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Predictive Factors for Coronary Artery Disease among Peritoneal Dialysis Patients without Diabetic Nephropathy

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ABSTRACT

Objectives: *Scientific literature indicates that the risk of coronary heart disease morbidity and death among peritoneal dialysis patients exceeds risk observed in non-renal patients. The aims of this study were to establish the independent predictors associated with increased risk of coronary heart disease in peritoneal dialysis patients without diabetic nephropathy.*

Materials and Methods: *A number of 116 end-stage renal disease patients without diabetic nephropathy undergoing peritoneal dialysis were evaluated for coronary heart disease and predictive risk factors were investigated and identified. Also intima-media thickness measurements, as an early sign of atherosclerosis, were analyzed in a subset of patients in correlation with a number of traditional and non-traditional cardiovascular risk factors.*

Results: *The study sample was found to be characterized by a high prevalence of traditional risk factors: hypertension (95.7%), dyslipidemia (93.1%) and metabolic syndrome (58.6%), but also of dialysis-related risk factors: inflammation (82.8%) and anemia (55.2%). Independent variables found to be associated in regression analysis with coronary heart disease were: age, smoking status, nephroangiosclerosis, albumin, C-reactive protein and iPTH levels. Intima-media thickness was significantly higher in patients with coronary heart disease, values greater than 0.89 mm being associated with increased risks for coronary heart disease, acute coronary syndrome and cardiovascular death.*

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Conclusions: *The prevalence of traditional cardiovascular risk factors in these peritoneal dialysis patients is extremely high, but there are also some other factors involved, especially malnutrition and inflammation. Age higher than 55 years, smoking, albumin less than 3.5 g/dl, iPTH less than 150 pg/ml and nephroangiosclerosis were associated with highest odds ratio for coronary heart disease. An increasing CRP levels was associated with an increasing gradient for coronary heart disease risk.*

Keywords: end-stage renal disease, coronary heart disease, peritoneal dialysis, intima-media thickness

Chronic kidney disease, especially in its advanced stages, is a major public health problem due to increasing incidence but also due to the extremely high costs it incurs, both for the individual and the society. Despite many advances in renal replacement therapies, the prognosis for end-stage renal disease (ESRD) patients remains poor. The USRDS data showed an excess mortality rate among dialysis patients greater than 20% (1), with an estimate of 40-50% of the dialyzed patients dying due to cardiovascular diseases (2). The risk for cardiovascular death in dialysis patients greatly exceeds the risk among non-renal patients of same age (3), especially in younger patients, among whom cardiovascular mortality is up to 100 times higher than in the general population of similar age (4).

The incidence of cardiovascular diseases (CVD) in dialyzed patients is higher on the account of higher prevalence of traditional risk factors such as diabetes and hypertension (as identified and deeply described in the Framingham Study) as compared with the general population (5), but not only. Some non-traditional risk factors such as anemia, abnormal mineral metabolism, oxidative stress, inflammation, malnutrition, high homocysteine levels, and thrombogenic factors were also held accountable by various researchers (Table 1). More than 30 years ago, while observing an increased incidence of myocardial infarction (MI) in dialyzed population from Seattle, Lindner launched the hypothesis that ESRD could be associated with an early and accelerated atherosclerosis (6). Further angiographic and necroptic studies revealed an increased prevalence of coronary heart disease (CHD) in ESRD (7). Most subsequent studies addressed CHD among diabetes patients on hemodialysis, but fewer studies addressed non-diabetics treated by peritoneal dialysis (PD).

To elucidate some of these less known aspects pertaining this later group of subjects, this study investigated different clinical forms of CHD diagnosed in 116 ESRD patients without diabetic nephropathy treated by peritoneal dialysis. A high-resolution ultrasound measurement of carotid intima-media thickness (IMT) was employed as an early sign of atherosclerosis and as a predictor of future vascular events. A large number of traditional and non-traditional cardiovascular risk factors were evaluated (8,9). ❑

Traditional risk factors	Uremia-related risk factors
Treatable	Primary kidney disease
Smoking	Anemia
Diabetes	Abnormal mineral metabolism
Increased LDL-cholesterol	Malnutrition
Decreased HDL- cholesterol	Inflammation
Hypertension	Oxidative stress
Obesity	Hypervolemia
Insulin resistance and metabolic syndrome	Increased sympathetic tone
Untreatable	Nocturnal hypoxemia
Age	Hyperhomocisteinemia
Male gender	Advanced glycation end products
Menopause	Thrombogenic factors
Family history of cardiovascular diseases	Uremic toxins
Social stress	Endothelial dysfunction

TABLE 1. Cardiovascular risk factors in dialyzed patients
LDL - low density lipoprotein; HDL - high density lipoprotein

MATERIALS AND METHODS

Population

This case-control study was conducted in Fundeni Center of Internal Medicine-Nephrology in 2006-2011, with the support from the Center of Cardiology, Institute for Cardiovascular Diseases "Prof. C.C. Iliescu". Inclusion criteria were: patients with stable peritoneal dialysis without diabetic nephropathy as primary renal disease who survived at least 6 months after PD was initiated; patients who accepted to participate in the study upon informed consent were

considered eligible. The 6 months threshold was chosen in order to avoid potential biases related to late referral to nephrologists, early modality switching and to allow differential diagnosis with acute renal failure. Exclusion criteria were: age less than 18 years, acute infectious diseases (at inclusion and/or 3 months prior to inclusion in the study), diabetes requiring insulin treatment or diabetes with poor control, chronic hemodialysis or kidney transplant history, pregnancy or less than 6 months since delivery and severe psychiatric diseases.

A total of 116 patients were included in the study, 51 patients diagnosed with different forms of CHD, while the control group included 65 patients free of CHD.

Methods

All patients were evaluated at the time they were included in the study by anamnesis and review of all available medical records. The clinical parameters recorded at baseline were: age, gender, diabetic status, family history of cardiovascular disease, primary renal disease, duration of kidney failure and peritoneal dialysis, residual diuresis; smoking history and alcohol use; whole medication chart and peritoneal dialysis prescription; previous history of hypertension, angina pectoris, myocardial infarction (MI), and coronary revascularization, height, weight, waist and hip circumferences, and blood pressure (BP). All the laboratory tests and the carotid ultrasound were also performed at baseline. Laboratory parameters considered were: lipid profile (total cholesterol, LDL, HDL cholesterol, and triglycerides), hemoglobin, albumin, serum calcium, phosphate, and intact parathyroid hormone (iPTH) levels. Blood samples were taken after an overnight fast. Body mass index (BMI), waist-to-hip-ratio (WHR), mean arterial pressure (MAP) and pulse pressure (PP, as a measure of arterial stiffness) were calculated. WHR was assessed with an empty peritoneal cavity (without dialysis solution). Nutritional status was assessed using serum albumin and 7-points scale from Subjective Global Assessment (SGA) chart. Presence of the metabolic syndrome was evaluated according to International Diabetes Federation definition (10), and presence of dyslipidemia was assessed according to NCEP ATP III recommendations. Ultrasound measurements of the carotid were made bilaterally and always using the same equipment by a single observer blinded to the clinical and biochemical data. All measurements were conducted with an Aloka device, Tokyo, Japan, using a 7.5-MHz high resolution probe, with the accuracy of the electronic calipers of the instrument to the nearest 0.1 mm. IMT was defined as a low level echo gray band, which does not project into the arterial lumen and was measured during end-diastole as the distance from the leading edge of the second echogenic line of the far walls of the distal segment of the common carotid artery, the carotid bifurcation, and the initial tract of internal carotid artery on both sides. The averages of measurements taken during 3 cardiac cycles at end-diastole, for both right and left carotid arteries were calculated. The final IMT was computed as an average between left and right averages. This study complies with rules and regulations pertaining to ethical medical research.

Statistical analysis

Statistical analysis was carried out with SPSS for Windows v. 16 (IBM, USA). All data are expressed as mean ± standard deviation. The Student *t*-test was used to compare means between groups, and the chi-square test was used to compare proportions between groups. A p value less than 0.05 was considered statistically significant. Risk estimate was computed by using odds ratio (OR). Multivariate analysis by logistic regression was used in order to identify the independent variables associated with coronary heart disease. ❑

RESULTS

Overall, the study sample was characterized by a very high prevalence of traditional risk factors: hypertension (95.7%), dyslipidemia (93.1%) and metabolic syndrome (58.6%). 62.9% (73 pts.) had hypercholesterolemia, 67.2% (78 pts.) hypertriglyceridemia, 57.8% (67 pts.) low HDL levels and 53.4% (62 pts.) increased LDL levels; only 12.1% (14 pts.) had optimal HDL levels (>60 mg/dl). The prevalence of ESRD-related risk factors was also high: 82.8% (96 pts.) had CRP>3 mg/l and 55.2% (64 pts.) had hemoglobin levels less than 11 g/dl. Almost half of the patients (40.5%) had nephroangiosclerosis as the primary renal disease. With a mean age of 56.3 years, mean duration of chronic kidney failure was 75.8 months (9-

252 months) and mean duration of PD treatment was 36.6 months (6-86 months). 101 patients were treated using continuous ambulatory PD (CAPD) and 15 patients with automated PD (APD). Almost two thirds of the patients (60.3%) had a diuresis greater than 500 ml/day, which is otherwise one of the advantages of PD over hemodialysis (i.e. preservation of residual renal function for a longer period). The prevalence of CHD among the eligible subjects was 43.9% (95%CI: 35.1-53.1). 23 patients (19.8%) died during study duration: 4 non-cardiovascular deaths (sepsis or malignancies) and 19 cardiovascular deaths (15.5%) were recorded- 6 sudden cardiac deaths, 4 deaths due to acute miocardial infarction, 5 deaths due to heart failure and 4 deaths due to ischaemic stroke.

In the group of 51 patients with CHD most patients had stable angina pectoris (AP) (49 patients). However, some of these patients were included in more than one diagnosis categories during the study period, as some developed acute coronary syndrome (ACS) (Table 2). Coronary revascularization (percutaneous angioplasty with stent placement) was performed in 8 cases for ACS.

Univariate analysis was conducted for key variables concerning traditional risk factors (Table 3) and kidney disease and/or dialysis-related risk factors (Table 4). Patients with CHD were significantly older, had higher WHR, lower HDL levels and higher total cholesterol to-HDL ratios (as a marker of cardiovascular risk) than those without CHD with p value less than 0.05 for the statistical test applied (Table 3). Prevalence of patients older than 55 years, males, smokers and of diabetic patients was statistically significant higher in the group of patients with CHD. The highest OR were observed for: patients with severe hypertension with crude OR 6.16 (95%CI: 1.96-19.30), males with crude OR 4.38 (95%CI: 1.99-9.63), smokers with crude OR 2.71 (95%CI: 1.24-5.91), and diabetes with crude OR 2.59 (95%CI: 1.02-6.54). There were no significant differences between the two groups of patients concerning family history of cardiovascular diseases, BMI, waist circumferences, prevalence of hypertension, obesity, metabolic syndrome and dyslipidemia, BP (systolic, diastolic, MAP and PP), LDL and triglycerides levels and these variables will not be considered in the final regression model.

Patients with CHD had lower total cholesterol levels, but without reaching statistical significance. Published research highlighted the phenomenon of reverse causality between cholesterol levels and cardiovascular outcome in ESRD patients (i.e. poor outcome in those with lower cholesterol in connection with malnutrition and inflammation). In this study the relationship between total cholesterol level and CHD was also investigated. Subjects with total cholesterol >200 mg/dl were less likely to have CHD comparing those with cholesterol <150 mg/dl (crude OR 0.34; 95%CI: 0.13-0.88). There were no significant differences between patients with low and normal cholesterol and between those with high and normal cholesterol regarding the risk of CHD. Similar analysis was conducted for the subset of patients diag-

Types of coronary heart disease	Patients (%)
Stable angina pectoris	49 (96.07%)
Acute coronary syndrome • *Unstable angina* • *Myocardial infarction with/without ST elevation*	21 (41.17%) • 10 (19.6%) • 11 (21.56%)
Coronary revascularization (percutaneous angioplasty)	8 (15.68%)
Coronary heart disease (total)	**51**

TABLE 2. Frequency of coronary heart disease

	CHD (51 pts)	Without CHD (65 pts)	p	Crude OR (95% CI)
Mean age (years)	64.43±10.48	49.98±16.36	0.001	-
Age >55 years (Yes/No)	8/43	35/30	<0.001	6.27 (2.55-15.40)
Gender (M/F)	36/15	23/42	<0.001	4.38 (1.99-9.63)
Smoking (Yes/No)	25/26	17/48	0.01	2.71 (1.24-5.91)
WHR	0.86±0.04	0.82±0.04	0.03	-
Diabetes (Yes/No)	15/36	9/56	0.03	2.59 (1.02-6.54)
HDL-cholesterol (mg/dl)	35.92±11.58	44.22±16.26	0.003	-
Total cholesterol/HDL cholesterol ratio	5.33±1.67	4.66±1.81	0.04	-
Grade 3 hypertension (Yes/No)	47/4	42/23	0.001	6.43 (2.05-20.12)

TABLE 3. Traditional risk factors and coronary heart disease

CHD - coronary heart disease; OR - odds ratio; HDL - high density lipoprotein

nosed with ACS. ACS risk was significantly higher in patients with lower cholesterol <150 mg/dl) than in patients with cholesterol >200 mg/dl. The crude OR was 4.61 (95%CI: 1.20-17.65) in patients with low vs. high cholesterol levels.

Univariate analysis for nontraditional risk factors were conducted (Table 4). Nephroangiosclerosis, loss of residual diuresis (diuresis <500 ml/day), anemia, albumin levels <3.5 g/dl and iPTH <150 pg/dl were all associated with increased risk of CHD in the univariate analysis. Higher CHD risk was observed among patients with laboratory signs of inflammation, with statistically significant difference for fibrinogen and CRP levels. Patients with CHD had significant lower levels of hemoglobin, higher levels of serum phosphate and calcium-phosphate product (CaxP) and poor nutritional status (lower albumin and higher SGA scores) than patients without evidence of CHD. The highest OR were observed for: patients with nephroangiosclerosis with crude OR 8.00 (95%CI: 3.44-18.56), iPTH <150 pg/ml with crude OR 7.96 (95%CI: 3.05-20.75) and albumin <3.5 g/dl with crude OR 6.64 (95%CI: 2.87-15.36). There were no differences between patients with and without CHD in terms of duration of chronic renal failure or PD, PD prescription and serum calcium so these variables will not be considered in the final regression model. In patients with severe CHD, who developed ACS during the study, PD duration was significantly longer from those without ACS (45.52±18.73 months versus 33.72±19.01 months, p=0.01) (Figure 1).

There are studies suggesting a poor cardiovascular outcome in ESRD patients with adynamic bone disease characterized by a metabolically inactive bone and low levels of iPTH. The risk of CHD depending of the levels of iPTH was investigated. Patients with iPTH <150 pg/ml were more likely to associate CHD than patients with optimal iPTH (i.e. iPTH 150-300 pg/ml) (Table 5). iPTH >300 pg/ml was associated with increased risk of CHD comparing with patients with optimal iPTH levels.

The next analytical step, by means of logistic regression, addressed the following parameters that were found to be significant during the univariate analysis: age, gender, diabetes, smoking status, HDL <40 mg/dl (as traditional cardiovascular risk factors) and nephroangiosclerosis, anemia, CRP, preserved RRF, albumin <3.5 g/dl, iPTH and serum phosphate >5.5 mg/dl (as PD-related risk factors). In the final

	CHD (51 pts)	Without CHD (65 pts)	p	Crude OR (95% CI)
Nephroangiosclerosis (Yes/No)	34/17	13/52	<0.001	8.00 (3.44-18.56)
Hemoglobin (g/dl)	10.24±1.39	10.80±1.41	0.03	-
Anemia (Yes/No)	35/16	29/36	0.01	2.71 (1.26-5.85)
Fibrinogen (mg/dl)	544.12±126.69	500.14±106.94	0.04	-
C-reactive protein (mg/l)	23.98±30.91	11.22±19.16	0.007	-
Preserved residual diuresis (Yes/No)	22/29	48/17	0.001	0.26 (0.12-0.58)
SGA	5.45±3.36	3.51±3.50	0.003	-
Albumin (g/dl)	3.17±0.62	3.65±0.67	<0.001	-
Albumin <3.5 g/dl (Yes/No)	40/11	23/42	<0.001	6.64 (2.87-15.36)
Phosphate (mg/dl)	6.10±1.49	5.46±1.56	0.02	-
CaxP product (mg2/dl2)	54.25±15.93	47.87±14.24	0.02	-
iPTH <150 pg/ml (Yes/No)	23/26	7/58	<0.001	7.96 (3.05-20.75)

TABLE 4. Non-traditional risk factors and coronary heart disease

CHD - coronary heart disease; OR - odds ratio; SGA - subjective global assessment; CaxP - calcium x phosphorus; iPTH - intact parathyroid hormone

	CHD	Without CHD	p	Crude OR (95% CI)
iPTH<150 pg/ml *versus* iPTH=150-300 pg/ml	25/6	7/33	<0.001	18.07 (5.87-65.73)
iPTH>300 pg/ml *versus* iPTH=150-300 pg/ml	20/6	25/33	0.005	4.40 (1.54-12.57)

TABLE 5. iPTH levels and coronary heart disease

CHD - coronary heart disease; iPTH - intact parathyroid hormone

model, the variables that remained significant contributors to the CHD predictive model were: age, smoking status, nephroangiosclerosis, albumin, C-reactive protein and iPTH (Table 6).

For CRP levels the precision of the estimate is lower due to reduced number of subjects in some CRP categories; however, the results from the backward logistic regression suggest that there is a risk gradient with increasing CRP levels (i.e. higher CRP levels are predictive for an increased CHD risk in these patients, the highest risk seemed to be attributable to CRP levels higher than 10 mg/l).

IMT was analyzed as a surrogate marker for subclinical atherosclerosis. IMT measurements were available for 98 patients, for this reason IMT was not included in the final regression model. Overall, in the study sample, IMT was higher in males (0.97±0.30 vs. 0.86±0.21, p=0.03), smokers (1.01±0.33 vs. 0.87±0.20, p=0.01), in patients with diabetes (1.07±0.25 vs. 0.89±0.26, p=0.01) and in patients older than 55 years (0.99±0.27 vs. 0.81±0.22, p=0.002). Regarding the IMT mean values, there were no significant differences depending the presence of obesity (0.96±0.23 vs. 0.91±0.27, p=NS), metabolic syndrome (0.95 ±0.24 vs. 0.89±0.29, p=NS), dyslipidemia (0.93±0.27 vs. 0.82±0.20, p=NS) or hypertension (0.93±0.27 vs. 0.81±0.08, p=NS). IMT was significantly higher in patients with CHD (Figure 2), values >0.89 mm being associated with increased risk for CHD, ACS and cardiovascular death (Table 7). ❑

Variable	β coefficient	95% CI	p
Age			**0.04**
Age less than 55 years	1	-	-
Age higher than 55 years	3.86	1.03-14.40	
Smoking status			**0.01**
Non-smokers	1	-	-
Smokers	5.70	1.43-22.64	-
Nephroangiosclerosis			**0.005**
Other primary kidney disease	1	-	-
Nephroangiosclerosis	5.89	1.68-20.61	-
C-reactive protein			**0.01**
CRP <3 mg/l	1	-	-
CRP 3-9.9 mg/l	2.94	0.16-52.03	NS
CRP ≥10 mg/l	14.24	0.82-244.68	NS
Albumin			0.03
Albumin ≥3.5 g/dl	1	-	-
Albumin <3.5 g/dl	3.54	1.10-11.34	-
iPTH			**0.006**
iPTH <150 pg/ml	1	-	-
iPTH 150-300 pg/ml	0.07	0.01-0.42	0.003
iPTH >300 pg/ml	0.38	0.10-1.45	NS

TABLE 6. Multivariate analysis through logistic regression to establish the independent variables associated with coronary heart disease

CI - confidence interval; CRP - C-reactive protein; iPTH - intact parathyroid hormone

	Univariate analysis		
	Crude OR	95% CI	p
Coronary heart disease	2.41	1.05-5.49	0.04
Angina pectoris	2.49	1.07-5.75	0.03
Acute coronary syndrome	6.88	1.79-26.39	0.003
Cardiovascular death	4.3	1.13-16.36	0.02

TABLE 7. Risk (OR) for coronary heart disease and cardiovascular death in patients with intima-media thickness higher than 0.9 mm

OR - odds ratio; CI - confidence interval

DISCUSSION

Chronic kidney disease (CKD) is a public health problem, with increasing incidence and prevalence. The mortality of ESRD is 10- to 20-fold higher than that in the general population, almost half of these deaths being attributable to cardiovascular disease, especially CHD (11,12). Present study analyzed different aspects of CHD in PD patients without diabetic nephropathy as the primary kidney disease. Diabetic nephropathy was an exclusion criterion since there are many studies concerning increased cardiovascular risk in these patients, while data regarding patients with other primary renal disease are scarce.

The etiology of cardiovascular disease in CKD is complex. It may partly be a result of increased prevalence of classic cardiovascular risk factors. Prevalence of hypertension in ESRD is extremely high, estimated at around 60-85% for the hemodialysis (HD) patients and 50% in PD patients (2). There is a strong correlation between hypertension, CHD, left ventricular hypertrophy, heart failure and death in ESRD (13). The workgroup for KDOQI guidelines regarding dyslipidemia management (14) analyzed dyslipidemia management in dialyzed patients included in Dialysis Morbidity and Mortality Study. According ATP III definition, only 15.1% from these patients had normal lipids levels. Frequencies of hypertension and dyslipidemia were 95.7% and 93.1% respectively in our study sample. These very high prevalences are probably the main reasons why, in the univariate analysis, these two traditional risk factors were not associated with an increased risk for CHD. Grade 3 hypertension

was associated with increased risk for CHD and this is the main explanation why nephroangiosclerosis was a powerful predictive risk factor for CHD, both in univariate and in multivariate analysis.

In hemodialysis patients low cholesterol levels are independent predictors for increased mortality (15) and this is considered to be the result of association between different co morbidities, especially inflammation and malnutrition. Patients with cholesterol higher than 200 mg/dl were less likely to have CHD than patients with total cholesterol less than 150 mg/dl.

In dialysis patients HDL levels are usually low, and is estimated a mean HDL level at around 26 mg/dl comparing with 52 mg/dl in the general population (16). In the total study sample mean HDL level was 40.57 mg/dl; 57.8% patients had a lower level than that established by ATP III; only 12.1% patients had a HDL level above 60 mg/dl (considered optimum for cardiovascular protection). In the univariate analysis reduced HDL levels were associated with increased risk for CHD; however, this association didn't remain significant in the multivariate analysis. In the general population increased total cholesterol to-HDL ratio is a marker of high cardiovascular risk (17). Patients with CHD had a significant higher total cholesterol to-HDL ratio than those without CHD, reflecting a high cardiovascular risk. It must be pointed out however that both groups of patients, with and without CHD, had mean values for this ratio in the high risk zone (>4), which stands up for a high cardiovascular risk in the whole PD population.

Framingham study proved that metabolic syndrome (MetS) is associated with increased risk for CVD. MetS was not associated in our PD patients with increased risk for CHD. Same observation was done in other studies concerning patients with ESRD; in 200 patients with CKD stage 4 and 5 enrolled in a randomized study, prevalence of MetS was 30.5%, reaching more than 50% in PD patients, but its presence was not associated with increased risk for CVD and death (18). Obesity, estimated by BMI, is a major cardiovascular risk factor in general population, but in ESRD is a poor predictor for mortality. Also, in PD patients, waist circumference is not a good evaluator for abdominal adiposity (19). Direct measurements of visceral fat, like waist-to-hip ratio (WHR), are positive correlated with general and cardiovascular

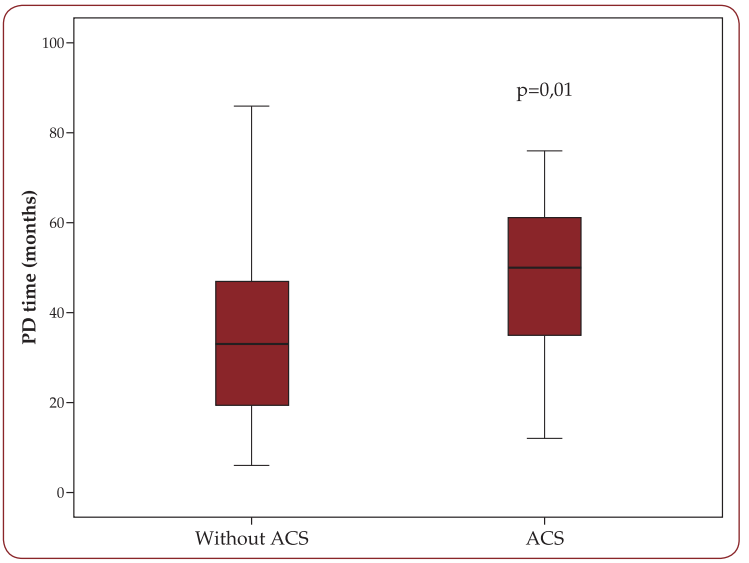

FIGURE 1. Increased risk for acute coronary syndrome in patients with longer PD duration

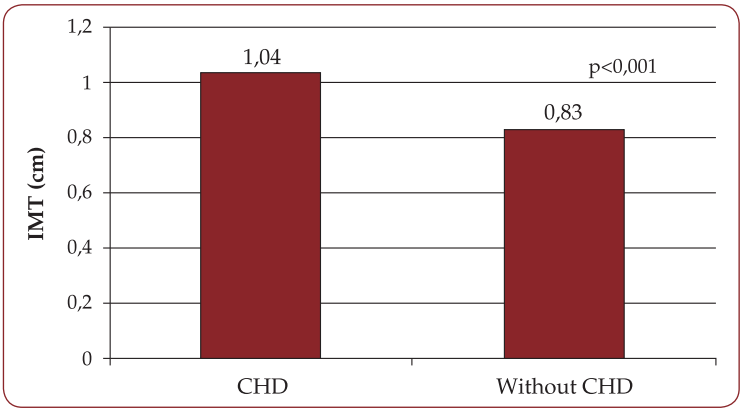

FIGURE 2. IMT and presence of coronary heart disease

mortality in ESRD (20). In the unvaried analysis BMI and waist circumference were not correlated with the presence of CHD, but patients with increased WHR had a statistically significant risk of CHD and ACS In this population WHR might be considered a much better anthropometric predictive factor than BMI (which is currently used in clinical practice) for risk of developing atherosclerotic disease.

At least 50% of the patients in dialysis are smokers or ex-smokers, and smoking at the start of the dialysis is independently associated with de novo heart failure, cerebrovascular disease and death (21,22). In unvaried analysis smoking was associated with increased risk of CHD in PD patients and this variable remained significant in the multivariate analysis.

From the parameters characterizing PD population, nephroangiosclerosis, anemia, loss of RRF, increased CRP levels (as a marker for inflammation), low serum albumin and in-

creased SGA score (as markers of malnutrition), increased serum phosphate and CaxP product and reduced serum iPTH were associated in the unvaried analysis with increased risk of CHD. A reduced residual diuresis in PD is associated with inflammation, poor nutritional status and increased general mortality through exacerbation of atherosclerosis (23). A diuresis less than 500 ml/day was associated with increased risk of CHD. There are many studies during the last years concerning a strong link between increased oxidative stress, inflammation, malnutrition, vascular calcifications, presence of extensive atherosclerosis and premature death in ESRD- the MIA syndrome (malnutrition-inflammation-atherosclerosis). In the multivariate analysis, from the parameters characterizing the renal disease, apart nephroangiosclerosis, the variables associated independently with increased risk for CHD were low albumin, increased CRP and iPTH less than 150 pg/ml. These results are in accordance with the data from other studies and point out the major impact of malnutrition and inflammation on the process of early and accelerated atherosclerosis in PD patients. Longer PD duration was not associated with increased risk of angina pectoris. Contrary to this, PD duration was associated with increased risk of developing ACS during the study period. It is possible that in PD a prolonged proinflammatory status favor the mechanisms involved in plaque vulnerability, which may predispose these patients to events conducting to ACS.

In the hemodialysis patients higher (>300 pg/ml) and also lower (<150 pgml) levels of iPTH are associated with increased risk of cardiovascular events and mortality (24). Results from the multivariate analysis suggest an increased risk for CHD for lower and higher iPTH levels compared with optimal iPTH, reaching statistical significance for iPTH <150 pg/ml. The precision of the estimate is lower than expected for iPTH probably due to the relatively low number of patients enrolled, so the study couldn't have enough statistical power to obtain statistical significance for increased CHD risk in patients with higher iPTH.

IMT emerged as a strong and independent predictor of cardiovascular events in the general population and in various disease states, including ESRD (25). Increased carotid IMT, in particular, is considered to be not only a critical lesion predisposing to plaque formation but also a valid marker for the severity of atherosclerosis in critical vascular beds, such as the coronary arteries (26). An increased IMT (i.e. higher than 0.89 mm) was associated with an increased risk for CHD in our PD patients.

In summary, the study supports an increased prevalence of traditional cardiovascular risk factors in PD patients without diabetic nephropathy as the primary renal disease, but there are also some other factors involved especially inflammation and malnutrition. Age, smoking, malnutrition and inflammation, reduced iPTH levels and nephroangiosclerosis are strong and independent predictors of CHD in these PD patients. Increased IMT is associated with elevated CHD risk in these patients. Framingham cardiovascular risk score is a good predictor for the presence of CHD and subsequently ACS in PD population without diabetic nephropathy.

Abbreviations

F - female
M - male
PD - peritoneal dialysis
CAPD - continuous peritoneal dialysis
APD - automated peritoneal dialysis
ESR - erythrocyte sedimentation rate
CaxP - calcium x phosphate product
iPTH - intact parathyroid hormone
CHD - coronary heart disease
BMI - body mass index
WHR - waist-to-hip ratio
SBP - systolic blood pressure
DBP - diastolic blood pressure
MAP - mean arterial pressure
PP - pulse pressure
RRF - residual renal function
SGA - subjective global assessment of nutritional status
ACS - acute coronary syndrome
AP - angina pectoris
CRP - C-reactive protein
IMT - intima-media thickness
ESRD - end stage renal disease
CVD - cardiovascular disease
MI - myocardial infarction
CKD - chronic kidney disease
MetS - metabolic syndrome

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