capusa · S. Stancu · L. Petrescu · I. Andreiana · G. Mircescu
"Dr. Carol Davila" Teaching Hospital of Nephrology, Bucharest, Romania

C. Capusa (✉) · S. Stancu · L. Petrescu · I. Andreiana · G. Mircescu
Nephrology Department, "Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania
e-mail: ccalexandr@yahoo.com

E. D. Nedelcu
Department of Radiology and Medical Imaging, Delta Hospital, Bucharest, Romania

Introduction

Arterial calcification is frequent in patients with chronic kidney disease (CKD) and is closely associated with a high cardiovascular risk [1–3]. The abdominal aortic calcification (AAC) score assessed on a lumbar radiogram is a predictor of cardiovascular morbidity and mortality, independent of the atherosclerosis traditional risk factors [4–7].

The renal arterial resistive index (RRI) measured by Doppler ultrasonography describes the percentage reduction of end diastolic blood flow in renal vessels in relation to the maximal systolic blood flow. High RRI values were found in patients with renal vascular damage due to atherosclerosis [8] and were correlated with renal histopathologic indices of arteriolosclerosis [9]. Moreover, in a

4-year follow-up study, RRI was shown to predict renal prognosis in CKD patients with almost the same sensitivity and specificity as proteinuria [10].

Our purpose was to investigate the relationship between AAC score and the RRI in non-dialysis CKD patients.

Subjects and methods

Subjects

This prospective, cross-sectional study enrolled 77 patients selected from those admitted to "Dr. Carol Davila" Teaching Hospital of Nephrology in a 6-month period. Inclusion criteria were age over 50 years, estimated glomerular filtration rate (eGFR) <60 ml/min/1.73 m^2 [modification of diet in renal disease (MDRD) equation] on two occasions in a 3-month period, and a positive history for systemic atherosclerosis (ischemic heart disease, cerebrovascular disease, peripheral vascular disease, ischemic nephropathy). Patients with end-stage renal disease (ESRD), obstructive nephropathy and valvular heart disease were excluded.

The study protocol was approved by the local Ethics Committee. All subjects signed an informed consent prior to any study procedure.

Methods

Physical examination included body mass index and blood pressure (measured with an aneroid sphygmomanometer in the sitting position with an appropriate-sized cuff). Serum lipid profile (total cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol and triglycerides), calcium-phosphate metabolism (total and ionized calcium, phosphate, and total alkaline phosphatase), inflammation parameters [C-reactive protein (CRP), albumin] and hemoglobin were assessed. Urinary protein, albumin and creatinine were measured in a 24 h urine sample.

Abdominal aortic calcifications (AAC) were evaluated on a lateral lumbar X-ray (acquired in the standing position), as described by Kauppila [5]. The measurements were performed by the same independent examiner who was unaware of the patient's characteristics or the purpose of the study.

For Doppler ultrasonography examination a real-time ultrasound device with color Doppler capacity (Acuson S2000; Siemens, Erlangen, Germany) and a 3.5 MHz convex-type transducer were used. The examination was performed with the patient in supine position and after at least 15 min rest. The signals were obtained from interlobar and arcuate arteries in the upper, middle, and lower parts of the kidney. The RRI was calculated as [(peak-systolic velocity − end-diastolic velocity)/peak systolic velocity]. The RRI value for each kidney was the mean of all 6 measurements. A mean RRI value was obtained for each patient by averaging the two kidneys' mean RRIs. The use of antihypertensive medication was not suspended before RRI measurement. In order to avoid inter-observer variability, all Doppler examinations were performed by the same examiner who was unaware of the study or the clinical details of the patients.

The ankle-brachial index (ABI)—an index of atherosclerotic peripheral vascular disease—and cardio-ankle vascular index (CAVI)—a marker of arterial stiffness—were measured with the subjects in supine position at rest for at least 10 min by trained technicians using the VaSera VS-1000 screening device (Fukuda Denshi, Tokyo, Japan) as described in the manufacturer's protocol.

For intima media thickness (IMT) determination B-mode ultrasonography imaging of the carotid artery was performed with a transducer frequency of 7 MHz. Up to 4 cm of the common carotid artery, the carotid bifurcation and the internal carotid 2 cm distally from bifurcation were scanned bilaterally using longitudinal and transverse sections. IMT was defined as the distance between the leading edge of the first echogenic line (lumen-intima interface) and the second echogenic line (media-adventitia interface) in plaque-free arterial segments. All measurements were performed under blind conditions.

Statistical analysis

Continuous variables are presented as mean or median and 95 % confidence interval, according to their distribution, and categorical variables as percentages. The mean bilateral CAVI, ABI and IMT values were used in analysis. Group comparisons were performed with Student's t-test, χ^2 test, Mann–Whitney U test, and the Kruskal–Wallis test, as appropriate. The Spearman test was used to assess correlations. A $p \leq 0.05$ was considered statistically significant.

The utility of the AAC score as a continuous variable to identify patients with pathological RRI (>0.7), ABI (<0.9) and IMT (>0.1 cm) as dichotomous was investigated using receiver operating characteristic (ROC) curve analysis [10–12]. In order to validate the ROC curve, a calibration analysis was performed with the Hosmer–Lemeshow goodnes-of-fit test [13]. The association between AAC (defined as a dichotomous variable, higher or lower than 5) and RRI, IMT, and ABI as covariates, and the atherosclerosis risk factors was investigated by multivariable-adjusted binomial logistic regression.

Table 1 Investigated parameters in study groups

	All	AAC score ≤5	AAC score >5	p*
Patients (n)	77	40	37	
Traditional risk factors for atherosclerosis				
Age (years)	69.2 (67.1–71.2)	66.7 (64–69.5)	71.8 (68.8–74.8)	0.006
Gender (M/F)	38/39	25/15	13/24	0.01
BMI (kg/m^2)	27.7 (26.4–28.9)	28.7 (26.9–30.5)	26.6 (24.7–28.4)	0.04
Smokers (n)	10 (17 %)	5	5	0.5
Cholesterol (mg/dl)	177 (167–193)	167 (160–182)	193 (175–211)	0.006
Triglycerides (mg/dl)	128 (111–140)	126 (85–140)	129 (111–147)	0.2
LDL-cholesterol (mg/dl)	94 (82–104)	94 (72–115.5)	94.5 (73–141)	0.2
HDL-cholesterol (mg/dl)	51.4 (48.5–54.8)	49.9 (46.6–54.5)	53.7 (47.8–64.1)	0.2
SBP (mmHg)	140 (134–145)	137 (129–146)	142 (134–151)	0.2
DBP (mmHg)	77.2 (74.1–80.4)	77.6 (73.7–81.4)	76.8 (71.3–82.2)	0.8
MBP (mmHg)	96.7 (90–100)	96.7 (90–103.3)	97.5 (90–101.7)	0.8
Non-traditional risk factors for atherosclerosis				
Chronic kidney disease				
Primary renal disease (%)				0.2
Vascular nephropathy	50	40	54	
Diabetic nephropathy	26	20	32	
Primary glomerulonephritis	8	12	3	
ADPKD	4	7	–	
Interstitial nephropathies	5	7	3	
Pyelonephritis	2	2	3	
n/a	5	12	5	
eGFR (MDRD)	33.5 (30.1–36.9)	33.7 (30.3–39)	30.2 (28–35.2)	0.1
CKD stage (%)				0.8
2	6	3	3	
3A	13	8	5	
3B	44	25	19	
4	28	12	16	
5	9	4	5	
Proteinuria (g/24 h)	0.5 (0.2–0.7)	0.47 (0.15–0.8)	0.56 (0.16–0.95)	0.7
Albuminuria (g/24 h)	0.11 (0.03–0.27)	0.05 (0.03–0.2)	0.18 (0.03–0.46)	0.1
Calcium-phosphate metabolism parameters				
Total calcium (mg/dl)	9.3 (9.1–9.4)	9.25 (8.9–9.5)	9.35 (9.1–9.5)	0.2
Ionized calcium (mg/dl)	4.03 (3.9–4.1)	4 (3.8–4.1)	4.06 (3.9–4.2)	0.2
Serum phosphate (mg/dl)	3.6 (3.4–3.8)	3.6 (3.3–3.9)	3.68 (3.3–4)	0.3
Serum alkaline phosphatase (U/L)	77 (69–84)	77 (68–79)	81 (60–99)	0.4
Inflammation markers				
CRP (mg/dl)	5 (3–8)	3 (2–7)	6 (4–12)	0.01
Serum albumin (g/dl)	4.32 (4.2–4.4)	4.4 (4.3–4.6)	4.1 (3.9–4.3)	0.002
Serum hemoglobin (g/dl)	12.3 (11.9–12.7)	12.7 (12.1–13.3)	12 (11.5–12.5)	0.03
Non-invasive measurements of atherosclerosis and arterial stiffness				
IMT (cm)	0.08 (0.07–0.08)	0.07 (0.07–0.08)	0.08 (0.08–0.09)	0.006
ABI	1.02 (0.97–1.06)	1.08 (1.04–1.21)	0.92 (0.84–1)	0.0002
CAVI	10.5 (10.01–11.07)	10.8 (10.07–11.53)	10.1 (9.3–10.9)	0.2

Table 1 continued

	All	AAC score ≤5	AAC score >5	p*
Renal resistive index	0.7 (0.68–0.72)	0.68 (0.64–0.69)	0.73 (0.7–0.75)	0.0008

AAC abdominal aortic calcification, *BMI* body mass index, *LDL*-cholesterol low-density lipoprotein cholesterol, *HDL*-cholesterol high-density lipoprotein cholesterol, *SBP* systolic blood pressure, *DBP* diastolic blood pressure, *MBP* mean arterial pressure, *eGFR* estimated glomerular filtration rate, *MDRD* modification of diet in renal disease, *n/a* not available, *ADPKD* autosomal dominant polycystic kidney disease, *CRP* C-reactive protein, *IMT* intima media thickness, *ABI* ankle-brachial index, *CAVI* cardio-ankle vascular index

* Abdominal aortic calcification score >5 versus ≤5

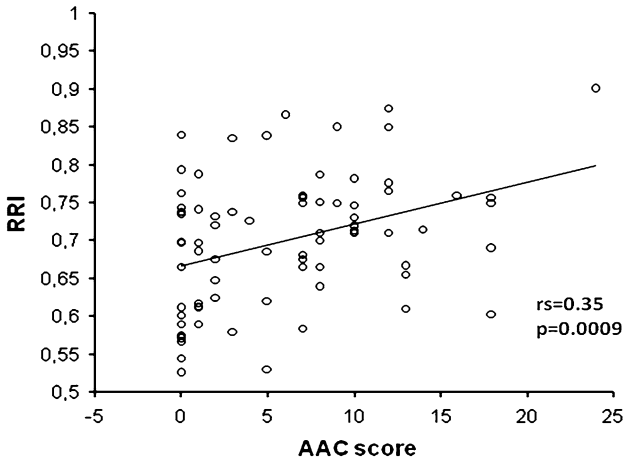

Fig. 1 Renal resistive index (RRI) correlation with abdominal aortic calcification (AAC) score

Analyse-it (Analyse-it Software, Ltd., Leeds, UK) and SPSS (SPSS Inc., Chicago, IL, USA) software were used to analyze the data.

Results

Most patients were in stage 3B or 4 CKD (44 and 28 %). Vascular nephropathies, diabetes mellitus and primary glomerulonephritis were the main primary renal diseases. Ninety-four percent of the patients were treated for arterial hypertension. Only 23 % of the subjects had no aortic calcification as assessed by the Kauppila score (Table 1).

Renal resistive index increased with the aortic calcification score ($rs = 0.35$, $p = 0.0009$, Fig. 1). A calcification score of five had the best sensitivity and specificity in identifying patients with a high RRI (>0.7) (Table 2). RRI also correlated with the other indices of atherosclerosis: ABI ($rs = -0.44$, $p = 0.0004$) and IMT ($rs = 0.22$, $p = 0.03$), but not with arterial stiffness (CAVI) (Table 1; Fig. 2). Furthermore, a calcification score of five was found to have the greatest sensitivity and specificity in identifying patients with an abnormal ABI (<0.9) and IMT (>0.1 cm), respectively (Table 2). The observed relationships between AAC score and RRI, ABI, IMT were validated by the Hosmer–Lemeshow test results (Table 2).

In order to further evaluate the impact of the aortic calcifications, groups defined according to an ACC score ≤5 or >5 were compared (Table 1). The patients with an AAC score >5 (48 %) were older, mostly female, had higher serum total cholesterol, lower serum hemoglobin and more pronounced inflammation (as suggested by higher CRP and lower serum albumin levels) as compared to their lower AAC counterparts. No other traditional or non-traditional investigated cardio-vascular risk factors differed between the two groups (Table 1). CKD etiology and severity were similar in both groups. However, in the whole cohort, the AAC score was negatively correlated with eGFR ($rs = -0.18$, $p = 0.05$).

The AAC score was negatively correlated with ABI ($rs = -0.51$, $p < 0.0001$) and positively with IMT ($rs = 0.27$, $p = 0.01$) in the whole cohort. Lower ABI ($p = 0.0002$) and higher IMT ($p = 0.006$) were seen in patients with a calcification score >5. However, arterial stiffness (CAVI) did not differ between groups (Table 1).

The association between AAC score and IMT, ABI, RRI was tested separately in three distinct multivariable-adjusted binomial logistic regression models, with the rest of the independent variables being the same. IMT, ABI and RRI were retained as independent predictors and made statistically significant contributions to the models (Table 3).

Discussion

The present study is the first to describe a relationship between vascular calcification and RRI in non-dialysis CKD patients. In our data, AAC was positively correlated with the RRI, and a Kauppila calcification score higher than 5 identified with reasonable accuracy patients with a pathologic RRI.

The impact of vascular nephropathies in the population over 60 years is highlighted by the important percentage of patients with this pathology in the studied group (50 %). We observed a high prevalence of aortic calcifications in our predialysis cohort (77 %). It is known that patients who

Table 2 ROC analysis for AAC score in predicting a pathological RRI (>0.7), ABI (<0.9) and IMT (>0.1 cm), respectively

Parameter	AUROC (95 % CI)	p	AAC score	Sensitivity (95 % CI)	Specificity (95 % CI)	Hosmer–Lemeshow test	
						χ^2	p
RRI	0.69 (0.56–0.81)	0.001	5	0.65 (0.48–0.80)	0.68 (0.51–0.82)	6.69	0.46
ABI	0.82 (0.66–0.98)	<0.0001	5	0.81 (0.48–0.97)	0.71 (0.55–0.84)	4.31	0.74
IMT	0.67 (0.49–0.84)	0.03	5	0.69 (0.38–0.90)	0.55 (0.42–0.68)	3.83	0.79

The cut-off value of AAC score with the best sensitivity and specificity was chosen

AUROC area under ROC curve, *CI* confidence interval, *AAC score* abdominal aortic calcification score, *RRI* renal resistive index, *ABI* ankle-brachial index, *IMT* intima media thickness

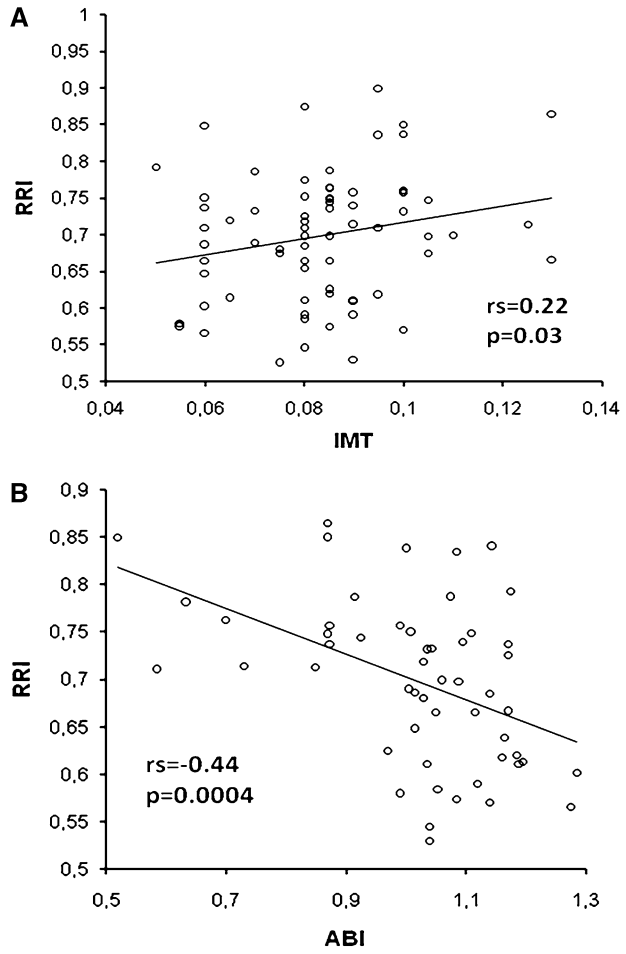

Fig. 2 **a** Renal resistive index (RRI) correlation with intima media thickness (IMT); **b** Renal resistive index (RRI) correlation with ankle-brachial index (ABI)

are on dialysis have a high prevalence of arterial calcifications which are associated with cardiovascular mortality [1, 2]. A number of studies have also demonstrated the high prevalence of vascular calcifications in predialyis patients, which suggests that this process starts early in the course of the disease [14, 15]. However, the relationship with CKD is unclear, as kidney damage can result from vascular lesions or, on the other hand, CKD could be a progression factor for vascular calcifications.

In our data, the lack of differences with regard to the majority of traditional cardiovascular risk factors, except for age and serum cholesterol, could be due to the positive history for systemic atherosclerosis, which was an inclusion criteria. Furthermore, as most of our patients were treated, blood pressure comparison might have been biased by the therapy.

Concerning the investigated atherosclerosis non-traditional risk factors, the present study yielded mixed results. Higher aortic calcification score was found as eGFR declines. This could be attributable to the previously reported imbalance between the inducers and inhibitors of calcification in CKD patients [16]. Also, higher inflammation was seen in subjects with extensive aortic calcification, a finding that is in line with other data linking inflammation with vascular calcification and atherosclerosis [17, 18]. On the other hand, no differences between the studied groups in calcium-phosphate metabolism parameters were observed, despite the common reported associations of hypercalcemia, hyperphosphatemia and high levels of alkaline phosphatase with increased risk of vascular calcification, at least in hemodialysis patients [19–22]. However, in non-dialysis CKD patients this correlation is less clear. Adeney et al. [15] observed an association between higher serum phosphate, still within the normal laboratory range, and prevalence of vascular calcification in patients with moderate CKD and no clinical cardiovascular disease, while others considered that calcium-phosphorus balance is not related to vascular calcification [23].

Abnormal ABI and increased carotid IMT are independent predictors of cardiovascular morbidity and mortality in CKD patients [24, 25]. Vascular calcification of the main arteries was associated with an ABI <0.9, while calcification of peripheral and distal arteries was associated with values >1.3 [26]. No ABI >1.3 was found in the studied cohort and median values were around 1, suggesting dominant calcification of the main arteries. Moreover, patients with AAC score >5 had lower ABI and higher IMT. In the logistic regression models ABI and IMT were

Table 3 Relationship between AAC score >5 and cardiovascular risk factors in three separate models of multivariable-adjusted binary logistic regression analysis

Model	Variable[a]	B	SE	Wald	df	p	Exp(B) (95 % CI)
ABI[†]	ABI	−1.24	0.46	7.15	1	<0.01	0.28 (0.11–0.71)
	Constant	−0.41	0.35	1.39	1	0.23	0.66
IMT[‡]	IMT	0.95	0.37	6.49	1	0.01	2.59 (1.24–5.41)
	Triglycerides	0.56	0.31	2.91	1	0.08	1.75 (0.91–3.36)
	Constant	−0.48	0.34	1.99	1	0.15	0.61
RRI[§]	RRI	1.13	0.46	5.90	1	0.01	3.09 (1.24–7.71)
	Constant	−0.46	0.33	1.88	1	0.17	0.63

Each model included one vascular marker, ABI, IMT or RRI, and the same cardiovascular risk factors

[†] Cox and Snell $R^2 = 0.22$; Nagelkerke $R^2 = 0.30$; ($\chi^2 = 11.42$; dif = 1; p = 0.001)

[‡] Cox and Snell $R^2 = 0.20$; Nagelkerke $R^2 = 0.27$; ($\chi^2 = 10.46$; dif = 2; p = 0.005)

[§] Cox and Snell $R^2 = 0.16$; Nagelkerke $R^2 = 0.22$; ($\chi^2 = 8.69$; dif = 1; p = 0.003)

[a] Variables entered at step 1 for each model: age, gender, eGFR (MDRD), mean arterial pressure, body mass index, HDL-cholesterol, LDL-cholesterol, triglycerides, diabetic status and ABI or IMT or RRI—depending on the model

retained in the final step and were associated, independently of the other cardiovascular factors, with Kauppila score. The associations of AAC score with ABI and IMT emphasizes the relationship of abdominal aortic calcification with the extension of atherosclerosis in other territories. In contrast, there was no relationship between CAVI and AAC score, suggesting an unexpected low correlation between aortic calcification and arterial stiffness. This could be due to the confounding effect of the high prevalence of patients with abnormal CAVI (80 %) in this cohort of advanced age (median age 69.2 years) and is consistent with the results of Mitchell et al. [27] who found that arterial stiffness and wave reflection increase with advancing age.

More important, RRI values in our patients increased along with the abdominal aortic calcification score. In the logistic regression model RRI was retained in the final model and was associated independently of the other cardiovascular factors with the AAC score. Furthermore, RRI was correlated with IMT and ABI, which are accepted indicators of systemic atherosclerosis. This relationship was first described by Pontremoli et al. [28], who showed that increased RRI is associated with early signs of target organ damage in essential hypertension. Also, it was demonstrated that RRI denotes renal arteriolosclerosis [9] and a high RRI (>0.7) had a similar strong association with the CKD progression as proteinuria and hypertension [10, 29]. Thus, according to our data, RRI could be an integrating marker of both intrarenal and extrarenal atherosclerosis.

We found that AAC score could predict a pathologic RRI (>0.7) in 69 % of cases and an ACC >5 had the best sensitivity (65 %) and specificity (68 %). Therefore, the Kauppila score could be a useful marker in RRI estimation and, consequently, of the intrarenal vascular status. It could stratify patients into categories of likelihood and help the clinician to select those patients who require assessment of RRI by ultrasound, which is a time-consuming and operator-dependent procedure. In addition, an AAC score of 5 allowed to identify patients with pathologic ABI (<0.9) and IMT (>0.1 cm) with reasonable sensitivity and specificity, which could make the Kauppila score a useful and convenient tool in the evaluation of the vascular status.

Some limitations of this study should be acknowledged. First, the data resulted from a cross-sectional design with a small sample size from a single center, which can limit the statistical power. Second, the selection criteria influenced the composition of the cohort by increasing the prevalence of both atherosclerosis and vascular calcifications. However, the final cohort reasonably describes the patients seen in day-to-day practice. Finally, Doppler ultrasonography is an operator-dependent method; nevertheless, the risk of inter-observer variability was reduced in our study because only one experienced examiner performed all ultrasound assessments.

The present study shows, for the first time to our knowledge, the relationship between abdominal aortic calcification and RRI in CKD patients. RRI appears to have a multifaceted significance because of its relationship with systemic atherosclerosis and renal arteriolosclerosis. With the due reserve on account of the small sample size and cross-sectional design, our study suggests that the Kauppila score might allow a fast, convenient and inexpensive indirect evaluation of the RRI. Additional research is warranted for validation.

Conflict of interest The authors have no conflict of interest to declare.

References

1. Mizobuchi M, Towler D, Slatopolsky E (2009) Vascular calcification: the killer of patients with chronic kidney disease. JASN 20:1453–1464

2. Sigrist M, Bungay P, Taal MW, McIntyre CW (2006) Vascular calcification and cardiovascular function in chronic kidney disease. Nephrol Dial Transpl 21:707–714
3. Parfrey PS, Foley RN (1999) The clinical epidemiology of cardiac disease in chronic renal failure. JASN 10:1606–1615
4. Wilson PW, Kauppila LI, O'Donnell CJ et al (2001) Abdominal aortic calcific deposits are an important predictor of vascular morbidity and mortality. Circulation 103:1529–1534
5. Kauppila LI, Polak JF, Cupples LA, Hannan MT, Kiel DP, Wilson PW (1997) New indices to classify location, severity and progression of calcific lesions in the abdominal aorta: a 25-year follow-up study. Atherosclerosis 132:245–250
6. van der Meer IM, Bots ML, Hofman A, del Sol AI, van der Kuip DA, Witteman JC (2004) Predictive value of noninvasive measures of atherosclerosis for incident myocardial infarction: the Rotterdam Study. Circulation 109:1089–1094
7. Hollander M, Hak AE, Koudstaal PJ et al (2003) Comparison between measures of atherosclerosis and risk of stroke: the Rotterdam Study. Stroke 34:2367–2372
8. Prabahar MR, Udayakumar R, Rose J et al (2008) Prediction of tubulo-interstitial injury by Doppler ultrasound in glomerular diseases: value of resistive and atrophic indices. J Assoc Physicians India 56:21–26
9. Ikee RKS, Hemmi N, Imakiire T, Kikuchi Y, Moriya H, Suzuki S, Miura S (2005) Correlation between the resistive index by Doppler ultrasound and kidney function and histology. Am J Kidney Dis 46:603–609
10. Sugiura T, Wada A (2011) Resistive index predicts renal prognosis in chronic kidney disease: results of a 4-year follow-up. Clin Exp Nephrol 15:114–120
11. Ankle Brachial Index Collaboration (2008) Ankle brachial index combined with Framingham risk score to predict cardiovascular events and mortality: a meta-analysis. JAMA 300(2):197–208
12. Kanters SD, Algra A, van Leeuwen MS, Banga JD (1997) Reproducibility of in vivo carotid intima-media thickness measurements: a review. Stroke 28:665–671
13. Tripepi G, Jager KJ, Dekker FW, Zoccali C (2010) Statistical methods for the assessment of prognostic biomarkers (part II): calibration and re-clasification. Nephrol Dial Transpl 25:1402–1405
14. Russo D, Miranda I, Ruocco C et al (2007) The progression of coronary artery calcification in predialysis patients on calcium carbonate or sevelamer. Kidney Int 72:1255–1261
15. Adeney KL, Siscovick DS, Ix JH et al (2009) Association of serum phosphate with vascular and valvular calcification in moderate CKD. JASN 20:381–387
16. Jono S, Shioi A, Ikari Y, Nishizawa Y (2006) Vascular calcification in chronic kidney disease. J Bone Mineral Metab 24:176–181
17. Demer LL, Tintut Y (2008) Vascular calcification: pathobiology of a multifaceted disease. Circulation 117:2938–2948
18. Moe SM, Chen NX (2005) Inflammation and vascular calcification. Blood Purif 23:64–71
19. Goodman WG, Goldin J, Kuizon BD et al (2000) Coronary-artery calcification in young adults with end-stage renal disease who are undergoing dialysis. N Engl J Med 342:1478–1483
20. Floege J, Ketteler M (2004) Vascular calcification in patients with end-stage renal disease. Nephrol Dial Transpl 19(Suppl 5):V59–V66
21. Oh J, Wunsch R, Turzer M et al (2002) Advanced coronary and carotid arteriopathy in young adults with childhood-onset chronic renal failure. Circulation 106:100–105
22. Raggi P, Boulay A, Chasan-Taber S et al (2002) Cardiac calcification in adult hemodialysis patients. A link between end-stage renal disease and cardiovascular disease? JACC 39:695–701
23. McCullough PA, Sandberg KR, Dumler F, Yanez JE (2004) Determinants of coronary vascular calcification in patients with chronic kidney disease and end-stage renal disease: a systematic review. J Nephrol 17:205–215
24. Ix JH, Katz R, De Boer IH et al (2009) Association of chronic kidney disease with the spectrum of ankle brachial index the CHS (Cardiovascular Health Study). JACC 54:1176–1184
25. Szeto CC, Chow KM, Woo KS et al (2007) Carotid intima media thickness predicts cardiovascular diseases in Chinese predialysis patients with chronic kidney disease. JASN 18:1966–1972
26. Adragao T, Pires A, Branco P et al (2012) Ankle–brachial index, vascular calcifications and mortality in dialysis patients. Nephrol Dial Transpl 27:318–325
27. Mitchell GF, Parise H, Benjamin EJ et al (2004) Changes in arterial stiffness and wave reflection with advancing age in healthy men and women: the Framingham Heart Study. Hypertension 43:1239–1245
28. Pontremoli R, Viazzi F, Martinoli C et al (1999) Increased renal resistive index in patients with essential hypertension: a marker of target organ damage. Nephrol Dial Transpl 14:360–365
29. Sugiura T, Wada A (2009) Resistive index predicts renal prognosis in chronic kidney disease. Nephrol Dial Transpl 24:2780–2785