Original Article

The Role of Dyslipidemia in Atherogenesis in Peritoneal Dialysis Patients

Damir Rebić[1], Edin Begić[2,3], Buena Aziri[3], Alen Džubur[4], Ena Gogić[4], Azra Durak-Nalbantić[4], Aida Hamzić-Mehmedbašić[1], Senad Hasanspahić[1], Nermir Granov[5]

[1]Department for General Nephrology, Clinic for Nephrology, Sarajevo, Bosnia and Herzegovina, [2]Department of Cardiology, General Hospital "Prim.Dr. Abdulah Nakaš", Sarajevo, Bosnia and Herzegovina, [3]Department of Pharmacology, School of Medicine, Sarajevo School of Science and Technology, Sarajevo, Bosnia and Herzegovina, [4]Department of Cardiology, Clinic for Heart, Blood Vessel and Rheumatic Diseases, Clinical Center University of Sarajevo, Sarajevo, Bosnia and Herzegovina, [5]Clinic for Cardiovascular Surgery, Clinical Center University of Sarajevo, Sarajevo, Bosnia and Herzegovina

Abstract

Background: To evaluate atherosclerotic changes in carotid arteries (CCA) in uremic patients before and after 18 months of continuous ambulatory peritoneal dialysis (CAPD) treatment, and to evaluate the impact of dyslipidemia and CAPD treatment on vascular remodeling.

Materials and Methods: We conducted a longitudinal, prospective study during 2020 and 2021 at the Clinic for Nephrology, Clinical Center University of Sarajevo. Patients with end-stage renal disease were included and were followed during 18 months of CAPD treatment. All patients were treated using commercially prepared biocompatible balanced dialysis solutions. Carotid intima-media thickness (IMT) and atherosclerotic plaques on the common carotid artery (CCA) were measured by echotomography.

Results: A total of 50 patients were included and were followed during 18 months of CAPD treatment. Lipid values in the serum of patients with CAPD were significantly lower after 18 months of CAPD treatment compared to the values before treatment, while the value of high-density lipoprotein (HDL) was significantly increased after 18 months of CAPD treatment. The values of IMT and the diameter of the CCA compared to the basal values were significantly lower ($P < 0.001$).

Conclusion: We demonstrated significantly lower lipid values and higher HDL levels following CAPD treatment. Correct selection of the targeted pharmacological intervention can substantially impact the regression of vascular changes in patients on peritoneal dialysis.

Keywords: Atherosclerosis, carotid intima-media thickness, dyslipidemia, end-stage renal disease, peritoneal dialysis

Address for correspondence: Dr. Damir Rebić, Clinic for Nephrology, Clinical Center University of Sarajevo, Bolnicka 25, Sarajevo - 71000, Bosnia and Herzegovina.
E-mail: damir.rebic@gmail.com
Submitted: 01-Jan-2023; **Revised:** 29-Jan-2023; **Accepted:** 01-Feb-2023; **Published:** 19-May-2023

Introduction

Cardiovascular diseases (CVD) present a big concern in end-stage renal disease (ESRD) when they are included in treatment with renal replacement therapy, but they can also develop during treatment with chronic dialysis, indicating the importance of assessment and timely action to modify the variable risk factors of CVD.[1,2]

The prevalence of CKD is increasing globally, ranging between 8% and 16%, and it is associated with atheromatous CVD owing to the deleterious effects of uremic toxins on the structure and function of arteries.[3–5] With a mortality rate that is 10–30 times greater than the general population, CVD are the major cause of death in patients with ESRD and CKD with dialysis treatment.[6,7]

Dyslipidemia is a risk factor for CVD both in the overal population and dialysis patients.[8] Besides the traditional risk factors for atherosclerosis, in recent years, new non-traditional, uremia-related risk factors have been elucidated, which play an

Access this article online

Quick Response Code:

Website: www.advbiores.net

DOI: 10.4103/abr.abr_1_23

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: WKHLRPMedknow_reprints@wolterskluwer.com

How to cite this article: Rebić D, Begić E, Aziri B, Džubur A, Gogić E, Durak-Nalbantić A, *et al*. The role of dyslipidemia in atherogenesis in peritoneal dialysis patients. Adv Biomed Res 2023;12:135.

important role in the development of early onset atherosclerosis in the process of chronic kidney failure.[9] Several observational studies have shown that total cholesterol and low-density lipoprotein (LDL) values are some of the most important independent factors of CVD and mortality.[8] Atherosclerosis contributes to a significant increase in CVD and mortality in patients on peritoneal dialysis (PD), the most common causes being myocardial infarction, cardiac failure, stroke, and sudden cardiac death.[10,11] The increased CV burden in CKD may be mediated by mechanisms other than atherosclerosis, such as arterial media calcification or stiffening.[12] Changes in the vascular system in uremic patients are attributed to the synergistic action of numerous factors, such as prothrombotic factors, dyslipidemia, anemia, hypertension, increased oxidative stress, disruption of the synthesis of parathormone (PTH), homocysteine, and nitric oxide, abnormalities of endothelial function, which leads to remodeling of the vascular system.[4,5,13,14]

High serum levels of indoles, phenols, and hippurates have been correlated with parameters of endothelial damage involved in carotid artery intima-media thickening and arterial stiffness.[3]

Malnutrition and cardiovascular complications are more often in uremic patients.[6] Furthermore, vascular calcification, as an integral element of the atherosclerosis process, is a commonly found complication in dialyzed patients and is associated with mineral and bone disorders, given that normal endothelium function is hampered by uremic toxins as well as by high inorganic phosphate levels.[9,15,16]

Evidence illustrates that carotid intima-media thickness (CIMT) is an early marker of atherosclerosis that carries prognostic value and is increased in PD patients.[11,17,18] In addition to being utilized as a risk assessment tool and a predictor of future cardiovascular events providing consistent and reliable information, it can also help assess the effectiveness of interventional therapy.[11,19]

Patients with impaired renal function have significant changes in lipoprotein metabolism whose exact role in the pathogenesis of atherosclerosis in these patients is still controversial.[20] No research has dealt with the issue of atherosclerosis in PD patients on the soil of Bosnia and Herzegovina thus far. The clinician's goal is to prevent the progression of the atherosclerotic process in patients with ESRD. The aim of this study is to evaluate atherosclerotic changes in carotid arteries (CCA) in uremic patients before inclusion and after 18 months of continuous ambulatory peritoneal dialysis (CAPD) treatment and to evaluate the impact of dyslipidemia and CAPD treatment on vascular remodeling, based on CIMT assessment.

Materials and Methods

In this longitudinal prospective study conducted during 2020 and 2021, at Clinic for Nephrology, Clinical Center University of Sarajevo, 50 patients with ESRD were included and were followed during 18 months of CAPD treatment. All patients were treated using commercially prepared biocompatible balanced dialysis solutions.

Carotid intima-media thickness and atherosclerotic plaques on the common carotid artery (CCA) were measured by echotomography using a high-resolution 7.5 MHz probe in B mode (General Electric, Boston, Massachusetts, United States of America). Carotid intima-media thickness CCA measurements were performed at a distance of 20 mm from the bifurcation in a plaque-free area. Three measurements were performed on the left and right CCA, and the mean values were used to estimate the CCA plaque score. The diameter of the CCA was measured as the intraluminal distance between the adventitia of the opposite walls of the artery at the end of the diastole.[5,6] Levels of cholesterol, triglycerides, high-density lipoprotein (HDL), LDL, lipoprotein (a) (Lp(a)), apolipoprotein B (Apo B), apolipoprotein AI (ApoA-I), body mass index, haemoglobin, C-reactive protein, calcium, phosphorate, calcium x phosphate (CaxP), PTH, albumin, Kt/Vurea (Kt/V · K – dialyzer clearance of urea · t – dialysis time · V – volume of distribution of urea), and protein equivalent of total nitrogen appearance were monitored on inclusion examination and after 18 months of CAPD treatment.

Statistical analysis

Statistical analysis was performed by Statistical Package for 27 Social Sciences (SPSS) version 22.0. Data were evaluated by standard statistical procedures and presented in tables. The $p<0.05$ is considered as statistically significant.

Results

The most common kidney disease that led to ESRD was diabetic nephropathy (48%) [Table 1]. The average age of subjects treated with CAPD was 60.5 years, and the gender structure of subjects was equally represented. The representation of patients with type 2 diabetes is 52%.

Lipid values in the serum of patients with CAPD were significantly lower after 18 months of CAPD treatment compared to the values before treatment, while the value of HDL was significantly increased after 18 months of CAPD treatment. The values of IMT and the diameter of the

Table 1: Demographic data of patients

Kidney disease		Clinical characteristics	
Diabetic nephropathy	24 (48%)	Age (years)	60.5 (26-76)
Nephroangiosclerosis	7 (14%)	Gender (male)	25 (50%)
Pyelonephritis	9 (18%)	Diabetes mellitus type 2	26 (52%)
Glomerulonephritis	7 (14%)	Smoking (yes)	18 (45%)
Reflux nephropathy	2 (4%)		
Polycystic kidney disease	1 (2%)		

Data are presented as mean value, range, or absolute numbers (percentage)

CCA compared to the basal values were significantly lower ($P < 0.001$), which was accompanied by a significant increase in the weekly Kt/V of urea and the rate of protein degradation [Table 2].

A significant increase in the number of patients without verified atherosclerotic plaques on CCA was observed at the end of the follow-up period compared to baseline values (26% vs. 44%). Proatherogenic lipid fractions before dialysis treatment positively correlated with CCA IMT and plaque score. After 18 months of CAPD treatment, HDL and ApoA-I levels were negatively correlated with CCA diameter, IMT, and plaque score, while cholesterol, LDL, Lp(a), and Apo B showed a significant positive correlation with the mentioned CCA parameters [Table 3]. An independent negative predictor of CCA diameter after 18 months of CAPD treatment was serum albumin, and LDL and age were positive predictors [Table 4]. The regression analysis model determined that HDL was in an independent negative, and CRP, CaxP, and LDL in a positive relationship with IMT CCA after 18 months of CAPD treatment [Table 5].

Discussion

Renal function is linked to an increase in CIMT as a result of the altered lipid metabolism and the inflammation induced by uremic toxins in PD patients.[19] It should be emphasized that, in patients treated with CAPD, several other factors specific to this type of dialysis can affect the level of serum lipids, especially secondary hyperparathyroidism, insulin resistance, peritoneal absorption of glucose, and finally, the etiology of the kidney disease itself, all of which further stimulate oxidative stress and systemic inflammation, leading to endothelial dysfunction, atherosclerosis, and ultimately, cardiovascular death.[6,11] Continuous ambulatory peritoneal dialysis itself is associated with a relatively more atherogenic lipid profile compared to the general population, as well as patients on hemodialysis.

Table 2: Clinical and biochemical parameters of the patients during the follow-up period

Parameter	Basal	After 18 months	*P*
Cholesterol (mmol/L)	6.5±1.6	5.5±1.3	<0.01
Triglycerides (mmol/L)	2.4±1.3	2.0±2.5	<0.05
High-density lipoprotein (HDL) cholesterol (mmol/L)	1.0±0.3	1.4±0.3	<0.001
Low-density lipoprotein (HDL) cholesterol (mmol/L)	4.7±1.4	3.6±0.8	<0.001
Lipoprotein (a) (g/L)	0.5±0.2	0.3±0.1	<0.001
Apolipoprotein B (Apo B) (g/L)	1.3±0.4	1.2±0.3	<0.001
Apolipoprotein AI (ApoA-I) (g/L)	1.4±0.4	1.8±0.3	<0.001
Body Mass Index (kg/m^2)	25.9±3.7	25.7±2.2	NS
C-reactive protein (mg/L)	11.1 (6.1-16.4)	4.5 (2.8-7.7)	<0.001
Calcium (mmol/L)	2.2±0.2	2.3±0.1	NS
Phosphor (mmol/L)	1.8±0.3	1.6±0.2	<0.01
calcium x phosphate (CaxP) (mmol/L)	3.9±0.6	3.6±0.5	<0.01
Paratahormone (pg/ml)	225.5 (97.8-387)	200.0 (100.0-410)	NS
Albumin (g/L)	30.9±2.6	31.5±2.0	<0.01
Kt/Vurea	1.8±0.6	2.1±1.6	<0.05
protein equivalent of total nitrogen appearance	0.98±0.13	1.11±0.1	<0.001
Carotid intima-media thickness (IMT)	0.73 (0.6-0.9)	0.70 (0.5-0.8)	<0.05
Carotid diameter (mm)	5.8 (5.2-6.4)	5.00 (4.9-5.4)	<0.001
Plaque score	4.15 (4.2-5.4)	3.95 (2.9-5.1)	<0.05

Data are presented as mean±standard deviation and as median and interquartile range

Table 3: Relationship between lipid profile and carotid artery parameters during the follow-up period

	Basal			After 18 months		
	Carotid intima-media thickness (IMT)	Carotid diameter	Plaque score	Carotid intima-media thickness (IMT)	Carotid diameter	Plaque score
Cholesterol (mmol/L)	0,47**	0,26	0,51**	0,42**	0,74**	0,64**
Triglycerides (mmol/L)	0,44**	0,14	0,31*	-0,03	0,03	0,1
High-density lipoprotein (HDL) cholesterol (mmol/L)	-0,05	-0,01	-0,05	-0,34*	-0,58**	-0,64**
Low-density lipoprotein (LDL) cholesterol (mmol/L)	0,5**	0,32*	0,54**	0,35*	0,58**	0,71**
Apolipoprotein B (Apo B) (g/L)	0,486**	0,16	0,494**	0,281*	0,262	0,447**
Apolipoprotein AI (ApoA-I) (g/L)	0,198	0,054	-0,03	-0,41**	-0,445**	-0,701**
Lipoprotein (a) (g/L)	0,437**	0,371**	0,496**	0,322*	0,583**	0,704**

*P<0.05; **P<0.001

Table 4: Independent predictors of carotid artery diameter after 18 months of continuous ambulatory peritoneal dialysis treatment

Model	B	Standard error	*P*	Exp (B)	95.0% confidence interval for Exp (B)	
					Lower limit	Upper limit
Albumin (g/L)	-1.111	0.459	0.015	0.329	0.134	0.809
Haemoglobin (g/L)	-0.155	0.074	0.037	0.857	0.741	0.991
Low-density lipoprotein (LDL) cholesterol (mmol/L)	1.402	0.652	0.032	4.063	1.131	14.591
Age	0.171	0.078	0.029	1.186	1.018	1.383

Table 5: Independent predictors of carotid intima-media thickness after 18 months of continuous ambulatory peritoneal dialysis treatment

Model	Unstandardized coefficients		Standardized coefficients	*t*	*P*
	B	Standard error	Beta		
C-reactive protein (mg/L)	0.142	0.031	0.423	4.615	<0.001
High-density lipoprotein (HDL) cholesterol (mmol/L)	-0.462	0.111	-0.379	-4.154	<0.001
Low-density lipoprotein (LDL) cholesterol (mmol/L)	0.409	0.133	0.387	3.080	0.004
Lipoprotein (a) (g/L)	1.604	0.011	0.489	5.066	0.048
Calcium x phosphate (CaxP) (mmol/L)	0.084	0.021	0.349	4.034	<0.001

In this study, dyslipidemia in our subjects was permanently present but significantly less compared to the period before dialysis treatment. Changes in the metabolism of lipoprotein fractions were also observed (after 18 months of CAPD treatment, a drop in Lp(a), slightly lower Apo B values, and an increase in ApoA-1 and HDL values). Similar results were published by other authors.[21] Studies based on CCA ultrasonography have established the existence of significant atherosclerotic arterial damage in patients with ESRD. Blacher *et al*. found that the internal diameter of the CCA in patients with impaired renal function is a marker of arterial stiffness and an independent predictor of total mortality.[22] Benedetto *et al*. also indicated that the rigidity of the CCA wall has a primary negative effect on the entire vascular system.[23] Through the conducted research, we determined that the average IMT of the CCA before the start of PD treatment was 0.73 mm. Stompor *et al*. found that the average IMT in patients treated for PD was 0.75 ± 0.17 mm.[24] The results of the Italian authors[25] indicate that, in patients with terminal kidney disease treated with dialysis (HDL, PD), the average diameter of the CCA is 6.86 mm, which is more than in our subjects, in whom we found an inner diameter of the CCA of 5.8 mm, basal. The same authors did not determine the presence of atherosclerotic plaques in 26 subjects (25%), and 25% of subjects had four or more plaques.[25] In our study, which differed in the number of subjects but also in the fact that basal parameters were measured before inclusion in the PD treatment program, we verified 26% of patients without plaques, 64% of subjects with one–four plaques, while four or more atherosclerotic plaques were found in 10% of patients. The basal CCA plaque score was 4.15. After 18 months of follow-up, the average IMT of the CCA was 0.7 mm, with a significant reduction in the diameter of the CCA. The plaque score was slightly lower at the end of the follow-up; it was 3.95. The proportion of patients without verified atherosclerotic plaques on CCA after 18 months of PD treatment is significantly higher compared to the baseline findings (26% vs. 44%). In the study by Benedetto *et al*., the second measurement of the CCA diameter after 12 months of PD treatment showed a statistically insignificant smaller CCA diameter compared to the initial values (6.88 vs. 6.86 mm).[25] Caliskan *et al*. determined that the average IMT of the CCA was 1.05 mm after the inclusion of TBZ patients in the PD treatment program,[26] while Stompor *et al*. found significantly lower IMT after a one-year PD treatment (0.66 vs. 0.75 mm), with a smaller number of subjects with atherosclerotic plaques on CCA (59.6 vs. 40.4 %).[24] At the beginning of the study, a positive correlation was verified between all atherogenic lipoprotein fractions, on one hand, and CCA IMT and plaque score, on the other hand, while CCA diameter positively correlated with LDL and Lp(a) levels. After 18 months of PD treatment, IMT, CCA diameter, and plaque score were negatively correlated with serum levels of HDL and ApoA-1, and significantly positively correlated with total cholesterol, LDL, Apo B, and Lp(a). Due to substantial protein losses, patients on PD have higher Lp(a) levels.[16] In particular, the Apo B/Apo A1 ratio is a marker of atherogenicity, and a higher ratio, defined by the thickness of carotid arteries, indicates atherosclerotic progression.[27] Even amidst conflicting evidence of lipid effects on the prognosis of patients on PD, the longitudinal cohort study by Zhan *et al*. revealed substantial correlations between the Apo B/ApoA-1 ratio, cardiovascular events, and all-cause mortality in this population.[27] Moreover, it has been suggested that in uremic patients, Lp(a), apolipoprotein E, and Apo B undergo modifications and are consequently linked to cardiovascular events.[7] Likewise, high Apo B levels as a result of overproduction in PD patients have been significantly correlated with CIMT values and vascular stiffness.[7]

In a study by Prichard *et al*., 20–40% of CAPD patients had elevated levels of total cholesterol and LDL.[28] Sevinc *et al*. suggested a positive linear relation between CIMT and synergistic effect of the traditional factors of atherosclerosis, and they are responsible for 32.8% increase in the carotid artery IMT.[9] Lai *et al*., however, reported no changes in carotid IMT as an atherosclerosis marker in adult PD patients, despite being age related, and no significant differences in the number of hospitalizations.[29]

Kumar *et al*. also found a positive correlation between IMT and atherosclerotic CCA plaques, on one hand, and dyslipidemia in the pre-dialysis period, on the other hand,[30] which was later proven in the population of dialysis patients.[31] The independent positive association of LDL and negative association of HDL with IMT CCA after 18 months of PD treatment support the claim of Cengiz *et al*. that changes in CCA are related to a disturbed lipid profile, primarily due to a reduced level of HDL and an increase in LDL.[32] We have confirmed that HDL represents a significant independent factor that influences the regression of CCA IMT in patients treated with CAPD, while LDL has a predictive influence on the rigidity of the CCA wall, assessed based on the CCA diameter. These results support the results of the Study of Heart and Renal Protection (SHARP) study[33] that lipid disorders should be aggressively treated in dialysis patients in order to reduce the risk of CVD and keep the LDL level below 3 mmol/L.[34]

Furthermore, a low serum albumin level is deemed an independent negative predictor of CCA diameter, thus yielding an adverse prognosis in dialysis patients.[35] In addition, through oxidative modifications of LDL, inflammation may potentially alter the structure and functionality of lipoprotein.[35] In the research of Szeto *et al*. conducted among PD patients over three years, it was found that serum albumin level is a strong predictor of cardiovascular complications.[36] This research confirmed the high prevalence of atherosclerosis in uremic patients, as well as the positive effect of CAPD treatment on stopping the process of arterial remodeling, which is in accordance with the results of recent studies.[37] Changes in the vascular system in uremic patients are attributed to the synergistic action of numerous factors, which modify the structural and functional features of the vascular system.[38] Although pharmacological interventions have significantly advanced in treating patients with CKD, traditional risk factors, including dyslipidemia, still have a great influence and significance for the progression of the atherogenesis process, which contributes to the high incidence of morbidity and mortality. Atherosclerosis and high values of proatherogenic lipid fractions are present even before dialysis treatment, which suggests intensive atherogenesis even in the predialysis period. Treatment of CAPD in the first 18 months has a positive effect on stopping the process of vascular remodeling and even on partial regression of these changes. The role of dyslipidemia in atherogenesis in patients with PD is unquestionable, but it is modified by the action of other traditional and non-traditional risk factors, especially inflammation and malnutrition.

A study by Guo *et al*. found an incidence of carotid artery calcification in CAPD patients of 54.8%.[15] Vascular calcification in CKD patients is influenced by a complex array of factors. Investigators observed that, in CAPD patients, age, elevated fibroblast growth factor 23 (FGF-23, a phosphaturic hormone released due to relative calcium-phosphate excess), and reduced klotho (an anti-aging protein that controls calcium and phosphorus metabolism and PTH secretion, opposes oxidative stress, and inhibits inflammation, apoptosis, and fibrosis) were important risk factors for carotid calcification. In view of this, vascular calcification in CAPD patients could potentially be tackled with new therapeutic alternatives regulating klotho or FGF-23.[15] By optimizing PD, controlling FGF-23 and klotho derangements, and diminishing inflammatory state, there is a plausibility of improving the prognosis of ESRD patients through lowering the risk of vascular calcification.[15] Vascular calcification in high-risk patients may also be prevented with low calcium dialysate.[15]

In addition, the monocyte to high-density lipoprotein cholesterol ratio is a relatively new marker reported to be linked to the thickness of the intima-media in the carotid artery, owing to the pro-inflammatory effect of monocytes as well as the anti-inflammatory and antioxidant effect of HDL. According to a retrospective study by Zhan *et al*., the monocytosis and monocyte differentiation into more pro-inflammatory and atherogenic ones as a result of the uremic settings are consequently associated with increased cardiovascular events in PD patients.[39] Interestingly, another study identified a decreased frequency of circulating angiogenic T-cells in PD patients and could serve as biomarkers of vascular dysfunction and early atherosclerosis stage.[40]

According to a multicentric study, in dialysis patients without a history of CVD, PD is an independent risk factor associated with lower CIMT.[17]

One of the limitations of our study is the small sample size. It is also important to note that this was a single-center study. On the other hand, one of the strengths of our study is that the regression analysis performed helped adjust any confounders. Moreover, no patients were lost to follow-up, thus minimizing the attrition bias.

Notwithstanding the breakthroughs with increased coronary intervention rates over the past years, as well as the availability of biocompatible solutions, cardiovascular mortality rates remain reasonably high in PD patients.[11,41]

The sample is interesting because patients who were followed from the moment they were in ESRD but not yet included in dialysis treatment, then followed as a longitudinal study after 18 months of PD treatment were included in the research. Peritoneal dialysis as a dialysis method is represented by only 3% of the dialysis population in Bosnia and Herzegovina as well as in the world, because the majority are on HDL treatment.[41]

Despite the fact that almost all of the included patients were on statins, with atorvastatin up to a maximum dose of 20

mg due to ESRD, our aim was not to determine the effect of statins because they cannot have much of a favorable effect considering the uremic milieu, but we believe that it gives a good effect of PD treatment as intracorporeal dialysis methods. With regard to antihypertensives in ESRD, either the patients were already on angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers, or these were included during PD treatment. A glycated hemoglobin was not monitored; most patients who are on insulin due to diabetes mellitus with kidney failure mostly do not need insulin substitution.

Conclusion

Carotid IMT measurement, as a reliable indicator of atherosclerosis in PD patients, is a simple and reproducible approach that should be implemented in routine follow-ups. Correct selection of the targeted pharmacological intervention can substantially impact the regression of vascular changes in patients on PD. Optimization of PD dose, ultrafiltration, and modality could lead to improvements in the design of clinical studies with cardiovascular endpoints in patients with renal disease.

Financial support and sponsorship

Nil.

Conflicts of interests

There are no conflicts of interest.

References

1. Matsushita K, Ballew SH, Wang AY, Kalyesubula R, Schaeffner E, Agarwal R. Epidemiology and risk of cardiovascular disease in populations with chronic kidney disease. Nat Rev Nephrol 2022;18:696-707.
2. Ortiz A, Wanner C, Gansevoort R, ERA Council. Chronic kidney disease as cardiovascular risk factor in routine clinical practice: A position statement by the Council of the European Renal Association. Eur J Prev Cardiol 2022;29:2211-5.
3. El Chamieh C, Liabeuf S, Massy Z. Uremic toxins and cardiovascular risk in chronic kidney disease: What have we learned recently beyond the past findings? Toxins (Basel) 2022;14:280.
4. Zanoli L, Mikhailidis DP. Narrative review of carotid disease and the kidney. Ann Transl Med 2021;9:1210.
5. Foudi N, Palayer M, Briet M, Garnier AS. Arterial remodelling in chronic kidney disease: Impact of uraemic toxins and new pharmacological approaches. J Clin Med 2021;10:3803.
6. Liao C Te, Kao TW, Chou YH, Wu MS, Chen YM, Chuang HF, *et al*. Associations of metabolic syndrome and its components with cardiovascular outcomes among non-diabetic patients undergoing maintenance peritoneal dialysis. Nephrol Dial Transplant 2011;26:4047-54.
7. Vlad CE, Foia L, Popescu R, Ivanov I, Luca MC, Delianu C, *et al*. Apolipoproteins A and B and PCSK9: Non-traditional cardiovascular risk factors in chronic kidney disease and in end-stage renal disease. J Diabetes Res 2019;2019:6906278.
8. Berberich AJ, Hegele RA. A modern approach to dyslipidemia. Endocr Rev 2022;43:611-53.
9. Sevinc C, Yilmaz G, Ustundag S. The relationship between calcification inhibitor levels in chronic kidney disease and the development of atherosclerosis. Ren Fail 2021;43:1349-58.
10. Querido S, Quadros Branco P, Silva Sousa H, Adragão T, Araújo Gonçalves P, Gaspar MA, *et al*. Peritoneal dialysis is a reasonable option in patients with cardiovascular disease Clin Nephrol 2017;87:111-6.
11. Asicioglu E, Velioglu A, Arikan H, Koc M, Tuglular S, Ozener C, *et al*. Baseline carotid intima-media thickness is associated with cardiovascular morbidity and mortality in peritoneal dialysis patients. Ther Apher Dial 2021;25:962-9.
12. Beddhu S, Boucher RE, Sun J, Balu N, Chonchol M, Navaneethan S, *et al*. Chronic kidney disease, atherosclerotic plaque characteristics on carotid magnetic resonance imaging, and cardiovascular outcomes. BMC Nephrol 2021;22:69.
13. Ng CH, Ong ZH, Sran HK, Wee TB. Comparison of cardiovascular mortality in hemodialysis versus peritoneal dialysis. Int Urol Nephrol 2021;53:1363-71.
14. Tracz J, Luczak M. Applying proteomics and integrative "Omics" strategies to decipher the chronic kidney disease-related atherosclerosis. Int J Mol Sci 2021;22:7492.
15. Guo N, Chen X, Cao Y, Lu G. Associations of serum soluble klotho and fibroblast growth factor 23 with carotid artery calcification in patients undergoing continuous ambulatory peritoneal dialysis: A retrospective study. Medicine (Baltimore) 2021;100:e26620.
16. Valdivielso JM, Rodríguez-Puyol D, Pascual J, Barrios C, Bermúdez-López M, Sánchez-Niño MD, *et al*. Atherosclerosis in chronic kidney disease. Arterioscler Thromb Vasc Biol 2019;39:1938-66.
17. Borràs M, Cambray S, Crespo-Masip M, Pérez-Fontán M, Bozic M, Bermudez-López M, *et al*. Peritoneal dialysis is an independent factor associated to lower intima media thickness in dialysis patients free from previous cardiovascular disease. Front Physiol 2018;9:1743.
18. Lawal OM, Balogun MO, Akintomide AO, Ayoola OO, Mene-Afejuku TO, Ogunlade O, *et al*. Carotid intima-media thickness: A surrogate marker for cardiovascular disease in chronic kidney disease patients. Clin Med Insights Cardiol 2019;13:1179546819852941.
19. Ohtake T, Kobayashi S. Chronic kidney disease and atherosclerosis: An important implication of carotid intima-media thickness. J Atheroscler Thromb 2021;28:471-3.
20. Twardawa M, Formanowicz P, Formanowicz D. Chronic kidney disease as a cardiovascular disorder-tonometry data analyses. Int J Environ Res Public Health 2022;19:12339.
21. Suh SH, Oh TR, Choi HS, Kim CS, Bae EH, Ma SK, *et al*. Korean Cohort Study for Outcomes in Patients with Chronic Kidney Disease (KNOW-CKD) Investigators. Non-High-Density Lipoprotein Cholesterol and Cardiovascular Outcomes in Chronic Kidney Disease: Results from KNOW-CKD Study. Nutrients 2022;14:3792.
22. Blacher J, Pannier B, Guerin AP, Marchais SJ, Safar ME, London GM. Carotid arterial stiffness as a predictor of cardiovascular and all-cause mortality in end stage renal disease. Hypertension 1998;32:570-4.
23. Benedetto AF, Mallamaci F, Tripepi G, Zoccali C. Prognostic value of ultrasonographic measurement of carotid intima media thickness in dialysis patients. J Am Soc Nephrol 2001;12:2458-64.
24. Stompór T, Kraśniak A, Sułowicz W, Dembińska-Kieć A, Janda K, Wójcik K, *et al*. Changes in common carotid artery intima-media thickness over 1 year in patients on peritoneal dialysis. Nephrol Dial Transplant 2005;20:404-12.
25. Benedetto AF, Tripepi G, Mallamaci F, Zoccali C. Rate of atherosclerotic plaque formation predicts cardiovascular events in ESRD. J Am Soc Nephrol 2008;19:757-63.
26. Caliskan Y, Ozkok A, Akagun T, Alpay N, Guz G, Polat N, *et al*. Cardiac biomarkers and noninvasive predictors of atherosclerosis in chronic peritoneal dialysis patients. Kidney Blood Press Res 2012;35:340-8.
27. Zhan X, Chen Y, Yan C, Liu S, Deng L, Yang Y, *et al*. Apolipoprotein B/apolipoprotein A1 ratio and mortality among incident peritoneal dialysis patients. Lipids Health Dis 2018;17:117.
28. Zhao M, Ren L, Zhou Z, Wang T, Li J. The association between statin use and risk of chronic kidney disease in community-dwelling older people in Shanghai, China. Clin Epidemiol 2022;14:779-88.
29. Lai S, Amabile MI, Bargagli MB, Musto TG, Martinez A, Testorio M, *et al*. Peritoneal dialysis in older adults: Evaluation of clinical, nutritional, metabolic outcomes, and quality of life. Medicine (Baltimore) 2018;97:e11953.
30. Kumar KS, Lakshmi AY, Srinivasa Rao PVLN, Das GC, Kumar VS.

Carotid intima-media thickness in patients with end-stage renal disease. Indian J Nephrol 2009;19:13-4.
31. Lamprea-Montealegre JA, Astor BC, McClelland RL, de Boer IH, Burke GL, Sibley CT, *et al*. CKD, plasma lipids, and common carotid intima-media thickness: Results from the multi-ethnic study of atherosclerosis. Clin J Am Soc Nephrol 2012;7:1777-85.
32. Cengiz K, Dolu D. Comparison of atherosclerosis and atherosclerotic risk factors in patients receiving hemodialysis and peritoneal dialysis. Dial Transplant 2007;36:205-16.
33. Baigent C, Landray MJ, Reith C, Emberson J, Wheeler DC, Tomson C, *et al*. SHARP investigators. The effects of lowering LDL cholesterol with simvastatin plus ezetimibe in patients with chronic kidney disease (Study of Heart and Renal Protection): A randomised placebo-controlled trial. Lancet 2011;377:2181-92.
34. Mizobuchi M, Towler D, Slatopolsky E. Vascular calcification: The killer of patients with chronic kidney disease. J Am Soc Nephrol 2009;20:1453-64.
35. Liu Y, Coresh J, Eustace JA, Longenecker JC, Jaar B, Fink NE, *et al*. Association between cholesterol level and mortality in dialysis patients: Role of inflammation and malnutrition. JAMA 2004;291:451-9.
36. Szeto CC, Chow KM, Lam CW, Cheung R, Kwan BC, Chung KY, *et al*. Peritoneal albumin excretion is a strong predictor of cardiovascular events in peritoneal dialysis patients: A prospective cohort study. Perit Dial Int 2005;25:445-52.
37. Mutluay R, Degertekin CK, Poyraz F, Yılmaz MI, Yücel C, Turfan M, *et al*. Dialysis type may predict carotid intima media thickness and plaque presence in end-stage renal disease patients. Adv Ther 2012;29:370-82.
38. Tobe SW, Raymond N, Ismail NA. Peritoneal dialysis: a clinical update congestive heart failure and PD. Contrib Nephrol. 2006;150:129-134.
39. Zhan X, Pan D, Wei X, Wen D, Yan C, Xiao J. Monocyte to high-density lipoprotein ratio and cardiovascular events in patients on peritoneal dialysis. Nutr Metab Cardiovasc Dis 2020;30:1130-6.
40. Carrillo-Lopez N, Rodriguez-Carrio J, Ulloa C, Mart In-Carro B, Rodriguez-Suarez C, Arcidiacono MV, *et al*. P1292decreases in angiogenic T cells are predictive biomarkers of vascular dysfunction and atherosclerosis in chronic kidney disease. Nephrol Dial Transplant 2020;35:gfaa142.P129.
41. Sachdeva B, Zulfiqar H, Aeddula NR. Peritoneal Dialysis. [Updated 2022 Aug 10]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK532979/.