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Calcified Plaques in Carotid and Femoral Arteries in Association with Left Ventricular Hypertrophy and Ejection Fraction in Hemodialysis Patients

Background/Objectives: Two principal cardiovascular findings in end-stage renal disease (ESRD) patients who undergo hemodialysis are left ventricular hypertrophy (LVH) and arterial disease due to rapidly progressive atherosclerotic vascular disease that can be characterized by arterial plaques. In this study we studied the relationship of LVH and ejection fraction with carotid and femoral artery plaques in ESRD patients undergoing hemodialysis.

Materials and Methods: Sixty-one ESRD patients who underwent maintenance hemodialysis (F=23, M=38) were considered. There were 50 non-diabetic hemodialysis patients (F=20, M=30) and 11 diabetic hemodialysis patients (F=3, M=8). For all the subjects echocardiography and B-mode ultrasonographic assessment of carotid-femoral arteries for plaque occurrence were performed.

Results: In this study there was a positive correlation between LVH and the duration of hemodialysis treatment; and also a significant association between LVH and plaque score. Positive correlation was also demonstrated between hypertension and plaque score. Also an inverse correlation of plaque score with LV ejection fraction was noted. Moreover, the association of plaque score with diabetes mellitus was positive.

Conclusion: The present study signifies the cardiac and vascular adaptation secondary to ESRD and demonstrates the potential contribution of structural and functional alteration in the large arteries to the pathogenesis of left ventricular hypertrophy, which requires more attention in hemodialysis patients.

Keywords: plaque score, carotid artery, femoral artery, hemodialysis, left ventricular hypertrophy, atherosclerosis

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Introduction

In patients with renal failure, cardiovascular complications are a major clinical problem, the most important of which is left ventricular hypertrophy (LVH) and the main cause of death in these patients is cardiac involvement.[1,2] with a mortality 10 to 30 times higher than the general population despite stratification for sex, race, and presence of diabetes.[3] Cardiac risk increases with much more frequency in uremic patients as compared with matched strata of general population.[1,2,4] It had been long known that atherosclerosis, particularly arterial plaques are more frequent in patients with chronic renal failure.[1] In fact patients with end-stage renal disease (ESRD) who receive hemodialysis, suffer from excessive mortality due to atherosclerotic cardiovascular disease (ACVD).[5] This is frequently attributed to a process of accelerated atherosclerosis (rapidly progressive atherosclerosis). Coronary artery calcification is very common in dialysis patients. Depending on the age of the patient population examined, 54 to

100 percent (mean 83%) of dialysis patients in case series have some degree of coronary artery calcification, with scores markedly above the general population.[6] The ACVD risk factors (such as hypertension), lipid abnormalities, glucose intolerance and left ventricular hypertrophy are especially more commonly observed in these groups.[5,7] In fact, LVH is the most frequent cardiac abnormality in patients with ESRD. LVH is associated with hypertension, increased arterial stiffness, and extensive vascular calcification in hemodialysis patients. Vascular calcification is the most important contributor to the development of patients undergoing hemodialysis. [8]Ultrasonic assessment of plaques in the carotid and femoral arteries are widely used as a surrogate marker of atherosclerosis in coronary arteries.[4] But prospective evaluations of the association of arterial plaque with LVH and also LV ejection fraction are little and appear to be lacking in patients with ESRD under hemodialysis. We therefore sought to examine whether any association exists between carotid and femoral arteries plaques with LVH and LV ejection fraction in hemodialysis patients. This may help to predict the prognosis of patients and therefore, to develop preventive and therapeutic programs.

Materials and Methods

This cross-sectional study was performed on 61 patients with ESRD undergoing hemodialysis treatment. Exclusion criteria were tobacco use, body mass index (BMI) of greater than 25, use of anti-hyperlipidemia medications, recent myocardial infarction (MI), active or chronic infection, vascular diseases, and pericarditis or pericardial effusion on echocardiography. For stratification of hypertensive patients according to the sixth and seventh report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure, we stratified hypertensive patients from stage one to three (stage zero was no hypertension). [9,10] Stages of hypertension in hemodialysis patients were considered before treatment and at the initiation of hemodialysis treatment. Carotid ultrasound was done by the same radiologist who was masked to the patients' history or laboratory data. A Honda-Hs-2000 7.5 MHZ linear probe was used for the studies. Cardiac measurements were done at the end diastolic phase. The sites of measurements were the distal common carotid artery, carotid bifurcation, and the proximal end of the internal carotid artery. Subjects were placed in the supine position with the neck hyperextended and head rotated during the procedure. Ultrasound was done for the right and left carotid and femoral arteries and scored from 0 (no plaque) to 4 (plaques present at all four sites); and regardless of the number and size of the plaques at each site, plaque occurrence in each site scored one point. A plaque was sonographically defined as an echogenic or hypoechogenic protrusion into the vascular lumen, with a local wall thickness more than 1 mm. Plaques were divided into 3 groups: soft, calcified (Figure 1) and mixed.

For echocardiography, one cardiologist who was masked to the patients' data performed all echocardiograms (2D doppler) . Regarding LVH, on the basis of septal thickness, we stratified the patients into no LVH (septal thickness between 6-11 mm), mild LVH (septal thickness between 11-15 mm), moderate LVH (septal thickness between 15-18 mm) and severe LVH (septal thickness >18 mm).

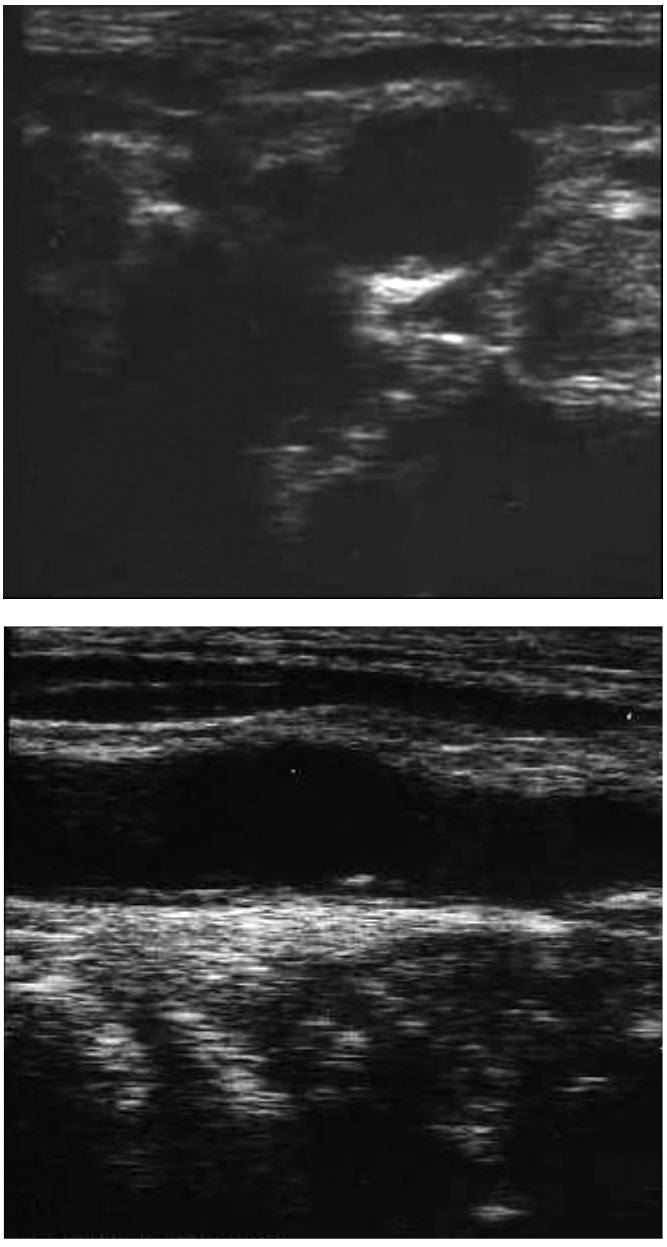

Figure 1: Calcified plaque of carotid artery

LVH was measured at the end diastolic phase. LV ejection fraction between 55 to 75% was considered normal .For statistical analysis; descriptive data were expressed as mean± SD and frequency distributions. Comparison between groups was performed using Chi-square test, Mann- Whitney U test, Kruskal and Wallis and Fisher's exact tests. For correlations, Spearman's rho test, partial correlation test with adjustment for of patient's age, Phi & Cramer´s V, Pearson and Eta tests were used. All the statistical analyses were performed using the SPSS (version 11.00). Statistical significance was inferred at a $P < 0.05$.

Results

Sixty-one patients (female/male: 23/38) with 50 non-diabetic hemodialysis patients (20 female and 30 male) and 11 diabetic hemodialysis patients (3 female and 8 male) were studied. Table 1 shows age, duration of hemodialysis and ejection fraction of patients. Tables 2 and 3 demonstrate the frequency distributions of hypertension (HTN) and LVH stages of patients. Table 4 shows the frequency distribution of plaque scores in total patients including diabetic and non-diabetic groups. Mean age of subjects was 57 ± 16 years with 47.8 ± 16 years in the diabetics and non-diabetics, respectively. The duration of hemodialysis treatment was 32 ± 31 months, which was 22.6 ± 22.4 and 34 ± 33 months in diabetics and non-diabetics, respectively. Mean LV ejection fraction was 47.7 ± 7 % and 51 ± 9 % in diabetics and non-diabetics. Plaque scores were: plaque score zero in 9.1% of diabetics and in 64% of non-diabetics, plaque scores of 1 and 2 in 63.6% of diabetics and 20% of non-diabetics, and plaque scores of 3 and 4 in 27.3% of diabetics and 16% of non-diabetics. All of the plaques were calcified. In this study there were no significant differences in age, percentage of LV ejection fraction and duration of hemodialysis treatment between males and females ($P > 0.05$). There was no significant LVH difference between the two genders ($P > 0.05$). No significant difference in duration of hemodialysis treatment, ages of the patients and percentage of LV ejection fraction existed between the diabetic and non-diabetic groups ($P > 0.05$). In this study there was a positive association between LVH and duration of hemodialysis treatment [in the diabetic group $r = 0.72$ ($P = 0.009$), and in the non-diabetics group $r = 0.292$ ($P = 0.021$)] (partial correlation test with adjustment for age).

Table1: Age, Duration of hemodialysis and Ejection Fraction of patients.

		Age (years)	D.H.T* (months)	EF** (percent)
Diabetic group	Mean±SD	57±16	22.6±22.4	47.7±7
	Min	27	3	30
	Max	78	60	55
Non-diabetic group	Mean±SD	47.8±16	34±33	51±9
	Min	15	2	25
	Max	78	108	70

*Duration of hemodialysis treatment.
**LV ejection fraction.

Table 2: Frequency distribution of stages of hypertension (HTN).

	DM group*		Non-DM group	
Stages of HTN	Number	Percent	Number	Percent
0	0	0	4	8
1	0	0	5	10
2	8	72.7	25	50
3	3	27.3	16	32

*DM=Diabetes Mellitus.

Table 3: Frequency distribution of Left ventricular hypertrophy (LVH) in hemodialysis patients.

	Total patients		Diabetic patients		Non diabetic patients	
	Number	Percent	Number	Percent	Number	Percent
No LVH	9	14.8	1	9	8	16
Mild LVH	25	41	4	36.4	21	42
Modrate LVH	20	32.8	4	36.4	16	32
Severe LVH	7	11.5	2	18.2	5	10

Table4: Frequency distribution of plaque score of carotid and femoral arteries.

	Plaque score	Frequency	Percent
Group one	0	1	9.1
	1	1	9.1
	2	6	54.5
	3	0	0.0
	4	3	27.3
Group two	0	32	64.0
	1	4	8.0
	2	6	12.0
	3	2	4.0
	4	6	12.0

Group1=Diabetic hemodialysis patients
Group2=Nondiabetic hemodialysis patients

No significant correlation of the percentage of LV ejection fraction (EF %) with the duration of hemodialysis treatment (P > 0.05) was found. Positive correlation of plaque score with the age of the patients (P = 0.003) was demonstrated. A weak linear inverse correlation of plaque score with the percentage of LV ejection fraction was seen (r =-0.404, P = 0.001). Significant positive correlation between plaque score and presence of diabetes mellitus was observed (P = 0.004). A weak significant linear positive correlation between plaque score with LVH (r =0.259,P = 0.023) was found. Also significant positive correlation between plaque score with the duration of hemodialysis (r =0.239,P=0.033), and significant positive correlation between plaque score with stages of HTN (r = 0.240, P = 0.032) was found.

Discussion

Patients with chronic kidney disease (CKD) on dialysis have a 2- to 5-fold increase in coronary artery calcification as compared to age-matched individuals with angiographically proven coronary artery disease.[11]

Positive correlation of plaque score with patient's age, and inverse correlation of plaque score with percentage of LV ejection fraction were found. Significant positive correlation between the plaque score and the presence of diabetes mellitus was also observed, which is in agreement with the results by Messerli.[12] In this study, the significant positive correlation between the plaque score and LVH, is in accordance with London et al.[13] but contrary to the findings of some researchers.[5] Also. we found a significant positive correlation between the plaque score and on the duration of hemodialysis, as stated by some studies.[11] However, the significant positive correlation between the plaque score with HTN in our study was contrary to Ahmet's study.[14]

Studies concerning the arterial plaques and LVH in hemodialysis patients show interesting findings. Strauman et al. in a study on 62 patients on maintenance hemodialysis observed a 65% prevalence of LVH. He showed that age, body mass index and duration of HTN were associated with LVH and asymmetric septal hypertrophy.[15] Greaves et al. in the evaluation of 30 hemodialysis patients and 54 patients under peritoneal dialysis compared with 38 ESRD patients not yet on dialysis demonstrated that left ventricular wall thickness was greater in the dialysis groups.[16] De Lima et al. in a study of 103 hemodialysis patients showed that systolic blood pressure was significantly associated with LV mass and it significantly and independently correlated with LVH and posterior wall hypertrophy.[17] Hojs in a study on 28 hemodialysis patients showed that age was the only significant determinant of the number of plaques. He concluded that hemodialysis patients had advanced atherosclerosis in the carotid arteries as compared with normal subjects.[18] Moreover, in his recent study, he showed no difference in plaque occurrence between 28 hemodialysis patients with 28 ESRD patients prior to hemodialysis.[18] Pascasio et al. observed a large number of vascular plaques in uremic patients that was statistically significant in all the vessels except for the carotids. He concluded that the process of advance atherosclerosis might get started early in the renal failure. He suggested that hemodialysis treatment may not be a potential factor to accelerate artherosclerosis, and finally concluded that the progression of atherosclerosis might be related to atherogenic factors in action before regular dialysis was commenced.[18] Savage et al. in a study on 24 dialysis patients noted a higher prevalence of plaques in the carotid and femoral arteries. Also, this study showed the relationship between femoral artery plaques and age.[5] Our results provide the evidence for the association of carotid-femoral plaques with hypertrophy of left ventricle, and especially the inverse correlation of plaque score with LV ejection fraction, suggesting that the arterial plaques and cardiovascular involvement (especially LVH) in hemodialysis patients could have an atherosclerotic basis, although other factors can contribute to this process. The relationship of carotid-femoral arterial plaques to LVH could confirm the cardial-arterial interaction and further highlights the importance of structural changes in large arteries in the pathogenesis of LVH in hemodialysis patients. Mallion believed that the prevalence of arterial changes is more evident in subjects with LVH.[19] He

believed that in LVH (particularly in concentric LVH), the arterial changes reproduce the ventricular changes in severity. But the question is whether carotid ultrasonography would provide any relevant extra information to echocardiograghically measured LVH in hemodialysis patients. Thus in the meantime, further clinical studies are required to evaluate the clinical significance of these findings on this important aspect of hemodialysis patients.

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