Cardiac evaluation of patients with chronic kidney disease: what lessons?

Avaliação cardiológica de pacientes portadores de doença renal crônica: quais as lições?

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ABSTRACT

Introduction: Patients with chronic kidney disease (CKD) experiment a synergistic effect of the traditional and the emerging uremia-related risk factors for atherosclerosis. **Objective:** Draw the epidemiologic profile of a group of CKD patients who underwent cardiac evaluation. **Methods:** Symptomatic patients, patients with ischemia on myocardial scintigraphy and/or systolic dysfunction on echocardiography, patients older than 50 years and diabetes *mellitus* (DM) as a cause of CKD, and those with two or more risk factors underwent coronary angiography. Asymptomatic, non-diabetic patients and patients with no risk factors were investigated with echocardiography. Those with a single risk factor were investigated with echocardiography and scintigraphy. **Results:** 46 patients (58.7% men) were enrolled. Their mean age was 50.7 ± 11.7 years. 91.3% were on dialysis, for 61.96 ± 55.1 months. Hypertension was the cause of CKD in 56.5%. Of the 28 patients (60.9%) who underwent angiography, 53.6% had coronary artery disease (CAD). The patients were divided into three groups: those with CAD (A), those without CAD (B) and those who didn't undergo coronary angiography (C). A significant difference occurred only between groups B and C, as regards an abnormal ABI (p = 0.026), with no ABI abnormality in group C, and as regards the mean age, which was higher in group B (p = 0.045). In group A, 53.3% of the patients were in the preoperative stage of parathyroidectomy. **Conclusion:** This study confirmed the high rate of cardiovascular disorders, including CAD, in patients with CKD, especially those on dialysis.

Keywords: Coronary disease. Renal insufficiency, chronic. Inflammation. Atherosclerosis.

RESUMO

Introdução: Pacientes com doença renal crônica (DRC) apresentam sinergismo entre fatores de risco tradicionais para aterosclerose e emergentes derivados do estado urêmico. **Objetivo:** Traçar o perfil epidemiológico de um grupo de pacientes com DRC submetido à avaliação cardiológica. **Métodos:** Pacientes sintomáticos – com isquemia em cintilografia miocárdica e/ou disfunção sistólica ao ecodopplercardiograma – com idade maior que 50 anos e diabetes *mellitus* (DM) como causa da DRC e aqueles com dois ou mais fatores de risco ateroscleróticos realizaram cineangiocoronariografia. Assintomáticos – não diabéticos e sem fatores de risco – foram investigados com ecodopplercardiograma e aqueles com único fator de risco, por meio de ecodopplercardiograma e cintilografia. **Resultados:** Foram estudados 46 pacientes, 58,7% homens, idade de 50-70 ± 11,7 anos, 91,3% dialíticos. Tempo de hemodiálise: 61,96 ± 55,1 meses. Hipertensão arterial foi causa da DRC em 56,5%. Dos 28 pacientes (60,9%) submetidos à cineangiocoronariografia, 53,6% apresentaram doença arterial coronariana (DAC). Os pacientes foram divididos em três grupos: com DAC (A), sem DAC (B) e não submetidos à cineangiocoronariografia (C). Diferença significativa ocorreu entre os Grupos B e C na frequência de índice tibiobraquial (ITB) anormal (p = 0,026), com ausência de ITB anormal no Grupo C e na média de idade, superior no B (p = 0,045). No Grupo A, 53,3% dos pacientes estavam em avaliação pré-paratireoidectomia (PTX). **Conclusão:** Este estudo confirmou a alta frequência de alterações cardiovasculares, inclusive de DAC, nos pacientes portadores de DRC, principalmente naqueles em diálise.

Palavras-chave: Doença das coronárias. Insuficiência renal crônica. Inflamação. Aterosclerose.

Introduction

Chronic kidney disease (CKD) patients are at high risk of cardiovascular diseases (CVD), which account for 40-50% of the deaths in this population.[1-4]

The high cardiovascular risk could be explained, in part, by a synergy between traditional risk factors and the newly emerging uremia-related risk factors, resulting in accelerated atherosclerosis and early death. Furthermore, the diagnosis of CKD, made when CVD is already advanced (epidemiologic causality), and the malnutrition, inflammation and atherosclerosis (MIA) syndrome present in these patients, would lead to accelerated atherosclerosis.[5,6]

The emerging factors, mineral and bone metabolism disturbances, hyperhomocysteinemia, oxidative stress and inflammation, which are mostly cause or consequence of endothelial dysfunction, grow in importance as the renal impairment progresses.[2,7,8] All risk factors interact and increase the cardiovascular mortality of CKD patients.[8-12]

Mineral and bone metabolism disturbances, characterized by abnormal serum levels of calcium, phosphorus and parathyroid-hormone (PTH), are associated with extraosseous (arterial, valvular and myocardial) calcifications, and play an important role in the pathogenesis of myocardial hypertrophy and fibrosis. Vascular calcification is strongly associated with cardiovascular events and death.[2]

In CKD, a paradoxical association between some risk factors and mortality has been observed. Curiously, systemic arterial hypertension and overweight apparently protect these patients, determining a reverse epidemiology. Serum cholesterol levels positively correlate with serum albumin levels, and negatively correlate with serum C-reactive protein (CRP) and interleukin-6 levels, in a reflection of the MIA syndrome.[6]

We assessed the clinical, demographic and laboratory characteristics of a group of stages 4 and 5 CKD patients, who underwent cardiac evaluation, including coronary angiography, in an attempt to know the epídemiologic profile of this population at cardiovascular risk.

Method

Sample

This case-series study was undertaken at the Cardiology Division of the *Hospital das Clínicas* (HC) of the Federal University of Pernambuco, Brazil, during the October 2008 – October 2009 period. The study was approved by the institutional Research Ethics Committee, and all participants signed their informed consent.

46 stages 4 and 5 CKD patients, over the age of 18 years, free from acute or chronic infectious diseases and with no severe liver disease, were included in the study. The patients were referred from the Nephrology Division of the same institution, with the following indications: pre-transplantation assessment, pre-parathyroidectomy (PTx) assessment, or cardiovascular signs/symptoms.

The following clinical and demographic parameters were assessed: age, sex, cause of CKD and time on dialysis. The patients were questioned about their symptoms, classic risk factors for coronary artery disease (CAD) (hypertension, diabetes mellitus, dyslipidemia and smoking), and use of cardioprotective medications. All the patients were scored according to Framingham`s criteria, and underwent general and cardiac physical examinations. Weight was measured in kilograms and height and abdominal circumference in centimeters. Two consecutive blood pressure readings were obtained, one from an upper limb without an arteriovenous fistula and another from the ipsilateral lower limb, for calculation of the ankle-brachial index (ABI). The latter is the ratio between the systolic blood pressures obtained in the lower limb and in the upper limb, with values below 0.9 being abnormal.

The following serum determinations were performed at the Central laboratory of the same institution: albumin (bromocresol green method, Abott, reference: 3.5-5.2 g/dL); high-sensitivity CRP (Aptec nephelometry, Bisys, reference: 0-1 mg/dL); total cholesterol (colorimetric enzymatic method); high-density lipoprotein (HDL, enzymatic method); low-density lipoprotein (LDL, enzymatic method); triglycerides (enzymatic method); fasting glucose (enzymatic method, reference: 70-99 mg/dL); calcium (o-cresolphthalein method, reference: 8.5-10.1 mg/dL); phosphorus (modified phosphomolybdate method, reference: 2.5-4.9 mg/dL); intact PTH (chemoluminescence, reference: 15-68.3 pg/mL); hematocrit (automated method, Beckman Coulter, reference: 47% ± 5 for men and 42% ± 5 for women.

A chest radiograph was obtained on an interdialytic day, for all patients, and it was considered abnormal when at least one of the following was found: increased cardiothoracic ratio, increased vascular markings, aortic calcification and increased diameter of the aortic root. Additionally, a 12-lead resting

electrocardiogram was obtained, with an abnormal result consisting of at least one of the following: a rhythm other than sinus-driven, conduction disturbances, chamber overload and alterations of ventricular repolarization.

For CAD assessment, the patients were stratified in risk groups, according to Gowdak *et al*.[12] The very high-risk group consisted of patients with symptoms suggestive of CAD or anginal equivalent. The high-risk group was composed of diabetics aged over 50 years and of patients with two or more classic CAD risk factors. Patients from the very high and high-risk groups underwent coronary angiography. The medium-risk group, consisting of asymptomatic non-diabetics, with a single classic CAD risk factor, was investigated with resting echocardiography and with resting and stress myocardial scintigraphy. The low-risk group, consisting of asymptomatic non-diabetics without CAD risk factors, was investigated with resting echocardiography.

Other criteria for coronary angiography indication were evidence of ischemia on resting/stress myocardial scintigraphy and the presence of systolic dysfunction (left ventricular ejection fraction under 45%) on resting echocardiography.

Obstructive coronary disease was defined by the presence of stenotic lesions of 50% or more of the arterial lumen, in at least one coronary artery and/or its main branches.

According to the coronary angiography-defined CAD status, the patients were divided into two groups: Group A, composed of those with CAD and Group B, composed of those without CAD. Another group (C), was composed of the medium and low-risk patients. A comparative analysis between the groups was performed.

Left ventricular hypertrophy (LVH) was diagnosed when the echocardiography-defined left ventricular mass index was > 134 g/m^2 (men) and > 110 g/m^2 (women).[13]

To assess the MIA syndrome, we used serum albumin as a nutritional parameter, serum CRP as an inflammation marker, and the ABI as an indicator of atherosclerosis. The MIA syndrome was diagnosed when all the following were present: serum albumin level < 3.5 g/dL, CRP level > 1 mg/dL and ABI < 0.9.

Statistical analysis

PTH levels were presented as median and first and third quartiles. The other variables were presented as means and standard deviations. Kolmogorov-Smirnov`s test was applied for normality supposition. For comparative analysis of the quantitative variables, we used Student`s t test for independent samples, with the chi-squared and Fisher`s exact tests being used for analysis of the qualitative variables. For between-groups comparison of the PTH levels, we used Mann-Whitney`s non-parametric test. The significance level was set at 5%. The Excel 2000 and SPSS v 8.0 software were used.

Results

Of the 46 patients (mean age 50.7 years) assessed, 58.7% were men and 42 (91.3%) were on dialysis, with a mean dialysis time of 61.96 ± 55.1 months. 4 (8.7%) patients were referred from the CKD conservative treatment outpatient service, and were characterized as having a very high risk. The main causes of CKD were hypertension (56.5%) and diabetes mellitus (17.4%). As for the traditional risk factors, 91.3% of the patients had hypertension, 23.9% diabetes and 23.9% dyslipidemia. 13.0% actively smoked and 41.3% were former smokers.

As shown in Table 1, there was a low rate of cardioprotective medication use, with aspirin as the most frequently used drug, by around 40% of those at very high and high risk. Table 2 shows the Framingham`s score for Groups A and B.

As for symptoms, 67.4% of the patients were asymptomatic, with dyspnea being the most frequent symptom (32.6%), and chest pain occurring in only 17.4%. 40% of Group A patients were asymptomatic.

Of all the patients, 30.4% were seen during their PTx preoperative assessment.

Obstructive CAD was diagnosed in 15 patients (32%) of the total sample. Of the 28 patients (61.9%) with coronary angiography indication, CAD was diagnosed in 53.6% (Group A). Tables 1 and 3 show the comparative analyses between Groups A and B. As can be seen, in spite of the lack of a significant difference between the PTH medians, the third quartile of the PTH of Group A was twice that of Group B. In addition, 53.3% of Group A patients were in the PTx perioperative period, compared with 15.4% of Group B (p = 0.055).

Medium and low-risk patients (n = 18, Group C) were non-invasively assessed. The comparative analysis between Groups B and C is shown in Table 4. The patients of these groups differed as for age, abdominal circumference and chest radiograph abnormalities, which were all more frequent in Group B.

Table 1 Clinical characteristics of the patients with an indication for coronary angiography

Characteristics	*Group A (n = 15)	**Group B (n = 13)	p-value
Age*** (years)	51.7 ± 10.6	55.5 ± 8.6	0.313
Male sex	10 (66.7%)	7 (53.8%)	0.700
Conservative	1 (6.7%)	3 (23.1%)	0.463
Time on dialysis*** (months)	69.3 ± 54.9	50.2 ± 48.0	0.339
Previous hypertension	14 (93.3%)	13 (100%)	1.000
Diabetes mellitus	4 (26.7%)	4 (30.8%)	1.000
Dyslipidemia	1 (6.7%)	5 (38.5%)	0.069
Former smoker	7 (46.7%)	5 (38.5%)	0.329
Previous coronary artery disease	2 (13.3%)	0 (0.0%)	0.484
Family coronary artery disease	3 (20.0%)	1 (7.7%)	0.600
Stroke	1 (6.7%)	2 (15.4%)	0.583
Peripheral arterial disease	1 (6.67%)	0 (0.0%)	0.464
Use of ACEI	3 (20.0%)	5 (38.5%)	0.410
Calcium-channel blocker	4 (26.7%)	2 (15.4%)	0.655
Beta-blocker	4 (26.7%)	5 (38.5%)	0.689
Aspirin	5 (33.3%)	6 (46.2%)	0.700
Statin	1 (6.7%)	4 (30.8%)	0.153
Angiotensin-receptor blocker	0 (0.0%)	1 (7.7%)	0.464
Pre-PTx	8 (53.3%)	2 (15.4%)	0.055
Pre-transplantation	3 (20.0%)	4 (30.8%)	0.670
Symptomatic	9 (60.0%)	8 (61.5%)	
Asymptomatic	6 (40.0%)	5 (38.5%)	1.000

ACEI: angiotensin-converting enzyme inhibitor; PTx: parathyroidectomy.
*Group A: with coronary artery disease on coronary arteriography; **Group B: without coronary artery disease on coronary arteriography; ***means and standard deviations;

Mean Echocardiography-defined left ventricular ejection fraction (LVEF) was 63 ± 9% (n = 44) and diastolic function (n = 43) was normal in only 34.9% of the patients. LVH was frequent, being detected in 71.4% (Group A), 50% (Group B) and 47% (Group C).

As for the MIA syndrome, no patient had the three parameters at the same time. The most frequently altered parameter in Group A was inflammation (Table 5).

Discussion

The unacceptably high mortality rate of CKD patients remains even after stratification of the known cardiovascular risk factors, such as age, sex, smoking, sedentariness, hypertension and diabetes mellitus.[1,2] Therefore, factors which are inherent in the uremic state are added to the classic factors to promote accelerated atherosclerosis and early mortality.

Cardiac assessment of CKD patients, chiefly those on dialysis, is a permanent challenge to cardiologists, as myocardial scintigraphy frequently yields false-positive results (because of the high rate of LVH), and because complications (increased blood pressure) frequently occur during pharmacological-stress echocardiography.[12]

Besides, chest pain is a poor indicator of CAD in this population.[14] Because of the high rates of microvascular dysfunction and LVH in CKD patients, angina without relevant CAD is reported to occur in 30-44% of these patients, in contrast with only 17% of the general population.[14] On the other hand, the absence of angina does not rule out CAD, a finding that has been attributed to diabetic neuropathy and uremia.[15]

We observed a low rate of chest pain (17.4%), and even in the group with CAD, a large number of patients was totally asymptomatic, confirming what

Table 2 10-year Framingham`s percentage risk of patients who underwent coronary arteriography

Risk	n	Minimum	Maximum	Mean	SD	p-value
Percentage Framingham`s risk female						
Group A*	4	1	8	5.3	3.0	0.987
Group B**	5	2	14	5.2	5.1	
Percentage Framingham`s risk male						
Group A	10	1	25	6.3	7.4	0.234
Group B	7	1	25	11.1	8.7	

SD: standard deviation.
*Group A: with coronary artery disease; **Group B: without coronary artery disease.

Table 3 Anthropometric and laboratory characteristics of the patients with an indication for coronary angiography

Characteristics	*Group A (n = 15)	**Group B (n = 13)	p-value
BMI***	(25.3 ± 3.6)	(26.3 ± 5.0)	0.565
Abdominal circumference *** (cm)	(89.6 ± 10.5)	(92.5 ± 14.1)	0.544
Blood glucose*** (mg/dL)	(100.3 ± 19.6)	(93.2 ± 17.8)	0.323
HDL-Cholesterol *** (mg/dL)	(55.9 ± 19.8)	(52.3 ± 16.5)	0.606
LDLcholesterol *** (mg/dL)	(83.7 ± 43.5)	(80.2 ± 34.6)	0.817
Triglycerides*** (mg/dL)	(157.5 ± 115.3)	(180.9 ± 103.0)	0.580
Calcium X phosphorus product ***	(52.8 ± 17.7)	(49.8 ± 10.5)	0.607
Hematocrit***	(35.5 ± 6.9)	(35.4 ± 8.0)	0.968
PTH (pg/mL)****	513.4 (P25 158.3; P75 1.529)	364.7 (P25 212.6; P75 738.4)	0.602
Echo mass index - male ***	(142.38 ± 56.60)	(117.94 ± 33.10)	0.329
Echo mass index – female***	(156.02 ± 37.01)	(142.32 ± 78.42)	0.733
Echo LVH yes	10 (71.4%)	6 (50.0%)	
No	4 (28.6%)	6 (50.0%)	0.422
ECG normal	1 (6.7%)	0 (0.0%)	
Abnormal	14 (93.3%)	13 (100.0%)	1.000
ABI abnormal			
Chest radiograph Normal	1 (7.7%)	1 (7.7%)	
Abnormal	12 (92.3%)	12 (92.3%)	1.000

BMI: body mass index; HDL: high density lipoprotein; LDL: low density lipoprotein; PTH: parathyroid hormone; Echo: echocardiography; LVH: left ventricular hypertrophy; ECG: electrocardiogram; ABI: ankle-brachial index; CAD:coronary artery disease.
*Group A: with CAD on coronary arteriography; **Group B: without CAD on coronary arteriography; ***means and standard deviations; ****medians.

Table 4 Clinical, anthropometric and laboratory characteristics of Groups B and C patients

Characteristics	*Group B (n = 13)	**Group C (n = 18)	p-value
BMI***	26.3 ± 5.0	23.6 ± 4.0	0.108
Age (years)***	55.5 ± 8.6	46.4 ± 13.3	0.041
Abdominal circumference *** (cm)	92.5 ± 14.1	82.6 ± 10.5	0.034
Blood glucose*** (mg/dL)	93.2 ± 17.8	85.9 ± 16.4	0.249
HDL-Cholesterol *** (mg/dL)	52.3 ± 16.5	50.8 ± 11.3	0.760
LDL-Cholesterol *** (mg/dL)	80.2 ± 34.6	91.7 ± 33.0	0.355
Triglycerides*** (mg/dL)	180.9 ± 103.0	132.9 ± 57.9	0.147
Calcium X phosphorus product ***	49.8 ± 10.5	55.0 ± 13.5	0.268
Hematocrit***	35.4 ± 8.0	36.7 ± 4.6	0.594
PTH (pg/mL)****	364.7 (P25 212.6; P75 738.4)	551.0 (P25 262.5; P75 1.433)	0.403
Echo mass index – male ***	117.94 ± 33.10	160.60 ± 73.51	0.174
Echo mass index – female ***	142.32 ± 78.42	106.57 ± 29.85	0.291
Echo LVH yes	6 (50.0%)	8 (47.1%)	
No	6 (50.0%)	9 (52.9%)	1.000
ECG normal	0 (0.0%)	1 (5.6%)	
Abnormal	13 (100%)	17 (94.4%)	1.000
ABI abnormal	4 (30.8%)	0 (0.0%)	0.026
Chest radiograph normal	1 (7.7%)	8 (44.4%)	
Abnormal	12 (92.3%)	10 (55.6%)	0.045

BMI: body mass index; HDL: high density lipoprotein; LDL: low density lipoprotein; PTH: parathyroid hormone; Echo: echocardiography; LVH: left ventricular hypertrophy; ECG: electrocardiogram; ABI: ankle-brachial index; CAD: coronary artery disease.
*Group B: without CAD on coronary angiography; **Group C: did not undergo coronary arteriography; ***means and standard deviations; ****medians.

Table 5 Distribution of the variables of the malnutrition, inflammation and atherosclerosis syndrome in Groups A and B patients

Characteristics	*Group A (n = 15)	**Group B (n = 13)	p-value
Albumin*** (g/dL)	(4.5 ± 0.6)	(4.5 ± 0.3)	0.819
Normal	(n = 13) 86.7%	(n = 13) 100.0%	
Abnormal	(n = 2) 13.3%	(n = 0) 0%	0.484
CRP*** (mg/dL)	(1.6 ± 1.4)	(1.4 ± 1.0)	0.746
Normal	(n = 9) 60.0%	(n = 9) 69.2%	
Abnormal	(n = 6) 40.0%	(n = 4) 30.8%	0.705
ABI***	(1.1 ± 0.1)	(1.0 ± 0.2)	0.053
Normal	(n = 14) 100.0%	(n = 9) 69.2%	
Abnormal	(n = 0) 0.0%	n = 4 30.8%	0.153
MIA syndrome			
No	(n = 14) 100.0%	(n = 13) 100.0%	
Yes	(n = 0) 0.0%	(n = 0) 0.0%	-

CRP: C-reactive protein; ABI: ankle-brachial index; MIA: malnutrition, inflammation and atherosclerosis; CAD: coronary artery disease. *Group A: with CAD on coronary arteriography; **Group B: without CAD on coronary arteriography; ***means and standard deviations.

was reported elsewhere.[14,15] Furthermore, because dyspnea, the main symptom reported by our patients, is frequent in patients on dialysis, due to volume overload, its presence does not always alert the nephrologist to the possibility of CAD. These peculiarities, among others, make the cardiovascular assessment of CKD patients a particularly difficult task.

In spite of the high rate of electrocardiographic abnormalities found, which is in agreement with the literature data,[16] there was no significant difference between Groups A and B. This decreases the importance of electrocardiography for the cardiac assessment of CKD patients.

It is noteworthy that liaison between nephrologist and cardiologist is still insufficient in Brazil. This is due, in part, to cardiologists` lack of knowledge about this particular population and the difficulty to find a cardiologist to whom the patient can be referred. In fact, most large cardiac studies exclude CKD patients, further contributing to the paucity of knowledge and strategies targeting this population.

We demonstrated that the cardiac evaluation of our patients was delayed, that is, it was performed in those with PTx indication and mean dialysis time of five years. Besides, the low rate of cardioprotective drug use found indicates the need of greater liaison between cardiologist and nephrologist. Other authors have also shown a low rate of cardioprotective drug use in CKD patients.[17] This fact is associated with high early and late mortality, and inferior therapeutic response to pharmacological and non-pharmacological interventions alike.[1,2]

CKD patients have both classic and uremia-related risk factors. The rate of classic risk factors, such as hypertension and smoking, was high, in accordance with what was reported by Gowdak *et al*.,[9] demostrating that the epidemiologic profile of CKD favors atherosclerosis. However, the mean 10-year Framingham`s risk of our patients with CAD was low (5.3% for women and 6.3% for men), which does not reflect the high cardiovascular risk seen in CKD, and characterizes this population as an exception, besides confirming the importance of other pro-atherosclerotic factors that are not quantified by this classic score.

The prevalence of CAD in our sample was 32.6%, a high rate, chiefly because it was mainly early CAD. In fact, our patients` mean age was 50 years. This prevalence increased to 53.6%, when those who underwent coronary arteriography were analyzed, which demonstrates the high CAD risk in the group selected for coronary angiography.

Because of the higher pre-test likelihood of CAD with non-invasive stratification of the CKD population, coronary angiography is indicated in high and very high-risk groups, as well as in symptomatic patients, those over the age of 50 years, diabetics, and/or those with structural alterations, such as a reduced LVEF, even when asymptomatic.[16]

The high LVH rate we found confirmed the data reported by Kundhal *et al*.,[18] who observed LVH in

74% of the dialysis population. There are several factors implicated in the development of LVH in the CKD population, such as arterial thickening (due to alterations of the calcium, phosphorus, PTH and vitamin D metabolism) and systolic hypertension (due to a chronic state of hypervolemia and anemia-related increased after-load).

Mineral and bone metabolism impairment was evident in this study, as shown by our patients' serum PTH levels. In fact, a PTH serum level over 300 pg/mL indicates considerable hyperparathyroidism. Furthermore, 53.3% of Group A patients were in the PTx perioperative stage, indicating more severe secondary hyperparathyroidism in these individuals.

Our study should alert nephrologists and cardiologists to the fact that CKD patients on the PTx waiting list are at risk of CAD. Hence, should patients being considered for PTx undergo coronary angiography? Because of our small sample size we could not answer this question. It would also be interesting to assess the impact of the PTx waiting time, as this is determinant of all the deleterious effects of the PTH on the heart.

PTH directly affects muscle cells in vessels and the heart, altering the energy metabolism and leading to calcium accumulation. Hyperparathyroidism has been suggested to play a role in the pathogenesis of myocardial fibrosis and hypertrophy, vascular calcification, endothelium-mediated vasodilation dysfunction and alterations in the diastolic function of CKD patients.[19] The complexity of the alterations surrounding the bone metabolism and vascular calcification, both in hyperparathyroidism and adynamic bone disease, in which PTH is reduced, has made it difficult to correctly associate PTH with CAD.[18] Decreased and increased PTH levels are likely to be associated with CVD.

As for the MIA syndrome, which is known to be associated with atherosclerosis, it was not diagnosed in any of our patients. Stenvinkel *et al.*[20] reported malnutrition in 44%, inflammation in 32% and carotid plaques in 72% of their patients, although an association of the three parameters occurred in only 30% of the cases. Inflammation was the parameter most frequently found in our CAD patients. Because of the results reported by Silva Júnior.,[3] who demonstrated that inflammation is the main determinant of the MIA syndrome, we cannot totally exclude the association of this syndrome with the CAD of our patients.

An abnormal ABI indicates peripheral atherosclerosis in the general population, being associated with a higher risk of CAD and carotid disease.[21] Gabriel *et al.*[21] observed ABI values over 1.3 to be associated with diffuse atherosclerotic disease, with calcification of the middle layer and vascular rigidity. This phenomenon would be more frequent in high-risk groups, such as diabetics, elders and those with CKD. The low rate of abnormal ABI we found could be explained by the high rate of hyperparathyroidism, once this metabolic disorder is associated with vascular calcification and increased arterial rigidity, which would then increase the ABI. We might thus have used a parameter that influenced the low diagnostic rate of atherosclerosis in our population.

We used serum albumin to diagnose the nutritional status of our patients. Although this is not sensitive enough for the diagnosis of malnutrition, albumin measurement was the available exam during the study period. Hypoalbuminemia may be due to a combination of inflammation and low protein-energy intake, contributing to reduced fat stores and muscle mass and being associated with the high mortality seen in patients on hemodialysis.[22,23] The combination of a normal serum albumin level and an increased body mass index (BMI) suggested a good nutritional status.

When the patients who did not undergo coronary arteriography (Group C) were assessed, we observed a younger population, with smaller abdominal circumference, lower rate of chest radiograph alterations and more favorable atherosclerosis parameters (ABI), that is, patients with less severity criteria. Obviously, CAD cannot be safely ruled out in these patients, but this is less likely because of their better clinical profile in comparison with Group B patients, that is, those who underwent coronary arteriography and did not have CAD.

Conclusions

We confirmed the high rate of cardiovascular alterations, including CAD in our CKD patients, chiefly those on dialysis.

Although the MIA syndrome was not diagnosed in any patient, we were able to demonstrate the importance of other uremia-related factors, such as mineral and bone metabolism disturbances, in the development of CAD.

Furthermore, we demonstrated that in spite of the high cardiovascular mortality in the CKD population, these patients are still under-assessed and undertreated with cardioprotective drugs, which is against common sense.

Finally, this study consolidates the notion that the CKD patient has particular characteristics that make him an exception as long as the cardiovascular risk is concerned.

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