

# Association of Serum Adiponectin Concentration with Aortic Arterial Stiffness in Chronic Kidney Disease: From the KNOW-CKD study

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## OBJECTIVES

- High serum adiponectin levels predict all-cause and cardiovascular mortality in chronic kidney disease (CKD).
- However, the relationship between serum adiponectin concentration and arterial stiffness in CKD is not well established.
- The aim of this study was to assess this relationship by measuring pulse wave velocity (PWV) in CKD patients.

## METHODS

- Serum adiponectin concentration was measured in 716 CKD patients in the prospective KoreaN Cohort Study for Outcome in Patients With Chronic Kidney Disease.
- The study group consisted of 415 men and 301 women; mean age was 53.1 years, and baseline estimated glomerular filtration rate (eGFR) was 51 ± 29 mL/min per 1.73 m<sup>2</sup>. Heart to femoral PWV (hfPWV) and mean brachial to ankle PWV (baPWV) served as indicators of aortic artery stiffness and arterial stiffness, respectively.

Table 1. Demographic, clinical, and biochemical characteristics of the study population

Serum adiponectin	1st quartile (n=179)	2nd quartile (n=179)	3rd quartile (n=179)	4th quartile (n=179)	P value
	(≤6.46 µg/ml)	(6.47–11.33 µg/ml)	(11.34–18.56 µg/ml)	(≥18.57 µg/ml)	
Age (year)	51.1±12.8	53.5±12.8	54.9±11.5	53.1±12.9	0.034
Male (%)	286(78.4)	232(63.9)	205(65.3)	169(46.6)	<0.001
SBP (mmHg)	126±13	126±14	125±14	125±14	0.701
DBP (mmHg)	77±10	77±10	77±11	77±10	0.890
Current/former Smoking (%)	216(59.2)	179(49.6)	168(46.2)	136(37.5)	<0.001
BMI (kg/m <sup>2</sup> )	25.0±3.2	25.0±3.7	23.6±3.2	23.1±3.2	<0.001
Diabetes (%)	127(35.9)	120(33.9)	114(33.0)	123(34.9)	0.872
Hypertension (%)	338(95.5)	335(94.6)	320(92.8)	331(94.0)	0.469
Coronary artery disease (%)	24(6.8)	30(8.5)	31(9.0)	27(7.7)	0.721
Cerebral vascular disease (%)	30(8.5)	28(7.9)	32(9.3)	31(8.8)	0.998
Ejection fraction (%)	63.3±6.5	64.0±5.9	64.1±6.0	63.1±7.1	0.422
iPTH (pg/ml)	49.9(31.3,61.7)	50.9(35.6,74.6)	44.3(28.7,67.6)	68.4(39.5,138)	<0.001
25(OH) vitamin D (pg/ml)	16.9(13.7,20.7)	16.2(13.8,21.8)	17.2(13.9,22.2)	15.5(12.3,20.6)	<0.001
1,25(OH) <sub>2</sub> vitamin D (pg/ml)	27.4(23.2,33.3)	26.9(23.8,33.5)	26.5(23.7,31.0)	25.7(21.3,29.7)	0.001
Total ALP (U/L)	59(48,73)	61(50,77)	62(50,77)	68(53,88)	0.002
Serum albumin (mg/dL)	4.36±0.32	4.23±0.41	4.19±0.34	4.01±0.54	<0.001
Baseline Cr (mg/dl)	1.51±0.79	1.55±0.83	1.82±1.04	2.27±1.53	<0.001
Baseline eGFR <sup>a</sup>	57.7±28.5	56.1±29.3	47.2±27.6	39.7±26.2	<0.001
UACR (mg/g)	158(28,510)	290(54,783)	348(37,1025)	465(148,1590)	<0.001
hfPWV (m/s)	0.94(0.81,1.09)	0.93(0.80,1.11)	0.97(0.86,1.18)	0.97(0.84,1.18)	0.067
Mean baPWV (m/s)	1.41(1.28,1.56)	1.43(1.30,1.65)	1.47(1.31,1.67)	1.47(1.34,1.69)	0.003
Pulse pressure (mmHg)	48.4±9.3	49.4±9.7	48.6±11.5	47.3±10.9	0.294
ACE inhibitor (%)	11(6.5)	17(10.1)	11(6.4)	22(12.7)	0.127
ARB (%)	142(84.5)	146(86.4)	142(83.0)	144(83.2)	0.562
Statin (%)	86(48.0)	92(51.4)	86(48.0)	78(43.6)	0.231
Fenofibrate (%)	7(3.9)	5(2.8)	2(1.1)	1(0.6)	0.014

Table 2. Significant correlations of several variables with serum adiponectin concentration

	Serum adiponectin			
	(Unadjusted)		(Adjusted for age and sex)	
	r	P value	r	P value
Age (year) <sup>a</sup>	0.076	0.041	-	-
BMI (kg/m <sup>2</sup> ) <sup>a</sup>	-0.281	<0.001	-0.240	<0.001
iPTH (pg/ml) <sup>a</sup>	0.314	<0.001	0.355	<0.001
25(OH) vitamin D (ng/ml) <sup>a</sup>	-0.141	0.001	-0.152	<0.001
1,25(OH) <sub>2</sub> vitamin D (ng/ml) <sup>a</sup>	-0.174	<0.001	-0.161	<0.001
Total ALP (U/L) <sup>a</sup>	0.155	<0.001	0.154	<0.001
Log-hfPWV (cm/s) <sup>a</sup>	0.094	0.012	0.185	<0.001
Log-mean baPWV (cm/s) <sup>a</sup>	0.107	0.004	0.155	<0.001

## RESULTS

Figure 1. Relationship between serum adiponectin concentration and chronic kidney disease stage (A) and a scatter plot showing estimated glomerular filtration rates (eGFRs) (B).

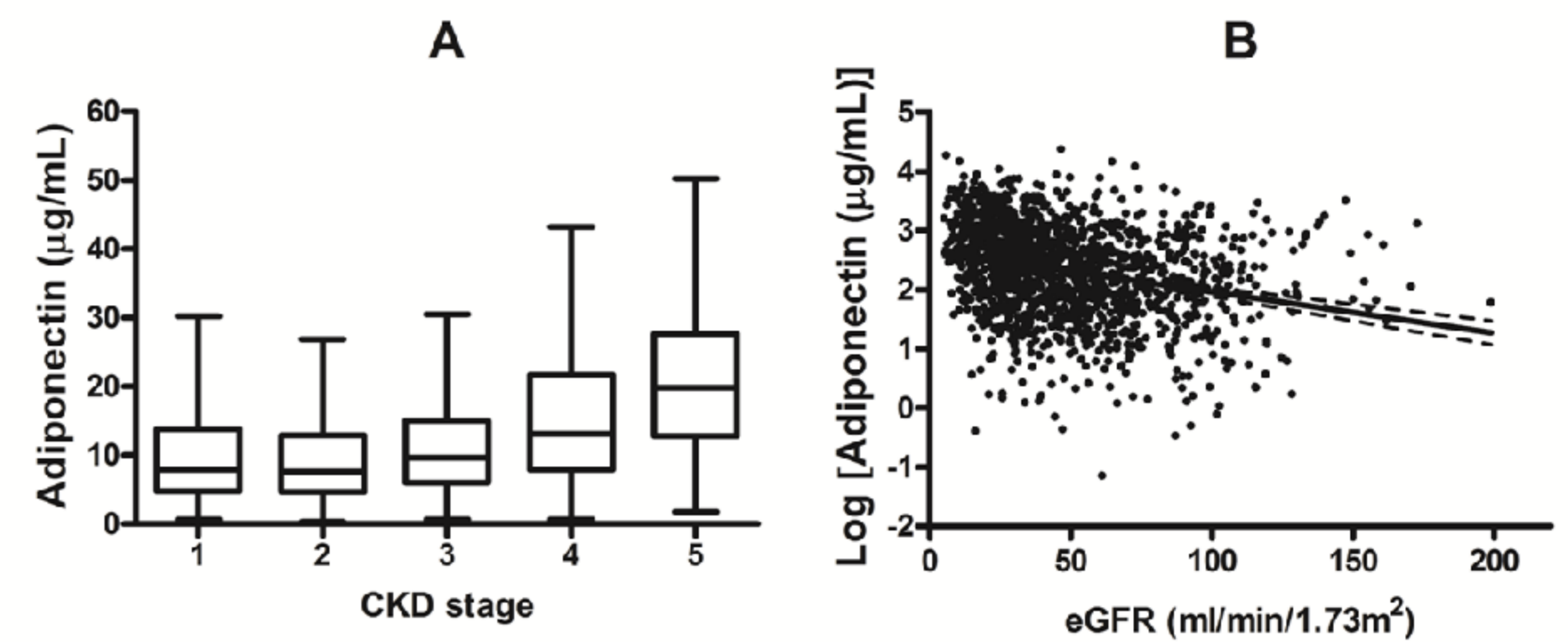


Figure 2. Scatter plots showing heart to femoral pulse wave velocity PWV (hfPWV) (A) and mean brachial to ankle PWV (baPWV) (B) as a function of serum adiponectin concentration with a fitted regression line.

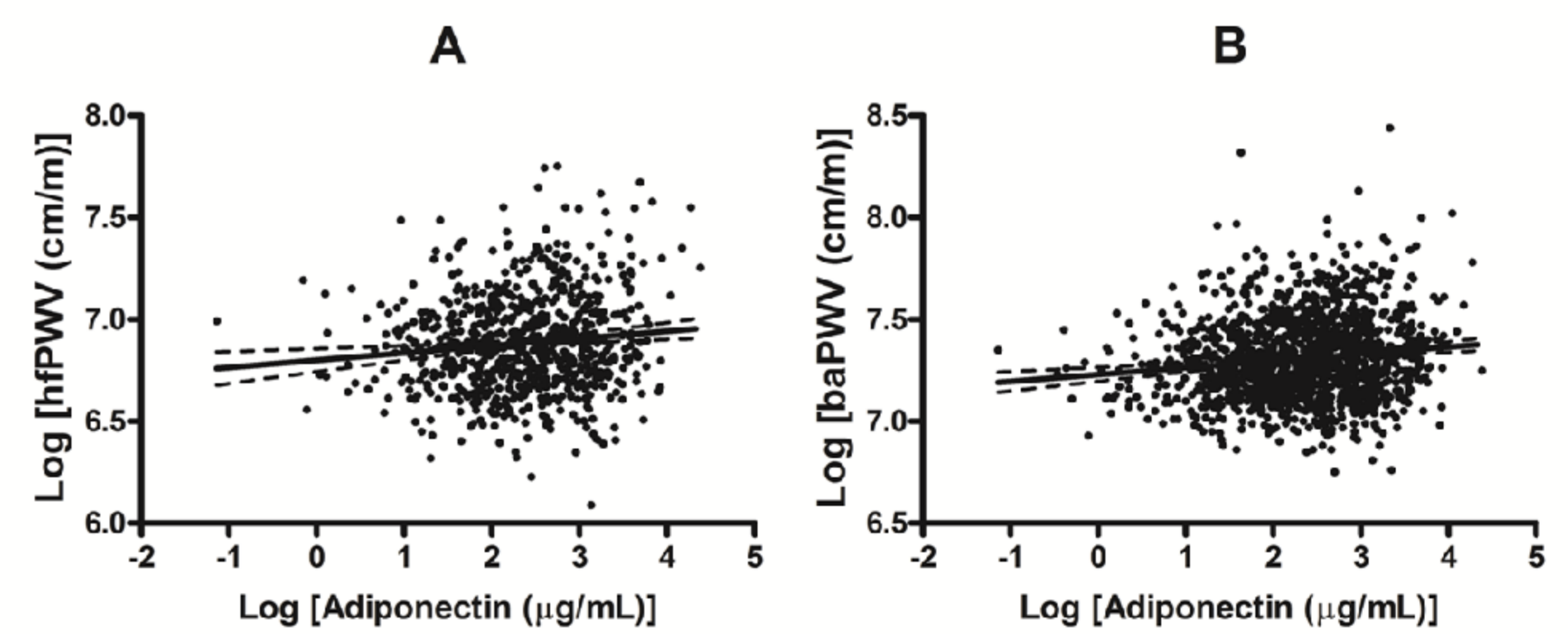


Table 3. Multivariable linear regression analysis of the association between log pulse wave velocity and log serum adiponectin concentration in patients with chronic kidney disease

	β Value (95% Confidence Interval)	R <sup>2</sup>	Adjusted R <sup>2</sup>	P value
<b>Log-hfPWV (cm/s)</b>				
Unadjusted	0.035(0.012, 0.058)	0.012	0.011	0.003
Model 1 <sup>a</sup>	0.032(0.013, 0.050)	0.402	0.399	0.001
Model 2 <sup>b</sup>	0.021(0.001, 0.040)	0.501	0.489	0.039
Model 3 <sup>c</sup>	0.023(0.001, 0.045)	0.516	0.497	0.041
<b>Log-mean baPWV (cm/s)</b>				
Unadjusted	0.033(0.015, 0.052)	0.018	0.016	<0.001
Model 1 <sup>a</sup>	0.025(0.009, 0.041)	0.325	0.322	0.002
Model 2 <sup>b</sup>	0.015(-0.003, 0.032)	0.418	0.404	0.098
Model 3 <sup>c</sup>	0.012(-0.007, 0.031)	0.438	0.415	0.222

<sup>a</sup> (standardized coefficient) values represent a change of pulse wave velocity per doubling of serum adiponectin.  
<sup>b</sup> Adjusted for age and sex.  
<sup>c</sup> Adjusted for age, sex, BMI ≥25 kg/m<sup>2</sup>, serum albumin, diabetes mellitus, history of hypertension, cardiovascular accident, cerebrovascular disease and peripheral vascular disease, current/former smoking, eGFR, log [UACR], pulse pressure, and medication with ARB and fenofibrate.  
<sup>d</sup> Adjusted for Model 2 plus levels of alkaline phosphatase, intact PTH, 25(OH) vitamin D and 1,25(OH)<sub>2</sub> vitamin D.

Table 4. Multivariable logistic regression analysis of the association between serum adiponectin concentration and the highest quartile of pulse wave velocities in patients with chronic kidney disease

	Odds Ratio (95% Confidence Interval)			
Serum adiponectin (µg/ml) <sup>a</sup>	Highest quartile of hfPWV	P value	Highest quartile of baPWV	P value
Unadjusted	1.37(1.10–1.72)	0.006	1.35(1.08–1.70)	0.009
Model 1 <sup>b</sup>	1.50(1.15–1.97)	0.003	1.27(0.97–1.66)	0.083
Model 2 <sup>c</sup>	1.66(1.18–2.32)	0.003	1.20(0.87–1.66)	0.266
Model 3 <sup>d</sup>	1.62(1.10–2.41)	0.015	1.23(0.85–1.80)	0.272

<sup>a</sup> Continuous natural log-transformed.  
<sup>b</sup> Adjusted for age and sex.  
<sup>c</sup> Adjusted for model 1 plus BMI ≥25 (kg/m<sup>2</sup>), serum albumin, diabetes mellitus, history of hypertension, cardiovascular accident, cerebrovascular disease and peripheral vascular disease, current/former smoking, estimated GFR, log [urine albumin creatinine ratio], pulse pressure, and medication with angiotensin receptor blockers and fenofibrate.  
<sup>d</sup> Adjusted for Model 2 plus levels of alkaline phosphatase, iPTH, 25(OH) vitamin D and 1,25(OH)<sub>2</sub> vitamin D.

## CONCLUSIONS

- In patients with CKD, serum adiponectin concentration significantly correlated with aortic stiffness, a major risk factor for cardiovascular mortality in CKD.
- Our results suggest a link between serum adiponectin concentration and aortic stiffness in patients with CKD.