Prevalence of Peripheral Arterial Disease in Hemodialysis Patients

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Introduction. The ankle-brachial index (ABI), measurement of carotid artery intima-media thickness (CIMT), and assessment of the thickness of interventricular septum (IVS), are noninvasive methods used to predict subclinical atherosclerosis in hemodialysis patients. This study aimed to determine the prevalence of peripheral arterial disease and to assess the correlations between ABI, CIMT, the thickness of IVS, and blood parameters in hemodialysis patients.
Materials and Methods. The ABI, CIMT, and the thickness of IVS were measured in 50 patients on hemodialysis. Data were collected regarding the levels of calcium, urine nitrogen, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, triglyceride, cholesterol, creatinine, albumin in serum, as well as erythrocyte sedimentation rate.
Results. Ten percent of the patients showed a reduced ABI (< 0.9). The mean values for ABI, CIMT, and IVS were 1.09 ± 0.13, 0.68 ± 0.11mm, and 9.83 ± 1.65 mm, respectively. The levels of calcium, cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, and triglyceride in the serum of the patients with normal ABI were significantly higher than in patients with reduced ABI. There was a negative correlation between ABI and levels of serum LDLC ($r = -0.29$, $P = .04$) and triglyceride ($r = -0.32$, $P = .02$).
Conclusions. The prevalence of peripheral arterial disease in the patients with CRF was 10% and it was correlated with several classical risk factors for atherosclerosis, including elevated LDL and cholesterol levels. CIMT and the thickness of IVS showed no apparent association with ABI.

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INTRODUCTION

Atherosclerosis, the major cause of cardiovascular disease (CVD), is the leading cause of death for both men and women all over the world.[1,2] In particular, people with end-stage renal disease (ESRD) have an increased risk of death of CVD. However, medical intervention can reduce the risk of CVD in these patients to a significant extent.[3]

Atherosclerotic diseases are not always detected by traditional risk assessment. Measurement of the carotid artery intima-media thickness (CIMT) and the ankle-brachial index (ABI) are two well-established screening tools used to diagnose subclinical atherosclerosis and predict all-cause and cardiovascular mortality in hemodialysis patients. However, studies that have investigated

the relationship between CIMT and ABI in different populations have produced conflicting results.[4] Definite peripheral arterial disease (PAD) has been defined as an ABI less than 0.90 and is associated with increased risk of cardiovascular morbidity and mortality.[5,6] The CIMT is a surrogate marker for atherosclerosis and can be used to diagnosis an accelerated disease process, or to study the efficacy of interventions.[7,8] Measurement of CIMT is a noninvasive and relatively inexpensive method that can be repeatedly used without producing adverse effects. Thus, it is a valuable tool for assessing potential associations between cardiovascular risk factors and echocardiographic parameters.[9] This study aimed to determine the prevalence of PAD by using the ABI, CIMT, and the thickness of the interventricular septum (IVS) in patients with ESRD undergoing hemodialysis.

MATERIALS AND METHODS
Patients and Baseline Assessments

In a cross-sectional study, 50 hemodialysis patients (30 men and 20 women) who were admitted to Rasul-Akram Hospital (Tehran, Iran), between September 2008 and September 2009, were approached. They were on 4-hour chronic hemodialysis 3 times per week. Patients who had myocardial infarction or cerebrovascular accident and those who did not consent to participate were excluded. Patients with diabetes mellitus and hypertension were included.

Data were collected from the clinical records. The patients were assessed for clinical symptoms and blood biochemical parameters, including hemoglobin, calcium concentration, albumin, urea nitrogen, creatinine, cholesterol, low-density lipoprotein cholesterol (LDLC), high-density lipoprotein cholesterol (HDLC), triglyceride, and erythrocyte sedimentation rate, before and after dialysis. The patients received supplementary therapy, including erythropoietin, fibrates, antihypertensive agents, atrovostatin (20 mg/d), folate (1 mg/d), vitamin B complex, and insulin.

The study protocol was approved by the Ethics Committee of Tehran University of Medical Sciences.

Assessment of Atherosclerosis

The CIMT and ABI were assessed using Doppler ultrasonography (Sonoline G40, Siemens Medical Solutions AG, Erlangen, Germany), all performed

by the one examiner, as described elsewhere.[10] Briefly, the cuff was placed on resting patient's upper arm or leg with the lower edge approximately 3 cm above the antecubital fossa or ankle's medial malleolus, respectively. Brachial artery pressures were measured and 3 readings averaged to obtain the ABI denominator. The higher of the two brachial systolic pressure readings were used to calculate the ABI. For each lower extremity, the systolic blood pressure measurements were obtained from the dorsalis pedis and posterior tibial arteries. The cutoff for every patient was chosen by detection of the flow (pulse) by the Doppler prob. Diagnosis of debilitating PAD was made based on the ABI values less than 0.9 at resting position and the clinical manifestations, as descried previously.[11]

To determine the CIMT using high-resolution carotid ultrasonography, subjects laid quietly on the bed in the supine position with semi-extended neck and the distal 1.0 cm to 1.5 cm of far wall of the right and left common carotid arteries from different scanning angles (anterior, later-posterior) were scanned. The measurements of the 3 readings for each side were averaged.

Echocardiography at M mode was used to determine the thickness of the IVS. The Doppler ultrasonography examinations were performed using MyLab 50 xvision (Biosound Esaote Inc, Granbury, Texas, USA).

Statistical Analyses

Values were expressed as means ± standard deviation. The Student *t* test, chi-square test, and Spearman correlation coefficient test were used to analyze the data. The SPSS software (Statistical Package for the Social Sciences, version 15.0, SPSS Inc, Chicago, Ill, USA) was utilized for analyses. *P* values less than .05 were considered significant.

RESULTS

Fifty hemodialysis patients were investigated in the study. Thirty patients were men (60%) and 20 were women (40%). The mean age of the patients was 55.0 ± 14.8 years (range, 23 to 83 years). The ABI values were greater than 0.9 in 90% of the patients (n = 45). The mean values for ABI, CIMT, and IVS were 1.09 ± 0.13 (range, 0.88 to 1.5), 0.68 ± 0.11mm (range, 0.4 mm to 0.9 mm), and 9.83 ± 1.65 mm (range, 7 mm to 14 mm), respectively.

The levels of calcium, cholesterol, LDLC, HDLC,

Characteristics of Hemodialysis Patients With Normal and Reduced Ankle-Brachial Index*

Characteristic	Reduced ABI Group (n = 5)	Normal ABI Group (n = 45)	P
Age, y	49.80 ± 6.05	55.60 ± 15.3	.06
IVS, mm	9.88 ± 1.71	9.40 ± 1.05	.10
CIMT, mm	0.67 ± 0.07	0.68 ± 0.12	.08
Duration of dialysis, mo	49.50 ± 6.36	37.75 ± 18.78	.09
Hemoglobin, g/dL	10.18 ± 1.77	9.98 ± 1.91	.13
Serum calcium, mg/dL	7.60 ± 0.52	8.44 ± 1.16	.01
Serum albumin, g/dL	3.24 ± 0.89	4.18 ± 1.04	.06
BUN, mg/dL	57.40 ± 38.20	66.84 ± 39.70	.07
Serum creatinine, mg/dL	6.80 ± 2.75	5.93 ± 3.15	.12
ESR, mm/h	50.20 ± 36.58	42.42 ± 26.82	.06
Serum cholesterol, mg/dL	232.00 ± 26.42	169.13 ± 48.57	< .001
Serum LDLC, mg/dL	166.04 ± 27.40	112.47 ± 42.30	< .001
Serum HDLC, mg/dL	32.60 ± 8.84	34.84 ± 10.39	.09
Serum triglyceride, mg/dL	219.80 ± 23.28	149.66 ± 64.64	< .001

*ABI indicates ankle-brachial index; IVS, interventricular septum; CIMT, carotid intima-media thickness; BUN, blood urea nitrogen; ESR, erythrocyte sedimentation rate; HDLC, high-density lipoprotein cholesterol; LDL, low-density lipoprotein cholesterol.

and triglyceride in the serum of the patients with normal ABI were significantly higher than in patients with reduced ABI (Table). There was a negative correlation between ABI and levels of serum LDLC (r = -0.29, P = .04) and triglyceride (r = -0.32, P = .02). Regression analysis did not show a significant correlation between ABI or CIMT and blood biochemical parameters including HDLC, erythrocyte sedimentation rate, calcium, urea nitrogen, and creatinine.

DISCUSSION

Atherosclerosis and cardiovascular diseases are major causes of morbidity and mortality in patients with ESRD. Several large clinical and epidemiological studies have shown that the chronic baseline kidney function is an independent predictor of survival in patients with ESRD.[12,13] In addition, echocardiographic studies have demonstrated that left ventricular hypertrophy begins at an early stage of chronic kidney failure, and its prevalence increases in association with deteriorating renal function.[14] The ABI and CIMT are two well-established screening tools for determining cardiovascular risk.[15] In this study, differentiation of clinical PAD from non-PAD conditions was made based on ABI values. Patients with reduced ABI (< 0.9) were considered suffering from PAD.[11] Ultrasonography measurements of CIMT was used for evaluation of generalized atherosclerosis in this study as described previously.[3,7] The morbidity and mortality caused by atherosclerotic vascular

disease is highly associated with ESRD, and CIMT measurement is often used as a noninvasive method to study vascular atherosclerosis in patients with chronic kidney failure.[3]

In patients with PAD, the ultrasonography measurements of CIMT are usually higher than in the normal population. However, in the current study, no significant association was found between ABI and CIMT. This discrepancy between the results from our study and others may be linked to the limited number of investigated patients with a reduced ABI (n = 5). The ABI and CIMT are well studied markers of atherosclerosis. Considerable evidence has shown that they are both independently associated with increased vascular morbidity and mortality, although some studies have shown little to no correlation between them.[16] However, their value in identifying high-risk patients among those with a low or intermediate estimated risk appears to be limited. CIMT is mainly useful in early atherosclerosis, but PAD (with an ABI < 0.9) develops mostly in patients who already have a high estimated vascular risk, including elderly smokers and diabetic patients.[17] The thickness of the IVS and its correlation with ABI were also evaluated in patients. It has been shown that high ABI values may be associated with increased thickness of IVS through non-atherosclerotic pathways.[18]

In hemodialysis patients, it has been shown that CIMT is comparable to the control group. It was mainly affected by traditional cardiovascular risk

factors and uremic risk factors did not specifically affect CIMT.[19]

In the current study, ABI was used to predict the PAD in patients with ESRD. As a limitation of this study, to validate the ABI findings, it will be required to compare the readings with a gold standard method. Angiography is regarded as a gold standard for validation of ABI values. However, this method is invasive and is considered a high risk method to use in diabetic patients with ESRD. To obviate this limitation, other non-invasive methods, including measurements of left ventricular septum thickness and CIMT, were used in this study as predictors. The results from our study showed no correlation between ABI measurements and IVS thickness. In reduced ABI group, an increase was observed in the thickness of IVS, but there was no significant different between the two groups. This discrepancy between our results and others is unclear, but the results might be biased by the small number of patients in the reduced-ABI group (n = 5). It has been also stated that despite recommendations, ABI measurement is not sensitive screening tool for detecting subclinical atherosclerosis in asymptomatic middle-aged individuals.[15]

One limitation of our study was the small number of investigated subjects, which mainly was caused by the exclusion of noneligible patients as explained earlier. Meanwhile, our findings showed that the levels of serum cholesterol, LDLC, and triglyceride were significantly higher in patients with PAD compared with those without PAD. There was a significantly inverse correlation between ABI and total cholesterol, LDLC and triglyceride. It has been reported that elevated total and LDLC levels is associated with a high carotid plaque score among dialysis patients.[20]

CONCLUSIONS

The current study provided broader insight about the prevalence of PAD in HD patients and the association of classical risk factors in Iranian population. This study showed that PAD in patients with ESRD is correlated with some classical risk factors for atherosclerosis, including elevated levels for LDL and cholesterol. The CIMT and IVS thickness showed no apparent association with ABI. Findings in the current study provided broader insights about the prevalence of PAD in hemodialysis patients and the association of classical risk factors in Iranian population.

CONFLICT OF INTEREST

None declared.

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