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Factors Relating to Vascular Damage in Patients on Continuous Ambulatory Peritoneal Dialysis

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SUMMARY

Chronic kidney disease (CKD) patients, especially the patients with end-stage renal disease (ESRD) who are on dialysis therapy are at high risk for developing cardiovascular diseases, based on the progression of arteriosclerosis which often limit the prognosis of these patients. Arteriosclerosis is initiated by endothelial dysfunction followed by thickening and stiffening of medial layer of arterial wall. In the present study, reactive hyperemia index (RHI), an index of endothelial function, and augmentation index (AI), an index of arterial stiffness, were measured in patients on continuous ambulatory peritoneal dialysis (CAPD), and factors related to these parameters of arteriosclerosis were analyzed. RHI was positively corelated with blood urea nitrogen (BUN) and adiponectin and negatively correlated with serum potassium (K) and C-reactive protein (CRP). On the other hand, AI was positively correlated with age, systolic blood pressure (BP) and serum potassium. In subsequent multiple regression analyses, BUN, serum K and CRP showed independent correlation with RHI, and systolic BP was the parameter independently correlated with AI. It is suggested that the inflammatory mechanism is involved in the development of endothelial dysfunction in CAPD patients and adequate protein intake may be protective against this. As for the arterial stiffness, long-term duration of systolic BP is supposed to contribute to the stiffening of arterial wall. In addition, exposure to hyperkalemia may facilitate the development of arteriosclerosis in the CAPD patients. These factors related to the indices of arteriosclerosis are assumed as candidates for the target of intervention attempting to prevent the progression of arteriosclerosis and the incidence of cardiovascular diseases thereby improving the long-term prognosis of ESRD patients on CAPD.

Key Words : Peritoneal dialysis, endothelial function, arterial stiffness, arteriosclerosis, inflammation

INTRODUCTION

It has become recognized that existence of chronic kidney disease (CKD) such as reduced renal function and proteinuria not only increases the risk of end-stage renal disease (ESRD) requiring renal replacement therapy but also the risk of developing cardiovascular diseases such as stroke and myocardial infarction[1~3]. Actually, cardiovascular diseases are the leading causes of death as well as infection in dialysis patients in Japan[4]. Considering that the number of patients on dialysis therapy is increasing globally, it is obvious that the prevention of cardiovascular diseases in ESRD patients is a matter of growing importance. As most cardiovascular diseases are caused by the failure of arteries feeding respective organs, care

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should be directed to the prevention of arteriosclerosis and atherosclerosis in order to reduce the incidence of cardiovascular events and improve the prognosis in dialysis patients. It is generally understood that the development and progression of arteriosclerosis is promoted by various risk factors such as hypertension, diabetes and dyslipidemia. Not only these traditional risk factors, but also the non-traditional risk factors such as oxidative stress and inflammation are thought to participate to the pathogenesis of arteriosclerosis in CKD patients[5~7]. Therefore, it is required to reduce the influences of these traditional and non-traditional risk factors comprehensively for the effective protection of cardiovascular organs from the development and progression of arteriosclerosis.

It is assumed that arteriosclerosis is initiated by endothelial dysfunction developing to the formation of intimal lesions such as plaque[8~10]. Then, in the medial layer of the arteries, the proliferation of vascular smooth muscle cells and the increase in extracellular matrices result in the thickening and stiffening of arterial walls[11]. In addition, the calcification of arterial wall often occurs in ESRD patients due to the impaired metabolism of calcium and phosphate[12~14]. With regard to the evaluation of these changes in vascular function and structure, several physiologic and image techniques have been applied in clinical practice[15].

Although the ESRD patients receiving renal replacement therapy are at high risk of developing cardiovascular diseases, the impacts of various risk factors on the progression of arteriosclerosis in peritoneal dialysis (PD) patients have not been well-documented because the number of patients are much fewer than hemodialysis (HD) patients. In the present study, we analyzed the relations of various parameters including traditional and non-traditional risk factors to the indices of vascular endothelial function and arterial stiffness in patients undergoing continuous ambulatory peritoneal dialysis (CAPD) in order to obtain information as to the targets of intervention for the effective prevention of cardiovascular events in PD patients and thereby improving the long-term prognosis of the patients.

METHODS

This study enrolled a total of 34 end-stage renal disease patients undergoing stable maintenance continuous ambulatory peritoneal dialysis (CAPD) as an outpatient for more than three months. Eighteen patients were on a regular CAPD regimen exchanging the 1.5 or 2 L bags of lactate-buffered dialysate containing 1.35, 1.5 or 2.5% dextrose as an osmotic agent (Dianeal, Baxter, Tokyo, Japan or Midpeliq, Terumo, Tokyo, Japan) three to four times daily. Sixteen patients were using the automated peritoneal dialysis (APD) system performing cyclic exchanges of 4.5 to 8 L dialysate solution nightly for 8 to 10 hours. Nineteen patients were using a 1.5 or 2 L dialysate bag containing icodextrin as an osmotic agent (Extraneal, Baxter, Tokyo, Japan or Nicopeliq, Terumo, Tokyo, Japan) once a day in order to promote ultrafiltration.

In the morning hours at the time of outpatient visit, office blood pressure (BP) was measured with a sphygmomanometer in the sitting position after resting for at least 15 min. Then, the blood sample was obtained from the antecubital vein for blood cell counts, routine blood chemistry and measurements of β_2-microglobulin, intact parathyroid hormone (PTH), B-type natriuretic peptide (BNP), adiponectin (ADN), malondialdehyde-modified low-density lipoprotein (MDA-LDL) and high-sensitivity C-reactive protein (HSCRP). β_2-microglobulin and ADN were assayed by latex immuno-agglutination method, and chemiluminescent immunoassay was used for the measurements of intact PTH and BNP. MDA-LDL and HSCRP were measured by ELISA colarimetry.

Reactive hyperemia index (RHI), an index of endothelial function, and augmentation index (AI), an index of arterial stiffness, were measured using the EndoPAT 2000 device (Itamar Medical, Israel)[16~19]. Measurements were performed by the manufacturer's instruction. Briefly, after a rest at supine for longer than 15 minutes in a quiet and temperature-controlled (21-24℃) room, beat-to-beat plethysmographic arterial pulse wave amplitude of the middle finger of both hands were simultaneously recorded using inflatable latex air cuffs. The measurement protocol consists of 3 consecutive recordings of 5 minutes each.

Table 1 Background characteristics and physical findings of the study subjects on peritoneal dialysis.

Gender, male/female	22/12
Age, year	55.7±14.5
Cause of renal failure	
Diabetic nephropathy	11 (32%)
Chronic glomerulonephritis	17 (50%)
Nephrosclerosis	5 (15%)
Lupus nephritis	1 (3%)
Duration on dialysis therapy, year	1.9±1.1
Body mass index, kg/m^2	24.7±3.9
Systolic BP, mmHg	142.5±15.5
Diastolic BP, mmHg	80.1±12.7
Heart rate, bpm	78.3±9.3
Cardio-thoracic ratio, %	50.4±5.6
Complications	
Cerebrovascular disease	3 (9%)
Arrhythmia	1 (3%)
Coronary artery disease	4 (12%)
Peripheral artery disease	1 (3%)
Dyslipidemia	24 (71%)
Hypothyroidism	2 (6%)
Rheumatoid arthritis	1 (3%)

Data are the mean±SD. BP, blood pressure.

Table 2 Medications given to the study subjects on peritoneal dialysis.

Antihypertensive drugs	
Diuretic	32 (94%)
α-adrenergic inhibitor	5 (15%)
β-adrenergic inhibitor	7 (21%)
Calcium channel blocker	25 (74%)
Renin-angiotensin system inhibitor	29 (85%)
Other	1 (3%)
Antianginal drug	3 (9%)
Antiplatelet drug	9 (26%)
Anticoagulant	1 (3%)
Antidiabetic drug	3 (9%)
Lipid-lowering drug	15 (44%)
Statin	11 (32%)
Other than statin	5 (15%)
Antihyperuricemic drug	1 (3%)
Potassium binder	1 (3%)
Phosphate binder	25 (74%)
Vitamin D	26 (76%)
Calcium mimetic	11 (32%)
Iron	9 (26%)
Erythropoiesis stimulating agent	33 (97%)

After a 5 minutes of baseline recording, the blood pressure cuff on one arm was inflated to 60 mmHg above the baseline systolic blood pressure for 5 minutes. Then, the arm cuff was deflated and another 5-minute recording was performed. RHI and AI were calculated using a computerized automated algorithm. RHI is the difference between the post-occlusion and pre-occlusion amplitude on the arm with occlusion divided by the same measurement on the control arm. AI was calculated as the ratio of the second to the first peak of the pulse wave expressed as a percentage.

The study protocol was in accordance with the recommendations of the World Medical Association for biomedical research involving human subjects (Fortaleza version, 2013) and was approved by the institutional review board (R-8-1). Informed consent was obtained from all subjects after explaining the study objective and design.

Clinical data were expressed as means±standard deviations (SD). Parametric data between the two groups were compared by unpaired Student's t test and Mann-Whitney U-test was applied for the comparisons of non-parametric data. Linear regression analysis was used to evaluate correlations between the two variables. Then, the multiple regression analysis was performed to evaluate dependency between variables. A p value less than 0.05 was considered to indicate statistical significance.

RESULTS

Table 1 shows the background characteristics of these 34 patients on CAPD enrolled in this study. Two-thirds were men and the average age was 56 years. Diabetic nephropathy and chronic glomerulonephritis were the frequent causes of end-stage renal failure followed by nephrosclerosis which correlated with the general situations of dialysis patients in Japan. Twenty-one of them (62%) had hypertensive range blood pressure, ≥140 mmHg in systole and/or ≥90 mmHg in diastole. In addition to hypertension, 71 % of study subjects had dyslipidemia as a traditional cardiovascular risk and seven patients were complicated by cardiovascular diseases. One patient had a history of angina pectoris and atrial fibrillation, and another patient had a history of angina pectoris and cerebral infarction.

The medications given to the study subjects were

Table 3 Routine laboratory data of study subjects on peritoneal dialysis.

Blood cell counts		Blood chemistry	
White blood cell, $\times 10^3/mm^3$	6.86±1.88	Total protein, g/dL	6.3±0.5
Red blood cells, $\times 10^4/mm^3$	346±45	Albumin, g/dL	3.2±0.4
Blood hemoglobin, g/dL	10.3±1.3	AST, U/L	15±8
Hematocrit, %	31.3±4.1	ALT, U/L	15±8
Platelet, $\times 10^3/mm^3$	23.7±7.4	Urea nitrogen, mg/dL	53±13
		Creatinine, mg/dL	9.39±3.62
		Uric acid, mg/dL	5.7±1.3
		Sodium (Na), mEq/L	137±3
		Potassium (K), mEq/L	4.2±0.6
		Calcium (Ca), mg/dL	8.5±0.5
		Phosphate, mg/dL	5.5±1.4
		HDL-cholesterol, mg/dL	52±14
		LDL-cholesterol, mg/dL	100±27

Data are the mean±SD. AST : aspartate aminotransferase, ALT : Alanine aminotransferase, HDL : high-density lipoprotein, LDL : low-density lipoprotein.

listed in Table 2. All the CAPD patients involved in this study were taking antihypertensive drugs. Most patients were taking loop diuretics for the purpose of maintaining urine volume as well as lowering blood pressure. In addition, antihypertensive drugs other than diuretics were given in 32 of 34 patients. Calcium channel blockers and inhibitors of renin-angiotensin system, especially angiotensin II receptor blockers (ARB), were the frequently used classes of antihypertensive drugs. Nearly half of the patients were taking lipid-lowering drugs, mostly statins, and two-thirds of the patient were taking xanthine oxidase inhibitors as antihyperuricemic drugs. For the maintenance of calcium and phosphate balance, three-fourths were given phosphate binder and vitamin D, and one-fourth were given calcium mimetics in order to suppress excessive PTH secretion. However, only one patient required potassium binder for hyperkalemia. Subcutaneous injection of erythropoiesis stimulating agent (ESA) was performed in almost every patient for the treatment of renal anemia so that the blood hemoglobin concentration was maintained at 10-12 g/dL according to the guideline of Japanese Society of Dialysis Therapy[20].

Table 3 shows the data of routine laboratory tests. Average values of blood hemoglobin and hematocrit were raised above 10 g/dL and 30 %, respectively, by the ESA treatment. Although blood urea nitrogen (BUN) and serum creatinine were considerably high as is the case with dialysis patients, average values of serum potassium (K), Calcium (Ca), phosphate and uric acid were maintained in the affordable ranges by the respective dietary intervention and drug therapies described above. Table 4 shows other parameters examined in the study subjects. Serum or plasma levels of peptides such as β_2-microglobulin, intact PTH, BNP and adiponectin were elevated due to the impaired renal metabolism. Average values of serum MDA-LDL, a product of oxidative reaction, and serum HSCRP, an inflammatory marker, were higher than the upper limit of normal range.

Table 4 Metabolic, endocrinological and other laboratory data of study subjects on peritoneal dialysis.

β_2-microglobulin, mg/L	24.6±8.8
Intact PTH, pg/mL	190±127
BNP, pg/mL	320±523
Adiponectin, μg/mL	28.6±14.9
MDA-LDL, U/L	112±51
HSCRP, mg/L	3.34±6.90
Reactive hyperemia index	2.10±0.58
Augmentation index, %	19.5±17.8

Data are the mean±SD. PTH : parathyroid hormone, BNP : B-type natriuretic peptide, MDA-LDL : malondialdehyde-modified low-density lipoprotein, HSCRP : High-sensitivity C-reactive protein.

Figure 1 compares RHI (left panel) and AI (right panel) between the male (n=22) and the female (n=12) patients on CAPD. These parameters of endotheli-

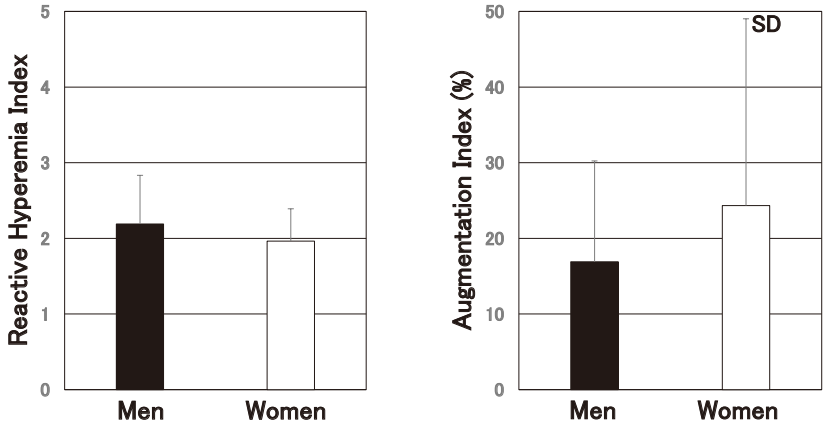

Figure 1

Reactive hyperemia index (left) and augmentation index (right) in male and female patients undergoing continuous peritoneal dialysis.

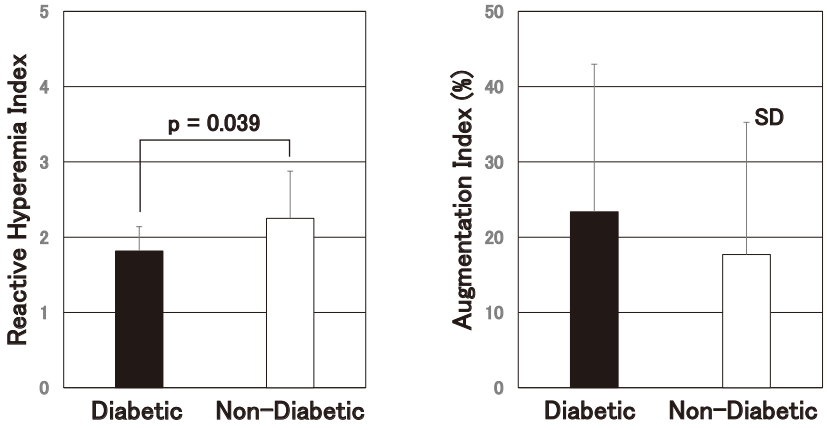

Figure 2

Reactive hyperemia index (left) and augmentation index (right) in diabetic and non-diabetic patients undergoing continuous peritoneal dialysis.

al function or arterial stiffness was not significantly affected by the difference in gender. Figure 2 also shows RHI and AI in 11 diabetic and 23 non-diabetic CAPD patients. As shown in the left panel, RHI was significantly lower in the diabetic patients than in the non-diabetic patients. However, AI was not significantly different between the two groups (right panel). During the cuff-inflation of one arm, the finger plethysmographic arterial pulse wave amplitude of non-inflated arm was increased, unchanged and decreased in 4, 24 and 6 patients, respectively.

The results of linear regression analyses of correlations between various parameters and RHI, a parameter of endothelial function, are listed in Table 5. Among the examined parameters, BUN and ADN showed positive correlations and serum K and log (HSCRP) showed negative correlation with RHI. Figure 3 depicts the correlations of BUN (left panel) and serum K (right panel) with RHI, and Figure 4 shows the correlations of ADN (left panel) and log (HSCRP) (right panel) with RHI. The multiple regression analysis adopting these parameters revealed that BUN, serum K and log (HSCRP) had independently significant correlation with RHI (Table 6). As to the parameter of arterial stiffness, Table 7 presents the results of linear regression analyses of correlations between various parameters and AI. It was indicated that age, systolic BP and serum K had positive correlation with AI as depicted in Figures 5 and 6. This was followed by the multiple regression analyses including these

Table 5 Correlations of examined parameters with reactive hyperemia index.

Parameter	Correlation coefficient, r	P value
Age	−0.047	0.7931
Body mass index	−0.120	0.4979
Duration on dialysis therapy	−0.099	0.5767
Systolic blood pressure	0.017	0.9241
Diastolic blood pressure	0.212	0.2292
Heart rate	0.106	0.5555
Blood hemoglobin	0.197	0.2632
Hematocrit	0.153	0.3868
AST	−0.166	0.3494
ALT	−0.129	0.4686
Total protein	−0.196	0.2665
Albumin	0.224	0.2032
Urea nitrogen	0.373	0.0300
Creatinine	0.201	0.2550
Uric acid	−0.229	0.1920
Sodium (Na)	−0.065	0.7136
Potassium (K)	−0.350	0.0422
Calcium (Ca)	−0.115	0.5169
Phosphate	0.173	0.3272
HDL-cholesterol	0.285	0.1025
LDL-cholesterol	0.264	0.1314
β_2-microglobulin	−0.064	0.7307
Intact PTH	0.115	0.5175
Log (BNP)	−0.074	0.6765
Adiponectin	0.373	0.0385
MDA-LDL	−0.002	0.9923
Log (HSCRP)	−0.381	0.0345

AST : aspartate aminotransferase, ALT : Alanine aminotransferase, HDL : high-density lipoprotein, LDL : low-density lipoprotein, PTH : parathyroid hormone, BNP : B-type natriuretic peptide, MDA-LDL : malondialdehyde-modified low-density lipoprotein, HSCRP : High-sensitivity C-reactive protein.

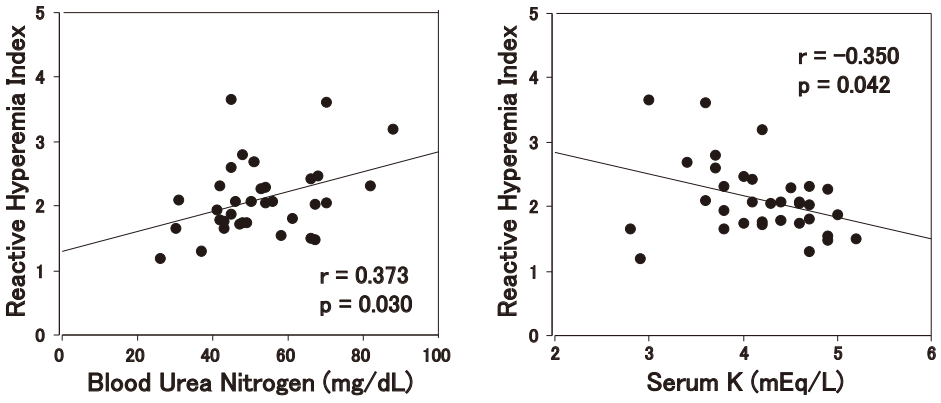

Figure 3

Correlations of reactive hyperemia index with blood urea nitrogen and serum potassium (K) in patients undergoing continuous peritoneal dialysis.

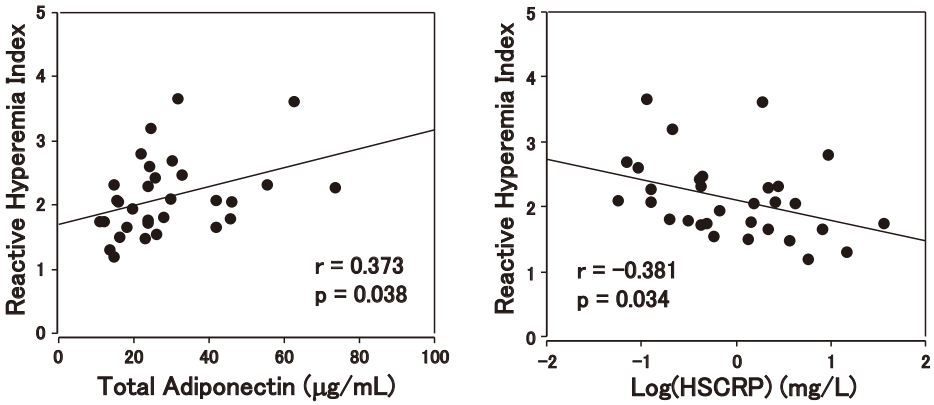

Figure 4

Correlations of reactive hyperemia index with serum total adiponectin and logarithmic value of serum high-sensitivity C-reactive protein in patients undergoing continuous peritoneal dialysis.

Table 6 Multiple regression analysis of parameters related to reactive hyperemia index.

Parameter	Standardized correlation coefficient r	P value
Urea nitrogen	0.610	0.0003
Potassium (K)	−0.650	<0.0001
Adiponectin	0.139	0.3014
Log (HSCRP)	−0.278	0.0357

HSCRP : High-sensitivity C-reactive protein.

three parameters which showed only systolic BP had independently significant correlation with AI (Table 8).

DISCUSSION

RHI is an index of endothelial function reflecting endothelium-dependent vasorelaxation after ischemia. On the other hand, AI is assumed to be an index of arterial stiffness because the faster pulse wave velocity increases the overlap of ejection wave and reflection wave resulting in an increased AI. In the present study, factors relating to these indices of endothelial dysfunction and arterial stiffness were analyzed in ESRD patients on CAPD. As in the results, BUN, serum K, adiponectin and HSCRP were significantly correlated with RHI. In addition, there was not gender difference in RHI, however, the CAPD patients with diabetes showed lower RHI than those without diabetes. With regard to the index of arterial stiffness, AI was significantly correlated with age, systolic BP and serum K.

BUN is affected not only by renal dysfunction but also by protein intake. The endothelium is known to produce nitric oxide (NO) from L-arginine by the action of endothelial NP synthase (eNOS) which dilate vessels. In addition to L-arginine, amino acids such as L-citrulline, L-ornithine and L-asparatate are metabolized and serve as the source to produce NO[21,22]. Therefore, the observed positive correlation between BUN and RHI may imply sufficient protein intake and amino acid supply contribute to the endothelial production of NO.

Renal failure patients are often complicated by hyperkalemia due to reduced or absent urinary excretion of K. Great care should be taken for hyperkalemia because it provokes possibly fatal ventricular arrhythmia in patients with reduced or abolished renal function. Generally, CAPD patients are less subject to hyperkalemia than HD patients because K is continuously transferred to the peritoneal dialysate in PD, while the K removal is limited during several hours in three days per week in HD. Actually, in present

Table 7 Correlations of examined parameters with augmentation index.

Parameter	Correlation coefficient, r	P value
Age	0.342	0.0480
Body mass index	−0.032	0.8593
Duration on dialysis therapy	0.126	0.4792
Systolic blood pressure	0.417	0.0141
Diastolic blood pressure	0.127	0.4741
Heart rate	0.032	0.8617
Blood hemoglobin	−0.211	0.2319
Hematocrit	−0.135	0.4475
AST	−0.124	0.4830
ALT	−0.148	0.4036
Total protein	−0.294	0.0912
Albumin	−0.263	0.1330
Urea nitrogen	0.037	0.8745
Creatinine	−0.022	0.9036
Uric acid	0.008	0.9633
Sodium (Na)	0.326	0.0601
Potassium (K)	0.413	0.0152
Calcium (Ca)	0.118	0.5068
Phosphate	0.196	0.2647
HDL-cholesterol	0.142	0.4226
LDL-cholesterol	0.059	0.7382
β_2-microglobulin	0.025	0.8919
Intact PTH	−0.086	0.6303
Log (BNP)	0.053	0.7639
Adiponectin	0.084	0.6539
MDA-LDL	−0.236	0.2006
Log (HSCRP)	−0.018	0.9229

AST : aspartate aminotransferase, ALT : Alanine aminotransferase, HDL : high-density lipoprotein, LDL : low-density lipoprotein, PTH : parathyroid hormone, BNP : B-type natriuretic peptide, MDA-LDL : malondialdehyde-modified low-density lipoprotein, HSCRP : High-sensitivity C-reactive protein.

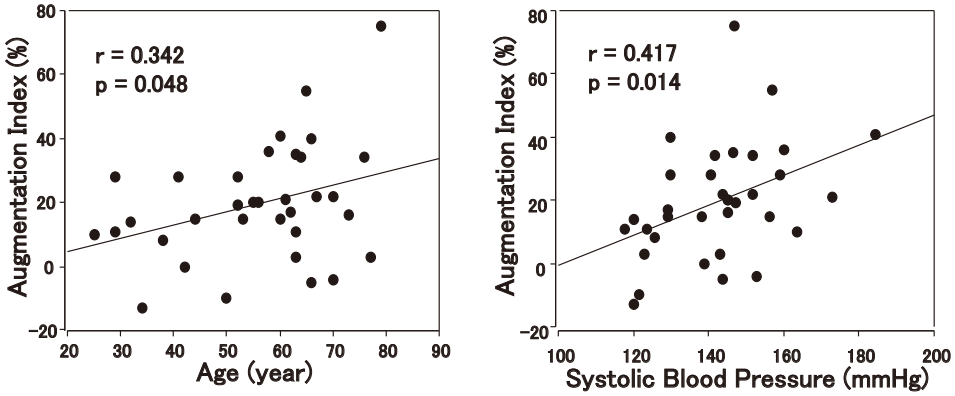

Figure 5

Correlations of augmentation index with age and systolic blood pressure in patients undergoing continuous peritoneal dialysis.

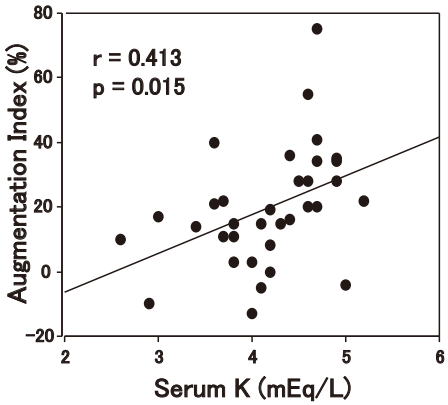

Figure 6
Correlation of augmentation index with serum potassium in patients undergoing continuous peritoneal dialysis.

Table 8 Multiple regression analysis of parameters related to augmentation index.

Parameter	Standardized correlation coefficient r	P value
Age	0.260	0.1164
Systolic blood pressure	0.358	0.0337
Potassium (K)	0.311	0.0657

study, average serum K of the involved CAPD patients was within the normal range and only one of 34 patients was prescribed the potassium binder. In this study, serum K was negatively correlated with RHI, an index of endothelial function, and positively correlated with AI reflecting the extent of arterial stiffness. As the high concentration of K induce contraction of vascular smooth muscle, an increase in serum K may cause the increased tension and stiffness of arterial wall. It is generally recognized that the activity of Na^+/K^+-ATPase, which promotes K^+ influx and Na^+ efflux, is essential for maintaining polarization and integrity of the cells including endothelium. It is also well-known that insulin is an important hormone incorporating glucose, major energy source of the cells, together with K^+ into the cells. Therefore, it is speculated that the insufficient actions of these key enzyme and hormone are the causes of the increase in serum K and the decrease in endothelial dysfunction in CAPD patients, although the extent of hyperkalemia is less prominent than HD patients. Actually, RHI was lower in CAPD patients with diabetes than in those without diabetes and the serum K was insignificantly higher by 0.2 mEq/L in the former than the latter.

ADN is a cytokine produced by adipocytes and has beneficial actions such as inhibiting the development of atherosclerosis and improving the glucose metabolism by enhancing insulin sensitivity[23,24]. Furthermore, it has been indicated that ADN inhibits proliferation of vascular smooth muscle cells, production of adhesion molecules by endothelium and activation of monocytes[25,26]. Therefore, it seems plausible that serum ADN was positively correlated with RHI in the current study. However, as ADN is composed of 244 amino acids, the metabolism is prolonged and the blood level is increased generally in patients with reduced or abolished renal function. Indeed, the average serum ADN level was much higher than the normal range in subjects without renal dysfunction. Considering that the plasma levels of peptide hormones such as atrial natriuretic peptide and BNP which have beneficial effects on cardiovascular system are also increased in renal failure patients, it seems elusive if the increased serum ADN had direct influence on the endothelial function in the CAPD patients examined in this study.

It is generally understood that the progression of arteriosclerosis is contributed by aging, smoking and lifestyle-related diseases such as diabetes, hypertension and dyslipidemia. In addition to these traditional risk factors, non-traditional factors such as oxidative stress and inflammation are thought to participate in the etiology and pathogenesis of vascular injuries[5~7]. It has been demonstrated that oxidative stress and inflammatory markers are increased in CKD patients including those on CAPD[27~30]. However, in the present study, serum MDA-LDL, a marker of oxidized lipids, failed to show correlation with RHI or AI. Quantitative evaluation of oxidative stress is difficult because the lifetime of reactive oxygen species is very short as less than a second. Therefore, the oxidized products are often measured as substitutes in clinical samples, however, this may be subject to inaccuracy as indirect markers of existed oxidative stress. As compared with this, C-reactive protein (CRP) is a relatively stable molecule in the circulating blood and plasma or serum HSCRP is frequently used as a marker of inflammation in the cardiovascular system[31~33]. Our

analysis in CAPD patients showed a positive correlation between serum log (HSCRP) and RHI, an index of endothelial function, suggesting the participation of inflammatory mechanism to the pathophysiology of arteriosclerosis in CAPD patients. This association is thought to be reasonable considering that serum CRP has been shown to be a predictor of prognosis in PD patients as well as in HD patients[34~36].

In multiple regression analysis, BUN, serum K and log (HSCRP) showed independent correlation with RHI. The values of these parameters on regression lines corresponding to RHI of 2.10 as the lower limit of desirable range were 53 mg/dL for BUN, 4.2 mEq/L for serum K and 1.1 mg/L for HSCRP, respectively. These values may be considered as references in managing CAPD patients in order to prevent progression of arteriosclerosis and incidence of cardiovascular diseases.

It seems natural that high age and high systolic BP were associated with high AI value in the current study because these factors are known to contribute to the thickening and stiffening of arterial wall. In renal failure patients, impaired vitamin D activation in the kidney causes hypocalcemia and hyperparathyroidism resulting in mineral and bone disorder, which on the long period combined with hyperphosphatemia, facilitates calcification of the vascular wall[12~14]. However, in this study, serum phosphate or intact PTH did not show significant correlation with AI. Such correlations, if present, may have been hidden by the relatively large intra-individual variations of serum phosphate and intact PTH in general.

As to the limitations of current study, AI was indirectly evaluated from the finger pulse wave, however, the intra-arterial direct recording of pressure wave in larger arteries is thought to be more appropriate for the evaluation of reflective pressure wave. Second, although various medications especially antihypertensive drugs are supposed to affect endothelial function and arterial stiffness, the number of study population is insufficient for evaluating the influences of each drug. And third, because of the cross-sectional nature of study design, observed correlations do not necessarily indicate causal relationships and validations by future prospective studies are required.

In conclusion, it is suggested that the inflammatory mechanism is involved in the development of endothelial injury and adequate protein intake may be preferable for preserving the endothelial function in ESRD patients on CAPD. On the other hand, long duration of high systolic BP is supposed to contribute to the stiffening of arterial wall. In addition, it is also suggested that hyperkalemia is detrimental to the maintenance of endothelial function and arterial elasticity in CAPD patients. These factors related to the extent of vascular injury are possibly the candidates for intervention suppressing the progression of arteriosclerosis and preventing cardiovascular events in CAPD patients.

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