DECLINE OF RENAL FUNCTION AT LATER STAGES OF CHRONIC KIDNEY DISEASE: THE RELATIVE IMPORTANCE OF PRESCRIPTION MEDICATION

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Introduction and Aims

◆ Accelerated loss of renal function is a common finding at later stages of chronic kidney disease (CKD). Many studies have alerted about the potential influence of common prescription medication on CKD progression

◆ Aims: to determine the rate of decline of renal function in advanced CKD, factors associated with faster progression, and the relative importance of common prescription medication in this renal outcome

Patients and Methods

◆ Longitudinal observational study in a cohort of adult patients with CKD stage 4 and 5 not on dialysis (2000-2014), who had at least 3 consecutive measures of eGFR (MDRD-4) in a follow-up period greater than 3 months. Patients with recent AKI or in ongoing treatment for glomerular disease or vasculitis were excluded.

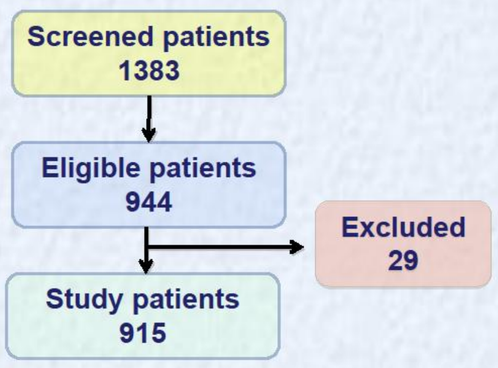
◆ The rate of renal failure progression was assessed by the slope of the regression line of eGFR over time (days). Expressed as ± ml/min/1,73 m^2/year.

◆ Outcome variables: slope eGFR (continuous variable), and faster progression (steeper than the mean slope value) (dummy variable).
◆ Covariates: demographic, BMI, diabetes, comorbidity index (Davies), smoking, SBP and DBP, proteinuria (24 h collection, g/g creatinine). Prescription medication included as potential determinants: diuretics, ACEi or ARB, dual blockade (ACEi+ARB or DRI), erythopoiesis stimulating agents (ESA), oral anticoagulants (OAC) (acenocumarol), xanthine-oxidase inhibitors (XOi) (allopurinol or febuxostat), proton-pump inhibitors (PPI), vitamin D analogues (VDA) (calcitriol or paricalcitol), ACEi or ARB withdrawal (wd), fibrates withdrawal, and VDA withdrawal. All patients were treated for controlling hyperphosphatemia and acidosis.

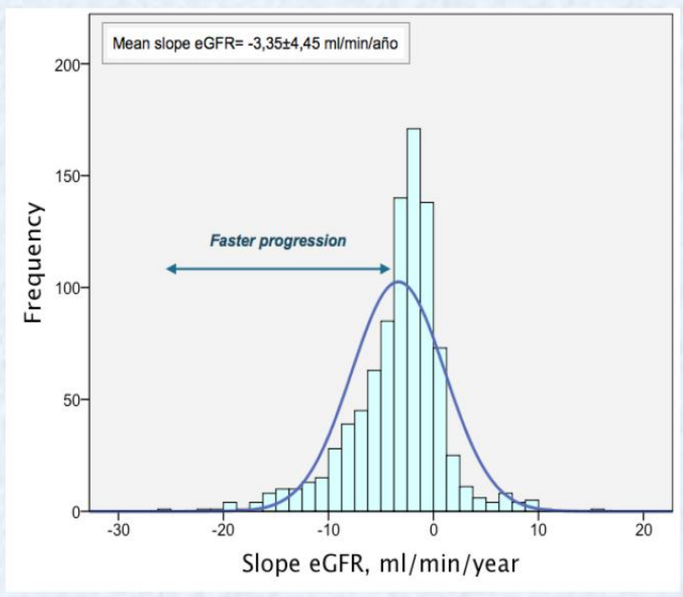
◆ Statistical methods. Multiple lineal or logistic regression analysis. Johnson´s relative weights analysis was used to estimate the relative importance of each potential determinant in the best regression models, and the results were expressed as percent contribution to multiple R

Results

Patient selection



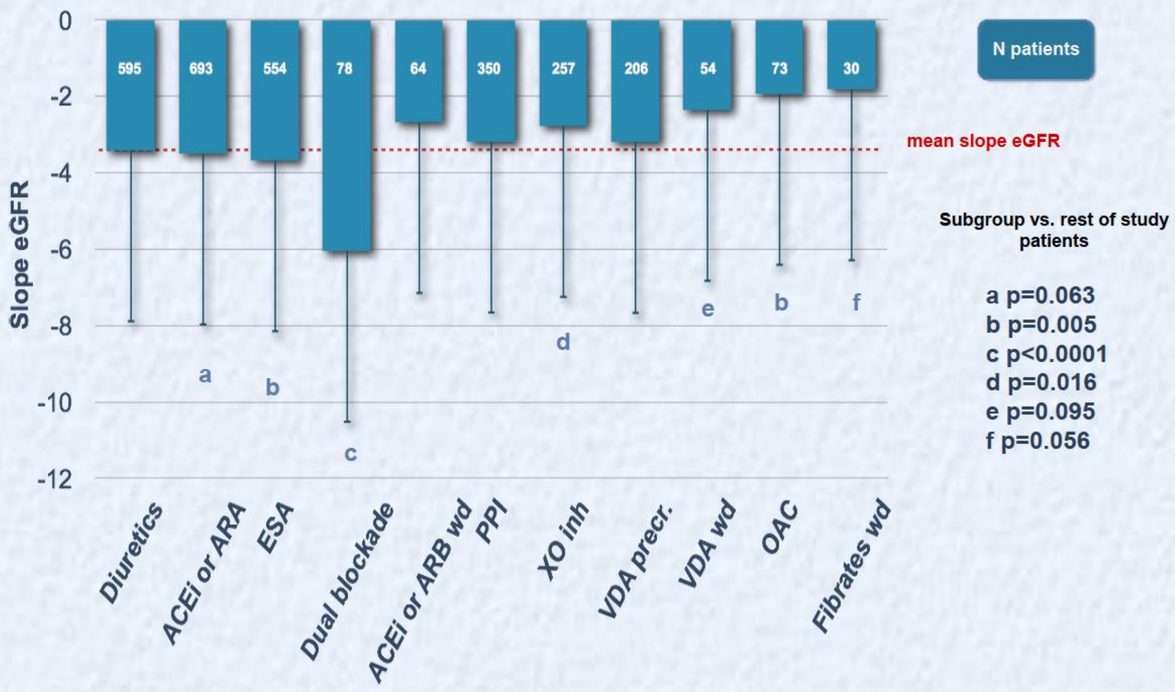
Frequency distribution of slope eGFR



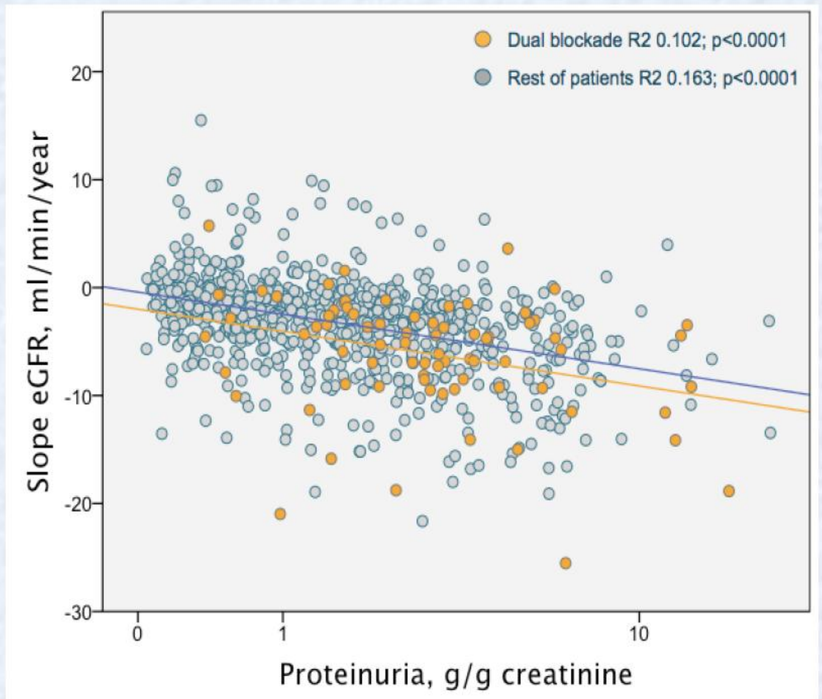
Clinical and biochemical characteristics of study patients

	Total	Slow progression	Fast progression	p
N patients	915	545	370	
Age, years	65±14	67±13	63±14	**<0.0001**
Gender, m/f	475/440	274 / 271	201 / 169	0.229
Comorbidity Index	380/445/ 90	226/268/51	154/177/39	0.821
Diabetes mellitus	330 (36%)	189 (35%)	141 (38%)	0.289
Current smokers	157 (17%)	81 (15%)	76 (21%)	**0.025**
B.M.I., kg/m²	29.5±5.8	29.8±5.9	29.1±5.8	**0.089**
Systolic BP, mmHg	158±27	154±26	163±27	**<0.0001**
Diastolic BP, mmHg	87±14	86±15	88±14	**0.003**
Baseline eGFR, ml/min/1,73 m²	14.7±4.5	14.6±4.6	14.8±4.5	0.517
Slope eGFR, ml/min/year	-3.35±4.45	-0.67±2.42	-7.28±3.78	**<0.0001**
Serum uric acid, mg/dl	7.6±1.9	7.6±2.0	7.5±1.5	0.408
Serum total calcium, mg/dl	9.2±0.8	9.3±0.8	9.1±0.8	**0.001**
Serum phosphate, mg/dl	4.7±1.0	4.6±1.1	4.8±0.9	**0.005**
Serum albumin, g/dl	3.96±0.44	4.02±0.41	3.86±0.45	**<0.0001**
Serum bicarbonate, mmol/l	21.5±4.0	21.6±4.1	21.4±3.9	0.453
PTH, pg/ml	263±216	257±228	273±198	0.256
Proteinuria, g/g creatinine	2.13±2.35	1.48±1.69	3.09±2.81	**<0.0001**
N measures per patient	7 [5 – 11]	11 [6 – 14]	6 [4 – 8]	**<0.0001**
Follow-up time, months	16 [8 – 30]	31 [12 – 40]	10 [6 – 17]	**<0.0001**

Slope eGFR according to prescription medication



Linear regression between slope eGFR and proteinuria



Multiple linear regression and relative weights analysis for slope eGFR

Covariate	Beta coeff.	Structure coeff.	Contribution multiple R	P
Age, years	0.129	+0.303	8.2	<0.0001
B.M.I., kg/m²	0.087	+0.158	3.7	0.005
Systolic Blood Pressure, mmHg	-0.136	-0.418	12.4	<0.0001
Proteinuria, g/g creatinine	-0.343	-0.823	57.2	<0.0001
Dual blockade	-0.101	-0.396	9.7	0.001
Fibrates withdrawal	0.083	0.134	2.5	0.005
ESA prescription	-0.086	-0.200	3.3	0.004
Oral anticoagulants	0.063	0.198	2.8	0.035

Multiple logistic regression for faster progression

Covariate	Odds Ratio	C.I. 95% OR	P
Age, years	0.982	0.972 – 0.993	0.001
B.M.I., kg/m²	0.962	0.938 – 0.987	0.004
Systolic Blood Pressure, x 10 mmHg	1.080	1.030 – 1.140	0.004
Proteinuria, g/g creatinine	1.416	1.302 – 1.540	<0.0001
Dual blockade	2.280	1.328 – 3.914	0.003
Analogues vitamin D withdrawal	0.462	0.228 – 0.936	0.032

Conclusions

◆ In addition to highly expected risk factors for CKD progression, common prescription medication (e.g. dual blockade, fibrates, vitamin D analogues, etc.) are also significantly and independently associated with the rate of decline of renal function at later stages of CKD

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