

Prognostic value of carotid intima media thickness and wall plaques in haemodialysis patients

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ABSTRACT

Introduction: Cardiovascular disease and other complications of atherosclerosis are the most common cause of death in patients with chronic renal failure in maintenance hemodialysis (MHD). Carotid ultrasonography is a simple non-invasive tool to investigate the vascular system, by means of intima media thickness (IMT) measurement and carotid wall calcifications. **Objective:** To determine IMT and the presence of plaques, and their possible clinical relationships; finally we tried to investigate whether they would predict cardiovascular morbidity and mortality in patients in MHD. **Methods:** We studied 60 MHD patients (age 68 ± 13 years, 48% male, 50% diabetics, time on MHD 32 ± 11 months) and a control group of 274 people matched for age and sex. Follow-up period was 66 ± 13 months. **Measurements:** Demographic and clinical data, serum levels of homocysteine (tHcy), folic acid (FA) and B6 and B12 vitamins. IMT was measured by high-resolution B-mode ultrasonography. **Results:** IMT was higher in MHD patients than in those in the control group (0.947 ± 0.308 vs 0.619 ± 0.176 mm; $p < 0.001$). IMT was related with age ($r = 0.268$; $p = 0.038$), diabetic ($r = 0.650$; $p < 0.001$) and hypertensive condition ($r = 0.333$; $p = 0.012$), but not with lipids, tHcy or FA. Patients who suffered from coronary artery disease, peripheral artery disease or stroke had higher IMT than those without those events (1.156 ± 0.371 vs 0.875 ± 0.285 mm; $p < 0.001$; 1.205 ± 0.374 vs 0.911 ± 0.231 mm; $p = 0.007$; 1.195 ± 0.264 vs 0.844 ± 0.251 ; $p < 0.001$ respectively). Something similar occurred with the presence of plaques. During the follow-up period 36 patients died

(60%), 67% of them due to cardiovascular causes. IMT was higher in patients who died than those who survived (1.020 ± 0.264 vs 0.858 ± 0.334 mm; $p = 0.044$). The survival rate during the observation period was significantly lower in the final IMT fourth (20%) than in the first (72%) ($p = 0.014$). The presence of carotid plaques was an independent predictor of cardiovascular mortality. **Conclusions:** These findings suggest that measurement of carotid IMT and the presence of wall plaques are useful tools to predict cardiovascular events and mortality in patients in MHD.

Key Words: Hemodialysis, Cardiovascular disease, Mortality, Intima-media thickness, Carotid plaques.

La ecografía carotídea es útil para predecir enfermedad coronaria y mortalidad en pacientes en hemodiálisis

RESUMEN

Introducción: La enfermedad cardiovascular es la principal causa de muerte en los pacientes urémicos en hemodiálisis (HD). La ecografía carotídea es una herramienta sencilla y no invasiva para conocer el estado aterosclerótico de los pacientes. **Objetivo:** Conocer las asociaciones clínicas del grosor íntima-media carotídeo (GIM) y de la placa carotídea y su valor predictivo sobre el riesgo de enfermedad coronaria y la mortalidad. **Metodología:** Estudio prospectivo en el que se incluyeron 60 pacientes estables en HD (68 ± 13 años, 48% hombres, 50% diabéticos, tiempo en HD de 32 ± 11 meses) y 274 controles, semejantes en edad y sexo. El período de seguimiento fue de 66 ± 13 meses. **Determinaciones:** Datos demográficos y clínicos, analítica general y niveles séricos de homocisteína y folato. Se midió el GIM mediante ecocardiografía 2D. Resulta-

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dos: El GIM fue mayor en los pacientes en HD que en el grupo control ($0,947 \pm 0,308$ frente a $0,619 \pm 0,176$ mm; $p < 0,001$). El GIM se correlacionó con la edad ($r = 0,268$; $p = 0,038$), con la condición de diabético ($r = 0,650$; $p < 0,001$) y la de hipertenso ($r = 0,333$; $p = 0,012$), pero no con colesterol total, HDL, LDL, triglicéridos, homocisteína o folato. Los pacientes con enfermedad coronaria, enfermedad vascular periférica o ictus tenían un GIM mayor que los que no presentaban dichas afecciones ($1,156 \pm 0,371$ frente a $0,875 \pm 0,285$ mm; $p < 0,001$; $1,205 \pm 0,374$ frente a $0,911 \pm 0,231$ mm; $p = 0,007$; $1,195 \pm 0,264$ frente a $0,844 \pm 0,251$; $p < 0,001$, respectivamente). Se encontraron datos similares respecto a la presencia de placas en la pared carotídea. Durante el período de seguimiento fallecieron 36 pacientes, 24 de los cuales (67%) por causa cardiovascular, cuyo GIM fue mayor ($1,020 \pm 0,264$ frente a $0,858 \pm 0,334$ mm; $p = 0,044$). La supervivencia a la finalización del período de estudio fue significativamente mejor en el cuartil inferior de GIM (72%) que en el superior (20%). La presencia de placas carotídeas fue predictor independiente de mortalidad cardiovascular. Conclusiones: El GIM y la presencia de placas carotídeas se relacionan con algunos de los factores clásicos de riesgo cardiovascular como la edad, la diabetes o la hipertensión en pacientes urémicos. Su medición es útil para predecir la enfermedad coronaria y la mortalidad a largo plazo en los paciente urémicos.

Palabras clave: Hemodiálisis, Enfermedad cardiovascular, Mortalidad, Grosor íntima-media carotídeo, Placas carotídeas.

INTRODUCTION

The risk of mortality from cardiovascular causes is significantly increased in patients with advanced chronic kidney disease (CKD) on haemodialysis (HD). When compared to the general population, dialysis patients have approximately 10 times higher risk of dying from heart disease.¹ Cardiovascular disease (CVD) and CKD share certain important risk factors.² Furthermore, CKD is an independent risk factor for the development of CVD.³ Patients on HD have significant changes in the structure of their arterial walls, as shown by the increase in intima-media thickness (IMT) in the carotid and femoral arteries.⁴ Epidemiological studies have demonstrated that the increase in IMT augments the risk of suffering an acute myocardial infarction or ischemic stroke in the general population.⁵ Furthermore, these structural changes in the arterial wall are predictors of cardiovascular mortality in the non-uremic population⁶ and in patients on HD.⁷ Other studies propose that measuring the diameter of carotid plaques has better predictive value than IMT for cardiovascular events.⁸

Some authors have observed that the increase in IMT is already appreciable in the predialysis stage⁹ and that it is

uraemia rather than the classic cardiovascular risk factors that is the independent predictor of IMT.¹⁰

The main objective of this work is to examine the clinical importance of measuring the IMT and analyzing the presence and characteristics of carotid plaques in the development of CVD and related mortality. We also attempt to study the possible correlations between IMT and the presence of plaques with other cardiovascular risk factors.

MATERIALS AND METHODS

Patients

The study population was selected for a separate study that we published previously.¹¹ For this work, all of the patients on an HD program at a single health centre were evaluated. The dialysis prescription was 12-13.5 hours per week, with tri-weekly modality and a prescribed 65% reduction in urea using a polysulfone F8 dialyzer (Fresenius, Bad Homburg, Germany).

Inclusion criteria were: patients of both sexes, more than 18 years old, clinically stable (defined as an absence of complications requiring hospitalization in the last 3 months, except for instances related to vascular access dysfunction) and with more than 6 months on the HD program.

Exclusion criteria for the study consisted of a poor history of compliance with treatment and medical indications.

A detailed clinical history was performed for each patient, along with a physical exam, after procuring a written consent form for participation in the study.

Control group

A group of 276 healthy volunteers were selected (similar in age and sex to the study group) in order to obtain control values for IMT, homocysteine, folic acid, vitamin B₁₂, and the presence of plaques.

Biochemical tests

Blood samples were taken at the start of the HD session from the middle of the week. They were taken from the arterial puncture of the fistula or from the arterial line in cases employing a catheter for vascular access. The general analysis was performed by an auto-analyzer using systematic techniques. iPTH values were determined using the immunoradiometric method, considering normal values to be those between 10 and 65 pg/ml. Folate and vitamin B₁₂ levels were determined simultaneously using radiometric methods

(SPNB, Dualcount Folic Acid/Vitamin B₁₂ in-vitro Diagnostic Test Kit, Diagnostic Products Corporation, Los Angeles, California, USA); normal reference values for the folate test were between 3.0 and 17.0 nmol/l, and for vitamin B₁₂: 200-950 pmol/l. Vitamin B₆ was measured by radioenzymatic methods (reference values: 20-160 nmol/l).

Total homocysteine values (a sum of the free form and the protein-bonded form) were measured using a fluorescent polarization immunoanalysis (IMX, Abbot Diagnostics, Abbot Park, IL, USA).

Methylenetetrahydrofolate reductase (MTHFR) genotype

The patient's DNA was subjected to two allele-specific amplifications using polymerase chain reaction (PCR), with one common oligonucleotide and another specific for either the Ala223 allele or the Val223 allele. The primers were designed from a sequence deposited in GenBank (U09806).

Carotid wall evaluation

The common left and right carotid arteries were studied using a 7.5 MHz linear transducer with a high-resolution b-mode ultrasound (Aloka, Tokyo, Japan). This apparatus is capable of detecting 0.1 mm changes in arterial wall thickness. In order to perform these measurements, we used the technique described by Bots.¹² The subjects were placed in supine position with the head rotated contralaterally against the carotid being examined. All measurements were made by the same researcher. The IMT was defined as the distance between the innermost refractive line of the vessel (corresponding to the arterial lumen-intima interface) and the next echogenic line outside the previous one (corresponding to the media-adventitia interface). All measurements were performed within 0.5 to 1 cm of the carotid bulb in the proximal arterial wall. In order to ensure the reproducibility of the measurements, the mean value of three measurements was considered. The intraobserver coefficient of variance was 5% (mean difference of 0.01 mm). The interobserver coefficient of variation was 8.3% when comparing the measurements made in healthy subjects (control group). A carotid plaque was defined as the existence of a minimum IMT increase of 50% in relation to the contiguous vascular wall.¹³

Follow-up period

The patients were observed for a mean time of 66 ± 13 months after the initial measurements, using ultrasound and laboratory tests. No data were lost for any of the patients. All causes of patient mortality were recorded. Derivatives of acute myocardial infarction, congestive heart failure, and

ischemic stroke were all placed in the category of death due to cardiovascular causes.

Statistical analysis

Continuous variables were expressed as a mean and standard deviation, and categorical values as a percentage. Initial values were compared using T and Chi-square tests as appropriate. The Kolmogorov-Smirnov test had been previously applied in order to verify a normal distribution of the data.

We used the Pearson's *r* coefficient for univariate correlations. For the survival study, we used the Kaplan-Meier test, using the logarithmic range test in order to compare curves. The relative risks of the different parameters under study were estimated using the Cox proportional model. Relative risk and its confidence interval (95%) were calculated using estimated regression coefficients and standard errors in the Cox regression analysis. We used the SPSS 13.0 statistical package for Windows (SPSS Inc., Chicago, IL, USA) for the analysis of the results.

RESULTS

In the end, 60 patients were included in the study. The characteristics of the study population and control groups are summarized in Table 1.

IMT was higher in the population on dialysis than in the control population (0.947 ± 0.308 vs. 0.619 ± 0.176 mm; *p* < 0.001). Considering that an increase in IMT greater than 0.9 mm is a marker for generalized atherosclerosis,¹⁴ 43.3% of our patients suffered this condition, while it is only present in 3.2% of the control subjects (*p* < 0.001).

In our study group, IMT was correlated with age (*r* = 0.268; *p* = 0.038), diabetic condition (*r* = 0.650; *p* < 0.001), and hypertension (*r* = 0.333, *p* = 0.012), but not with other cardiovascular risk factors, such as total cholesterol, HDL cholesterol, LDL cholesterol, triglycerides, smoking, homocysteine, and folate, except for iPTH, although this was inversely related (*r* = -0.400; *p* = 0.002). Nor was it related to albumin levels or length of time on HD. In the multivariate analysis, we observed that only age (*b* = 0.226; *p* = 0.030) and diabetic condition (*b* = 0.553; *p* < 0.001) remained in the equation.

Similar findings to the IMT results were found in the evaluation of the presence or absence of carotid plaques. We detected carotid plaques in 68% of patient subjects and in 1.8% of control subjects (*p* < 0.001). This finding was also associated with age (*r* = 0.247; *p* = 0.042), diabetic condition

Table 1. Characteristics of the study and control groups

	Patients	Controls	p
N	60	276	
Age (years)	68 ± 13	66 ± 12	
Men (%)	48	50	
Diabetics (%)	50		
HTA (%)	87		
Hcys (̑mol/l)	32.4 ± 8.9	12.9 ± 7.2	<0.001
Folic Acid (nmol/l)	7.74 ± 7.3	5.2 ± 4.12	<0.001
B12 (pmol/l)	546.6 ± 222	436.2 ± 189	<0.001
Cholesterol (mg/dl)	184.4 ± 35.2		
HDL (mg/dl)	35.7 ± 8.4		
LDL (mg/dl)	108.1 ± 25.8		
Tryglicerides (mg/dl)	187.0 ± 35.2		
iPTH (pg/ml)	229.8 ± 304.8		

($r = 0.642$; $p < 0.001$) hypertension ($r = 0.365$; $p = 0.004$), LDL cholesterol levels ($r = -0.280$; $p = 0.031$) and inversely with PTH ($r = -0.405$; $p = 0.001$). Again, in the multivariate analysis, only age ($b = 0.245$; $p = 0.027$) and diabetic condition remained in the equation ($b = 0.512$; $p < 0.001$).

Patients with an unfavourable genotype for MTHFR did not have greater IMT, nor did they present plaques more frequently than those with favourable genotypes, although given the small sample size (only 7 patients had the unfavourable genotype), we cannot extract reliable conclusions.

Intima-media thickness and cardiovascular events

We found higher IMT in those patients that had previously had some type of cardiovascular event than in patients that

had not. Therefore, IMT was highest in those patients with chronic ischemic heart disease ($1.15 ± 0.28$ vs. $0.87 ± 0.28$; $p < 0.001$), ischemic stroke ($1.20 ± 0.37$ vs. $0.91 ± 0.27$; $p = 0.007$) or peripheral vascular disease ($1.20 ± 0.27$ vs. $0.84 ± 0.25$; $p = 0.001$). The presence of carotid plaques was also higher in this group (83 vs. 48%; $p = 0.010$; 79 vs. 50%; $p = 0.025$, and 89 vs. 53%; $p = 0.045$, respectively). There were no differences in patients with or without a history of heart failure in relation to IMT or the presence of carotid plaques.

Survival study

During the follow-up period, 36 patients died (60% of the total); 24 of these deaths were due to cardiovascular events. Table 2 summarizes the characteristics of the two groups: survivors and deceased (from any cause).

Table 2. Characteristics of surviving and deceased patients (due to any cause)

	Survivors	Deceased	p
N	24	36	
Age (years)	61 ± 14	72 ± 10	0.001
Men (%)	48	50	NS
Diabetics (%)	42	55	NS
HTA (%)	86	87	NS
Hcys (̑mol/l)	32.2 ± 8.7	32.5 ± 9.2	NS
Folic Acid (nmol/l)	7.74 ± 7.3	8.5 ± 9.0	NS
B12 (pmol/l)	515 ± 169	568 ± 251	NS
B6 (nmol/l)	25.9 ± 22.4	37.7 ± 61	NS
Cholesterol (mg/dl)	178 ± 35	188 ± 35	NS
HDL (mg/dl)	34 ± 8	37 ± 8	NS
LDL (mg/dl)	103 ± 25	111 ± 26	NS
TG (mg/dl)	178 ± 68	193 ± 82	NS
Albumin (g/dl)	4.6 ± 0.19	3.92 ± 0.28	0.028
TPI	255 ± 260	213 ± 333	NS
Time on HD (months)	58 ± 36	65 ± 35	NS
IMT (mm)	0.86 ± 0.34	1.02 ± 0.27	0.044
Carotid plaques (%)	42	69	0.031

Table 3. Univariate and multivariate analyses of death from cardiovascular causes and in general

		RR	95 % CI	p
Univariate Analysis				
Mortality from any cause				
- Age	1 year	1.044	1.008-1.081	0.016
- Albumin	1 g/dl	0.265	0.087-0.808	0.020
- Total cholesterol	1 mg/dl	1.016	1.005-1.027	0.003
Cardiovascular mortality				
- Age	1 year	1.042	1.011-1.087	0.039
- Plaques	Yes	3.331	1.142-9.718	0.028
- Albumin	1 g/dl	0.244	0.060-0.988	0.044
- Total cholesterol	1 mg/dl	1.016	1.003-1.029	0.018
Multivariate analysis				
Mortality from any cause				
- Age	1 year	1.034	1.005-1.069	0.028
- Albumin	1 g/dl	0.221	0.096-0.794	0.022
Cardiovascular mortality				
- Age	1 year	1.024	1.004-1.067	0.041
- Plaques	Yes	2.915	1.222-8.323	0.032
- Albumin	1 g/dl	0.234	0.084-0.990	0.046

The group of deceased patients had a more advanced age ($p = 0,001$) and less albumin ($p = 0,028$), not finding any differences between the diabetic or hipertensive condition or other cardiovascular risk factors (homocistein, folate or lipids). The IMT was greater in deceased patients than in alive patients ($1,02 \pm 0,27$ vs $0,86 \pm 0,34$; $p = 0,044$) and this happened for diabetic and non-diabetic patients. The percentage of patients with carotid plaques was greater among the deceased individuals.

By comparing the deceased patients from cardiovascular events with those who died from other causes, we observed that the first group had more frequently diabetes mellitus (76 vs. 10%; $p < 0,001$), arterial hypertension (96 vs. 63%; $p = 0,023$), greater IMT ($1,09 \pm 0,27$ vs. $0,85 \pm 0,18$; $p = 0,011$) and carotid plaques (80 vs. 45%; $p = 0,045$).

By dividing the patients into quartiles based on IMT, we analyzed survival and found that it was significantly lower in the 4th quartile (20%, IMT $> 1,20$ mm) compared to the first (80%, IMT $< 0,67$ mm; $p = 0,014$). And, if we only analyze those patients who died from cardiovascular causes, this significance increases to $p = 0,004$ (8 vs. 79%). This circumstance occurred both in diabetic and non-diabetic patients when analyzed separately.

The Cox univariate regression analysis (Table 3) demonstrated that age, albumin, and total cholesterol were all related to mortality from any cause. Limiting the analysis to just cardiovascular mortality, age, albumin, and cholesterol are accompanied by the presence of a carotid plaque as predictive parameters. IMT had no correlation with any type of death.

In the multivariate analysis, age and albumin were independent predictors of mortality from any cause, and these factors, along with the presence of carotid plaques, were predictors for cardiovascular mortality.

DISCUSSION

Carotid IMT is higher in patients on HD than in the general population. Furthermore, those patients who have presented cardiovascular events have a still higher IMT. Carotid plaques are also more frequent in these individuals. Both parameters were higher in our deceased patients, making carotid plaques an independent predictor of cardiovascular-caused mortality.

Increased IMT is considered to be a marker of atherosclerotic changes,¹⁴ reflecting remodelling processes of the vascular wall. In the general population, IMT is related to other cardiovascular risk factors such as arterial hypertension, diabetes, dyslipidemia, and smoking.¹⁵ Furthermore, increased IMT can facilitate an ischemic stroke or coronary syndrome.^{5,16} Our uremic study group on HD had significantly higher IMT than the general population, with significantly elevated levels in patients who died during the course of the study. IMT in our patients was markedly higher than in other studies, which could be due to the fact that half of the patients were diabetics, which is a much higher proportion than in the other studies.

We found no correlation between IMT and other cardiovascular risk factors except for diabetes mellitus,

arterial hypertension, and PTH. Similar data were found regarding the presence or absence of carotid plaques.

The progressive increase in IMT can start its development in the pre-dialysis stage. Therefore, Preston¹⁴ suggested that changes in the arterial wall start in the early stages of CKD and that it is associated with traditional cardiovascular risk factors, such as LDL and HDL levels, hypothesizing on the positive effect of statins on IMT. This could be the reason that IMT was not correlated to the length of time on the HD program in our patients nor in other studies.⁷ Our work also confirms that serum LDL cholesterol levels can be determining factors in IMT,¹⁸ although this relationship was not seen with other cardiovascular risk factors such as smoking.

The inverse relationship between IMT and PTH was an interesting result. The progression of atherosclerosis has frequently been related to hyperparathyroidism. Ronstand¹⁹ described the different mechanisms by which this could occur: increased lipid deposits in the vascular wall, proliferation of smooth muscle cells, calcification, etc. following an analysis of the medical literature on the subject. However, some authors have found no relationship between the progression of atherosclerosis as measured by carotid ultrasound and PTH in patients with primary hyperparathyroidism.²⁰ Finally, other results have shown that hyperparathyroidism favours vascular calcifications in diabetic patients starting HD.²¹ In our group of patients, we found that PTH was lower in those with higher IMT and carotid plaque levels. Furthermore, the analysis of diabetic patients compared to non-diabetic patients showed that PTH was significantly lower in diabetics (103.2 vs. 356.2 pg/ml; $p = 0.001$), which justifies these findings. Diabetic patients have also been shown to suffer frequently from adynamic bone disease, which favours the processes of atherosclerosis and vascular calcification.

With respect to the presence of carotid plaques, less has been discussed on their prevalence and related factors. In general, as occurred also in our patients, the presence of plaques is described in over 60% of uremic patients,²²⁻²⁵ with the exception of the study by Savage,²⁶ who observed this condition in only 12% of patients (as we have mentioned, this study was carried out with young patients with little prevalence of diabetes). The association with other cardiovascular risk factors is frequent. As in the study by Malatino,²⁷ we found no correlation with albumin levels, a circumstance negatively described by Savage.²⁶

IMT is higher in patients who have suffered cardiovascular events. The presence of plaques is also more frequent in this population. An increase in IMT is an independent predictor for the appearance of cardiovascular events, such as ischemic stroke and coronary syndromes^{5,16} in the general population. We found that patients with higher IMT or

carotid plaques suffered more frequently from cardiovascular events, ischemic strokes, and coronary syndromes, which favours the assumption that changes observed in the carotid artery can be extrapolated to other areas of the circulatory system. Brzosko²⁸ made similar findings upon analyzing IMT in 21 patients on HD during a 40-month study.

In the general population, the presence of carotid plaques predicts the appearance of cardiovascular events.^{29,30} However, in the population on haemodialysis, it appears that the relationship is not so clear. Some authors have related the appearance of cardiovascular events with the sum of the thickness of all plaques found,³¹ others with the sum and bilateral location of all plaques found,³² and finally, others propose diverse scores based on the number of plaques or possible calcification.²⁵ We found this relationship by analyzing the presence or absence of plaques. Maeda³³ performed a similar analysis with comparable results.

Some controversy exists on the possible relationship between survival and carotid IMT or the measurement of arterial elasticity as evaluated by the wavelength of the patient's pulse. Blancher³⁴ proposed that the carotid wall rigidity could be a good predictor of mortality in uremic patients. Other authors, however, use the value of IMT. In an analysis of 138 patients over 30 months, Benedetto³⁵ found an association between IMT and the mass of the left ventricle, describing IMT as an independent predictor for cardiovascular mortality. Nishizawa³⁶ found an association between IMT and cardiovascular deaths, but not with other causes of death in a 438 patient study over 30 months. Kato⁷ was the first author to describe IMT as a predictor for mortality, whether cardiovascular in origin or otherwise. Savage²⁶ found no differences in IMT between 48 HD patients and 24 healthy subjects. This study did show a greater number of patients with plaques, all of which were calcified, in comparison with the control group, who had fewer and softer plaques. Savage also observed that IMT had an inverse relationship with albumin levels. In our case, we detected that hypoalbuminemic patients died with greater frequency, and a correlation with IMT that was not significant.

Several authors have analyzed the possibility that IMT is a predictor for mortality. Some have demonstrated that an increase in IMT is a cardiovascular risk factor and a predictor for mortality. Kato⁷ studied 219 patients on HD for 54 months and showed that IMT and a diabetic condition were independent predictors of mortality from cardiovascular causes or any other. Analysis of the data showed that for every 0.1 mm increase in IMT, cardiovascular mortality increased by 41% and general mortality by 31%. Nishizawa³⁶ analyzed data on 438 patients on HD for 30 months and found that an increase in IMT indicated an increase in cardiovascular mortality, but found

no such relationship with mortality in general. Benedetto³⁵ produced similar results, demonstrating that IMT is only an independent predictor of death from cardiovascular causes, increasing the risk of death by 24% for each 0.1 mm increase in IMT. In contrast, Blancher³⁴ studied 138 patients (91 on HD and 47 on peritoneal dialysis) for 30 months and did not observe that IMT was an independent predictor of cardiovascular death after an adjusted analysis, opting for carotid arterial distensibility as a better predictor. Iglesias del Sol³⁷ followed 374 patients during 4.2 years and did not find that increases in IMT had any predictive value for risk of dying from cardiovascular events, although this study did not work with uremic patients. With respect to carotid plaques, Schwaiger²⁵ studied 165 patients on HD over 13 years, and proved that the presence of carotid plaques was a predictor for cardiovascular events and mortality from any cause. In our case, the multivariate analysis showed that age and albumin levels were predictors of mortality due to any cause, but by analyzing only those cases of death by cardiovascular causes, the presence of carotid plaques was also an independent predictor of mortality. Thus, the presence of carotid plaques tripled the risk of dying from any cause or from a cardiovascular event. As a global factor, IMT does not predict mortality in our patients. However, taking into account only non-diabetic patients, IMT is an independent predictive factor (a 0.1 mm increase produces an increase in probability of death from any cause by 43%). The fact that IMT is not a predictor for mortality in the group of diabetic patients could be influenced by the presence of multiple cardiovascular risk factors in this group of patients.

Definitively, IMT and the presence of carotid plaques increase the risk of cardiovascular events and death. Measuring IMT by carotid ultrasound is a simple and non-invasive tool that can help verify the level of atherosclerotic processes in uremic patients who suffer from several important cardiovascular risk factors. Recognizing the risk represented by an increase in IMT must lead us to optimize the treatment for these patients in order to reduce it: statins, antiplatelets, ACE inhibitors/ARA II, tobacco cessation, etc., which must be applied as early as possible.

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