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CLINICAL STUDY

The relationship between AASI and arterial atherosclerosis in ESRD patients

Shu Zhang[1,2], Hui-Juan Mao[1], Bing Sun[1], Ning-Ning Wang[1], Bo Zhang[1], Ming Zeng[1], Lin Xu[1], Xiang-Bao Yu[1], Jia Liu[1], and Chang-Ying Xing[1]

[1]Department of Nephrology, The First Affiliated Hospital of Nanjing Medical University, Nanjing, China and [2]Department of Nephrology, Yangzhou No. 1 People's Hospital, Yangzhou, China

Abstract

Objective: To explore the relationship between ambulatory blood pressure and arterial atherosclerosis and provide simple and easy reference indicators for the prediction, prevention and prognosis of cardiovascular events in end-stage renal disease (ESRD) patients. *Method*: This prospective study consecutively collected clinical data of 114 ESRD hospitalized patients in the Department of Nephrology, the First Affiliated Hospital of Nanjing Medical University during August 2012 to December 2012. The data included laboratory data, the ambulatory blood pressure monitoring (ABPM), carotid ultrasound, two-dimensional echocardiography and the prognosis scores of the death risk. *Results*: (1) A series of ABPM parameters were closely associated with atherosclerosis ($p \leq 0.05$). Ambulatory Arterial Stiffness Index (AASI) was the most representative parameter of ABPM and also the best indicator for atherosclerosis (logistic regression analysis, $p = 0.005$). (2) AASI was a comprehensive index of atherosclerosis ($p < 0.001$), which was associated with the increase of left ventricular diameter ($p = 0.028$) and the risk of death ($p < 0.001$). The independent risk factors of AASI were the growth of the age ($p < 0.001$), elevated serum fibrinogen ($p = 0.009$) and reduced serum albumin ($p = 0.022$). *Conclusion*: AASI, as the representative of ABPM parameters, related well to atherosclerosis, which implied a broader application of ABPM in ESRD patients.

Keywords

ABPM, AASI, atherosclerosis, ESRD

History

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Introduction

Hypertension is the most common complication of chronic kidney disease (CKD), the incidence of which in end-stage renal disease (ESRD) patients is 70% ~ 90% in China nowadays. Ambulatory blood pressure monitoring (ABPM) is accepted as ''gold standard'' for the diagnosis of hypertension currently.[1] Based on ABPM, a series of derivative indicators can be obtained by some appropriate formula translation, such as nocturnal blood pressure dipping, blood pressure variability (BPV), morning blood pressure surge, etc. Ambulatory Arterial Stiffness Index (AASI), as a new ambulatory blood pressure parameter, not only predicted atherosclerosis but also reflected cardiovascular disease (CVD) and target organ damage,[2] which had been explored and confirmed the relationship with atherosclerosis[3] in hypertension or diabetes patients with normal or mild renal function impairment. ESRD population had a higher and more severe incidence of atherosclerosis than non-CKD and non-uremic population with an earlier onset.[4] Influence factors such as anemia, oxidative stress, coagulation disorders, uremic toxins and bone-mineral metabolism accelerate the progression of atherosclerosis and increase ESRD patients' cardiovascular mortality. ESRD population was different from the general population in some cardiovascular epidemiology, for example, its cardiovascular mortality increased because of the low weight and low cholesterol.[5] The relationship between AASI and atherosclerosis in ESRD patients is still unknown. This study focused on ESRD population, trying to explore the relationship between ambulatory blood pressure and arterial atherosclerosis and provide simple and easy reference indicators for the prediction, prevention and prognosis of cardiovascular events in ESRD patients.

Address correspondence to Hui-Juan Mao and Chang-Ying Xing, Department of Nephrology, The First Affiliated Hospital of Nanjing Medical University, Nanjing 210029, China. Tel and Fax: 86-25-68136039; E-mail: maohuijuan72@hotmail.com

Objects

Clinical data of 114 cases of hospitalized ESRD patients were consecutively collected in the Department of Nephrology, the First Affiliated Hospital of Nanjing Medical University during August 2012 to December 2012 after permission of the ethic committee of the hospital and consent of patients.

Inclusion criteria were as follows: (1) Older than 18 years and (2) CKD stage 5 patients, whose estimated glomerular filtration rate (eGFR) was less than 15 mL/(min.1.73 m^2)

(MDRD formula), whether predialysis or having maintenance hemodialysis (MHD) for more than three months.

Exclusion criteria were as follows: (1) Severe cardiac dysfunction, according to New York Heart Association classification of class IV; (2) Arrhythmia, including persistent atrial fibrillation, frequent atrial or ventricular premature beats; (3) stroke, myocardial infarction, infection, surgery or trauma, occurred in recent three months; (4) artificial arteriovenous fistula made in right arm; and (5) others, such as malignancies, decompensated liver sclerosis, intellectual or mental disorder.

Data collection

History collection and physical examination

The history of kidney disease and its therapy, family history, complications and co-morbidities were obtained by face-to-face communication with patients. Height, weight and abdominal circumference were measured in the morning before breakfast. For MHD patients, physical examination was done on the next morning of the dialysis day.

Laboratory test

All patients were taken fasting venous blood in the morning, to MHD patients, on the intermittent dialysis day. Blood samples were tested immediately in the clinical laboratory center of the hospital. Test items were hemoglobin, biochemical markers, homocysteine, high-sensitivity C-reactive protein, insulin, glycosylated hemoglobin, fibrinogen, prealbumin, transferrin, etc. Using MDRD formula, eGFR was evaluated [Eq. (1)]. The homeostasis model of insulin resistance was used to evaluate the degree of insulin resistance [Eq. (2)].

$$\mathrm{e}GFR[ml/(\min\cdot 1.73m^2] = 186 \times (Scr, \mathrm{mg}/dL)^{-1.164} \times (\mathrm{age})^{-0.203} \times (0.724\,\mathrm{female}) \quad (1)$$

$$HOMA{-}IR = (\text{fast blood sugar}, mol/L) \times (\text{fast insulin}, \mu U/ml)/22.5 \quad (2)$$

Device test

Ambulatory blood pressure monitoring

ABPM was performed by a non-invasive pulse wave collector, BPro6000 device (Singapore International Health STATS), which was a portable, non-cuff, wrist ABPM. Patients were requested to have a rest for 10 min before the measurements. All the patients adopted the right radial artery to perform ABPM. Operations were carried out according to the instruction strictly. Measurement interval was 15 min during daytime (6:00–24:00) and 30 min during nighttime (0:00–6:00). The valid records should have at least 80% of the total records. Imported data into the supporting software of the device can analyze daytime/nighttime systolic blood pressure (SBP)/diastolic blood pressure (DBP), nocturnal blood pressure dipping, etc. automatically. Diagnostic criteria reference of hypertension was JNC7.[6]

The original blood pressure parameters can be transformed into other ambulatory blood pressure parameters through appropriate formulas. BPV represents the extent of fluctuation in blood pressure during a certain time [Eq. (3)].

$$BPV = (SD \text{ of blood pressure}/\bar{X} \text{ of blood pressure}) \times 100\% \quad (3)$$

Morning blood pressure surge refers to the abrupt and steep acceleration of BP in the early morning. In this study, it was calculated as follows: mean systolic BP during the two hours after awakening minus mean systolic BP during the one hour that included the lowest sleep BP. AASI is a novel index derived from the linear relationship between 24-h ambulatory SBP and DBP. It is calculated by 1 minus the slope (B) of diastolic on systolic pressure during 24-h ambulatory monitoring [Eq. (4)]. More stiffness the artery is, more closer to 0 the regression slope (B) is, and more closer to 1 AASI is.

$$AASI = 1 - B \quad (4)$$

Pulse pressure (PP) and SBP ratio is expressed as PP/SBP.

Carotid ultrasound

Carotid ultrasound was carried out by the designated physician according to the standard procedure. Atherosclerosis was defined as carotid intima-media thickness (IMT) ≥ 0.9 mm,[7] or carotid artery plaque formation. Carotid artery plaque formation was defined as a focal structure that encroached into the arterial lumen of at least 0.5 mm or 50% of the surrounding IMT value, or demonstrated a thickness > 1.5 mm as measured from the media-adventitia interface to the intima-lumen interface.[8]

Two-dimensional echocardiography

Two-dimensional echocardiography was performed by the designated physician according to the standard procedure. The left ventricular end diastolic diameter (LVDd), interventricular septal thickness, left ventricular posterior wall thickness (LVPWT) and left ventricular ejection fraction (EF) were recorded. Using Devereux formula, left ventricular mass (LVM) and left ventricular mass index (LVMI) were determined [Eq. 5 and 6)].

$$(LVM, g) = 1.04 \times \left[(LVDd + IVST + LVPWT)^3 - (LVDd)^3\right] - 13.6 \quad (5)$$

$$\left(LVMI, g/m^2\right) = LVM/\text{body surface area} \quad (6)$$

Prognostic parameters

Charlson Comorbidity Index (CCI) is commonly used in the evaluation of one-year mortality. Considering the factor of age, CCI can be converted into Charlson-Age Comorbidity Index (CACI). Patients were divided into three groups according to CACI score: low risk group (2–3 points), moderate risk group (4–5 points) and high risk group (≥ 6 points), calculated according to previous literature.[9]

Statistical analyses

Statistical analyses were conducted with SPSS, 19.0 software package (Chicago, IL). The normally distributed data were

presented by $x \pm SD$; the non-normally distributed data were presented by the median and the interquartile range; Student's t and chi-square test were used for the comparison between groups; one-way ANOVA or Wilcoxon rank-sum test was used for comparing multiple groups. Pearson's rank correlation or Spearman's rank correlation test were used to evaluate the relationship between risk factors. To determine the independent determinants, multiple linear regression analysis or logistic regression analysis were performed. A $p < 0.05$ was regarded as a statistically significant difference.

Results

Clinical features

In the 114 cases, 50 were female and 32 were postmenopausal (Table 1). Age ranged from 21 to 87 years (average 55.8 ± 15.5), and 43 patients (37.7%) were under 50 years old. Sixty-five patients were on MHD; 37 patients were smokers, among them 14 patients had stopped smoking for at least one year.

Concomitant disease: 107 (93.9%) had hypertension, 25 (25.9%) had diabetes, 14 (12.3%) had coronary disease and 17 (14.9%) had stroke history.

The causes of ESRD: 45 (39.4%) were chronic glomerulonephritis, 18 (15.8%) were diabetic nephropathy, 9 (7.9%) were benign arteriolar nephrosclerosis, 7 (6.1%) were polycystic kidney, 4 (3.5%) were hyperuricemia nephropathy, 6 (2.6%) were lupus nephritis, 2 (1.8%) were interstitial nephritis, 1 (0.9%) was obstructive nephropathy and the rest 22 patients (19.3%) had unknown causes.

The presence of atherosclerosis was confirmed by carotid ultrasound in 76 (66.7%) patients. eGFR in predialysis patients were 7.1 ± 2.5 mL/min 1.73 m^2, while in MHD patients were 5.6 ± 2.3 mL/min 1.73 m^2. The maintenance dialysis duration ranged from 3 to 322 months (median 60 months and average 72 months).

The correlation between blood pressure parameters and atherosclerosis

First, we compared all the ambulatory blood pressure parameters between predialysis group and MHD group, but had no statistical differences (Table 2). Based on these results, we did not separate the predialysis from MHD patients any more in subsequent statistical analysis. Second, we divided all the cases into two groups, atherosclerosis group and negative group. We found parameters such as 24-h-DBP, daytime

Table 2. Comparison of ambulatory blood pressure (ABP) parameters between MHD and predialysis group.

ABP parameters	MHD	Predialysis	p Values
Daytime SBP load (%)	55.2 ± 39.8	57.2 ± 39.2	0.802
Nighttime SBP load (%)	71.2 ± 37.1	74.0 ± 36.3	0.705
24-h SBP (mmHg)	137.3 ± 19.4	137.6 ± 20.8	0.954
Daytime SBP (mmHg)	138.5 ± 19.8	139.0 ± 21.4	0.915
Nighttime SBP (mmHg)	132.3 ± 19.4	133.9 ± 22.1	0.702
24-h DBP (mmHg)	81.5 ± 15.1	83.5 ± 13.5	0.465
Daytime DBP (mmHg)	82.4 ± 15.4	84.2 ± 13.9	0.530
Nighttime DBP (mmHg)	78.7 ± 14.9	81.2 ± 14.0	0.369
24-h PP (mmHg)	63.7 ± 19.5	62.8 ± 20.7	0.817
Daytime PP (mmHg)	56.1 ± 17.1	54.6 ± 14.8	0.627
Nighttime PP (mmHg)	53.7 ± 16.5	52.6 ± 14.8	0.733
Nocturnal BP drop (%)	4.4 ± 5.0	3.7 ± 5.2	0.462
24-h SBPV	6.7 ± 1.5	6.5 ± 1.2	0.662
24-h DBPV	5.6 ± 1.4	5.5 ± 0.9	0.865
Morning peak of SBP (mmHg)	30.7 ± 9.4	31.2 ± 9.5	0.849
Morning peak of DBP (mmHg)	14.9 ± 5.8	15.9 ± 5.3	0.501
Morning peak of PP (mmHg)	16.8 ± 5.2	16.7 ± 5.7	0.963
AASI	0.51 ± 0.11	0.50 ± 0.09	0.505
SBP/PP	0.40 ± 0.09	0.38 ± 0.07	0.192

Notes: DBP, diastolic blood pressure; SBP, systolic blood pressure; PP, pulse pressure; SBPV, systolic blood pressure variability; DBPV, diastolic blood pressure variability; and AASI, Ambulatory Arterial Stiffness Index.

Compared all the ambulatory blood pressure parameters between predialysis group and MHD group, no statistical difference was found.

Table 1. The general information of ESRD patients in this study.

General situation	Total ($\bar{X} \pm SD$)	MHD ($\bar{X} \pm SD$)	Predialysis ($\bar{X} \pm SD$)
Age (years)	55.8 ± 15.5	54.8 ± 16.1	57.8 ± 15.5
Weight (kg)	61.2 ± 12.1	61.4 ± 12.5	61.0 ± 11.9
BMI (kg/m^2)	22.4 ± 3.2	22.4 ± 3.4	22.4 ± 3.2
Abdomen circumference (cm)	85.9 ± 10.5	87.8 ± 11.1	83.8 ± 9.4
hs-CRP (mg/L)	6.9 ± 11.3	7.3 ± 9.9	6.5 ± 12.7
Albumin (g/L)	37.1 ± 5.7	39.3 ± 4.7	34.0 ± 5.7
Prealbumin (g/L)	0.30 ± 0.13	0.30 ± 0.13	0.30 ± 0.12
Hemoglobin (g/L)	93.2 ± 24.9	103.6 ± 25.5	81.4 ± 18.4
Serum creatinine (μmol/L)	806.6 ± 323.2	873.2 ± 318.4	684.8 ± 294.5
Urea (mmol/L)	24.7 ± 9.0	23.2 ± 8.7	27.2 ± 9.0
Uric acid (mmol/L)	468.1 ± 153.3	402.7 ± 105.1	557.6 ± 167.1
Total cholesterol (mmol/L)	4.6 ± 1.3	4.5 ± 1.3	4.7 ± 1.3
Triglycerides (mmol/L)	1.4 ± 1.6	1.6 ± 1.3	1.3 ± 0.8
High-density lipoprotein (mmol/L)	1.1 ± 0.4	1.1 ± 0.4	1.2 ± 0.4
Low-density lipoprotein (mmol/L)	2.8 ± 0.9	2.8 ± 0.9	2.8 ± 0.9
Plasma fibrinogen (g/L)	3.7 ± 1.3	3.7 ± 0.9	3.9 ± 1.2
Transferrin (g/L)	1.9 ± 0.5	1.9 ± 0.6	1.9 ± 0.4
eGFR (mL/min.1.73 m^2)	6.2 ± 2.5	5.6 ± 2.3	7.5 ± 2.5
HOMA-IR	0.16 ± 0.45	0.18 ± 0.49	0.13 ± 0.37
Homocysteine (μmol/L)	23.5 ± 9.7	24.7 ± 10.6	21.7 ± 8.0

Notes: MHD, maintenance hemodialysis; BMI, body mass index; hs-CRP, high-sensitivity C-reactive protein; eGFR, estimated glomerular filtration rate; and HOMA-IR, homeostasis model assessment of insulin resistance.

Table 3. Comparison ambulatory blood pressure (ABP) parameters between atherosclerosis group and negative group.

ABP parameters	Negative group	Atherosclerosis group	*t/z* value	*p* Values
Daytime SBP load (%)	55.1 ± 41.3	57.3 ± 39.5	−0.281	0.808
Nighttime SBP load (%)	69.2 ± 39.5	73.9 ± 37.0	−0.460	0.589
24-h SBP (mmHg)	136.5 ± 18.9	138.2 ± 21.2	−0.363	0.708
Daytime SBP (mmHg)	138.8 ± 19.8	138.7 ± 21.4	0.025	0.980
Nighttime SBP (mmHg)	131.2 ± 18.3	134.4 ± 22.4	−0.679	0.499
24-h DBP (mmHg)	88.4 ± 12.7	79.1 ± 14.4	3.000	0.004*
Daytime DBP (mmHg)	89.5 ± 13.4	79.6 ± 14.7	3.152	0.002*
Nighttime DBP (mmHg)	84.7 ± 12.7	77.3 ± 14.9	2.383	0.019*
24-h PP (mmHg)	54.1 ± 17.3	67.9 ± 20.7	−3.009	0.004*
Daytime PP (mmHg)	49.1 ± 13.5	59.0 ± 16.7	−2.822	0.006*
Nighttime PP (mmHg)	46.4 ± 12.0	57.1 ± 16.7	−3.149	0.002*
Nocturnal BP drop (%)	5.4 ± 4.5	3.2 ± 5.0	1.968	0.051
24-h SBPV	6.6 ± 1.0	6.7 ± 1.6	−0.198	0.844
24-h DBPV	5.7 ± 0.9	5.5 ± 1.4	0.541	0.591
Morning peak of SBP (mmHg)	31.8 ± 10.5	30.5 ± 8.8	0.474	0.638
Morning peak of DBP (mmHg)	16.6 ± 6.0	14.4 ± 5.0	1.424	0.161
Morning peak of PP (mmHg)	16.4 ± 5.6	17.5 ± 5.6	−0.652	0.517
AASI	0.45 ± 0.06	0.53 ± 0.11	−3.778	< 0.001*
SBP/PP	0.35 ± 0.06	0.42 ± 0.08	−3.508	0.001*

Notes: This table compared the ambulatory blood pressure parameters between atherosclerosis group and negative group. The results showed that a series of ABPM parameters (*) related well to atherosclerosis. DBP, diastolic blood pressure; SBP, systolic blood pressure; PP, pulse pressure; SBPV, systolic blood pressure variability; DBPV, diastolic blood pressure variability; and AASI, Ambulatory Arterial Stiffness Index.

average DBP (daytime-DBP), nighttime average diastolic blood pressure (nighttime-DBP), 24-h average PP (24-h-PP), daytime average PP (daytime-PP), nighttime average PP (nighttime-PP), AASI, SBP/PP ratio, had statistical significant differences between the two groups. Multivariable logistic regression analysis showed that AASI was the best and the most representative parameter in indicating atherosclerosis ($p = 0.005$) (Table 3).

The risk factors of AASI

As the representative of ambulatory blood pressure parameters, and having close relationship with other blood pressure parameters, AASI had been made a correlation analysis with traditional risk factors and uremia related risk factors of CVD. Menopause ($p = 0.010$), stroke history ($p < 0.001$), diabetes history ($p < 0.001$) and diabetic nephropathy ($p = 0.047$) were all the risk factors for the increase of AASI, while dialysis itself had no effect on AASI. The single factor analysis found that age, serum albumin, serum prealbumin and plasma fibrinogen were correlated with AASI (Table 4). The multiple regression analysis of AASI relevant risk factors showed that the growth of the age, the increase of serum fibrinogen and the decrease of serum albumin were all independent risk factors for AASI (Table 5).

AASI and cardiac structure and prognosis scores

Based on two-dimensional echocardiography, cardiac structure was evaluated. AASI was positively correlated with LVDd, and the correlation between AASI and LVM or LVMI was close to statistical significance (Table 6).

Furthermore, ASSI was significantly positively correlated with two prognostic parameters: CCI and CACI (Table 7). In addition, the average level of AASI increased successively in the three rating groups divided by CACI score (Figure 1).

Table 4. Single factor analysis of AASI-related risk factors.

Parameters	Correlation coefficients (*r* value)	*p* Values
Age (years)	0.586	< 0.001*
Weight (kg)	0.070	0.503
BMI (kg/m^2)	0.137	0.182
Abdomen circumference (cm)	0.127	0.221
hs-CRP (mg/L)	−0.194	0.059
Education degree	0.108	0.401
Albumin (g/L)	−0.282	0.006*
Prealbumin (g/L)	−0.372	0.003*
Hemoglobin (g/L)	−0.130	0.210
Serum creatinine (μmol/L)	−0.296	0.004*
Serum urea (mmol/L)	−0.137	0.182
Uric acid (mmol/L)	−0.052	0.616
Total cholesterol (mmol/L)	0.024	0.814
Triglycerides (mmol/L)	−0.090	0.387
High-density lipoprotein cholesterol (mmol/L)	0.036	0.731
Low density lipoprotein (mmol/L)	0.004	0.969
Plasma fibrinogen (g/L)	0.225	0.030*
Serum transferrin (g/L)	0.002	0.988
eGFR (mL/min 1.73 m^2)	0.127	0.234
HOMA-IR	−0.018	0.873
Homocysteine (μmol/L)	−0.196	0.225

Notes: BMI, body mass index; hs-CRP, high-sensitivity C-reactive protein; eGFR, estimated glomerular filtration rate; and HOMA-IR, homeostasis model assessment of insulin resistance.

*$p < 0.05$.

The single factor analysis of AASI related risk factors found that age, serum albumin, serum prealbumin and plasma fibrinogen were associated with AASI.

Discussion

ABPM and atherosclerosis

Hypertension is not only the cause of atherosclerosis but also the result of atherosclerosis. Long-term uncontrolled hypertension is often accompanied with a series of CVDs.

Table 5. Multiple regression analysis of AASI related risk factors.

Variables	Regression coefficients	Standardized coefficients	p Value
Age (years)	0.004	0.591	<0.001*
Plasma fibrinogen (g/L)	0.093	0.256	0.009*
Albumin (g/L)	−0.003	−0.241	0.022*

Notes: *$p<0.05$.
The multiple regression analysis of AASI-related risk factors found that the growth of the age, elevated plasma fibrinogen and reduced serum albumin were the independent risk factors of AASI.

Table 6. AASI and cardiac remodeling.

	AASI	
Cardiac structural parameters	Correlation coefficients (r value)	p Value
LVDd (mm)	0.241	0.028*
IVST (mm)	0.060	0.590
LVPWT (mm)	0.160	0.148
EF %	−0.050	0.660
LVM (g)	0.200	0.070
LVMI (g/m^2)	0.192	0.082

Notes: LVDd, left ventricular end diastolic diameter; IVST, interventricular septal thickness; LVPWT, left ventricular posterior wall thickness; EF, left ventricular ejection fraction; LVM, left ventricular mass; and LVMI, left ventricular mass index.
*$p<0.05$.
AASI positively correlated with left ventricular end diastolic diameter (LVDd), while the correlation with LVM and LVMI was just close to statistical significance.

Table 7. AASI and prognostic parameter.

Prognostic parameters	Correlation coefficients (r value)	p Value
CCI	0.489	<0.001*
CACI	0.568	<0.001*

CCI, Charlson Comorbidity Index and CACI, Charlson-Age Comorbidity Index.
*$p<0.05$.
AASI was significantly positively correlated with CCI and CACI.

Controlling blood pressure to ideal level is essential for reducing cardiovascular complications and prolonging longevity. Currently, three diagnostic methods of hypertension are commonly used in clinical condition, including clinic blood-pressure monitoring, home blood-pressure monitoring and ambulatory blood-pressure monitoring (ABPM). A model research[10] evaluated cost-effectiveness of these three methods. Because of the higher diagnostic accuracy and less misdiagnosis, ABPM was the best cost-effectiveness method for hypertension diagnosis. Accompanied by more and more widely use, the feature of ABPM on evaluating arteriosclerosis has also been appreciated.

AASI was invented in 2006 as an indicator for arterial stiffness in general population, and it was calculated basing on the 24-hour ABPM.[11] It is well correlated with markers of arterial stiffness, easily obtained and has good reproducibility.[12] Further studies have found that AASI was also related to the decline of glomerular filtration rate,[13] carotid intima-media thickening and left ventricular hypertrophy.[14] Researchers gradually realized that elevated AASI was not only the marker of atherosclerosis but also a comprehensive indicator of cardiovascular dysfunction and target organ damage. Uremia was at high risk of hypertension, arteriosclerosis and cardiovascular events. There was so far no study on the correlation between ambulatory blood pressure parameters, especially AASI and arteriosclerosis in ESRD population.

Blood pressure fluctuation in MHD patients resulted from weight gain (fluid overload) during the interlude of hemodialysis, hemodynamic instability and the use of erythropoietin[15] at the time of hemodialysis. In this study, we did not find any statistical differences of blood pressure parameters between the predialysis group and the MHD group. It was possibly due to monitoring blood pressure in the interlude of hemodialysis, thus weakening the influence of dialysis process. The value of AASI for predicting cardiovascular events was independent of the mean arterial pressure, in both hypertension and normal pressure patients.[16] Some studies have shown that AASI maintained a good consistency with pulse wave velocity even in the process of adjusting antihypertensive treatment.[17] In this study, a series of 24-h ambulatory blood pressure parameters (AASI, day/night/24-h DBP, day/night/24-h PP, SBP/PP ratio) except SBP were closely related to atherosclerosis. The main differences between the atherosclerosis group and negative group were the increase of AASI, PP and the decrease of DBP. Logistic regression analysis found that AASI was correlated with atherosclerosis significantly and also the most representative parameter among all the ambulatory blood pressure parameters.

Another parameter of ABPM, non-dipper shaped blood pressure at night was also known as a risk factor for cardiovascular events. Taking antihypertensive drugs at bedtime can improve the circadian rhythm of blood pressure significantly and reduce the risk of cardiovascular events in CKD patients.[18] In this study, most of the patients had non-dipper pattern, whose nocturnal BP decline was only $3.2 \pm 5.0\%$ in the atherosclerosis group and $5.4 \pm 4.5\%$ in the negative group. The results suggested that we should prescribe long-acting preparation or change the time of taking antihypertensive medicine for these ESRD patients. This study confirmed the clinical value of 24-hour ABPM in ESRD patients. In the face of a series of abnormal blood pressure parameters, especially the higher value of AASI, clinicians should not only control blood pressure but also consider the risk of atherosclerosis and try to prevent cardiovascular complications actively.

The risk factors of AASI

Kollias et al.[19] summarized all the clinical studies about AASI from 2006 to 2011 and found that age was consistently the independent risk factor of AASI in most of the relevant studies. Along with the growth of the age and the decline in blood vessel elasticity, the change of blood pressure showed a rise in systolic pressure, a drop in diastolic pressure and a rise in AASI. Besides, some studies also showed that AASI related to urinary albumin excretion and

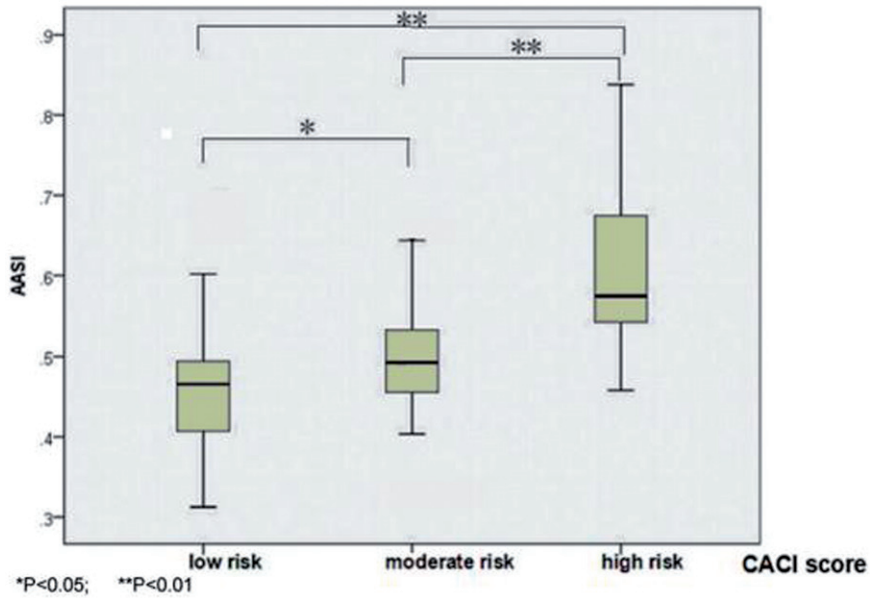

Figure 1. The average level of AASI in the three CACI rating groups.

kidney function decline.[13] In this study, age, menopause, diabetes, stroke history, serum albumin, prealbumin and plasma fibrinogen were all risk factors of AASI. Among them, age, serum albumin and plasma fibrinogen were independent risk factors.

Protein-energy malnutrition was a common issue in ESRD patients, and poor nutrition status would lead to vascular dysfunction and increase cardiovascular death.[20] In this study, those patients with lower serum creatinine had a higher level of AASI. The interpretation was that the malnourished patients had less meat intake and less muscle tissue metabolism, while malnutrition increased the risk of atherosclerosis.

Fibrinogen is also called clotting factor I. Under the action of thrombin, it converts to fibrin by covalent cross-linking. When fibrinogen increased, the fibrinolytic activity decreased and the stability of atheromatous plaque would be destroyed. Fibrinogen was also a kind of acute phase inflammation protein, which promoted the formation of atherosclerosis by stimulating vascular smooth muscle cell proliferation, increasing vascular collagen content and inhibiting endothelial function. Some studies have confirmed that fibrinogen related to atherosclerosis diseases, such as coronary heart disease, stroke and so on.[21] In this study, the level of plasma fibrinogen was positively correlated with AASI. After adjusting other factors, plasma fibrinogen was still an independent risk factor for high AASI.

In this study, we also found that diabetic patients, no matter with or without diabetic nephropathy, always had higher AASI than other concomitant diseases. Poor blood glucose control,[22] insulin resistance,[23] oxidative stress[24] may be the pivotal factors leading to cardiovascular complications.

The relationship between AASI and cardiac structure and prognosis

Cardiac structural changes are quite common in ESRD patients. Under the influence of hypertension, high-volume load and metabolic disorder, a series of adaptive changes happened, characterized by myocardial hypertrophy, ventricular wall thickening or ventricular cavity expansion. A previous study revealed that AASI can reflect LVH in hypertension patients.[14] But clinical situations was not exactly the same in ESRD patients as general population, for factors such as anemia[25] or arteriovenous fistula[26] can lead to cardiac structural abnormality independent of hypertension. Our results found that AASI related to ventricular cavity expansion, but its correlation with LVM and LVMI was just close to statistic significance in ESRD patients. To expand the samples may have statistic significance.

CCI and CACI score are still the most common and reliable method for assessing risk of death in ESRD patients.[27] The higher the score is, the higher risk of death they have. This study showed that AASI had positive correlation with CCI and CACI significantly and the average level of AASI increased successively in the three rating groups divided by CACI score.

Summary

A series of ABPM parameters abnormality (AASI, 24-h/daytime/nighttime-DBP, 24-h/daytime/nighttime PP, SBP/PP) can imply atherosclerosis in ESRD patients. AASI was the best and the most representative parameter of ABPM, which can indicate atherosclerosis. Meanwhile, the increase of AASI closely related to heart remodeling and the risk of death of ESRD patients. In addition, the independent risk factors of AASI were old age, malnutrition and elevated fibrinogen. It is necessary to extend the application of ABPM in ESRD patients.

Declaration of interest

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