Chronic Kidney Disease as an Independent Risk for Long-Term Adverse Outcomes in Patients Hospitalized With Heart Failure in Japan

— Report From the Japanese Cardiac Registry of Heart Failure in Cardiology (JCARE-CARD) —

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Background: Previous studies have demonstrated that renal dysfunction is common in patients with heart failure (HF), but it is not known whether chronic kidney disease (CKD) is associated with increased risks of long-term adverse outcomes in unselected HF patients encountered in current routine clinical practice in Japan.

Methods and Results: The Japanese Cardiac Registry of Heart Failure in Cardiology (JCARE-CARD) prospectively studied a broad sample of patients hospitalized with worsening HF and their outcomes with an average of 2.4 years of follow-up. The study cohort (n=2,013) were classified into 3 groups by estimated glomerular filtration rate (eGFR): ≥60 (n=579), 30–59 (n=1,025), and <30 ml·min⁻¹·1.73 m⁻² or patients with dialysis (n=409); 1,372 patients (70.3%) had an eGFR <60 ml·min⁻¹·1.73 m⁻² and 62 patients were treated with dialysis. The multivariable adjusted risk for all-cause death or rehospitalization increased with reduced eGFR; an adjusted hazard ratio (HR) 1.520 (95% confidence interval (CI) 1.186–1.949) for eGFR 30–59 ml·min⁻¹·1.73 m⁻² (P=0.001) and HR 2.566 (95%CI 1.885–3.492) for eGFR <30 ml·min⁻¹·1.73 m⁻² or patients with dialysis (P<0.001).

Conclusions: CKD is common in HF and was independently associated with long-term adverse outcomes in a broad cohort of Japanese patients. (Circ J 2009; 73: 1442–1447)

Key Words: Heart failure; Kidney; Prognosis; Survival

Decreased renal function has been consistently demonstrated as an independent risk for all-cause mortality, as well as cardiovascular adverse outcomes in patients with chronic heart failure (HF).¹⁻⁴ However, those previous studies have been of patients enrolled in large-scale clinical trials with restricted inclusion criteria, such as markedly reduced left ventricular ejection fraction (LVEF ≤35%) and lower serum creatinine levels (≤2 mg/dl).² Cohort studies from Canada and Japan have been also limited because they used data from a single center specializing in HF.³⁸ The Acute Decompensated Heart Failure National Registry (ADHERE) evaluated 118,465 hospitalization episodes of acute decompensated HF and found a graded association between reduced renal function and in-hospital death,⁴ a result that was, however, also limited by the short period of follow-up. Moreover, most of the previous studies were performed mainly in the United States and Europe, so the impact of renal dysfunction on long-term outcomes has not been assessed in a broad cohort of HF patients encountered in routine clinical practice in Japan.

Glomerular filtration rate (GFR) is now estimated by the Modification of Diet in Renal Disease (MDRD) equation.¹⁰

Figure 1. Distribution of estimated glomerular filtration rate (eGFR) at baseline among the total of 2,013 patients.
The details of JCARE-CARD have been described previously. Briefly, eligible patients were those hospitalized for worsening HF as the primary cause of admission. For each patient, baseline data recorded on the form included (1) demography, (2) causes of HF, (3) precipitating cause, (4) comorbidities, (5) complications, (6) clinical status, (7) electrocardiographic and echocardiographic findings, (8) serum B-type natriuretic peptide (BNP), and (9) treatments including discharge medications.

**Renal Function**

Of the total cohort of 2,675 patients enrolled in JCARE-CARD, 1,951 had the data required to estimate GFR at the time of hospital discharge using the modified MDRD equation: 

$$eGFR = \frac{186 \times (\text{serum creatinine} + 0.2)}{\text{age in years} \times (1.210 \text{ if male} - 1.476 \text{ if female})} \times 1.234 \text{ if African American}$$

and the estimated GFR (eGFR) is a more precise approximation of renal function than serum creatinine alone because age, gender, and race/ethnicity all significantly affect the level of the latter. To examine the prevalence of renal dysfunction in HF and determine whether it is independently associated with outcome, we analyzed data from the Japanese Cardiac Registry of Heart Failure in Cardiology (JCARE-CARD), which is a prospective database of the clinical characteristics, treatments, and outcomes of a broad sample of patients hospitalized with worsening HF at teaching hospitals in Japan.

**Methods**

**Patients**

The details of JCARE-CARD have been described previously. Briefly, eligible patients were those hospitalized for worsening HF as the primary cause of admission. For each patient, baseline data recorded on the form included (1) demography, (2) causes of HF, (3) precipitating cause, (4) comorbidities, (5) complications, (6) clinical status, (7) electrocardiographic and echocardiographic findings, (8) serum B-type natriuretic peptide (BNP), and (9) treatments including discharge medications.

<table>
<thead>
<tr>
<th>Table 1. Baseline Patient Characteristics According to Baseline eGFR</th>
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<tbody>
<tr>
<td>Characteristic</td>
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<td></td>
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<tr>
<td>DEMOGRAPHIC</td>
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<tr>
<td>Age, years (mean±SD)</td>
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<tr>
<td>Male, %</td>
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<tr>
<td>BMI, kg/m²</td>
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<tr>
<td>CAUSE OF HF, %</td>
</tr>
<tr>
<td>Ischemic</td>
</tr>
<tr>
<td>Hypertensive</td>
</tr>
<tr>
<td>Dilated cardiomyopathy</td>
</tr>
<tr>
<td>MEDICAL HISTORY, %</td>
</tr>
<tr>
<td>Hypertension</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
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<tr>
<td>Hyperuricemia</td>
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<tr>
<td>Stroke</td>
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<td>Anemia</td>
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<td>COPD</td>
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<td>Smoking</td>
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<tr>
<td>Prior MI</td>
</tr>
<tr>
<td>Chronic AF or AFl</td>
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<tr>
<td>Sustained VT/VF</td>
</tr>
<tr>
<td>PROCEDURE, %</td>
</tr>
<tr>
<td>PCI</td>
</tr>
<tr>
<td>CABG</td>
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<tr>
<td>PPM</td>
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<tr>
<td>CRT</td>
</tr>
<tr>
<td>ICD</td>
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<tr>
<td>Hb concentration at discharge, g/dl</td>
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<tr>
<td>NYHA functional class</td>
</tr>
<tr>
<td>Admission</td>
</tr>
<tr>
<td>Discharge</td>
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<tr>
<td>SERUM BNP, pg/ml</td>
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<tr>
<td>Admission</td>
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<tr>
<td>Discharge</td>
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<tr>
<td>Echocardiographic parameters on admission</td>
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<tr>
<td>LVEDd, mm</td>
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<tr>
<td>LVESd, mm</td>
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<tr>
<td>LVEF, %</td>
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<tr>
<td>Echocardiographic parameters at discharge</td>
</tr>
<tr>
<td>LVEDd, mm</td>
</tr>
<tr>
<td>LVESd, mm</td>
</tr>
<tr>
<td>LVEF, %</td>
</tr>
</tbody>
</table>

Values are percent or mean±SD.

eGFR, estimated glomerular filtration rate; BMI, body mass index; HF, heart failure; COPD, chronic obstructive pulmonary disease; MI, myocardial infarction; AF, atrial fibrillation; AFl, atrial flutter; VT/VF, ventricular tachycardia/ventricular fibrillation; PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting; PPM, permanent pacemaker; CRT, cardiac resynchronization therapy; ICD, implantable cardioverter defibrillator; Hb, hemoglobin; NYHA, New York Heart Association; BNP, B-type natriuretic peptide; L.V, left ventricular; EDd, end-diastolic diameter; ESd, end-systolic diameter; EF, ejection fraction.
Outcomes
The status of all patients was surveyed at least 1 year after discharge and the following information was obtained: (1) survival, (2) cause of death, and (3) rehospitalization for exacerbation of HF that required more than continuation of the usual therapy from prior admission. Only patients who survived the initial hospitalization were included in the follow-up analysis. Follow-up data were obtained for 1,617 of 2,013 patients (80.3%). Mean postdischarge follow-up was 862 ± 267 days (2.4 ± 0.7 years).

Statistical Analysis
Patient characteristics and treatments were compared using the Pearson chi-square test for categorical variables and 1-way ANOVA for continuous variables. The relationship between eGFR and outcome was evaluated among patients with multivariate adjustment. Baseline clinical variables, treatment factors, and the data of the severity of HF at discharge were used in developing the postdischarge Cox proportional hazard models. A P value < 0.05 was used for criteria for variables to stay in the model. SPSS version 16.0 J for Windows was used for all statistical analyses (Chicago, IL, USA).

Results
Patient Characteristics
The mean age of the study group was 71.5 years and 58.7% were men. HF etiology was ischemic in 32.3%, hypertensive in 26.9%, and dilated cardiomyopathic in 16.9%. The mean LVEF was 42.5 ± 17.6% on admission and 44.8 ± 16.4% at discharge.

Figure 1 shows the distribution of eGFR among the total cohort. The mean eGFR was 49.5 ± 19.8 ml·min⁻¹·1.73 m⁻², ranging from 5.6 to 169.1 ml·min⁻¹·1.73 m⁻² among 1,951 patients not treated with dialysis; 1,372 patients (70.3%) had an eGFR < 60.0 ml·min⁻¹·1.73 m⁻². Including 62 (3.1%) patients treated with dialysis, 1,434 (71.2%) patients had an eGFR < 60 ml·min⁻¹·1.73 m⁻². Including 62 (3.1%) patients had an eGFR < 60 ml·min⁻¹·1.73 m⁻² or on dialysis. Only 52 (2.6%) patients had a normal eGFR.

Table 1 is a comparison of the clinical characteristics for the total cohort (n = 2,013) and the patients classified into 3 groups according to eGFR.

Using the revised MDRD equation for estimating GFR in Japanese, the mean eGFR was 50.9 ± 24.9 ml·min⁻¹·1.73 m⁻², which was slightly higher than the value in our original analysis. Including patients treated with dialysis, 1,359 (66.5%) patients had an eGFR < 60 ml·min⁻¹·1.73 m⁻². The total cohort of patients was classified into 3 groups according to eGFR as follows: ≥ 60 ml·min⁻¹·1.73 m⁻² (n = 674), 30–59 ml·min⁻¹·1.73 m⁻² (n = 918), and < 30 ml·min⁻¹·1.73 m⁻² or on dialysis (n = 421).

Patients with reduced eGFR were older and more often women. They more often had ischemic or hypertensive heart disease as the cause of HF, but less often dilated cardiomyopathy. They also had more extensive comorbidities, including hypertension, diabetes mellitus, hyperuricemia, stroke, anemia, prior myocardial infarction, and sustained ventricular tachycardia or ventricular fibrillation. New York Heart Association (NYHA) functional class and serum BNP level were higher both on admission and at discharge in patients with reduced eGFR. However, echocardiographic LV diameters and LVEF did not differ among groups.

Patients with reduced eGFR were less frequently prescribed by angiotensin-converting enzyme inhibitors, β-blockers, digitalis, or warfarin (Table 2). In contrast, they were prescribed more calcium-channel blockers, α-blockers, nitrates, aspirin, and antiplatelet agents at discharge.

Outcomes
During an average follow-up of 2.4 years after hospital discharge, the all-cause death rate was 21.6%. The rate of rehospitalization for worsening HF was 35.7%. The rate of all-cause death or rehospitalization was 43.6%. All-cause death or rehospitalization because of worsening HF increased with reduced eGFR: 26.6% for eGFR ≥ 60 ml·min⁻¹·1.73 m⁻², 44.1% for eGFR 30–59 ml·min⁻¹·1.73 m⁻², and 68.8% for eGFR < 30 ml·min⁻¹·1.73 m⁻² or on dialysis (P < 0.001; Table 3, Figure 2).

On multivariate analysis with eGFR ≥ 60 ml·min⁻¹·1.73 m⁻² as the reference and adjustment for all-cause death or rehospitalization, patients with eGFR < 30 ml·min⁻¹·1.73 m⁻² or on dialysis had a significantly elevated risk (an adjusted hazard ratio (HR) 2.566 [95% CI 1.885–3.492]) (P < 0.001), as did those with eGFR 30–59 ml·min⁻¹·1.73 m⁻² (HR 1.520 [95% CI 1.186–1.949]) (P = 0.001) (Table 3). Therefore, long-term adverse outcomes were significantly associated with eGFR, even after adjustment for all other covariates.
The Cox regression model used in the analysis adjusted for the following covariates: demographic (age, sex, BMI), cause of HF (ischemic, dilated cardiomyopathy), medical history (hypertension, diabetes mellitus, hyperuricemia, stroke, smoking, chronic AF or AFl, sustained VT/VF), procedure (PPM, CRT), Hb concentration at discharge, NYHA functional class at discharge, serum BNP at discharge, LVEF at discharge, and medication use (ACEI, β-blocker, diuretics, digoxilis, CCB, α-blocker, nitrates, aspirin, antiplatelet, warfarin). Patients with eGFR ≥60 ml·min⁻¹·1.73 m⁻² were the reference group. Serum BNP and LVEF at discharge were entered into the model as categorical variables (ie, serum BNP at discharge ≥240 pg/ml or <240 pg/ml or unknown and LVEF at discharge <40% or ≥40% or unknown).

HR, hazard ratio; CI, confidence interval. See Tables 1 and 2 for other abbreviations.

The independent predictors associated with death or rehospitalization among those entered into the Cox proportional hazard analysis were eGFR, hemoglobin, age, NYHA functional class, sustained ventricular tachycardia and ventricular fibrillation, serum BNP level at discharge, and the use of cardiac resynchronization therapy (Table 4). There was 1.4% increase in all-cause death or rehospitalization, for each 1-ml·min⁻¹·1.73 m⁻² decrease in eGFR (P<0.001).

The results of subgroup analysis for death or rehospitalization stratified by sex, age (≥65 vs <65 years), etiology (ischemic vs nonischemic), comorbidity (hypertension vs no hypertension) are shown in Table 5; eGFR <60 ml·min⁻¹·1.73 m⁻² was associated with poor outcomes in each subgroup, similar to the primary analysis.

Table 3. HRs for Outcomes According to Baseline eGFR

<table>
<thead>
<tr>
<th>Outcome</th>
<th>eGFR (ml·min⁻¹·1.73 m⁻²)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>≥60 (n=478)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>30–59 (n=831)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>&lt;30 or dialysis (n=308)</td>
<td></td>
</tr>
<tr>
<td>All-cause death (%)</td>
<td>50 (10.5%)</td>
<td></td>
</tr>
<tr>
<td>Unadjusted HR (95% CI)</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>Adjusted HR (95% CI)</td>
<td>1.257 (0.851–1.858)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Rehospitalization (%)</td>
<td>106 (22.2%)</td>
<td></td>
</tr>
<tr>
<td>Unadjusted HR (95% CI)</td>
<td>1.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Adjusted HR (95% CI)</td>
<td>1.612 (1.231–2.112)</td>
<td></td>
</tr>
<tr>
<td>All-cause death or rehospitalization (%)</td>
<td>127 (26.6%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Unadjusted HR (95% CI)</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>Adjusted HR (95% CI)</td>
<td>1.520 (1.186–1.949)</td>
<td></td>
</tr>
</tbody>
</table>

Figure 2. Kaplan-Meier event-free curves from all-cause death (A), rehospitalization for worsening heart failure (HF: B), and all-cause death or rehospitalization because of worsening HF (C) according to baseline estimated glomerular filtration rate (ml·min⁻¹·1.73 m⁻²).

The independent predictors associated with death or rehospitalization among those entered into the Cox proportional hazard analysis were eGFR, hemoglobin, age, NYHA functional class, sustained ventricular tachycardia and ventricular fibrillation, serum BNP level at discharge, and the use of cardiac resynchronization therapy (Table 4). There was 1.4% increase in all-cause death or rehospitalization, for each 1-ml·min⁻¹·1.73 m⁻² decrease in eGFR (P<0.001).

The results of subgroup analysis for death or rehospitalization stratified by sex, age (≥65 vs <65 years), etiology (ischemic vs nonischemic), comorbidity (hypertension vs no hypertension) are shown in Table 5; eGFR <60 ml·min⁻¹·1.73 m⁻² was associated with poor outcomes in each subgroup, similar to the primary analysis.
Table 4. Multivariate Predictors of Death or Rehospitalization by Cox Proportional Hazard Models

<table>
<thead>
<tr>
<th>Variable</th>
<th>HR</th>
<th>95% CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>0.727</td>
<td>0.592–0.892</td>
<td>0.002</td>
</tr>
<tr>
<td>eGFR (per 1 ml·min⁻¹·1.73 m⁻² decrease)</td>
<td>1.014</td>
<td>1.009–1.020</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hb (per 1 g/dl decrease)</td>
<td>1.061</td>
<td>1.013–1.110</td>
<td>0.012</td>
</tr>
<tr>
<td>Age (per 10 year increase)</td>
<td>1.166</td>
<td>1.066–1.275</td>
<td>0.001</td>
</tr>
<tr>
<td>NYHA functional class (per 1 increase)</td>
<td>1.177</td>
<td>1.011–1.371</td>
<td>0.036</td>
</tr>
<tr>
<td>Sustained VT/VF</td>
<td>1.445</td>
<td>1.052–1.984</td>
<td>0.023</td>
</tr>
<tr>
<td>Serum BNP at discharge ≥240 pg/ml</td>
<td>1.591</td>
<td>1.216–2.083</td>
<td>0.001</td>
</tr>
<tr>
<td>CRT</td>
<td>2.147</td>
<td>1.185–3.890</td>
<td>0.012</td>
</tr>
</tbody>
</table>

See Tables 1 and 3 for abbreviations.

Table 5. Subgroup Analysis of Death or Rehospitalization by Baseline eGFR

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>n</th>
<th>HR for death or rehospitalization eGFR &lt;60 vs ≥60</th>
<th>95% CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>921</td>
<td>1.619</td>
<td>1.203–2.179</td>
<td>0.001</td>
</tr>
<tr>
<td>Female</td>
<td>661</td>
<td>1.630</td>
<td>1.063–2.499</td>
<td>0.025</td>
</tr>
<tr>
<td>Age ≥65 years</td>
<td>1,139</td>
<td>1.705</td>
<td>1.268–2.291</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age &lt;65 years</td>
<td>443</td>
<td>1.766</td>
<td>1.130–2.780</td>
<td>0.013</td>
</tr>
<tr>
<td>Ischemic etiology</td>
<td>514</td>
<td>1.942</td>
<td>1.224–3.083</td>
<td>0.005</td>
</tr>
<tr>
<td>Nonischemic etiology</td>
<td>1,068</td>
<td>1.556</td>
<td>1.162–2.084</td>
<td>0.003</td>
</tr>
<tr>
<td>Hypertension</td>
<td>830</td>
<td>1.538</td>
<td>1.069–2.213</td>
<td>0.020</td>
</tr>
<tr>
<td>No hypertension</td>
<td>741</td>
<td>1.851</td>
<td>1.323–2.590</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

See Tables 1 and 3 for abbreviations.

Discussion

The present study used the JCARE-CARD database to demonstrate that significant renal dysfunction was very common in patients hospitalized with HF. More importantly, renal dysfunction was independently associated with all-cause death or rehospitalization for worsening HF during the long-term follow-up.

The prevalence of CKD in this study (70%) was higher than that reported in previous cohort studies and clinical trials. The previous cohort studies found 47–64% of HF patients with an eGFR <60 ml·min⁻¹·1.73 m⁻². In contrast, the CHARM study found only 36% of patients with eGFR <60 ml·min⁻¹·1.73 m⁻². Recent meta-analysis also demonstrated that 29% of patients had at least moderate renal dysfunction. Therefore, the prevalence of renal dysfunction in the present study is greater than that reported in most previous studies, but similar to that reported in the ADHERE study. These discrepancies are attributable to differences between studies in the patients being evaluated. The present study group included patients who were more elderly and had more comorbidities, such as hypertension and diabetes, than those in previous studies, because the JCARE-CARD registered an unselected group of HF patients and did not exclude those who had higher levels of serum creatinine and were treated with dialysis. It was thus highly expected that these patients would have a higher prevalence of renal dysfunction, which might reflect current routine clinical practice.

The present study demonstrated that renal dysfunction was associated with adverse long-term outcomes in patients with HF, which extends the previous results from randomized clinical trials conducted with selected patients to a diverse cohort of HF patients. Although evidence from those trials showed significant adverse outcomes for renal dysfunction in patients with HF, they were recognized as unrepresentative of the general HF population encountered in “real world” clinical practice. Therefore, uncertainty about the applicability of the findings to the population of patients with HF at large persists and it is critically important to analyze data from registries that enroll HF patients without any exclusion criteria. The results from JCARE-CARD confirmed the previous results that renal dysfunction is associated with long-term adverse outcomes in HF patients.

The present study also extends the findings of the ADHERE database, in which renal dysfunction was associated with higher in-hospital mortality. However, the ADHERE limited its follow-up to hospitalization. The present study has provided the first demonstration that renal dysfunction is associated with the adverse outcomes during long-term follow-up of 2.4 years. The event-free curves diverged within the early period and these differences remained statistically significant during the follow-up (Figure 2). Both the ADHERE and JCARE-CARD have clearly demonstrated a high prevalence of renal dysfunction and its prognostic implications in patients hospitalized with HF during the acute as well as chronic phases. These findings should reassure physicians that earlier evaluation and management of CKD is critically important to prevent adverse outcomes for patients with HF, and is an opportunity to significantly improve outcomes. Moreover, in the present study, the study patients with renal dysfunction were less frequently prescribed by angiotensin-converting enzyme inhibitor inhibitors and β-blockers (Table 2). A previous study reported the same therapeutic nihilism for HF patients with renal dysfunction and that they might have had better outcomes if they had received these medications. Although we adjusted the medication used at discharge in our analysis, it is still possible that adverse outcomes associated with renal dysfunction are related to inadequate treatment. These findings should reassure physicians that the use of standard medications, as well as the development of an effective treatment strategy, is critical for HF patients with renal dysfunction to prevent adverse outcomes.
Several explanations have been postulated for the observed prognostic implications of renal dysfunction in HF. First, renal dysfunction might be a marker of traditional risk factors such as age, hypertension, and diabetes, as well as nontraditional risks associated with this dysfunction such as hyperuricemia and anemia (Table 1), and therefore may reflect the severity of organ damage in both the kidney and the heart. However, the significant impact of renal dysfunction on outcomes in the present study, even after adjustment for various other risk factors (Tables 3, 4), demonstrates that renal dysfunction is an independent predictor for adverse outcomes even if it may partly represent underlying cardiovascular diseases. Second, renal dysfunction may be directly associated with cardiac dysfunction that is related to the severity of the underlying diseases. However, in the present study, the prevalence of dilated cardiomyopathy was less in patients with renal dysfunction, echocardiographic LVEF did not differ among groups (Table 1), and long-term adverse outcomes were significantly associated with eGFR even after adjustment for variables that reflected severity of HF (ie, NYHA functional class, serum BNP, and LVEF) (Tables 3, 4). These findings indicate that the effects of renal dysfunction on outcome are not sequelae of systolic dysfunction in HF; instead, it may become an independent risk in both systolic and diastolic HF.

**Study Limitations**

First, the documentation of serum creatinine level at hospital discharge might not accurately reflect the course of renal function after discharge. Second, the JCARE-CARD is not a prospective randomized trial, and despite covariate adjustment, other measured and unmeasured factors, which we could not completely exclude, might have influenced outcomes. Third, the data were dependent on the accuracy of documentation and abstraction by the individual medical centers that participated in the program. However, it was not the objective of this survey to restrict enrollment to a narrowly defined population of HF, as is usually included in clinical trials, but rather to include a broad range of patients reflecting the current reality of clinical practice. Finally, we used the MDRD equation modified for Japanese patients in the present study. Even when the revised equations for estimating GFR in Japan were used, the characteristics of the 3 groups classified by baseline eGFR confirmed the validity of our original analysis (data not shown).

More importantly, the relationship between eGFR and outcome was unaffected by the equations employed.

**Conclusion**

In current routine clinical practice in Japan CKD is common in patients hospitalized with HF. Renal dysfunction is independently associated with adverse long-term outcomes in these patients and should be considered a higher risk in HF patients, independent of systolic function or comorbidities, and every preventive and treatment strategy should be used to manage these high risk patients.

**Acknowledgments**

The JCARE-CARD investigators and participating cardiologists are listed in the Appendix of our previous publication. This study could not have been carried out without the help, cooperation and support of the cardiologists in the survey institutions. We thank them for allowing us to obtain the data. This study is supported by the Japanese Circulation Society and the Japanese Society of Heart Failure. This study is supported by grants from Health Sciences Research Grants from the Japanese Ministry of Health, Labor and Welfare (Comprehensive Research on Cardiovascular Diseases), the Japan Heart Foundation, and Japan Arteriosclerosis Prevention Fund.

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