Original Article

Carotid Artery Intima Media Thickness as a Surrogate Marker of Atherosclerosis in Patient with Chronic Renal Failure on Hemodialysis

Jayanta Paul, Somnath Dasgupta, Mrinal Kanti Ghosh[1]

Departments of Medicine, and [1]Radiology, Burdwan Medical College, West Bengal, India

Abstract

Background: In patients with chronic renal failure (CRF), carotid artery intima media thickness (CAIMT) is increased when the patients are on hemodialysis. Vascular events caused by atherosclerosis are the major cause of death in patients undergoing hemodialysis. **Aims:** This study was done to find out the relationship between carotid artery intima media thickness and hemodialysis in chronic renal failure patients independent of classical risk factors and also the relationship between CAIMT of hemodialyzed patients and nonhemodialyzed CRF patients. **Materials and Methods:** In this observational study, CAIMT of 78 CRF patients was examined by B-mode ultrasonography. Glomerular filtration rate (GFR) was calculated by using the "Modification of Diet in Renal Disease" formula. CRF patients, who had been on regular hemodialysis treatment (treated thrice weekly) for at least 6 months, were identified as hemodialyzed patients. Data were analyzed by software Statistical package for the social Sciences (SPSS) (17th version). **Results:** There was significant positive correlation between CAIMT and hemodialysis (P=0.045) independent of traditional risk factors. Hemodialyzed patients had higher mean CAIMT (1136.30±21.21 μm, P<0.001) than mean CAIMT of age and sex matched nondialyzed patients (959.30±23.01 μm). **Conclusion:** Hemodialysis is an independent risk factor for atherosclerosis in CRF patents. Hemodialyzed patients have significantly higher CAIMT than nondialyzed CRF patients.

Keywords: Atherosclerosis, Carotid artery intima media thickness, Chronic renal failure, Dialysis, Traditional risk factors of atherosclerosis

Address for correspondence: Dr. Jayanta Paul, Post Graduate Student, Department of Medicine, Burdwan Medical College, West Bengal, India.
E-mail: dr.jayantapaul@gmail.com

Introduction

In patients with chronic kidney dysfunction, cardiovascular disease (CVD) is twice as common as in the general population.[1] Cardiovascular events are also the leading cause of death in chronic hemodialysis patients.[2] Patients undergoing hemodialysis (HD) have progressive atherosclerosis.[3] Besides the renal disease itself, hemodialysis may also be one of the risk factors for atherosclerosis.[4] The cardiovascular mortality rate is 20–40 times higher for adults on dialysis than for the general population.[5,6]

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Carotid artery intima media thickness (CAIMT) was also an independent predictor of Cardiovascular (CV) death in nondiabetic hemodialysis patients.[7] Ultrasound measurements of the intima media thickness (IMT) in the carotid arteries were used as an indicator of carotid atherosclerosis.[8] In several recent studies, ultrasound measurements of IMT in carotid arteries were also used as the indicator of atherosclerosis in dialysis patients. Benedetto *et al,*[9] found that carotid artery IMT represented an independent predictor of cardiovascular death in dialysis patients. In patients on HD, the CAIMT has been found to be a strong predictor of cardiovascular or all-cause mortality.[10,11]

The aims of our study were to find out (1) the relationship between CAIMT as a surrogate marker of atherosclerosis and hemodialysis independent of traditional risk factors, (2) relationship between CAIMT of hemodialyzed CRF patients and CRF patients without hemodialysis.

Materials and Methods

In this prospective observational study, the study subjects included 78 patients with CRF (GFR <60 ml/min per 1.73 m^2 for 3 months or more with or without kidney damage).[12] Consecutive samples were taken. All subjects underwent a careful interview and clinical, radiological, biochemical examination with an evaluation of patient history based on hospital and outpatients records.

In this study, blood pressure, fasting blood sugar, 24 h total urine albumin excretion, hypertension, dyslipidemia, smoking were included as modifiable traditional risk factors. Age and sex were nonmodifiable traditional risk factors. Hypertension was diagnosed when a patient had received medicine for hypertension or had systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg after taking 5 min rest. Fasting blood sugar was measured by a "glucose oxidase-peroxidase" method. Diabetes was diagnosed according to "American Diabetes Association" when a previous or current 12 h fasting glucose level is 7 mmol/l or greater (≥126 mg%). Total cholesterol was estimated by "cholesterol oxidase-peroxidase" method. Patients who used cholesterol lowering medication or had a total serum cholesterol level ≥200 mg/dl were classified as having hypercholesterolemia or dyslipidemia.[13] Twenty four hours total urine albumin excretion is the "gold stander" for measurement of albuminuria,[14] and here it was measured by Esbach's albuninometer. Kidney damage was defined as a microalbuminuria between 17–300 mg/g for men and 25–300 mg/g for women.[15] Serum creatinine was estimated by kinetic alkaline picrate (Jaffe) method. Estimated GFR (eGFR) was calculated using the modification of diet in renal disease (MDRD) formula:[16] eGFR=186.3 × (serum creatinine−1.154) × (age−0.203) × 1.212 (if black) × 0.742 (if female).

Venous blood was taken in the morning after an overnight fast for at least 12 hours for biochemical analysis. All biochemical measurements were estimated through Department of Biochemistry, Burdwan Medical College.

Smoking history was assessed by participant's self report. Participants were classified as never-smokers if they responded that they had smoked fewer than 100 cigarettes or 5 packs of cigarettes during their lifetime.[17] CRF patients, who had been on regular hemodialysis treatment (treated thrice weekly) for at least 6 months,[18] were identified as hemodialyzed patients in this study.

Examination of the carotid arteries was performed with a 7 MHz B-mode ultrasound system. CAIMT defined as a low-level echo gray band that does not project into the arterial lumen, was measured at the diastolic phase as the distance between the leading edge of the first and second echogenic lines of the far walls of the distal segment of the common carotid artery, the carotid bifurcation, and the internal carotid artery on both sides[18] and was measured with a duplex ultrasound system with 7.5 MHz scanning frequency in the B-mode, pulsed Doppler mode and color mode. The B-mode scanning protocol included the scanning of the right and left common carotid arteries (3 cm before the carotid bifurcation), carotid bifurcation, as well as of the internal carotid artery 2 cm distally from the carotid bifurcation.[19] CAIMT measurements were always performed in plaque-free arterial segments.[18]

All examinations and measurements were performed by same examiner to exclude examiner bias.

Statistical study

Chi-square test, Independent samples *t*-test, and Linear multivariate regression analysis were performed for result and analysis. *P* value less than 0.05 was taken as statistically significant. All these analysis were performed using a commercially available software SPSS (window version 17.0) on personal computer. Data were expressed as means±SE (Standard Error).

Results

Out of 78 CRF patients, 46.15% patients were on hemodialysis and 53.85% were without hemodialysis. 80.56% of hemodialyzed patients were male and 19.44% were female. 61.90% of nondialyzed patients were male and 38.10% were female. Mean age of hemodialyzed patients was 51.47±2.17 years and mean age of nondialyzed patients was 50.47±2.27 years [Table 1]. Independent samples *t*-test for equality of means found that there was no significant difference of mean age between hemodialyzed and nondialyzed patients (*P*=0.752) [Table 2]. Chi-square test also showed that there is no significant difference in gender distribution between hemodialyzed and nondialysis CRF patients (*P*>0.05). So in this study, CAIMT of 36 hemodialyzed patients were compared with age and sex matched 42 nondialyzed CRF patients.

There was significant positive correlation between CAIMT and hemodialysis independent of traditional risk factors, *P*=0.045 [Table 3]. Hemodialyzed CRF patients

Table 1: Mean CAIMT and age of dialyzed and nondialyzed CRF patients

	Patients	Mean value
CAIMT	Nondialysis	959.30±23.02 µm
	Dialysis	1136.30±21.21 µm
Age	Nondialysis	51.47±2.17 years
	Nondialysis	50.47±2.27 years

CAIMT: Carotid artery intima media thickness; CRF: Chronic renal failure

Table 2: Independent samples *t*-test for equality of means

Variables	Sig. (2-tailed) (*P* value)
CAIMT	
Equal variances assumed	<0.001
Equal variances not assumed	<0.001
Age	
Equal variances assumed	0.755
Equal variances not assumed	0.752

CAIMT: Carotid artery intima media thickness; Variances are hemodialysis and nonhemodialysis CRF patients; Table 2 summarizes correlation between dependent variable (CAIMT) and different independent variables

Table 3: Linear multivariate regression analysis of traditional risk factors correlating with CAIMT

Independent variables	Standardized coefficients	*P* value
Age	0.123	0.047
Sex	0.206	0.002
Smoking	0.146	0.047
Hypercholesterolemia	0.154	0.021
Hypertension	0.203	0.003
Hemodialysis	0.137	0.045
Glomerula filtration rate	0.244	0.001
24 hours total urine protein	0.210	0.003
Fasting blood sugar	0.141	0.035

Here dependent variable: CAIMT: Carotid artery intima media thickness

had higher mean CAIMT (1136.30±21.21 μm) than age- and sex-matched CRF patients without hemodialysis (959.30±23.02 μm) [Table 1]. Independent samples *t*-test for Equality of Means found that there was significant difference of mean CAIMT between hemodialysis and non-dialysis CRF patients (P<0.001) [Table 2].

In this study, there was also independently positive significant correlation of age (P=0.047), sex (P=0.002), smoking (P=0.047), hypercholesterolemia (P=0.021), hypertension (P=0.003), 24 h total urine protein excretion (P=0.003), fasting blood sugar (P=0.035) with CAIMT. Here GFR was negatively correlated with CAIMT (P=0.001) [Table 3].

Discussion

Life expectancy is reduced in CRF patients comparing with normal population. Death due to cardiovascular disease (CVD) is common among hemodialysis patients. The relative risk of CVD death in this group of patients was high as 10–30 times.[20-22]

In this study, higher value of mean carotid artery intima media thickness in CRF patients on hemodialysis was found than in age- and sex-matched CRF patients without dialysis. These results are in accordance with other authors.[23,24] Increased carotid artery IMT is considered as a marker of early atherosclerotic changes.[25] The normal intima-medial thickness of common carotid artery as evaluated by B-mode ultrasound imaging was 0.74±0.14 mm[26] and CAIMT at or above 1 mm is associated with atherosclerosis and a significantly increased CVD risk in any age group.[27,28] Therefore, in our study, CRF patients on hemodialysis were suffering from atherosclerosis (mean CIAMT=1136.30±21.21 μm) and patients without hemodialysis were also associated with higher CAIMT (mean CAIMT=959.30±23.02 μm) than normal.

As per several studies,[29] known traditional risk factors such as age, sex, hypercholesterolemia, hypertension, fasting blood sugar, and smoking were also implicated in inducing atherosclerosis in CRF patients in our study.

There are some limitations in this study: (1) premature atherosclerosis, serum homocysteine, lipoprotein (a), obesity, physical activity, atherogenic diet, proinflammatory factors, and prothrombotic factors could not be included due to the limitations of budget and study design, (2) small number of participants.

Conclusion

Hemodialysis is an independent risk factor of atherosclerosis in CRF patients. Measurement of CAIMT has a value to diagnose the atherosclerosis in CRF patients on hemodialysis after traditional risk factors have been taken into consideration. Aggressive control of modifiable traditional risk factors may reduce the progression of atherosclerosis in hemodialysis patients because they are also independent risk factors of atherosclerosis.

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