ORIGINAL RESEARCH

Worsening of Renal Function During 1 Year After Hospital Discharge Is a Strong and Independent Predictor of All-Cause Mortality in Acute Decompensated Heart Failure

Tomoya Ueda, MD; Rika Kawakami, MD; Yu Sugawara, MD; Sadanori Okada, MD; Taku Nishida, MD; Kenji Onoue, MD; Tsunenari Soeda, MD; Satoshi Okayama, MD; Yukiji Takeda, MD; Makoto Watanabe, MD; Hiroyuki Kawata, MD; Shiro Uemura, MD; Yoshihiko Saito, MD

***Background*—**Renal impairment is a common comorbidity and the strongest risk factor for poor prognosis in acute decompensated heart failure (ADHF). In clinical practice, renal function is labile during episodes of ADHF, and often worsens after discharge. The significance of worsening of renal function (WRF) after discharge has not been investigated as extensively as baseline renal function at admission or WRF during hospitalization.

***Methods and Results*—**Among 611 consecutive patients with ADHF emergently admitted to our hospital, 233 patients with 3 measurements of serum creatinine (SCr) level measurements (on admission, at discharge, and 1 year after discharge) were included in the present study. Patients were divided into 2 groups according to the presence or absence of WRF at 1 year after discharge (1y-WRF), defined as an absolute increase in SCr >0.3 mg/dL (>26.5 μmol/L) plus a ≥25% increase in SCr at 1 year after discharge compared to the SCr value at discharge. All-cause and cardiovascular mortality were assessed as adverse outcomes. During a mean follow-up of 35.4 months, 1y-WRF occurred in 48 of 233 patients. There were 66 deaths from all causes. All-cause and cardiovascular mortality were significantly higher in patients with 1y-WRF (log-rank $P<0.0001$ and $P<0.0001$, respectively) according to Kaplan–Meier analysis. In a multivariate Cox proportional hazards model, 1y-WRF was a strong and independent predictor of all-cause and cardiovascular mortality. Hemoglobin and B-type natriuretic peptide at discharge, as well as left ventricular ejection fraction <50%, were independent predictors of 1y-WRF.

***Conclusions*—**In patients with ADHF, 1y-WRF is a strong predictor of all-cause and cardiovascular mortality. **(*J Am Heart Assoc*. 2014;3:e001174 doi: 10.1161/JAHA.114.001174)**

Key Words: acute decompensated heart failure • prognosis • worsening of renal function after discharge

In spite of great advances in the management of heart failure (HF), the prognosis of HF patients remains poor.[1,2] The reasons for poor prognosis are not clear, but most HF patients have 1 or more disorders in addition to HF, such as chronic kidney disease, hypertension, chronic lung disease, and anemia, which possibly makes HF refractory to treatment. A large proportion of patients with acute decompensated HF (ADHF) have various degrees of heart and renal dysfunction concomitantly.[3,4] Earlier cross-sectional studies have demonstrated that baseline renal function, as reflected by the estimated glomerular filtration rate (eGFR), is a strong prognostic predictor in HF.[5–7]

However, during the management of ADHF, renal function often deteriorates.[8] Reduced renal perfusion due to low cardiac output often leads to prerenal failure and the use of angiotensin-converting enzyme inhibitors or angiotensin receptor blockers that can worsen renal function; also, hypovolemia secondary to loop diuretics usually elevate serum creatinine (SCr) level. Therefore, in addition to baseline renal function, worsening of renal function (WRF) has gained attention in recent years. Some previous studies have reported that WRF during the first hospitalization for ADHF is a strong and independent predictor of adverse outcomes.[8–12] However, there were very few reports about WRF after discharge.[13,14] Therefore, how WRF during long-term follow-up influences the prognosis of patients with ADHF remains unclear. In this context, the aim of the present study

From the First Department of Internal Medicine (T.U., R.K., Y. Sugawara, S. Okada, T.N., T.S., S. Okayama, Y.T., M.W., H.K., S.U., Y. Saito,) and the Department of Regulatory Medicine for Blood Pressure (K.O., Y. Saito,), Nara Medical University, Kashihara, Nara, Japan.

Correspondence to: Rika Kawakami, MD, First Department of Internal Medicine, Nara Medical University, 840 Shijo-cho, Kashihara, Nara, Japan, 634-8522. E-mail: rkawa@naramed-u.ac.jp

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is to determine the clinical impact of WRF during the year after discharge (1y-WRF) on prognosis in ADHF patients in the Nara Registry and Analyses for Heart Failure 2 (the NARA-HF Study 2) cohort study.

Methods

Study Sample and Data Collection

The NARA-HF Study 2 recruited 611 consecutive patients emergently admitted to our department or the coronary care unit at our hospital with documented ADHF (either acute new-onset or acute-on-chronic HF) between January 2007 and December 2012. The diagnosis of HF was based on the Framingham Criteria.[15] Patients with both reduced and preserved left ventricular ejection fraction (LVEF) were included, but patients with acute myocardial infarction, acute myocarditis, and acute HF with acute pulmonary embolism were excluded. The study protocol was approved by the ethics committee in Nara Medical University, and written informed consent was obtained from all patients according to the Declaration of Helsinki Ethical Principles for Medical Research Involving Human Subjects.

Of the 611 patients, 378 patients were excluded because 116 patients died within 1 year after discharge, 56 patients were treated with dialysis, 4 patients were prescribed vasopressin type 2 receptor antagonists, 186 patients did not have available SCr values at 1 year after discharge, and 16 patients were lost to follow-up. Consequently, we included 233 patients in whom SCr levels were measured 3 times: on admission, at discharge, and at 1 year after discharge. For each patient, baseline data included age, sex, body mass index, HF etiology, medical history, vital signs, laboratory and echocardiographic data, and medications on admission and at discharge. For loop diuretics other than furosemide, we converted the dose to furosemide equivalent doses: 4 mg of torasemide and 30 mg of azosemide were considered equivalent to 20 mg of furosemide, respectively.[16,17]

Definitions

We measured SCr on admission, at discharge, and at 1 year after discharge. WRF was defined, according to previously published studies, as an absolute increase in SCr >0.3 mg/dL (>26.5 μmol/L) in combination with a ≥25% increase in SCr.[10,12] We evaluated the occurrence of 1y-WRF at the time point from discharge to 1 year of follow-up. Patients were divided into the 1y-WRF group (n=48) and the non-WRF group (n=185) according to the presence or absence of 1y-WRF.

Outcomes

The primary endpoints were all-cause and cardiovascular mortality. Cardiovascular death was defined as death due to HF, acute myocardial infarction, sudden death, stroke, or vascular diseases such as aortic dissection. We reviewed medical records to determine vital status and the cause of death. When this information was unavailable, we telephoned patients or their families. Information regarding cardiovascular events such as nonfatal acute myocardial infarction, nonfatal stroke, and unexpected rehospitalization due to recurrence of ADHF was also obtained.

Statistical Analysis

Continuous variables were expressed as means ± SD, and between-group differences were compared using Student *t* test. Categorical variables were summarized as percentages and analyzed using the χ^2 test. Cumulative event-free rates during follow-up were derived using the method of Kaplan–Meier. Univariate and multivariable analyses of mortality were performed using Cox proportional hazards models. Multivariable Cox proportional hazards models performed using forced inclusion models incorporated the 8 prognostic factors that were identified during past studies in HF patients: age, sex, body mass index, hemoglobin, eGFR, B-type natriuretic peptide (BNP), LVEF, and systolic blood pressure. We constructed 6 models adjusting for covariates: Model 1, unadjusted; Model 2, adjusted for age, sex, and body mass index; Model 3, adjusted for all factors in Model 2, plus hemoglobin, eGFR, and BNP; Model 4, adjusted for all factors in Model 3, plus LVEF and systolic blood pressure; Model 5, adjusted for the same factors as Model 4 except replacing eGFR at 1 year after discharge from eGFR at discharge; Model 6, adjusted for the same factors as Model 4 except replacing eGFR between hospital discharge and 1 year after discharge from eGFR at discharge. eGFR was calculated using the Japanese equations that take into account age, sex, and SCr.[18] Multivariate logistic regression was used to identify independent predictors of 1y-WRF.

Results were reported as hazard ratio (HR), 95% confidence interval (CI), and *P* values. HR for outcomes in the WRF group were compared with those in the non-WRF group. A *P* value <0.05 was used as the criterion for variables to stay in the model. JMP version 10 for Windows (SAS Institute Inc, Cary, NC) was used for all statistical analyses.

Results

Baseline Characteristics

As shown in Table 1, the mean age was 72.2±11.6 (mean±SD) years, and 43.3% of the patients were women. Based on the aforementioned definition, 1y-WRF occurred in 48 patients (20.6%). To investigate the impact of 1y-WRF on ADHF prognosis, we divided patients into 2 groups according

Table 1. Baseline Characteristics of HF Patients With and Without 1y-WRF

Characteristic	Total (n=233)	Non-WRF (n=185)	1y-WRF (n=48)	*P* Value
Demographic				
Age, y	72.2±11.6	71.7±11.9	73.9±10.4	0.3178
Female, %	43.3	46.5	31.2	0.0577
BMI, kg/m^2	23.8±3.8	23.9±3.9	23.2±3.7	0.2804
Cause of HF, %				
Ischemic	44.6	42.2	54.2	0.1360
Dilated cardiomyopathy	19.3	20.5	14.6	0.3515
Valvular	16.3	16.2	16.7	0.9400
Hypertensive	3.9	4.3	2.1	0.4728
Medical history, %				
Hypertension	76.0	74.6	81.3	0.3363
Diabetes mellitus	45.1	46.0	41.7	0.5955
Dyslipidemia	45.5	43.8	52.1	0.3035
Previous myocardial infarction	32.2	29.7	41.7	0.1147
Atrial fibrillation	30.0	31.9	22.9	0.2268
Procedures, %				
PCI	27.9	26.0	35.4	0.1924
CABG	7.7	6.5	12.5	0.1644
CRT/ICD	3.0	2.2	6.3	0.1393
NYHA class on admission, %				
III or IV	88.8	87.0	95.8	0.0842
Vital signs on admission				
Systolic blood pressure, mm Hg	142.8±32.6	143.1±33.9	141.5±27.0	0.9655
Diastolic blood pressure, mm Hg	82.1±22.3	82.7±23.6	80.0±16.6	0.8090
Heart rate, beats/min	96.5±29.1	96.0±29.4	98.1±28.2	0.4998
Echocardiographic parameters				
LVEF, %	45.1±16.0	45.8±16.4	42.3±13.9	0.1954
EF ≥50%, %	38.2	41.1	27.1	0.0753
LVEDD, mm	55.4±10.3	55.4±10.4	55.5±9.8	0.9483
Laboratory data on admission				
Hemoglobin, g/dL	12.0±2.4	12.1±2.4	11.6±2.1	0.2235
eGFR, mL/min per 1.73 m^2	52.7±23.8	53.4±23.5	49.9±25.0	0.2653
CKD stage 3A or 3B, %	49.8	49.2	52.1	0.7208
CKD stage 4 or 5, %	16.3	15.1	20.8	0.3410
Sodium, mEq/L	139.3±3.3	139.4±3.2	138.8±3.5	0.3227
Plasma BNP, pg/mL	959±900	917±870	1122±998	0.0866
Laboratory data at discharge				
Hemoglobin, g/dL	11.8±2.1	11.9±2.2	11.2±1.7	0.0336
eGFR, mL/min per 1.73 m^2	49.8±24.2	49.7±24.2	50.1±24.3	0.7685
Sodium, mEq/L	138.6±3.6	138.6±3.5	138.5±3.7	0.9942
Plasma BNP, pg/mL	311±289	288±289	401±277	0.0023

Data are shown as percentages, means±SD. BMI indicates body mass index; BNP, B-type natriuretic peptide; CABG, coronary artery bypass grafting; CKD, chronic kidney disease; CRT, cardiac resynchronization therapy; EF, ejection fraction; eGFR, estimated glomerular filtration rate; HF, heart failure; ICD, implantable cardioverter defibrillator; LVEDD, left ventricular end-diastolic diameter; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; PCI, percutaneous coronary intervention; 1y-WRF, worsening of renal function during the year after discharge.

to the presence or absence of 1y-WRF. Table 1 compares the baseline clinical characteristics of the 2 groups. Age, body mass index, and the sex distribution were similar in both groups. There were no significant differences in the etiology of HF or the proportion of comorbidities between the 2 groups. Moreover, New York Heart Association functional class, vital signs on admission, LVEF, and left ventricular end-diastolic diameter were also similar. SCr on admission was equal between the 1y-WRF group and the non-WRF group (1.27 and 1.13 mg/dL, respectively, P=0.1163). There were also no significant differences in laboratory findings on admission. However, at discharge, the 1y-WRF group had significantly lower hemoglobin and higher BNP compared to the non-WRF group.

Medications

Table 2 compares the medications on admission and at discharge of the patients in the 2 groups. The proportion of patients treated with angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, β-blockers, loop diuretics, mineralocorticoid receptor blockers, and calcium channel blockers were similar in the 2 groups, both on admission and at discharge. There were no significant differences in the furosemide equivalent dose at all time points (on admission, at discharge, and at 1 year after discharge) between the 1y-WRF and non-WRF groups. However, dose increases for loop diuretics between hospital discharge and 1 year afterwards were significantly larger in the 1y-WRF group than in the non-WRF group.

Prognosis and Outcome

During the mean follow-up period of 35.4 months, 66 (28.3%) patients died; 38 (16.3%) were from cardiovascular causes. As shown in the Kaplan–Meier survival curves, the 1y-WRF group had a much higher rate of all-cause death (log-rank P<0.0001) and cardiovascular death (log-rank P<0.0001) (Figure 1). Table 3 shows the unadjusted and adjusted HRs for outcomes in the 2 groups: 1y-WRF predicted all-cause and cardiovascular mortality (HR, 3.136; 95% CI, 1.893–5.127; P<0.0001 and HR, 4.571; 95% CI, 2.388–8.783; P<0.0001, respectively). Even after adjusting for age, sex, and cardiovascular risk factors such as plasma BNP levels, LVEF, etc., associations between 1y-WRF and all-cause and cardiovascular mortality remained significant (Table 3). Moreover, in the models including the absolute value of eGFR at 1 year after discharge (Table 3, Model 5) and the ΔeGFR between hospital discharge and 1 year after discharge (Table 3, Model 6), 1y-WRF remained a strong independent predictor of all-cause and cardiovascular mortality.

Table 2. Medications on Admission and at Discharge, and Loop Diuretic Dose

Medication	Total (n=233)	Non-WRF (n=185)	1y-WRF (n=48)	*P* Value
Admission, %				
ACE inhibitor or ARB	61.8	59.5	70.8	0.1484
β-blocker	30.5	29.7	33.3	0.6289
Loop diuretic	50.2	49.2	54.2	0.5388
MR blocker	22.8	22.7	22.9	0.9749
Ca channel blocker	33.9	31.9	41.7	0.2024
Statin	29.2	27.6	35.4	0.2865
Discharge, %				
ACE inhibitor or ARB	91.9	91.9	91.7	0.9595
β-blocker	57.9	57.8	58.3	0.9506
Loop diuretic	85.8	83.8	93.8	0.0776
MR blocker	38.2	35.1	50.0	0.0589
Ca channel blocker	27.0	26.0	31.3	0.4610
Loop diuretic dose, mg				
On admission	18.9±26.4	19.1±24.0	18.1±22.1	0.7579
At discharge	31.8±24.2	31.7±24.8	31.9±22.1	0.9372
At 1 y after discharge	34.9±25.8	33.7±26.4	39.8±23.2	0.1027
Dose increased	3.18±19.9	1.95±19.7	7.92±19.8	0.0464

Dose increased refers to an increase between discharge and 1 y afterwards. ACE indicates angiotensin-converting enzyme; ARB, angiotensin receptor blocker; Ca, calcium; MR, mineralocorticoid receptor; 1y-WRF, worsening of renal function during the year after discharge.

Factors Affecting 1y-WRF

Table 4 shows the multivariate analysis of factors associated with 1y-WRF. Hemoglobin and BNP at discharge, as well as LVEF <50%, were independent risk factors for 1y-WRF, but not age and eGFR at discharge.

Discussion

The present study demonstrates that 1y-WRF is a strong and independent risk factor for all-cause mortality and cardiovascular events in patients with ADHF. During the past decade, many studies reported a significant association between renal impairment and prognosis in HF. Many of these studies defined renal impairment as baseline SCr or WRF during hospitalization. In the present study, we evaluated longitudinal

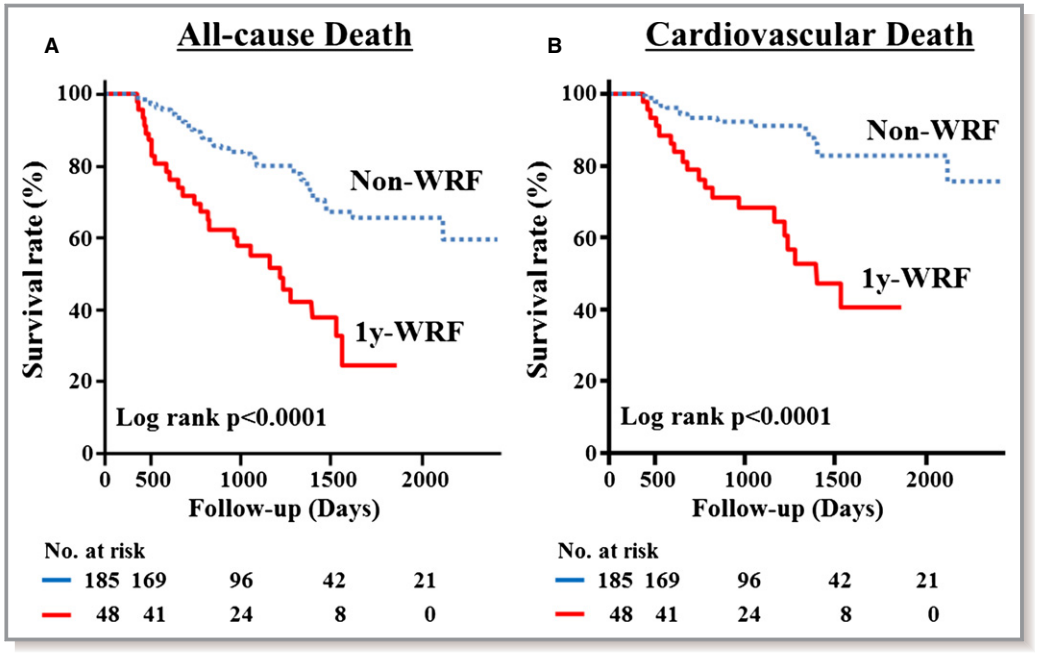

Figure 1. Kaplan–Meier event-free survival curves for (A) all-cause death and (B) cardiovascular death in patients with non-WRF (dotted line; n=185) compared with patients with 1y-WRF (solid line; n=48). WRF indicates worsening of renal function.

changes in renal function over the year after hospital discharge as a prognostic factor in ADHF. A large proportion of patients with ADHF have chronic kidney disease, which can exacerbate ADHF, and vice versa. This concept is currently accepted as the cardiorenal connection. More than half of the patients with ADHF in our study had eGFR <60 mL/min per 1.73 m^2 at admission, and ≈20% of the patients who were alive for >1 year after discharge had WRF, defined as an absolute increase in SCr >0.3 mg/dL (>26.5 μmol/L) in combination with a ≥25% increase in SCr at 1 year after discharge. These figures are comparable to or slightly higher than those in previous studies, which were conducted in Europe and recruited patients with systolic heart failure. Many cross-sectional studies have demonstrated that impaired renal function is an independent risk factor for poor outcomes in HF. In our study, however, the close association between 1y-WRF and all-cause mortality or cardiovascular events remained after adjustment for several factors including the absolute value of eGFR at 1 year after discharge. These observations provide clinically relevant information to physicians, namely, the importance of maintaining renal function when treating patients with HF. This concept is currently accepted as the cardiorenal connection, the mechanism of which may involve a complex interplay between HF and renal dysfunction through hemodynamic, pathological, and humoral dysregulation.

Although in-hospital WRF was observed in ≈20% of the study patients, it was not significantly associated with all-cause mortality or cardiovascular events (log-rank *P*=0.7636 and log-rank *P*=0.5908, respectively) (Figure 2). In prior studies, in-hospital WRF was reported to be a risk factor for poor outcomes in HF.[8–12] However, some recent reports showed it was not,[14,19,20] which is consistent with our results. In our study, only 2 patients had both in-hospital and 1y-WRF; in other words, most of patients with in-hospital WRF had preserved renal function at 1 year after discharge. Their transient WRF may be due to hemodynamic alterations rather than histological deterioration.

The mechanisms for 1y-WRF and in-hospital WRF may differ, but this was not discernable from a clinical cohort study. The proportion of patients with hypertension and diabetes mellitus, as well as previous myocardial infarction, which are risk factors for WRF in outpatients, was similar in the 1y-WRF and non-WRF groups. There were no significant differences in LVEF or eGFR between the 2 groups. However, the plasma BNP level was significantly higher in the 1y-WRF group than in the non-WRF group, and multiple logistic regression showed that plasma BNP level, LVEF <50%, and anemia were significant risk factors for 1y-WRF (Tables 1, 2, and 4). Thus, it is plausible that more advanced HF is more likely to be accompanied by WRF. Alternatively, the high levels of plasma BNP in the WRF group might be associated with continuing high venous pressure and negative effects on the kidney due to congestion.[21] In our study, the furosemide equivalent dose of loop diuretics at discharge was similar in the 1y-WRF and non-WRF groups, but at 1 year, the 1y-WRF

Table 3. HR and 95% CI for All-Cause and Cardiovascular Death According to 1y-WRF Status

	All-Cause Death		Cardiovascular Death	
	HR (95% CI)	*P* Value	HR (95% CI)	*P* Value
Model 1				
1y-WRF	3.136 (1.893 to 5.127)	<0.0001	4.571 (2.388 to 8.783)	<0.0001
Model 2				
1y-WRF	2.990 (1.774 to 4.974)	<0.0001	4.641 (2.372 to 9.125)	<0.0001
Age, y	1.031 (1.007 to 1.058)	0.0110	1.002 (0.974 to 1.033)	0.9028
Male sex	0.877 (0.531 to 1.461)	0.6103	0.903 (0.464 to 1.805)	0.7663
Model 3				
1y-WRF	2.622 (1.529 to 4.449)	0.0006	4.561 (2.264 to 9.341)	<0.0001
Age, y	1.011 (0.984 to 1.041)	0.4316	0.992 (0.960 to 1.028)	0.6560
Male sex	1.209 (0.692 to 2.134)	0.5063	1.215 (0.582 to 2.617)	0.6064
Hemoglobin, g/dL	0.860 (0.731 to 1.008)	0.0631	0.872 (0.711 to 1.062)	0.1758
eGFR, 10 mL/min per 1.73 m^2	0.931 (0.813 to 1.054)	0.2654	1.029 (0.876 to 1.193)	0.7143
Plasma BNP, 100 pg/mL	1.132 (1.050 to 1.208)	0.0020	1.123 (1.015 to 1.222)	0.0259
Model 4				
1y-WRF	2.423 (1.414 to 4.114)	0.0015	4.500 (2.227 to 9.249)	<0.0001
Age, y	1.015 (0.987 to 1.046)	0.3071	1.001 (0.967 to 1.038)	0.9657
Male sex	1.155 (0.662 to 2.036)	0.6123	1.227 (0.589 to 2.644)	0.5881
Hemoglobin, g/dL	0.826 (0.695 to 0.976)	0.0240	0.863 (0.699 to 1.055)	0.1529
eGFR, 10 mL/min per 1.73 m^2	0.926 (0.806 to 1.053)	0.2497	1.015 (0.863 to 1.178)	0.8508
Plasma BNP, 100 pg/mL	1.126 (1.041 to 1.205)	0.0042	1.107 (0.996 to 1.209)	0.0581
LVEF, %	0.982 (0.961 to 1.003)	0.0921	0.991 (0.963 to 1.017)	0.4997
SBP, mm Hg	1.003 (0.984 to 1.021)	0.7878	0.984 (0.960 to 1.008)	0.1895
Model 5				
1y-WRF	2.223 (1.217 to 4.070)	0.0096	4.451 (1.989 to 10.354)	0.0003
Age, y	1.017 (0.989 to 1.048)	0.2459	1.000 (0.966 to 1.037)	0.9991
Male sex	1.129 (0.648 to 1.986)	0.6691	1.238 (0.596 to 2.659)	0.5702
Hemoglobin, g/dL	0.825 (0.693 to 0.977)	0.0251	0.865 (0.699 to 1.059)	0.1634
Plasma BNP, 100 pg/mL	1.130 (1.045 to 1.209)	0.0033	1.105 (0.995 to 1.207)	0.0614
LVEF, %	0.983 (0.961 to 1.003)	0.0996	0.991 (0.963 to 1.017)	0.5134
SBP, mm Hg	1.003 (0.985 to 1.022)	0.7455	0.984 (0.960 to 1.008)	0.1818
eGFR at 1 y, 10 mL/min per 1.73 m^2	0.948 (0.803 to 1.104)	0.5046	0.997 (0.806 to 1.205)	0.9780
Model 6				
1y-WRF	2.819 (1.470 to 5.421)	0.0019	3.907 (1.713 to 9.151)	0.0012
Age, y	1.018 (0.990 to 1.048)	0.2053	1.001 (0.967 to 1.037)	0.9757
Male sex	1.115 (0.641 to 1.960)	0.7021	1.217 (0.585 to 2.618)	0.6017
Hemoglobin, g/dL	0.815 (0.686 to 0.962)	0.0151	0.867 (0.703 to 1.058)	0.1612
Plasma BNP, 100 pg/mL	1.131 (1.046 to 1.210)	0.0030	1.108 (0.997 to 1.208)	0.0559
LVEF, %	0.981 (0.960 to 1.002)	0.0705	0.991 (0.964 to 1.016)	0.4935
SBP, mm Hg	1.003 (0.985 to 1.022)	0.7425	0.985 (0.961 to 1.009)	0.2163
ΔeGFR, mL/min per 1.73 m^2	1.009 (0.987 to 1.032)	0.4507	0.992 (0.968 to 1.019)	0.5574

Hemoglobin, plasma BNP and SBP values were at the time of discharge. eGFR values are at the time of discharge in Models 3 and 4 and at 1 year after discharge in Model 5. ΔeGFR is the change in eGFR between hospital discharge and 1 year after discharge in Model 6. BNP indicates B-type natriuretic peptide; eGFR, estimated glomerular filtration rate; HR, hazard ratio; LVEF, left ventricular ejection fraction; SBP, systolic blood pressure; 1y-WRF, worsening of renal function during the year after discharge.

Table 4. Predictors of 1y-WRF in the Multivariate Analysis

	Odds Ratio	95% CI	*P* Value
Age, y	1.017	0.981 to 1.055	0.3605
Hemoglobin, g/dL	0.819	0.664 to 0.999	0.0491
eGFR, mL/min per 1.73 m^2	1.007	0.990 to 1.023	0.4303
Plasma BNP, 100 pg/mL	1.121	1.004 to 1.249	0.0421
LVEF <50%	2.219	1.025 to 5.087	0.0430
Increase in loop diuretic dose, mg	1.007	0.991 to 1.025	0.3947

Hemoglobin, plasma BNP, and eGFR values are at the time of discharge. Increase in loop diuretic dose refers to the increase in dose from the time of discharge to 1 year after discharge. BNP indicates B-type natriuretic peptide; eGFR, estimated glomerular filtration rate; LVEF, left ventricular ejection fraction; 1y-WRF, worsening of renal function during the year after discharge.

group had a nonsignificantly higher dose compared to the non-WRF group. As earlier reports reported that WRF has been attributed to hypoperfusion of the kidney due to intravascular volume depletion secondary to overdose of diuretics,[12,13,22,23] patients with HF should be treated with the lowest effective dose of loop diuretics, to avoid WRF. In our institution, physicians would take BNP levels into account to prevent overuse of loop diuretics.

Since the definition of WRF is not uniform, there are many ways to assess changes in WRF. We chose a strict definition, an absolute SCr increase >0.3 mg/dL (>26.5 μmol/L) in combination with a ≥25% increase in SCr, which has been used by previous studies.[10,12] Some investigators have used an absolute SCr increase >0.3 mg/dL from baseline. Therefore, we examined other definitions of 1y-WRF, such as an absolute SCr increase >0.3 mg/dL between discharge and follow-up at 1 year (53 patients with 1y-WRF). Using this definition, the Kaplan–Meier survival analysis showed that the 1y-WRF group had a much higher rate of all-cause death (log-rank $P<0.0001$) and cardiovascular death (log-rank $P<0.0001$) (data not shown).

Study Limitations

There are several limitations to this study. The major limitation is that the sample size was moderate, the study was retrospective in nature, and that it was based at a single center. We did not collect data on variables that can potentially influence ADHF prognosis such as respiratory function and QRS complex widening on admission. We could not compare the influence of thiazides between the 2 groups because there are no official dose-conversion formulas for converting between loop diuretics and thiazides.

Conclusions

WRF at 1 year after hospital discharge for ADHF is a strong predictor of all-cause and cardiovascular death.

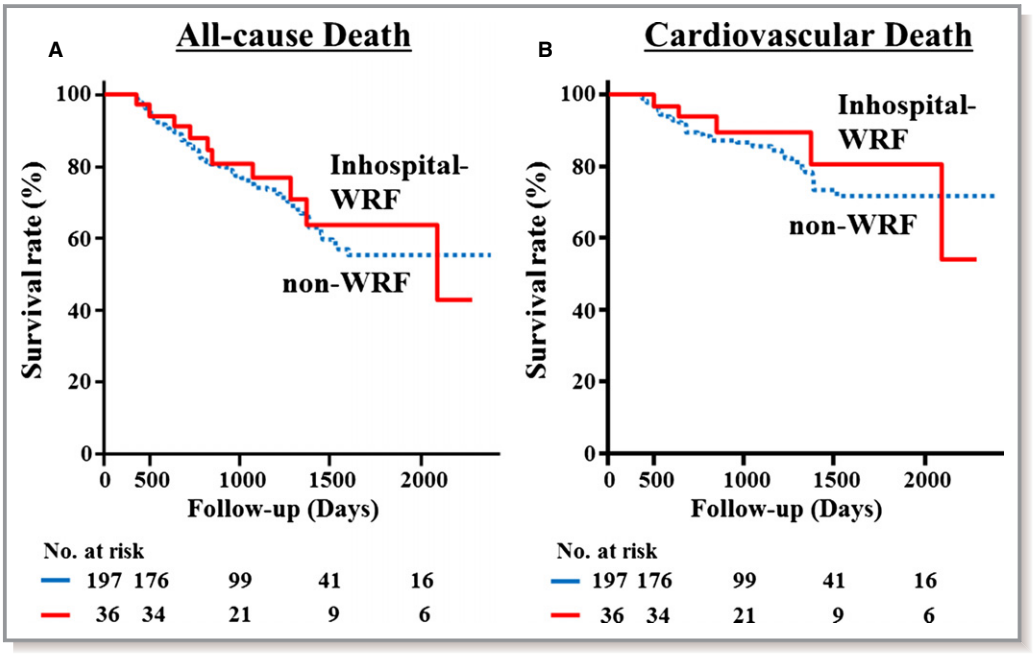

Figure 2. Kaplan–Meier event-free survival curves for (A) all-cause death and (B) cardiovascular death in patients with non-WRF (dotted line; n=197) compared with patients with in-hospital-WRF (solid line; n=36). WRF indicates worsening of renal function.

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Disclosures

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