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PROTOCOL PAPER

Current Medical and Social Conditions and Outcomes of Hospitalized Heart Failure Patients

— Design and Baseline Information of the Cohort Study in Hiroshima —

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Background: Information regarding current medical and social conditions and outcome of Japanese heart failure (HF) patients is needed.

Methods and Results: The registry and follow-up study regarding the medical and social conditions and outcomes of hospitalized heart failure patients (REAL-HF) is maintained by 8 regional core hospitals, which provide an interprofessional team approach for HF patients, in Hiroshima Prefecture. We planned to enroll all adult patients hospitalized with symptomatic HF (congestive HF and/or low output syndrome) in 1 year from March 2017. We registered the clinical characteristics of each patient, including physical activity (able to walk independently), during the indexed hospitalization. Information regarding living circumstances, cognitive function test, questionnaire for quality of life (QOL), and interprofessional team approaches was also collected. For patients discharged home, we planned to follow all-cause death, all-cause unscheduled readmission, and the conditions of outpatient cardiac rehabilitation and home nursing-care services at 3 and 12 months after discharge. A total of 1,218 patients has been registered initially. Follow-up is ongoing, and data analysis is expected to be completed in 2019.

Conclusions: The REAL-HF will provide a significant database on the current real conditions of hospitalized HF patients in a local district of Japan, elucidating medical and social risk factors of worsened QOL and prognosis.

Key Words: Follow-up study; Heart failure; Medical and social conditions; Multicenter registry

In the face of the heart failure (HF) pandemic,[1] the question of how to manage patients with chronic HF is a worldwide issue from a clinical and social perspective. The number of Japanese HF patients with left ventricular (LV) dysfunction has been increasing, and is expected to reach 1.3 million by 2030, which means a future epidemic of HF in Japan.[2] As for clinical characteristics of HF patients in Japan, the Japanese Cardiac Registry of Heart Failure in Cardiology (JCARE-CARD) enrolled 2,675 patients with chronic HF and assessed patient background, severity, treatment, and outcomes.[3] The Chronic Heart Failure Analysis and Registry in the Tohoku District (CHART) study analyzed 1,154 patients with stable HF and sought to clarify their prognosis and predictors for mortality.[4] Whereas these large-scale studies focus on the real conditions of Japanese HF patients, the conditions have been changing substantially in this decade. First, there has been a drastic increase in the elderly population in Japan. The Framingham Study found that HF affects 1% of persons in their 50 s and rises progressively with age to affect 10% of persons in their 80 s.[5] Additionally, developments in the health-care technology and system have increased the survival rate in patients with acute disorder including cardiovascular disease, resulting in a profound improvement in HF prognosis. These HF patients in Japan inevitably need long-term management after hospital treatment for acute HF, thereby emphasizing the importance of HF care in the chronic phase. As an important step toward successfully managing the medical and social issues of HF patients, we need to understand their current real conditions and outcomes.

Hiroshima Prefecture is a typical local district of Japan

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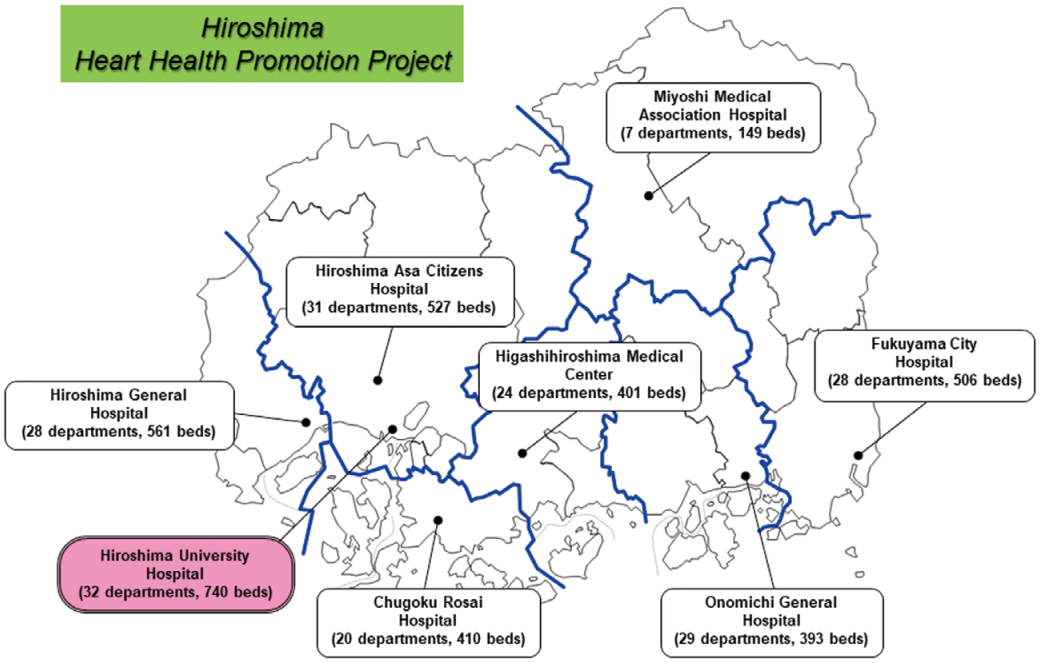

Figure 1. Participating institutions in the Hiroshima Heart Health Promotion Project. Bold lines, borders of the 7 medical regions of Hiroshima Prefecture.

with a total population of 2,800,000, containing both urban and rural areas. The Hiroshima Heart Health Promotion Project started in 2012 and focused on maintaining HF patient activities of daily living and preventing readmission through an interprofessional team approach. Hiroshima University Hospital and the other 7 regional core hospitals are participating in this project. The registry and follow-up study regarding medical and social conditions and outcomes of hospitalized HF patients (REAL-HF) is a prospective cohort representing patients with symptomatic HF hospitalized in these 8 institutions, which aims to provide an epidemiologic database of current real conditions (both medical and social) and outcomes of Japanese HF patients, especially those requiring hospitalization.

Methods

Study Overview and Objectives

REAL-HF is a prospective multicenter study designed to elucidate the real medical and social conditions of hospitalized HF patients, and also to identify their real outcomes after discharge. It will help to identify crucial medical and social factors affecting the outcomes of hospitalized HF patients. Hiroshima University institutional review board (IRB) has approved this prospective study. IRB approval from each participating institution is also required for participation in this study. The protocol has been published in the Japan UMIN Clinical Trials Registry (ID: UMIN000025651).

In all recruited HF patients, baseline information during the indexed hospitalization is collected based on the extraction and review of medical records. Given that the information is anonymized, the IRB has waived the need for patient consent. For patients who can be discharged home, the information regarding outcomes is collected 3 and 12 months after discharge after obtaining written informed consent.

The primary objective of REAL-HF is to clarify current real conditions and outcomes of hospitalized HF patients in local districts of Japan. The secondary objective is to determine which medical and social factors should be prioritized and managed to improve quality of life (QOL) and prognosis in the current and future Japanese society. There are no exclusion criteria, except for age and patient refusal.

Patient Registration

We planned to register all adult patients (age ≥20 years) hospitalized with symptomatic HF in 1 of the 8 institutions participating in the Hiroshima Heart Health Promotion Project (**Figure 1**). The term for registration is 1 year from March 2017. The 8 institutions are the regional core hospitals in Hiroshima Prefecture, and are located in urban, maritime, and intermountain areas. All the institutions have provided interprofessional team approaches for HF patients.

The process of the study is shown in **Figure 2**. The diagnosis of symptomatic HF was confirmed on the presence of at least 2 major criteria or 1 major criterion in conjunction with 2 minor criteria according to the Framingham Study (congestive HF),[6] or on the presence of low output syndrome (general fatigue, coldness of limbs, cyanosis, digestive symptoms, and hepatic and/or renal dysfunction due to low cardiac output) diagnosed by primary physicians.

The case sheet for collecting information is shown in **Supplementary Appendix 2**. At the time of admission, we

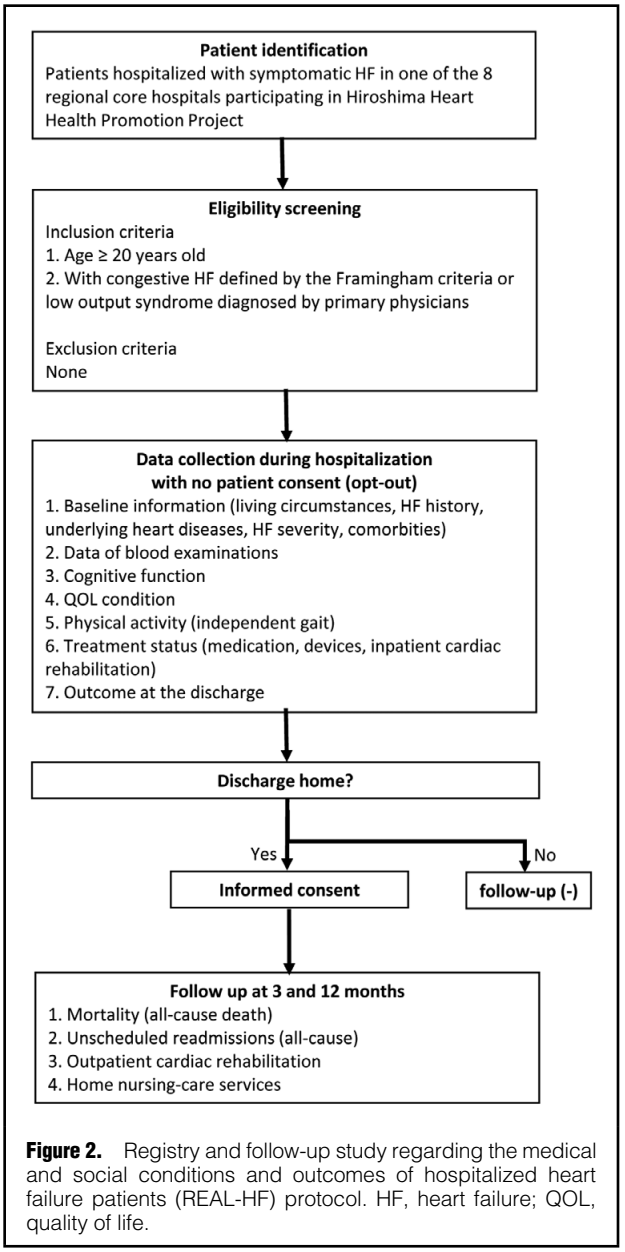

Figure 2. Registry and follow-up study regarding the medical and social conditions and outcomes of hospitalized heart failure patients (REAL-HF) protocol. HF, heart failure; QOL, quality of life.

Table. Entire Cohort: Baseline Information

Variable	n=1,218
Age (years)	79±13
Male	667 (54.8)
BMI (kg/m^2)	22±4
Living circumstances	
Alone	264 (21.7)
With family member	892 (73.2)
With only spouse	390 (32.0)
Nursing home	62 (5.1)
History of symptomatic HF	
First time	814 (66.8)
Second time	208 (17.1)
≥Three times	196 (16.1)
Underlying heart disease†	
Ischemic	319 (26.2)
Valvular	430 (35.3)
Hypertensive	369 (30.3)
Others	424 (34.8)
HF severity at admission	
NYHA I	19 (1.6)
NYHA II	178 (14.6)
NYHA III	652 (53.5)
NYHA IV	369 (30.3)
Comorbidity	
Hypertension	779 (64.0)
Diabetes mellitus	365 (30.0)
Dyslipidemia	262 (21.5)
Atrial fibrillation	533 (43.8)
CKD	499 (41.0)
Obesity (BMI ≥28)	69 (5.7)
Smoking	314 (25.8)
COPD	104 (8.5)
Biomarker (pg/mL)‡	
BNP (n=1,062)	602 (345–1,129)
NT-proBNP (n=134)	4,431 (2,028–11,313)
EF (%) (n=1,114)§	45.9±16.3
HFpEF (EF ≥50%)§	
≤64 years (n=141)	32 (22.7)
65–84 years (n=540)	227 (42.0)
≥85 years (n=433)	230 (53.1)

Data given as n (%), mean±SD or median (IQR). †Some patients had 2 or more underlying heart diseases. ‡Serum BNP or NT-proBNP measured at the time of admission. §Echocardiogram at the time of admission. BMI, body mass index; BNP, brain natriuretic peptide; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; EF, ejection fraction; HF, heart failure; HFpEF, heart failure with preserved ejection fraction; NT-proBNP, N-terminal pro-brain natriuretic peptide; NYHA, New York Heart Association.

recorded the living circumstances before admission (living alone at home or living with housemate at home [and relationship to housemate] or living in a nursing home) as important social background. We also recorded the clinical characteristics including past history of symptomatic HF, underlying heart disease as the etiology of HF at the time of admission, ongoing HF symptom severity (undue fatigue, palpitation, shortness of breath and/or angina on New York Heart Association [NYHA] class), and presence of comorbidities exacerbating HF. Hypertension was defined as peripheral blood pressure >140/90 mmHg and/or assumed if the patient was taking medication for hypertension. Diabetes mellitus was diagnosed using fasting blood sugar ≥126 mg/dL or 2-h blood sugar ≥200 mg/dL and hemoglobin A1c (National Glycohemoglobin Standardization Program) ≥6.5% as the standard and/or assumed if the patient was taking medication for diabetes. Dyslipidemia was diagnosed on abnormal lipids (total cholesterol >220 mg/dL, low-density lipoprotein cholesterol >140 mg/dL, high-density lipoprotein cholesterol <40 mg/dL, and triglycerides >150 mg/dL), and/or assumed if the patient was taking medication for dyslipidemia. The presence of paroxysmal or chronic atrial fibrillation was determined based on electrocardiography and/or past history. Chronic kidney disease was diagnosed if there was persistent proteinuria or if the estimated glomerular filtration rate was

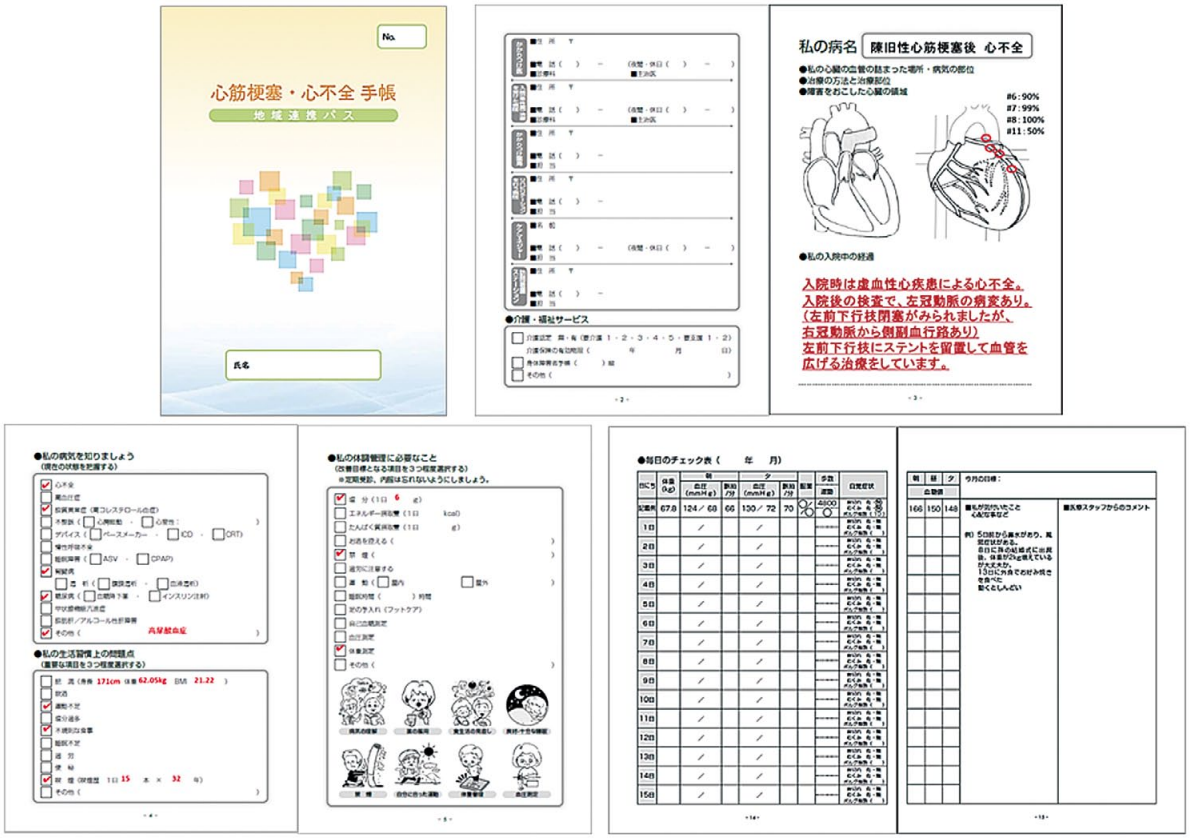

Figure 3. Our established notebook for heart failure management.

<60 mL/min/1.73 m^2 or if the patient was receiving dialysis. The presence of chronic obstructive pulmonary disease diagnosis and/or treatment, and of current or former smoking was determined. Finally, we recorded the clinical data of blood examinations, LV ejection fraction (EF) on echocardiography, and cardiothoracic ratio on chest X-ray.

Additionally, at the time of hospital discharge, we recorded the clinical characteristics including clinical data and treatment status (medication and treatment by device). Note that we collected the results of cognitive function test (Mini Mental State Examination) and QOL questionnaire (EuroQol 5 dimensions) scores, and the condition of physical activity (able to walk independently). The presence or absence of inpatient cardiac rehabilitation and each interprofessional team approach for HF management during the indexed hospitalization was also recorded, according to our established notebook for HF management (**Figure 3**).

Prospective Follow-up

For patients discharged home, we planned to conduct follow-up observation after discharge. In patients who are admitted to hospital from a nursing home, we regard the nursing home as home for them. At 3 and 12 months after discharge, information regarding all-cause death, all-cause unscheduled readmissions, outpatient cardiac rehabilitation, and home nursing-care services is collected through face-to-face or telephone interviews (**Supplementary Appendix 2**).

Patients hospitalized for HF are reportedly at high risk for all-cause re-hospitalization.[7] The primary endpoints of this study are defined as all-cause death and all-cause unscheduled readmission due to both cardiovascular and non-cardiovascular diseases requiring treatment. As for outpatient cardiac rehabilitation, its introduction and completion (5-month program, which is allowed under health insurance in Japan) are checked. Note that, as important social information, the presence or absence and level of certification of public nursing-care need in the Japanese nursing insurance system (explained in **Supplementary Appendix 3**) are checked. The conditions of cardiac rehabilitation and home nursing-care services are defined as the secondary endpoints.

Patient Confidentiality

This study does not include any protocol-specified alteration of treatment or any other aspect of hospital care. Hiroshima University Hospital plays a central role in this study and collects the data from the other 7 institutions through mail. Patient confidentiality is preserved because direct patient identifiers, such as name, address, and identification number, are not collected.

Statistical Analysis

Descriptive statistics are used to summarize baseline characteristics and outcomes for the subjects and for specific subgroups of interest.

Results

A total of 1,218 patients hospitalized with symptomatic HF has been initially registered. **Table** lists the baseline information of the entire cohort. Note that the patients enrolled in REAL-HF were older compared with those of the previous large HF cohorts in Japan (71±13 years old in JCARE-CARD and 69±13 years old in CHART). The super-elderly (≥85 years old) made up a considerable portion of the cohort (n=477, 39.2%), in whom more than half of the patients (53.1%) had preserved EF (≥50%).[8]

Follow-up of the cohort is ongoing. All data collection and analysis are scheduled to end in 2019.

Discussion

The increasing number of chronic HF patients and the considerable changes over time in their clinical and social characteristics are critical issues in Japan. REAL-HF is designed to clarify current real conditions and outcomes of hospitalized HF patients in 1 local district in Japan, in order to contribute to the improvement in Japanese HF management. We believe that this study will provide a typical epidemiologic database of hospitalized HF patients in Japan.

In Europe and the USA, many large-scale epidemiological and clinical studies have been conducted to clarify the real conditions of chronic HF patients, which are documented in the recent guidelines.[8] In Japan, there have been some large-scale studies targeting HF patients (JCARE-CARD,[3] CHART,[4] Heart Institute of Japan-Department of Cardiology [HIJC],[9] and acute decompensated heart failure syndromes [ATTEND] registry[10,11]). They mainly focus on the clinical characteristics of patients with HF, such as HF causes, history, clinical data, and treatment status. These studies clinically clarify the real conditions of HF patients, while they poorly document the HF patients' complex problems including social background, such as living alone, elderly caregiver, and physical disability. More recently, a multicenter cohort of Japanese HF patients focusing on both the medical and social conditions (Kitakawachi Clinical Background and Outcome of Heart Failure [KICKOFF] Registry) has been reported.[12] That study describes the social background of patients in Japan, especially super-elderly patients, based on a community-based registry. It provides unique and useful information regarding lifestyle, family support, dietary and drug management, exercise habits, and long-term care insurance of Japanese HF patients. The study region, however, is restricted to a satellite community near a metropolis, and the number of enrolled patients is relatively small. The study region of REAL-HF covers the whole of Hiroshima Prefecture, which is a typical local district of Japan containing both urban and rural areas, and which may be regarded as the perfect example of a prefecture in Japan. The present sample size reached >1,200 in total and included more elderly HF patients with preserved EF. REAL-HF is expected to elucidate the current medical and social conditions of Japanese HF patients based on a larger cohort.

The multidisciplinary team approach is expected to reduce the mortality and all-cause hospitalizations of HF patients.[13] In 2012, Hiroshima University Hospital and the other 7 regional core hospitals in Hiroshima Prefecture built a regional network to provide an interprofessional team approach for HF patients. In each hospital, the specific team is composed of multidisciplinary medical care personnel, including cardiologists, cardiovascular surgeons, nurses, physical therapists, nutritionists, pharmacists, and social workers. The activities of the team include inpatient/outpatient rehabilitation with aerobic exercise, patient education about HF, and lifestyle guidance using our established notebook for HF management (**Figure 3**). The participating hospitals routinely meet to discuss and improve the team approach. We previously reported single-center data showing that our institutional team approach reduced all-cause hospitalizations and medical costs in patients with an elevated serum HF biomarker (N-terminal pro-brain natriuretic peptide).[14] The participating hospitals have the potential to apply specific and effective interprofessional team approaches for HF care based on the results of REAL-HF.

Conclusions

REAL-HF is a prospective multicenter study in the Hiroshima area, elucidating the real medical and social conditions and outcomes of hospitalized HF patients in Japan. Results from this study will help the interprofessional teams to determine which medical and social factors should be prioritized and managed for HF patients. It is expected to improve HF health care comprehensively, resulting in reduced demand for medical resources for HF patients, in the current and future Japanese society.

Disclosures

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Supplementary Files

Please find supplementary file(s);
http://dx.doi.org/10.1253/circrep.CR-18-0006