Renal Failure

ISSN: 0886-022X (Print) 1525-6049 (Online) Journal homepage: informahealthcare.com/journals/irnf20

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To cite this article: Mehmet Büyükbakkal, Başol Canbakan, Bariş Eser, Özlem Yayar, Zafer Ercan, Özgür Merhametsiz, Ayhan Haspulat & M. Deniz Ayli (2015) The relation between apelin levels, echocardiographic findings and carotid intima media thickness in peritoneal dialysis patients, Renal Failure, 37:3, 433-438, DOI: 10.3109/0886022X.2014.996108

To link to this article: https://doi.org/10.3109/0886022X.2014.996108

Published online: 12 Jan 2015.

RENAL FAILURE

http://informahealthcare.com/rnf
ISSN: 0886-022X (print), 1525-6049 (electronic)

Ren Fail, 2015; 37(3): 433–438
 DOI: 10.3109/0886022X.2014.996108

informa
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CLINICAL STUDY

The relation between apelin levels, echocardiographic findings and carotid intima media thickness in peritoneal dialysis patients

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Abstract

Background: Cardiovascular disease (CVD) is the most important cause of morbidity and mortality in patients with end stage renal disease (ESRD). Apelin expressed in endothelial and other tissues including brain and kidney is an adipocytokine defined recently and is emerging an important mediator of cardiovascular homeostasis. The aim of this study was to test whether apelin levels might be associated with carotid artery atherosclerosis and left ventricular mass index (LVMI) in peritoneal dialysis patients. *Patients and methods*: Fifty peritoneal dialysis patients (25 female, mean age 41.4 ± 11.9 years, mean dialysis vintage 65.0 ± 35.4 months) and 18 healthy individuals (9 female, mean age 41.7 ± 6.8 years) were included in this cross-sectional study. Serum apelin 12 levels, echocardiographic findings and carotid intima media thickness (CIMT) were recorded as well as clinical and laboratory data. *Results*: There were no differences between the patient and the control groups with regard to demographic characteristics. In patient group, LVMI, CIMT, CRP and apelin levels were elevated compared to control group. However there was no association between apelin, LVMI and CIMT. There was a positive correlation between apelin and CRP, which was not statistically significant. When patients were divided into two groups according to the mean serum apelin levels, LVMI, CIMT and CRP were higher in the high apelin group but this difference did not reach statistical significance. *Conclusion*: We observed an increased inflammation and CVD risk in peritoneal dialysis patients. However, serum apelin levels seem not to be associated with cardiovascular risk in this group of patients.

Keywords

Apelin, carotid artery intima media thickness, C-reactive protein, end stage renal disease, left ventricular mass index, peritoneal dialysis

History

Received 21 August 2014
Revised 29 October 2014
Accepted 22 November 2014
Published online 12 January 2015

Introduction

The incidence of cardiovascular disease (CVD) in patients with end stage renal disease (ESRD) is high and this disease is the most important cause of morbidity and mortality.[1] The increased prevalence of several traditional and chronic renal failure related risk factors such as hypertension, hyperlipidemia, diabetes mellitus, anemia, hyperparathyroidism, hypervolemia, left ventricular hypertrophy (LVH) and increased oxidative stress are responsible for this increased morbidity and mortality.[2] In addition to these risk factors, some metabolic problems due to absorption of glucose from peritoneal cavity as an osmotic agent and peritoneal damage via advanced glycosylation end products contribute to accelerated atherosclerosis in peritoneal dialysis (PD) patients.[3]

Apelin, released from white adipose tissue, is an adipocytokine defined recently. It is expressed in endothelial cells and also other tissues including brain and kidney. The localization of expressed receptors is clearly linked to different functions played by apelin in the organism. Apelin via vascular receptors participates in control of blood pressure (BP) and alerts new blood vessel formation. It is one of the most potent stimulants through detected receptors in cardiomyocytes.[4] In addition to positive inotropic effect, apelin induces vasodilation via nitric oxide and helps cardiac compensation without causing LVH.[5]

Serum apelin level because of the role in the regulation of fluid and association of endothelial function may be related to increased risk of death due to CVD in patients with ESRD. The aim of this study is to test whether apelin levels might be associated with carotid artery atherosclerosis and increased left ventricular mass index (LVMI) in peritoneal dialysis patients.

Subjects and methods

The study protocol was approved of the Institutional Review Board of Diskapi Yildirim Beyazit Training and Research Hospital, and written informed consents were obtained from all the patients before enrollment.

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Patients

Fifty PD patients (25 males/25 females) and 18 clinically healthy individuals (9 males/9 females) were included in this cross-sectional study. All the patients had been on continuous peritoneal dialysis (CAPD) for more than 3 months (mean CAPD duration 65, 0 ± 35, 4 months) and were clinically stable without active infection. Age, gender, body mass index (BMI), waist circumference, waist to hip ratio, systolic, diastolic and mean BP, smoking behavior, dialysis duration, Kt/V values and all medications (Antihypertensives, anti-hyperlipidemics, phosphate binders, vitamin D, iron and erythropoietin) were recorded. Chronic renal failure was attributed to hypertension in 10 cases, diabetic nephropathy in six cases, glomerulonephritis in five cases, polycystic kidney disease in five cases, urolithiasis in four cases, amyloidosis in three cases, tubulointerstitial nephritis in two cases and was undetermined in 15 cases. All the clinical data including last 6 months laboratory results were also recorded. Patients with malignancy, liver disease, acute coronary events, autoimmune disease, dialysis-related peritonitis and other infections were excluded in order to avoid the possible effects of these serious conditions. The rates of comorbid diseases were found to be as follows; hypertension 30 (60%), diabetes mellitus 6(12%), atherosclerotic heart disease 4 (8%) and cerebrovascular accident 2 (4%). Forty-one patients (82%) were on a four to five exchanges per day schedule with standard dialysis bag and nine patients (18%) were on automated peritoneal dialysis. Thirty patients (69%) were receiving one or more antihypertensive drugs (calcium channel blockers, angiotensin-converting enzyme inhibitors, angiotensin-II receptor antagonists, alpha and beta blockers) at the time of the study. Twenty-nine patients (58%) were on recombinant human erythropoietin therapy. The control subjects did not have any history of hypertension, diabetes mellitus, renal or CVD and were receiving no drugs at the time of the study.

BP was measured three times in the sitting position, using a manual sphygmomanometer, after the subjects had been resting for 15 min and the mean of the three readings was used for the analysis. The mean arterial pressure (MAP) was calculated as diastolic BP + 1/3 × (systolic BP − diastolic BP) and BMI was calculated by weight in ''kg'' and height in ''m^2'' were estimated for all subjects. Waist circumference was measured midway between the lowest rib and the iliac crest while empty abdomen. The waist to hip ratio was also measured as the ratio between the circumferences of the waist and the hip at the widest trochanters.

Laboratory methods

Blood samples for hematological and biochemical measurements were obtained after 12-h fasting. Serum creatinine, albumin, calcium, phosphorus, uric acid, parathyroid hormone (PTH), HDL-cholesterol, triglyceride, ferritin, hemoglobin and hematocrit measurements were carried out by standard methods in the routine clinical laboratory. Average of the monthly serum albumin concentrations calculated in CAPD patients by using pre-study 6 month-period measured albumin levels. LDL-cholesterol was calculated using Friedewald formula. Serum CRP levels were measured by immunonephelometric method. Kt/V urea and creatinine clearance were calculated using 24-h collected dialysate and urine the day before. After specimen collection, Kt/V urea and creatinine clearance were assessed using the Renal Soft software application, version 2.0 (Baxter Healthcare Corporation, Deerfield, IL). Urea volume distributions were calculated using the Watson equation.[6]

Measurement of serum apelin levels

Of patients and control subjects, blood samples were taken from a peripheral vein in after an overnight fast. After standing at room temperature for about one hour, blood samples were centrifuged at 2000 rpm for 10 min and serum was separated. It was immediately frozen at $-80\,^{\circ}C$ until analyzed. Serum apelin-12 levels were measured by immunoenzymatic assays using commercially available ELISA kit for standard human apelin (Phoenix Pharmaceuticals, Burlingame, CA).

Carotid artery intima media thickness measurement

Ultrasonographic examination of carotid arteries was carried out using a 4.12 MHz multifrequency B mode probe attached to high resolution ultrasound machine (Mindray DC7). Within 1 week after blood sampling, all the patients were evaluated on an empty abdomen in supine position in a semi-dark room by the same radiologist who was unaware of clinical and laboratory data to exclude examiner bias. Carotis intima media thickness (CIMT) was measured 1 cm above the carotid bifurcation on a plaque-free arterial segment at the end-diastolic phase. The mean value of right and left CIMT used for statistically analysis. Presence of plaque was defined as a localized protrusion of the vessel wall into the lumen with an area greater than the intima media thickness of neighboring sites on visual assessment.[7] Each measurement was repeated four times.

Echocardiography

All echocardiographic measurement was made according to the recommendations of the American Society of Echocardiography.[8] The ultrasonographic study was performed within 1 week after blood sampling. All patients were evaluated on an empty abdomen, in supine position and in a semi-dark room by the same cardiologist who was unaware of clinical and laboratory data. Ejection fraction (EF), left ventricle end systolic diameter (LVESD), left ventricle end diastolic diameter (LVEDD), left ventricular posterior wall thickness (LVPWT), interventricular wall thickness (IVWT) and left ventricular relaxation time (LVRT) were recorded. Body surface area (BSA) was calculated using *DuBois and DuBois* formula [$BSA = (\text{weight (kg)}^{0.425} \times \text{height (cm)}^{0.725}) \times 0.007184$].[9] And LVMI was calculated using *Devereux* formula [$LVMI\ (g/m^2) = (1.04\ [(IVWT + LVEDD + LVPWT)^3 – LVEDD^3] – 14\ g)/BSA$].[10] The evaluation of LVH was based on data from the Framingham Heart Study and the presence of LVH was defined on the basis of an LVMI greater than 131 g/m^2 and 100 g/m^2 for males and females, respectively.[11,12]

Statistical analysis

''SPSS for Windows 17'' used for data analysis. The result of analysis of continuous variables was expressed as mean ± SD

and the result of discrete variables was expressed percentage value with frequency distribution. The median value for apelin level was used as cutoff point. According to this point, low and high apelin groups have been formed. We made pairwise comparison of demographic, clinical and laboratory data between each group of apelin. Kolmogrov–Smirnov test was used for normality assumption of continuous variables. *T* test was used for normal distribution, and Mann Whitney *U* test used for abnormal distribution. Dual comparison of discrete variables performed by Chi-square test. $p < 0.05$ was accepted statistically significant.

Results

The somatometric, hemodynamic and biochemical characteristics of patient and control groups are presented in Table 1. In all CAPD patients Kt/V value was at least 1.7. CAPD patients exhibited significantly higher mean values of waist-to-hip ratio, systolic, diastolic and mean BP, creatinine, uric acid, serum phosphorus, CaxP Product, triglyceride, hsCRP and apelin compared to the control group. However, the mean values of hemoglobin, albumin, HDL-cholesterol were significantly lower than in CAPD patients compared to controls. No significant difference was observed between the two groups as regards age, BMI, waist circumference, ferritin, serum calcium and LDL-cholesterol. In addition, serum apelin levels were not statistically different in PD patients using and not using erythropoietin ($p = 0.88$)

On the other hand, we observed that our CAPD patients included in the study had significantly lower EF and significantly higher LVEDD, LVESD, LVMI and the presence of LVH than control subjects. Additionally, CAPD patients had a significantly increased right and left CIMT compared with control subjects. There was no significant difference between the two groups in the presence of any arterial plaque. All echocardiographic and carotid Doppler ultrasonographic features in CAPD patients and control subjects are presented in Table 2.

In CAPD patients, apelin does not correlate with age, waist circumference, waist-to-hip ratio, duration of dialysis, systolic BP, diastolic BP and MAP, BMI, ultrafiltration amount, Kt/V value, creatinine clearance and dose of erythropoietin as shown in Table 3. On the other hand, correlation between serum apelin level and laboratory data was not detected in patients undergoing PD as shown Table 4. Furthermore, there was no correlation between serum levels of apelin and right and left CIMT values and echocardiographic findings such as EF, LVEDD, LVESD and LVMI in the patient group. These data are presented in Table 5.

Mean serum level of apelin was 0.5 ng/mL in the patient group. According to this, the group was divided into two groups as high and low apelin groups. In comparison, LVMI and CRP value in high apelin group was higher than low apelin group, but this difference was not statistically significant ($p = 0.45$ and $p = 0.08$) (Table 6).

Table 1. Comparison between somatometric, hemodynamic and biochemical data in CAPD patients and control subjects.

	CAPD patients Mean ± SD *n*: 50	Controls Mean ± SD *n*: 18	*p*-Value
Age (years)	41.4 ± 11.9	41.7 ± 6.8	NS
BMI (kg/m^2)	25.5 ± 3.8	25.1 ± 3.8	NS
Waist circumference (cm)	94.6 ± 10.5	93 ± 10.8	NS
Waist-to-hip ratio	0.96	0.9	0.009
Duration of CAPD (months)	65.0 ± 35.4		
Systolic BP (mmHg)	128.3 ± 19.6	115.8 ± 11.8	0.013
Diastolic BP (mmHg)	80.7 ± 11.8	74.4 ± 6.1	0.009
Mean BP (mmHg)	96.9 ± 16.8	88.2 ± 7.5	0.01
Hemoglobin (g/dL)	11.4 ± 2.0	14.4 ± 1.4	<0.001
Ferritin (ng/mL)	297.8 ± 394.6	226.3 ± 190.7	NS
Creatinine (mg/dL)	9.6 ± 1.9	0.8 ± 0.2	<0.001
Albumin (g/dL)	3.7 ± 0.4	4.3 ± 0.1	<0.001
Uric acid (mg/dL)	5.2 ± 0.8	4.6 ± 1.1	0.02
Serum Calcium (mg/dL)	9.1 ± 0.6	9.2 ± 0.1	NS
Serum Phosphorus (mg/dL)	5.0 ± 1.3	3.0 ± 0.3	<0.001
CaxP Product (mg^2/dL^2)	46.0 ± 12.7	28.4 ± 3.5	<0.001
PTH (pg/mL)	536.4 ± 534.7	–	
Trigliceryde (mg/dL)	184.9 ± 112.9	130.3 ± 90.2	0.02
LDL-C (mg/dL)	114.7 ± 35.7	114.6 ± 23.5	NS
HDL-C (mg/dL)	38.5 ± 11.4	46.2 ± 8.7	0.012
hsCRP (mg/dL)	1.6 ± 2.2	0.3 ± 0.3	0.002
Erythropoietin dose (U/week)	4620 ± 4457		
Apelin (ng/mL)	0.53 ± 0.20	0.35 ± 0.11	<0.0001

Notes: BMI, body mass index; CAPD, contunious ambulatory peritoneal dialysis; BP, blood pressure; PTH, parathormon; hsCRP, high sensitive C-reactive protein.

Table 2. Echocardiographic and carotid doppler ultrasonographic features in CAPD patients and control subjects.

Carotis Doppler USG and Echocardiographic findings	Patient group	Control group	*p*-Value
Left CIMT (mm)	0.79 ± 0.20	0.65 ± 0.14	0.004
Right CIMT (mm)	0.78 ± 0.20	0.62 ± 0.11	0.001
Carotid arteriel plaque, *n* (%)	6 (%12)	3 (%16)	NS
EF (%)	60.7 ± 5.5	65.1 ± 2.3	<0.001
LVEDD (cm)	4.7 ± 0.5	4.3 ± 0.3	0.005
LVESD (cm)	3.0 ± 0.4	2.8 ± 0.2	0.019
LVMI (g/m^2)	134.4 ± 40.6	69.8 ± 15.5	<0.001
LVH	32 (%64)	0 (%0)	<0.001

Notes: USG, ultrasonography; CIMT, carotid intima media thickness; EF, ejection fraction; LVEDD, left ventricle end diastolic diameter; LVESD, left ventricle end systolic diameter; LVMI, left ventricular mass index; LVH, left ventricular hypertrophy.

Table 3. Correlation between somatometric findings, dialysis adequacy and apelin level in CAPD patients.

Patient group	Apelin ng/mL	
	r	*p*
Age	−0.03	0.81
Waist circumference	−0.12	0.40
Waist to hip ratio	−0.01	0.98
Duration of dialysis	−0.03	0.81
Systolic BP	−0.01	0.94
Diastolic BP	−0.08	0.54
Mean BP	−0.19	0.16
BMI	−0.09	0.50
UF amount	0.13	0.36
Kt/V	−0.07	0.61
Creatinine clearence	0.03	0.83
Dose of erythropoietin	0.03	0.78

Notes: BP, blood pressure; BMI, body mass index; UF, ultrafiltration.

Table 4. Correlation between laboratory results and serum apelin level in the patient group.

Patient group	Apelin ng/mL	
	r	*p*
Glucose	−0.14	0.30
Creatinine	0.02	0.85
Albumin	−0.09	0.53
Hemoglobin	−0.06	0.63
Iron	0.12	0.39
Iron binding capacity	−0.03	0.83
Ferritin	0.05	0.68
ESR	0.04	0.76
hsCRP	0.27	0.056
Ca	−0.14	0.33
P	−0.03	0.79
CaxP	−0.06	0.66
Uric acid	−0.15	0.28
PTH	0.19	0.16
HDL-Cholesterol	0.09	0.51
LDL-Cholesterol	0.02	0.84
Triglyceride	0.05	0.71

Notes: ESR, erythrocyte sedimentation rate; hsCRP, high sensitive C-reactive protein; PTH, parathormon.

Table 5. Correlation between carotid Doppler ultrasound and echocardiographic findings and apelin level in the patient group.

Patient group	Apelin ng/mL	
	r	*p*
Right CIMT	−0.01	0.96
Left CIMT	0.04	0.75
EF	0.01	0.90
LVESD	0.10	0.48
LVEDD	0.07	0.58
LVMI	0.04	0.74

Notes: CIMT, carotid intima media thickness; EF, ejection fraction; LVESD, left ventricle end systolic diameter; LVEDD, left ventricle end diastolic diameter; LVMI, left ventricular mass index.

Table 6. According to apelin groups of patient LVMI and CRP levels.

Patient group	Apelin > 0.50 ng/mL ($n = 26$)	Apelin < 0.50 ng/mL ($n = 24$)	*p*
LVMI	139.0 ± 45.3	130.3 ± 34.3	0.45
hsCRP	2.1 ± 2.9	1.0 ± 0.9	0.08

Notes: LVMI, left ventricular mass index; hsCRP, high sensitive C-reactive protein.

In the patient group, the median value of BMI was 25 kg/m^2. According to this, the group was divided into two groups as large and small BMI groups. Serum level of apelin in patients with large BMI group was higher than those with small BMI, but the difference was not statistically significant ($p = 0.10$) (Table 7).

Table 7. Serum apelin level in patients with high or low BMI in the patient group.

Patient group	Apelin (ng/mL)	*p*
High BMI (*n*: 24)	0.57 ± 0.21	0.10
Low BMI (*n*: 26)	0.48 ± 0.16	

Note: BMI, body mass index.

Discussion

Advances in biomarker discovery have provided important opportunities for diagnostic approach and follow-up in clinical practice. A biomarker is a substance used as an indicator of biologic state. It is a characteristic that is objectively measured as an indicator of normal biologic process or pharmacologic responses to a therapeutic intervention.[13] Biomarkers can help understanding of disease mechanisms, predicting disease process, recognizing and monitoring.

After inflammation was recognized as an important contributing factor to atherosclerosis,[14] its importance has increased. Additionally, biomarkers have been one of the main areas of research and practice of CVD. Cardiovascular mortality in dialysis patients is 10–20 times higher than general population and CVD is responsible for nearly half of the deaths in these patients.[15] The prevalence of major cardiovascular risk factors such as dyslipidemia, hypertension, smoking, diabetes mellitus and left ventricular dysfunction is increased in CKD patients, as the also risk factors such as malnutrition, inflammation and oxidative stress for CKD itself. These risk factors directly contribute to increase in cardiovascular mortality.[3] In this study, it was investigated that the relation between serum apelin level as a biomarker and inflammatory markers, echocardiographic findings and CIMT as an early finding of atherosclerosis in PD patients. In ESRD patients under renal replacement therapy, serum apelin level compared with healthy controls.

There were many studies on serum apelin level in patients undergoing renal replacement therapy. It was affected by many factors such as diabetes mellitus, obesity, heart failure and chronic kidney disease. Recently, Malyszko et al. pointed out that apelin levels were lower in hemodialysis (HD) patients with coronary artery disease (CAD) than those without CAD.[5] In 2010, El-Shehaby et al.[16] showed the apelin levels are lower in HD patients. They also observed that apelin was related to echocardiographic features. In a different study, serum apelin levels was low in HD patients with dilated cardiomyopathy compared to patients with dilated cardiomyopathy and normal renal function. Consequently, it was expressed that this finding may be due to uremic state rather than the cardiac involvement.[17] However, Zhang et al. has observed that serum apelin-13 level was higher in HD patients without heart failure compared with healthy controls in a study.[18] In another study recently carried out, it has been shown that plasma apelin 36 level in HD patients were found to be similar with healthy controls, but plasma apelin-12 level was found higher in HD patients than healthy controls.[19] El-Shehaby et al.[16] showed that plasma apelin level was similar before and after HD session. Nevertheless, Zhang et al. has shown that the serum levels of apelin decreased significantly after HD session, probably because apelin isoforms may be lost via dialysis as the molecular weight of it gets smaller.[18] In the literature, there are few studies comparing the serum

level of apelin in PD patients with healthy controls. In a study carried out by Malyszko et al. regarding assessment of endothelial function on dialysis patients, they measured serum levels of apelin in HD, PD patients and control subjects. In PD patients, serum apelin level was obviously higher than HD patients, but slightly higher than control subjects. But, there was no comment about statistical significance.[20] In 2014, Yavuz S. et al. reported that serum apelin levels in children were similar in PD, HD and control groups.[21] In our study we found that apelin level was significantly higher in PD patients than healthy individuals. To our knowledge, this is the first study to demonstrate this finding.

Apelin is synthesized as a 77 amino acid preproprotein that is sequentially cleaved into at least circulating active peptides, apelin 36, apelin 17, apelin 13 and apelin 12. Since the sequencing of the 12 amino acids in the structure of apelin is the same in all apelin forms, the basic apelin structure is called apelin 12. In addition, the biological activity of apelin is determined by the N-terminopyroglutamat which prevents the destruction of apelins. Apelin has some important effects on cardiovascular physiology.[5,22] It is a peripheral vasodilator, powerful inotrope and may affect fluid homeostasis.[4] In a recent study, exogenous administration of apelin improved of left ventricular systolic function in dogs with advanced heart failure.[23] In 2008, Azizi et al investigated the effect of hypertonic saline infusion or water loading on osmolality, apelin and arginine vasopressin (AVP). Increasing plasma osmolality was accompanied by a parallel, linear increase in plasma AVP concentration and by a decrease in plasma apelin concentration. In contrast, decreasing plasma osmolality by water loading reduced plasma AVP concentration and rapidly increased plasma apelin concentration. Thus, the regulation of apelin secretion contributes to the maintenance of body fluid homeostasis.[24] Serum concentration of apelin may be increased in hypervolemic patients as a compensatory mechanism and help volume control. PD patients are often more hypervolemic than HD patients. Chen YC et al compared extracellular volume and blood pressure between HD and PD patients. They reported that overhydration and hypertension are more common in PD patients than in HD patients.[25] Thus, in PD patients, serum apelin level can be higher than HD patients because they are more often hypervolemic than HD patients. In a different study performed by Koç et al., they found that LVMI was significantly higher in CAPD patients with uncontrolled hypertension. This situation was also explained by presence of hypervolemia.[26] Karadağ et al found that relationships between apelin-36 level and diastolic BP, left atrium diameter, and EF in PD patients. All these parameters related with volume status of the patients.[27] Increased incidence of ultrafiltration failure and the presence of hypervolemia in most of the patients receiving long term PD treatment may lead to increase in serum levels of apelin. However, in another study involved 21 PD patients carried out by Kazancıoğlu et al., it was found negative correlation between serum level of apelin and amount of body water. This unexpected result may be due to limited number of patients.[28] In our study, it is detected that LVMI and serum apelin level in patient group was significantly higher than control group. As the patient group was divided into two groups as high and low apelin groups, LVMI is higher in high apelin group than low apelin group, but not statistically significant. Relationship between volume and serum level of apelin in PD patients must be demonstrated more clearly. Thus, future trials will need to involve large number of patients and prolonged follow-up.

It is suggested that apelin is a beneficial peptide related oxidative stress and inflammatory condition as a result of few studies.[29,30] Oxidative stress and inflammation are associated with premature deaths from CVD in patients with ESRD.[31] Oxidative stress level may be regulated by apelin expression and secretion to prevent excessive lipid accumulation and formation of reactive oxygen products in differentiated adipocytes.[32] El-Shehaby et al. investigated whether circulating apelin levels reflect cardiovascular homeostasis and inflammation in HD patients. They suggested that plasma apelin level was found to be positively correlated with LVESD, LVEDD, IVS, RV, LA and aorta, while it was negatively correlated with hs-CRP and IL-6 level in ESRD patients.[16] However, in a study performed by Malyszko et al.,[33] it was detected that positive correlation between serum apelin and CRP levels. The same work group also showed that serum level of apelin was positively correlated with visfatin, an important proinflammatory mediator.[20] In our study, serum CRP levels were significantly higher in patient group than controls and between CRP and apelin level had positive correlation, but unfortunately there was no statistically significant importance. However, in patients with high apelin levels tend to be higher CRP levels, although, statistically significance was not observed. Many factors such as uremia, bioincompatible membranes and solutions may cause reactive oxygen species formation in HD and PD patients.[34] Therefore, serum apelin levels may vary depending on the oxidative stress in these patients.

After interaction with many factors leads to impaired endothelial cells, development of endothelial dysfunction causes deterioration in angiogenesis and atherosclerotic plaque formation. It has been shown that CIMT is an early sign of atherosclerosis and it has prognostic significance for cardiovascular disease.[35] In our study, right and left CIMT in patient group was significantly higher than controls. However, we did not find any relationship between CIMT and serum apelin levels. Kadoglou et al. investigated the influence of atorvastatin treatment on CIMT and serum levels of novel adipokines. They found that atorvastatin treatment significantly improved lipid profile across with increased apelin levels in diabetic patients after 12 months. But CIMT levels did not alter significantly after treatment.[36] This condition reveals that the effectiveness of serum apelin levels must be analyzed to determine cardiovascular risk with well-designed large clinical study in peritoneal dialysis patients.

Apelin is more produced in obese individuals who have excessive adipose tissue. Its serum concentration was shown to be higher in patients with obesity and correlated with the BMI.[37] In 2006, Beltowski suggested that elevated apelin levels have some beneficial effects such as potential protective effects on obesity related complications.[38] In our study, there was no correlation between apelin level and BMI. However, when we divided patients into two groups as large and small BMI, we found large BMI group had higher levels of serum apelin. But this difference was not statistically significant.

Our study has some limitations. First, due to nature of the cross-sectional study, evaluation of relationship was difficult between only one value of apelin, which is influenced by many factors, and causally related conditions such as inflammation and atherosclerosis. And second, limited number of patients was insufficient for detailed analysis. In conclusion, despite these limitations, our study showed that patient group had high cardiovascular risk due to high LVMI, increased CIMT and CRP levels. Additionally serum apelin levels were found significantly higher than healthy controls. In spite of high level of LVMI, BMI, CRP and serum apelin, there were no statistically significant correlations. Therefore, further studies are needed to clarify the role of apelin in PD patients.

Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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