Arterial stiffness and functional properties in chronic kidney disease patients on different dialysis modalities: an exploratory study

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Abstract
Background. Abnormalities of vascular function and accumulation of oxidative stress have been associated with chronic kidney disease (CKD). Dialysis modalities, peritoneal dialysis (PD) and haemodialysis (HD) may differentially impact on vascular function and oxidative stress.

Methods. Patients undergoing living donor transplantation were studied for vascular stiffness using pulse wave velocity measurements, and inferior epigastric arteries were harvested to examine in vitro stiffness and functional properties and evidence of oxidative stress. Forty-one patients were studied representing PD (n = 12), HD (n = 14) and non-dialysed recipients (n = 15).

Results. We demonstrated differences in stiffness from in vivo and in vitro measurements such that non-dialysis < HD < PD groups. The stiffness measurements did not correlate with duration of CKD nor dialysis duration, but did so with phosphate levels (r = 0.356, P = 0.02). From the in vitro isometric force experiments, HD arteries demonstrated decreased contractility and endothelium-dependent relaxation compared with PD and non-dialysis vessels. Level of oxidative stress (as indicated by the 8-isoprostanate level) was 30% higher in HD arteries than in PD arteries. Protein expression of inducible nitric oxide synthase, NADPH subunits and xanthine oxidase was upregulated in HD arteries, while superoxide dismutase was downregulated. The compromised vascular function in HD arteries was improved by pharmacological means that eliminated oxidative stress.

Conclusions. We report associations between vasomotor function and oxidative stress in the vasculature of patients receiving different dialysis therapies. Oxidative stress, which may be differentially augmented during PD and HD, may play an important role in the vascular dysfunction in dialysis populations.

Keywords: chronic kidney disease; haemodialysis; oxidative stress; peritoneal dialysis; vasomotor function

Introduction
Chronic kidney disease (CKD) is a well-recognized risk factor for cardiovascular disease (CVD). Furthermore, the leading cause of death in both CKD and dialysis populations remains to be CVD [1,2]. There is increasing evidence that the cardiac and vascular abnormalities develop early in CKD and become more severe as the disease progresses to end stage. The complex process of vascular calcification and the consequent arterial stiffening have received substantial attention in all CKD populations. However, whether and how different dialysis modalities might impact on the vascular function has not been the focus of much study.

Vascular dysfunction is characterized by aberrations in endothelial secretion, smooth muscle contractility and mechanical property. Increased arterial stiffness results in elevated left ventricular stress and reduced coronary perfusion, and the subsequent hypertrophy and cardiomyopathy predispose to congestive heart failure and sudden death in dialysed CKD patients [1–3]. Endothelial dysfunction has been described in the vasculature of patients on both peritoneal dialysis (PD) and haemodialysis (HD), and is implicated as the initial pathological step in the progression of vascular damage [4,5]. Elevated production of vasoconstrictors, such as norepinephrine, endothelin-1 and angio-
tensin II, has been suggested to be associated with uraemia [6–8]. However, very few studies have focused on arterial wall properties in patients on PD [4], and there is a lack of information on the comparative impact of PD and HD on arterial stiffness and vascular function.

Oxidative stress, characterized by excessive production of reactive oxygen species (ROS), has been associated with the pathogenesis of hypertension, diabetes and CKD [9–12]. Oxidative stress is caused by an imbalance between the production and neutralization of ROS [9–11,13]. Vascular endothelial and smooth muscle cells contain ROS-generating enzymes, among which NAD(P)H oxidase, xanthine oxidase and inducible nitric oxide synthase (iNOS) are believed to play a dominant role in vascular disease [9]. Superoxide dismutase (SOD) is the main endogenous anti-oxidant responsible for superoxide removal [11]. Oxidative stress could cause endothelial dysfunction through scavenging of NO and produce peroxynitrite by uncoupling endothelial nitric oxide synthase [9–13]. Oxidative stress could also impair calcium signalling pathway, leading to the reduction of vascular reactivity [9, 14]. However, to what extent oxidative stress has an impact on the vasomotor function in CKD patients on PD and HD remains unknown.

The present study investigates differences in vascular structure and function in a cohort of patients undergoing living donor kidney transplantation. Given that patients were either on PD or HD, or were not receiving dialysis, we were able to explore the possibility that differences in dialysis exposure may contribute to vascular structural and functional changes as well as oxidative stress production.

Materials and methods

Study population and sample preparation

Patients who were to undergo live donor kidney transplantation at St. Paul’s Hospital (Vancouver, BC, Canada) were approached for participation in the study, which was approved by the ethics board of Providence Health Care/University of British Columbia. Written informed consent was obtained from recipients (n = 41). Demographics, cardiovascular risk factors, medications and dialysis modality or renal function (if not on dialysis) were collected at the time of transplantation. The estimated glomerular filtration rate (eGFR) was calculated from the Modification of Diet in Renal Disease formula. All patients consented to undergo in vivo pulse wave velocity (PWV) measurements and to the use of the discarded inferior epigastric artery as described previously [15–17]. ‘APD’ denotes the artery from patient who had not been on dialysis procedure (n = 15) at the time of transplantation, while ‘AHA’ and ‘AH’ denote those from patients who had been on either peritoneal dialysis (PD, n = 12) or haemodialysis (HD, n = 14), respectively.

Procedures for in vitro stiffness, in vivo PWV, isometric force measurement, 8-isoprostane measurement, western immunoblotting and statistics are available as Supplementary Data in Nephrology Dialysis Transplantation online.

Results

Study cohorts

Table 1 describes the cohort of recipients by modality at the time of transplant. There were some differences between those on HD and PD (significantly less female and higher haemoglobin level in the HD vs PD group). However, the clinical significance of the Hb difference is questionable. As expected, the PD group (6 mL/min) had higher renal residual function than the HD group (2 mL/min). Laboratory parameters were otherwise similar in two groups. There were no differences between the number of months since GFR <30 and the number of months since the first nephrologist consult (which were used as an indication of the exposure to nephrology care) among three groups. In those receiving dialysis therapies, the duration of CKD, defined as the number of months since the first nephrology consult to the dialysis start date or transplantation, was not different. Those on PD did have a substantially longer mean exposure of 47 vs 26 months in those on HD.

Table 1. Demographics and clinical features of the live kidney transplantation recipients, P-value indicates statistic difference between PD and HD groups.

<table>
<thead>
<tr>
<th></th>
<th>Non-dialysis (n = 15)</th>
<th>PD (n = 12)</th>
<th>HD (n = 14)</th>
<th>P-value (t test, Wilcoxon or χ²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female (%)</td>
<td>27</td>
<td>75</td>
<td>21</td>
<td>0.006</td>
</tr>
<tr>
<td>Age (years)</td>
<td>50 ± 12</td>
<td>47 ± 11</td>
<td>51 ± 15</td>
<td>0.445</td>
</tr>
<tr>
<td>Creatinine (μmol/L)</td>
<td>423 ± 130</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>eGFR (mL/min/1.73 m²)</td>
<td>13.6 ± 4.0</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Diabetes (%)</td>
<td>6</td>
<td>25</td>
<td>21</td>
<td>0.838</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>NA</td>
</tr>
<tr>
<td>Calcium (mmol/L)</td>
<td>2.34 ± 0.16</td>
<td>2.36 ± 0.11</td>
<td>2.45 ± 0.18</td>
<td>0.127</td>
</tr>
<tr>
<td>Phosphate (mmol/L)</td>
<td>1.63 ± 0.41</td>
<td>1.74 ± 0.44</td>
<td>1.56 ± 0.59</td>
<td>0.377</td>
</tr>
<tr>
<td>Haemoglobin (g/L)</td>
<td>112 ± 11</td>
<td>111 ± 15</td>
<td>127 ± 11</td>
<td>0.006</td>
</tr>
<tr>
<td>Length of dialysis (months)</td>
<td>0.0</td>
<td>47 ± 57</td>
<td>26 ± 21</td>
<td>0.296</td>
</tr>
<tr>
<td>Number of months since GFR &lt;30</td>
<td>78 ± 99</td>
<td>70 ± 53</td>
<td>59 ± 46</td>
<td>0.615</td>
</tr>
<tr>
<td>Since 1st nephrologist consult (months)</td>
<td>141 ± 124</td>
<td>115 ± 80</td>
<td>92 ± 72</td>
<td>0.488</td>
</tr>
<tr>
<td>Duration of CKD</td>
<td>141 ± 124</td>
<td>68 ± 85</td>
<td>66 ± 75</td>
<td>0.949</td>
</tr>
<tr>
<td>ACEi/ARB</td>
<td>47 ± 52</td>
<td>50 ± 52</td>
<td>29 ± 47</td>
<td>0.281</td>
</tr>
<tr>
<td>Beta blockers</td>
<td>40 ± 51</td>
<td>50 ± 52</td>
<td>21 ± 43</td>
<td>0.137</td>
</tr>
<tr>
<td>Calcium channel blockers (%)</td>
<td>67 ± 49</td>
<td>33 ± 49</td>
<td>21 ± 43</td>
<td>0.515</td>
</tr>
<tr>
<td>Aspirin (%)</td>
<td>27 ± 46</td>
<td>42 ± 52</td>
<td>43 ± 51</td>
<td>0.954</td>
</tr>
<tr>
<td>Statins (%)</td>
<td>47 ± 52</td>
<td>33 ± 49</td>
<td>21 ± 43</td>
<td>0.495</td>
</tr>
</tbody>
</table>

Duration of CKD = number of months since the first nephrologist consult until the initiation of dialysis or transplantation.

PTH, parathyroid hormone; ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; NA, not applicable.
Arterial stiffening in PD patients

PWV measurements were not significantly different among three groups. However, PD and HD patients showed higher PWV than the non-dialysed recipients (7.9 ± 1.5 m/s), with values in the recognized ‘pathological range’ of >8.3 m/s (HD = 8.3 ± 1.8 m/s, PD = 9.2 ± 4.1 m/s).

**Fig. 1.** (A) *In vitro* arterial stiffness measurement (K value) was deduced from stress–strain curves as described previously. (B) Linear relation between PWV and K values. (C–F) Relations between K value and duration of CKD, length of dialysis, phosphate and calcium levels.
Tissue stiffness measured in vitro, however, demonstrated significant differences according to the dialysis modality. Figure 1A demonstrates that $A_{PD}$ was 25% stiffer than $A_{non-dialysis}$ ($P = 0.01$), and that there was a trend of increase in the stiffness: $A_{non-dialysis} < A_{HD} < A_{PD}$ although the difference between $A_{PD}$ and

![Graph of KCl](image)

![Graph of Agonists](image)

![Graph of Concentration–response curves](image)

Fig. 2. Maximum force (mN) generated in arteries in response to (A) membrane depolarization (80 mmol/L KCl) and (B) pharmacological agonist stimulation, e.g. phenylephrine (PE), angiotensin II (ANG), endothelin-1 (ET) and serotonin (5-HT). *$P < 0.05$. (C) Concentration–response curves of each agonist.
A_{\text{HD}} was not statistically significant (P = 0.09). Importantly, the correlation between PWV (in vivo) stiffness and tissue (in vitro) stiffness measurements were strongly correlated to each other (r = 0.653, P = 0.002) (Figure 1B).

In tissue preparations, we could not demonstrate an association of K value (stiffness) with the length of dialysis and duration of CKD (Figure 1C–D). However, stiffness was found to be significantly correlated to the phosphate level (r = 0.356, P = 0.02) but not calcium (Figure 1E–F).

Depressed contraction and endothelium-dependent relaxation in A_{\text{HD}}

The KCl-stimulated vasocontraction was significantly depressed in both dialysis modality groups. There were differences between PD and HD when each was compared to non-dialysis patients; Figure 2A describes these differences in contractile force generated in A_{PD} as compared to A_{non-dialysis} (56% less), and 70% less contraction in A_{HD} as compared to A_{non-dialysis}.

We compared the agonist-induced vasoconstriction among A_{non-dialysis}, A_{PD} and A_{HD}. Comparing with the A_{non-dialysis}, the phenylephrine (PE), endothelin (ET-1) and serotonin (5-HT)-stimulated maximum contraction was greatly depressed in both dialysed groups. A more pronounced reduction was observed in the A_{HD}, which generated 60 and 40% less force compared with the A_{non-dialysis} and A_{PD}, respectively, in the PE, ET-1 and 5-HT-stimulated contraction. The angiotensin II (ANG II)-induced contraction was similar among three groups (Figure 2B). The concentration–response curves of each agonist are shown in Figure 2C. Note that the pEC_{50} values of each agonist were similar among three groups.

Although the pEC_{50} values were similar among three groups (non-dialysis = 6.73 ± 0.24; PD = 7.00 ± 0.67; HD = 6.77±0.49), we observed a trend of reduction in ACh-induced relaxation (E_{\text{max}}) in the artery: non-dialysis > PD > HD group (Figure 3). The relaxation response in the A_{PD} was 80% of that in the A_{non-dialysis} (P = 0.03). The relaxation was further reduced in the HD group, which was only 65% of that in the A_{non-dialysis} (P < 0.0001). The PD group trended towards better relaxation than the HD, although not statistically significant (P = 0.11).

Elevated oxidative stress in the A_{HD}

In order to explore possible mechanisms of compromised arterial functions, and knowing that dialysis modalities can be associated with oxidative stress level [9,14], we examined tissue levels of isoprostane 8-epi-PGF_{2} and protein expression of SOD1, SOD2, xanthine oxidase and subunits of NAD(P)H oxidase, and iNOS. The level of isoprostane 8-epi-PGF_{2}, a marker of oxidative stress [13,19], was higher in the A_{HD} by 30% as compared to the A_{PD}, which in turn was 20% higher than those levels in the A_{non-dialysis}. Figure 4A describes these differences in tissue oxidative stress markers by group.

The expression of SOD1 and SOD2 also varied by dialysis modality, and it was greater in the A_{PD} as compared to A_{HD}. Xanthine oxidase was elevated in the A_{HD} while its expression was similar in both A_{non-dialysis} and A_{PD}. The expression of p47phox, the regulatory subunits of NAD(P)H oxidase, was increased in the A_{HD}, while the expression of gp91phox, the catalytic units, was similar in all groups. iNOS expression was clearly evident in the A_{HD}, but not in the arteries from other groups (Figure 4B).

Reversibility of vasomotor dysfunction

A_{HD} could be improved by oxidative stress-eliminating agents. Figure 5 describes the impact of SOD, allopurinol and 1400W that greatly improved PE-induced contraction in the A_{HD}. Apocynin did not significantly alter contractile function of A_{HD} (data not shown).

Figure 6A–D describes the pronounced improvement in the E_{\text{max}} of ACh-induced relaxation by the above agents in the A_{HD} (Figure 6A–D). Figure 6E shows that in A_{PD}, only SOD and allopurinol improved relaxation in the artery, whereas 1400W hampered the relaxation.

Discussion

The current translational study has the unique advantage of examining human vessels, from individuals at CKD stage 4/5, so as to investigate differences in contractility and endothelial function as well as structural property. Although numerous animal studies have examined the pathologic modifications in the vasculature during CKD development, the complex vascular pathology in CKD seen in middle-aged and elderly patients is impossible to reproduce in laboratory animals; thus, they may have limited applicability to the human condition.

By taking advantage of a unique situation of planned living kidney transplantation, we were able to systematically subject tissues obtained at the time of transplantation in order to explore the differences in arterial stiffness and vasomotor function between cohorts of CKD patients treated by either PD or HD, comparing these parameters with...
CKD patients not on dialysis. The demographic parameters such as age, medications and the length of CKD amongst the recipients are similar, which somewhat strengthens our hypothesis that observed differences in vascular properties may possibly be attributed either to the dialysis modalities or to the duration of dialysis, or both. We performed a series of comprehensive functional studies to compare the arterial function of patients either non-dialysis PD HD

![Bar graph presenting the levels of isoprostane 8-epi-PGF$_2$ in the arterial protein homogenate. Values were normalized to the level from renal arteries from three live kidney donors.](B) Representative western immunoblots showing the expression of protein of interest in arteries. β-Actin is the loading control. Table is the densitometric analysis (normalized to β-actin). *P < 0.05 vs PD.

<table>
<thead>
<tr>
<th></th>
<th>Non-dialyzed</th>
<th>PD</th>
<th>HD</th>
</tr>
</thead>
<tbody>
<tr>
<td>SOD-1</td>
<td>0.328±0.035</td>
<td>0.291±0.055</td>
<td>0.154±0.009 *</td>
</tr>
<tr>
<td>SOD-2</td>
<td>0.160±0.030</td>
<td>0.247±0.040</td>
<td>0.110±0.025 *</td>
</tr>
<tr>
<td>Xanthine Oxidase</td>
<td>0.198±0.034</td>
<td>0.148±0.045</td>
<td>0.440±0.075 *</td>
</tr>
<tr>
<td>p47phox</td>
<td>0.104±0.022</td>
<td>0.153±0.039</td>
<td>0.424±0.069 *</td>
</tr>
<tr>
<td>gp91phox</td>
<td>0.109±0.005</td>
<td>0.094±0.015</td>
<td>0.120±0.020</td>
</tr>
<tr>
<td>iNOS</td>
<td>0.052±0.002</td>
<td>0.055±0.004</td>
<td>0.128±0.014 *</td>
</tr>
</tbody>
</table>
on PD, HD or those who were dialysis independent. The three novel observations were: (i) $A_{PD}$ exhibited increased stiffness than $A_{HD}$ and $A_{non-dialysis}$; (ii) despite this, $A_{HD}$ had reduced contractile function, blunted endothelium-dependent relaxation and elevated oxidative stress relative to $A_{PD}$; and (iii) the vasomotor dysfunction in the $A_{HD}$ could be improved by pharmacological means that eliminate oxidative stress.

Fig. 5. (A) Bar graph shows the percent change of PE-induced maximal contraction in the presence of SOD, allopurinol and 1400W in $A_{PD}$ and $A_{HD}$. *$P < 0.05$ vs $A_{PD}$. Concentration–response curves of PE-induced contraction in $A_{HD}$ with the pre-incubation of (B) SOD, (C) allopurinol and (D) 1400W.
Fig. 6. Bar graph shows the percent change of ACh-induced relaxation in the presence of SOD, allopurinol and 1400W in \( A_{PD} \) and \( A_{HD} \). *P < 0.05 vs \( A_{PD} \). Concentration–response curves of ACh-stimulated relaxation in \( A_{HD} \) with the pre-incubation of (B) SOD, (C) allopurinol, (D) 1400W and (E) in \( A_{PD} \) with the 1400W pretreatment.
From the stiffness measurements, those on dialysis had elevated arterial stiffness compared to those not on dialysis. Reduction in GFR has been demonstrated to adversely affect arterial compliance such as medial calcification, insulin resistance, increased sympathetic nerve activity or activation of the local vascular renin–angiotensin system [20]. Some clinical studies describe the increase in vascular stiffness in PD patients [21], which could be due to the uraemia-dependent inflammation, hypoalbuminaemia and homocysteine [20,22,23]; we did find similar findings in the tissues examined herein.

Arterial wall elastic properties may also be influenced by calcium and phosphorus metabolism and the duration of dialysis therapy. In our study cohort, we could not demonstrate a significant correlation between stiffness and duration of CKD or length of dialysis. However, phosphate was associated with increased stiffness. Note that the phosphate levels are higher in patients on PD, despite not achieving statistical significance due to our small sample size; we prefer to limit inferences about statistical differences in this parameter. Recent data have described very small differences in serum phosphate levels even within the normal range, which could be associated with vascular disease [24]. The relationship between phosphate and stiffness in these studies was also within very small ranges close to normal, thus adding some validity to our finding here.

We are the first to characterize and explore the differential vasomotor (dys)function at CKD stage 4/5, including different dialysis modalities, using a comprehensive set of functional studies performed on live tissue. The aberrant response to KCl in the two dialysed groups may suggest the differential regulation of blood volume and potassium response to KCl in the two dialysed groups may suggest functional studies performed on live tissue. The aberrant different dialysis modalities, using a comprehensive set of functional vasomotor (dys)function at CKD stage 4/5, including here.

Close to normal, thus adding some validity to our finding here.

Arterial stiffness in CKD patients on different dialysis modalities

Given the exploratory nature of this study, we cannot determine which of these explanations is most viable or their relative contribution within an individual.

The A_HD demonstrated impaired endothelial relaxation. We note that elevated plasma markers of endothelial injury and NO synthase inhibitors have been reported in HD patients [31,32]. It is described that the extracorporeal HD procedure can lead to pro-oxidative changes via complement activation, leucocyte activation and inflammatory responses, thereby impairing endothelial function [5,10,12,21]. The elevated oxidative stress markers seen in A_HD could result from the imbalance in superoxide-removing and superoxide-generating enzymes levels [10,11,33]. Thus, our studies raise the possibility that compromised vascular function in A_HD is due to oxidative stress [9–14]. To bolster this observation, we demonstrated improvement of vasomotor function in A_HD using antioxidants, which is consistent with our hypothesis as well as with other experimental models of diabetes, heart failure, hypertension and hypercholesterolaemia [5,9–14]. Note that a clinical trial has demonstrated that administration of antioxidants in HD patients with preexisting cardiovascular disease improves cardiovascular outcome [34]. The lack of beneficial effects of the antioxidants in A_PD may suggest two possibilities: either there is an absence of augmented oxidative stress in PD patients or those on PD have additional inhibitors that preclude them from responding to antioxidants.

This study, as an exploratory study of human vessels, has several limitations: (i) The patients on PD and HD are not ‘matched’ in any way, and the exposures to therapy (both dialysis duration and some medications) are not the same. We can only describe and hypothesize based on other observations whether the therapies are contributing to differences seen in vasculature. (ii) In an adult study, all patients have some degree of preexisting confounders for vascular disease, i.e. diabetes, dyslipidaemia and hypertension. The clustering of cardiovascular risk factors may have synergistic deleterious effects on the vasculature. However, the incidence of these concomitant diseases was not significantly different among recipient groups. (iii) Most importantly, the cross-sectional nature of the study does not allow us to confirm whether the dialysis procedures per se are the sole cause of the differential vascular function and oxidative stress production. The selection of modality may be due to a variety of factors; thus, without serial vascular function measurements (which, however, is not practical with respect to tissue studies), we cannot separate the impact of dialysis from disease duration and other exposures. (iv) More non-dialysed and PD patients are on medications such as ACEi/ARB/beta blockers prior to the transplantation, and the impact of these drugs on our findings cannot be determined. Numerous clinical studies have reported the beneficial effects of renin–angiotensin system blockers on the improvement of endothelial function and oxidative stress burden. It might account for the apparent difference in responses to SOD, allopurinol and 1400W between PD and HD groups. Lastly, the nature of the population studied (transplant eligible) may actually bring some ‘conservative bias’ to the findings. The functional changes we described here would likely represent
the least severe of all CKD populations, given that they are well enough to undergo transplantation. Thus, the signal we have demonstrated here with respect to the severity of vascular dysfunction may actually be much more profound if we were to study long-term dialysis patients not eligible for transplantation due to high cardiovascular disease burden or patients receiving cadaveric transplantation with longer dialysis exposure.

Nonetheless, using this unique opportunity to examine blood vessels from transplant recipients, we demonstrate that although arterial stiffness is increased in patients on PD, they appear to have better vascular function as compared to those receiving HD. The vasomotor dysfunction observed in the HD vasculature appears to be responsive in vitro to pharmacological antioxidants. Our data indicate that oxidative stress, which has been shown to be differentially amplified during different dialysis modality implementations, could explain the differential findings between PD and HD. We recognize that cross-sectional studies such as this cannot answer questions regarding comparative effects of different types of renal replacement therapy on arterial stiffness, vascular function and the cardiovascular risk before and after transplantation. This project has the advantage of examining human vessels from well-characterized individuals at different stages of CKD; the results presented herein are provocative but remain exploratory, and require confirmation by future longitudinal studies.

**Supplementary data**

Supplementary data is available online at http://ndt.oxfordjournals.org.

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**Conflict of interest statement.** None declared.

**References**

Factors associated with aortic stiffness and its change over time in peritoneal dialysis patients

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Abstract
Background. An increase in aortic stiffness, as reflected by an increase in pulse wave velocity (PWV), is an important predictor of cardiovascular mortality in dialysis patients. Decreased serum concentration of calcification inhibitor, such as fetuin-A, is inversely related to mortality in haemodialysis patients. Our aim is to investigate the factors associated with aortic stiffness and its change over time in peritoneal dialysis (PD) patients.

Methods. As a prospective observational study, we analysed 67 PD patients, aged 50 ± 14 years (mean ± SD) and with dialysis duration of 26 (5–58) months (median, interquartile range). At baseline, age, mean arterial pressure (MAP), left ventricular mass (LVM) index, diabetes, serum albumin, calcium (Ca), phosphorus (P) and intact parathyroid hormone (iPTH), uric acid, total bilirubin, high-sensitivity C-reactive protein (hsCRP), fetuin-A, and residual renal function were included in association analysis with aortic stiffness represented by heart-to-femoral PWV (hfPWV). We also evaluated simple vascular calcification score (SVCS) with plain radiograph of the pelvis and both hands. PWV was measured both at baseline and at 1 year. Change of aortic stiffness was determined by ΔPWV (difference between 1-year PWV and baseline PWV). Time-averaged concentrations were used to evaluate the relation between biologic markers and changes of aortic stiffness.

Results. hfPWV was 1022 ± 276 cm/s at baseline, and hfPWV determined at 1 year was 1069 ± 317 cm/s. Mean serum fetuin-A concentration was 0.34 ± 0.08 g/L. At baseline, aortic PWV positively correlated with age, smoking status, diabetes, MAP, total cholesterol and LDL cholesterol. On the other hand, aortic PWV inversely correlated with fetuin-A, log PTH, haemoglobin and albumin. In a multiple regression model, association of serum fetuin-A (β = −0.329, P = 0.003) with aortic PWV remained significant, along with age (β = 0.512, P < 0.001), MAP (β = 0.215, P = 0.047) and log PTH (β = −0.269, P = 0.025). At follow-up, ΔMAP (β = 0.500, P < 0.001) and time-averaged TG (aTG) (β = 0.259 P = 0.019) were determinants of ΔPWV.

Conclusions. For our PD patients, serum fetuin-A was an independent determinant of aortic stiffness, as well as age, MAP and log PTH. Although 1 year is not sufficient to observe the change of aortic stiffness, some patients exhibited >15% increase of PWV during this period. ΔMAP and aTG were factors affecting the change of PWV. Follow-up over a longer period is necessary to elucidate factors that determine changes of aortic stiffness over time from PD patients.

Keywords: aortic stiffness; peritoneal dialysis; PWV; serum fetuin-A

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