Studying the relationship between the risk factors of cardiovascular diseases and carotid intima-media thickness (CIMT) in renal patients undergoing hemodialysis admitted to Razi Hospital and Caspian Dialysis Center in Rasht, 2017

Estudiar la relación entre los factores de riesgo de enfermedades cardiovasculares y el grosor íntima-media carotídeo (CIMT) en pacientes renales sometidos a hemodiálisis ingresados en el Hospital Razi y el Centro de Diálisis Caspian en Rasht, 2017

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Abstract

The increase in CIMT is known as an early warning sign of atherosclerosis. CIMT examination using ultrasonography is a non-invasive, precise, and practical way to detect atherosclerosis. As cardiovascular diseases are of the main causes of mortality in dialysis patients, this study tried to examine the relationship between cardiovascular risk factors and CIMT in renal patients undergoing hemodialysis.

This case-control study was conducted on 60 hemodialysis patients and 60 non-dialysis patients at Razi Hospital and Caspian Diabetic Center in Rasht in 2017. After examining the risk factors of cardiovascular diseases, ultrasonography was performed to measure CIMT. Finally, data were analyzed using SPSS21 and appropriate statistical methods.

Mean CIMT in dialysis patients (0.88 ± 0.16 mm) was significantly higher than the non-dialysis patients (0.69 ± 0.14 mm) (P<0.0001). Mean CIMT in terms of gender and smoking was statistically significant only in non-dialysis patients (P = 0.025 and 0.028, respectively). Age (P<0.0001, β = 0.004), gender (P<0.027, β = 0.05), systolic blood pressure (P = 0.024, P = 0.001) Body mass index (BMI) (P = 0.017, β = 0.005) and TG (P <0.0001, β = 0.002) were considered as factors related to CIMT. Moreover, CRP (P <0.0001, β = 0.132), intact parathyroid hormone (iPTH) (P <0.0001, β = 0.003) and Ca-P product (P = 0.023, P <0.001) 0 = β) were considered for having the most importance among the new generation of risk factors associated with CIMT.

The results showed that the mean CIMT in dialysis patients was significantly higher than that of non-dialysis patients. Furthermore, age, gender, systolic blood pressure, BMI and TG had direct connection with CIMT. CRP, iPTH and Ca-P product were identified as the most important new generation risk factors for CIMT.

Keywords: Ultrasonography, cardiovascular diseases, carotid artery, intima layer, media layer, hemodialysis

Resumen

El aumento en CIMT se conoce como un signo de advertencia temprana de aterosclerosis. El examen CIMT mediante ultrasonografía es una forma no invasiva, precisa y práctica para detectar aterosclerosis. Como las enfermedades cardiovasculares son las principales causas de mortalidad en pacientes en diálisis, este estudio trató de examinar la relación entre los factores de riesgo cardiovascular y CIMT en pacientes renales sometidos a hemodiálisis.

Este estudio de casos y controles se realizó en 60 pacientes en hemodiálisis y 60 pacientes sin diálisis en el Hospital

Razi y el Centro de Diabetes Caspio en Rasht en 2017. Después de examinar los factores de riesgo de enfermedades cardiovasculares, se realizó una ecografía para medir CIMT. Finalmente, los datos se analizaron usando SPSS21 y métodos estadísticos apropiados.

La CIMT media en pacientes en diálisis (0,88 ± 0,16 mm) fue significativamente más alta que en los pacientes sin diálisis (0,69 ± 0,14 mm) (P <0,0001). La CIMT media en términos de sexo y tabaquismo fue estadísticamente significativa solo en pacientes sin diálisis (p = 0,025 y 0,028, respectivamente). Edad (P <0.0001, β = 0.004), sexo (P <0.027, β = 0.05), presión arterial sistólica (P = 0.024, P = 0.001) Índice de masa corporal (IMC) (P = 0.017, β = 0.005) y TG (P <0.0001, β = 0.002) se consideraron factores relacionados con CIMT. Además, la CRP (P <0.0001, β = 0.132), la hormona paratiroidea intacta (PTHi) (P <0.0001, β = 0.003) y el producto Ca-P (P = 0.023, P <0.001) 0 = β) fueron considerados por tener la mayor importancia entre la nueva generación de factores de riesgo asociados con CIMT. Los resultados mostraron que la CIMT media en pacientes en diálisis fue significativamente más alta que la de pacientes sin diálisis. Además, la edad, el sexo, la presión arterial sistólica, el IMC y el TG tenían una conexión directa con CIMT. El producto CRP, iPTH y Ca-P se identificaron como los factores de riesgo de nueva generación más importantes para CIMT.

Palabras clave: Ultrasonografía, enfermedades cardiovasculares, arteria carótida, capa íntima, capa de medios, hemodiálisis

Introduction

In previous studies, hyperlipidemia, hypertension and diabetes are considered as a risk factor for cardiovascular diseases[1]. In addition, aging and smoking are among other risk factors for these diseases[2]. In recent studies, serum phosphorus, iPTH, Ca-P product, CRP, and serum homocysteine are considered as new cardiovascular risk factors as well[3,6].

CIMT, measured by non-invasive ultrasonography, is now known as an alternative marker for atherosclerosis[7] i.e. IMT is generally known as a primary marker for atherosclerosis[8].

IMT is independent of other lesions created and this increase in thickness is seen in 70% of people over 60 years of age, which is the only clinical finding in 26% of the population. Prati et al. reported an increase in IMT as 4.9% in men and 11.7% in women in the general population[9].

IMT examination by ultrasonography is a non-invasive, precise, and practical way to detect atherosclerosis[10,11]. Moreover, it is considered for risk evaluation in primary prevention in clinical trials as an endpoint for cardiovascular events[12].

Studies have reported that increase in IMT is associated with an increased risk of ischemic stroke and coronary artery diseases[10,13].

Many researchers, including Jukka and Salonen, have stated the increase in CIMT as the primary form of atherosclerosis[14]. As the researchers have stated, increase in IMT has a high predictive value for future atherosclerosis[15]. Cross-sectional studies have suggested the relationship between IMT and cardiovascular risk factors and peripheral arteriosclerosis[16]. Recently, futuristic studies have suggested that an increase in CCIMT has connection with an increased risk of myocardial infarction[17,18]. Besides the results of the correlation between IMT and cardiovascular events, some studies have discussed the relationship between CIMT and cerebral and neurological complications. The 6-year study by O'Leary et al. evaluated the correlation between IMT and the risk of stroke and suggested that IMT increase had a significant relationship with an increased risk of cardiac infarction in patients without heart disease in the past[18].

Chronic kidney disease decreases the quality of life, and increases health costs and mortality[1,19]. Many CKD patients suffer from cardiovascular diseases at the same time[18,20]. Studies suggest that the risk of cardiovascular complications increases in the early stages of renal diseases. Moreover, the patients with CKD have an increased risk of cardiovascular disease like hyperlipidemia, hypertension, and diabetes (20).

Except in the very severe forms, Atherosclerosis is often asymptomatic, so a direct evaluation of the vessel wall in the early stages of the disease seems necessary. CIMT is known as a reliable and dependable index for atherosclerosis that favorably shows the correlation between cardiovascular risk factors in patients with CKD[21,22]. Atherosclerosis, which is the most common cause of mortality in patients with the end stage renal disease (ESRD), usually has good progression over the years before the symptoms start to reveal[23,24]. Studies have suggested that patients undergoing hemodialysis have significant arterial wall changes in the IMT of the carotid and femoral arteries[25].

Considering these, it is important to note that atherosclerosis is a systemic process and an increase in IMT could be as a predictor of the disease[26]. Furthermore, recent studies of CIMT and new risk factors for cardiovascular diseases state a direct correlation between serum phosphorus increase, calcium-phosphorus metabolism disorders, serum homocysteine, parathyroid hormone, and serum CRP with CIMT[27,3-6]. There are differences in the reported prevalence of predictive factors for CIMT in renal patients. Given this and for determining the effect of these factors on the disease process, as well as the lack of comprehensive studies on Iranian populations, we decided to study the relationship between the risk factors of cardiovascular diseases with increase in CIMT in patients with CKD undergoing hemodialysis referring to Razi Hospital and Caspian Dialysis Center of Rasht in 2017.

Methods: The study was designed as a case-control and the population included dialysis patients in dialysis unit of Razi Hospital and Caspian Dialysis Center of Rasht. The sampling method was gradual in the patients group. Thus, CIMT and other variables were measured in the patients who referred to the dialysis unit with the inclusion criteria and the consent to participate. With 95% level of confidence and 90% test power, in examining the bilateral statistical differences of the two hypotheses according to the sampling formula, 120 patients were studied in two groups of 60:

1. Case group: Patients with renal disease undergoing hemodialysis (the renal patients undergoing continuous hemodialysis for at least three months)

2. Control group: People without ESRD: the control group was selected from the patients admitted to Razi Hospital with available blood pressure information and included people with no known cardiovascular diseases and a normal electrocardiogram. The control group was selected from other units of the hospital and was similar in term of age to the case group.

The patients were ensured that their information would remain confidential and the results of the research would be published in general form of the data without mentioning the names or personal specifications. Furthermore, patients' consent was free of any coercion, threat, and seduction. Information about the implementation method, the purpose, the benefits, the nature and duration was presented to them, and their questions were given proper answers. The study costs were on the research group. After explaining the purpose of the study to the participants, if they were satisfied, they entered the research phase.

Blood pressure was measured by Mercury sphygmomanometer with a precision of 5 mm Hg on the right arm of the patients after five minutes of rest. Korotkoff phase was taken from 1 to 5 in systolic and diastolic pressures. Hypertension was defined based on jnc8 criterion: systolic blood pressure above 150mmHg and/or diastolic blood pressure above 90mmHg for patients more than or equal 60 years old, systolic blood pressure above 140 mmHg and/or diastolic blood pressure above 90 mmHg for patients less than 60 years old 3 times in one week intervals, or patients receiving antihypertensive medications. Diagnosis of the patients with renal disease and its introduction were done by a nephrologist and based on classified criteria.

Blood glucose, total cholesterol, HDL cholesterol, LDL cholesterol and triglyceride were recorded in both groups. The serum phosphate, serum CP, iPTH and CRP levels were recorded in dialysis patients. For determining the level of serum homocysteine, dialysis patients were referred to a specific laboratory to receive blood samples. The normal range of fasting blood glucose was considered 70-100 mg/dL, total cholesterol<200 mg/dL, HDL cholesterol 40-50 mg/dL, LDL cholesterol 100-129 mg/dL, triglyceride <100 milligrams G / dL, serum phosphorus 2.5-4.5 mg/dL, and CRP<1 mg/dL. The exclusion criteria were the patients with acute renal failure, as well as patients undergoing surgery or angioplasty in the carotid arteries.

Measuring IMT: IMT measurements were done by non-invasive ultrasound method at Razi Educational Treatment Center of Rasht. The study used an ultrasound and linear transducer with a frequency of 5-12 MHz. The sensitivity of the ultrasound device is up to 0.1 millimeters. One radiologist did all measurements. Patients were initially in supine position with their heads rotated 45 degrees to the contralateral side and B-mode scans was performed in transverse and longitudinal sections with proper movements of transducer to detect the three areas with the greatest thickness in the both sides including the internal carotid bulb area (0-20 mm after the location of the common carotid artery bifurcation), 0-20 mm before the common carotid bifurcation and also 20-60 mm before the bifurcation. After that, a high quality longitudinal image was obtained in the mentioned areas, the image was fixed, and to obtain a more accurate view in all patients, zoom was used by placing the measurement indicator electronically by the device. The largest IMT was measured at three points on the right and left sides. Finally, the average maximum IMT was calculated as the mean of the maximum IMTs in the above areas (a total of 6 measurements)[7,12,15,31]. Data were analyzed by SPSS 21. Chi-square test was used to compare qualitative variables and to determine the difference in ratios in two groups. Linear regression analysis was used to show the relationship between the main variable and the dependent variable. In addition, the significance level of the tests was P<0.05.

Results

The results showed that the age range of patients was 20-85. According to the data mentioned in Table 1, the mean age (P<0.0001), gender (P = 0.028), systolic blood pressure (P<0.0001), diastolic blood pressure (P<0.0001), hypertension (P<0.0001), HDL cholesterol (P<0.0001) and TG (P <0.0001), in patients (P <0.0001), total cholesterol level (P <0.0001), LDL cholesterol level (P<0.0001) had significant differences in dialysis and non-dialysis subjects. However, BMI (P = 0.160), diabetes (P = 0.648), history of CVA (P = 0.17) and smoking (P = 0.532) were not significantly different in two groups. The results also showed that the mean and standard deviation of CIMT in dialysis patients (0.88 ± 0.16 mm, with a median of 0.9 mm) compared to non-dialysis patients (0.69 ± 0.14 mm with a median of 0.7 mm) were more, and this difference was statistically significant based on Mann Whitney U test (P<0.0001) (Table 1).

Table 1: Comparison of CIMT in dialysis and non-dialysis subjects

Variable		Dialysis patients	Non-dialysis patients	P*
CIMT thickness	Mean	0.88	0.69	0.0001
	Standard deviation	0.16	0.14	
	Middle	0.90	0.70	
	25 percentile	0.80	0.60	
	75 percentile	1.00	0.80	

*P value, Mann Whitney u Test

According to Table 2, CIMT in dialysis (P=0.005) and non-dialysis (P=0.001) patients statistically has significant differences in terms of age group. Furthermore, the data in this table showed that gender differences of CIMT was statistically significant only in non-dialysis patients (P=0.028), which men had a higher mean CIMT than women. It should be noted that CIMT has not been significantly different regarding gender in dialysis patients. Moreover, the results indicated that CIMT was significantly related to smoking only in non-dialysis patients (P = 0.025), which CIMT has a higher mean in smokers than non-smokers. It is worth mentioning that CIMT was not significantly different regarding smoking in dialysis patients. CIMT was not significantly different regarding diabetes, history of CVA and BMI in dialysis and non-dialysis patients (P>0.05) (Table 2).

Table 2: Comparison of CIMT regarding demographic characteristics and underlying diseases in dialysis and non-dialysis subjects

Variable		CIMT thickness					
		Dialysis patients		P	Non-dialysis patients		
		Mean	SD		Mean	SD	P
Age group	50 years≥	0.78	0.17	0.005*	0.53	0.11	0.001*
	51-60	0.94	0.14		0.67	0.13	
	60 ≤	0.92	0.13		0.76	0.11	
Gender	Female	0.90	0.17	0.506	0.64	0.17	0.028*
	Man	0.87	0.15		0.73	0.11	
Hypertension	No	0.94	0.14	0.286	0.69	0.12	0.821
	Yes	0.88	0.16		0.69	0.19	
BMI	underweight	0.91	0.12	0.359	0.69	0.25	0.839
	Normal	0.86	0.18		0.68	0.13	
	Overweight	0.89	0.13		0.71	0.18	
	Obese	0.91	0.17		0.70	0.19	
Diabetes	No	0.89	0.17	0.575	0.69	0.12	0.954
	Yes	0.87	0.13		0.69	0.22	
CVA history	No	0.88	0.16	0.184	0.70	0.15	0.524
	Yes	0.96	0.05		0.65	0.00	
Smoking history	No	0.90	0.15	0.189	0.67	0.15	0.025
	Yes	0.84	0.17		0.76	0.07	

*P value

The results of Table 3 showed that in dialysis patients, CIMT was significantly correlated with age (r = 0.285, r = 0.002), systolic blood pressure (r = 0.361, P = 0.0001), diastolic blood pressure (r=0.391, P= 0.0001), total cholesterol level (r = 0.795, P = 0.0001), LDL (r = 0.822, P = 0.0001), HDL (r = 0.769, r = 0.0001)) and blood TG level (r = 0.762, P<0.0001). This correlation was significant in dialysis patients, except for systolic blood pressure with no significant correlation with CIMT. (r = 0.216, P=0.097 (Table 3).

Table 3: Correlation between CIMT and quantitative variables in dialysis patients

Dialysis subjects		CIMT thickness
Age	r	0.285
	P	0.002
Systolic blood pressure	r	0.361
	P	0.0001
Diastolic blood pressure	r	0.391
	P	0.0001
BMI	r	-0.20
	P	0.829
Total blood cholesterol level	r	0.795
	P	0.0001
Cholesterol level (LDL)	r	0.822
	P	0.0001
Blood Cholesterol Level (HDL)	r	-0.769
	P	0.0001
Blood triglyceride	r	0.762
	P	0.0001
Duration of dialysis	r	00.40
	P	0.763
Phosphorus	r	0.595
	P	0.000
Calcium serum	r	0.629
	P	0.000
CRP	r	0.969
	P	0.000

*Correlation Coefficient
**P value

According to Table 4, in the correlation analysis of quantitative variables with CIMT, by Spearman correlation coefficient, it was found that age (r = 0.632, P<0.0001), total cholesterol level (r =0.852, P =0.0001), LDL (r = 0.723, r = 0.0001), HDL (r = 0.630, P=0.0001) and TG level (r = 0.446, P = 0.0001) were significantly correlated with CIMT in non-dialysis patients. Based on the correlation coefficient, the absolute value of the correlation coefficient between 0 and 0.25 was very weak, from 0.26 to 0.49 weak, from 0.5 to 0.69 average, from 0.7 to 0.89 high, and from 0.9 to 1 is very high.

Table 4: Correlation between CIMT and quantitative variables in non-dialysis patients

Non-dialysis patients		CIMT thickness
Age	r	0.632
	P	0.0001
Systolic blood pressure	r	-0.164
	P	0.211
Diastolic blood pressure	r	-0.015
	P	0.908
BMI	r	-0.143
	P	0.275
Total blood cholesterol level	r	0.582
	P	0.0001
Cholesterol level (LDL)	r	0.723
	P	0.0001
Blood Cholesterol Level (HDL)	r	-0.630
	P	0.0001
Blood triglyceride	r	0.466
	P	0.0001

*Correlation Coefficient
**P value

The results of stepwise multiple linear-regression analysis showed that in the matched model, non-dialysis patients had a lower CIMT compared to dialysis patients: on average, 0.113 ± 0.034 mm less than CIMT (P = 0.001, β = 0.05). It should be noted that in addition to dialysis in multiple analysis, age (P = 0.0001, β = 0.004), gender (P = 0.027, β = 0.05), systolic blood pressure (P=0.024, β=0.001), BMI (P = 0.017, P = 0.005) and TG (P = 0.0001, β = 0.002) were also considered as other factors related to CIMT (Table 5).

Table 5: Multiple linear regression model to examine the relationship between CIMT with dialysis by modulating the effects of individual variables, background and lipid profiles

Model	Unstandardized Coefficients		P	0.95% Confidence Interval for B	
	B	Std. Error		Min.	Max.
(Constant)	-0.013	156	0.935	-0321	0.295
Non-dialysis patients compared to patients with dialysis	-0.113	0.034	0.001	-0.180	-0.45
Age	0.004	0.001	0.0001	0.003	0.006
Gender (Men to Women)	0.050	0.022	0.027	0.006	0.095
Systole	0.001	0.001	0.024	0.000	0.002
BMI	0.005	0.002	0.0117	0.001	0.008
Blood triglyceride	0.002	0.000	0.0001	0.001	0.003
CIMT: Dependent variable					

*P value

Multiple stepwise-regressions were used to determine the relationship between new generation risk factors in dialysis patients (Table 6). In the final model, CRP (P <0.0001, β = 0.132), iPTH (P<0.0001, β = 0.003) and Ca-P product (β = 0.001, P = 0.023) were the most important new generation factors associated with CIMT (Table 6).

Table 6: Multiple stepwise linear-regression for determining the relationship between new generation risk factors in the dialysis group

Model	Unstandardized Coefficients		P	95.0% Confidence Interval for B	
	B	Std. Error		Min.	Max.
(Constant)	0.234	0.025	0.000	0.183	0.284
CRP	0.132	0.009	0.0001	0.114	0.151
iPTH	-0.003	0.001	0.0001	-0.004	-0.001
Ca.P Product	0.001	0.001	0.023	0.000	0.003
CIMT: Dependent variable					

*P value

Discussion and conclusion: Today, it is believed that coronary artery and atherosclerosis diseases are in fact a chronic inflammatory process, which are more likely to be seen in hemodialysis patients due to their specific conditions, like trauma to the large vessels of the organs and electrolyte disorder[28]. Researchers have focused on the study of arterial structures, especially carotid arteries using non-invasive methods like ultrasonography as a predictor of cardiovascular disease[29,30]. Studies have shown that the increase in the thickness of Intima-Media layer of the carotid arteries is directly related to cardiovascular and cerebrovascular events. Furthermore, it seems that measured thickness of this carotid artery layer is a prognostic factor for cerebrovascular and cardiovacular diseases. Although this increase can be influenced by various factors, and since cardiovascular diseases are of the most important causes of mortality in patients with dialysis, more examination in dialysis patients seems crucial.

In the present study, mean CIMT in dialysis patients was significantly higher compared to non-dialysis patients. In line with the present study, Shakeri et al also suggested that the mean of CCIMT in hemodialysis patients was significantly higher compared to the healthy subjects[31]. In the study by Prasad et al., CIMT in patients with ESRD under peritoneal dialysis was significantly higher in control group compared with those with normal renal function[32]. Differences in the reported values of CIMT in various studies may be due to defects such improper matching of the control group with the patients, IMT reading errors, and insufficient number patients. However, the results of the present and other studies mentioned vividly indicate a higher CIMT in ESRD patients compared with healthy subjects. As hemodialysis patients are vulnerability to cardiovascular disease and atherosclerosis is the most common cause of death in ESRD patients, higher CIMT in hemodialysis patients can be because of higher incidence of atherosclerosis in these patients. It is worth noting that despite significant progress in recognizing the pathophysiology of atherosclerosis in patients with CKD, its exact mechanism is not known yet.

In recent years, serum phosphorus, iPTH, Ca-P product and CRP have been stated as new risk factors for cardiovascular disease. In addition, new studies have shown that cumulative intake of calcium-containing phosphate and vitamin D-containing product is associated with IMT in ESRD patients[3-6]. In this study, CRP, iPTH and Ca-P product were the most important new generation factors associated with CIMT. In the study by Ossareh et al., there was no correlation between CIMT and serum calcium, serum phosphorus, Ca-P product, PTH level, or total calcium or calcitriol administered during hemodialysis[33]. This lack of correlation was also reported in the study by Szeto et al. However, some authors reported a positive relationship between IMT and Ca-P product, or cumulative consumption of calcium, with phosphate receptors and vitamin A-containing products[34]. On the other hand, some studies have suggested that homocysteinemia is also related to CIMT[35] independently and positively, but this conclusion was not attained in our study. These contradictory results also reveal the need for more extensive studies in this regard. On the other hand, in different studies, the correlation between CIMT and inflammation has been reported in hemodialysis patients, as healthy people. Zoccali et al. found a strong correlation between asymmetric dimethylarginine and CRP in hemodialysis patients, and they identified the two as the only predictors of intimal

lesions progression[36]. In the study by Ossareh et al., CRP-positive patients had a higher CIMT, which is able to justify the correlation between inflammation and CIMT[33].

In the present study, mean CIMT in all patients - dialysis and non-dialysis - in older age groups was significantly higher compared to those in younger age groups. Additionally, mean CIMT in all patients had a positive and significant correlation with age. Furthermore, in multiple analyses, age was considered to be correlated to CIMT. Like ours, in the study of Sami Moghadam, the mean age in hemodialysis patients with higher CIMT was significantly more compared to those with low CIMT[37]. In addition, in the study of Patel et al., a significant correlation was found between age and CIMT. Increasing age naturally increases the relative thickness of the carotid artery due to the effect of different factors. Moreover, in some studies, the correlation is shown between the number of atherosclerotic plaques and the age of dialysis patients. In addition, with aging, the possibility of vascular endothelial degeneration increases due to factors like increased blood pressure, oxidative stress, and hyperglycemia. Hence, the relationship between CIMT and age of patients can be indicative of progression of atherosclerotic changes following age.

In addition, in the present study men had significantly higher mean CIMT compared to women, only in non-dialysis patients. In multiple analyses, gender was considered to be related to CIMT. Ossareh et al., found a significant difference in CIMT between men and women undergoing hemodialysis, which was significantly higher in men than in women[33]. In a study, Marcos et al. show that being male is a factor associated with CIMT[38]. Lower CIMT in women was previously reported in patients with coronary artery disease. Studies have suggested that the incidence of atherosclerosis is higher in men, and the cause is still not completely determined, but lower estrogen levels in men's circulation, with a role in vasodilatation, can explain this.

In the present study, CIMT was significantly more in non-smokers non-dialysis patients compared with smokers. In this regard, in Szeto et al., as in the present study, CIMT in non-dialysis patients was significantly correlated with smoking[34]. In Dzitoeva et al., it was also shown that non-dialysis patients with a history of smoking have a higher CIMT compared to other patients[39]. On the other hand, Hojas et al. found no correlation between smoking and CIMT in hemodialysis patients[40]. As in many studies, smoking is one of the risk factors for atherosclerosis and cardiovascular disease; it is natural that smokers have a higher CIMT compared to others.

In this study, CIMT in terms of diabetes and BMI were not significantly different in all patients, including dialysis and non-dialysis ones, while independently, BMI was considered to be related to CIMT. In the study by Sami, diabetes was not correlated with CIMT-related factors in hemodialysis patients as in the present study[37]. In the study by Rosvall et al., this correlation was not reported[41]. Nonetheless, in Sanchez-Alvarez et al., diabetes mellitus was one of the risk factors for atherosclerosis in hemodialysis patients[42]. These contradictory results show the need for more studies to examine the relationship between CIMT and diabetes. In many studies, such as Singh et al., obesity is proposed as one of the factors associated with CIMT[43]. These results confirm that metabolic changes in overweight individuals ultimately lead to events in the body that accelerate the process of atherosclerosis and, the development of cardiovascular disease, consequently.

Moreover, in many studies, hypertension is one of the risk factors for atherosclerosis in people with CKD[44]. In the present study, CIMT was statistically significant in all patients given the presence of hypertension, so that people with hypertension had more CIMT. Additionally, in all patients, CIMT had a significant correlation with systolic and diastolic blood pressure and systolic blood pressure was a factor correlated with CIMT. Patel et al. found a positive correlation between CIMT and systolic and diastolic blood pressure[45]. Furthermore, Ossareh found a positive correlation between CIMT and mean blood pressure before dialysis[33].

In the present study, CIMT had a significant correlation with total cholesterol, LDL, HDL and blood TG levels in all patients, and TG was considered as a factor correlated with CIMT. In various studies, hypercholesterolemia is considered as one of the risk factors for atherosclerosis in patients with CKD. Patel found a positive correlation between CIMT and levels of LDL and HDL[45]. Ossareh discovered a positive correlation between CIMT and serum cholesterol levels[33]. In addition, Prasad et al. reported total cholesterol and triglyceride to be higher in peritoneal dialysis patients than the control group[32].

Overall, the results showed that CIMT in dialysis patients was significantly higher than non-dialysis patients and its value is correlated with age, diastolic blood pressure, total cholesterol, LDL, HDL, and TG levels in dialysis patients. Furthermore, age, gender, systolic blood pressure, BMI and TG were considered as factors correlated with CIMT. CRP, iPTH and Ca-P product were among the most important new-generation risk factors for CIMT. Given the limited studies for examining the relationship between the risk factors of cardiovascular disease and the carotid intima-media thickness in hemodialysis patients, we suggest that more studies should be conducted with more sample size and in multiple treatment centers for confirmation of the results obtained. In addition, we suggest that cervical CIMT examination by color Doppler ultrasonography should be performed in dialysis patients to determine the early cardiovascular complications and control the risk factors leading to it. Additionally, a study entitled CIMT evaluation based on dialysis type, separately for peritoneal dialysis and hemodialysis, is suggested.

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