ORIGINAL ARTICLE

Association of renal function with the ambulatory arterial stiffness index and pulse pressure in hypertensive patients

Yaqiong Wang^{1,2}, Yarong Hu^{1,2}, Yan Li^{1,2}, Hua Li^{1,2}, Shaoli Chu^{1,2}, Dingliang Zhu^{1,2} and Pingjin Gao^{1,2,3}

Arterial stiffness exemplified by the ambulatory arterial stiffness index (AASI) and pulse pressure (PP) predicts cardiovascular morbidity and mortality. The present cross-sectional study assessed the association of renal function with AASI and 24-h PP in hypertensive inpatients. Subjects included 948 hypertensive inpatients with drug treatment (mean age, 53.3 years; male, 67.1%). The AASI was defined as 1 minus the regression slope of diastolic over systolic blood pressure readings obtained from 24-h recordings. Renal function was evaluated by serum creatinine and urinary albumin excretion was expressed by the urinary albumin-to-urinary creatinine ratio (ACR), and estimated glomerular filtration rate (eGFR) was calculated by the modification of diet in renal disease formula and chronic kidney disease-epidemiology collaboration formula. As AASI and 24-h PP increased, serum creatinine concentrations and ACR increased, and eGFR decreased. Multiple linear regression showed that AASI and 24-h PP were associated with eGFR-EPI ($B = -12.00$, $P = 0.001$ vs. $B = -0.14$, $P = 0.002$) and ACR ($B = 0.56$, $P = 0.004$ vs. $B = 0.01$, $P = 0.017$) independent of other cardiovascular risk factors. After additional adjustment for 24-h PP, the association of AASI with eGFR-EPI had borderline significance ($P = 0.053$), whereas the significant associations of 24-h PP with serum creatinine and ACR persisted ($P = 0.009$ and $P = 0.006$) after adjusting for confounding factors and AASI. Multiple logistic regression analysis showed that each s.d. increase in 24-h PP (that is, 13 mm Hg) was associated with a higher risk of suffering from microalbuminuria (MA) by 39% ($P = 0.038$) after additional adjustment for AASI. In conclusion, AASI is more closely associated with eGFR compared with 24-h PP in hypertensive inpatients. However, for MA 24-h PP is a better predictor.

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INTRODUCTION

Arterial stiffness is a strong predictor of cardiovascular morbidity and mortality in patients with hypertension.^{1,2} Pulse pressure (PP), a traditional marker of arterial stiffness, has been shown to be associated with cardiovascular mortality.^{3–5} In 2006, Li *et al.*⁶ proposed a novel, easy-to-obtain index of arterial stiffness, called the ambulatory arterial stiffness index (AASI). The AASI is defined as 1 minus the regression slope of diastolic blood pressure (DBP) plotted against systolic blood pressure (SBP) obtained from individual 24-h blood pressure (BP) recordings. AASI is correlated with classical measurements of arterial stiffness and predicts cardiovascular mortality in hypertensive patients and in the general population.^{6–8}

Generally, renal insufficiency is one of the important target organ damage (TOD) in hypertensive patients. Cardiovascular events progressively increase as renal function declines in patients, even in cases of mild renal insufficiency.⁹ Alteration of arterial stiffness, a subclinical

sign of TOD in hypertension, has been reported to be correlated with renal function within the normal range¹⁰ or in renal dysfunction.^{11–17} As a surrogate index of arterial stiffness, PP is correlated with early signs of renal dysfunction.^{18,19} Similar to PP, AASI is also associated with TOD²⁰ and renal abnormalities^{21,22} in untreated patients with primary hypertension. However, clinically most hypertensive patients receive state-of-the-art anti-hypertensive therapy, which may have a protective role for arterial and renal function.^{23–26} Therefore, it is largely unknown whether AASI and PP are indicators for renal function in these treated inpatients. Therefore, the present study aimed to determine the association of indices of renal function, such as serum creatinine, estimated glomerular filtration rate (eGFR) and microalbuminuria (MA) with AASI and PP in a large group of primary hypertensive inpatients with drug treatment, and to determine which index is more closely correlated with renal damage.

¹State Key Laboratory of Medical Genomics, Shanghai Key Laboratory of Vascular Biology, Vascular Evaluation Center and Department of Hypertension, Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China; ²Shanghai Institute of Hypertension, Shanghai, China and ³Laboratory of Vascular Biology, Institute of Health Sciences, Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences, Shanghai, China
Correspondence: Dr P Gao, Shanghai Institute of Hypertension, Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, 197 Ruijin 2nd Road, Shanghai 200025, China.
E-mail: gaopingjin@yahoo.com.cn

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METHODS

Study population

From January 2006 to December 2008, 1660 consecutive inpatients with antihypertensive treatment from the Department of Hypertension, Shanghai Ruijin Hospital were included in the present study. Exclusion criteria included life-threatening disease, secondary hypertension, atrial fibrillation and other arrhythmias. We excluded 712 patients for the following reasons: blood measurements were not available at baseline ($n=567$); ambulatory blood pressure readings were <10 times during daytime or <5 times during nighttime or <20 times during 24 h ($n=11$); not all of the cardiovascular risk factors had been recorded ($n=114$) and the patient's age was 90 years ($n=20$). Therefore, the total number of patients included in the present analysis was 948. T2DM was diagnosed using the following criteria: (i) fasting plasma glucose levels ≥ 7.0 mmol l⁻¹ on two occasions; (ii) two 2-h postprandial plasma glucose readings ≥ 11.1 mmol l⁻¹ after a glucose load of 75 g; (iii) two casual glucose readings ≥ 11.1 mmol l⁻¹ or (iv) treatment with oral hypoglycemic drugs or parenteral insulin. The study protocol was approved by the ethics committee of Ruijin Hospital, and written informed consent was obtained from all participants.

Ambulatory BP and AASI

Ambulatory BP was recorded using an oscillometric SpaceLabs 90217 (SpaceLabs Inc., Redmond, WA, USA) monitor that obtained blood pressure readings at 20-min intervals from 0600 hours to 2200 hours and at 30-min intervals from 2200 hours to 00600 hours. From 24-h BP readings, we computed the regression slope of DBP on SBP. AASI was 1 minus the regression slope. We did not force the slope through the origin.

Glomerular filtration rate and urinary albumin excretion

Glomerular filtration rate was estimated by the modification of diet in renal disease (MDRD) formula²⁷ and chronic kidney disease-epidemiology collaboration (CKD-EPI) formula.²⁸ Urinary albumin excretion was assessed from a morning fasting spot urine sample by the urinary albumin-to-urinary creatinine ratio (ACR). Urinary creatinine concentration was measured by an automatic biochemistry analyzer (Beckman CX7, Chaska, MN, USA) and urinary albumin concentration was measured by means of particle-enhanced turbidimetric immunoassay (Beckman CX7). MA was defined as an albumin-creatinine ratio ≥ 22 (males) or ≥ 31 (females) mg per g creatinine.²⁹

Statistical analysis

Data are expressed as either mean $\pm$ s.d. or median (interquartile range) for skewed variables. The ACR was log transformed. One-way analysis of variance was used to analyze differences among the quartiles of AASI and 24-h PP distribution. Comparisons of proportions were performed using the χ^2 -test. In multivariate analyses, we used linear regression models to study the association of indices of renal function with AASI and 24-h PP. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated by exponentiation of logistic regression coefficients. Statistical significance was defined as $P < 0.05$. All statistical analyses were performed using SPSS Version 11.5 (SPSS, Chicago, IL, USA).

RESULTS

Clinical characteristics of the inpatients

Of the 948 inpatients, whose mean age was 53.3 ± 13.9 years, 67.1% were men, 30.6% were smokers and 24.0% had diabetes mellitus. The mean AASI was 0.43 ± 0.15 and 24-h PP was 49.1 ± 12.9 mm Hg. All participants were taking oral antihypertensive agents, including diuretics (10.1%), β -blockers (20.7%), vasodilators (calcium channel blockers and α -blockers; 89.8%), and inhibitors of the renin-angiotensin-aldosterone system (angiotensin-converting enzyme inhibitors and angiotensin II receptor blockers, 36.7%). Univariate analysis showed that AASI was positively related to age ($r=0.415$, $P < 0.001$) and 24-h mean blood pressure (MBP; $r=0.158$, $P < 0.001$), and negatively related to height ($r=-0.151$, $P < 0.001$) and pulse rate ($r=-0.111$, $P=0.001$).

The main clinical characteristics of the study population across the quartiles of AASI and 24-h PP distribution are shown in Tables 1 and 2. Patients with a higher AASI were older, had higher 24-h SBP and MBP, higher prevalence of diabetes (all $P < 0.001$), and a lower 24-h pulse rate ($P < 0.001$) and 24-h DBP ($P=0.018$). Moreover, serum creatinine concentration ($P=0.029$), ACR ($P < 0.001$), the prevalence of eGFR < 90 ml min⁻¹ per 1.73 m² (both $P < 0.001$) and MA ($P=0.001$) were increased with AASI, whereas the value of eGFR ($P < 0.001$) was decreased with AASI. As the patients we studied were all being treated, we analyzed the use of antihypertensive medications in the quartiles of AASI groups and found a significant difference only in the use of vasodilators ($P=0.042$, Table 1). The results of the above parameters among the quartiles groups divided by 24-h PP were similar with those grouped by AASI, except for the use of inhibitors of the renin-angiotensin-aldosterone system (Table 2).

Correlation between serum creatinine, eGFR, ACR and risk factors

As shown in Table 3, stepwise multiple regression analysis showed that serum creatinine concentrations were negatively correlated with sex and positively correlated with age, 24-h MBP and the use of diuretics. eGFR calculated by the MDRD formula was related to age ($B=-0.60$), sex ($B=3.59$), 24-h MBP ($B=-0.34$) and diuretics ($B=-7.25$). However, eGFR measured by the CKD-EPI formula was associated with age ($B=-0.83$), 24-h MBP ($B=-0.25$), diuretics ($B=-5.70$) and the use of inhibitors of the renin-angiotensin-aldosterone system ($B=-2.31$). Log-transformed ACR was positively correlated with sex, 24-h MBP, total to HDL cholesterol ratio, diabetes, diuretics and the use of inhibitors of the renin-angiotensin-aldosterone system.

Association of renal indices with AASI and 24-h PP

Multiple linear regression analysis was performed to evaluate the relationship of renal indices such as serum creatinine, eGFR and urinary albumin excretion with AASI and 24-h PP (Table 4). In unadjusted analysis, both AASI and 24-h PP were related to serum creatinine concentration, eGFR and urinary albumin excretion. In the adjusted models shown in Table 4, we found that serum creatinine ($B=16.58$, $P=0.005$ vs. $B=0.27$, $P < 0.001$), urinary albumin excretion ($B=0.56$, $P=0.004$ vs. $B=0.01$, $P=0.017$) and eGFR-EPI ($B=-12.00$, $P=0.001$ vs. $B=-0.14$, $P=0.002$) were independently correlated with AASI and 24-h PP after adjusting for several potentially confounding variables. However, when eGFR was assessed by the MDRD formula, the association between eGFR and 24-h PP was weakened ($P=0.101$). Furthermore, in the fully adjusted model, that is, adjusting for AASI, 24-h PP and other confounding variables, AASI had a borderline statistical significance with eGFR-EPI ($P=0.053$), whereas 24-h PP remained associated with serum creatinine ($P=0.009$) and urinary albumin excretion ($P=0.006$). Additionally, in the subgroup of 24-h SBP < 130 mm Hg, the association of AASI with eGFR-EPI, and the relationship between 24-h PP and urinary albumin excretion still persisted (Supplementary Table 1).

Multiple logistic regression analysis showed that each s.d. increase in AASI (that is, 0.15) and 24-h PP (that is, 13 mm Hg) entailed a higher risk of suffering from eGFR-EPI < 90 ml min⁻¹ per 1.73 m² by 80% (OR=1.80; 95% CI: 1.55–2.08) and 79% (OR=1.79; 95% CI: 1.54–2.07) in the unadjusted model (Table 5). When we adjusted for some confounders in the model, both AASI and 24-h PP lost their statistical significance for eGFR-EPI < 90 ml min⁻¹ per 1.73 m² ($P=0.073$ and $P=0.337$). However, 24-h PP maintained its prognostic value for MA after additional adjustment for AASI ($P=0.038$). Each s.d. increase in 24-h PP was associated with a higher risk of suffering

Table 1 Characteristics of the study population by quartiles of AASI distribution

AASI percentile limits	< 0.34	≥ 0.34/< 0.42	≥ 0.42/< 0.53	≥ 0.53	P
Number	237	237	237	237	—
Mean characteristic ± s.d. (or median (interquartile ranges))					
Age (years)	45.6 ± 12.6	51.6 ± 12.3	56.0 ± 13.2	60.0 ± 13.1	<0.001
BMI (kg m ⁻²)	25.3 ± 3.4	25.5 ± 3.4	26.0 ± 3.2	25.4 ± 3.6	0.155
Serum triglycerides (mmol l ⁻¹)	1.6 (1.0–2.3)	2.0 (1.3–2.7)	1.8 (1.3–2.6)	1.8 (1.4–2.5)	0.661
Total-to-HDL cholesterol ratio	4.2 ± 1.4	4.2 ± 1.2	4.3 ± 1.2	4.1 ± 0.1	0.430
Serum creatinine (μmol l ⁻¹)	78.9 ± 21.1	81.4 ± 23.5	83.1 ± 25.4	87.6 ± 33.2	0.029
Serum uric acid (μmol l ⁻¹)	355.2 ± 89.5	350.5 ± 88.4	355.0 ± 88.3	364.1 ± 93.6	0.419
ACR (mg g ⁻¹)	8.1 (5.5–16.6)	10.5 (6.4–29.6)	12.5 (7.3–29.2)	16.2 (8.4–44.3)	<0.001
eGFR-MDRD (ml min ⁻¹ per 1.73 m ²)	95.7 ± 21.3	90.3 ± 19.7	87.2 ± 23.0	82.6 ± 25.1	<0.001
eGFR-EPI (ml min ⁻¹ per 1.73 m ²)	101.2 ± 16.4	95.1 ± 16.5	89.8 ± 18.3	84.1 ± 20.6	<0.001
24-h SBP (mm Hg)	122.7 ± 13.4	126.8 ± 15.4	131.1 ± 15.8	140.4 ± 17.3	<0.001
24-h DBP (mm Hg)	82.3 ± 9.9	82.1 ± 10.8	80.7 ± 11.7	79.5 ± 12.2	0.018
24-h MBP (mm Hg)	95.8 ± 10.3	97.1 ± 11.4	97.8 ± 11.6	100.7 ± 11.8	<0.001
24-h Pulse rate (b.p.m.)	70.1 ± 7.9	70.9 ± 8.2	70.2 ± 8.7	67.7 ± 9.0	<0.001
Number with characteristic (%)					
Sex (male)	165 (69.6)	165 (69.6)	158 (66.4)	149 (63.1)	0.377
Smoking	77 (32.5)	81 (34.2)	62 (26.1)	70 (29.7)	0.236
Diabetes mellitus	35 (16.1)	50 (22.1)	66 (29.2)	77 (33.8)	<0.001
Microalbuminuria	16 (14.3)	26 (26.3)	32 (28.3)	45 (37.5)	0.001
eGFR-MDRD <90 ml min ⁻¹ per 1.73 m ²	94 (39.7)	122 (51.5)	144 (60.5)	150 (63.6)	<0.001
eGFR-EPI <90 ml min ⁻¹ per 1.73 m ²	51 (21.5)	69 (29.1)	113 (47.5)	123 (52.1)	<0.001
Diuretics	20 (8.4)	21 (8.9)	22 (9.2)	33 (14.0)	0.156
β-blockers	58 (24.5)	42 (17.7)	44 (18.5)	52 (22.0)	0.230
Vasodilators	213 (89.9)	202 (85.2)	217 (91.2)	219 (92.8)	0.042
Inhibitors of RAAS	83 (35.0)	88 (37.1)	81 (34.0)	348 (40.7)	0.450

Abbreviations: AASI, ambulatory arterial stiffness index; ACR, urinary albumin-to-urinary creatinine ratio; BMI, body mass index; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; HDL, high-density lipoprotein; MBP, mean blood pressure; MDRD, modification of diet in renal disease; RAAS, renin-angiotensin-aldosterone system; SBP, systolic blood pressure. Vasodilators included calcium channel blockers and α-blockers; inhibitors of RAAS included angiotensin-converting enzyme inhibitors and angiotensin II receptor blockers. P-value for trend across the quartiles of the AASI distribution.

from MA by 39% (OR=1.39; 95% CI: 1.02–1.90) after adjusting for several potentially confounding factors.

DISCUSSION

The present study investigated the association of renal function with the novel indices AASI and 24-h PP in a large hypertensive inpatient cohort. Our results indicated that both AASI and 24-h PP were associated with eGFR and urinary albumin excretion. AASI is more strongly correlated with eGFR than 24-h PP, and 24-h PP might be superior to AASI as a marker for MA.

Stiffening of the arteries has an important role in the pathogenesis of cardiovascular events and it is a classic feature in individuals with renal dysfunction. Arterial enlargement and increased stiffness have been observed in the early stages of (CKD),^{14–16} suggesting that arterial remodeling occurs early in the course of renal diseases. Moreover, recent studies have suggested an association between impaired renal function and decreased arterial stiffness in essential hypertensive patients.^{11–13,20,21}

In the present study, AASI and 24-h PP were inversely correlated with eGFR-MDRD and eGFR-EPI, independent of other cardiovascular risk factors, such as MBP. However, after adjusting for all the potential confounders, including AASI, 24-h PP and other risk factors, AASI ($P=0.053$), but not 24-h PP ($P=0.081$), was independently related to eGFR-EPI. These findings are in agreement with the observations of Mulè *et al.*²² that increased AASI was associated

with GFR in 143 untreated hypertensive patients, which was independent of traditional cardiovascular risk factors, including 24-h MBP and 24-h PP. However, in contrast to the previous studies, we assessed GFR by the CKD-EPI and MDRD formulas, which are noninvasive and easily achieved methods, rather than by a radioisotopic technique. Some studies have shown that the CKD-EPI formula is more accurate than the MDRD equation and it can replace it for routine clinical use.^{28,30,31} Our results showed that the value of eGFR measured by the MDRD formula was lower than that estimated with the CKD-EPI formula. In a study by Ratto *et al.*²¹ the risk of a mild reduction in eGFR increased almost twofold for each s.d. increase in AASI. However, in our study, multivariate logistic regression analysis showed that neither AASI nor 24-h PP was related to the presence of mild renal insufficiency (eGFR <90 ml min⁻¹ per 1.73 m²) after adjusting for potential confounders. In addition, we found that AASI was correlated with eGFR-EPI ($P=0.051$) in the subgroup of 24-h SBP <130 mm Hg, whereas 24-h PP was more closely associated with eGFR-MDRD ($P=0.026$) and eGFR-EPI ($P=0.003$) in the subgroup of 24-h SBP ≥130 mm Hg. These findings suggest that AASI might be an indicator of arterial dysfunction at the early stage and 24-h PP better reflects the advanced stage of vascular lesions.

Our study showed that although AASI and 24-h PP were also associated with urinary albumin excretion, 24-h PP might be a better predictor of MA than AASI. This finding is different from the results of Leoncini *et al.*²⁰ and Ratto *et al.*²¹ The reasons for this discrepancy

Table 2 Characteristics of the study population by quartiles of 24-h PP distribution

PP Percentile Limits	< 40.2	≥ 40.2/< 46.8	≥ 46.8/< 55.6	≥ 55.6	P
Number	237	237	237	237	—
<i>Mean characteristic ± s.d. (or median (interquartile ranges))</i>					
Age (years)	48.3 ± 10.8	50.1 ± 13.2	53.1 ± 13.6	61.8 ± 13.7	<0.001
BMI (kg m ⁻²)	25.2 ± 3.5	25.5 ± 3.2	25.9 ± 3.5	25.6 ± 3.5	0.194
Serum triglycerides (mmol l ⁻¹)	1.7 (1.1–2.4)	1.8 (1.1–2.7)	1.9 (1.5–2.6)	1.9 (1.3–2.5)	0.391
Total-to-HDL cholesterol ratio	4.3 ± 1.4	4.1 ± 1.1	4.3 ± 1.3	4.2 ± 1.1	0.499
Serum creatinine (μmol l ⁻¹)	80.8 ± 24.0	78.5 ± 16.4	80.3 ± 26.6	91.5 ± 33.5	<0.001
Serum uric acid (μmol l ⁻¹)	352.2 ± 96.0	360.4 ± 83.1	349.9 ± 85.2	362.2 ± 94.8	0.370
ACR (mg g ⁻¹)	7.4 (5.3–11.5)	9.8 (5.6–22.1)	13.3 (7.9–32.2)	20.0 (9.7–52.3)	<0.001
eGFR-MDRD (ml min ⁻¹ per 1.73 m ²)	92.6 ± 22.9	92.4 ± 17.4	92.4 ± 23.9	78.6 ± 23.5	<0.001
eGFR-EPI (ml min ⁻¹ per 1.73 m ²)	97.3 ± 17.8	97.7 ± 14.3	94.4 ± 18.9	80.7 ± 19.8	<0.001
24-h SBP (mm Hg)	115.0 ± 10.8	125.9 ± 9.9	132.9 ± 11.8	147.2 ± 15.4	<0.001
24-h DBP (mm Hg)	79.3 ± 9.9	82.6 ± 9.6	82.1 ± 11.3	80.5 ± 13.4	0.001
24-h MBP (mm Hg)	91.5 ± 9.7	97.1 ± 9.2	99.3 ± 10.8	103.5 ± 12.2	<0.001
24-h pulse rate (b.p.m.)	70.1 ± 7.7	71.9 ± 8.8	69.5 ± 8.2	67.5 ± 9.0	<0.001
<i>Number with characteristic (%)</i>					
Sex (male)	162 (68.4)	161 (67.9)	157 (66.2)	157 (66.2)	0.941
Smoking	75 (31.6)	74 (31.2)	67 (28.3)	74 (31.2)	0.846
Diabetes mellitus	30 (13.6)	38 (17.2)	60 (26.7)	100 (43.3)	<0.001
Microalbuminuria	10 (9.9)	25 (21.6)	33 (30.6)	51 (42.9)	<0.001
eGFR-MDRD < 90 ml min ⁻¹ per 1.73 m ²	112 (6.3)	112 (1.7)	108 (6.8)	178 (19.0)	<0.001
eGFR-EPI < 90 ml min ⁻¹ per 1.73 m ²	67 (28.3)	62 (26.2)	80 (33.8)	147 (62.0)	<0.001
Diuretics	24 (10.1)	19 (8.0)	21 (8.9)	32 (13.5)	0.208
β-blockers	50 (21.1)	49 (20.7)	45 (19.0)	52 (21.9)	0.880
Vasodilators	202 (85.2)	210 (88.6)	220 (92.8)	219 (92.4)	0.020
Inhibitors of RAAS	80 (33.8)	77 (32.5)	84 (35.4)	107 (45.1)	0.017

Abbreviations: ACR, urinary albumin-to-urinary creatinine ratio; BMI, body mass index; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; HDL, high-density lipoprotein; MBP, mean blood pressure; MDRD, modification of diet in renal disease; PP, pulse pressure; RAAS, renin-angiotensin-aldosterone system; SBP, systolic blood pressure. Vasodilators included calcium channel blockers and α-blockers; inhibitors of RAAS included angiotensin-converting enzyme inhibitors and angiotensin II receptor blockers. P-value for trend across the quartiles of the 24-h PP distribution.

Table 3 Covariables of renal indices in stepwise multiple regression

	Serum creatinine	eGFR-MDRD	eGFR-EPI	Log ACR
R ²	0.22	0.16	0.40	0.24
Intercept	66.2	150.0	162.6	-1.423
<i>Partial regression coefficients (B ± s.e.)</i>				
Age	0.28 ± 0.06	-0.60 ± 0.05	-0.83 ± 0.04	—
Sex (1=male, 2=female)	-23.45 ± 1.74	3.59 ± 1.53	—	0.14 ± 0.06
24-h MBP	0.33 ± 0.07	-0.34 ± 0.06	-0.25 ± 0.04	0.02 ± 0.00
Total to HDL cholesterol ratio	—	—	—	0.06 ± 0.02
Diabetes mellitus	—	—	—	0.25 ± 0.06
Diuretics	8.36 ± 2.64	-7.25 ± 2.33	-5.70 ± 1.71	0.20 ± 0.08
Inhibitors of RAAS	—	—	-2.31 ± 1.13	0.17 ± 0.06

Abbreviations: ACR, urinary albumin-to-urinary creatinine ratio; eGFR, estimated glomerular filtration rate; HDL, high-density lipoprotein; MBP, mean blood pressure; MDRD, modification of diet in renal disease; RAAS, renin-angiotensin-aldosterone system. Inhibitors of RAAS included: angiotensin-converting enzyme inhibitors and angiotensin II receptor blockers. The stepwise multiple regression model included age, sex, body mass index, 24-h MBP, total to HDL cholesterol ratio, current smoking habit, diabetes mellitus, the use of diuretics, β-blockers, vasodilators and inhibitors of RAAS.

between studies might be that the objective population we included was from a specific hypertensive ward, it had more cardiovascular complications and all patients were treated with antihypertensive agents. Numerous studies have shown a decrease in arterial stiffness with various pharmacological classes of antihypertensive agents.^{24,31–33}

Moreover protecting the kidneys by reducing BP, antihypertensive drugs can also have direct effects on intrarenal mechanisms of damage, such as increased glomerular pressure and proteinuria.^{26,34,35} Additionally, the use of hypertensive agents might affect the degree of nocturnal BP fall, which is considered as an important factor for

Table 4 Association of renal indices with AASI and 24-h PP

Variables	Serum creatinine		eGFR-MDRD		eGFR-EPI		Log ACR	
	B ± s.e.	P	B ± s.e.	P	B ± s.e.	P	B ± s.e.	P
AASI								
Unadjusted	26.80 ± 5.78	<0.001	−37.05 ± 4.92	<0.001	−45.06 ± 3.98	<0.001	0.89 ± 0.19	<0.001
Adjusted	16.58 ± 5.84	0.005	−11.64 ± 5.26	0.027	−12.00 ± 4.91	0.001	0.56 ± 0.19	0.004
Fully adjusted	7.86 ± 6.70	0.242	−9.76 ± 6.07	0.108	−8.28 ± 4.28	0.053	0.18 ± 0.24	0.455
24-h PP								
Unadjusted	0.39 ± 3.30	<0.001	−0.43 ± 0.06	<0.001	−0.52 ± 2.28	<0.001	0.02 ± 0.00	<0.001
Adjusted	0.27 ± 0.07	<0.001	−0.101 ± 0.07	0.101	−0.14 ± 0.05	0.002	0.01 ± 0.00	0.017
Fully adjusted	0.22 ± 0.08	0.009	−0.05 ± 0.08	0.532	−0.09 ± 0.05	0.081	0.01 ± 0.00	0.006

Abbreviations: ACR, urinary albumin-to-urinary creatinine ratio; AASI, ambulatory arterial stiffness index; eGFR, estimated glomerular filtration rate; PP, pulse pressure. In the serum creatinine model, adjusted for age, sex, 24-h MBP and diuretics; MDRD, modification of diet in renal disease; fully adjusted for PP or AASI additionally. In the eGFR-MDRD model, adjusted for age, sex, 24-h MBP and diuretics; fully adjusted for PP or AASI additionally. In the eGFR-EPI model, adjusted for age, 24-h MBP, diuretics and inhibitors of RAAS; fully adjusted for PP or AASI additionally. In the log ACR model, adjusted for sex, 24-h MBP, total to HDL cholesterol ratio, diabetes mellitus, diuretics and inhibitors of RAAS; fully adjusted for PP or AASI additionally.

Table 5 Multiple logistic regression analysis on the association of the presence of eGFR <90 ml min^{−1} per 1.73 m² and MA with AASI and 24-h PP

Variables	eGFR-MDRD < 90		eGFR-EPI < 90		MA	
	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P
AASI						
Unadjusted	1.52 (1.33–1.75)	<0.001	1.80 (1.55–2.08)	<0.001	1.46 (1.17–1.82)	0.001
Adjusted	1.17 (1.00–1.37)	0.055	1.18 (0.99–1.42)	0.073	1.30 (1.00–1.70)	0.058
Fully adjusted	1.12 (0.93–1.35)	0.219	1.18 (0.95–1.45)	0.129	1.07 (0.78–1.48)	0.676
24-h PP						
Unadjusted	1.56 (1.35–1.81)	<0.001	1.79 (1.54–2.07)	<0.001	1.78 (1.43–2.21)	<0.001
Adjusted	1.17 (0.98–1.40)	0.089	1.10 (0.90–1.35)	0.337	1.44 (1.11–1.87)	0.006
Fully adjusted	1.10 (0.90–1.35)	0.387	1.01 (0.80–1.27)	0.931	1.39 (1.02–1.90)	0.038

Abbreviations: AASI, ambulatory arterial stiffness index; eGFR, estimated glomerular filtration rate; MA, microalbuminuria; MDRD, modification of diet in renal disease; PP, pulse pressure. In the eGFR-MDRD model, adjusted for age, sex, 24-h MBP and diuretics; fully adjusted for PP or AASI additionally. In the eGFR-EPI model, adjusted for age, 24-h MBP, diuretics and inhibitors of RAAS; fully adjusted for PP or AASI additionally. In the MA model, adjusted for sex, 24-h MBP, Thr, diabetes mellitus, diuretics and inhibitors of RAAS; fully adjusted for PP or AASI additionally.

AASI in hypertensive patients.³⁶ In fact, our study showed that the association of AASI with eGFR and urinary albumin excretion was weakened after adjusting for the same confounders and night-to-day ratio of SBP. However, some studies have reported that 24-h PP outperformed AASI in assessing arterial stiffness³⁷ and in predicting renal damage.^{18,19}

Arterial stiffness is a common feature of aging and is exacerbated by several disorders such as hypertension, diabetes and renal disease. Mean 24-h PP is an estimate of arterial stiffness at a single point on the pressure stiffness curve, and it is critically dependent on the average distending pressure over the 24 h of measurement. In contrast, AASI is based on the concept that the average distending pressure varies during the day and that the relation between DBP and SBP, with this changing distending pressure, largely depends on the structural and functional characteristics of the large arteries.⁶ Therefore, AASI and PP reflect different characteristics of the arterial system and may provide different information. It is noteworthy that we demonstrated a different relationship of renal function with AASI and 24-h PP, and confirmed that AASI and 24-h PP could also assess the cardiovascular–renal risk, even in patients with antihypertensive medications.

Some limitations of this study should be noted. First, the cross-sectional design meant that the potential predictive variables and

outcome variables were obtained nearly simultaneously, and the information about causality could not be provided. Second, the population of our research was treated inpatients; although we adjusted for some confounders, the complicated effect of antihypertensive agents could not be avoided.

In conclusion, this study provided evidence that the indices of arterial stiffness, AASI and 24-h PP are associated with renal function, such as eGFR and urinary albumin excretion. AASI might more closely correlate with eGFR, and 24-h PP might be superior to AASI in assessing MA in a large group of primary hypertensive inpatients.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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Supplementary Information accompanies the paper on Hypertension Research website (<http://www.nature.com/hr>)