Original Article

Effects of Glucose Metabolism on Aortic Pulse Wave Velocity in Hemodialysis Patients with and without Diabetes

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To compare the clinical features of aortic stiffness and its contributors between hemodialysis (HD) patients with and those without diabetes, we performed a cross-sectional study of stably treated HD patients (*n*=242). Aortic stiffness was assessed by measuring carotid-femoral pulse wave velocity (cfPWV). Annual laboratory data, comorbid conditions, and contributors to cfPWV were compared between HD patients with and those without diabetes. Of the 242 patients, 94 had diabetes. The comparison showed that patients with diabetes had a shorter duration of HD; higher systolic blood pressure (SBP), cfPWV, and rate of macrovascular complications; and lower ankle-brachial blood pressure index and concentrations of serum albumin and calcium. Stepwise multiple regression analysis identified age, duration of HD, SBP, heart rate (HR), and HbA1c as independent determinants of cfPWV in nondiabetic HD patients, while only SBP, HbA1c, and duration of diabetes were independent contributors of cfPWV in HD patients with diabetes. Our results indicate that glucose metabolism plays an important role in the promotion of aortic stiffness in both diabetic and nondiabetic HD patients. In particular, hyperglycemia's effect on aortic compliance in HD patients with diabetes is so strong that it negates the effects of the uremic milieu and aging. Follow-up studies are needed to ascertain whether or not strict diabetes management could improve aortic compliance. (*Hypertens Res* 2008; 31: 1365–1372)

***Key Words*: aortic pulse wave velocity, end-stage renal disease, hemodialysis, glucose metabolism**

Introduction

Cardiovascular diseases (CVD) account for more than 50% of deaths among patients with end-stage renal disease (ESRD) (*1*, *2*). Moreover, ESRD patients with diabetes have higher comorbidity and poorer outcomes than nondiabetic ESRD patients (*3*). Several studies reported that hemoglobin A1c (HbA1c) level is a prognostic factor in diabetic ESRD patients treated with hemodialysis (HD) (*4–6*). In addition, a recent Canadian study (*7*) showed that a high proportion of HD patients had inadequate glycemic control, evidenced by HbA1c levels >7.0%, and had a significantly higher rate of microvascular complications.

Increased aortic stiffness, as assessed by pulse wave velocity (PWV), is an independent poor prognostic factor for CVD and all-cause mortality in patients with ESRD (*8*, *9*). We recently demonstrated in a cross-sectional study that HbA1c level, HD duration, heart rate (HR), and mean blood pressure are independent determinants of aortic stiffness in HD patients without diabetes (*10*). However, it remains unclear whether the determinants of aortic stiffness in ESRD patients vary according to the presence or absence of diabetes, and whether or not aortic stiffness relates to vascular complica-

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tions in ESRD patients.

We hypothesized that additional information regarding arterial pathophysiology may be obtained by comparing determinants of aortic stiffness between diabetic and nondiabetic ESRD patients.

Methods

Study Design and Patients

A total of 292 patients with or without diabetes were placed on HD for >180 d from June 2003 to December 2006 at Murakami Memorial Hospital. Excluded from the study were patients in a critical state, specifically those with severe cerebrovascular disease (8 cases), severe peripheral arterial occlusive disease with amputated lower extremities and/or active gangrene (5 cases), severe joint deformity due to rheumatoid arthritis (3 cases) or ankylosing spondylitis (1 case), complicating noncontrolled neoplasm (3 cases), decompensated liver cirrhosis (2 cases), severe congestive heart failure (6 cases), and severe anemia with a hematocrit level of less than 25% (3 cases). Also excluded were one patient who changed treatment from HD to peritoneal dialysis and 9 patients who transferred to other institutions. Informed consent was not obtained from another 9 patients. Thus, 242 patients were analyzed. Of these, 85 were diagnosed with diabetes at the start of HD. HbA1c was measured every 3 months in nondiabetic patients. All patients whose HbA1c level exceeded 5.8% received a repeat measurement of blood glucose at 2 h after a meal and/or a 75 g oral glucose tolerance test. These tests identified 9 patients who developed diabetes after the introduction of HD; all 9 were classified into the diabetic group.

Data Collection

The clinical data were collected by chart reviews and interviews. All patients were reviewed for duration of dialysis (months), smoking habit, use of antihypertensive medication, macrovascular complication including coronary artery disease (angina or previous myocardial infarction), and cerebrovascular disease (stroke or transient ischemic attack). Patients with an ankle-brachial blood pressure (BP) index (ABPI: the ratio of ankle to brachial systolic BP) of less than 0.9 were considered positive for peripheral vascular disease. The diabetic patients were also reviewed for duration of diabetes, type of diabetes, diabetes medications (diet-controlled, oral hypoglycemics, and insulin), and microvascular complications including retinopathy, neuropathy, and gastropathy. The cause of ESRD was not identified in each patient, thus diabetic nephropathy was not assumed.

Blood chemistry was determined twice per month before HD, and included measurement of serum creatinine, urea, uric acid, magnesium, calcium, phosphate, sodium, potassium, and chloride, as well as hematocrit. Serum albumin, blood lipids, hypersensitive C-reactive protein (hs-CRP), and β-2-microglobulin were measured once every month. Intact parathyroid hormone (i-PTH) was measured every 3 months. HbA1c assays were performed monthly in diabetic patients and every 3 months in nondiabetic patients using a latex immunoassay. Atrial natriuretic peptide (ANP) was measured before the HD session at midweek, and the cardio-thoracic ratio (CTR) was measured before the HD session on the first day of the week. Volume overload and/or congestion were checked and excluded.

We used annual average blood biochemistry parameters of HD patients for analyses (if the duration of HD was less than 12 months, we used average values from the start of HD to the examination). Moreover, multiple blood samples were taken before HD under nonfasting conditions. Desmeules *et al.* (*11*) demonstrated that non-HDL cholesterol levels were equivalent in fasting and nonfasting samples. Indeed, the lipid profile measured in our patients correlated significantly with the overnight-fasting values (total protein: $r=0.552$, $p<0.0001$; albumin: $r=0.667$, $p<0.0001$; total cholesterol: $r=0.776$, $p<0.0001$; triglycerides: $r=0.763$, $p<0.0001$; HDL cholesterol: $r=0.679$, $p<0.0001$; low-density lipoprotein [LDL] cholesterol: $r=0.765$, $p<0.0001$), and they were similar in our cohort. Carotid-to-femoral PWV (cfPWV) was measured by the method of Hasegawa (*12*), using a PWV meter (VaSera VS-1000, Fukuda Denshi, Tokyo, Japan) on the morning before the midweek HD with the patient in a supine position after a 5-min bed rest. Pulse waves were recorded by using sensors placed on the skin at the left carotid and right femoral arteries. Heart sounds S1 and S2 were detected by a microphone placed on the right edge of the sternum at the level of the second intercostal space. Electrocardiograms were recorded with electrodes placed on both arms and the right leg. The PWV meter measures the time intervals between pulse waves at the carotid and femoral probes (T), and between S2 and the notch of the carotid pulse wave (T_c). cfPWV was calculated as:

$$\text{cfPWV (m/s)} = 1.3 \times L/(T + T_c)$$

where L is the measured distance between the heart-sound microphone and the femoral probe. The actual distance between the aortic orifice and the femoral site was estimated to be $1.3 \times L$ (*12*). $T + T_c$ indicates the time for the pulse wave to travel from the aortic orifice to the femoral artery. PWV increases as a function of diastolic BP (DBP) at the time of measurement in normal subjects (*13*). Therefore, the PWV meter automatically reports raw- and BP-standardized PWV values. The latter represents the pressure-independent elastic property of the aorta. The cfPWV was measured for 10 consecutive pulses, and the average was used for analysis. The coefficient of variation of PWV was less than 5%.

The ABPI was determined at the time of the cfPWV measurements using the same device, which simultaneously measures arm and ankle (brachial and posterior tibial) artery BP by oscillometry. ABPI represented the ratio of the lower value

Table 1. Clinical Characteristics of Hemodialysis Patients with or without Diabetes

Characteristic	Diabetics	Non-diabetics	*p* value
n	94	148	
Male/female	55 (58.5)/39 (41.5)	88 (59.5)/60 (40.5)	0.92
Age (years)	64.8±11.9	64.3±11.3	0.76
Current smoking (%)	24 (25.5)	35 (24.1)	0.92
Duration of hemodialysis (m)	45.4±54.6	85.4±82.0	<0.01
Body mass index (kg/m^2)	21.1±3.3	21.4±3.0	0.52
Systolic blood pressure (mmHg)	166±24	146±26	<0.01
Diastolic blood pressure (mmHg)	89±14	89±16	0.95
Heart rate (bpm)	69±10	69±11	0.87
Cardiothoracic ratio (%)	50.4±5.3	51.0±5.9	0.42
Antihypertensive medications	64 (68.1)	89 (60.1)	0.27
ACEI/ARB	45 (47.9)	57 (38.5)	0.19
Calcium channel blocker	50 (53.2)	70 (47.6)	0.48
Carotid-femoral pulse wave velocity (m/s)	11.0±2.1	9.2±2.0	<0.01
Ankle-brachial blood pressure index	0.87±0.23	1.00±0.18	<0.01
Blood samples			
Hematocrit (%)	30.1±2.4	30.7±3.1	0.64
Total protein (g/dL)	6.71±0.56	6.67±0.44	0.67
Albumin (g/dL)	3.98±0.34	4.10±0.33	<0.01
Calcium (mg/dL)	8.76±0.76	9.10±0.82	<0.01
Phosphate (mg/dL)	5.33±1.21	5.51±1.10	0.27
Calcium-phosphate product	47.0±12.4	50.3±11.7	0.04
Intact parathormone (ng/mL)	104±90	141±136	0.03
β-2-Microglobulin	23.6±7.9	24.7±7.2	0.30
Total cholesterol (mg/dL)	162±38	157±29	0.21
Triglycerides (mg/dL)	119±59	108±56	0.13
LDL-C (mg/dL)	100±29	97±24	0.40
HDL-C (mg/dL)	38±12	39±12	0.74
HbA1c (%)	6.4±1.1	5.2±0.5	<0.01
Hypersensitive C-reactive protein (mg/dL)	0.36±0.35	0.42±0.57	0.32
Atrial natriuretic peptide (pg/mL)	122±104	107±67	0.22
Macrovascular complications	50 (53.2)	55 (37.2)	0.03
Coronary artery disease	21 (22.3)	22 (14.8)	0.17
Stroke	19 (20.2)	10 (6.7)	<0.01
Peripheral vascular disease	41 (43.6)	42 (28.4)	0.03
Relating to diabetes			
Diabetes type I/II	3 (2.3)/91 (96.8)		
Diabetes duration (years)	19.0±10.9		
Microvascular complication	78 (83.0)		
Retinopathy	72 (76.6)		
Neuropathy	50 (53.2)		
Gastropathy	4 (4.3)		
Oral hypoglycemics	16 (17.0)		
Insulin	40 (42.6)		

Data are mean±SD or count (%). ACEI/ARB, angiotensin converting enzyme inhibitor and/or angiotensin receptor 1 blocker; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; HbA1c, hemoglobin A1c.

of the ankle systolic blood pressure (SBP) divided by the SBP of the arm without vascular access.

Statistical Analysis

Data are presented as means±SD or actual numbers. Bivariate analysis was used to compare diabetic and nondiabetic

Table 2. Univariate Correlations of Carotid-Femoral Pulse Wave Velocity and Other Variables in 94 Hemodialysis Patients with Diabetes and 148 Hemodialysis Patients without Diabetes

Dependent variables	Diabetics		Non-diabetics	
	Correlation coefficient	*p* value	Correlation coefficient	*p* value
Age	0.094	0.371	0.420	<0.0001
Duration of hemodialysis	−0.089	0.397	0.149	0.073
Duration of diabetes	0.304	0.003		
Body mass index	−0.121	0.246	0.009	0.916
Systolic blood pressure	0.272	<0.0001	0.394	<0.0001
Heart rate	0.104	0.320	0.213	0.010
Cardiothoracic ratio	0.061	0.563	0.173	0.040
Antihypertensive medications	0.093	0.374	0.093	0.264
ACEI/ARB	0.063	0.511	−0.011	0.892
Calcium channel blocker	0.058	0.583	0.031	0.711
Current smoking	0.040	0.706	0.094	0.260
Albumin	0.115	0.270	−0.176	0.036
Calcium	−0.099	0.334	0.128	0.129
Phosphate	−0.142	0.175	−0.017	0.842
Calcium-phosphate product	−0.145	0.164	0.026	0.762
Intact parathormone	−0.074	0.480	0.134	0.114
β-2-Microglobulin	−0.017	0.872	0.038	0.651
Total cholesterol	0.067	0.524	0.037	0.662
Triglycerides	0.057	0.587	−0.018	0.830
LDL-C	0.051	0.627	0.131	0.122
HDL-C	0.040	0.703	−0.156	0.065
Hemoglobin A1c	0.394	<0.0001	0.168	0.048
Hypersensitive C-reactive protein	0.032	0.762	0.030	0.728
Atrial natriuretic peptide	0.051	0.683	0.134	0.147
Relating to complications				
Number of macrovascular complications	0.072	0.494	0.264	0.001
Coronary artery disease	−0.054	0.606	0.170	0.041
Stroke	0.053	0.612	0.109	0.191
Peripheral arterial disease	0.108	0.303	0.221	0.008
Number of microvascular complications	0.334	0.001		
Retinopathy	0.286	0.006		
Neuropathy	0.330	0.001		
Gastropathy	−0.092	0.380		
Insulin use	0.272	0.008		

ACEI/ARB, angiotensin converting enzyme inhibitor and/or angiotensin receptor blocker; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol.

HD patients. Categorical variables were subjected to the χ^2 or Fisher's exact test, as appropriate. Continuous variables were subjected to an unpaired *t*-test or Wilcoxon's rank-sum test, as appropriate. The associations between cfPWV and a number of other parameters were assessed using correlation analysis that was appropriate for the normal distribution (Pearson's correlation) or non-normal distribution (Spearman's correlation). Differences in the associations of cfPWV with various parameters were investigated by comparing the slope (β) of the appropriate regression line ($y=\alpha+\beta x$) between diabetic and nondiabetic HD patients. Correlations that were significantly below the 10% level were entered in a multiple regression model with cfPWV as the dependent variable to determine the variables that independently predicted cfPWV. A *p* value less than 0.05 indicated statistical significance. All analyses were performed using a statistical software package (SPSS 11.0 for Windows; SPSS, Chicago, USA).

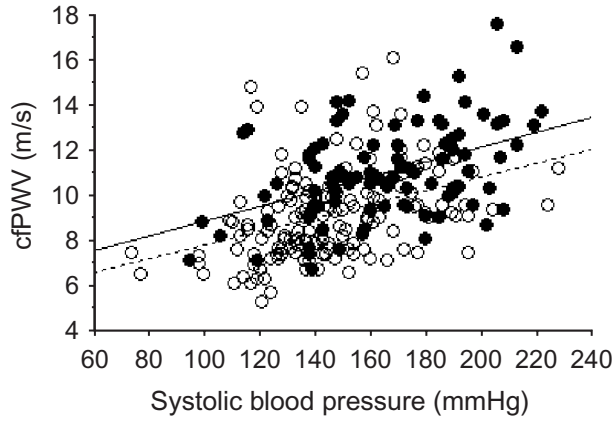

Fig. 1. *Relationships between cfPWV and systolic blood pressure in a cohort of 242 HD patients with (solid symbols, straight line) and without (open symbols, dotted line) diabetes ($y=0.03x+5.59$; $r^2=0.20$ in diabetic patients, $y=0.03x+4.78$; $r^2=0.16$ in nondiabetic patients).*

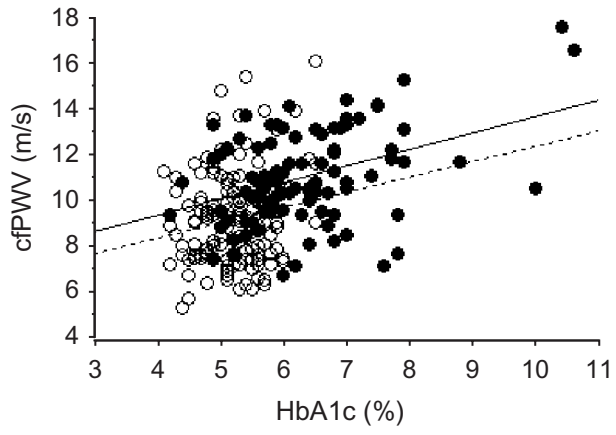

Fig. 2. *Relationships between cfPWV and HbA1c in a cohort of 242 HD patients with (solid symbols, straight line) and without (open symbols, dotted line) diabetes. The y-intercept is larger the diabetes patients ($y=0.72x+6.43$; $r^2=0.16$ in diabetic patients, $y=0.67x+5.69$; $r^2=0.03$ in nondiabetic patients).*

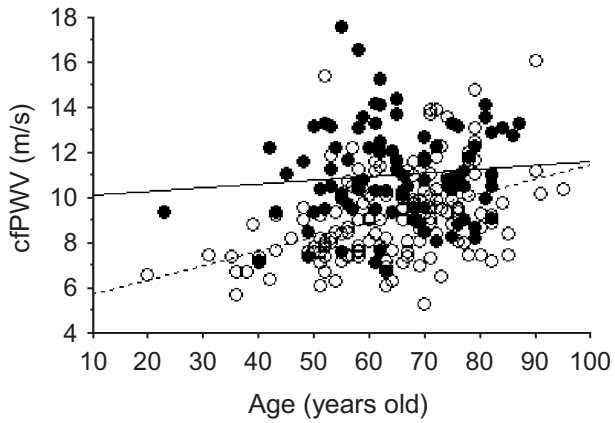

Fig. 3. *Relationship between cfPWV and age in a cohort of 242 hemodialysis patients with (solid symbols, straight line) and without (open symbols, dotted line) diabetes ($y=0.02x+9.96$; $r^2=0.09$ in diabetic patients, $y=0.06x+5.07$; $r^2=0.18$ in nondiabetic patients).*

Results

Characteristics of Patients with and without Diabetes

Table 1 summarizes the clinical features of the HD patients. All patients underwent hospital-based HD, with the majority on dialysis for three 4 h sessions per week. Out of the 242 patients registered in this study, 94 were diabetics. There were no significant differences in the male/female ratio, mean age, ratio of current smokers, and body mass index between HD patients with and those without diabetes. The duration of HD was shorter and SBP was higher in HD patients with diabetes than in those without. The cfPWV value was higher, while the ABPI value was lower in diabetic HD patients than in nondiabetics. Blood chemistry analyses showed lower serum concentrations of albumin, calcium, calcium-phosphate product, and i-PTH in diabetic patients, but no difference between groups in the levels of total protein, hematocrit, phosphate, total cholesterol, triglycerides, both LDL and HDL cholesterol, and hs-CRP. A higher proportion of patients with diabetes than without had documented macrovascular complications, especially stroke and peripheral vascular disease.

Almost all of the diabetic patients in this study (96.8%) were type 2, with reasonable glycemic control for most (78% of patients had HbA1c levels less than 7.0%). Diabetes duration was 19.0±10.9 years and ranged from 1 to 57 years. Forty patients used insulin and 14 used oral hypoglycemic agents, while 2 patients used both types of medications together. Of the 16 patients using oral hypoglycemic agents, 7 were taking a β-glucosidase inhibitor, 4 were on sulfonylurea, 4 were on pioglitazone, and 1 used both an α-glucosidase inhibitor and sulfonylurea. Because diabetic nephropathy has not been established as the cause of ESRD, it was excluded from the evaluation of microvascular complications, which were identified in 78 patients. Three patients had three types of microvascular complications, 43 patients had 2, and 32 patients had only 1 complication. Sixteen were free of microvascular complications.

Table 3. Predictors of Carotid-Femoral Pulse Wave Velocity Identified by Stepwise Regression Analysis in 94 Hemodialysis Patients with Diabetes and 148 Hemodialysis Patients without Diabetes

Hemodialysis patients with diabetes			Hemodialysis patients without diabetes		
Independent variables	β coefficient	p value	Independent variables	β coefficient	p value
SBP	0.356	<0.001	Age	0.440	<0.001
HbA1c	0.296	0.001	Duration of HD	0.244	0.002
Duration of diabetes	0.230	0.013	SBP	0.361	<0.001
			HR	0.230	0.001
			HbA1c	0.256	<0.001
	Adjusted r^2=0.323			Adjusted r^2=0.438	
	F value=15.4			F value=19.2	

SBP, systolic blood pressure; HbA1c, hemoglobin A1c; HD, hemodialysis; HR, heart rate.

Determinants of cfPWV in HD Patients with and without Diabetes

Table 2 lists the univariate correlations of cfPWV with other variables in HD patients with and without diabetes. In 94 HD patients with diabetes, the duration of diabetes, SBP, HbA1c, number of microvascular complications, presence of retinopathy and neuropathy, and insulin use positively correlated with cfPWV. In contrast, 148 HD patients without diabetes showed positive correlations between cfPWV and age, SBP, HR, CTR, HbA1c, number of macrovascular complications, presence of coronary artery disease, and presence of peripheral arterial disease, while showing a negative correlation with serum albumin. A weak correlation was also found between duration of HD and cfPWV in HD patients without diabetes. Thus, only SBP and HbA1c correlated with cfPWV in both diabetic and nondiabetic HD patients (Figs. 1 and 2). A significant difference existed in the rate of aging (β, slope of line) of cfPWV between diabetic and nondiabetic subjects (β=0.016 *vs*. 0.064, respectively; $p<0.05$, Fig. 3).

Next, we performed a stepwise multiple regression analysis to further explore the independent impact of cfPWV (Table 3). SBP (β=0.356, $p<0.001$), HbA1c (β=0.296, $p=0.001$), and duration of diabetes (β=0.230, $p=0.013$) were independent contributors to cfPWV in HD patients with diabetes. In HD patients without diabetes, age (β=0.440, $p<0.001$), duration of HD (β=0.244, $p=0.002$), SBP (β=0.361, $p<0.001$), HR (β=0.230, $p=0.001$), and HbA1c (β=0.256, $p<0.001$) independently contributed to cfPWV.

Discussion

In this cross-sectional study, we identified differences in contributing factors for cfPWV between HD patients with and those without diabetes. Only SBP and HbA1c contributed to cfPWV in both diabetic and nondiabetic HD patients, while three independent determinants of cfPWV in nondiabetic HD patients—age, duration of HD, and HR—did not contribute to cfPWV in diabetic HD patients. On the other hand, duration of diabetes was an independent determinant of cfPWV in diabetic HD patients. These results suggest that the pathogenesis of arteriosclerosis in HD patients is heterogeneous and is influenced by the presence of diabetes.

Many studies demonstrated that age was a significant determinant of arterial stiffness (*14–18*), while others found a correlation between aortic stiffness and age in ESRD patients treated with HD (*19*, *20*). Unexpectedly, diabetic patients in our study showed no correlation between aortic stiffness and age. In addition, there was a significant difference in the rate of aging (β, slope of line) of cfPWV between diabetic and nondiabetic subjects. However, our results are consistent with a previous report that described the loss of the normal age-associated change in aortic compliance in diabetic patients (*21*). Moreover, there was no association between HD duration and cfPWV in HD patients with diabetes, suggesting that these patients already had considerable atherosclerotic deterioration at the initiation of HD and that the diabetic milieu attenuated the effective power of HD duration on aortic stiffness.

HbA1c independently contributed to aortic stiffness in HD patients with and those without diabetes, though the coefficient was higher and p-value was lower in diabetic patients than in nondiabetic patients. We speculated that the distribution of HbA1c in diabetic patients extended over a wider range than in nondiabetic patients, thus HbA1c in diabetic patients had a stronger effect on the increase in aortic stiffness than in nondiabetic patients. As shown in Fig. 2, the y-intercept in diabetic HD patients was higher than in nondiabetic HD patients, probably suggesting that the increase in HbA1c has a much worse effect on cfPWV in diabetic than nondiabetic patients. Furthermore, the diabetes duration independently contributed to cfPWV in HD patients with diabetes. In a Japanese population-based study, fasting blood glucose and HbA1c correlated with brachial-ankle PWV (baPWV) (*22*, *23*). Furthermore, the duration of diabetes was an independent risk factor for increased cfPWV in Japanese diabetic patients (*24*). Thus, we speculate that the degree and length of exposure to hyperglycemia affect arterial wall stiffness, regardless of the presence or absence of comorbid renal disease. On the other hand, SBP's effect on aortic stiffness is constant in HD

patients with or without diabetes. This suggests that, to prevent aortic stiffening, it is important to strictly control blood pressure for both diabetic and nondiabetic HD patients.

Our evidence suggests that volume overload likely increases aortic stiffness in diabetic patients, whose cushioning function of large arteries probably decreases more than that of nondiabetic patients, although our result that CTR correlated with cfPWV in nondiabetic, but not in diabetic, HD patients was contrary to our expectation. As a possible explanation of this finding, because of the high prevalence of ischemic coronary disease and/or nonischemic diabetic cardiomyopathy in diabetic patients (*25*), the mechanism underlying CTR is more complex in diabetic patients than in nondiabetic patients.

The association of HR and PWV has not been elucidated, although recent studies have reported that HR significantly influences PWV. In the J-TOPP study, HR increased in association with increased baPWV in patients with untreated essential hypertension (*14*). The cardiac cycle correlated weakly with cfPWV in healthy subjects, and a weak correlation was also found in ESRD patients (*26*). On the other hand, Albaladejo *et al*. showed that cfPWV increased with HR in males but not in females (*27*). In our study, HR was an independent contributor to cfPWV in nondiabetic HD patients, but not in diabetic HD patients. The reason for the lack of such a correlation in our diabetic cohort is not clear at present. However, we speculate that the effect of the degree of glycemia on aortic stiffness was so strong that it counteracted the association between HR and cfPWV. In a similar fashion, serum albumin may have correlated with cfPWV in nondiabetic patients but not in diabetic patients. To our knowledge, only a few studies have evaluated the influence of serum albumin on aortic stiffness in patients with or without ESRD (*10*, *28*). Further evaluation is necessary to understand this correlation.

The number of macrovascular complications and the prevalence of both coronary artery disease and peripheral artery disease correlated with cfPWV in HD patients without diabetes but not in those with diabetes. It is possible that the cfPWV values in HD patients with diabetes could have changed between the onset of a macrovascular complication and a measurement of cfPWV. Thus, aortic stiffness in HD patients with diabetes may vary more than in HD patients without diabetes, because blood glucose levels fluctuate more broadly in these patients, potentially affecting arterial stiffness. A similar relationship was reported by Koji *et al*. (*29*). These investigators demonstrated that the number of diseased coronary arteries increased significantly with an increase in baPWV in subjects without metabolic syndrome but not in those with metabolic syndrome. They speculated that the metabolic syndrome may directly produce clinically significant atherosclerotic stenosis of coronary arteries independent of an increase in arterial stiffness. The association between the number of microvascular complications and cfPWV in our diabetic patients suggests that both the degree of glycosylation and the duration of exposure to hyperglycemia promote microvasculopathy and reduce aortic compliance.

It will be interesting to learn whether or not arterial stiffness can be improved. A prospective study demonstrated that resolution of the metabolic syndrome was associated with attenuation of the progression of arterial damage (*30*). On the other hand, inhibition of the renin-angiotensin-aldosterone axis seems a particularly attractive approach to reducing arterial stiffness (*31–33*). Based on these studies, we predicted that administration of an angiotensin-converting enzyme inhibitor (ACEI) and/or an angiotensin receptor 1 blockade (ARB) could lower cfPWV, although we could not demonstrate that ACEI and/or ARB had a beneficial effect on aortic stiffness in either the diabetic or nondiabetic cohort. Indeed, at our institution, ARB is the first-choice medication for patients with hypertension and/or for patients at high risk for atherosclerotic diseases, although the duration of such treatment varied widely among patients. Thus, we consider that the lack of documentation on the beneficial effect of ARB is a limitation of this cross-sectional study.

In conclusion, high blood glucose level affects aortic stiffness in ESRD patients with diabetes as well as in those without diabetes. In particular, aortic compliance in HD patients with diabetes was susceptible to abnormal glucose metabolism, and this effect negated the influences of the uremic milieu and/or aging. Further studies are necessary to clarify whether or not long-term reinforcement of blood glucose control and/or the inhibition of the renin-angiotensin-aldosterone axis have any real beneficial effect on arterial stiffness in HD patients.

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