入院時所見（入院時とは、入院してから24時間以内のことです）

入院時の状況

救急部での初期治療 ： □あり　□なし

CCUあるいはICUへの入室 ： □あり（入室日数　日）　□なし

身長

cm　□不明

体重

kg　□不明

血圧（治療開始前）

／　mmHg

心拍数（治療開始前）

bpm

入院時症状および身体所見

労作時呼吸困難：	□あり	□なし	□不明
安静時呼吸困難：	□あり	□なし	□不明
倦怠感：	□あり	□なし	□不明
頸静脈怒張：	□あり	□なし	□不明
Ⅲ音：	□あり	□なし	□不明
ラ音：	□あり	□なし	□不明
末梢浮腫：	□あり	□なし	□不明

入院時血液検査所見

BUN：	mg／dl	□不明
クレアチニン：	mg／dl	□不明
ナトリウム：	mg／dl	□不明
ヘモグロビン：	g／dl	□不明

入院時胸部レントゲン所見

□未施行　（次の質問にお進みください）

□施　行

心胸郭比：			%	□不明
肺うっ血所見：	□あり	□なし		□不明
胸水：	□あり	□なし		

動脈血ガス　（入院して最初の所見をご記載ください）

□未施行　（次の質問にお進みください）

□施　行

測定時点での酸素吸入：	□あり	□なし		□不明
pH：				
酸素飽和度 SaO2：			%	
酸素分圧 PaO2：			mmHg	
炭酸ガス分圧 PaCO2：			mmHg	

Swan-Ganzカテーテルの所見　（入院して最初の所見をご記載ください）

□未施行　（次の質問にお進みください）

□施　行

体血圧：		／	mmHg	□不明
心拍数：			bpm	□不明
右房圧：			mmHg	□不明
肺動脈圧：	収縮期 mmHg	拡張期 mmHg		□不明
肺動脈楔入圧：			mmHg	□不明
心拍出量：			L／分	□不明

入院前の薬物治療

今回の入院の直前に行われていた薬物治療です。
JCARE-CARDの退院時薬物治療の調査と同じ形式となっています。

ACE阻害薬

□レニベース　□ロンゲスまたはゼストリル　□コバシル
□タナトリルまたはノバロック　□カプトリル　□インヒベース
□エースコール　□標記以外のACE阻害薬　□無

アンジオテンシン受容体拮抗薬(ARB)

□ニューロタン　□デイオバン　□ブロプレス
□ミカルデイス　□標記以外のARB　□無

β遮断薬

□アーチスト：_____mg／日　□メインテート：_____mg／日
□セロケンまたはロプレソール(徐放錠含む)：_____mg／日
□無

利尿剤

□サイアザイド系利尿薬　□ラシックス　□ダイアート
□アルダクトンA　□エプレレノン　□標記以外の利尿薬
□無

ジギタリス

□有　□無

経口強心薬　(ジギタリス以外)

□アカルディ　□ダナトーパ　□その他
□無

Ca拮抗薬

□ノルバスクまたはアムロジン　□アダラート(徐放錠含む)
□ヘルベッサー(徐放錠含む)　□標記以外のCa拮抗薬
□無

α遮断薬

□カルデナリン　□標記以外のα遮断薬　□無

亜硝酸薬

□有　□無

抗不整脈薬　(β遮断薬・Ca拮抗薬除く)

□アンカロン　□ソタコール　□ベプリコール
□リスモダン　□アスペノン　□メキシチール
□タンボコール　□サンリズム　□シベノール
□標記以外の抗不整脈薬　□無

アスピリン

□有　□無

抗血小板薬　(アスピリン以外)

□パナルジン　□プレタール　□標記以外の抗血小板薬
□無

ワーファリン

□有　□無

スタチン

□メバロチン　□ローコール　□リピトール
□リポバス　□標記以外のスタチン　□無

入院中治療／薬物治療

（入院中に投与した薬物はすべて対象となります）

注意：後発品（ジェネリック）は該当する一般名の薬剤を選択してください。

利尿薬

ループ利尿薬【静注・持続静注】	投与	あり・なし
ループ利尿薬【経口】	投与	あり・なし
サイアザイド系・非サイアザイド系【経口】	投与	あり・なし
アルダクトンA【経口】	投与	あり・なし
（　　）【静注・経口】	投与	あり・なし

ナトリウム利尿ペプチド

ハンプ（カルペリチド）	投与	あり・なし

強心薬

ジゴキシン【静注】	投与	あり・なし
ジゴキシン【経口】	投与	あり・なし
ドパミン	投与	あり・なし
ドブタミン	投与	あり・なし
ノルエピネフリン	投与	あり・なし
アムコラル（アムリノン）	投与	あり・なし
ミルリーラ（ミルリノン）	投与	あり・なし
コアテック（塩酸オルプリノン）	投与	あり・なし
アデール（塩酸コルホルシンダロパート）	投与	あり・なし
アカルディ【経口】	投与	あり・なし
（　　）【静注・経口・筋注・皮下注】		
（　　）【静注・経口・筋注・皮下注】		
（　　）【静注・経口・筋注・皮下注】		

血管拡張薬

ニトロプルシド【静注】	投与	あり・なし
ニトログリセリン【静注】	投与	あり・なし
ニトログリセリン【経口】	投与	あり・なし
硝酸イソソルビド【静注】	投与	あり・なし
硝酸イソソルビド【経口】	投与	あり・なし
（　　）【静注・経口・筋注・皮下注】		
（　　）【静注・経口・筋注・皮下注】		
（　　）【静注・経口・筋注・皮下注】		

抗不整脈薬

（　　）【静注・経口】	投与	あり・なし
（　　）【静注・経口】	投与	あり・なし
（　　）【静注・経口】	投与	あり・なし
（　　）【静注・経口】	投与	あり・なし

その他（急性心不全の治療薬）

（　　）【静注・経口・筋注・皮下注】
（　　）【静注・経口・筋注・皮下注】
（　　）【静注・経口・筋注・皮下注】
（　　）【静注・経口・筋注・皮下注】
（　　）【静注・経口・筋注・皮下注】

慢性心不全の標準的薬物治療（経口）の開始時期

1）ACE阻害薬開始時期：入院：＿＿＿＿日目

2）ARB開始時期：入院：＿＿＿＿日目

3）β遮断薬開始時期：入院：＿＿＿＿日目

入院中治療／非薬物治療

（今回の入院中に施行した治療が対象となります）

□人工呼吸管理

□冠動脈インターベンション（PCI）

□冠動脈バイパス（CABG）

□電気的除細動

□ペースメーカー

□血液浄化（ECUM,CVVH,CHDFなど）

□IABP

□PCPS

□左心補助装置（LVAS）

□心肺蘇生（CPR）

記入はこれで終わりです。
ご協力、どうもありがとうございました。

JCARE-CARD 研究

入院中死亡症例　死因調査

施設名：

登録医師名：

JCARE-CARD に登録された患者 ID：

入院日：

退院日（死亡日）：

1）死因（該当する項目に○を付けて下さい。）

1．心不全死

2．不整脈死

3．突然死（発症後 24 時間以内の死亡）

4．上記以外の心血管系による死亡
→具体的な死因【できるだけ具体的にご記入下さい】

〔　　〕

5．心血管系以外による死亡

2）剖検の有無

1．あり　　2．なし

3）入院中死亡前の非薬物治療の有無

（1）永久ペースメーカー植込み　　1．あり　2．なし

（2）両心室ペーシング　　1．あり　2．なし

（3）植込み型除細動器（ICD）　　1．あり　2．なし

（4）左室補助装置　　1．あり　2．なし

（5）心臓移植　　1．あり　2．なし

V. 発 表 論 文

Circ J 2007; **71:** 449–454

Characteristics and Outcomes of Patients With Heart Failure in General Practices and Hospitals

—— Japanese Cardiac Registry of Heart Failure in General Practice (JCARE-GENERAL) ——

Hiroyuki Tsutsui, MD; Miyuki Tsuchihashi-Makaya, PhD*;
Shintaro Kinugawa, MD; Daisuke Goto, MD; Akira Takeshita, MD**
for the JCARE-GENERAL Investigators

Background The characteristics and outcomes of patients discharged from hospitals with a diagnosis of heart failure (HF) have been described by a number of previous epidemiological studies. However, very little information is available on this issue in general practice in Japan.

Methods and Results The Japanese Cardiac Registry of Heart Failure in General Practice (JCARE-GENERAL) is designed to study the characteristics, treatment and outcomes prospectively in a broad sample of outpatients with HF who were managed by cardiologists in hospital (Hospital-HF) and primary care physicians in general practice (GP-HF). Out of 2,685 patients with HF, 1,280 patients were Hospital-HF and 1,405 GP-HF. Compared to the Hospital-HF patients, GP-HF patients were more likely to be elderly and female, and they had a higher prevalence of hypertensive heart disease as a cause of HF. Angiotensin-converting enzyme inhibitors, angiotensin receptor blockers and β-blockers were more prescribed to Hospital-HF than GP-HF patients. At the follow-up of 1.2 year, after adjustment, the mortality was comparable between the Hospital-HF and GP-HF groups, whereas HF-related admission was higher in the Hospital-HF group than in in the GP-HF group.

Conclusions Based on the JCARE-GENERAL, the characteristics, treatment and outcomes of GP-HF patients differed from those of Hospital-HFpatients in Japan. (*Circ J* 2007; **71:** 449–454)

Key Words: General practice; Heart failure; Hospital; Outcome; Registry

Heart failure (HF) is a complex clinical syndrome that can result from any structural or functional cardiac disorder that impairs the ability of the ventricle to fill with or eject blood. The cardiac manifestations of HF are dyspnea and fatigue, which may limit exercise tolerance, and fluid retention, which may lead to pulmonary congestion and peripheral edema. HF is a leading cause of morbidity and mortality in industrialized countries[1] It is also a growing public health problem, mainly because of aging populations and the increase in the prevalence of HF in the elderly[2] The clinical characteristics, treatment and outcomes of these patients have been well described by a number of hospital-based registries performed in the United States of America[3] Europe[4–6] and Japan[7–11] However, most patients with HF are managed not only by hospital cardiologists but also by primary healthcare physicians in the community (general practitioners). Accordingly, primary care physicians must play a key role in the identification and management for these patients. Nevertheless, much less is known of HF in general practice. There have been no studies reported that provide information on the characteristics, treatment and outcomes in this setting in Japan.

The Japanese Cardiac Registry of Heart Failure in General Practice (JCARE-GENERAL) was developed to provide a large, national prospective registry database describing the clinical characteristics, treatment and outcomes of outpatients with HF. The main aim of the present study was to compare the characteristics and outcomes between patients managed by hospital cardiologists with those managed by primary care physicians in general practice.

Methods

The JCARE-GENERAL is a prospective multicenter registry designed to compile a large clinical database on the characteristics, treatment and outcomes of the outpatients with HF in Japan. Baseline data were collected during November 2004. Follow-up data were collected 1 year after the enrollment.

Study Patients

Eleven participating areas, Hakodate, Shiogama, Mishima, Kahoku in Ishikawa, Motosu in Gifu, Ibaraki, Kasai, Hata in Kochi, Ube, Higashi in Fukuoka, and Kurume, have been selected throughout Japan (Fig 1). In

(Received August 17, 2006; revised manuscript received January 19, 2007; accepted January 23, 2007)

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This work is supported by the grants from the Japanese the Ministry of Health, Labour and Welfare, the Japan Heart Foundation, and Japan Arteriosclerosis Prevention Fund.

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Fig 1. The Japanese Cardiac Registry of Heart Failure in General Practice (JCARE-GENERAL) study areas in Japan.

each participating area, hospital cardiologists and primary healthcare physicians enrolled HF outpatients into the present study. HF patients managed by the hospital cardiologists were categorized as "Hospital-HF" and those managed by primary care physicians in general practice as "GP-HF".

HF was defined as a complex clinical syndrome that can result from any structural or functional cardiac disorder that impairs the ability of the ventricle to fill with or eject blood. For this registry, patients with current HF symptoms as well prior HF were enrolled. The presence of HF was confirmed by the simultaneous presence of at least 2 major criteria or 1 major criterion in conjunction with 2 minor criteria according to the Framingham criteria (Table 1)[12] Patients must have been at least 15 years old at the time of enrollment. Eligibility is not contingent on the use of any particular therapeutic agent or regimen.

Data Collection and Processing

The study protocol, study procedures and data-collection forms were reviewed by the co-investigators at each study area during the central meetings and also presented to all participating physicians during training sessions before commencing the present study. The participating physicians were encouraged to register all patients meeting the entry criteria as consecutively as possible. Duplicated registry of the same patient at different institutions was avoided by checking for their prior enrollment to this registry. Compliance with these methods of registry was not strictly monitored. For each case, baseline data recorded on the form included: (1) demography including age and sex; (2) underlying causes of HF; (3) atrial fibrillation; (4) prior history of HF; and (5) medication. The status of all patients was surveyed and the following information was obtained: (1) whether they survived to the follow up; (2) their cause of death; and (3) hospital admissions due to an exacerbation of HF that required more than continuation of their usual therapy on admission. The cause of death was classified as cardiac or non-cardiac death by the participating physician in each patient based on the clinical information. Death from cardiac causes was defined as death due to cardiac events including sudden cardiac death, fatal myocardial infarction and HF death. Death from causes other than cardiac diseases such as cancer was defined as non-cardiac death.

Ischemic heart disease was considered an etiology of HF if the patient had one of the following: (1) a documented history of myocardial infarction, angina or prior coronary revascularization; (2) pathologic Q waves on the electrocardiogram; or (3) greater than 75% stenosis in one or more coronary arteries on coronary angiograms. Valvular heart disease was determined on the basis of the presence of long standing mitral or aortic valve involvement documented by physical examination and echocardiography or angiography. Hypertensive heart disease was considered present if there was a history of hypertension in the medical records or sustained hypertension and left ventricular (LV) hypertrophy confirmed by electrocardiogram or echocardiogram. Dilated cardiomyopathy was diagnosed by the presence of global LV dilatation with impaired systolic function occurring in the absence of known cardiac or systemic causes.

Table 1 Framingham Criteria for HF

Major criteria
Paroxysmal nocturnal dyspnea
Neck vein distension
Rales
Radiographic cardiomegaly (increasing heart size on chest X-ray)
Acute pulmonary edema
S3 gallop
Increased central venous pressure (>16 cm water at right atrium)
Circulation time ≥25 s
Hepatojugular reflux
Pulmonary edema, visceral congestion, or cardiomegaly at autopsy
Minor criteria
Bilateral ankle edema
Nocturnal cough
Dyspnea on ordinary exertion
Hepatomegaly
Pleural effusion
Decrease in vital capacity by one-third from maximum value recorded
Tachycardia (rate ≥120/min)
Major or minor criteria
Weight loss ≥4.5 kg in 5 days in response to treatment

The diagnosis of HF was established by the simultaneous presence of at least 2 major criteria or 1 major criterion in conjunction with 2 minor criteria.
HF, heart failure.

Patient Confidentiality

The JCARE-GENERAL protocol was organized to ensure compliance with the Guidelines for the Epidemiological Research published by the Japanese Ministry of Health, Labour and Welfare. The original study protocol was approved by the institutional review board at Kyushu University. Informed consent was attained for each patient. The present study did not include any protocol-specified alterations of treatment or any other aspects of hospital care. Patient confidentiality was preserved because direct patient identifiers, such as name, address and identification number, were not collected.

Statistical Analysis

Data are expressed as means±SD. Differences in clinical characteristics, treatment and outcomes were evaluated using the chi-square test or Student's t-test. Survival was estimated with the Kaplan and Meier methods. Differences in survival between the groups were evaluated using the log rank test. After the adjustment for age, sex, etiology of HF, atrial fibrillation and prior history of HF, the relative risk for outcomes including all-cause death, cardiac death and HF-related admission was estimated for the Hospital-HF and GP-HF groups. They were adjusted as categorical

Table 2 Patient Characteristics

	All (n=2,685)	Hospital-HF (n=1,280)	GP-HF (n=1,405)	p value
Age, year (mean±SE)	74±12	71±13	77±10	<0.01
≥75 years, %	56	46	64	<0.01
Male, %	46	55	38	<0.01
Underlying causes of HF, %				
Ischemic	30	27	32	<0.05
Hypertensive	35	22	47	<0.05
Valvular	26	27	25	NS
Cardiomyopathic	15	22	9	<0.05
Others	12	12	12	NS
Unknown	5	4	5	NS
Atrial fibrillation, %	40	42	37	<0.01
Prior history of HF, %	83	90	77	<0.01

GP, general practice. Other abbreviation see in Table 1.

Table 3 Medication Use

	All (n=2,685)	Hospital-HF (n=1,280)	GP-HF (n=1,405)	p value
ACEIs, %	31.5	40.4	23.5	<0.01
ARBs, %	30.9	32.7	29.4	NS
ACEIs or ARBs, %	59.2	68.7	50.6	<0.01
ACEIs and ARBs, %	3.3	4.4	2.3	<0.01
β-blockers, %	27.4	38.3	17.5	<0.01
Diuretics, %	62.0	66.1	58.2	<0.01
Digitalis, %	43.0	45.4	40.8	<0.05
Calcium antagonists, %	37.1	33.4	40.5	<0.01

ACEIs, angiotensin-converting enzyme inhibitors; ARBs, angiotensin receptor blockers. Other abbreviations see in Tables 1,2.

Table 4 Death and HF-Related Admission Rate

	No. of patients		All cause death (%)		Cardiac death (%)		HF-related admission (%)	
	Hospital-HF	GP-HF	Hospital-HF	GP-HF	Hospital-HF	GP-HF	Hospital-HF	GP-HF
Crude rate	1,251	1,377	6.7	5.9	2.9	1.7	11.3	6.8
Age-adjusted rate (95%CI)			7.6 (2.7–12.5)	5.3 (1.9–8.7)	3.0 (0.2–6.1)	1.5 (0.3–3.3)	12.1 (6.0–18.3)	6.8 (2.3–11.3)
Age groups								
–39 years	36	4	11.1	0	5.6	0	8.3	0
40–49 years	52	16	1.9	0	1.9	0	13.5	6.3
50–59 years	132	72	3.0	0	3.0	0	8.3	5.6
60–69 years	237	200	3.4	1.5	1.7	0.5	10.1	4.0
70–79 years	439	503	6.6	3.8	2.7	1.4	11.8	7.2
80–89 years	314	472	10.5	8.3	3.8	2.8	13.1	6.4
90– years	38	108	13.2	18.5	2.6	1.9	7.9	13.9
Sex groups								
Male								
Crude rate	685	508	8.7	7.3	2.9	1.8	12.0	6.9
Age-adjusted rate (95%CI)			10.2 (4.9–15.6)	6.4 (2.7–10.0)	3.1 (0.2–5.9)	1.5 (0.5–3.5)	13.0 (7.4–18.6)	6.8 (1.3–12.3)
Female								
Crude rate	563	858	4.4	5.1	2.8	1.6	10.5	6.9
Age-adjusted rate (95%CI)			4.9 (0.8–8.9)	4.9 (2.3–7.5)	2.9 (0.2–6.1)	1.6 (0.5–2.8)	11.4 (5.2–17.6)	6.9 (3.3–10.5)

The mean follow-up periods for HP-HF and GP-HF were 431±93 days and 424±91 days, respectively.
CI, confidence interval. Other abbreviations see in Tables 1,2.

variables, except for age, which was a numerical variable. Two tailed tests of significance are reported. $p<0.05$ was considered to be statistically significant.

Results

Patient Characteristics

The present study included 2,685 outpatients with HF from 11 areas in Japan; 1,280 patients from 55 hospitals as Hospital-HF and 1,405 patients from 180 general practitioners as GP-HF. The mean number of patients at each hospital and GP was 23±27 and 8±9, respectively. The mean age was 74±12 years (range 15 to 101), and 56% of patients were >75 years of age (Table 2). The mean age and the proportion of aged patients were greater in GP-HF patients compared to Hospital-HF patients (Table 2). Overall, 46% were men and 54% women. The GP-HF patients were more often women (45% vs 62%, $p<0.01$).

Ischemic heart disease was the predominant cause of HF in both groups, but this was more prevalent in the GP-HF group. Hypertensive heart disease was more common in the GP-HF group than in the Hospital-HF group and it was the leading cause of HF in this group of patients. In contrast, cardiomyopathy was less common in GP-HP patients.

The prevalence of atrial fibrillation was greater and the prior history of HF was more frequent in Hospital-HF patients than in the GP-HF group (Table 2).

Medication Use

Angiotensin-converting enzyme (ACE) inhibitors were administered to 32% of the patients, angiotensin receptor blockers (ARBs) to 31%, β-blockers to 27%, diuretics to 62% and digitalis to 43% (Table 3). ACE inhibitors and ARBs were more prescribed to Hospital-HF than GP-HF patients (Table 3). Beta-blockers were prescribed to approximately 38% of Hospital-HF patients whereas they were prescribed to only 18% of GP-HF patients. Prescription rates of diuretics and digitalis were also higher in Hospital-HF patients. In contrast, calcium antagonists were prescribed more often to GP-HF patients.

Mortality and HF-Related Admission

Among 2,685 patients, 57 patients were lost during the follow up (2.1%). The mean follow-up periods for patients with HP-HF and GP-HF were 431±93 and 424±91 days, respectively, which were not significantly different.

During the follow-up, 165 patients (6.3%) died; 59 (36%) from cardiac causes, 53 (32%) from non-cardiac causes and 53 (32%) from unknown causes. The rates of all-cause death as well as cardiac death tended to be greater in Hospital-HF

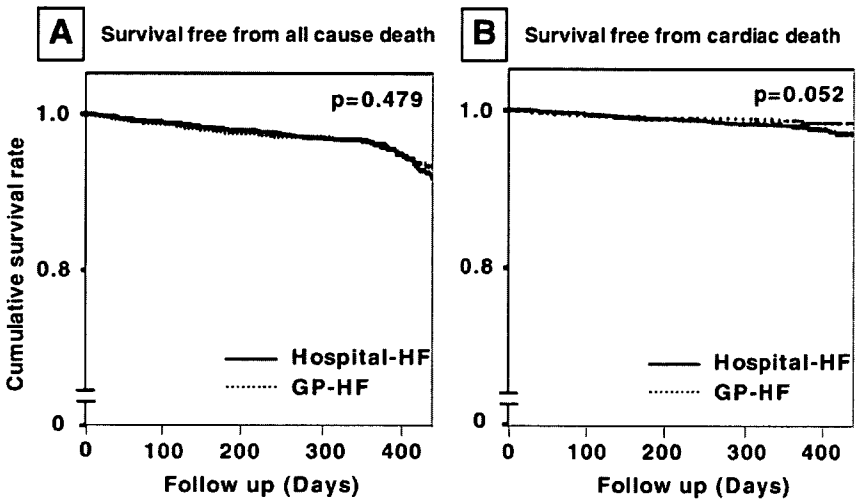

Fig 2. Cumulative survival rates. Survival estimates free from all-cause death (A) and cardiac death (B) during the follow up were derived from the Kaplan and Meier methods. HF, heart failure; GP, general practice.

Table 5 Adjusted Relative Risk for Outcomes by Hospital-HF and GP-HF

	Relative risk (95%CI)	*p value*
All cause death		
Hospital-HF	*1*	
GP-HF	*0.83 (0.59–1.18)*	*0.30*
Cardiac death		
Hospital-HF	*1*	
GP-HF	*0.69 (0.39–1.22)*	*0.20*
HF-related admission		
Hospital-HF	*1*	
GP-HF	*0.62 (0.47–0.82)*	*<0.01*

Adjusted for age, sex, etiology of HF, atrial fibrillation, and prior history of HF.
Abbreviations see in Tables 1,2,4.

patients than GP-HF (Table 4, Fig 2). For the age and sex categories studied, these rates were higher in Hospital-HF patients than in GP-HF, except for all-cause death in female patients (Table 4). However, after adjusting for age or variables including age, sex, causes of HF, atrial fibrillation and prior history of HF, the rates of all-cause death and cardiac death did not differ between Hospital-HF and GP-HF patients (Tables 4, 5).

During the same study period, 235 patients (9%) had a hospital admission due to an exacerbation of HF. The HF-related hospital admission rate was significantly higher in Hospital-HF than in GP-HF patients ($p<0.01$; Table 4), which did not alter even after adjustment (Table 5).

Discussion

The characteristics and outcomes of outpatients with HF in general practice have been poorly described, despite the importance of this disease to public health. The JCARE-GENERAL is the first diverse, large-scale, prospective multicenter database of this population in Japan. An important finding is that HF outpatients in the general practice were more likely to be elderly and women with hypertension as a predominant cause of HF. Evidence-based medications for HF, including ACE inhibitors, ARBs and β-blockers, were less prescribed to GP-HF patients compared to Hospital-HF patients. In contrast, calcium antagonists were prescribed more often to GP-HF patients. At the follow-up of 1.2 years after adjustment, the mortality was comparable between Hospital-HF and GP-HF patients, whereas HF-related admission was higher in Hospital-HF than in GP-HF patients, which might be caused by them having more definite and severe HF.

We have previously reported the characteristics and outcomes of patients hospitalized to the cardiology departments in Fukuoka, Japan[9–11] These studies highlighted several important features of "real world" patients with HF, which were not found in large-scale clinical trials. One key feature was the old age of HF patients. The mean age of the patients was 69 years; 70% were ≥65 years of age. Women especially were mostly over 70 years of age. This is consistent with previous community-based studies[13,14] Another important feature was a relatively good survival prognosis; the 1-year mortality rate being 8.3%. A prognosis of patients with decreased ejection fraction (<40%) was still good; the 1-year mortality rate being 9.1%. At the first glance, this finding appears to be contradicted by the generally held notion that advanced age and more comorbidity may be related to poor survival. In contrast to the relatively low mortality, rates of readmission due to worsening HF were as high as 40% within 1 year after discharge. This value was comparable to those in prior studies (a 3- to 6-month readmission rate 30 to 50%)[15,16] The most commonly identified precipitating cause for hospital readmission was lack of compliance with medical and dietary treatment (48%)[10]

Even though our previous studies have provided a valuable insight into the clinical characteristics, outcomes and the potential effective treatment strategies for HF patients, the generality of these results is questioned because our previous studies were conducted in hospitalized patients with HF[9–11] Outpatients with HF are managed mostly in the community by primary care physicians. Nevertheless, few studies provide objective information about these patients. Therefore, it is of critical importance to analyze the realistic data for HF outpatients in general practice, and to form a database on a national basis for future investigations. For this purpose, JCARE-GENERAL was designed to focus on the demographic and clinical characteristics, treatment strategies and outcomes in "real-world" outpatients managed by primary care physicians in general practice.

The present study demonstrated that, compared to Hospital-HF patients, GP-HF patients were more often elderly and female, and had a higher prevalence of hypertensive heart disease as a cause of HF. In concordance with the

present study, previous studies have shown that the majority of HF patients are elderly and women in the community![17–20] In contrast, more severe cases of HF are referred to hospital cardiologists, and these patients are most comparable to the HF patients included in the randomized clinical trials with respect to a high proportion of younger and male patients. This might explain, at least in part, our findings that Hospital-HF patients had higher rates of mortality and HF-related hospital admission than GP-HF patients.

Another important feature of the present study is the description of the contemporary pharmacological management of HF in general practice in Japan. Even though previous randomized controlled trials have shown that drugs such as ACE inhibitors can improve the survival of HF patients, GP-HF patients were significantly less likely to be prescribed the evidenced-based medications?[21,22] However, these medications are indicated when LV systolic function is reduced and not when it is preserved. GP-HF patients are elderly and more likely to be female and hypertensive, which is more often associated with preserved LV systolic function and may explain, at least in part, the difference in the medication use between Hospital-HF and GP-HF patients![1]

Limitations

Several crucial limitations inherent in the present study should be considered when these data are interpreted. First, although the present study intended to determine the differences between HF patients in general practice and those treated by the hospital cardiologists, the selection or referral bias might be a potential limitation of the present study. This form of bias occurs when younger patients, particularly those at lower risk, are treated by the hospital cardiologists. Elderly patients are then disproportionately represented in general practice. Therefore, the present study compared the outcomes after adjustment for the differences between patients in hospital and general practice. However, more importantly, it is not known whether HF patients treated by general practices have a different outcome from those managed in hospitals. Second, the JCARE-GENERAL data are based on the decisions made by the participating primary care physicians and hospital cardiologists according to the Framingham diagnostic criteria, which may be incomplete or imprecise. The lack of a precise, universal definition of HF makes this type of registry difficult and open to many criticisms. However, it is not the objective of this survey to restrict enrollment to the narrowly defined population of HF usually included in clinical trials but rather to include a broad range of patients reflecting the current reality of clinical practice rather than trials. Moreover, the information regarding the study protocol was regularly provided at national as well as local meetings in each area. Third, even though data validation included manual verification and correction of all numeric fields in the present study, the validation of the registered data regarding the diagnosis by comparison with the source data were not performed. Further, even though the participating physicians were encouraged to register all patients meeting entry criteria as consecutively as possible, it was not verified whether all patients were indeed registered. Fourth, the present study did not determine the prevalence of patients who met 2 major Framingham criteria for HF or 1 major and at least 2 minor criteria. Fifth, the information on cardiac structure and function especially by using echocardiography were not available in the present study, which might make it difficult to diagnose structural heart disease as a cause of HF and its disease severity, and further differentiate between patients with reduced and preserved systolic function. Nevertheless, the main focus of the present study as well as most other epidemiological studies is to obtain information on the realistic picture of HF based on the symptoms, rather than LV systolic dysfunction. Sixth, the majority of HF patients in the present study had prior history of HF although it was more prevalent in Hospital-HF than in GP-HF patients (Table 2). The data regarding the length between the initial diagnosis of HF and the enrollment to this registry were not available in the study patients and might differ between Hospital-HF and GP-HF patients, which could be a potential variable affecting their outcomes. Seventh, the present study defined cardiac death as death due to cardiac events including sudden cardiac death, fatal myocardial infarction and HF death. The cause of death was diagnosed in each patient by the participating physician based on the clinical information and not verified by the death certificate.

Conclusions

The JCARE-GENERAL has provided the first, valuable information on the characteristics, management and outcomes in a broad sample of "real world" outpatients with HF in general practice in Japan. They were different from those managed by cardiologists in hospital. The mortality was comparable between Hospital-HF and GP-HF patients, whereas HF-related admission was higher in Hospital-HF patients. By helping to characterize this disease state better, it will ultimately have a significant impact on public health at the national level in Japan.

Acknowledgments

The JCARE- GENERAL is supported by the Japanese Society of Heart Failure. It is supported by grants from the Health Sciences Research Grants from the Japanese Ministry of Health, Labour and Welfare, the Japan Heart Foundation, and Japan Arteriosclerosis Prevention Fund.

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Appendix 1

JCARE-GENERAL Investigators

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≪心不全の疫学を探る――日本発の日本人のための心不全エビデンス≫ JCARE 研究

眞茅みゆき　筒井裕之*

要旨

- 高齢者が多くを占める慢性心不全では，循環器専門医とともに一般開業医(かかりつけ医)の役割が大きい．
- 地域の病院，一般開業医で治療を受けている慢性心不全患者を登録した JCARE-GENERAL 研究の結果では，開業医に通院する患者の特徴として，高齢，高血圧性心疾患が多いことが示され，病院と開業医の年齢調整死亡率には，有意な差を認めなかった．
- JCARE-GENERAL のような観察研究は，大規模臨床試験では得ることのできない治療効果の検証や，新たな臨床試験の対象を選定するうえでの基盤となり，日本人のためのエビデンスの構築が可能になると考えられる．

はじめに

人口の高齢化・生活習慣の欧米化に伴う虚血性心疾患の増加により慢性心不全患者は増加の一途をたどっているが，今後さらに増加していくと予想される．最近の米国での報告では，1970～1974年と1990～1994年のそれぞれの観察期間における心不全の発症率を比較したところ，発症率が14%上昇している[1]．

慢性心不全患者は増悪による入院を繰り返し，医療コストの増大にもつながることから，欧米では重要な社会問題として捉えられている．さらに，高齢者が多くを占める慢性心不全では，定期的なフォローアップによる管理が重要であり，循環器専門医とともに一般開業医(かかりつけ医)の役割が大きい．しかしながら，日本のみならず欧米においても，地域における慢性心不全の治療，管理の実態は十分に把握されているとはいえない．そこで，われわれは，地域の病院，一般開業医で治療を受けている慢性心不全患者を登録し，追跡調査を行うことにより，心不全の病態，治療，予後の実態を明らかにすることを目的に，「地域住民の中で外来治療を受けている慢性心不全患者を対象とした調査研究(Japanese Cardiac Registry of Heart Failure in General Practice：JCARE-GENERAL 研究)」を実施した[2]．

本稿では，JCARE-GENERAL 研究の結果から，地域における慢性心不全患者の実態を概説する．

JCARE-GENERAL 研究の概要

2003年より開始した JCARE-GENERAL 研究は，全国の11地域(Fig. 1)の内科・循環器科の診療を行っている医療機関を対象に，外来に通院中の慢性心不全患者を1ヵ月間登録し，その患者背景，治療内容，予後を調査するものである(Table 1)．登録時の必須項目としては，心不全の基礎疾患，心房細動の合併，心不全の既往の有無，投薬

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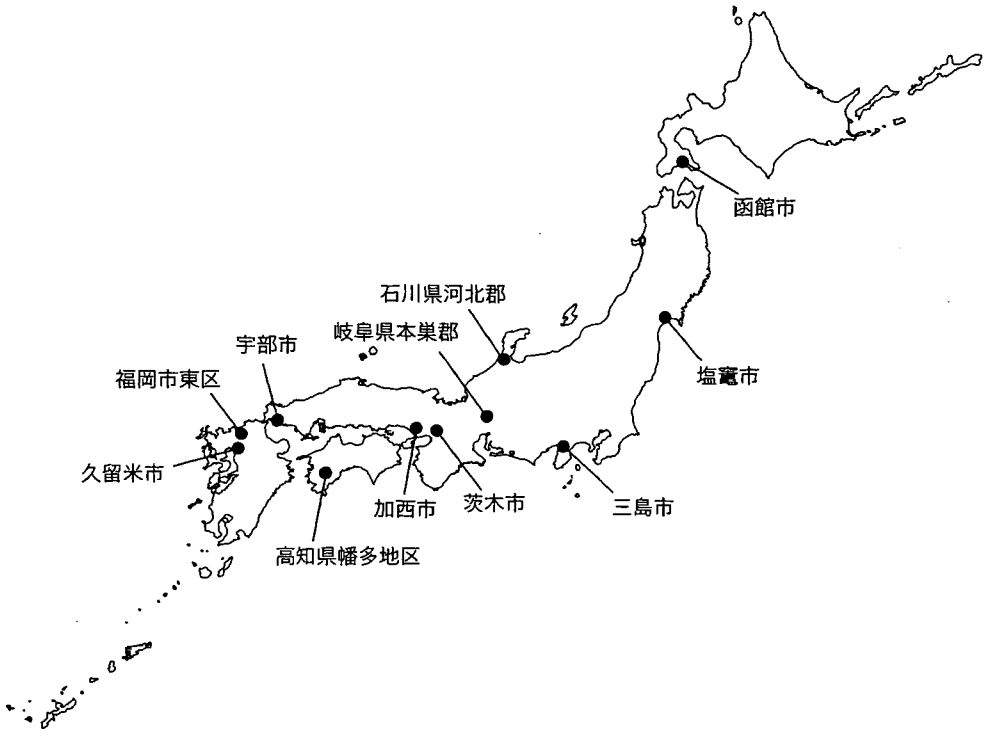

Fig. 1. JCARE-GENERAL 研究における研究対象地域

Table 1. JCARE-GENERAL の概要

目的	外来治療を受けている慢性心不全患者を全国の複数の地域で登録し，患者の臨床像や治療内容などの実態を明らかにするとともに，予後(生命予後と心不全増悪による再入院)の規定因子を明らかにする．
研究デザイン	前向き観察研究
研究参加施設	全国 11 地域(Fig. 1)において，内科・循環器科を標榜する施設
方法	インフォームドコンセントが得られた患者について，各医療機関の主治医が，患者の退院時に以下の調査項目をホームページから直接登録する． 調査項目：登録日，患者 ID，年齢，性別，基礎疾患(虚血，高血圧，心筋症，弁膜症，不明，その他)，心房細動，新規に診断された心不全患者か否か，外来患者総数，心エコー所見(可能な地域のみ)，投薬(ACE 阻害薬，ARB，β遮断薬，利尿薬，ジギタリス製剤，Ca 拮抗薬，スタチン) 登録 1 年後に予後調査(生死，心不全増悪による入院)
調査期間	登録：2003 年 10 月を中心とした 1ヵ月間
対象	慢性心不全の診断にて外来治療を受けている患者
診断基準	心不全の症状(息切れや倦怠感)や徴候(ラ音や浮腫)があり，それらが他疾患によるものではない患者で，心機能障害を有する患者(European Society of Cardiology ガイドラインの診断基準)
除外症例	無症候性心不全
症例数	2,685 例
年齢	15 歳以上

内容であり，1 年後に生命予後と心不全増悪による入院の有無を調査した．さらに，可能な地域では，心エコー所見も調査した．

この研究では，幅広い重症度の患者の臨床像や治療と予後との関連に加えて，主に循環器医が診療する病院と一般開業医に通院する慢性心不全患

Table 2. 患者背景

	全症例 (*n*= 2,685)	病院通院患者 (*n*= 1,280)	開業医通院患者 (*n*= 1,405)	*p* 値
年齢(歳：平均±標準偏差)	74±12	71±13	77±10	<0.01
≧75 歳(%)	56	46	64	<0.01
男性(%)	46	55	38	<0.01
心不全の基礎疾患(%)				
虚血性	30	27	32	<0.05
高血圧性	35	22	47	<0.05
弁膜症	26	27	25	NS
心筋症	15	22	9	<0.05
その他	12	12	12	NS
不明	5	4	5	NS
心房細動(%)	40	42	37	<0.01
心不全の既往(%)	83	90	77	<0.01

NS：not significance

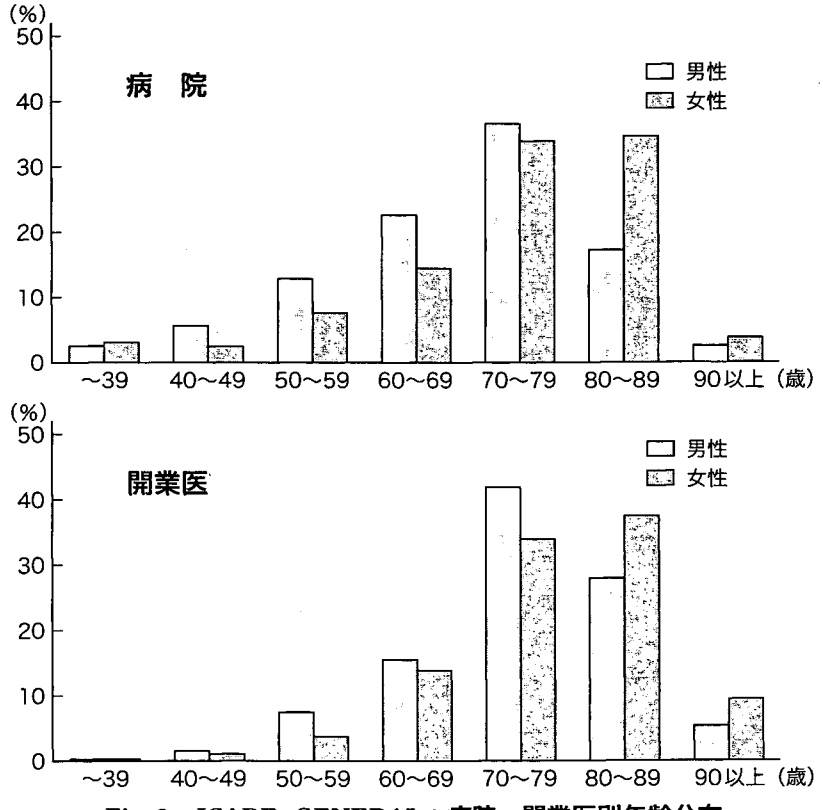

Fig. 2. JCARE-GENERAL：病院，開業医別年齢分布

者の臨床像の違いを明らかにすることを目的としている．

慢性心不全患者の臨床像――病院と開業医における心不全患者の比較○

循環器医が診療する病院に比べ，開業医に通院する心不全患者は高齢であることが示された(Table 2)．また，病院，開業医ともに，女性の高齢者が多いことが特徴である(Fig. 2)．さらに，開業医では病院と比較し，女性が多かった．基礎疾患は，開業医に通院する心不全患者では虚血性心疾患，高血圧性心疾患がより多く，とくに高血圧