FACTORS PREDICTING SUBCLINICAL ATHEROMATOSIS PROGRESSION IN CHRONIC KIDNEY DISEASE. THE NEFRONA STUDY.

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BACKGROUND

Subclinical atheromatous disease (AD) is a noninvasive marker of arterial injury that predicts incident cardiovascular events in both the general population and among patients with chronic kidney disease (CKD). However, data on risk factors for progression of AD in CKD are scarce. The aim of the study is to evaluate predictors of changes in AD in a cohort of chronic kidney disease patients.

METHODS

Multicenter, prospective and observational study of 1553 CKD patients (709 stage 3, 578 stages 4-5 and 266 on dialysis) without previous cardiovascular events from the NEFRONA cohort. A carotid and femoral ultrasound examination was performed at baseline and 24 months follow-up after. A unique reader performed the evaluation of the images. Progression of AD was defined as formation of new atherosclerotic plaques. CKD progression was defined as doubling of serum creatinine or the onset of dialysis. The statistical level of significance was fixed to 0.05.

RESULTS

26.9% were diabetics and 33.4% were former or habitual smokers. Prevalence of atheromatous plaque at baseline was 69 % and progression of AD occurred in 60% patients after 24 months without differences between CKD Stage. A higher rate of plaque progression occurred in patients with plaque at baseline and/or CKD progression. **(Figure 1**). Variables significantly and positively predicting AD progression in multivariate regression analysis are shown in **Figure 2**. Predictors of AD progression varied in the different CKD Stages and in patients with or without plaque at baseline. Thus, in early stages of CKD factors were similar to those described in the general population, whereas in late stages specific factors appear **(Table 1)**.

Fig. 1 Progression of plaque after 24 months stratified by plaque at baseline & CKD progression.

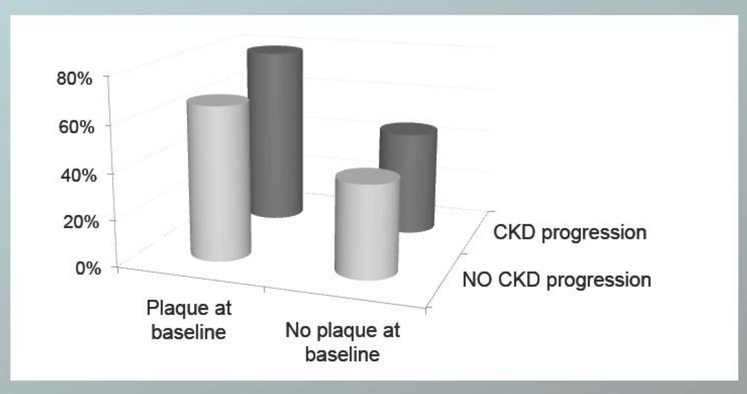

Fig. 2 Predictors of plaque progression after 24 months in a multivariate logistic regression analysis.

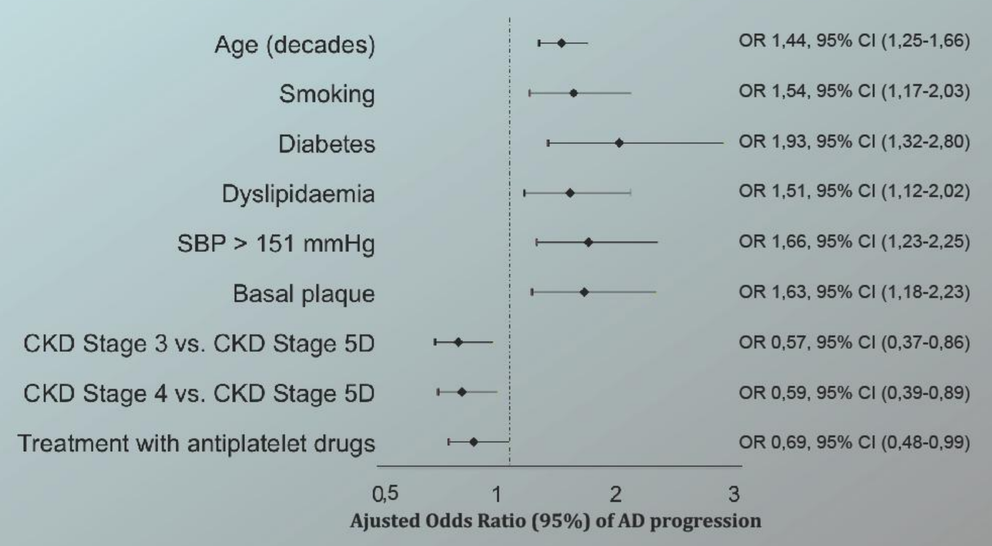

Table 1 Multivariate logistic regression to model plaque progression at 24 months stratified by CKD stage 3, 4-5 and 5D

	CKD stage 3		*CKD stage 4-5*		*CKD 5D*	
	β (S.E.)	p-value	β (S.E.)	p-value	β (S.E.)	p-value
Age (decades)	0.37 (0.1)	<0.01	0.64 (0.17)	<0.01	0.44 (0.16)	<0.01
Smoking (current & former vs. no)	0.62 (0.18)	<0.01	1.37 (0.38)	<0.01		
Diabetes	0.52(0.21)	0.01				
SBP[a] (highest tertile vs. rest)	0.39 (0.19)	0.03	1.04 (0.25)	<0.01		
P[b] (highest tertile vs. rest)	-1.65 (0.78)	0.03				
Age*P	0.51 (0.18)	<0.01				
Phosphate binders	-0.86 (0.38)	0.02				
25-OH-vitamin D (highest tertile vs. rest)	-0.46 (0.18)	0.01			-4.20 (1.79)	0.02
Plaque at baseline			3.08 (0.88)	<0.01		
Ln Ferritin			2.06 (0.81)	0.01		
Age*LnFerritin			-0.41 (0.20)	0.04		
Age*Plaque at baseline			-0.45 (0.21)	0.03		
Smoking*Plaque at baseline			-1.09 (0.45)	0.02		
BMI					-0.42 (0.17)	0.01
Dyslipidemia					1.59 (0.40)	<0.01
Cholesterol > 180 mg/dL[c]					-1.01 (0.41)	0.02
Uric acid					0.35 (0.14)	<0.01
cIMT					0.51 (0.16)	<0.01
Ln 25-OH-vitamin D*BMI					0.13 (0.06)	0.04

Results are expressed as β Coefficient and S.E. (Standard error). The following variables were introduced to build multivariate models by CKD stages because they were significant on bivariate testing or potential confounders: sex, CKD stage, age (decades), diabetes, smoking, dyslipidemia, SBP[a] (highest tertile>150 mmHg in CK stage 3 and > 156 mmHg in CKD stage 4-5), Pulse pressure, BMI, basal plaque, cIMT, ferritin, uric acid, CRP, Total cholesterol> 180 mg/dL[c] (the level of 180 was selected based in clinical criteria), LDL-cholesterol, hematocrit, statins, antiplatelet drugs, triglycerides, 25-OH-vitamin D (Vitamin D highest tertile in CKD Stage 3 ≥ 18.1, in CKD Stage 5D ≥ 11.5) , Phosphorous[b] (P highest tertile in CKD stage 3 ≥ 3.6 mg/dL), PTH. Finally, only significant variables in multivariate analysis in each group of CKD were included in the final model. **CKD stage 3**. Hosmer Lemeshow= 0.64, AUC= 0.706. **CKD stage 4-5**. Hosmer Lemeshow= 0.18 AUC= 0.75. **CKD stage 5D**. Hosmer Lemeshow=0.18, AUC=0.814.

CONCLUSIONS

In CKD (Stage 3, 4-5 & 5D), atheromatous disease progression after 24 months is notorius. Presence of plaque at baseline and ESRD are two factors highly predicting AD progression. Ultrasound monitoring may be a useful tool in cardiovascular risk assessment in CKD patients.

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