Elderly patients with chronic kidney disease: what is their course at one year?

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SUMMARY

Introduction: *Aging is associated to several structural and functional kidney changes. Recently, there is a great interest in the detection of Chronic Kidney Disease (CKD) in the general population. A classification of CKD, based on several stages of the estimated glomerular filtration rate (eGFR), has been established. In this study we followed up, clinically and biochemically, during one year eighthy patients older than 65 years so as to ascertain the applicability and utility of such classification to those patients.*

Patients and methods: *80 clinically stable patients, with a median age of 83 years, recruited within january and april 2006, were followed up during one year. We separated them in two groups: Group 1: 38 patients with serum creatinine < = 1,1 mg/dl (range 0,7-1,1) and with no proteinuria; and Group 2: 42 patients with serum creatinine > 1.1 mg/dl (range 1,2-3) and with proteinuria < 3 g/24 hours. Clinically we registered morbimortality and treatments received, and biochemically we measured serum creatinine and eGFR at the time of recruitment and after one year of follow up using two equations: Cockroft and abreviated MDRD. Statistical comparisons were made using the general lineal model for repeated measures of the SPSS 11.0 program.*

Results: *10% of the patients died during the follow up. Cardiac problems were the kind of morbidity more frequently found. Only a small proportion (23%) of group 2 patients were receiving erithropoietin (EPO) treatment. Estimated GFR and proteinuria remained stable at the end of one year independently of basal GFR; we found no significant differences between groups in the rest of analitical parameters.*

Conclusion: *In old patients with no significant proteinuria, the similarity of their clinical evolution and the stability of their eGFR (independently of its basal value), as well as the lack of differences in other analitical parameters, appears not to confer any advantages to the use of matematical formulae to clasifie them according to their eGFR.*

Key words: *Creatinine. Chronic kidney disease. Filtrate glomerular estimate. Elderly.*

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RESUMEN

Introducción: **El envejecimiento conlleva diversos cambios estructurales y funcionales en el riñón. Recientemente se está prestando un gran interés a la detección precoz de la Enfermedad Renal Crónica (ERC) en la población general, a partir de la estimación mediante fórmulas matemáticas del filtrado glomerular (FG); por otra parte, se ha establecido una clasificación de la ERC en diversos estadios según el FG estimado (FGe). En este estudio se analizó la evolución clínica y del FGe en un grupo de pacientes ancianos con FGe basal disminuido, con el objetivo de valorar si la aplicación de dicha clasificación tiene utilidad práctica en este tipo de pacientes.**

Pacientes y métodos: **80 pacientes clínicamente estables con una media de edad de 82,4 ± 6,5 años, reclutados entre enero y abril de 2006 fueron seguidos durante un año (grupo 1: 38 pacientes con creatinina sérica (Crs) < = 1,1 mg/dl (rango 0,7-1,1) y sin proteinuria; y grupo 2: 42 pacientes, con Cr s > 1,1 mg/dl (rango 1,2-3) y con proteinuria < 3 g/día). El 70% del total de pacientes tenía un estadio 3 ó 4 de ERC, de acuerdo con el FGe (MDRD abreviado). Clínicamente se estudiaron la morbi-mortalidad y los fármacos empleados. Analíticamente se determinó la Crs y se estimó el FG basal y un año después según fórmulas de Cockroft y MDRD abreviado. La estadística se realizó con el programa SPSS 11.0 usando un modelo lineal general para medidas repetidas.**

Resultados: **Un 10% de los pacientes falleció antes del año. La patología cardíaca fue la comorbilidad más frecuente. Sólo el 23% de los pacientes del grupo 2 recibía terapia con eritropoyetina (EPO) al final del estudio. La función renal (FR) y la proteinuria permanecieron estables al cabo del año con independencia del grado de FG previo; no hubo diferencias significativas en el resto de los parámetros analíticos analizados.**

Conclusión: **En pacientes ancianos que no presentan proteinuria significativa la evolución clínica similar (independientemente del grado de FG basal) y la estabilidad de los diversos parámetros analíticos asociados al descenso de la función renal en el tiempo, permiten simplificar su seguimiento sin necesidad de recurrir a la estimación del FG mediante fórmulas matemáticas.**

Palabras clave: Creatinina. Enfermedad renal crónica. Filtrado glomerular estimado. Anciano.

INTRODUCTION

Aging is associated to a number of changes in the structure and function of various organs.[1] In the kidney, among other

changes, the glomerular filtration rate (GFR) decreases at an average rate of 0.8 mL/min/year.[2] It is known that a marked decrease in GFR leads to the occurrence of various manifestations associated to chronic renal failure (CRF), including anaemia[3], osteodistrophy[4], metabolic acidosis[5] and so on.

On the other hand, a great interest is currently being paid to early detection of «occult kidney disease» in the general population from GFR estimation. For this purpose, a number of mathematical equations based on serum creatinine (SCr) have been devised. Thus, depending on GFR, chronic kidney disease (CKD) is divided into several stages. A GFR ranging from 60 and 30 mL/min is considered indicative of stage 3 CKD.[6] This classification has been considered applicable to the whole population.

In a prior study,[7] we reported that all elderly patients enrolled, including those with SCr values within the normal range, already had decreased GFR values, and approximately one third were in stage 3. Today, a laboratory finding of a decreased GFR in asymptomatic elderly patients with no other associated signs of CKD (anaemia, etc.) is a reason for referral to the nephrology outpatient clinic. This study was therefore intended to establish whether such classification has a practical value in this specific group of patients or is only imposing an unnecessary overload on nephrology clinics. For this purpose, a clinical a laboratory monitoring was performed in a group of patients over 65 years of age, analysing the changes in their kidney function and their morbidity and mortality for one year.

PATIENTS AND METHODS

Patients

Eighty patients > 65 years of age (mean, 82.4 ± 6.5 years; range, 69-97 years) seen during the January-April 2006 period were enrolled. Of these, 38 patients were recruited at the geriatrics outpatient clinic (Group 1, SCr ≤ 1.1 mg/dL (range 0.7-1.1) and 42 patients at the general nephrology outpatient clinic (group 2, SCr > 1.1 mg/dL (range 1.2-3). Overall, 68.8% of patients were females (84.2% in group 1 and 54.8% in group 2, p < 0.005). A history of diabetes mellitus (DM) and high blood pressure (HBP) was found in 37.3% and 81.3% of patients respectively. Comparison of both groups showed no significant differences in DM or HBP distribution. Study patients were clinically stable and underwent a clinical and laboratory re-evaluation one year later.

Patient distribution by CKD stage at baseline using the Cockcroft-Gault formula was as follows: stage 1, 0%; stage 2, 7.9%; stage 3, 66.6%; stage 4, 20.6%; stage 5, 4.7%. The distribution obtained with the abbreviated MDRD formula was: stage 1, 0%; stage 2, 30%; stage 3, 60%; stage 4, 10%; stage 5, 0%.

Established treatments with statins, antihypertensives, calcium salts, iron, and erythropoietin (EPO).

Methods

A prospective, observational study. The baseline assessment was performed at a scheduled patient visit to the clinic during January-April 2006. All patients underwent clinical and laboratory monitoring for one year, and a re-evaluation was done in the January-April period of 2007. Hospital admissions and their reasons were recorded, as well as the occurrence of cardiovascular events and mortality. Laboratory monitoring was based on GFR estimation using the Cockcroft-Gault[8] and abbreviated MDRD formulas.[9]

Laboratory tests were performed one week before patients attended the scheduled visits at the geriatrics and nephrology clinics both at baseline and at one year. The following parameters were measured in venous blood using standard hospital methods: creatinine, urea, uric acid, lipid profile, albumin, calcium, phosphorus, alkaline phosphatase, electrolytes, haemoglobin, and haematocrit. In group 2, 24-hour urine protein was measured.

Statistical analysis

SPSS 11.0 software was used for statistical analysis. Data are given as proportions, means, and standard deviations. A lineal model for repeated measures was used to assess change in kidney function over time. The significance level was 95%.

RESULTS

Ten percent of patients died before the end of the study year (four due to impairment in overall status, two from fracture complications, one from a tumour, and one from a stroke). Hospital admission of 21.8% of patients was required during the year; 27.8% of these admissions were for cardiac disease, and 22.2% for infections. No significant differences in mortality, admission, and cardiovascular events were found between the groups.

As regards use of drugs, 27.7% were receiving statins, 82.8% antihypertensive drugs, 10.3% calcium salts, and 14.5% iron. No significant differences were found between the groups in use of these drugs. Only some group 2 patients (23%) were receiving EPO (p < 0.003). These were older patients (89 ± 5 *vs* 81 ± 6 years, p < 0.001) with higher SCr levels (2.0 ± 0.5 *vs* 1.2 ± 0.2 mg/dL; p 0.000) and lower eGFRs according to the MDRD formula (32 ± 10 *vs* 54 ± 15 mL/min; p 0.000).

Figure 1 shows the change in kidney function (KF) at one year in the 72 patients who completed the study. While significant differences exist in SCr levels and GFR between both groups (p = 0.000), it may be seen that both SCr levels and GFR (estimated by MDRD and Cockcroft-Gault) do not significantly differ from baseline values.

In group 2, proteinuria showed no significant changes at one year: baseline, 0.14 ± 0.23 g/24 hours (range 0-3 g/24 h), *vs* 1 year, 0.23 ± 0.46 g/24 h (range 0-1.96 g/24 h).

Figure 2 shows the change in anaemia over time by group. All patients had a haematocrit value higher than 35% both at baseline and at one year of follow-up. No significant differences were found between the groups in all other laboratory parameters tested at baseline and one year.

Similarly, no significant changes over time were found when GFR values were compared between diabetic and non-diabetic patients (table I).

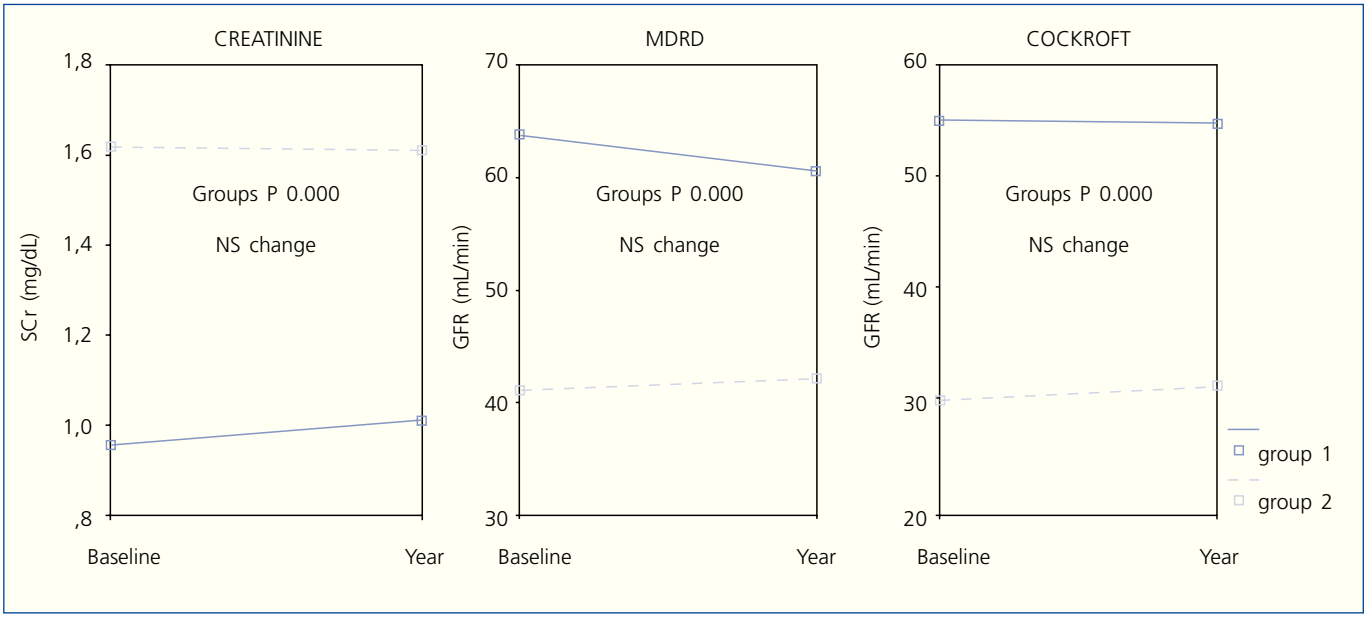

Figure 1. Change in kidney function at one year. While significant differences (at baseline and one year) exist in kidney function in both groups (P 0.000), analysis of repeated measures at one year showed no significant changes from baseline values. Group 1: SCr ≤ 1.1 mg/dL; Group 2: SCr > 1.1 mg/dL. NS: Non significant.

DISCUSSION

There are few studies reporting the progression of CKD in the elderly population. One such report is the Hemmelgarm study,[10] describing CKD progression during two years of follow-up in a population > 66 years. Progression was slow, except in diabetic patients and in those with a GFR < 30 mL/min, in agreement with other studies[11,12] where association of estimated GFR to mortality, as well as progression to end-stage CRF, was seen to be lower in the elderly population as compared to young patients.

With the current CKD classification, most patients diagnosed the condition are elderly subjects.[13] However, only a small proportion of them will require renal replacement therapy, often dying before from cardiovascular disease.[14] This study assessed the clinical and laboratory changes over one year in patients over 65 years of age with different grades of baseline GFR. A significant proportion of patients had cardiovascular risk factors (HBP and/or DM), and cardiac disease was the main morbidity cause among the studied groups. One may therefore wonder what benefits may these patients derive from referral to nephrology clinics, whether emphasis should rather be placed on cardiovascular prevention, and where and how would their monitoring be most adequate.

Aging is associated to a decrease in GFR.[2] In a previous study,[7] our group found that despite the fact that all elderly patients studied had a decreased GFR (even with SCr within the normal laboratory ranges), no characteristic signs of CRF were seen in most of them. Moreover, SCr showed higher statistical correlation levels with the laboratory changes associated to CRF than the GFRs estimated from mathematical formulas. That study concluded that GFR estimations provided no advantages over a simple SCr measurement for assessing KF in the elderly. Moreover, since part of the GFR decrease in these patients is associated to age and the main cause of mortality is cardiovascular disease, the current classification

Table I. Change in kidney function depending on the presence of diabetes mellitus

	Diabetics	Non-diabetics	P
SCr (B/A) (mg/dL)	B 1.23 ± 0.43 A 1.22 ± 0.36	B 1.31 ± 0.5 A 1.34 ± 0.5	NS
MDRD (B/A) (mL/min)	B 54.6 ± 15 A 54.4 ± 15	B 51.3 ± 16 A 49.8 ± 16	NS
Cockroft (B/A) (mL/min)	B 45.4 ± 14 A 47.9 ± 17	B 42.3 ± 18 A 42.1 ± 16	NS

A comparison of the change in kidney function between diabetic and non-diabetic patients. B: baseline; A: one year later.

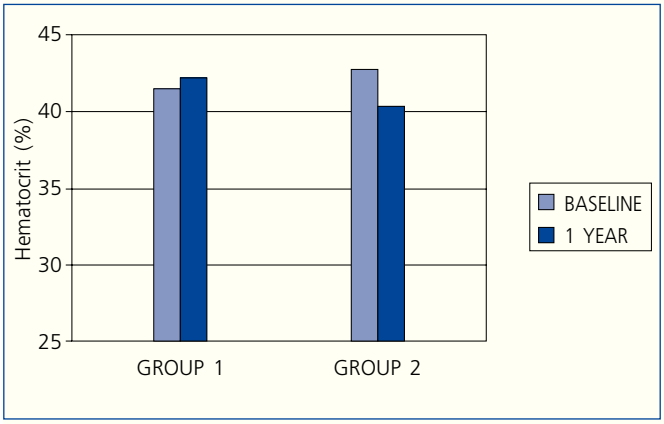

Figure 2. Change in haematocrit at one year in both groups.

of CKD may induce unnecessary confusion and alarm and does not appear to have practical advantages for management of this type of patients.

In this study, we performed a clinical and laboratory follow-up to ascertain what happened with GFR. It was seen that, though significant variations existed in GFR levels in both groups, when compared after one year of follow-up, no differences were found, irrespective of such baseline levels.

With GFR decrease, various laboratory changes associated to CRF occur (anaemia, changes in bone and mineral metabolism, metabolic acidosis, etc.). When such changes were looked for, the group of patients with SCr within the normal laboratory range (group 1, SCr < = 1.1 mg/dL), despite having a decreased GFR, showed a baseline haematocrit higher than 35%, that remained one year later at similar levels without the need for using agents to stimulate erythropoiesis. Group 2 patients (SCr > 1.1 mg/dL) were also seen to have a baseline haematocrit higher than 35% that was maintained one year later. The proportion of patients receiving erythropoietin therapy was low. No differences were found between the groups in all other laboratory parameters studied. When the parameters associated to use of erythropoietin in these elderly patients were analysed, SCr levels > 2 mg/dL and advanced age were found to be the two factors that appear to contribute to the need for EPO therapy to prevent the occurrence of anaemia associated to CRF.

It therefore appears that, in standard clinical practice, CKD detection and management in elderly patients could continue to be performed as done to date, in a simpler form, with a simple measurement of SCr and a systematic urine analysis (Multistix) to rule out the presence of kidney disease requiring specialised care. This approach would allow for dispelling the confusion felt by many physicians who are not used to CKD management when they see this type of patients.[15] It would also allow for avoiding or reducing unnecessary referrals and overload for the nephrology teams.[16] We therefore postulate that elderly patients with SCr higher than 1.1 mg/dL but no changes secondary to CRF (anaemia, etc.) or proteinuria need not be routinely referred to specialised care. In fact, the recommendations recently published in the Consensus Document on CKD of the SEN and the Society of Family and Community Medicine state that patients over 70 years of age with a stable GFR > 30 mL/min and albuminuria < 0.5 g/24 h may be monitored at primary care without the need for referral, provided adequate control is maintained of blood pressure and all other vascular risk factors (recommendation 11).[17]

In conclusion, in elderly patients showing no significant proteinuria or laboratory changes associated to CKD (anaemia), the similar clinical course (irrespective of baseline GFR) and the stability of the various laboratory parameters associated to the decrease in kidney function over time allow for simplification of follow-up, with no need to resort to GFR estimation using mathematical formulas.

REFERENCES

1. Beck LH. Changes in renal function with aging. *Clin Geriatr Med* 1998; 14 (2): 199-209.
2. Mimran A. Renal function and aging. *Nephrologie* 1990; 11 (5): 275-80.
3. Astor BC, Muntner P, Levin A, Eustace JA, Coresh J. Association of kidney function with anemia: the Third National Healt and Nutrition Examination Survey(1988-1994). *Arch Intern Med* 2002; 162: 1401-1408.
4. Cozzolino M, Gallieni M, Brancaccio D, Arcidiacono T, Bianchi G, Vezzoli G. Vitamin D retains an important role in the pathogenesis and management of secondary hyperparathyroidism in chronic renal failure. *J Nephrol* 2006; 19 (5): 566-577.
5. Kraut JA, Kurtz I. Metabolic acidosis of CKD: diagnosis, clinical characteristics, and treatment. *Am J Kidney Dis* 2005; 45 (6): 978-993.
6. Kidney Disease Outcome Quality Inititative: K/DOQI clinical practice guidelines for chronic kidney disease: evaluation , classification and stratification. *Am J Kidney Dis* 2002; 39: S76-S92.
7. Heras M, Guerrero MT, Sánchez R, Fernández-Reyes MJ, Muñoz A, Hernández V, Prado F, Álvarez-Ude F. Utilidad clínica de la creatinina plasmática como marcador de función renal y de riesgo cardiovascular en ancianos. *Nefrología* 2006; 26 Supl. (6): 58.
8. Cockroft DW, Gault MH. Prediction of creatinine clearance from serum creatinine. *Nephron* 1976; 16: 31-41.
9. Levey AS, Greene T, Kusek JW, Beck GJ. Simplified equation to predict glomerular filtration rate from serum creatinine. *J Am Soc Nephrol* 2000; 11: 828 (A).
10. Hemmelgarn BR, Zhang J, Manns BJ, Tonelli M, Larsen E et al. Progresion of kidney dysfunction in the community-dwelling elderly. *Kidney Int* 2006; 69: 2155-2161.
11. O'Hare AM, Bertenthal D, Covinisky KE, Landefeld CS et al. Mortality risk stratification in chronic kidney disease: one size for all ages. *J Am Soc Nephrol* 2006; 17: 846-853.
12. Derose S Crooks P, Rutkowski M, Levin N et al. Age, GFR, and the risk of ESRD or death. ASN (Abstrac). *J Am Soc Nephrol* 2007; 18: 46A.
13. Eknoyan G. On epidemic cardiovascular disease in patients with chronic renal disease and progressive renal failure: a first step to improve the outcomes. *Am J Kidney Disease* 1998; 32: S1-S4.
14. Locatelli F, Pozzoni P. Chronic kidney disease in the elderly: is it really a premise for overwhelming renal failure? *Kidney Int* 2006; 69 (12): 2155-2166.
15. Robles NR. Cálculo del filtrado glomerular: una visión escéptica. *Nefrología* 2007; 27 (4): 405-407.
16. Torregrosa I, Solis M, Pascual B et al. Resultados preliminares de la implantación de un protocolo conjunto de manejo de la enfermedad renal crónica entre atención primaria y nefrología. *Nefrología* 2007; 27 (2): 162-167.
17. Documento de consenso sobre la Enfermedad renal crónica. SEN-semFYC.www.senefro.org