

Original article

PTH levels and not serum phosphorus levels are a predictor of the progression of kidney disease in elderly patients with advanced chronic kidney disease[☆]

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ABSTRACT

Background: At present, there is a high incidence of elderly patients with advanced chronic kidney disease (CKD) and it is important to know the long term progression and the factors that influence it.

Objectives: To analyse the progression of advanced CKD in elderly patients and the influence of bone-mineral metabolism.

Methods: Retrospective study of 125 patients ≥ 70 years of age with CKD stages 4–5 who started follow-up from January 1, 2007 to December 31, 2008, showing the progression of CKD (measured by the slope of the regression line of the estimated glomerular filtration rate [eGFR] by MDRD-4) over 5 years.

Results: Progression in the entire group (median and 25th and 75th percentiles): -1.15 ($-2.8/0.17$) ml/min/1.73 m²/year, CKD-4: -1.3 ($-2.8/0.03$) ml/min/1.73 m²/year, CKD-5: -1.03 ($-3.0/0.8$) ml/min/1.73 m²/year; the slope of the regression line was positive in 35 patients (28%: CKD does not progress) and negative in 90 patients (72%: CKD progresses). Negative correlation (Spearman) (slower progression): PTH, albumin/Cr ratio and daily Na excretion (all baseline measurements). No correlation with eGFR, serum P, urinary P excretion, protein intake and intake of P (all baseline measurements). In the linear regression analysis (dependent variable: slope of progression): albuminuria and PTH (both at baseline measurements) influenced this variable independently. Logistic regression (progresses vs. does not progress): PTH, albuminuria and eGFR (all at baseline measurements) influenced significantly.

Conclusions: In our group of elderly patients, impairment of renal function is slow, particularly in CKD-5 patients. Albuminuria and PTH at baseline levels are prognostic factors in the evolution of renal function.

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El nivel de la hormona paratiroidea (PTH) y no el de fósforo sérico es predictor de la progresión de la enfermedad renal en pacientes mayores con enfermedad renal crónica avanzada

R E S U M E N

Palabras clave:

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Antecedentes: En la actualidad hay una elevada incidencia de pacientes ancianos con enfermedad renal crónica avanzada (ERCA), siendo importante conocer la evolución a largo plazo y qué factores influyen.

Objetivos: Analizar la evolución de la ERCA en pacientes ancianos y la influencia del metabolismo óseo-mineral.

Métodos: Estudio retrospectivo de 125 pacientes ≥ 70 años con ERC 4-5, que iniciaron seguimiento desde el 1 de enero de 2007 al 31 de diciembre de 2008, observándose la progresión de la ERC (medida con la pendiente de la línea de regresión del filtrado glomerular estimado [FGe] obtenido mediante MDRD-4) durante 5 años.

Resultados: Progresión grupo completo (mediana y percentiles 25 y 75): $-1,15$ ($-2,80/0,17$) ml/min/ $1,73$ m²/año, ERC-4: $-1,3$ ($-2,8/0,03$) ml/min/ $1,73$ m²/año, ERC-5: $-1,03$ ($-3/0,8$) ml/min/ $1,73$ m²/año; pendiente de línea de regresión positiva en 35 pacientes (28%: ERC no progresa) y negativa 90 pacientes (72%: ERC progresa). Correlación (Spearman) negativa (progresión más lenta): hormona paratiroidea (PTH), albuminuria/Cr, excreción diaria de Na (todos basales). No se correlacionó con FGe, P sérico, excreción urinaria de P, ingesta proteica e ingesta de P (todas basales). Regresión lineal (variable dependiente: pendiente de progresión): albuminuria y PTH (ambos a nivel basal) influyeron de forma independiente en dicha variable. Regresión logística (progresa vs. no progresa): PTH, albuminuria y FGe (todos basales) influyeron de forma significativa.

Conclusiones: En nuestro grupo de pacientes de edad avanzada el deterioro de la función renal es muy lento, especialmente en los pacientes en estadio 5. La albuminuria y la PTH al inicio del seguimiento son factores pronósticos en la evolución de su función renal.

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Introduction

In recent years the number of elderly patients with advanced chronic kidney disease (ACKD) has increased. In some series it has been estimated that the number has doubled during the past 25 years.^{1,2} Factors, such as increased life expectancy and medical advances, have contributed to an increase in time exposure for the development of ACKD, mainly associated with atherosclerosis and diabetes mellitus (DM); in the past, these patients died before reaching ACKD.³

Patients with ACKD have specific characteristics: increased comorbidity, difficulty regarding the vascular access, need (sometimes not met) for family support for transportation to the haemodialysis centre or help with peritoneal dialysis. Renal replacement therapy may improve survival but it may also increase morbidity, decrease quality of life and involves enormous costs. The need to find factors that prevent or slow down the progression of CKD in this aged patients is a primary objective in health care.

Recent observational studies on the general population,⁴⁻⁶ without stratifying by age, suggest that elevated serum phosphate (P) and parathyroid hormone (PTH) levels may be responsible for a faster rate of CKD progression, although the aetiopathogenic mechanisms are not totally clear. Among

the possible underlying mechanisms are the vascular and renal tubular calcification, causing cell damage and fibroblast proliferation. An elevated serum phosphate level induces osteoblast differentiation of vascular smooth muscle cells and subsequent mineralisation of the vascular wall due to vesicle and apoptotic body secretion.⁷⁻⁹ In animal studies, treatment with phosphate binders slows down the vascular calcification process, even in the presence of high levels of calcium and calcitriol.¹⁰ Another proposed mechanism is phosphate induced endothelial injury due to down-regulation of annexin II (involved in various biological processes of the endothelial cell and in angiogenesis),¹¹ FGF-23 (acting on the FGFR1-klotho receptor) increases as GFR declines in an attempt to facilitate the urinary excretion of phosphate, may also play a role in CKD progression, but the mechanism is not well defined. One recent study showed that FGF23 was the marker most significantly related to CKD progression in patients with diabetic nephropathy.¹²

Since these parameters are at least partially modifiable with treatment, it is important to evaluate them in a population of older patients with ACKD.

The purpose of our study was to analyse whether parameters of bone and mineral metabolism predict CKD progression in a group of elderly patients (≥ 70 years of age) followed at our ACKD clinic for 5 years.

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