

# Estimation of glomerular filtration rate in primary care: prevalence of chronic kidney disease and impact on referral to nephrology

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## SUMMARY

Data were collected in 18.922 patients attending Primary Care Centers in Alcañiz (Spain), mean age  $59,96 \pm 17$  years, 42,9% males and 57,1% females. The prevalence of eGFR was: stage 3 (30-59 ml/min/1,73 m<sup>2</sup>) 15,7%; stage 4 (15-29 ml/min/1,73 m<sup>2</sup>) 0,6%; stage 5 no dialysis (GFR < 15 ml/min/1,73 m<sup>2</sup>) 0,1%. This prevalence increased with age and 32% of patients attending Primary Care services over 65 years presented a eGFR < 60 ml/min/1,73 m<sup>2</sup>. Of the total patients with eGFR < 60 ml/min/1,73 m<sup>2</sup>, 26% had normal serum creatinine levels. Protocol implementation could implied for the Renal Unit an increase in the number of patients, specially the oldest ones. This study documents the substantial prevalence of significantly abnormal renal function among patients at Primary Care level and the importance of Primary Care collaboration in their early identification and appropriate management.

Key words: Epidemiology. Chronic kidney disease. Primary care. Cardiovascular risk factors.

## RESUMEN

La incidencia de Enfermedad Renal Crónica (ERC) en los 18.922 pacientes con determinación bioquímica realizada en los Centros de Salud del Sector Sanitario de Alcañiz a lo largo de 2006 fue del 16,4% (mujeres 19,1%, varones 12,9%,  $p < 0,0001$ ). Por estadios K/DOQI la mayoría de los casos pertenecen al estadio 3. Encontramos Insuficiencia renal oculta en 810 pacientes (4,3%), todos ellos mujeres. Esta elevada prevalencia de ERC y de ERC oculta puede detectarse de forma precoz mediante la inclusión en los resultados de laboratorio del cálculo del filtrado glomerular por la fórmula MDRD y hace necesaria la implantación de un protocolo que facilite una colaboración estrecha con Atención Primaria. El control y seguimiento de pacientes con ERC estable y sin complicaciones recaería principalmente sobre el Médico de Cabecera, siendo necesario mantener su formación y el apoyo por parte de nefrología.

Palabras clave: Epidemiología. Enfermedad renal crónica. Atención primaria. Consultas nefrología. Factores de riesgo cardiovascular.

## INTRODUCTION AND OBJECTIVES

In recent years, large studies have reinforced consideration of chronic kidney disease (CKD) as a public health problem because of its high prevalence in the general population (5.1% in Spain according to data from the EPIRCE study),<sup>1</sup> its attendant increase in morbidity and mortality mainly of a cardiovascular origin,<sup>2,3</sup> and the possibility of improving such course by early intervention.<sup>4,5</sup>

An adequate coordination between nephrology and primary care is required to manage such a significant condition.<sup>6</sup> Being aware of this, in January 2006 the Department of Quality, primary care coordinators, and the Departments of Nephrology and Biochemistry of the Alcañiz health sector, after receiving support from the sector management, created a work group that prepared a common protocol for detection and update in CKD within a wider proposal for optimisation of laboratory requests and criteria for referral to specialised care.

In the analysis of the implementation process, this preliminary study was conducted with two objectives:

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1. To estimate the prevalence of CKD and occult CKD among all laboratory tests performed in the healthcare centres of the Alcañiz health sector.
2. To analyse the predictable impact of this protocol on patients characteristics and on the activity and care pressure at nephrology outpatient clinics.

## MATERIALS AND METHODS

**Study design:** A cross-sectional epidemiological study in patients performed blood chemistry tests at their healthcare centres during 2006.

**Inclusion criteria:** Patients of both sexes older than 18 years performed chemical tests for any reason at healthcare centres of the Alcañiz health sector (consisting of Alcañiz Hospital and 12 healthcare centres covering a total of 83,456 inhabitants) from January 1 to December 31, 2006.

Chemistry tests were performed in a central laboratory at the Department of Biochemistry of the Alcañiz Hospital. Sex, age, and plasma creatinine values requested in the laboratory forms were recorded using a computerised process.

Plasma creatinine was measured by a modified kinetic Jaffé method using a C-Architec 8000 autoanalyser (Abbot Científica).

Estimated glomerular filtration rate (eGFR) was calculated using the abbreviated MDRD formula.<sup>7,8</sup>

Occult chronic kidney disease was defined as coexistence of an eGFR < 60 mL/min/1.73 m<sup>2</sup> with normal serum creatinine, < 1.1 mg/dL in females and < 1.2 mg/dL in males.<sup>9</sup>

Results were analysed providing the following criteria for referral to nephrology outpatient clinics:

- A) First group of criteria:
- < 65 years: eGFR < 60 mL/min/1.73 m<sup>2</sup>
  - 65-80 years: eGFR < 30 mL/min/1.73 m<sup>2</sup>
  - > 80 years: eGFR < 20 mL/min/1.73 m<sup>2</sup>
- B) Second group of criteria:
- < 65 years: eGFR < 45 mL/min/1.73 m<sup>2</sup>
  - 65-80 years: eGFR < 30 mL/min/1.73 m<sup>2</sup>
  - > 80 years: eGFR < 20 mL/min/1.73 m<sup>2</sup>

Patients referred for CKD in 2006 were reviewed, and the proportion of them who would meet these criteria was calculated from all eGFR determinations made at healthcare cen-

tres. The characteristics of both groups were analysed (age, sex, plasma creatinine, eGFR, and K/DOQI stages of CKD).

## Statistical analysis

Quantitative variables were described using means and standard deviations, and qualitative variables using proportions with calculation of the 95% confidence interval (CI). Statistical significance of the differences between proportions was assessed using a Chi-square test. Means of independent groups were compared using ANOVA or Student's t tests. A value of  $p < 0.05$  was considered significant. SPSS 10.0 software was used for statistical calculations.

## RESULTS

During the 12 months, 22,250 measurements of plasma creatinine were performed in 21,321 patients from the healthcare centres. Of all measurements, 1,321 (5.94%) were discarded because they were repeat tests in the same patient, and 2,007 (9.02%) because the age was not recorded in the request form, and eGFR could therefore not be calculated using the MDRD formula. Data from a total of 18,922 patients were recorded.

Table I gives the mean age, plasma creatinine, and eGFR values, overall and by sex, and distribution by age groups.

Overall prevalence of CKD, defined as an eGFR < 60 mL/min/1.73 m<sup>2</sup>, was 16.4 %, and was significantly higher in females as compared to males (19.1% versus 12.9%,  $p < 0.0001$ ). Distribution by K/DOQI stages showed most patients to have stage 3 CKD (table II).

Occult renal failure, according to the definition proposed in Materials and methods, was found in 810 patients, 4.3% of the Spanish population. It should be noted that occult CKD was only found in females. The proportion of females with occult CKD was 7.5%, and the condition was more commonly detected in the group > 65 years (3.9% of women under 65 years of age versus 12.1% of those over 65 years,  $p < 0.001$ ). This means that 39.3% of the 2,061 women with an eGFR < 60 mL/min/1.73 m<sup>2</sup> had normal plasma creatinine values, lower than 1.1 mg/dL.

During 2006, there were 194 first visits to our nephrology clinics, in 103 of which (53.1%) an eGFR < 60 mL/min/1.73 m<sup>2</sup> was found. The first group of referral criteria was met in 41 of these visits, and the second group of criteria was met in

**Table I. Patient characteristics and estimated GFR, overall and by sex**

Variables	Total 18,922	Males 8,115 (42.9%)	Females 10,807 (57.1%)	P Male/Female
Age (years)	59.96 ± 17.7	61.07 ± 16.6	59.13 ± 18.4	< 0.0001
Age by groups				
18-65 years	10,450 (55.2%)	4,400 (54.2%)	6,050 (56%)	P = 0.02
66-80 years	6,476 (34.2%)	2,867 (35.3%)	3,609 (33.4%)	
> 80 years	1,996 (10.5%)	848 (10.4%)	1,148 (10.6%)	
PCr (mg/dL)	0.97 ± 0.26	1.08 ± 0.32	0.88 ± 0.23	< 0.0001
GFR mL/min/1.73 m <sup>2</sup>	75.89 ± 17.4	78.02 ± 17.3	74.29 ± 17.3	< 0.0001

**Table II. Overall and sex prevalence of eGFR < 60 mL/min/1.73 m<sup>2</sup> and K/DOQI stages of CKD**

	Overall	Males	Females	P
GFR < 60 mL/min/1.73 m <sup>2</sup>	3,107 (16.4%)	1,046 (12.9%)	2,061 (19.1%)	p < 0.0001
K/DOQI stages				
– 3 (GFR 30-60 mL/min)	2,979 (15.7%)	997 (12.3%)	1,982 (18.3%)	p < 0.0001
– 4 (GFR 15-30 mL/min)	116 (0.6%)	44 (0.5%)	72 (0.7%)	
– 5 (GFR < 15 mL/min)	12 (0.1%)	5 (0.1%)	7 (0.1%)	

33 visits. The number of patients who would require revision at our clinics based on these criteria would be:

– According to the first group: The number of first visits for CKD would increase from 41 to 422, 2.2% of patients performed tests. This increase would mainly occur at the expense of females, patients younger than 65 years, and patients with stage 3 CKD.

– According to the second group: The number of first visits for CKD would increase from 33 to 113, 0.6% of patients undergoing tests. Increases would mainly occur in females and patients with stage 3-4 CKD (table III).

## DISCUSSION

This study was intended to assess the prevalence of CKD in patients over 18 years of age who were performed chemical tests for any reason at their healthcare centers during 2006. Among 18,922 patients, 3,107 (16.4%) had CKD, with an eGFR < 60 mL/min/1.73 m<sup>2</sup>.

The EROCAP study<sup>9</sup> reported a higher prevalence, 21.3%, maybe because of the different methodology used. For this multicentre study, the first two patients attending the healthcare centre on three consecutive days were selected. In primary care, laboratory tests are usually performed for chronic conditions such as diabetes, high blood pressure, dyslipidemia, and so on, avoiding the coincidence with acute conditions that may cause transient impairment of kidney function (the main reasons for visits include acute respiratory condi-

tions, rheumatological conditions with NSAID intake, and gastroenteritis). Our study recorded the usual laboratory tests, performed in more clinically stable states, which would explain this lower incidence of CKD.

Assessment of kidney function using plasma creatinine values reveals a significant rate of occult CKD.<sup>10,11</sup> In our series, occult CKD was found in 4.3% of patients, and showed two characteristics worth mentioning: all 810 cases were recorded in females, with a higher frequency among those older than 65 years.

The high frequency of CKD poses a significant healthcare problem. Early diagnosis, management, and follow-up of CKD would depend on support and training of primary care physicians and on reconsideration of the procedures followed at our practices. In a first phase, we nephrologists have considered use of poorly restrictive referral criteria,<sup>12</sup> which in our case would represent multiplying by 10 the number of patients to be seen for a decrease in eGFR, mainly at the expense of women, patients under 65 years of age, and those with stage 3 CKD, which is an unfeasible option. A review of the large population studies by Go et al and O'Hare et al<sup>2,3</sup> shows that the risk of cardiovascular events inherent to CKD markedly increases from a GFR < 45 mL/min/1.73 m<sup>2</sup>, and this could therefore be considered a referral criterion in patients under 65 years of age. This would virtually multiply by three the number of patients to be seen at our practice, an option that, in principle, appears more feasible. Use of more restrictive criteria, such as a decrease in GFR below 30 mL/min/1.73 m<sup>2</sup>, could maybe deprive patients with a high risk of cardiovascular morbidity and mortality and progression to end-stage CKD from nephrological review. All other patients with CKD could continue to be supervised by their general practitioners, provided kidney function remained stable and adequate control was maintained.<sup>13,14</sup>

As conclusions, it may be stated that the high prevalence of CKD may be detected early in primary care by including in the laboratory results the eGFR calculated by the MDRD formula, and that a protocol to facilitate management of these patients implying a close collaboration with primary care and use of reasonable criteria for referral to the nephrology outpatient clinics should be implemented. Joint monitoring of the results is required to assess results, correct defects, and improve our procedures.

## REFERENCES

- Otero A, Gayoso P, García F, De Francisco AL, on behalf of the EPIRCE study group: epidemiology of chronic renal disease in the Galician population: results of the pilot Spanish EPIRCE study. *Kidney Int* 2005; (Supl. 99): S16-S19.

**Table III. Characteristics of patients referred to nephrology outpatient clinics according to the second group of criteria for GFR calculated by the MDRD formula**

	Referred in 2006 meeting criteria	Study prediction
Referral based on criteria B for GFR	33 (17%)	113
Sex Male/Female	63.6/36.4%	42.5/57.5%
Mean age	75.8 ± 9	67.1 ± 14
< 65 years	5 (15%)	50 (44.2%)
70-80 years	15 (45%)	48 (42.5%)
> 80 years	13 (39%)	15 (13.3%)
PCr	3.52 ± 1.3	2.39 ± 1.2
GFR (mL/min/1.73 m <sup>2</sup> )	19.8 ± 9	29.7 ± 11
K/DOQI stage		
– 3	5 (15%)	46 (40.7%)
– 4	13 (39%)	55 (48.7%)
– 5	15 (45%)	12 (10.6%)

2. Go AS, Chertow GM, Fan D, McCulloch CE, Hsu C-Y. Chronic kidney disease and the risk of death, cardiovascular events, and hospitalization. *New Engl J Med* 2004; 351: 1296-1305.
3. O'Hare AM, Bertenthal D, Covinsky KE, Landefeld CS, Sen S, Mehta K, Steinman MA, Borzecki A, Walter LC. Mortality risk stratification in chronic kidney disease: One size for all ages? *J Am Soc Nephrol* 2006; 17: 846-854.
4. International Society of Nephrology Commission for the Global Advancement of Nephrology Study Group 2004. Prevention of chronic kidney and vascular disease: toward global health equity -the Bellagio 2004 Declaration. *Kidney Int* 2005; (Supl. 98): S1-S6.
5. De Zeeuw D, Hillege HL, De Jong PE. The kidney, a cardiovascular risk marker, and a new target for therapy. *Kidney Int* 2005; (Supl. 98): S25-S29.
6. Alcázar R, De Francisco AL. Acción estratégica de la SEN frente a la enfermedad renal. *Nefrología* 2006; 26: 1-4.
7. Levey AS, Bosch JP, Lewis JB, Greene T, Rogers N, Roth D. A more accurate method to estimate glomerular filtration rate from serum creatinine: a new prediction equation. Modification of Diet in Renal Disease Study Group. *Ann Intern Med* 1999; 130: 461-470.
8. Gansevoort RT, Bakker SJ, De Jong PE. Early detection of progressive chronic kidney disease: is it feasible? *J Am Soc Nephrol* 2006; 17: 1218-1220.
9. De Francisco AL, De la Cruz JJ, Cases A, De la Figuera M, Egocheaga MI, Górriz JJ, Llisterri JJ, Marín R, Martínez Castela A. Prevalencia de insuficiencia renal en Centros de Atención Primaria en España: Estudio EROCAP. *Nefrología* 2007; 27: 300-312.
10. Fernández-Fresnedo G, De Francisco AL, Rodrigo E, Piñera C, Herráez I, Ruiz JC, Arias M. Insuficiencia renal «oculta» por valoración de la función renal mediante la creatinina sérica. *Nefrología* 2002; 22: 144-151.
11. Duncan L, Heathcote J, Djurdjev O, Levin A. Screening for renal disease using serum creatinine: who are we missing? *Nephrol Dial Transplant* 2001; 16: 1042-1046.
12. Torregrosa I, Solís M, Pascual B, Ramos B, González M, Ramos C, Puchades MJ, García R, Pons S, Abarca A, Mahiques E, Alcocer H, Sanmartín A, Navarro J, Miguel A. Resultados preliminares de la implantación de un protocolo conjunto de manejo de la enfermedad renal crónica entre atención primaria y nefrología. *Nefrología* 2007; 27: 162-167.
13. St Peter WL, Schoolwerth AC, McGowan T, McClellan WM. Chronic kidney disease: issues and establishing programs and clinics for improvement patient outcomes. *Am J Kidney Dis* 2003; 41 (5): 903-924.
14. De Francisco AL. Revisiones SEN. Academia de Nefrología. La necesidad de enfrentarnos a la ERC como enfermedad epidémica. En: Euromedice Ediciones Médicas SL, 2006.