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Peripheral arterial disease and kidney failure: a frequent association

Salvador Tranche-Iparraguirre[1], Rafael Marín-Iranzo[2], Rebeca Fernández-de Sanmamed[1], Alba Riesgo-García[3], Eduardo Hevia-Rodríguez[4], Juan B. García-Casas[5]

[1] Centro de Salud El Cristo. Oviedo, Asturias. Spain
[2] Centro Médico de Asturias. Oviedo, Asturias. Spain
[3] Hospital Valle del Nalón. Langreo, Asturias. Spain
[4] Centro de Salud Vallobín-Concinos. Oviedo, Asturias. Spain
[5] Facultad de Medicina. Oviedo, Asturias. Spain

ABSTRACT

Objectives: To determine the prevalence of kidney disease in people older than 49 years old with peripheral arterial disease and to analyse its relationship with risk factors and cardiovascular disease. **Material and method:** Prospective epidemiological study 3 years in duration with selection by simple random sampling in the general population aged over 49 years. Data on demographic, clinical, prevalence of risk factors and cardiovascular disease were registered. We defined peripheral arterial disease (PAD) by ankle-brachial index (ABI) ≤ 0.9 and chronic kidney disease (CKD) according to estimated glomerular filtration rates by the MDRD <60 ml/min/1.73m^2. Baseline data are presented. **Results:** 511 people were included. The mean age was 66.6 (9.7) years (SD), 37% were men. The prevalence of PAD was 12.4% (N=63) of the sample, average age 72.6 years, 46% men. The presence of CKD stages 3-5 was 39.7%. Patients with PAD and CKD compared with those with normal renal function were older (75.6 vs. 70.6, p=0.08), predominantly women (64% vs 47.4%, p=ns), and showed higher values for systolic and diastolic blood pressure (159.2 vs 146.1, p=ns and 85.7 vs 80.3 mmHg, p=0.09), CRP (1.23 vs 0.38 mg/dl, p=0.05) and albumin creatinine ratio (90.2 vs 26.4 mg/g, p=ns). In this group, the prevalence of cardiovascular risk factors and associated cardiovascular disease, were significantly higher without reaching statistical significance. **Conclusions:** Kidney failure is present in 39.7% of patients with PAD and it defines a subgroup of patients with high cardiovascular risk.

Key Words: Peripheral arterial disease. Chronic kidney disease. Primary Care.

Enfermedad arterial periférica e insuficiencia renal: una asociación frecuente

RESUMEN

Objetivos: *Determinar la prevalencia de insuficiencia renal en población mayor de 49 años de edad con enfermedad arterial periférica y analizar su relación con factores de riesgo y enfermedad cardiovascular.* ***Material y métodos:*** *Estudio epidemiológico prospectivo de 3 años de duración con selección por muestreo aleatorio simple en población general de edad superior a 49 años. Se recogieron datos demográficos, clínicos, prevalencia de factores de riesgo y enfermedad cardiovascular. Se definió enfermedad arterial periférica (EAP) por índice tobillo-brazo ≤ 0,9 e insuficiencia renal crónica (IRC) según valores de filtrado glomerular estimado por la fórmula MDRD < 60 ml/min/1,73 m^2. Se presentan datos basales.* ***Resultados:*** *Se incluyeron 511 personas de 66,6 (9,7) años de edad media (desviación estándar), 37% varones. La prevalencia de EAP fue del 12,4% (n = 63) de la muestra, de 72,6 años de edad media, 46% varones. La presencia de enfermedad renal crónica en estadios 3-5 fue del 39,7%. Los pacientes con EAP e IRC, en comparación con los que tenían función renal normal, eran de mayor edad (75,6 vs. 70,6, p = 0,08), predominantemente mujeres (64 vs. 47,4%, p = no significativa [ns]), presentaban cifras más elevadas de presión arterial sistólica y diastólica (159,2 vs. 146,1, p = ns y 85,7 vs. 80,3 mmHg, p = 0,09), proteína C reactiva (1,23 vs. 0,38 mg/dl, p = 0,05) y cociente albúmina-creatinina (90,2 vs. 26,4 mg/g, p = ns). En este grupo, la prevalencia de factores de riesgo cardiovascular y enfermedad cardiovascular asociada fueron notablemente superiores, sin alcanzar significación estadística.* ***Conclusiones:*** *La insuficiencia renal está presente en el 39,7% de los pacientes con EAP y delimita un subgrupo de pacientes con elevado riesgo cardiovascular.*

Palabras clave: *Enfermedad arterial periférica. Enfermedad renal crónica. Atención Primaria.*

Correspondence: Salvador Tranche Iparraguirre
Centro de Salud El Cristo.
A. Flórez Estrada, 23, 33006 Oviedo. Asturias. Spain.
stranchei@gmail.com
stranchei@medynet.com

INTRODUCTION

In clinical practice, the term «peripheral arterial disease» PAD tends to refer to vascular disease in the lower limbs,

defined as being caused by stenosis or thrombosis of leg arteries, and one manifestation of systemic atherosclerosis.[1]

Although the presence of intermittent claudication has traditionally been used as a PAD marker to give an approximate calculation of its prevalence in the general population, the ankle-brachial index (ABI) is currently considered to have more diagnostic precision, and it is recommended for both individual diagnoses and epidemiological studies.[1,2] An ABI below 0.9 is 95% sensitive and 100% specific for the presence of stenosis in the vascular array of the lower limbs, which is indicative of atherosclerosis in that region.[3,4] ABI is also recognised as a marker of cardiovascular risk, and it has an excellent correlation with the development of coronary artery complications, the incidence rate of strokes and death by cardiovascular or other causes in the general population, particularly in the geriatric population.[5,6]

It is well understood that the presence of end-stage kidney failure in patients with kidney replacement therapy and PAD is accompanied by increases in lower limb amputations, hospitalisation, and total and cardiovascular mortality.[7-9] There is a growing interest in examining the correlation between kidney function and PAD, not only during end-stage kidney failure, but also throughout all stages of kidney disease. The NHANES 1999-2000 epidemiological study analysed the prevalence of PAD in patients with kidney disease, defined as those having an estimated glomerular filtration rate (eGFR) measured with the Cockcroft-Gault formula below 60ml/min/1.73 m². Prevalence in this population was 24% compared with 3.7% in the population whose eGFR was higher than 60ml/min/1.73 m² (odds ratio [OR]: 9.7, 95% confidence interval [CI]: 5.6-16.7), $P<.001$). This correlation was independent from other variables such as age, diabetes, hypertension, hypercholesterolaemia, coronary artery disease and ictus (OR: 2.5, 95% CI: 1.2-5.1), $P<.011$).[10] Very similar results were obtained in NHANES 1999-2004.[11] Longitudinal follow-up studies have also shown increased risk of developing PAD in patients with an eGFR below 60ml/min compared to those with a higher glomerular filtration rate (GFR).[12,13]

Chronic kidney disease (CKD) and PAD have more than just atherosclerosis as a common underlying factor in their anatomical pathology. They also share risk factors such as diabetes, arterial hypertension and smoking, and it is possible that gaining control over these risk factors would reduce or slow the progression of both diseases. This would explain the reciprocal relationship between both entities; that is, patients with reduced kidney function will have higher incidence and prevalence rates for arterial disease, and in turn, kidney failure will be more common in patients with chronic ischaemia of the lower limbs. However, this last postulate has not received much study.

OBJECTIVES

Main objective

Determine the prevalence of chronic kidney disease (CKD) defined as an eGFR <60 ml/min/1.73 m² in a population aged 49 years and older with PAD.

Secondary objective

Analyse the relationship between patients with PAD and kidney failure and classic cardiovascular risk factors and vascular disease at other levels.

MATERIAL AND METHOD

Population and sample

The study population includes all individuals 49 years old or older (n=76 660) residing in Oviedo, Asturias, Spain, identified in the database containing individual health card data. For the purpose of calculating PAD prevalence, 1000 individuals were selected from the initial population through simple random sampling. This number was established based on the following suppositions: estimated prevalence of 0.10 based on other studies, with a Type I error of 0.05 and desired precision 0.03, giving us a sample size (453) that was increased according to an estimate of 60% drop-outs and non-responses. The final sample size was 996 individuals. Terminal and immobilised patients were excluded. Deceased patients, those who moved their residence and those who declined to participate in the study were considered lost and they were not substituted. The study was approved by the Clinical Research Ethics Committee of Asturias.

The main objective of this study is to verify the relationship between PAD and cardiovascular disease in a population 49 years or older during a 3 year follow-up period. This project is a sub-study to determine whether patients with both PAD and chronic kidney disease (CKD) show a more unfavourable risk profile, both at baseline and during disease evolution. Initial data are shown here.

Data registry

We elaborated a protocol for collecting demographic data (age and sex), clinical data (weight, height, body mass index), systolic blood pressure (SBP), diastolic blood pressure (DBP), presence of cardiovascular risk factors (smoking, dyslipidaemia, hypertension, diabetes, obesity), cardiovascular disease (ischaemic heart disease, heart failure, cerebrovascular accident, peripheral arterial disease), in addition to data corresponding to hypertension,

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dyslipidaemia, diabetes and anti-platelet drugs. All patients underwent an electrocardiogram and a general biochemical study that included serum concentrations of glucose, uric acid, creatinine, total cholesterol, HDL cholesterol, triglycerides, fibrinogen, C-reactive protein and lipoprotein(a).

Hypertension was diagnosed in the presence of SBP figures ≥140mmHg and/or DBP ≥90mmHg on 3 separate visits, or in individuals who were already receiving dietary or pharmacological antihypertensive treatment. Arterial blood pressure figures represent average readings from three measurements taken 2 minutes apart.

All subjects who had consumed tobacco during the past month were considered smokers; those who had been smokers but who had not smoked in the past year were considered former smokers.

Subjects with baseline glycaemia figures ≥126mg/dl on 2 occasions, or with a an oral glucose tolerance test reading above 200mg/dl at 2 hours were considered diabetic, along with subjects already receiving anti-diabetic treatment, whether in the form of insulin or oral anti-diabetic drugs.

Hypercholesterolaemia was declared for total cholesterol scores above 240mg/dl on 2 occasions at least 3 weeks apart, and high triglyceride levels were declared for levels above 200mg/dl on 2 occasions or for subjects already receiving lipid lowering treatment.

Subjects were considered obese if their body mass index (weight in kilograms divided by height in metres squared) was greater than or equal to 30kg/m^2.

Presence of cardiovascular disease was considered for ischaemic heart disease, heart failure, cerebrovascular accident and abdominal aortic aneurysm if events were documented by either hospital admission or by a specialist study. There was no active search for subclinical cardiovascular disease (lacunar stroke, silent ischaemic heart disease, etc.).

To determine ABI, each subject remained in dorsal decubitus during 5 minutes, and the ratio of the systolic pressure at the ankle (posterior tibial artery) to that at the dominant arm (humeral artery) was calculated separately for each of the limbs. We used a pocket non-directional Doppler ultrasound (Mini/Audio/Aqua/Dopplex®) with an 8MHz VP8 transducer. PAD was considered to be present if the index was less than or equal to 0.90.

The abbreviated or modified Modification of Diet in Renal Disease formula (MDRD) was used to estimate GFR, and a rate of less than 60ml/min/1.73m^2 was considered indicative of kidney failure.[14,15] CKD stages are those described in K/DOQI guidelines, and they included the modifications recently suggested by Levey et al. and Tonelli et al.[16,17]

Albuminuria was measured as the albumin-creatinine ratio (mg/g) in a sample collected during morning hours. It was classified as optimal for values <10 mg/g; normal-high, 10-29.9mg/g; high, 30-299mg/g; very high, 300-1999mg/g; and nephrotic for values >2000mg/g.

Abbreviated or modified MDRD formula:

$$\text{GFR (ml/min/1.73 m}^2\text{)} = 186 \times [\text{serum creatinine (mg/dl)}] -1.154 \times (\text{age}) -0.203 \times (0.742 \text{ if female}) \times (1.212 \text{ if black})$$

Quantitative variables are given as a mean and 95% CI. Qualitative variables are given with their frequency distributions. Association between variables was assessed using ^{2} or Fisher's exact test for qualitative variables, and Student's t-test for quantitative variables. In all cases, values of or Fisher's exact test for qualitative variables, and Student's t-test for quantitative variables. In all cases, values of $P<.05$ were considered statistically significant. Statistical analysis was performed using the software suite SPSS 15.0.

RESULTS

There were 511 subjects at the start of the study (exclusion criteria are listed in Figure 1); 37.4% were male and the mean age was 66.6 years. From their medical histories, we concluded that the prevalence of hypertension was 31.2%,
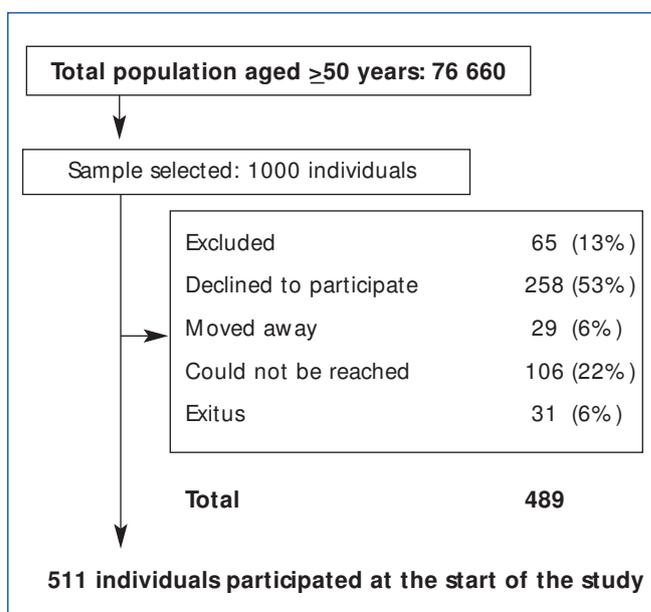

Total population aged ≥50 years: 76 660		
Sample selected: 1000 individuals		
Excluded	65	(13%)
Declined to participate	258	(53%)
Moved away	29	(6%)
Could not be reached	106	(22%)
Exitus	31	(6%)
Total	**489**	

511 individuals participated at the start of the study

Figure 1. Study population flow.

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16.6% were smokers, 7.8% had diabetes and 26.7% had a lipid metabolism disorder. General data are described in Table 1.

In total, 63 cases (12.4%) in the sample had PAD as defined by an ABI≤0.9. The PAD patient group was 46% male with a mean age of 72.6 years. This group presented slightly elevated SBP (150.3mmHg), baseline glycaemia (113.8mg/dl) and microalbuminuria (51.46mg/g). Their cardiovascular risk factors included hypertension (40.3%), dyslipidaemia (24.2%), microalbuminuria (22.9%), smoking (19.4%) and diabetes mellitus (12.9%). The microalbuminuria section also includes 1 patient with urinary albumin values above 300mg/g (Table 2).

A total of 25 (39.7%) PAD patients had an eGFR<60ml/min/1.73 m². Table 3 shows distribution by different CKD stages according to eGFR and urinary excretion of albumin for both the general sample and for patients with PAD. Patients with both PAD and kidney failure were older, with higher values for SBP and DBP, baseline glycaemia, C-reactive protein and urinary albumin excretion, although there were no cases in which differences

Table 1. General sample data

Variable	Value (SD)
N (people)	511
% males	37.4
Age in years	66.66 (9.7)
SBP (mmHg)	141.4 (21.5)
DBP (mmHg)	81.9 (10)
BMI (kg/m²)	28.08 (4.6)
Glucose (mg/dl)	102.8 (29.6)
Creatinine (mg/dl)	1.01 (0.19)
Total cholesterol (mg/dl)	222.7 (38)
LDL cholesterol (mg/dl)	138.2 (33.69)
HDL cholesterol (mg/dl)	62.1 (16.04)
Triglycerides (mg/dl)	113.8 (68.4)
CRP (mg/dl)	0.4 (0.2)
Albumin-creatinine ratio (mg/g)	16.43 (66.4)
Microalbuminuria (%)	9
Coronary artery disease	6.1
Stroke (%)	2.5
Heart failure (%)	1.2
Abdominal aortic aneurysm (%)	0.8

SD: standard deviation; HDL: high-density lipoproteins; BMI: body mass index; LDL: low-density lipoproteins; DBP: diastolic blood pressure; SBP: systolic blood pressure; CRP: C-reactive protein.

Table 2. Characteristics of patients with peripheral arterial disease

Variable	Value (SD)
N	63
Men (%)	29(46)
Age (years)	72.67(10.8)
SAP (mmHg)	150.37(30.4)
DAP (mmHg)	82.16(12.7)
BMI (kg/m²)	28.01(4.6)
Glucose (mg/dl)	113.8(54.1)
Creatinine (mg/dl)	1.08(0.3)
Total cholesterol (mg/dl)	215.81(38.6)
LDL cholesterol (mg/dl)	129.4(35.3)
HDL cholesterol (mg/dl)	61.71(17.1)
Triglycerides (mg/dl)	116.52(55.4)
CRP (mg/dl)	0.72(1.7)
Albumin-creatinine ratio (mg/g)	51.5 (170.9)
Microalbuminuria (%)	22.9
Coronary disease (%)	16.1
Stroke (%)	3.2
Heart failure (%)	6.5
Kidney failure (%)	39.7
Abdominal aortic aneurysm (%)	6.3
Overall cardiovascular disease (%)	17.5

SD: standard deviation; BMI: body mass index; DBP: diastolic blood pressure; SBP: systolic blood pressure; CRP: C-reactive protein.

were significant (Table 4). The group with CKD had a higher prevalence of abdominal aortic aneurysm and a tendency towards a higher presence of coronary artery disease, heart failure and global cardiovascular disease, but this was not statistically significant (Table 5).

DISCUSSION

This is the first study in our country to analyse the prevalence of CKD in the population with PAD. In PAD patients aged ≥50 years, the prevalence of CKD (defined by eGFR, MDRD formula, <60ml/min/1.73 m²) was 39.7%.

The prevalence of PAD in our population (12.4%) corresponds to that reported in other population studies that used ABI≤0.9 as a criterion. According to the National Health and Nutrition Examination Survey (NHANES 1999-2004), prevalence in the population aged 60 years and older was 12.2%; it was 19.1% in an epidemiological study in the Netherlands, but this was in a general population aged 55 years and older.[18,19] However, a recent Spanish study of a

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Table 3. Estimated glomerular filtration rate and urinary albumin excretion by chronic kidney disease stages

Stage eGFR (ml/min/1.73m²)	General sample N (%)	Population with PAD N (%)	Microalbuminuria mg/g			
			< 10	10-29	30-300	300-1999
1 (≥ 90)	24 (4.7)	3 (4.8)	3	0	0	0
2 (60-89)	347 (68.2)	35 (55.5)	21	5	9	0
3 (30-59)	133 (26.2)	24 (38.1)	11	6	6	1
4 (15-29)	3 (0.6)	1 (1.6)	0	1	0	0
5 (< 15)	0	0	0	0	0	0

PAD: peripheral artery disease; eGFR: estimated glomerular filtration rate.

population aged 49 years and older in 28 different health centres describes a prevalence of 7.6% for PAD. This is justified when we recall that Spain has low figures for cardiovascular risk according to international risk tables.[20] Explaining this difference in prevalence is difficult, because when we compare both populations, we observe that age (72.67 vs 70.7 years), hypertension prevalence (40.3% vs 11.9%), smoking (19.4% vs 11.9%) and hypercholesterolaemia (24.2 vs 10.2%) are much higher in our study. The opposite is true for diabetes (12.9% vs 17%), obesity (1.6 vs 8.2%) and cardiovascular disease, especially myocardial infarction (6.1% vs 29%) and ictus (3.2% vs 24%), which were higher in the other study.

Nearly 40% of the patients with PAD suffered from CKD, which was higher than the 29.7% given by the EROCAP study and the 35% given by the YP Liew study which contained more than 1000 patients.[21,22] The association of the two diseases is very common. O'Hare analysed the prevalence of PAD in 2229 subjects aged 40 years and older and established 2 groups according to eGFR (greater or less than 60ml/min/1.73 m²). PAD prevalence in the group with normal kidney function was 3.7%, and reached 24% of subjects with a low eGFR. The OR was 3.0 (95% CI [1.7-5.3], $P<.001$), and 2.5 (95% CI [1.2-5.1], $P=.011$), after adjusting for risk factors such as cholesterol, age, ATH and coronary artery disease.[10] The same tendency can be found in

Table 4. Comparison of clinical variables among patients with peripheral arterial disease with and without associated chronic kidney disease

Variable	PAD with CKD Value (SD)	PAD without CKD Value (SD)	P
Males [n(%)]	9(36)	20 (52.6)	ns
Age (years)	75.6(9.5)	70.6(11.4)	.08
SBP (mmHg)	159.2(34.4)	146.1(25.1)	ns
DBP (mmHg)	85.7(15)	80.3(10.1)	.09
BMI (kg/m²)	29.4(4.1)	27.2 (4.7)	.07
Glucose (mg/dl)	118.3(57.7)	110.7(52.2)	ns
Creatinine (mg/dl)	1.3(0.28)	0.95(0.13)	<.001
Total cholesterol (mg/dl)	205.9(36.8)	222.5(38.9)	ns
LDL cholesterol (mg/dl)	121.1(32.3)	135.1 (36.5)	ns
HDL cholesterol (mg/dl)	60.8(18.1)	62.3(16.6)	ns
Triglycerides (mg/dl)	120.7(59.4)	113.7(53.3)	ns
CRP (mg/dl)	1.2(2.6)	0.38(0.4)	.05
Albumin-creatinine ratio (mg/g)	90.2(261.9)	26.4(56.5)	ns

SD: standard deviation; PAD: peripheral artery disease; HDL: high-density lipoproteins; BMI: body mass index; CKD: chronic kidney disease; LDL: low-density lipoproteins; ns: not significant; DBP: diastolic blood pressure; SBP: systolic blood pressure; CRP: C-reactive protein

Table 5. Prevalence of cardiovascular risk factors in patients with peripheral arterial disease with and without associated chronic kidney disease

Variable	PAD with CKD	PAD without CKD	*P*
	%	%	
Arterial hypertension	48	35.1	ns
Smoking	16	21.6	ns
Diabetes	12	13.5	ns
Dyslipidaemia	80	73	ns
Microalbuminuria	28	21.6	ns
Coronary disease	16	8.1	.08
Stroke	4	2.7	ns
Heart failure	8	5.4	ns
Abdominal aortic aneurysm	16	0	.012
Overall cardiovascular disease	24	10.8	ns

PAD: peripheral artery disease; CKD: chronic kidney disease; ns: not significant.

a sub-analysis of the ARIC study in which the relative risk of developing PAD, comparing patients with eGFR >90ml/min/1.73 m^2 and eGFR ≤60ml/min/1.73 m^2, was 1.04 (95% CI, 0.91-1.18) and 1.82 (95% CI, 1.13-2.14) respectively.[12]

Analysing known risk factors that are shared by both diseases shows that the group with PAD and CKD was made up of older subjects, predominantly women (64%), and for all variables except the lipid profile, values were higher than in patients with a normal kidney function. The only parameters for which there were statistically significant differences were plasma creatinine and C-reactive protein. Various studies undertaken in patients with stage III, IV or V kidney failure presented results similar to our own with regard to the prevalence of cardiovascular risk factors.[23,24]

The differences in serum creatinine are logical due to the correlation between creatinine and kidney function, and this is consistent with findings from other studies in which increased serum creatinine is accompanied by increase in the PAD incidence rate.[21,25]

Differences in the lipid profile may be explained by the possibility of pharmacological treatment currently being used, given that the prevalence of dyslipidaemia is higher in patients with renal conditions.

Urinary excretion of albumin is higher in the group of subjects with kidney disease [90.16 (261.9) vs 26.36 (56.53)], although the difference is not statistically significant. CKD is not defined solely on the basis of decreased GFR; it also entails the presence of persistent kidney injury during at least 3 months, demonstrated by

direct methods (kidney biopsy) or indirectly by the presence of albuminuria or proteinuria or abnormalities in imaging tests or in urine sediment.[14] Baber states that the association between decreased GFR and decreased microalbuminuria has to do with a high prevalence of PAD, and this could be useful for identifying a subgroup with vascular disease, although this could not be verified in our study.[11]

In the present study, the prevalence rates of ischaemic heart disease, ictus and heart failure were all listed separately; all of these entities were far more prevalent in the group with concomitant kidney and vascular disease, although prevalence figures were considerably lower than those published in other studies.[26,27]

We have not found literature analysing the association of abdominal aortic aneurysms (AAA) in the population with PAD and kidney failure. Our results may be consistent with the findings of Nakamura et al. in a small study that observed poorer kidney function in patients with AAA than in the hypertensive population, and with those of Barba et al. documenting a much higher prevalence of AAA in the PAD population than in the general population. Chue postulates that CKD, in addition to being related to atherosclerosis, might increase arterial rigidity through a series of complex processes related to uraemia. In conjunction with other risk factors, especially hypertension, this could be associated with an increased risk of aneurysm. However, the incidence and prevalence rates of AAA in CKD patients are unknown.[28-31]

The presence of PAD is a sign of generalised atherosclerosis, and it is associated with higher cardiovascular morbidity and mortality rates. Several population studies corroborate this

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finding; some well-designed studies with long follow-up periods show a close relationship between decreased kidney function (identified by serum creatinine levels or eGFR), and total/cardiovascular morbidity and mortality. [26,27] It would therefore seem that this group is a target population for treatment to prevent cardiovascular events, and a detection strategy must therefore be implemented in order to identify the at-risk population.

Unfortunately, the exact mechanisms contributing to the high prevalence of CKD among patients with peripheral arterial disease are still unknown. Classic cardiovascular risk factors, which are very prevalent in CKD patients, may contribute aetiologically to PAD development, but they only explain a small part of this association. [32] Atheromatous lesions are not restricted to a single area; rather, they become more widespread and severe, and therefore PAD patients frequently suffer from renal artery stenosis, as described in the prospective study by Marin et al. which monitored 418 patients admitted to hospital with severe PAD. An unsuspected stenosis was discovered in the renal artery in 27% of the cases, together with decreased kidney function and increased prevalence of ischaemic heart disease. Since they share aetiopathogenesis, differing stages of ischaemic nephropathy and nephroangiosclerosis might coexist, which would explain the decrease in GFR. [33] The role which alterations in the calcium-phosphorus metabolism may play in causing increased vascular calcification and therefore increased PAD and/or kidney disease, especially in the subgroup of patients with both CKD and PAD, is beyond the scope of this study.

A number of authors cite other, less traditional and less commonly-studied risk factors, such as inflammatory markers, increase in lipoprotein(a), oxidative stress, endothelial dysfunction and hyperhomocysteinaemia as factors that could contribute to atherosclerosis development in these patients. [32] We found high lipoprotein(a) and C-reactive protein values in the first group, which supports this theory.

Our study has certain limitations. Firstly, the sample size could be called small; it was appropriate for estimating PAD prevalence, but probably insufficient for finding statistically significant differences between the two groups with regard to the risk factor and cardiovascular disease distributions. Secondly, its objective was to measure CKD prevalence in patients with PAD, and not vice versa (prevalence of PAD in CKD patients). This made it difficult to compare it with major studies that did not have the same design. Limitations include the cross-sectional design; since associations are not prospective, we cannot establish a causal relationship between PAD and kidney failure in either direction. Due to these limitations, and particularly the sample size, we may only venture the hypothesis that CKD in the population with vascular disease poses a larger cardiovascular risk. We may be able to confirm this with follow-up data from the study.

CKD is present in nearly 40% of patients with PAD. The presence of decreased kidney function must be taken into account not only for proper adjustment and use of a number of drugs, but also because the copresence of the two conditions is likely to delimit a patient subgroup with a high risk of cardiovascular events. This group may benefit from early diagnosis and treatment, and studies providing an in-depth analysis of the relationship between both conditions are therefore necessary.

Conflicts of interest

The authors affirm that they have no conflicts of interest related to the content of this article.

REFERENCES

1. Hirsch AT, Haskal ZJ, Hertzer NR, Bakal CW, Creager MA, Halperin JL, et al. ACC/AHA 2005 Practice Guidelines for the management of patients with peripheral arterial disease (lower extremity, renal, mesenteric, and abdominal aortic): a collaborative report from the American Association for Vascular Surgery/Society for Vascular Surgery, Society for Society for Vascular Medicine and Biology, Society of Interventional Radiology, and the ACC/AHA Task Force on Practice Guidelines. Circulation 2006;113(11):e463-654.

2. Khan NA, Rahin SA, Anand SS, Simel DI, Panju A. Does the clinical examination predicts lower extremity peripheral arterial disease? JAMA 2006;295(5):536-46.

3. Fowkes FG. The measurement of atherosclerotic peripheral arterial disease in epidemiological surveys. Int J Epidemiol 1988;17:248-54.

4. Norgren L, Hiatt W, Dormandy J, Nehler M, Harris K, Fowkes F. Inter-society consensus for the management of peripheral arterial disease (TASC II). Eur J Vasc Endovasc Surg 2007;33:S1-S75.

5. Mostaza JM, Vicente I, Cairols M, Castillo J, González Juanatey JR, Pomar JL, et al. Índice tobillo-brazo y riesgo cardiovascular. Med Clin (Barc) 2003;121:68-73.

6. Lee AJ, Price JF, Russell MJ, Smith FB, van Wijk MC, Fowkes FG. Improved prediction of fatal myocardial infarction using the ankle brachial index in addition to conventional risk factors: the Edinburgh Artery Study. Arterioscler Thromb Vasc Biol 2005;25:1463-9.

7. Rajagopalan S, Dellegrottaglie S, Furniss AL, Gillespie BW, Satayathum S, Lameire N, et al. Peripheral arterial disease in patients with end-stage renal disease: observations from the Dialysis Outcomes and Practice Patterns Study (DOPPS). Circulation 2006;114(18):1914-22.

8. Fishbane S, Youn S, Flaster E, Adam G, Maesaka JK. Ankle-arm blood pressure index as a predictor of mortality in hemodialysis patients. Am J Kidney Dis 1996;27:668-72.

9. O'Hare A, Johansen K. Lower-extremity peripheral arterial disease among patients with end-stage renal disease. J Am Soc Nephrol 2001;12(12):2838-47.

10. O'Hare A, Glidden DV, Fox CS, Hsu C. High prevalence of peripheral arterial disease in persons with renal insufficiency. Results from the National Health and Nutritional examination survey. 1999-2000. Circulation 2004;109:320-3.

11. Baber U, Mann D, Shimbo D, Woodward M, Olin JW, Muntner P. Combined role of reduced estimated glomerular filtration rate and microalbuminuria on the prevalence of peripheral arterial disease. Am J Cardiol 2009;104(10):1446-51.

12. Wattanakit K, Folsom AR, Selvin E, Coresh J, Hirsch AT, Weatherley BD. Kidney Function and Risk of Peripheral Arterial Disease: Results from the Atherosclerosis Risk in Communities (ARIC) Study. J Am Soc Nephrol 2007;18:629-36.

13. O'Hare AM, Vittinghoff E, Hsia J, Shlipak MG. Renal insufficiency and the risk of lower extremity peripheral arterial disease: results from the Heart and Estrogen/Progestin Replacement Study (HERS). J Am Soc Nephrol 2004;15(4):1046-51.

14. National Kidney Foundation. K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. Kidney Disease Outcome Quality Initiative. Am J Kidney Dis 2002;39(2 Suppl 1):S1-266.

15. Levey AS, Bosch JP, Breyer-Lewis J, Greene T, Rogers N, Roth A. A more accurate method to estimate glomerular filtration rate from serum creatinine: a new prediction equation. Ann Intern Med 1999;130:461-70.

16. Tonelli M, Muntner P, Lloyd A, Manns BJ, James MT, Klarenbach S, et al. Using proteinuria and estimated glomerular filtration rate to classify risk in patients with chronic kidney disease. Ann Intern Med 2011;154:12-21.

17. Levey AS, Tangri N, Stevens LA. Classification of chronic kidney disease: A step forward. Ann Intern Med 2011;154:65-7.

18. Ostchega Y, Paulose-Ram R, Dillon CF, Gu Q, Hughes JP. Prevalence of peripheral arterial disease and risk factors in persons aged 60 and older: data from the National Health and Nutrition Examination Survey 1999-2004. J Am Geriatr Soc 2007;55(4):583-9.

19. Meijer WT, Hoes AW, Rutgers D, Bots ML, Hofman A, Grobbee DE. Peripheral arterial disease in the Elderly. The Rotterdam study. Arterioscler Thromb Vasc Biol 1998;18:185-92.

20. Alzamora MT, Forés R, Baena-Díez JM, Pera G, Toran P, Sorribes M, et al. The Peripheral Arterial disease study (PERART/ARTPER): prevalence and risk factors in the general population. BMC Public Health 2010;10:38.

21. Liew YP, Bartholomew JR, Demirjian S, Michaels J, Schreiber MJ Jr. Combined effect of chronic kidney disease and peripheral arterial disease on all-cause mortality in a high-risk population. Clin J Am Soc Nephrol 2008;3(4):1084-9.

22. de Francisco ALM, De la Cruz JJ, Cases A, de la Figuera M, Egocheaga MI, Gorriz JL, et al. Prevalencia de insuficiencia renal en centros de Atención Primaria de España: estudio EROCAP. Nefrología 2007;27(3):300-12.

23. Guerrero A, Montes R, Muñoz-Terol J, Gil-Peralta A, Toro J, Naranjo M, et al. Peripheral arterial disease in patients with stages IV and V chronic renal failure. Nephrol Dial Transplant 2006;21:3525-31.

24. Rajagopalan S, Dellegrottaglie S, Furniss AL, Gillespie BW, Satayathum S, Lameire N, et al. Arterial disease in patients with end-stage renal disease: observations from the Dialysis Outcomes and Practice Patterns Study (DOPPS). Circulation 2006;114(18):1914-22.

25. Selvin E, Köttgen A, Coresh J. Kidney function estimated from serum creatinine and cystatin C and peripheral arterial disease in NHANES 1999-2002. Eur Heart J 2009;30(15):1918-25.

26. Culleton BF, Larson MG, Wilson PWF, Evans JC, Parfrey PS, Levy D. Cardiovascular disease and mortality in a community-based cohort with mild renal insufficiency. Kidney Int 1999;56:2214-9.

27. Go AS, Chertow GM, Fan D, McCullock CE, Hsu CY. Chronic kidney disease and the risks of death, cardiovascular events, and hospitalization. N Engl J Med 2004;351:1296-305.

28. Nakamura S, Yoshihara F, Kamide K, Horio T, Nakahama H, Inenaga T, et al. Renal function in patients with abdominal aortic aneurysm. Comparison with hypertensive patients. Kidney Blood Press Res 2006;29(2):67-73.

29. Barba A, Estallo L, Baguer M, Vega de Ceniga M. Detection of abdominal aortic aneurysm in patients with peripheral artery disease. Eur J Vasc Endovasc Surg 2005;30(5):504-8.

30. Chue CD, Moody WE, Steeds RP, Towned JN, Ferro JC. Unexpected benefits of participation in a clinical trial: abdominal aortic aneurysms in patients with chronic kidney disease. QJM 2011.doi: 10.1093/qjmed/hcr172. First published online: September 19, 2011.

31. Chue CD, Towned JN, Steeds RP, Ferro JC. Arterial stiffness in chronic kidney disease: causes and consequences. Heart 2010;96:817-23.

32. Jaar BG, Plantinga LC, Astor BC, Fink NE, Longenecker C, Tracy RP, et al. Novel and traditional cardiovascular risk factors for peripheral arterial disease in incident-dialysis patients. Adv Chronic Kidney Dis 2007;14(3):304-13.

33. Marín R, Díaz Corte C, Cosío J, Rodríguez E, Barreiro A, Estevan JE, et al. Estenosis de arteria renal no sospechada en pacientes con arteriopatía periférica: prevalencia, significado clínico y factores de riesgo asociados. Nefrologia 1997;17:62-71.