Clinical Study

Predictors of a Rapid Decline of Renal Function in Patients with Chronic Kidney Disease Referred to a Nephrology Outpatient Clinic: A Longitudinal Study

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Background. Predicting the progression of kidney failure in patients with chronic kidney disease is difficult. The aim of this study was to assess the predictors of rapid kidney decline in a cohort of patients referred to a single outpatient nephrology clinic. **Design.** Longitudinal, prospective cohort study with a median follow-up of 3.39 years. **Methods.** Data were obtained from 306 patients with chronic renal failure based on serum creatinine-estimated glomerular filtration rate ($\text{eGFR}_{\text{creat}}$) $< 90 \text{ mL/min/1.73 m}^2$. After excluding patients who died ($n = 30$) and those who developed end-stage renal failure ($n = 6$), 270 patients were included. This population was grouped according to the rate of kidney function decline. Rapid kidney function decline was defined as an annual $\text{eGFR}_{\text{creat}}$ loss $> 4 \text{ mL/min/1.73 m}^2$. We recorded nonfatal cardiovascular events at baseline and during follow-up in addition to biochemical parameters. **Results.** The mean loss in renal function was $1.22 \text{ mL/min/1.73 m}^2$ per year. The mean age was 75 ± 8.8 years old, and the mean baseline $\text{eGFR}_{\text{creat}}$ was $42 \pm 14 \text{ mL/min/1.73 m}^2$. Almost one-fourth of the sample (23.3% [63 patients]) suffered a rapid decline in renal function. In a logistic regression model with rapid decline as the outcome, baseline characteristics, lower serum albumin (OR: 0.313, 95% CI: 0.114–0.859), previous cardiovascular disease (OR: 1.903 95% CI: 1.028–3.523), and higher proteinuria (g/24 h) (OR: 1.817 CI 95%: 1.213–2.723) were the main predictors of rapid kidney decline. On multivariate analysis, including baseline and follow-up data, we obtained similar adjusted associations of rapid kidney decline with baseline serum albumin and proteinuria. The follow-up time was also shorter in the group with rapid rates of decline in renal function. **Conclusion.** Renal function remained stable in the majority of our population. Previous cardiovascular disease and cardiovascular incidents, lower serum albumin, and higher proteinuria at baseline were the main predictors of rapid kidney decline in our population.

1. Introduction

Chronic kidney disease (CKD) is an important public health problem characterized by poor health outcomes and high healthcare-related costs. Cross-sectional studies including adult subjects with a broad range of ages have demonstrated a declining glomerular filtration rate (GFR) as age advances [1]. Older people with advanced CKD are at increased risk of death, kidney failure, myocardial infarction, and stroke, compared with otherwise similar people with a normal or mildly

decreased GFR. To illustrate this point, a 5% random sample of people enrolled in Medicare from 1996 to 2000 and followed up for two years indicated that a patient with CKD was at least five times more likely to die than to reach end-stage renal disease (ESRD) [2]. Although death is the most common of these adverse outcomes, it does not mean that older patients cannot benefit from timely specialist referral. Several clinical studies have developed models to predict the risk of progression to end-stage renal disease (ESRD), cardiovascular events, and all-cause mortality in people with CKD [3, 4].

The Chronic Renal Insufficiency Cohort (CRIC) study was designed to examine the risk factors for the progression of chronic renal insufficiency (CRI) and cardiovascular disease (CVD) among patients with CRI [5–8]. Concurrent with this study, at least four longitudinal studies with a similar goal were published: the African American Study of Kidney Disease and Hypertension Cohort Study (AASK); the Canadian Study of Prediction of Death, Dialysis and Interim Cardiovascular Events (CanPREDDICT); the Chronic Kidney Disease Prognosis Consortium; and the German Chronic Kidney Disease (GCKD) cohort [9–14]. These large epidemiological studies included patients with different stages of kidney failure, ages, and ethnicities, and they used classic (eGFR and albuminuria), as well as newer, biomarkers (serum fibroblast growth factor-23, vascular endothelial growth factor) [15, 16] for the prediction of specific renal and cardiovascular events. Most studies performed to develop risk scores have focused on ESRD, but in many populations (particularly in primary care), cardiovascular risk exceeds the risk of progression to ESRD. The rate at which this decline occurs also varies based on the underlying cause of CKD, comorbidities, and age. Data from the PREVEND study, a prospective, population-based cohort study [17], provided the somewhat surprising finding that eGFR had lower rates of progression among the group with more impaired renal function at baseline. However, studies evaluating the rate of decline in eGFR among populations with CKD have typically demonstrated a slightly more rapid rate of decline in this subgroup [18]. Despite the progress achieved in identifying risk factors for adverse outcomes in people with CKD, we do not have a widely applicable and effective tool to guide clinical decisions. With appropriate management, patients with rapid kidney decline might benefit from slower loss of kidney function.

We conducted a longitudinal study to assess the clinical and biochemical parameters involved in rapid kidney disease progression in a cohort of CKD patients referred to a nephrologist at a single centre.

2. Methods

We conducted a longitudinal, observational, and prospective cohort study of a sample of 306 patients derived from primary care with the diagnosis of renal failure, defined by an estimated eGFR < 90 mL/min/1.73 m². The nephrology clinic covers the Health Care Area of the city of Leganés, in greater Madrid, with a population of 187,227. After excluding patients who died ($n = 30$) and those who developed end-stage renal failure ($n = 6$), 270 patients were included. This study was approved by the Ethics Committee of the Hospital Severo Ochoa.

2.1. Patients. The patients were aged 43 to 96 years. All of them were referred during the study period, from 2005 to 2013, to our outpatient clinic by their general practitioners, with diagnoses of renal insufficiency. All of the patients were evaluated prospectively for the diagnosis of chronic renal failure based on an estimated glomerular filtration rate < 90 mL/min/1.73 m². We decided also to include patients with stage II CDK according to the NKF (those with

a glomerular filtration rate > 60 and < 90 mL/min/1.73 m²) because some authors have previously described the influence of a milder degree of renal impairment. So Anavekar and colleagues [19] concluded that, in patients with acute myocardial infarction complicated by left ventricular dysfunction, at a GFR of less than 81.0 mL per minute per 1.73 m², the rate of renal events increased with declining estimated GFR, although the adverse outcomes were also cardiovascular. Our patients were elderly and had a high rate of cardiovascular comorbidity.

All of the patients had complete medical histories and clinical examinations. The routine medical examination included body weight, height, and body mass index (BMI), calculated as weight in kg/height in m². Blood pressure (BP) was measured as the average of 3 or more readings using an appropriate adult cuff size. All of the patients signed an informed consent form to participate in the study.

The visits were scheduled annually, but patients with a minimum of 6 months of follow-up were scheduled for at least three visits. In case of any medical event or complication, the review was delayed until the patient stabilized. The minimum was three visits, and the maximum was eight in those patients followed up during 8 years.

We recorded cardiovascular (CV) events (heart failure, acute myocardial infarction, and stroke) at baseline and during the follow-up period, in addition to biochemical parameters. Acute heart failure was diagnosed on the basis of the presence of at least one symptom (dyspnoea or orthopnoea) and one sign (rales, peripheral oedema, ascites, or pulmonary vascular congestion on chest radiography) of heart failure. Acute myocardial infarction was diagnosed when there was evidence of myocardial necrosis in association with clinical signs of myocardial ischaemia. Necrosis was diagnosed on the basis of a rising or falling pattern on troponin assay, performed in the hospital. Stroke (ischaemic or haemorrhagic) was defined as an acute reduction of cerebral blood flow causing transient or permanent loss of neurologic function. Cardiovascular events were documented from the medical records of the emergency department or inpatient unit. Events that occurred in other centres were included only when a medical report of the treating centre was available. Other covariates included in the follow-up were those with biological relevance (age, sex, and BMI), the number and types of antihypertensive drug treatments, the percentage of patients on lipid-lowering treatment, and biochemical variables considered to have greater relevance (serum uric acid, glucose, albumin, total cholesterol and triglycerides, haemoglobin, and proteinuria). We also considered HbA1c $> 7\%$ at any time to be a surrogate marker of metabolic control of diabetes mellitus in patients who suffered from it.

2.2. Analytical Methods. Blood samples were obtained after an overnight fast between 8:00 a.m. and 10:00 a.m. one week before the visit. Routine biochemical measurements were determined from each serum sample using a HITACHI modular autoanalyser.

Glycated haemoglobin (HbA1c) was assessed exclusively in diabetic patients. Albuminuria assays were conducted with

the morning's first voided urine using the albumin/creatinine ratio. In cases of albuminuria values >400 mg/g creatinine, proteinuria determination was performed using a 24 h urine collection. Serum creatinine was determined by the Gaffe2 method standardized from mass spectrometry with isotope dilution.

The glomerular filtration rate (GFR) at baseline and during follow-up was estimated by the following formula:

$$\text{eGFR-EPI}_{\text{creat}} = 141 \times \min(\text{SCr}/k, 1)^\alpha \times \max(\text{SCr}/k, 1)^{-1.209} \times 0.993^{\text{Age}} [\times 1.018 \text{ female}] [\times 1.159 \text{ if black}],$$
 where SCr is serum creatinine in mg/dL, k is 0.7 for females and 0.9 for males, α is -0.329 for females and -0.411 for males, min is the minimum of SCr/ k or 1, and max is the maximum of SCr/ k or 1 [20].

The whole cohort was grouped according to the rate of kidney function decline. Rapid kidney function decline was defined as an annual $\text{eGFR}_{\text{creat}}$ loss > 4 mL/min/1.73 m², as supported by the scientific literature [21].

A variation in $\text{eGFR}_{\text{creat}} \pm 1$ mL/min/1.73 m² relative to the basal value was considered stable renal function.

2.3. Statistical Analysis. The results are expressed as the mean and standard deviation (SD) for continuous variables. Categorical variables are expressed as absolute and relative frequencies. For the univariate analysis, the statistical tests for numeric variables were the t -test and Mann-Whitney U test, and for categorical variables, we used the χ^2 test and Fisher's exact test. For the multivariate analysis, logistic regression was used, as well as Wald's method, selecting variables by their clinical and biological importance and their statistical significance in the univariate analysis. Decline in renal function was assessed by $\text{eGFR}_{\text{creat}}$ slope, defined as the regression coefficient between $\text{eGFR}_{\text{creat}}$ and time, expressed in mL/min/1.73 m² per year. After confirming that all of the required conditions were met, forward stepwise multiple linear regression analysis was used to identify the factors that were independently associated with rapid decline in renal function. This analysis was performed with baseline and follow-up data. Covariates considered for selection in this analysis were chosen on the basis of their significance in univariate analysis or by their clinical or biological relevance.

The level of statistical significance was set at 0.05 with 95% confidence intervals. All of the analyses were performed using IBM SPSS Statistics software, version 20.

3. Results

Decline in renal function in the study subjects as a whole and after categorization by different percentiles is described in Table 1. The mean loss of renal function was 1.22 mL/min/1.73 m² per year. In the first quartile (25% with the greatest degree of deterioration of renal function), the loss was 3.71 mL/min/1.73 m² or greater. In the second and third quartiles the changes were -0.86 mL/min/1.73 m² and $+1.08$ mL/min/1.73 m², respectively.

3.1. Baseline Characteristics of the Study Population. The mean age was 75 ± 8.8 years, and the mean follow-up was

TABLE 1: Decrease in renal function in mL/min/1.73 m², categorized by percentiles.

Number of subjects	270
Mean	-1.2215
Median	-0.8625
Percentiles	
25%	-3.7175
50%	-0.8625
75%	1.08900

3.39 ± 2.27 years (max 8.44, min 0.58). The mean basal eGFR was 42 ± 14 mL/min/1.73 m². Among the 270 patients in the sample, 63 (23.3%) had an annual loss > 4 mL/min/1.73 m². At the time of enrolment, 34% of the patients (92) had already experienced at least one cardiovascular event, including heart failure, acute myocardial infarction, and stroke.

Table 2 describes the baseline clinical and biochemical parameters according to the rate of decline in renal function.

Patients with rapid decline of renal function had a higher incidence of previous cardiovascular events (44.4% versus 30.9%) and diabetes mellitus (55.6% versus 38.3%). Baseline proteinuria was higher, and serum albumin was lower in patients with rapid decline. The remainder of the variables analysed showed no differences between the groups.

Table 3 describes the clinical and biochemical parameters during follow-up, according to the rate of decline of renal function. The incidence of congestive heart failure was higher in the group with rapid decline, whereas myocardial ischaemia and stroke were not different between the groups. Serum albumin was lower, and proteinuria was higher in the participants with rapid decline. Both groups used diuretics in similarly high percentages.

In the logistic regression model with rapid $\text{eGFR}_{\text{creat}}$ as outcome (Figure 1), entering exclusively baseline characteristics, only previous cardiovascular disease, lower serum albumin, and proteinuria were independently associated with a rapid $\text{eGFR}_{\text{creat}}$ decline.

On multivariate analysis (Figure 2) including baseline and follow-up data, we obtained similar adjusted associations of rapid kidney decline with baseline serum albumin and proteinuria. The follow-up time was also shorter in the group with rapid rates of decline in renal function.

4. Discussion

In our study, more rapid progression of kidney failure in elderly patients was related to previous cardiovascular disease and cardiovascular incidents and with the biomarkers serum albumin and proteinuria. Congestive heart failure during follow-up was a more powerful predictor of rapid kidney decline than stroke or myocardial infarction. There exists a bidirectional relationship between cardiac and renal dysfunction. Acute or chronic dysfunction of the heart or the kidneys can reciprocally induce acute or chronic dysfunction. The term "cardiorenal syndrome" has been applied to this interaction, but its definition and classification are

TABLE 2: Baseline characteristics of patients with and without rapid kidney function decline, defined by an annual loss of >4 mL/min/1.73 m² in creatinine-based estimated glomerular filtration rate.

	No rapid decline Annual eGFR _{creat} loss $\leq$ 4 mL/min/1.73 m ² N = 207	Rapid decline Annual eGFR _{creat} loss $>$ 4 mL/min/1.73 m ² N = 63	P value
Sex (male %)**	116 (56)	47 (66.7)	0.134
Age > 65 years (%)**	180 (87)	54 (85.7)	0.800
Age (years)*	75.2 $\pm$ 8.7	74.2 $\pm$ 8.9	0.589
Previous CV event (%)	64 (30.9)	28 (44.4)	0.047
Serum creatinine (mg/dL)*	1.5 $\pm$ 0.3	1.5 $\pm$ 0.5	0.068
Serum uric acid (mg/dL)*	6.9 $\pm$ 1.7	7.0 $\pm$ 1.5	0.679
Haemoglobin (g/dL)*	13.2 $\pm$ 1.5	13.1 $\pm$ 1.6	0.329
Body mass index (kg/m ²)*	29.9 $\pm$ 4.6	30.2 $\pm$ 5.5	0.592
eGFR-EPI _{creat} (mL/min/1.73 m ²)*	39 $\pm$ 12	41 $\pm$ 14	0.290
Systolic blood pressure (mm Hg)*	138 $\pm$ 19	138 $\pm$ 18	0.588
Diastolic blood pressure (mm Hg)*	76 $\pm$ 10	76 $\pm$ 14	0.994
Glucose (mg/dL)*	116 $\pm$ 35	124 $\pm$ 46	0.125
Total cholesterol (mg/dL)*	189 $\pm$ 41	181 $\pm$ 38	0.162
Serum triglycerides (mg/dL)*	150 $\pm$ 118	160 $\pm$ 91	0.606
Proteinuria (g/24 h)*	0.23 $\pm$ 0.53	0.77 $\pm$ 1.27	<0.001
Serum albumin (g/dL)*	4.2 $\pm$ 0.3	4.1 $\pm$ 0.3	0.004
HbA1c (%)***	7 $\pm$ 1.7	7.5 $\pm$ 1.5	0.170
HDL cholesterol (mg/dL)*	50 $\pm$ 16	52 $\pm$ 17	0.583
LD cholesterol (mg/dL)*	109 $\pm$ 35	101 $\pm$ 35	0.247
Serum cystatin C (g/L)*	1.71 $\pm$ 0.54	1.73 $\pm$ 0.46	0.770
Diabetes mellitus, n (%)	79 (38.3)	35 (55.6)	0.016
Tobacco use, n (%)	95 (46.9)	36 (57.1)	0.118

CV: cardiovascular; eGFR-EPI_{creat}: estimated glomerular filtration rate according to creatinine; HbA1c: glycated haemoglobin. ** Data are presented as n (%).

*Data are presented as the mean $\pm$ SD.

***Performed in diabetic patients only.

FIGURE 1: Logistic regression model with rapid eGFR_{creat} as the outcome including baseline data adjusted for age, sex, baseline albumin, basal proteinuria, and the presence of diabetes mellitus.

TABLE 3: Comparative analysis during the follow-up according to declining rates of renal function.

	No rapid decline Annual eGFR _{creat} loss ≤ 4 mL/min/1.73 m ² N = 207	Rapid decline Annual eGFR _{creat} loss > 4 mL/min/1.73 m ² N = 63	P value
HbA1c > 7% at any time during follow-up (%)**	43 (20.8)	21 (33.3)	0.040
Incident CV event (%)**	32 (15.5)	14 (22.2)	0.211
Acute myocardial infarction (%)**	39 (19.0)	20 (30.8)	0.046
Stroke (%)**	30 (14.6)	12 (18.5)	0.458
Congestive heart failure (%)**	36 (17.6)	23 (35.4)	0.002
Lipid-lowering treatment n (%)**	103 (49.3)	35 (55.6)	0.600
Diuretic treatment, n (%)	151 (72.9)	49 (77.8)	0.638
ACEI, n (%)**	90 (43.7)	26 (41.9)	0.807
ARB, n (%)**	68 (33)	18 (29)	0.556
CHB, n (%)**	65 (31.7)	23 (37.1)	0.084
BB, n (%)**	67 (32.8)	21 (33.3)	0.429
Serum uric acid (mg/dL)*	7.3 ± 4.2	7.5 ± 1.5	0.743
Haemoglobin (g/dL)*	13.2 ± 2.2	12.8 ± 1.6	0.183
Glucose (mg/dL)*	116 ± 32	124 ± 44	0.118
Total cholesterol (mg/dL)*	182 ± 36	178 ± 39	0.522
Serum triglycerides (mg/dL)*	137 ± 97	142 ± 72	0.727
Proteinuria (g/24 h)*	0.32 ± 0.58	0.80 ± 1.27	0.001
Serum albumin (g/dL)*	4.2 ± 0.3	4.1 ± 0.3	0.008
Follow-up time, years*	3.7 ± 2.3	2.2 ± 1.8	<0.001

CV: cardiovascular; ACEI: angiotensin-converting enzyme inhibitor; ARB: angiotensin receptor blocker; CHB: calcium channel blockers; BB: beta blocker.

**Data are presented as n (%). *Data are presented as the mean ± SD.

FIGURE 2: Logistic regression model with rapid eGFR_{creat} as the outcome including baseline and follow-up data adjusted for age, sex, previous cardiovascular event, baseline serum albumin and proteinuria, mean proteinuria and mean serum albumin during follow-up, and presence of diabetes mellitus.

not clear [22–25]. Another finding of our study was the stability of renal function during the follow-up in a majority of patients, even in those with advanced degrees (stage 3B of the classification renal K/DOQI) of renal insufficiency. This finding agreed with those of previous studies [26] that showed a lower risk of ESRD with advanced age at all levels of eGFR.

Shlipak et al. [27] performed a population-based longitudinal study including 4380 individuals from the CHS (Cardiovascular Health Study) older than 65 years of age, and they obtained similar results to ours. Compared to our study, the mean eGFR in Schlipak's study was higher (80 mL/min/1.73 m² versus 42 mL/min/1.73 m², resp.). Their group with rapid kidney function decline also had higher prevalence of diabetic patients, and the eGFR at baseline was higher as well. These authors also found that rapid kidney disease progression was strongly associated with heart failure and not with myocardial ischaemia or stroke. In our study, the patients with more frequent heart failure during follow-up had also a more rapid rate of renal function decline, and the eGFR at baseline was similar between the patients with different rates of decline in renal function. Similar results were obtained by Rahman et al. [7] in a prospective study of 3,939 people with CKD enrolled in the Chronic Renal Insufficiency Cohort (CRIC). The study authors analysed the association between prevalent CVD and risk of progression of CKD. Prevalent CVD (myocardial infarction, heart failure, stroke, and peripheral vascular disease) was determined by self-reporting at baseline. The authors concluded that a history of heart failure was an independent risk factor for the development of ESRD or for a 50% decline in eGFR.

The greater impact of congestive heart failure over other major cardiovascular events could be the result of a decrease in renal plasma flow due to low cardiac output and/or chronic use of diuretics or the result of excessive activation of the renin-angiotensin-aldosterone system.

Mean proteinuria during follow-up was also a predictor of rapid deterioration of renal function, both in the whole sample and in diabetic patient subset. Albuminuria or the albumin-to-creatinine ratio (A/C > 30 mg/g creatinine) in the first voided urine of the morning has been defined as a diagnostic and prognostic biomarker of renal disease [28, 29]. The presence of this biomarker represents established kidney damage, which was an expected finding.

A surprising finding of our study was the relationship between lower serum albumin at baseline and more rapid deterioration of kidney function. Hypoalbuminemia has been defined traditionally as a powerful marker of malnutrition and as a protein acute-phase reactant, the synthesis of which decreases with inflammation regardless of nutritional status. There has also been abundant evidence correlating malnutrition-inflammation conditions with volume expansion in dialysis patients [30]. The interactions among volume overload, myocardial function, and progression of kidney disease are close and complex. In our study, there were no data on C-reactive protein or other markers of inflammation that would have allowed us to assess the influence of these factors.

Overhydration is another determinant of serum albumin concentrations in patients with renal insufficiency. Volume

overload occurs very early in the course of kidney disease as a result of the inability of the insufficient kidney to eliminate excess water and salt. Generally, this increase in extracellular water remains unnoticed in routine clinical examinations. More accurate methods of measurement of body water volume, such as bioimpedance, are needed to prove this finding. We could hypothesize that our patients were in a state of chronic volume overload, which resulted in lower levels of baseline serum albumin. It was reported that excess extracellular water was an independent factor involved in myocardial structural damage [31], and it was present in early phases of CKD. Over time, myocardial remodelling progresses, leading to diastolic dysfunction and higher left ventricular filling pressure. Tsai et al. [32], in a prospective cohort study of patients with advanced CKD, concluded that fluid overload was an independent risk factor associated with rapid eGFR decline.

Chen et al. [24], in a longitudinal study of 395 patients, examined whether the association between albumin and indexed echocardiographic left atrial diameter (LAD) was independently associated with renal outcomes in patients with CKD stages 3–5. They concluded that albumin was independently associated with indexed LAD, and they suggested that the combination of increased LAD and hypoalbuminemia was independently associated with rapid progression to dialysis.

In our study, there was no difference in blood pressure between the groups with rapid decline of renal function and the group that remained stable in this regard. Traditionally, poorly controlled hypertension has been associated with more rapid progression of renal disease. In our patients, the control of hypertension was very strict and similar in both groups. The patients were on treatment with five antihypertensive drugs in the same percentages in both groups, with special mention of diuretics, which were necessary in 72% and 77.8% of patients with not rapid and rapid declines in renal function, respectively. Our population had high cardiovascular risk, with a previous cardiovascular event as a predictor of rapid progression of kidney failure in a logistic regression model. We might hypothesize that left ventricular systolic or diastolic dysfunction and low cardiac output could be factors determinant of lower levels of blood pressure.

In clinical practice, we emphasize early intervention to control volume excess in early stages of CKD to prevent future cardiac dysfunction or the worsening of underlying heart disease. A prescription of a low sodium diet and careful use of diuretics could be our main tools to prevent volume overload and cardiovascular damage.

Our study had several important limitations. Estimates of glomerular filtration rate (GFR) that are based on serum creatinine are routinely used; however, they are imprecise and can potentially lead to overdiagnosis of chronic kidney disease. The direct measurement of kidney function with radioactive isotopes is too time-consuming and burdensome to be performed in routine clinical practice. The equation that we used to estimate glomerular filtration has been validated in younger population, but its applicability in cohorts of elderly patients remains uncertain. Additionally, the assessment of chronic volume overload has been performed by inaccurate

methods and could represent another limitation. In contrast, the findings of other authors have been conclusive regarding the relationships of excess extracellular water and myocardial structural damage with rapid kidney function decline [31]. Furthermore, in a study measuring total body water by bioimpedance spectroscopy, an association of fluid overload with rapid eGFR decline was also found [31]. However, it is necessary to emphasize that our study was performed with CKD patients in different stages of kidney failure.

5. Conclusion

Renal function remained stable in the majority of our surviving population. Cardiovascular disease, mainly heart failure (previous or incident), was an independent predictor of rapid kidney function decline in elderly patients. Lower serum albumin at baseline, probably as a marker of chronic volume overload, also had a significant predictive value for the deterioration of kidney function over time. Further studies are needed to investigate the pathogenic relationship between volume overload and the progression of kidney disease in different stages of renal failure.

Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

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