



Implementation of a Nephrology-Primary Health Care joint protocol for the management of chronic renal disease. Preliminary results

I. Torregrosa, M. Solís, B. Pascual, B. Ramos, M. González, C. Ramos, M. J. Puchades, R. García, S. Pons, A. Abarca, E. Mahiques, H. Alcocer, A. Sanmartín*, J. Navarro* and A. Miguel

Nephrology Department. Clinical University Hospital of Valencia. *On behalf of the health care centers of the Fifth Department of the Health Care Agency of Valencia.

SUMMARY

During the last years there has been an important advance in the knowledge of chronic kidney disease (CKD). In order to adapt our clinical practice to these new data, a protocol of management of CKD between Nephrology and Primary Health Care has been developed. The protocol includes several items like cardiac and renal protection strategies, diagnosis and treatment of complications, use of drugs and clear derivation criteria. Implementation of the protocol has been only partial and has implied, for the Renal Unit, an increase in the number of patients, specially the oldest ones, but a clear improve in the quality of the information too, and a first positive step in the right way to face the challenge of CKD. In view of analysed data we propose some modifications for the protocol.

Key words: **Chronic Kidney Disease. Nephrology. Primary Health Care. Protocol.**

RESULTADOS PRELIMINARES DE LA IMPLANTACIÓN DE UN PROTOCOLO CONJUNTO DE MANEJO DE LA ENFERMEDAD RENAL CRÓNICA ENTRE ATENCIÓN PRIMARIA Y NEFROLOGÍA

RESUMEN

En los últimos años se ha producido un importante avance en el conocimiento de la enfermedad renal crónica (ERC). Con el objetivo de adaptar la práctica clínica a los nuevos conocimientos se ha puesto en marcha en el Departamento 5 de la Agencia Valenciana de Salud un protocolo conjunto de manejo de la ERC entre Atención Primaria y Nefrología. El protocolo desarrolla una serie de puntos entre los que se incluyen medidas de cardio y renoprotección, detección y manejo de complicaciones, uso de fármacos y criterios claros de derivación. La implantación de este protocolo hasta el momento ha sido parcial y ha supuesto, para el Servicio de Nefrología, un aumento del número de consultas y un aumento de la remisión de pacientes mayores de 80 años, pero también una mejora clara en la información con la que llegan los pacientes y un primer paso, consideramos que claramente positivo, en la dirección correcta para afrontar el reto de la ERC. A la luz de los datos analizados se proponen también algunas modificaciones del protocolo.

Palabras clave: **Enfermedad Renal Crónica. Nefrología. Atención primaria. Protocolo.**

Correspondence: Alfonso Miguel Carrasco
Jefe de Servicio de Nefrología
Hospital Clínico Universitario de Valencia
Avda. Blasco Ibáñez, 17 - 46010 Valencia
E-mail: juan.a.miguel@uv.es

INTRODUCTION

In recent years there has been an important change in the conception that nephrologists have about chronic renal disease (CRD), which has been motivated by new knowledge such as: the high prevalence of chronic renal disease within the general population,, both in Spain,¹⁻⁵ where we are expecting soon important data from the EPIRCE study, and in other countries;⁶⁻⁷ the high cardiovascular morbimortality associated to chronic renal disease;⁸⁻¹⁸ and the possibility of improving this morbimortality and the course of end-stage chronic renal failure by means of early intervention.¹⁹⁻²⁷ This new conception necessarily implies a radical change in the way of facing the problem since it is impossible to manage such a large population just from our nephrology clinics. We may still go on as if nothing has changed, or much better, face the problem from a new perspective. From our reasoning, the only possible way implies good relations and coordination between Nephrology and Primary Health Care.

The Clinical Hospital of Valencia belongs to the Fifth Department of the Health Care Agency of Valencia, which includes 16 health care areas and one specialty center and assists a total of 324,714 inhabitants. The Nephrology Department also provides care to the Fourth Department, in which the Hospital of Sagunto is included since the latter has not a nephrology department, and that assists 135,171 inhabitants and has 9 health care centers and two specialty centers.

The aim of the study was to know the impact of the onset of a joint protocol to manage CRD between Primary Care and Nephrology on health care activity and assistance load at the outpatient nephrology clinics.

METHODOLOGY

In October of 2005, the Nephrology Department decided to put in place, together with Primary Care, an action protocol on CRD. After having received the support by the hospital and health care administration managers, the first step was to hold a meeting with the coordinators of the 16 primary care centers (PCCs) of the fifth department and explain the project to them. The 8 PCCs belonging to the Hospital of Sagunto were not initially included. A working team was created including two primary care physicians and two nephrologists, and as a result in December of 2005 a protocol was ready. One of the main objectives for elaborating the protocol was that the latter had to be short and simple, with clear intervention

guidelines and referral criteria. Its creation was based on several studies and published guidelines,²⁸⁻⁴¹ as well as our own experience. Primary care physicians were in charge of broadcasting it among coordinators, and the latter among the other professionals at the PCCs. Nephrologists would do the same at the nephrology department. Several months later, a new monitoring meeting would be held during which the protocol could be corrected according to the outcomes. Primary care physicians committed themselves to refer patients according to the protocol and the nephrologists to send back to Primary Care clinical information as well as a copy of laboratory results after each visit.

The following sections are included and developed in the protocol:

1. A justification of the need for a protocol.
2. Diagnosis and classification of chronic renal disease.
3. Assessment of renal involvement: the target population is indicated (the population with arterial hypertension, diabetes, high vascular risk (according to European guidelines), or previous renal disease, and the convenience for the use of formulas for the calculation of GFR and the determination of the albumin/creatinine or proteinuria/creatinuria ratios (PCR) in an isolated urine sample is stressed. Criteria for the suspicion of nephroangiosclerosis and ischemic renal disease are established.
4. Criteria for referral to specialized care:
 - a. Stage 1-2:
 - i. Age > 70 and PCR < 1: management at the primary care setting.
 - ii. Age < 70 or PCR > 1: referral to nephrology for assessment (management at the primary care setting)
 - b. Stage 3: referral to nephrology (joint management).
 - c. Stage 4-5: referral to nephrology (preferential management by Nephrology).
5. Management of CRD patients according to the stage and including heart and kidney protection measures, and management of CRD complications.
6. Renal side effects from most commonly used medications at Primary Care.
7. Quality indicators and organizational and improvement proposals.

In addition, the Hospital Laboratory Department was asked, and accepted, to include in the laboratory work-up the albumin/creatinine ratio in an isolated urine sample and GFR by the abbreviated MDRD for-

mula.³⁴⁻³⁵ This formula was used for practical reasons since it does not require the weight value for its calculation and it is sufficiently valid and accepted.³⁶⁻⁴¹

The main fear from the part of the Nephrology Department was (and still is) that the onset of the protocol would imply loads of requests from Primary Care with the resulting collapse of the clinics, which are already saturated and with no real possibility to grow proportionally with the demand.

All the consultation requests due to CRD suspicion sent from the PCCs to the nephrology department during two 3-months periods, before (February, March, and April of 2005) and after (February, March, and April of 2006) the protocol onset, have been reviewed. All the requests sent from Primary Care for another reason have been excluded, as well as those coming from specialists other than Primary Care physicians, those originated at the Hospital itself, and all coming from the Sagunto Hospital area. The number of requests as well as age of the patients and quality of the information provided (age, CRD stage, glomerular filtration rate (GFR), albuminuria or proteinuria, personal history) have been compared for each period.

RESULTS

During the period corresponding to the year 2005, 78 consultation requests were received, as compared to 102 during the period of 2006, which represents a 30.8% increase.

The characteristics of referred patients are shown in Table I. Table II shows the information received with the consultation request: age, stage, glomerular filtration rate, possibility of determining the stage and GFR (with age and plasma creatinine), even though albuminuria and proteinuria were not specified (by any means, in isolated urine or 24-h urine). Finally, and in order to compare the quality of the information provided, the latter was categorized into three subgroups: complete information when age, personal history, stage (provided or that could be calculated with provided data), GFR (provided or that could be calculated), and albuminuria; sufficient information when-

Table I. Patients characteristics

Period	2005	2006
Number of patients	78	102
Age	67.8 (90-14)	69.3 (88-31)
> 70 years (%)	55.1	52.3
> 80 years (%)	22.5	29.2

Table II. Information provided with the request for consultation

Period	2005	2006
Age, provided %	78.9	82.4
Stage, provided %	0.0	14.7
Stage, calculable %	55.8	82.3
GFR, provided %	9.6	42.6
GFR, calculable %	55.8	76.5
Albuminuria, provided %	30.8	26.5
Personal history %	75.0	91.2

ver age, personal history, and GFR (calculated or that could be calculated) were provided; and insufficient information whenever these minimal data were not provided. If the patient was diabetic, we considered that albuminuria was a fundamental piece of information and thus if it was not provided the information was classified as insufficient (thus, all diabetics may be included into the categories of complete or insufficient information). Whenever the reason for consultation was albuminuria and this piece of information was not provided, this was also considered as insufficient information. Table III shows the comparison between both periods.

DISCUSSION

An 30.8% increase in the number of consultations for suspicion of CRD has occurred. This increase may be partially although not completely attributable to the protocol since at the Fourth Department the protocol was not implemented and the number of consultations from that department has increased by 61% (28 patients during the year 2005 versus 45 during 2006). It is likely that the great amount of information that has been presented on CRD, such as articles in scientific journals, conferences sponsored by the pharmaceutical industry (some firms have already discovered the potential that CRD represents with regards to cardiovascular risk prevention and sponsor informative meetings), and even joint meetings between Primary Care and Nephrology (in May of 2005, the First Joint Session

Table III. Quality of the information received with the request for consultation

Period	2005	2006
Complete information %	23.1	20.6
Sufficient information %	19.2	48.5
Insufficient information %	57.7	30.9

between Primary Care and Nephrology took place at the Community of Valencia), is clearly related with the increase in the number of consultation requests. Ninety five point two percent of all referred patients adhered to the protocol. However, it is striking that although stage 1 and 2 CRD under the age of 70 years represents a referral criterion according to the protocol, the number of referrals due to isolated microalbuminuria have not increased, in deed, they have decreased. Most patients are referred because of stage 3 and 4 CRD (70.6% and 25.5% of the consultations, respectively). It is likely that the number of requests for consultations would be considerably increased if all patients with isolated microalbuminuria were referred. Another important issue is the age of referred patients: the percentage of patients older than 80 has changed from 22.5% to 29.2%.

There are two possible solutions to face the progressive increase in the number of consultations: the first one is to make referral criteria more restrictive, and the second one is necessarily linked to the fact that we nephrologists are able to attend all patients without having to take care of them forever, that is to say, many patients may benefit from a nephrology assessment for 2, 3, or 4 visits, and then being referred back to Primary Care, provided they are stable, to be followed-up there. Although this may seem obvious, it usually does not happen so, and many times the tendency is to keep the patient and follow him/her up for all his/her life, even for long periods of time. On the other hand, if we are able to get coordinated with Primary Care, another big group of patients may be followed-up jointly by alternating the visits, which implies improving health care and decreasing the assistance load. In order this system works, it is essential that nephrologists become aware that sharing information with Primary Care is essential by providing at each visit at least a little piece of clinical and analytical information. Thus, it might be convenient in our protocol to restrict referral of microalbuminuria to those cases in which it progressively increases in spite of treatment.

About age, an increase in the number of referrals of patients older than 80 years has occurred. It may be thought that these patients should not be referred to the nephrology clinic, but we believe that many of them do benefit from referral, in the first place because there is currently no age limit to start on renal replacement therapy (in fact, we are witnessing dialysis onset in patients older than 85 years) and therefore these patients will also benefit from earlier referral; and in the second place, because although they may not require dialysis, a good management of CRD-associated factors, particularly anemia, will have an impact on improving quality of life and reducing the associated morbimortality. We frequently attend at the

emergency services CRD patients with creatinine values that *a priori* may not seem too high but with associated anemia that favors heart failure onset or decompensation. One solution would be to decrease the GFR referral threshold in elderly patients from 60 to 45 or 40 mL/min, to referred back to Primary Care those patients with no complications and stable stage 3 CRD, and jointly follow-up the remaining ones.

Finally, it is necessary to monitor the outcomes resulting from the application of the protocol to avoid the final result of only increasing the workload that would negatively affect health care.

A second part of the study comprised the assessment of the quality of the information sent from Primary Care. The GFR was included in 42.6% of the consultation requests from the second period (2006) versus 9.6% in the period of 2005. Considering the number of patients in whom GFR was provided or could be calculated from age, gender and plasma creatinine (abbreviated MDRD), the percentage has changed from 55.8% (2005) to 76.5% (2006). In 2005, we did not receive a single request with the CRD stage value. In 2006, in spite of the protocol, only in 14.7% of the cases it was indicated, although in up to 82.3% it could be obtained from the data provided. About proteinuria, measured by any means (24-h urine or from an isolated sample), an improvement in the information provided has not occurred. The number of consultations in which this data is provided is less than one third of the cases. Even in diabetic patients, albuminuria is not provided in 43% of the cases. Taken together, the number of consultation requests with insufficient information (according to the above-mentioned criteria) has changed from 57.7 % (2005) to 30.9 % (2006). We may thus conclude that implementation of the protocol has entailed a clear improvement of the information provided, which is essential to organization of the clinic, although a lot is still left to be done. Once again, the solution implies a joint outcomes monitoring between Primary Care and Nephrology in order to correct the defects and improve the application.

ACKNOWLEDGEMENT

This study has been done with the collaboration of Pfizer Corporation.

REFERENCES

1. Fernández-Fresnedo G, De Francisco AL, Rodrigo E, Pinera C, Herraiz I, Ruiz JC, Arias M: Insuficiencia renal oculta por valoración de la función renal mediante la creatinina sérica. *Nefrología* 22: 95-7, 2002.

2. Otero A, Abelleira A, Camba MJ, Pérez C, Armada E, Esteban J y cols.: Prevalencia de insuficiencia renal oculta en la provincia de Ourense. *Nefrología* 23 (Supl. 6): 26, 2003.
3. Simal F, Martín Escudero JC, Bellido J, Arzua D, Mena FJ, González I, Álvarez AA, Tabuyo MB, Molina A: Prevalencia de la enfermedad renal crónica leve y moderada en población general. Estudio Hortega. *Nefrología* 24: 329-32, 334, 336-7, 2004.
4. Otero A, Abelleira A, Gayoso P: Occult chronic renal disease (OCD) and associated vascular risk factors (VRF). Epidemiological study. *Nefrología* 25: 275-87, 2005.
5. 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* (Supl. 99): S16-9, 2005.
6. Coresh J, Astor BC, Greene T, Eknoyan G, Levey AS: Prevalence of chronic kidney disease and decreased kidney function in the adult US population: third National Health and Nutrition Examination Survey. *Am J Kidney Dis* 41: 1-12, 2003.
7. Chadban SJ, Briganti EM, Kerr PG, Dunstan DW, Welborn TA, Zimmet PZ, Atkins RC: Prevalence of kidney damage in Australian adults: the AusDiab kidney study. *J Am Soc Nephrol* 14 (Supl. 2): S131-8, 2003.
8. Cullerton BF, Larson MG, Wilson PW, Evans JC, Parfrey PS, Levy DE: Cardiovascular disease and mortality in a community-based cohort with mild renal insufficiency. *Kidney Int* 56: 2214-9, 1999.
9. Hillege HL, Fidler V, Diercks GF, Van Gilst WH, De Zeeuw D, Van Veldhuisen DJ, Gans RO, Janssen WM, Grobee DE, De Jong PE, PREVEND Study Group: urinary albumin excretion predicts cardiovascular and noncardiovascular mortality in general population. *Circulation* 106: 1777-82, 2002.
10. Sarnak MJ, Levey AS, Schoolwerth AC, Coresh J, Cullerton B, Hamm L, McCullough PA, Kasiske BL, Kelepouris E, Klag MJ, Parfrey P, Pfeffer M, Raij L, Spinosa DJ, Wilson PW: Kidney disease as a risk factor for development of cardiovascular disease. *Hypertension* 42: 1050-1065, 2003.
11. Weiner DE, Tighiouart H, Amin MG, Stark PC, MacLeod B, Griffith JL, Salem DN, Levey AS, Sarnak MJ: Chronic kidney disease as a risk factor for cardiovascular disease and all-cause mortality: a pooled analysis of community-based studies. *J Am Soc Nephrol* 15: 1307-15, 2004.
12. Yuyun MF, Khaw KT, Luben R, Wech A, Bingham S, Day NE, Wareham NJ; European prospective Investigation into Cancer in Norfolk (EPIC_Norfolk) population study. *Int J Epidemiol* 33: 189-98, 2004.
13. Keith DS, Nichols GA, Guillón CM, Brown JB, Smith DH: Longitudinal follow-up and outcomes among a population with chronic kidney disease in a large managed care organization. *Arch Intern Med* 164: 659-63, 2004.
14. Go AS, Chertow GM, Fan D, McCulloch CE, Hsu C: Chronic kidney disease and the risks of death, cardiovascular events, and hospitalization. *N Eng J Med* 351: 1296-305, 2004.
15. Foley RN, Wang C, Collins AJ: Cardiovascular risk factor profiles and kidney function stage in the US general population: the NHANES III study. *Mayo Clin Proc* 80: 1267-9, 2005.
16. Foley RN, Murray AM, Shuling L, Herzog CA, McBean AM, Eggers PW, Collins AJ: Chronic kidney disease and the risk for cardiovascular disease, renal replacement, and death in the United States Medicare Population, 1998 to 1999. *J Am Soc Nephrol* 16: 489-95, 2005.
17. Schrier RW: Role of diminished renal function in cardiovascular mortality. marker or pathogenetic factor? *J Am Coll Cardiol* 47: 1-8, 2006.
18. Go AS, Lo JC: Epidemiology of non-dialysis-requiring chronic kidney disease and cardiovascular disease. *Curr Opin Nephrol Hypertens* 15: 296-302, 2006.
19. Mann JF, Gerstein HC, Pogue J, Bosh J, Yusuf S: Renal insufficiency as a predictor of cardiovascular outcomes and the impact of ramipril: the HOPE randomized trial. *Ann Intern Med* 134: 629-36, 2001.
20. Asselbergs FW y cols.: Effects of fosinopril and pravastatin on cardiovascular events in subjects with microalbuminuria. *Circulation* 110: 2809-16, 2004.
21. Pinkau T, Hilgers KF, Veelken R, Mann, JFE: How does minor renal dysfunction influence cardiovascular risk and the management of cardiovascular disease? *J Am Soc Nephrol* 15: 517-23, 2004.
22. 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* (Supl. 98): S1-6, 2005.
23. De Zeeuw D, Hillege HL, De Jong PE: The kidney, a cardiovascular risk marker, and a new target for therapy. *Kidney Int* (Supl. 98): S25-9, 2005.
24. Remuzzi G, Ruggenti P, Perna A, Dimitrov BD, de Zeeuw D, Hille DA, Shahinfar S, Carides GW, Brenner BM, RENAAL Study Group: Continuum of renoprotection with losartan at all stages of type 2 diabetic nephropathy: a *post hoc* analysis of RENAAL trial results. *J Am Soc Nephrol* 15: 3117-25, 2004.
25. Pohl MA, Blunenthal S, Cordonnier DJ, De Álvaro F, Deferrari G, Eisner G, Esmatjes E, Gilbert RE, Hunsiker LG, De Faria JB, Mangili R, Moore J Jr, Reisin E, Ritz E, Scherthner G, Spitalowitz S, Tindall H, Rodby RA, Lewis EJ: Independent and additive impact of blood pressure control and angiotensin II receptor blockade on renal outcomes in the irbesartan diabetic nephropathy trial: clinical implications and limitations. *J Am Soc Nephrol* 16: 3027-37, 2005.
26. Casas JP, Chua W, Loukogeorgakis S, Vayanse P, Smeeth L, Hingorami AD, MacAllister RJ: Effect of inhibitors of the renin-angiotensin system and other antihypertensive drugs on renal outcome: systematic review and meta-analysis. *Lancet* 366: 2026-33, 2005.
27. Remuzzi G, Macía M, Ruggenti P: Prevention and treatment of diabetic renal disease in type 2 diabetes: the BENE-DICT study. *J Am Soc Nephrol* 17 (Supl. 2): S90-7, 2006.
28. Documento de Consenso 2002 sobre pautas de detección, prevención y tratamiento de la nefropatía diabética en España. *Nefrología* 22: 521-530, 2002.
29. Nacional Kidney Foundation. K/DOQI clinical practice guidelines for chronic kidney disease. *Am J Kidney Dis* 39 (Supl. 1): S1-S246, 2002.
30. Górriz JL, Sancho A, Pallardó LM, Amoedo ML, Martín M, Sanz P, Barril G, Selgas R, Selgueira M, Palma A, De la Torre M, Ferreras I: Significado pronóstico de la diálisis programada en pacientes que inician tratamiento sustitutivo renal. Un estudio multicéntrico español. *Nefrología* 22: 49-59, 2002.
31. Marín R: Guías SEN: Riñón y enfermedad cardiovascular. *Nefrología* 24 (Supl. 6), 2004.
32. Levey AS, Eckardt KU, Tsukamoto Y, Levin A, Coresh J, Rosser J, Zeeuw D, Hostetter TH, Lameire N, Eknoyan G: Definition and classification of chronic kidney disease: a position statement from Kidney Disease: Improving Global Outcomes (KDIGO). *Kidney Int* 67: 2089-100, 2005.
33. Alcázar R, De Francisco ALM: Acción estratégica de la SEN frente a la enfermedad renal. *Nefrología* 26: 1-4, 2006.
34. 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* 130: 461-470, 1999.

35. Levey AS, Greene T, Kusek JW, Beck JB, Group MS: A simplified equation to predict glomerular filtration rate from serum creatinine (abstract). *J Am Soc Nephrol* 11: A0828, 2000.
36. Rodrigo E, De Francisco AL, Escallada R, Ruiz JC, Fresnedo GF, Piñera C, Arias M: Measurement of renal function in pre-ESRD patients. *Kidney Int* 61 (Supl. 80): S11-S17, 2002.
37. Lin J, Knight EL, Hogan ML, Singh AK: A comparison of prediction equations for estimating glomerular filtration rate in adults without kidney disease. *J Am Soc Nephrol* 14: 2573-80, 2003.
38. Stevens LA, Levey AS: Measurement of kidney function. *Med Clin North Am* 89: 457-73, 2005.
39. Rosner MH, Bolton WK: Renal Function Testing. *Am J Kidney Dis* 47: 174-83, 2006.
40. Gansevoort RT, Bakker SJ, De Jong PE: Early detection of progressive chronic kidney disease: is it feasible? *J Am Soc Nephrol* 17: 1218-1220, 2006.
41. Villafruela JJ: Valoración rutinaria de la afectación renal en atención primaria: claves para el futuro. *Nefrología* 25 (Supl. 4): S57-S65, 2005.