ORIGINAL ARTICLE

Renal Failure Is an Independent Predictor of Mortality in Hospitalized Heart Failure Patients and Is Associated With a Worse Cardiovascular Risk Profile

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Introduction and objectives. Most clinical trials that demonstrated the negative impact of renal failure on survival in patients with congestive heart failure (CHF) included a relatively small proportion of subjects with a high creatinine level and were performed in patients with depressed left ventricular systolic function. Our aim was to investigate the clinical characteristics and prognosis of hospitalized CHF patients with depressed or preserved systolic function and different degrees of renal dysfunction.

Patients and method. The study included 552 consecutive CHF patients admitted to a hospital department of cardiology between 2000-2002. Renal function was determined from the estimated glomerular filtration rate (GFR), and patients were divided into three groups: GFR>60, GFR 30-60, and GFR<30 mL/min per 1.73 m^2 (severe renal failure), containing 56.5%, 35.5%, and 8.0% of patients, respectively.

Results. Patients with severe renal failure had the worst cardiovascular risk profile: older age, higher prevalence of cardiovascular risk factors, anemia, inflammatory markers in plasma, and less prescription of angiotensin-converting enzyme (ACE) inhibitors. Survival in this patient group was significantly poorer than in other groups (relative risk or RR=2.4; 95% CI, 1.3-4.4) in those with either depressed (RR=3.8; 95% CI, 1.4-10.6) or preserved (RR=2.9; 95% CI, 1.2-6.9) systolic function, independent of other prognostic factors. The negative impact of severe renal failure on prognosis was reduced by ACE inhibitor use.

Conclusions. Renal failure is common and a strong predictor of mortality in hospitalized CHF patients with or without depressed systolic function. It is associated with a worse risk profile.

Key words: *Renal failure. Heart failure. Left ventricular systolic function. Survival. Angiotensin-converting enzyme inhibitors.*

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La insuficiencia renal es un predictor independiente de la mortalidad en pacientes hospitalizados por insuficiencia cardíaca y se asocia con un peor perfil de riesgo cardiovascular

Introducción y objetivos. El impacto negativo de la insuficiencia renal (IR) en la supervivencia de los pacientes con insuficiencia cardíaca congestiva (ICC) se ha descrito en ensayos clínicos realizados, principalmente, en pacientes con función sistólica deprimida (FS-D). El objetivo es valorar las características clínicas y el pronóstico en pacientes hospitalizados por ICC y diferentes grados de disfunción renal en los grupos con FS-D y función sistólica preservada (FS-P).

Pacientes y método. Se analizó a 552 pacientes ingresados entre el año 2000 y el 2002 en el servicio de cardiología con ICC. La función renal se valoró utilizando la tasa de filtración glomerular (TFG) y se consideraron 3 grupos: TFG > 60, 30-60 y < 30 ml/min/1,73 m^2 (IR grave) presente en el 56,5, el 35,5 y el 8,0% de los pacientes, respectivamente.

Resultados. La IR grave se asoció con el perfil de riesgo cardiovascular más adverso: mayor edad, mayor prevalencia de factores de riesgo cardiovascular, anemia, marcadores de inflamación y una menor prescripción de inhibidores de la enzima de conversión de la angiotensina (IECA). Los pacientes con IR grave tenían una supervivencia inferior a la de los otros grupos (riesgo relativo ([RR] = 2,4; intervalo de confianza [IC] del 95%, 1,3-4,4), tanto en FS-D (RR = 3,8; IC del 95%, 1,4-10,6) como en FS-P (RR = 2,9; IC del 95%, 1,2-6,9) e independiente de otras variables con influencia pronóstica. La prescripción de IECA en los enfermos con IR atenuó el impacto negativo de ésta sobre el pronóstico.

Conclusiones. La IR es un predictor común y potente de mortalidad en pacientes hospitalizados por ICC, tanto con FS-P como FS-D, y se asocia con un perfil de riesgo más elevado.

Palabras clave: *Insuficiencia renal. Insuficiencia cardíaca. Función sistólica ventricular izquierda. Supervivencia. Inhibidores de la enzima de conversión de la angiotensina.*

ABBREVIATIONS

ACE inhibitor: angiotensin-converting enzyme inhibitor.
CHF: congestive heart failure.
GFR: glomerular filtration rate.

INTRODUCTION

Congestive heart failure (CHF) is one of the main causes of hospitalization, in-hospital mortality and health spending.[1,2] Different types of hospital and clinical department (tertiary and area hospitals, cardiology departments, internal medicine departments) receive patients with this problem, some 30%-50% of whom present with preserved left ventricular systolic function.[3-5] There is some controversy surrounding the prognosis of this form of CHF compared to that in which systolic function is reduced,[5-12] as well as the prognostic factors associated with mortality.

In studies which largely involved outpatients with CHF and preserved left ventricular systolic function, end-stage kidney disease was found to be independently and significantly associated with increased mortality[13]; indeed, even mild to moderate forms of kidney failure increased the risk of death.[14-17] When analyzing the independent association between kidney failure and mortality in patients with CHF it should be remembered that kidney failure is associated with an increased prevalence of other cardiovascular risk factors (e.g., diabetes mellitus and high blood pressure) that could increase mortality.[18]

As far as we know, the relationship between kidney failure and mortality in patients hospitalized with decompensated CHF, and in particular those with preserved left ventricular systolic function, has not been analyzed. Patients with the latter type of CHF are usually elderly, more likely to be women, and to show a higher prevalence of diabetes and high blood presure,[19,20] factors that could influence the association between kidney failure and mortality.

Making use of a prospective registry of patients hospitalized for CHF in the cardiology department of a university hospital, the aim of the present study was to determine whether kidney failure is a predictor of mortality when left ventricular systolic function is preserved and when reduced. In addition, an analysis was made to determine whether the degree of kidney failure is associated with different cardiovascular risk profiles.

PATIENTS AND METHODS

Study Population, Selection Criteria, and Definitions

Between 1 January 2000 and 31 December 2002, 630 patients with CHF, as defined by the modified Framingham criteria (major criteria: paroxysmal nocturnal dyspnea, orthopnea, pulmonary crackling, jugular vein engorgement, third heart sound, radiological signs of pulmonary congestion, and cardiomegaly; minor criteria: exercise dyspnea, peripheral edema, hepatomagaly, and pleural effusion), were admitted to the cardiology department of a tertiary hospital in northwestern Spain. This diagnosis was reached when at least 2 major criteria or 1 major plus 2 minor criteria were met. Patients who were readmitted were excluded and only data for the first admission of any patient during the study period were taken into account. To be included, patients were also required to have undergone blood tests to determine their serum creatinine concentration at admission (before any other diagnostic tests were made or therapeutic decisions taken). The final study population was composed of 552 patients.

The glomerular filtration rate (GFR) was used to represent kidney function. This was estimated using the equation proposed in the Modification of Diet in Renal Disease study ($186 \times \text{serum Cr}^{-1.154} \times \text{age}^{-0,203} \times 1.210$ [for black patients only] $\times$ 0.742 [if female]).[21] Three groups were recognized in terms of the GFR values obtained: >60, 30-60, and <30 mL/min/1.73 m^2. In the present patients, the GFR established by the above formula was strongly correlated to creatinine clearance as determined by the Cockroft-Gault equation (r=0.84; P<.001).

The prognostic influence of GFR was analyzed for all patients as a whole, and for the subgroups with preserved and reduced left ventricular systolic function. The classification of patients within the latter subgroups was established according to their left ventricular ejection fraction. This was determined echocardiographically in 469 patients using the modified Simpson method, taking 50% as the cut-off value. Patients who did not undergo this procedure (15.03% of the total study population) were not a priori selected; such testing was performed at admission as judged clinically necessary by the attending cardiologist.

Variables Analyzed

The following variables were recorded: demographics cardiovascular risk factors, CHF etiology, clinical status, the results of complementary tests (chest x-ray, electrocardiogram, blood analysis), and the treatment prescribed at discharge. The selection of patients to be included in the study and the collection of data were undertaken by 2 cardiologists with ample experience of

treating CHF. Clinical data were collected in a prospective manner over the entire study period. However, for the analysis of survival, information was obtained from the hospital's general records; a telephone interview was also performed (April 2003).

Trustworthy data regarding the final status of 26 patients were unavailable. This small group of patients showed no significant differences to the remaining patients in their clinical characteristics.

Statistical Analysis

Categorical or dichotomous variables were expressed as percentages and compared using the χ^2 or Fisher exact test. Continuous variables were expressed as means ± standard deviation (SD); the Student *t* test was used for comparing the different groups. Survival curves were produced using the Kaplan-Meier method. These were plotted for the patients as a whole and for the 2 subgroups (those with preserved and those with reduced left ventricular systolic function) to determine the relationship between the degree of kidney failure and survival, and to determine the survival of patients with respect to the different GFR quartiles. The log rank test was used to compare differences in survival.

Multivariate analysis was performed using the Cox proportional hazard model (2-step). In the first step, all variables significant in univariate analysis were introduced (analyzed separately for the whole group of patients and the 2 subgroups) and the conditional forward method used. In the second step, the variables found to be significant in the first step were introduced. The resulting regression coefficients were used to estimate relative risks. The validity of the proportional risk model was corroborated by calculating the log-log functions for each of the covariables introduced. Significance was set at $P<.05$.

RESULTS

Clinical Characteristics of the Overall Study Population

The 552 patients of the present study had a mean age of 71.5 years. Men made up 58.7% of the population, 49% had ischemic heart disease and 63% had high blood pressure. The majority (69%) fell into NYHA class III/IV at the time of admission, and 56% showed reduced systolic function. The mean GFR was 66.9±30.4 mL/min/m^2 (Figure 1). Severe kidney failure (GFR<30 mL/min/1.73 m^2) was detected in 44 patients (8.0%), 196 (35.5%) had moderate kidney failure (GFR 30-60 mL/min/1.73 m^2), and 312 (56.5%) had a GFR of >60 mL/min/1.73 m^2 (no/mild kidney failure).

At discharge, 63% of patients were prescribed angiotensin converting enzyme (ACE) inhibitors, 42% were prescribed beta-blockers, and 16% were prescribed spironolactone. Table 1 shows all the variables analyzed.

Distinctive Clinical Characteristics of Patients With Different Degrees of Kidney Failure

The patients with severe kidney failure (GFR<30 mL/min/1.73 m^2) had a mean serum creatinine level of 7.1 mg/dL (2.7±0.9 mg/dL when excluding four patients receiving dialysis) and a mean GFR of 21.2 mL/min/1.73 m^2. They were also significantly older and showed a greater prevalence of cardiovascular risks such as high blood pressure (86% of patients in this group), diabetes mellitus, and ischemic heart disease (Table 1). In addition, these patients more commonly fell into higher NHYA classes. Although the proportion of patients with acute pulmonary edema (as shown by chest x-rays) was similar to that seen among patients with moderate kidney failure, it was higher than that seen among patients with no/mild impairment of kidney function. Severe kidney failure was also associated with a greater prevalence of anemia (seen in almost 80% of these patients) and with higher erythrocyte sedimentation rates and plasma fibrinogen levels. The patients of this group were those most commonly prescribed nitrates, diuretics and calcium antagonists at discharge; ACE inhibitors and spironolactone were prescribed less often (for only 36% and 3% of patients respectively). No significant differences were seen between the three kidney failure severity groups with respect to the prescription of beta-blockers. Neither the prevalence of left ventricular systolic dysfunction nor atrial fibrillation was correlated to the degree of kidney failure.

Survival

Impact of Kidney Failure on the Prognosis of Patients as a Whole

Mean follow-up time was 1.4±0.9 years, and was possible for 526 patients (95.3%). Twenty three patients (53.5%) with severe kidney failure (GFR<30 mL/min/1.73 m^2) died, 44 (23.7%) died in the moderate severity group (GFR, 30-60 mL/min/1.73 m^2), and 46 (15.6%) died in the group with no/mild kidney failure (>60 mL/min/1.73 m^2). Twelve patients (total) died during hospitalization; this death rate was 5 times higher among those with severe kidney failure than among those with no/mild kidney failure (41.7% compared to 50.0% in the moderate severity group) and 8.3% among those with no/mild kidney failure). Kaplan-Meier analysis showed notably higher mortality among the severe kidney failure patients (mean survival, 1.34 years; 95% confidence interval [CI], 0.99-1.68 years) (Figure 2). Although the prognosis for patients with moderate kidney failure was poorer than for those with no/mild

TABLE 1. Clinical Characteristics and Treatment of Patients Hospitalized for Congestive Heart Failure: Total Patients and Subgroups of Patients With Different Degrees of Kidney Failure (According to the Glomerular Filtration Rate in mL/min/1.73 m²)*

	Total patients (N=552)	GFR<30 (N=44)	GFR, 30-60 (N=196)	GFR>60 (N=312)	P†	P‡
Age, mean±SD, years	71.5±11.5	77.5±10.8	75.4±9.3	68.2±11.8	<.001	<.001
Hospitalization, mean±SD, days	12.5±8.5	12.1±9.4	13.6±10.5	11.8±6.7	.052	.015
Men, %	58.7	54.5	47.4	66.3	<.001	<.001
Risk factors						
High blood pressure, %	62.9	86.4	67.0	57.1	<.001	.030
Hyperlipidemia, %	43.0	41.9	45.5	41.6	.680	.404
Diabetes mellitus, %	26.1	41.9	28.8	22.3	.013	.110
Smokers, %	28.3	20.9	18.8	35.2	<.001	<.001
Etiology						
Ischemic heart disease, %	49.3	79.5	51.5	43.6	<.001	<.001
Valve disease, %	19.0	6.8	23.0	18.3		
Dilated cardiomyopathy, %	9.1	0	3.1	14.1		
Other cardiomyopathy, %	22.6	13.6	22.4	24.0		
Clinical examination						
BMI, mean±SD	28.1±4.6	26.9±5.7	28.2±4.0	28.2±4.8	.578	.947
BMI, 25-30, %	41.2	56.3	45.7	37.3	.009	.492
BMI>30, %	34.2	18.8	32.9	36.6		
NYHA III or IV, %	69.0	77.3	75.8	63.5	.007	.004
JVE, %	43,7	41.5	45.5	42.9	.817	.575
Pulmonary crackles, %	76.8	93.0	79.7	72.6	.006	.080
Third heart sound, %	8.0	2.4	4.8	10.9	.020	.020
Peripheral edema, %	39.5	42.9	36.0	32.5	.360	.435
Laboratory analyses						
GFR, mean±SD, mL/min/1.73 m²	66.9±30.4	21.2±8.2	46.9±8.3	86.1±25.7	<.001	<.001
Creatinine, mean±SD, mg/dL	1.6±4.8	7.1±16.1	1.4±0.3	0.9±0.2	<.001	<.001
Hemoglobin, mean±SD, g/dL	13.4±7.9	11.3±1.8	12.6±1.9	13.4±2.1	<.001	<.001
Anemia, %	44.1	79.5	52.3	34.0	<.001	<.001
Leucocytes/µL, mean±SD	8497±4779	9799±4320	8737±6039	8161±3825	.071	.190
ESR, mean±SD, mm/h	35.2±28.0	58.7±33.1	39.3±26.3	28.4±25.8	<.001	<.001
Fibrinogen, mean±SD, mg/dL	440.5±156.3	532.5±175.5	451.1±172.5	413.6±129.5	.002	.073
Glucose, mean±SD, mg/dL	142.4±86.4	158.6±67.6	144.4±69.1	138.8±97.7	.333	.481
Atrial fibrillation, %	30.7	26.2	31.3	31.0	.683	1.000
Echocardiography, %	86.8	84.1	84.7	88.5	.409	.225
LVEF<50%, %	55.7	43.2	57.4	56.3	0.279	.842
Cardiac catheter, %	41.2	20.5	34.4	48.4	<.001	.002
Treatment						
ACE inhibitors, %	62.8	36.1	55.6	70.3	<.001	.001
Beta-blockers, %	41.6	52.8	36.7	43.2	.136	.180
Spironolactone, %	16.4	2.8	16.1	18.2	.062	.620
Diuretics, %	74.6	86.1	81.7	69.0	.002	.003
Digoxin, %	21.2	19.4	20.0	22.1	.830	.646
Anticoagulants, %	27.9	22.2	24.4	30.7	.244	.146
Antiaggregants, %	59.9	72.2	60.0	58.4	.279	.774
Calcium antagonists, %	23.7	44.4	25.6	20.1	.004	.175
Nitrates, %	41.6	63.9	48.3	35.0	<.001	.004

*SD indicates standard deviation; LVEF, left ventricular ejection fraction; BMI, body mass index; JVE, jugular vein engorgement; ACE inhibitors, angiotensin converting enzyme inhibitors; NYHA, New York Heart Association functional class; GFR, glomerular filtration rate; ESR, erythrocyte sedimentation rate.
†Significanlty different between groups with different degrees of kidney failure.
‡Significantly different between groups with GFR>60 mL/min/1.73 m² and GFR, 30-60, mL/min/1.73 m².

kidney failure (mean survival, 2.45 years; 95% CI, 2.26-2.63 years, compared to 2.76 years; 95% CI, 2.64-2.89 years), the difference was much less marked than between the severe kidney failure and no/mild kidney failure patients. At one year of follow-up, survival increased progressively over the first 3 GFR quartiles (72.2%, 82.4%, and 90.8% respectively). A slight decrease was seen, however, for the highest quartile (86.3%) (Figure 3).

Independent of other variables significantly related to long term survival in univariate analysis, the influence of severe kidney failure was confirmed by the multivariate Cox model; the maximum relative risk (RR) was 2.36 (95% CI, 1.26-4.42). In contrast, moderate kidney failure was not significantly associated with long term survival. Other independent variables related to higher mortality were age and anemia. Treatment with ACE inhibitors was protective (Table 2).

The Role of ACE Inhibitors in the Influence of Kidney Failure on Prognosis

Differences were seen in the influence of severe kidney failure on survival between patients prescribed and not prescribed ACE inhibitors at discharge. These agents clearly attenuated the negative effect of this condition on prognosis; indeed, the significant relationship between kidney failure and survival disappeared in those prescribed these drugs (*P*=.309). In contrast, the negative influence of severe kidney failure on survival was highy siguificant in those not prescribed ACE inhibitors (*P*<.001) (Table 3).

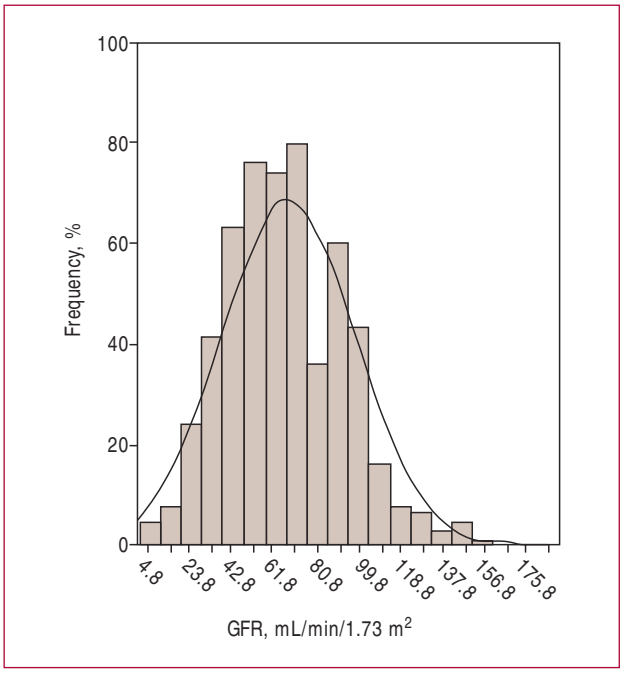

Figure 1. Frequency histogram showing different glomerular filtration rates (GFR) in the study population.

Influence of Kidney Failure on the Prognosis of Patients With Preserved and Reduced Systolic Function

Kidney failure was nighy prevalent in both subgroups of patients (those with preserved and those with reduced

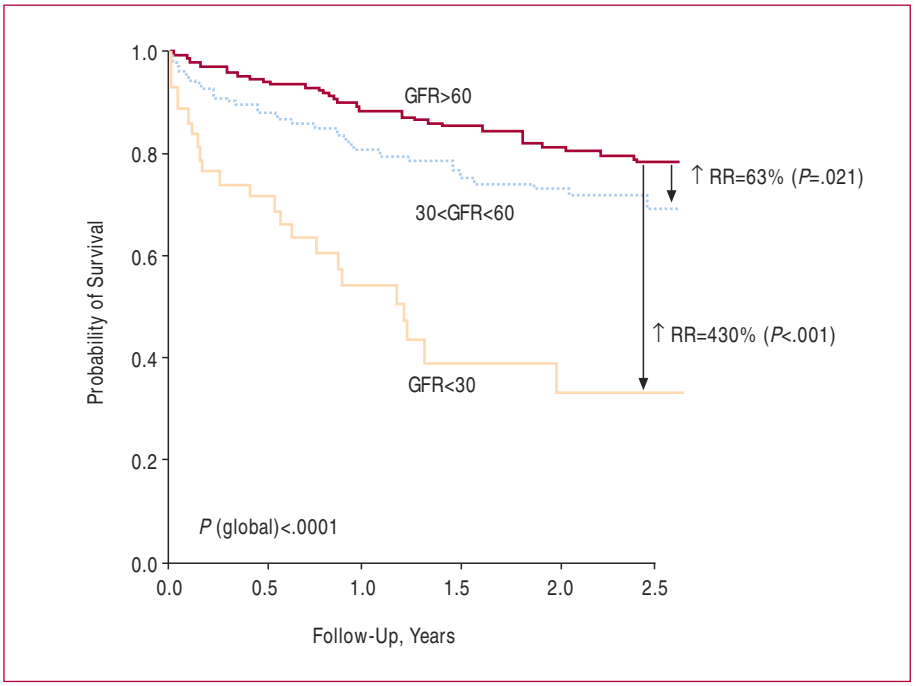

Figure 2. Kaplan-Meier survival curves for patients with severe, moderate, and no/mild kidney failure. GFR indicates glomerular filtration rate; RR, relative risk.

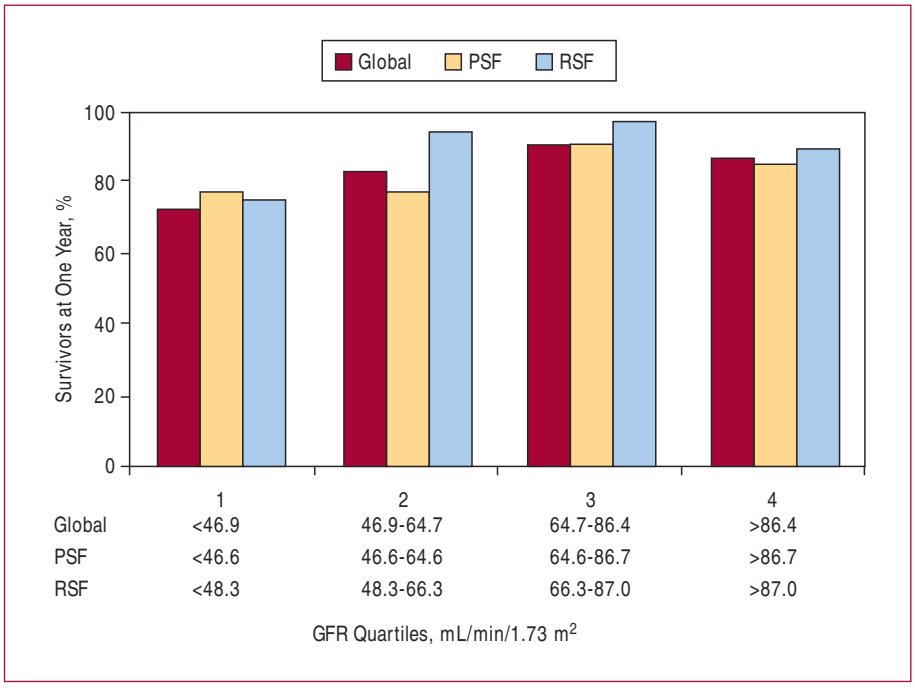

Figure 3. Annual survival of total patients, those with preserved left ventricular systolic function (PSF) and reduced left ventricular systolic function (RSF) with respect to glomerular filtration rate quartiles.

left ventricular systolic function) (Figure 4), affecting approximately half the members of each. Although severe kidney failure affected a relatively small proportion of patients (10% of preserved systolic function patients and 6% of those with reduced function), it was the variable with the strongest negative influence on survival—especially so amongst those with reduced systolic function (Figure 5). In the "preserved" subgroup, survival was reduced from 2.75 years (95% CI, 2.56-2.95 years) in patients with no/mild kidney failure to 1.66 years (95% CI, 1.16-2.17 years) in those with severe kidney failure. In the "reduced" subgroup survival was reduced from 2.83 years (95% CI, 2.66-3.00 years) in those with normal kidney function to 1.17 years (95% CI, 0.66-1.67 years) in those with severe kidney failure. With respect to the GFR quartiles and survival, the trends in the results for the whole patient group and the 2 subgroups (those with preserved and those with reduced left ventricular systolic function) were similar: an improvement over the first three quartiles and a slight worsening when GFR values were >87 mL/min/1.73 m^2 (Figure 3).

The influence of severe kidney failure on prognosis was powerful and independent of other variables significantly associated with survival in both the preserved and reduced systolic function subgroups (Table 4).

TABLE 2. Variables With Independent Influence on Survival in the Total Patient Population Hospitalized for Congestive Heart Failure, Adjusted for Sex, High Blood Pressure, Hyperlipidemia, Alveolar Edema, NYHA Functional Class, Atrial Fibrillation, Ejection Fraction, Beta-Blockers, Anticoagulants, and Digoxin

	RR (95% CI)	*P*
GFR>60 mL/min/1.73 m^2	1.0	
GFR, 30-60 mL/min/1.73 m^2	1.04 (0.65-1.66)	.886
GFR<30 mL/min/1.73 m^2	2.36 (1.26-4.42)	.007
Age	1.03 (1.01-1.05)	.015
Anemia	1.95 (1.24-3.05)	.004
ACE inhibitors	0.51 (0.33-0.80)	.003

*CI indicates confidence interval; ACE inhibitors, angiotensin converting enzyme inhibitors; RR, relative risk; GFR, glomerular filtration rate.

DISCUSSION

The results show that kidney failure is independently associated with mortality among patients hospitalized for CHF. This association was seen both in patients with preserved and reduced left ventricular systolic function. This association was independent of age, the presence of diabetes mellitus, blood pressure, or any other risk factors for mortality. Of all the factors found to be independently associated with mortality, kidney failure was the most important, especially amongst patients belonging to the reduced systolic function subgroup. Patients with more severe kidney failure showed a worse cardiovascular risk profile; this shows that, in patients with CHF, cardiovascular and renal disease develop in a parallel manner. Ezekowitz et al[22] recently described kidney failure to be very prevalent amongst patients with CHF and ischemic heart disease, and that this coexistence was associated with more advanced coronary atherosclerosis. Similary, in our patients, an

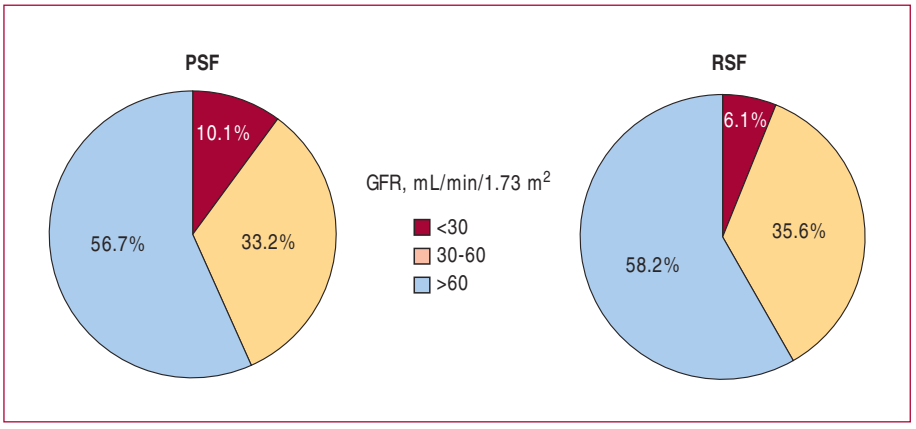

Figure 4. Proportion of patients with different degrees of kidney failure in the preserved (PSF) and reduced left ventricular function (RSF) subgroups.

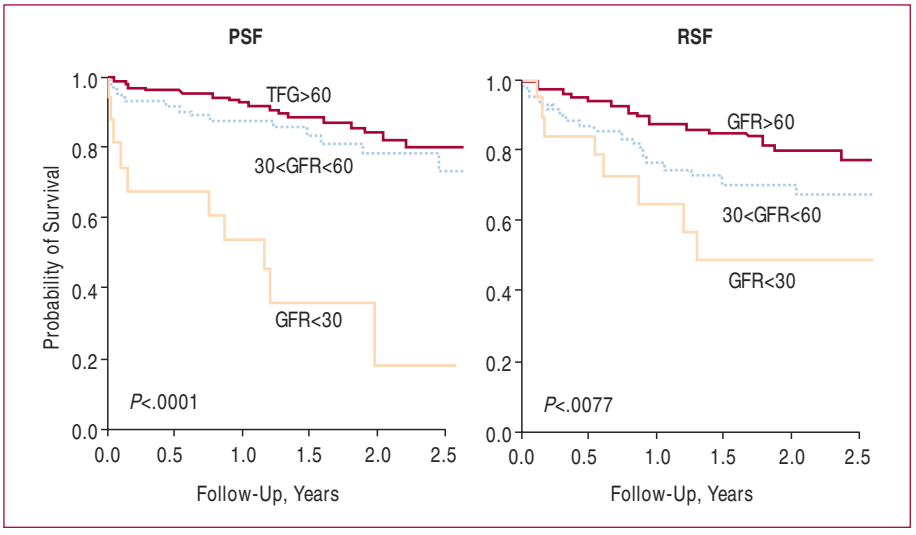

Figure 5. Kaplan-Meier survival curves for patients with congestive heart failure with severe, moderate and no/mild kidney failure in the preserved (PSF) and reduced (RSF) left ventricular systolic function subgroups. GFR indicates glomerular filtration rate.

inverse relationship was seen between GFR values and the prevalence of ischemic heart disease.

The present results underline the importance of kidney failure as a powerful risk factor for mortality in patients hospitalized due to CHF, whether their left ventricular systolic function is preserved or not. They also show that patients with moderate kidney failure can have apparently normal serum creatinine levels—something often seen in the elderly population.

Several papers have reported an association between the deterioration of kidney function and the prognosis of patients with different types of clinical cardiovascular disease.[13-17,23-25] Such deterioration is associated with a greater risk of cardiovascular complications and death in patients with high blood pressure, diabetes mellitus, ischemic heart disease (especially) and CHF.[26-33] In the VALIANT study (patients with ventricular dysfunction and CHF following a myocardial infarction), the deterioration of kidney function was found to be associated with a significant increase in mortality and cardiovascular complications. This increased risk was independent of other variables with influence on patient

TABLE 3. Influence of Kidney Function on Prognosis and the Effect of Prescribing Angiotensin Converting Enzyme Inhibitors

	RR Not Adjusted (95% CI), *P*		RR Adjusted for Age and Anemia (95% CI), *P*	
	Without ACE Inhibitors	With ACE Inhibitors	Without ACE Inhibitors	With ACE Inhibitors
GFR>601,0	1.0	1.0	1.0	1.0
GFR, 30-60	0.94 (0.50-1.77), .851	1.84 (0.95-3.56), .069	0.82 (0.43-1.57), .555	1.33 (0.66-2.70), .427
GFR<30	3.40 (1.72-6.72), <.001	2.13 (0.49-9.15), .309	2.43 (1.16-5.12), .019	1.51 (0.35-6.61), .581

*CI indicates confidence interval; ACE inhibitors, angiotensin converting enzyme inhibitors; GFR, glomerular filtration rate (mL/min/1.73 m^2); RR, relative risk.

TABLE 4. Variables With Independent Influence on Survival in Patients With CHF With Preserved and Reduced Left Ventricular Systolic Function*

	RR (95% CI)	*P*
Subgroup with PSF†		
GFR>60 mL/min/1.73 m²	1.0	
GFR, 30-60 mL/min/1.73 m²	1.44 (0.75-2.77)	.278
GFR<30 mL/min/1.73 m²	2.86 (1.17-6.99)	.021
Age	1.04 (1.01-1.07)	.016
Anemia	1.95 (1.24-3.05)	.003
High blood pressure	0.40 (0.22-0.76)	.005
Subgroup with RSF‡		
GFR>60 mL/min/1.73 m²	1.0	
GFR, 30-60 mL/min/1.73 m²	1.02 (0.47-2.23)	.955
GFR<30 mL/min/1.73 m²	3.79 (1.36-10.56)	.011
ACE inhibitors	0.33 (0.16-0.71)	.004

*CI indicates confidence interval; ACE inhibitors, angiotensin converting enzyme inhibitors; PSF, preserved systolic function; RSF, reduced systolic function; RR, relative risk; GFR, glomerular filtration rate.
†Adjusted for hyperlipidemia, alveolar edema, ACE inhibitors, and anticoagulants.
‡Adjusted for age, etiology, diabetes mellitus, hyperlipidemia, and anemia.

prognosis.[26] A recent analysis of the SAVE study results (patients with ventricular dysfunction following a myocardial infarction) revealed a similar picture, and indicated that treatment with captopril was especially important in patients who also suffered kidney failure.[27]

The increased risk of death in outpatients with moderate kidney failure and CHF is well known, especially in those with reduced left ventricular systolic dysfunction.[14-17] Several mechanisms have been proposed to account for this. Kidney failure might be a marker of more advanced CHF, is associated with a greater prevalence of other cardiovascular risk factors, and might limit the use of drugs known to have a positive impact on prognosis (such as ACE inhibitors).[34,35] In the present study, kidney failure was also found to be an independent predictor of mortality after adjusting for CHF severity markers and other risk factors, both in the preserved and reduced systolic function subgroups. It may be that the relationship between kidney failure and CHF is bidirectional: the former might accelerate the progression of the latter, and the latter influence the appearance of the former.[36]

To some extent the present results suggest such relationships since patients with more advanced kidney failure had a worse cardiovascular risk profile. However, further research is needed to determine the exact nature of the relationship between kidney failure and CHF, in particular to establish whether the stabilization of kidney failure is associated with improved survival.

As mentioned above, the association between mortality and kidney failure was noted in both the preserved and reduced systolic function subgroups of patients. Bearing in mind the physiopathology of CHF with preserved left ventricular systolic function, it is possible that the pathogenesis of both CHF and kidney failure is the same, and that they reflect a parallel progression of cardiovascular and renal disease. Several clinical trials are currently underway to determine the most adequate treatment for CHF with preserved left ventricular systolic dysfunction. Given the high prevalence of kidney failure associated with this clinical form of CHF, and its association with mortality, it is in such patients that the effectiveness of therapeutic strategies with respect to the degree of kidney failure should be investigated.

Given the important relationship between kidney failure and the prognosis of patients with CHF, we believe it wise to assess renal function—at least in terms of the GFR—as part of clinical evaluation and follow-up strategies. The presence of kidney failure should oblige potentially treatable causes be sought, and calls for the use of drugs known to be beneficial—ACE inhibitors and beta-blockers. The results of recent studies highlight the prognostic benefits of treatment with these agents in patients with CHF and kidney failure.[14,15,22,27] In one study[14] it was observed that ACE inhibitors significantly reduced mortality in a group of women patients. Similarly, in a study involving 6427 patients,[22] ACE inhibitors and beta-blockers significantly improved the prognosis of patients with CHF and kidney failure.

The present work also identified other factors that independently influenced patient prognosis. A very strong association was seen between the presence of anemia and CHF; anemia would appear to negatively (and significantly) affect patient prognosis.[37] From a physiopathological viewpoint there are several mechanisms that could account for the association between anemia and kidney failure in patients with CHF; in fact, kidney failure could be a factor in the development of anemia.[34] The present results showed a significant correlation between anemia and kidney function. However, further work is needed to determine whether the stabilization of kidney failure in patients with CHF has any favorable effect on the presence of anemia, to establish whether the correction of anemia has any effect on the survival of such patients, and to assess whether such correction prevents further deterioration of kidney function.

CONCLUSIONS

Kidney failure is a powerful predictor of mortality in patients hospitalized for CHF, irrespective of whether left ventricular systolic function is preserved or reduced. In the present patients, kidney failure was associated with a worse cardiovascular risk profile, suggesting that cardiovascular and renal disease progress together in CHF. Treatment with ACE inhibitors can attenuate the increased risk of death due to kidney failure.

It is recommended that the assessment of kidney function be included in clinical examinations of patients with CHF. Further experimental and clinical research is needed to clarify the mechanisms that justify the association between CHF and kidney failure, and to determine the best therapeutic strategies to follow, both in patients with reduced but especially with preserved left ventricular systolic function.

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