

Association of carotid atherosclerosis with anthropometric parameters and inflammatory markers in dialysis patients

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Abstract

Aim: Cardiovascular disease is the leading cause of morbidity and mortality in patients in dialysis treatment. Atherosclerosis is accelerated in long-term maintenance haemodialysis. Several reports have investigated carotid artery intima-media thickness (CIMT) and the presence of carotid artery plaque (CAP), as surrogate markers of carotid atherosclerosis in ESRD patients. The aim of this study was to assess the prevalence of atherosclerotic carotid artery changes in dialysis patients and determine the potential link with classic and non-classic risk factors contributing to its development.

Methods: 72 dialysis patients who agreed to participate (40 males) were included in this study: 39 patients on peritoneal dialysis (PD) and 33 patients on haemodialysis (HD). Mean age was 53.8±12.1 years old. Mean time on dialysis 40.0±35.6 months. CIMT and presence of CAP were obtained by B-mode ultrasonography. CRP, fibrinogen, calcium, phosphate, PTH, alkaline phosphatase, uric acid, serum albumin, and lipid profile were examined. In addition, anthropometric indices were measured. We analyzed the differences of these parameters in groups with and without atherosclerosis and their link to atherosclerosis.

Results: Atherosclerosis was found in 50 (69.4 %) patients, in 44 (62 %) men, in 25 (75.7%) HD patients and in 25 (64%) PD patients. Old age, diabetic nephropathy (DN), high phosphate (P), high pulse pressure (PP) and high BMI were found to be significantly linked with atherosclerosis. High CaxP product and fibrinogen were marginally significantly linked to atherosclerosis.

Conclusion: Atherosclerosis was highly prevalent in dialysis patients in this Albanian study. In our study, the older, the obese, the more inflamed and the high phosphoremic patients were more prone to atherosclerosis.

Keywords: atherosclerosis, carotid artery, dialysis.

Introduction

Chronic renal failure (CRF) is associated with premature atherosclerosis and increased cardiovascular morbidity and mortality in predialysis and haemodialysis (HD) patients (1,2). In patients with CRF, cardiovascular disease (CVD) is twice as common as in the general population (3). Compared with the general population, dialysis patients have more than 10 times higher relative risk for cardiovascular mortality (1).

Many studies have revealed that haemodialysis patients have advanced arterial wall changes as shown by increased intima-media thickness (IMT) of the carotid arteries as an index of thickening of arterial wall (4,5). Increased carotid artery IMT is considered a marker of early atherosclerotic changes (6) and carotid artery intima-media thickness (CAIMT) is increasingly used as a surrogate marker of early atherosclerosis. It was also shown that CAIMT is a strong predictor of future myocardial infarction and stroke (7).

Also, atherosclerosis and calcifications of vascular wall are found highly prevalent in peritoneal dialysis patients (8).

Several reports have investigated carotid artery intima-media thickness (CIMT), carotid artery calcification (CAAC) and carotid atherosclerosis (CAP) in ESRD patients. The CAIMT was found to be increased in subjects with impaired renal function (9-11), though contrasting results have also been published. Correlation between atherosclerosis and age, diabetes, diastolic blood pressure, acute phase proteins (such as CRP and fibrinogen), obesity, waist circumference as well as lipoprotein (a) and fetuin A were observed in CKD patients with and without dialysis treatment (8,13-19).

The aim of this study was to assess the prevalence of carotid artery atherosclerosis in dialysis patients and to analyze the potential link between various classic and non-classic factors and atherosclerosis.

Methods

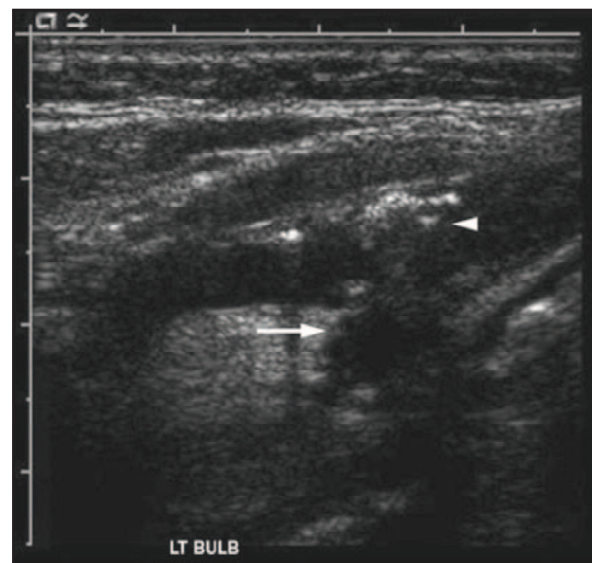
This study consisted of 72 stable dialysis patients (40 males) who agreed to participate and treated for more than 6 months. Of these, 39 patients were on peritoneal dialysis (PD) and 33 pts on maintenance haemodialysis (HD). Mean age was 53.8 ± 12.1 years old and mean time on dialysis 40.0 ± 34.6 months.

These subjects were randomly selected from our database. All HD patients had native fistulas or arteriovenous grafts, haemodialysed 3 times per week, 4 hours per treatment, with standard bicarbonate-containing dialysate bath, using high-flux dialysis membrane. PD patients were on continuous ambulatory PD (4-5 exchanges/ day with 2000 ml) dialyzed using conventional lactate-buffered glucose-based PD solutions (Dianeal PD4; 40 mmol/ L lactate, pH 5.3 to 5.5 containing 1.36, 2.27, or 3.86% dextrose as appropriate; Baxter Healthcare).

Doppler of carotid arteries

Carotid artery intima-media thickness (IMT) and presence of plaque were measured by B-mode ultrasonography using a real-time ultrasonograph with a 10-MHz in-line. The carotid artery was scanned bilaterally in the longitudinal and transverse projections. The examination included approximately 4 cm of the common carotid artery, the carotid bulb, and 1 cm each of the internal and external arteries. The image was focused on the far wall of the arteries. The site of the most advanced atherosclerotic lesion that showed the greatest distance between the lumen-intima interface and the media-adventitia interface was located in both the right and left carotid arteries. Was considered thickened intima-media >0.9 mm.

Figure 1. Mode ultrasound view of carotid artery



Covariates

Blood pressure was measured with a standard mercury sphygmomanometer, after the patient had rested for at least five minutes in the supine position. Pulse pressure was calculated as the difference between systolic and diastolic blood pressure. The average of three measurements was used for analysis.

Laboratory test of serum albumin, lipids, calcium, phosphorus, PTH, alkaline phosphatase fibrinogen, PCR, uric acid, lipids were taken on dialysis day, before dialysis session on the mid-week day for HD patients and in a normal day for peritoneal dialysis patients.

Data for age, gender, time on dialysis, cause of CKD, smoking habits and medication were taken from patients file.

Weight, height, waist circumference were measured for each participant after dialysis session and BMI was calculated.

We analyzed the differences of these parameters in groups with and without atherosclerosis and their link with atherosclerotic carotid artery changes in our study population.

Statistical analysis

The Statistical Package for Social Sciences (SPSS), version 19.0, was used for all the statistical analyses. Mann-Whitney U test, a non-parametric equivalent of the t-test, was used for comparison of mean values of numerical variables. Conversely, Fisher's exact test was used for comparison of proportions of the categorical variables.

Results

Mean age was significantly higher among patients with atherosclerosis compared to individuals without atherosclerosis (57.8 years vs. 45.1 years, $P < 0.001$). Conversely, there were no significant sex differences ($P = 0.125$).

There was a statistically significant difference in the cause of CKD between groups (overall $P = 0.030$), but no significant difference in the ratio PD/HD ($P = 0.316$).

Body mass index was significantly higher among atherosclerotic patients ($P = 0.05$). Waist circumference was also higher in atherosclerotic patients, a finding which nevertheless was not statistically

significant most probably due to the small sample size.

Fibrinogen level were higher in atherosclerotic patients, with borderline statistical significance ($P = 0.069$). There was no significant difference between groups with regard to CRP.

Mean P level and PP were significantly higher in atherosclerotic patients (respectively $P = 0.022$ and $P = 0.045$).

On the other hand, there were no significant differences between groups with regard to the other parameters.

Discussion

The prevalence of atherosclerosis in our study was 79.8% in the overall sample, 75.7% in the HD group and 64% in the PD group, which are similar to the previously reported prevalence rates of atherosclerosis in dialysis patients (12).

Older age is known to be associated with atherosclerosis in HD patients (13) and PD patients (8) as well as in the general population. In our study, also, this finding was evident with a mean age significantly higher among patients with atherosclerosis compared to individuals without atherosclerosis (57.8 years vs. 45.1 years, $P < 0.001$).

In respect to CKD underline cause Sanchez-Alvares et al (14) and Ekart et al (15), respectively, pointed to diabetes mellitus and hypertension as contributors to increased risk for atherosclerosis in dialysis patients. Similarly, in our study there was a statistically significant difference in the cause of CKD between groups (overall $P = 0.030$) with ND in first place, followed by nephroangiosclerosis being the diagnosis most commonly associated with atherosclerosis.

We found no significant difference regarding the dialysis modality PD vs. HD ($P = 0.316$), although PD was expected to be associated with higher atherosclerosis, considering more expressed metabolic and lipid profile derangements of the treated patients.

Body mass index was significantly higher among atherosclerotic patients ($P = 0.059$). Waist circumference was also higher in atherosclerotic patients, a finding which nevertheless was not statistically significant most probably due to the small sample size. In a recent study in PD patients, waist

Table 1. Distribution of characteristics by atherosclerosis status

Variable	No atherosclerosis (N=22)	Atherosclerosis (N=50)	P-value*
Age (years)	45.05±13.63	57.78±9.17	<0.001
Men	9 (40.9%)	31 (62.0%)	0.125
Time on dialysis (months)	43.14±26.52	38.70±39.13	0.083
CKD cause:			
NAS	2 (9.1%)	9 (18.0%)	0.030
ND	-	10 (20.0%)	
Other	20 (90.9%)	31 (62.0%)	
PD	14 (63.6%)	25 (50.0%)	0.316
P	4.35±1.44	5.01±1.30	0.022
Corrected Ca	8.49±0.90	8.32±0.84	0.599
CaxP	36.91±12.63	42.05±12.83	0.069
PTH	459.71±416.22	513.04±481.05	0.821
ALP	162.82±234.31	139.42±108.16	0.769
Fibrinogen (mg/dl)	412.64±129.33	475.04±131.38	0.069
PCR	6.30±5.83	6.62±6.59	0.932
Uricemia	5.70±1.11	5.90±1.00	0.466
S-albumine (g/dl)	3.56±0.49	3.49±0.48	0.632
Cholesterol (mg/dl)	183.86±46.65	169.56±50.21	0.165
Triglycerides (mg/dl)	158.14±89.05	162.28±85.16	0.691
RRF (ml/min)	2.68±2.69	2.63±2.85	0.944
PP (mmHg)	43.64±17.94	50.40±16.19	0.045
LV-i	140.75±57.47	157.09±50.23	0.146
Ca salts therapy	17 (77.3%)	39 (81.3%)	0.752
Vit D suppl.	17 (77.3%)	35 (72.9%)	0.776
Statin therapy	4 (18.2%)	19 (39.6%)	0.102
BMI	22.71±3.81	24.57±4.17	0.05
Waist circumference	0.92±0.13	0.98±0.16	0.208

* Mann-Whitney test was used for comparison of numerical variables and Fisher's exact test for comparison of the categorical variables.

circumference was found to be linked to CAIMT (16). Inflammation may be involved in atherogenesis in predialysis patients as well as in those treated with haemodialysis. High serum CRP (17) and low serum albumin (18) has been found associated with atherosclerosis in other studies, which noted the presence of inflammation in atherosclerotic patients. These findings were not confirmed in our study. Anyway, fibrinogen level were higher in atherosclerotic patients, with borderline statistical significance (P=0.06). These findings could be linked to relatively small number of patients in our study. Mean Phosphate and CaxP product level were higher in atherosclerotic patients in our study

(P=0.022 and P= 0.069, respectively), a similar finding to that of Ishimura et al (19), that found an association of serum phosphate with carotid intima-media thickness in haemodialysis patients.

PP was significantly higher in atherosclerotic patients (P=0.045).

On the other hand, there were no significant differences between groups with regard to the other parameters examined in our study.

In conclusion, atherosclerosis was highly prevalent in CKD patients on dialysis treatment in this Albanian sample. In our study, the older, the obese, the more inflamed and the high phosphoremic patients were more prone to atherosclerosis.

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