Comparison of co-management of patients with chronic kidney disease in primary care

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Abstract

Introduction: The prevalence of chronic kidney disease and end-stage renal disease is increasing, and therapeutic co-management may be a solution.

Objective: to determine the impact of nephrologist-directed care compared to primary care physician-directed management in patients with CKD.

Methods: A prospective randomized study was performed. Those patients with stage 3 and 4 CKD were eligible for the study.

Results: There was no difference in the 2-year survival rate without rehospitalization between the two groups (log-rank test = 0.2).

Conclusions: APMs informed about the guidelines could obtain results similar to nephrologists in caring for patients with CKD.

Keywords: chronic kidney disease, primary care, nephrology, survival, quality of life

source: DeCS

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Resumen

Introducción: La prevalencia de la enfermedad renal crónica y la enfermedad renal en etapa terminal está en aumento, el comanejo terapéutico puede ser una solución.

Objetivo: determinar el impacto de la atención por parte de los nefrólogos en comparación con el manejo dirigido por los médicos de atención primaria en pacientes con ERC.

Método: Se realizó un estudio aleatorio prospectivo, aquellos pacientes con ERC estadio 3 y 4 fueron elegibles para el estudio.

Resultados: No hubo diferencia en la tasa de supervivencia a los 2 años sin rehospitalización entre los 2 grupos (prueba de rango logarítmico = 0,2)

Conclusiones: los MAP informados sobre las pautas podrían obtener resultados semejantes a los nefrólogos en el cuidado de los pacientes con ERC.

Palabras clave: enfermedad renal crónica, atención primaria, nefrología, supervivencia, calidad de vida

fuente: DeCS

Introduction

The prevalence of chronic kidney disease (CKD) and subsequent end-stage renal disease (ESRD) is increasing, particularly in patients older than 65.

Despite steady improvements in renal replacement therapies (RRT), morbidity and mortality of such patients remain high, with the survival of patients with ESRD as low as 60% and 30% at 1 and 5 years, respectively[1].

Many factors are associated with this poor outcome, including late nephrologist referral. The most commonly reported explanations for the association of late referral with poor prognosis are delayed intervention by specialists and complications related to emergency dialysis. A delay in specialist care exposes patients to potential undertreatment of CKD complications, such as cardiovascular disease (CVD), anemia, bone and mineral disorders, and increased susceptibility to infections, or to the urgent implementation of RRT, which is associated with increased morbidity and mortality and length of hospitalization[2,3]. In addition, the initiation of urgent hemodialysis (HD) instead of planned HD deprives the patient of the possibility of opting for another type of RRT, such as peritoneal dialysis (PD) or preemptive renal transplantation (RT). The European Guidelines for Good Practice recommend that patients be referred to nephrologists when creatinine clearance (CA) < 60 ml/min and imperatively when CA < 30 ml/min[4].

However, "real life" practice shows that early referral to nephrologists of patients with CKD is uncommon. The impact of guidelines on primary care physicians (PCPs) is difficult to assess but probably limited, as most recommendations appear in specialized journals[5]. Other important barriers to timely referral include patient unfamiliarity, fear of dialysis, and underestimation of the severity of CKD by primary care physicians. There is also no financial incentive for early referral, which hinders the implementation of the guidelines among PCPs. The practical implementation of early referral also remains questionable, as nephrologists are unlikely to be able to follow up on all patients with CKD(6,7) regularly.

There is a need to develop and implement new strategies through collaboration between primary care physicians and nephrologists. However, before the increase in medical resources dedicated to renal care, the impact of specialized care on renal patients should be thoroughly assessed.

Therefore, the objective was to determine the impact of specialized care by nephrologists (co-management) compared with primary care physician-directed management on survival, RRT planning, and quality of life in patients with CKD who were discharged from hospitalization.

Method

A prospective randomized study was conducted from November 2017 to the end of June 2021 for those patients with CKD stage 3b-4 (Estimated glomerular filtration rate (eGFR) between 44 and 15 ml/min/1.73 m^2), according to the abbreviated MDRD-GFR formula and aged between 18 and 80 years were eligible for the study. Patients with CKD were enrolled during hospitalization and randomized into two arms: co-management by MAP and nephrologists (interventional arm) versus management by MAP with written instructions and consultations by nephrologists on demand (standard care) in 20 primary care practices in the city of Ambato. This study was approved by the Universidad Regional Autónoma de Los Andes (UNIANDES).

Exclusion criteria included patients previously known to nephrologists or patients with a diagnosis of acute renal failure (ARF) or those whose estimated life expectancy was < 1 year, and those who refused or were unable to sign a written consent.

Our CKD care model included a 30-minute consultation with a nephrologist, during which a clinical examination and assessment of laboratory values were performed, with time also allotted for dietary and lifestyle counseling.

Only primary care physicians' management was performed with written nephrology instructions based on KDOQI clinical practice guidelines[8]. Treatment advice was provided to primary care physicians on request by e-mail or telephone. Neither primary care physicians nor nephrologists were aware of patient assignment or outcome. The primary outcome was death or emergency hospitalization during the 24 months after inclusion. Secondary outcomes were the initiation of urgent RRT, a decline in renal function, and declining quality of life two years after inclusion[21].

Clinical, demographic, and laboratory data were collected at inclusion and year 1 and 2 in patients who accepted the study. The modified Charlson score was used as the comorbidity score[9]. Renal

function decline was calculated by the difference between baseline and year 1 and 2 values in FGE and creatinine clearances measured by 24-hour urine collections.

Values were expressed as mean and standard deviation or median and interquartile ranges according to their distribution. Parametric and nonparametric tests were used to test for significant differences between the demographic and baseline characteristics of the study groups. A two-sided significant *p*-value $p < 0.05$ was established. To compare the evolution of characteristics during follow-up between MAP and combined management, we first created a "post" variable to consider the time after randomization: post = 0 represents the time before randomization, post = 1 is the time after randomization at one year and two years. Then, linear and mixed logistic regression was used to account for the repeated measures; participant characteristics were the dependent variables, and time ("post") and the randomized group were the independent variables.[22]

Kaplan-Meier survival curves were drawn for univariate analysis of the main composite outcome (death or rehospitalization) within two years after randomization. The log-rank test was used to compare survival curves. In addition, a Cox proportional hazards model was used to investigate independent risk factors for the main composite outcome and implementation of emergency RRT. Database and statistical processing of the data were performed and analyzed in SPSS 26 statistical software (SPSS Inc., Chicago, IL, USA). Descriptive statistics were used for the results collection, presentation and interpretation.

Results

The authors identified 528 patients with GFR between 15 and 45 mL/min/1.73 $m^{2,}$ of whom 139 had refused randomization, and 147 were already being followed up by a nephrologist, leaving 242 patients to be randomized.

The primary combined outcome was achieved in 61 % (71/116) and 69 % (87/126) of patients in the PAM and combined treatment groups ($p = 0.25$). There was no difference in the 2-year survival rate without rehospitalization between the 2 groups (log-rank test = 0.2). Renal replacement therapy was implemented in 12 and 13 patients in the MAP and combined management groups, respectively. The rate of emergency RRT versus planned or no dialysis was similar in both groups (9 and 7% in MAP and combined management groups, respectively, $p = 0.62$). Emergency RRT was associated with age, GFR and comorbidity score (Table 1).

Table 1. Cox regression analysis for planned vs. emergency RRT

Features	unadjusted model		fitted model	
	HR (95% CI)	p	HR (95% CI)	p
Years	0,94 (0,91-0,98)	0.001	0,92 (0,88-0,96)	0.001
Male gender	4,19 (0,96-18,2)	0.06	2,25 (0,50-10,20)	0.29
Charlson score	1,22 (0,97-1,53)	0.09	1,42 (1,19-1,70)	0.001
FGE	0,92 (0,88-0,97)	0.002	0,93 (0,88-0,98)	0.005
Combined management	0,67 (0,27-1,71)	0.40	1,99 (0,72-1,48)	0.18

Source: statistical analysis, $p \leq 0.05$. GFR: estimated glomerular filtration rate, HR: hazard ratio.

Of note, only 42 patients in the co-management group and 18 in the MAP group had undergone the three planned 24-h ambulatory blood pressure mapping (ABPM). There was also no difference in the left ventricular hypertrophy (LVH) rate or cardiac ejection fraction. However, the number of patients who underwent echocardiography was reduced from 209 at baseline to 79 (29 in the MAP-only treatment group) at two years, and these results should be interpreted with caution.

No significant change was observed in laboratory data at two years in the levels of creatinine, FGE, ferritin, transferrin saturation, calcium, phosphate, bicarbonate, albumin and proteinuria evolution.

Concerning medications, most patients in both groups were taking renin-angiotensin blockers (ARBs), diuretics, and beta-blockers at a 2-year follow-up. However, patients in the co-management group were treated less with diuretics after randomization (p = 0.007). For all other medications, there was no difference between the two groups in prescriptions of

aspirin, insulin, oral antidiabetics, iron, and vitamin D after randomization.

Patients who refused the study or were excluded due to the previous follow-up by nephrologists had a statistically significant decrease in survival. Long-term mortality was 54% in the refusal group, 32% in those previously known to nephrologists versus 16.5% in the randomized group ($p < 0.001$).

Among the 122 patients who responded to the questionnaire at baseline and during follow-up, the means of all KDQOL scales were similar in the two arms of the trial at baseline, with little change as follow-up progressed.

Discussion

In patients with moderate to severe CKD, co-management by primary care physicians and nephrologists compared with management by primary care physicians who received guidelines and had access to nephrologist advice did not result in a substantial improvement in hospital-free survival. The few telephone calls for advice in the standard care group suggest that nephrologist input was not an attenuating factor in our study.

Although blood pressure (BP) is consistently mismanaged and poorly controlled in patients with CKD, our patients differed from everyone else in actual practice because their baseline BP patterns were already within the common range. This may explain why no demonstrable regression of LVH and the evolution of renal functionalities prevailed identically in the two sets at a 2-year follow-up. On the other hand, conjunctive management did not translate into better nephrological outcomes in terms of renal function deterioration and planned RRT rate nor into lower mortality and recurrence of hospitalizations at 2-year follow-up. Good adherence of the APMs to the guidelines may have contributed to this lack of differences and may also explain the similar evolution in most laboratory parameters during this study between the two groups[10, 11].

Quality of life (QoL) has not been intensively studied in patients with CKD and there is a paucity of longitudinal studies investigating the change in QoL over the entire duration of CKD. Lately, QoL was found to be associated in CKD patients with shorter and longer sleep periods, which could have a noticeable effect on CKD progression. However, in this 2-year time interval, we did not observe any significant alteration in the quality of life or difference between the two treatment teams[12,13].

In relation to the expectations of CKD patients in terms of research, it was shown in a survey that most of them favor research on treatments to stop the progression of CKD. Consequently, several models of care have been developed over the last 20 years to slow better the progression of ESRD in CKD patients[14].

Recently there has been a real emphasis on embedded or nurse-driven care to increase patient compliance; however, multidisciplinary or nurse-coordinated models yielded conflicting results[15]. The Masterplan study enrolled 740 patients with CKD who were randomized to common standard care by a nephrologist or boosted by nurse practitioner care. This trial demonstrated a minor decrease in renal function, although cardiovascular mortality did not change substantially[16]. This analysis further taught that lifestyle interventions were difficult to sustain over time due to the changing emphasis on goals and less linkage of nurses to patients[17]. Strategies encouraging integrated care involving health care officials appear to be most effective in developing countries with measurably delayed CKD[18].

Although the two professions favor a simplified collaborative care model between general practitioners and nephrologists, the search for a model that combines efficiency and economy of human resources remains conceptualized[19].

The trial had several limitations. First, they did not enroll the number of patients concluded in the sample size calculation within the authorized time for recruitment, and the follow-up era was limited to 2 years. Therefore, underpowering (type 2) error could be feasible, although our results agree with previous studies. Nevertheless, per-protocol exploration of the results has been similar to our intention-to-treat study[20].

Conclusions

Although the results did not show a virtue of scheduled care by a nephrologist in this frail population such as CKD patients, such data have to be put because of the constraints of our analysis; however, they further suggest that guideline-informed APMs could obtain similar outcomes as nephrologists in the care of CKD patients.

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