Original Article

CLOSE RELATIONSHIP OF CAROTID INTIMAE-MEDIA THICKNESS WITH LEFT VENTRICULAR HYPERTROPHY AND EJECTION FRACTION IN END-STAGE RENAL DISEASE PATIENTS UNDERGOING HEMODIALYSIS TREATMENT

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ABSTRACT

Background: Two principle findings of cardiovascular disease in end-stage renal disease patients undergoing regular hemodialysis is left ventricular hypertrophy (LVH) and arterial disease due to rapidly progressive atherosclerotic vascular disease that can be characterized by an enlargement and hypertrophy of arteries (Intimae-media complex thickening (IMT)). In this study we sought to study the relationship of left ventricular hypertrophy with Intimae-media complex thickening in end-stage renal disease patients undergoing regular hemodialysis.

Patients and Methods: This cross-sectional study was done on Sixty-one patients with end-stage renal disease (ESRD) undergoing regular hemodialysis treatment (F=23 M=38) consisting of 50 non diabetic hemodialysis patients (F=20 M=30) and 11 diabetic hemodialysis patients (F=3 M=8). For all patients echocardiography was done and carotid-Intimae-media thickness by B-mode Ultra-sonography was measured.

Results: There was positive correlation between stages of LVH with duration of hemodialysis treatment. Positive correlation between stages of LVH with stages of hypertension was seen. More over significant correlation between stages of LVH with carotid-IMT and also positive correlation between stages of LVH with presence of chest pain was found. More thickening of Intimae-media complex in diabetic group, and association of diabetes mellitus with the presence of chest pain as well as positive correlation between stages of HTN with IMT was also demonstrated. More over linear inverse correlation between IMT with percent of LV ejection fraction were observed.

Conclusion: Thickening of intimae-media complex is more evident in hemodialysis subjects with LVH, when there is an LVH; the IMT is similar in severity to the LVH.

KEYWORDS: Intimae-media Thickness, Hemodialysis, Left ventricular hypertrophy, Atherosclerosis, Diabetes Mellitus

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INTRODUCTION

Cardiovascular disease is the principal cause of morbidity and mortality in dialysis patients[1]. Principle findings of cardiovascular disease is left ventricular hypertrophy(LVH) as determined by echocardiography[2] and arterial disease due to rapid progressive atherosclerotic vascular disease[3] that characterized by an enlargement and hypertrophy of arteries (Intimae-media complex thickening (IMT)) as can be determined by B-mode ultra-sonography[2,3]. Left ventricular mass increases progressively as renal function deteriorates and is exceedingly frequent in patients undergoing dialysis[4]. In fact left ventricular hypertrophy and arte-

rial disease are the two principle risk factors for cardiovascular mortality in hemodialysis patients[5]. Carotid intimae – media thickness (IMT) is a marker of early atherosclerosis its anatomic extent and progression. IMT is increased in subjects with several risk factors and is a predictor of cardiovascular events and end-organ damage[6]. Clinical manifestation of cardiovascular disease often arises in a stage of well-advanced atherosclerosis. However, arterial vessel wall changes occur during a presumably long sub clinical lag phase characterized by functional disturbances and by gradual thickening of intimae-media[6]. IMT of large peripheral arteries especially carotid can be assessed by B-mode ultrasound in a relatively simple way, the measurement of IMT has emerged as one of the methods of choice for determining early atherosclerotic changes, the anatomic extent of atherosclerosis and its progression[6] and showing the effectiveness of medical therapies too[6-8]. Therefore considerable attention has been directed toward the use of B- mode ultrasound that can directly assess the IMT which corresponds to the thickness of the histology of intimae and media[6-10]. Evidence shows that carotid-IMT is a strong predictor of cardiovascular disease in the general population[6], however the question arises whether ultra-sonographic studies of carotid arteries for IMT are useful to find any relationship between ESRD-related vascular changes (IMT) with left ventricular hypertrophy and chest pain of hemodialysis patients? As various studies show the cardiovascular mortality rate is elevated in those with end-stage renal disease (ESRD) diabetes mellitus and especially in those with diabetes mellitus and especially in those with diabetes and ESRD[10], therefore our aim was to study on a group of hemodialysis patients consisting of diabetics and no diabetics to find any association between IMT with LVH and IMT with severity of hypertension and chest pain.

PATIENTS AND METHODS

This cross-sectional study was done on 61 patients with end-stage renal disease (ESRD) undergoing regular hemodialysis treatment between September 2002 and December 2003. The exclusion criteria included patients who were cigarette smoking, body mass index (BMI) more than 25, those on anti lipid drug therapy, recent MI and vascular diseases as well as pericarditis and pericardial effusion in echocardiography and active or chronic infection. 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[11,12] (stage of zero equal to no HTN) stages of the hypertension of HD patients were considered before treatment and at the first start of hemodialysis treatment. Carotid sonography was done by a single sonologist unaware of history or lab data of patients using a Honda-Hs-2000 Sonograph with 7.5 MHz linear probe. The procedure was done at the end of diastolic phase. The sites of measurements were at the distal common carotid artery, area of bifurcation and at the first proximal internal carotid artery. IMT was measured at the plaque free areas. For examination patients were in supine position with neck hyperextension and rotation of head for facilitation of procedure performing. Using sonography the carotid artery found to have tree different echoes. Intimae- media thickness (IMT) was defined as the distance from leading edge of lumen-Intimae interface of the far wall to the leading edge of the media- adventitia interface of the far wall. IMT more than 0.8 mm was considered abnormal. For heart echocardiography (2D & Doppler) one single cardiologist who was unaware of the patients' data performed all echo-cardiographies for left ventricular hypertrophy and LV ejection fraction. On the base of sepal thickness we stratified the patients into no LVH (septal thickness between 6-11 mm) mild (septal thickness between 11-15 mm) moderate (septal thickness between 15-18 mm) and severe LVH (septal thickness >18 mm) LVH measurements were done at the end diastolic phase and LV ejection fraction between 55to 75% was consid-

ered normal. Mean of right and left carotid IMT was considered for statistical analysis. For statistical analysis descriptive data are expressed as Mean± SD. Comparison between groups were performed using chi-square (x^2 test), Mann Whitney U test as well as Kruskal & Wallis and Fisher's exact tests. For correlations Spearman rho test, Partial correlation with adjustment for age, Phi & Cramer's V test and Eta test were used. All statistical analysis were performed with SPSS (version 11.00) and statistical significance was inferred at a p value < 0.05.

RESULTS

The total patients were 61(F=23 M=38) consisting of 50 non diabetic hemodialysis patients (F=20 M=30) and 11 diabetic hemodialysis patients (F=3 M=8). Table-I show the mean ± SD of patients data. Table II, III and IV show the frequency distribution of chest pain, stages of HTN and stages of LVH of patients. Mean ± SD of ages of patients were 46.5±16 years. The patients have been on hemodialysis for 32 ± 31 months. Mean ± SD of LV ejection fraction were 51±8.9 percent and 39.3% of patients had chest pain. In this study there were no significant difference of age, percent of LV ejection fraction, Carotid-IMT, and duration of hemodialysis between males and females (p>0.05). There was no significant different of LVH between two sexes (p>0.05). There was not significant difference in the presence of chest pain and also no significant difference of DM between two sexes (p>0.05). No significant relationship between sex of the subjects and stages of Hypertension (p>0.05) was found. In this study there was a positive association between stages of LVH and duration of hemodialysis

Table-I: Mean ± SD, minimum and maximum of patients data

		Age (years)	*D.H.T* (months)*	*IMT** (mm)*	*EF*** (percent)*
Total patients	Mean±SD	46.5±16	32±31	1.06±0.3	51±8.9
	Min	15	2	0.50	25
	Max	78	108	1.70	70
Diabetic group	Mean±SD	57±16	22.6±22.4	1.3±0.3	47.7±7
	Min	27	3	0.80	30
	Max	78	60	1.70	55
Non-diabetic group	Mean±SD	47.8±16	34±33	1±0.25	51±9
	Min	15	2	0.50	25
	Max	78	108	1.60	70

* Duration of hemodialysis treatment.
** Carotid Intimae-media thickness.
*** LV ejection fraction.

Table-II: Frequency distribution of stages of hypertension (HTN)

Stages of HTN	*Total patients*		*DM* group*		*Non-DM group*	
	Number	*Percent*	*Number*	*Percent*	*Number*	*Percent*
0	4	6.6	0	0	4	8
1	5	8.2	0	0	5	10
2	33	54.1	8	72.7	25	50
3	19	31.1	3	27.3	16	32

*DM=Diabetes Mellitus.

Table-III: Frequency distribution of chest pain in hemodialysis patients

Chest pain	*Total patients*		*Diabetic patients*		*Non-Diabetic patients*	
	Number	*Percent*	*Number*	*Percent*	*Number*	*Percent*
Yes	24	39.3	9	81.8	15	30
No	37	60.7	2	18.2	35	70

Table-IV: 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
Moderate LVH	20	32.8	4	36.4	16	32
Severe LVH	7	11.5	2	18.2	5	10

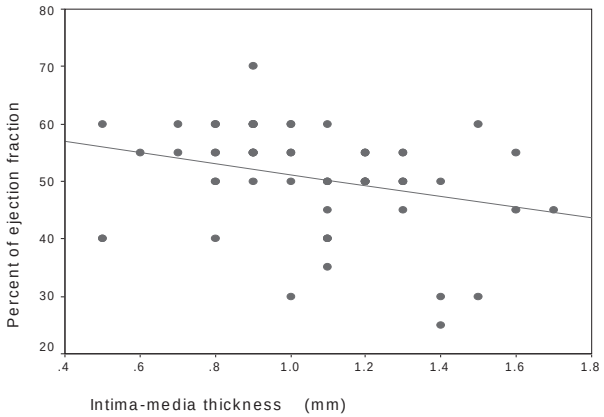

Figure-1: Inverse correlation between IMT with percent of LV ejection fraction (r= - 0.353 p=0.005) (partial correlation test after adjustment for ages)

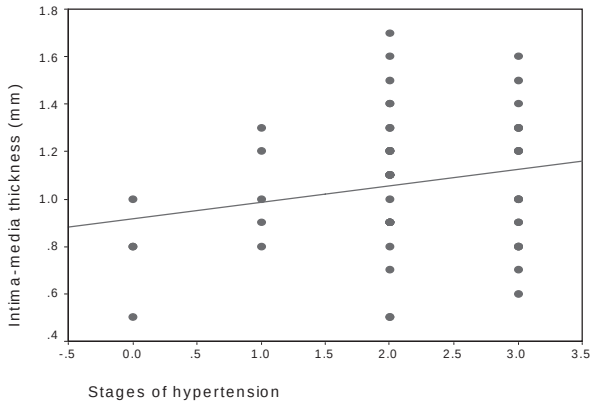

Figure-2: Positive correlation between IMT and stages of HTN (r = 0.266 p=0.020) (partial correlation test after adjustment for ages)

treatment (p<0.01) and no significant relation between stages of LVH and ages of the patients (p>0.05) was existed. There was a positive relationship between stages of LVH and stages of HTN (r= 0.580 p<0.001). No significant correlation between DM and LVH (p>0.05) was found. Significant relationship between stages of LVH with carotid-IMT (p>0.05) was seen. Significant positive correlation between presence of chest pain and DM (p<0.001) was also demonstrated. Association between the presence of DM with presence of HTN as well as sex with presence of DM were negative (p>0.005). There was a significant difference of carotid-IMT between diabetic and non-diabetic group (1.3±0.3 versus 1±0.25mm respectively) (p<0.05). No correlation between DM and with percent of LV ejection fraction was found (p>0.05). No significant difference existed in duration of hemodialysis, age and percent of LV ejection fraction between diabetic and non diabetic group (p>0.05). No significant Correlation of percent of LV ejection fraction with duration of hemodialysis treatment (p>0.05) was found. In some patients a significant correlation between presence of chest pain and stages of LVH (p<0.001) was observed. About HTN there was not any difference between stages of HTN with chest pain (p> 0.05). No positive correlation between IMT with duration of hemodialysis treatment was observed (p>0.05) more over linear inverse correlation between IMT with percent of LV ejection fraction (r= - 0.353 p=0.005) (figure1) was found. Positive association between IMT and stages of HTN (r = 0.266 p=0.020) (figure 2) were also observed.

DISCUSSION

The principle findings of the present study were positive correlation between stages of LVH with duration of hemodialysis treatment and between stages of LVH with stages of hypertension. Significant positive relationship between stages of LVH with carotid-IMT and also positive correlation between stages of LVH with presence of chest pain were demonstrated. Moreover, more thickening of Intimae-media complex in diabetic group than non-diabetics and association of diabetes mellitus with the presence of chest pain were also noted. Positive correlation between stages of HTN with IMT, and linear inverse correlation between IMT with percent of LV ejection fraction were other important findings of this study. Strauman et al. in a study on 62 patients on maintenance hemodialysis observed 65% prevalence of LV hypertrophy. He showed that age, body mass index and duration of HTN was associated with LV hypertrophy and asymmetric septal hypertrophy[13]. Greaves et al. in the evaluation of 30 HD 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 dialysis group[14]. De Lima et al. in

the study of 103 HD patients showed that systolic blood pressure was significantly associated with LV mass and was significantly and independently correlated with LVH and posterior wall hypertrophy[15]. Nishizawa et al in a study on 438 patients with ESRD treated with hemodialysis showed a significantly greater risk for death from cardiovascular causes in patients who had significant higher IMT[16]. Papagianni et al. in a study on 12 HD Patients also found a significant relationship between IMT and systolic blood pressure[8]. Lin et al. in a research on forty normotensive HD Patients demonstrated that LV mass was significantly positively related to carotid- IMT[17]. London et al studied 70 uncomplicated ESRD patients and observed a significant correlation of ventricular wall thickness and as well as left ventricular mass with carotid-IMT[18]. Zoccali et al. in an evaluation of 254 patients undergoing dialysis concluded that LV mass is a strong and independent predictor of survival and cardiovascular events in these patients[4]. Muiesan et al. in a study to evaluate the structural association between the carotid artery and left ventricle in a general population in northern Italy showed the common carotid-IMT was significantly greater in the subjects with concentric left ventricular hypertrophy[19].Our results provide the first direct evidence that diabetic patients with ESRD undergoing hemodialysis treatment had more accelerated atherosclerosis and more involvement by ischemic heart disease(IHD) than non diabetic hemodialysis patients. We could show the association of carotid-IMT with hypertrophy of left ventricle and especially inverse correlation of IMT with LV ejection fraction means that thickening of intimae-media complex and cardiovascular involvement especially LVH in hemodialysis patients could have an accelerated atherosclerotic base albeit other factors are involved in this process. We have also demonstrated that carotid artery –IMT is related to LV hypertrophy although the confirmation of this cardial-arterial interaction further highlights the importance of structural changes in large arteries in the pathogenesis of LVH in hemodialysis patients. Mallion[20] believed that the prevalence of thickening in intimae-media is more evident in subjects with LVH and also the presence of concentric remodeling of the left ventricle without LVH has already been associated with an increase in IMT and as he believed that when there is an LVH this IMT is similar in severity to the LVH and in particular concentric, but the question is whether carotid ultrasonography added relevant information to echocardiography measured LVH in hemodialysis patients, although IMT had a prediction power for cardiovascular death independent of LVH. Thus larger studies needs to allow to better appreciation of the relative value of ultra-sonography measured IMT in these patients.

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