

## Impact of Hospital Practice Factors on Mortality in Patients Hospitalized for Heart Failure in Japan

- An Analysis of a Large Number of Health Records From a Nationwide Claims-Based Database, the JROAD-DPC -

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**Background:** An inverse relationship exists between hospital case volume and mortality in patients with heart failure (HF). However, hospital performance factors associated with mortality in HF patients have not been examined. We aimed to identify these using exploratory factor analysis and assess the relationship between these factors and 7-day, 30-day, and in-hospital mortality among HF patients in Japan.

**Methods and Results:** We analyzed the records of 198,861 patients admitted to 683 certified hospitals of the Japanese Circulation Society between 2012 and 2014. Records were obtained from the nationwide database of the Japanese Registry Of All cardiac and vascular Diseases-Diagnostic Procedure Combination (JROAD-DPC). Using exploratory factor analysis, 90 hospital survey items were grouped into 5 factors, according to their collinearity: "Interventional cardiology", "Cardiovascular surgery", "Pediatric cardiology", "Electrophysiology" and "Cardiac rehabilitation". Multivariable logistic regression analysis was performed to determine the association between these factors and mortality. The 30-day mortality was 8.0%. Multivariable logistic regression analysis showed the "Pediatric cardiology" (odds ratio (OR) 0.677, 95% confidence interval [CI]: 0.628–0.729, P<0.0001), "Electrophysiology" (OR 0.876, 95% CI: 0.832–0.923, P<0.0001), and "Cardiac rehabilitation" (OR 0.832, 95% CI: 0.792–0.873, P<0.0001) factors were associated with lower mortality. In contrast, "Interventional cardiology" (OR 1.167, 95% CI: 1.070–1.272, P<0.0001) was associated with higher mortality.

**Conclusions:** Hospital factors, including various cardiovascular therapeutic practices, may be associated with the early death of HF patients.

Key Words: Cardiac rehabilitation; Electrophysiology; Exploratory factor analysis; Heart failure

Heart failure (HF) is one of the most common causes of hospitalization, with high in-hospital mortality and rehospitalization rates.<sup>1</sup> Numerous studies from clinical trials and registries have identified a number of clinical and biochemical factors as potential prognostic factors for poor outcomes among HF patients.<sup>2-6</sup> These factors include demographics, medical history, symptoms and signs, and laboratory biomarkers. However, the outcomes of HF patients may be influenced not only by individual characteristics, but also by hospital practices. Admission to higher-volume hospitals is associated with lower mortality of HF patients, as well as acute myocardial

infarction, which means hospital case volume is an indicator of the quality of hospital practice.<sup>7</sup> In Japan, the case volume-outcome relationship has been confirmed in HF using a nationwide administrative database of patients with cardiovascular diseases (Japanese <u>Registry Of All cardiac</u> and vascular <u>Diseases</u>: JROAD).<sup>8</sup> Multivariable regression analysis has also shown that a higher hospital volume is independently associated with lower rates of 7-day, 30-day, and in-hospital mortality.<sup>8</sup>

Hospital case volume is a representative clinical indicator, but may not be an appropriate factor for assessing optimal medical care for HF, because HF care involves various

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hospital practices, including interventional or non-interventional treatment of coronary artery disease (CAD), arrhythmia, and congenital heart disease; for example, the evidence-based HF therapies for left ventricular dysfunction. However, there are no studies demonstrating the relationship between hospital practice factors and outcomes in HF, partly because hospital therapeutic practices around HF are considered to be numerous and varied, as with other cardiovascular diseases. Moreover, analyses of the interrelationship between these factors are very complicated. For example, the number of coronary artery bypass grafting (CABG) cases will be associated with the number of cardiovascular surgeons and other arterial surgeries.

Exploratory factor analysis is a statistical grouping technique that simplifies multivariate data when there is a large number of intercorrelated variables.<sup>9.10</sup> It is used to eliminate multicollinearity and identify the "factors" of independent prognostic markers.<sup>9</sup> Exploratory factor analysis groups many variables into a smaller set of independent "factors" according to basic underlying relationships among variables.

Table 1. Baseline Characteristics of Study	Patients
n	198,861
Male, n (%)	104,893 (52.7%)
Age, years (mean±SD)	77.8±12.9
Length of hospitalization, days (mean±SD)	22.8±20.9
NYHA class, n (%) (n=178,268)	
I	14,132 (7.9%)
II	49,854 (28.0%)
III	59,577 (33.4%)
IV	54,705 (30.7%)
Comorbidity, n (%)	
Hypertension	100,927 (50.8%)
Diabetes mellitus	52,156 (26.2%)
Hyperlipidemia	33,938 (17.1%)
COPD	13,935 (7.0%)
Ischemic heart disease	61,332 (30.8%)
Cardiomyopathy	10,641 (5.7%)
Charlson comorbidity index, (median, [IQR])	2 [1, 3]
Discharge medication, n (%) (n=177,229)	
ACEI	33,388 (18.8%)
ARB	52,560 (29.7%)
Calcium-channel blocker	44,307 (25.0%)
β-blocker	82,590 (46.6%)
Loop diuretic	85,664 (48.3%)
Spironolactone	61,370 (34.6%)
Oral antidiabetic drugs	26,664 (15.0%)
Insulin	3,496 (2.0%)
Statin	42,150 (23.8%)
Warfarin	50,775 (28.6%)
DOAC	11,004 (6.2%)
Aspirin	53,228 (30.0%)

ACEI, angiotensin-converting-enzyme inhibitor; ARB, angiotensin II receptor blocker; COPD, chronic obstructive pulmonary disease; DOAC, direct oral anticoagulant; NYHA, New York Heart Association.

"Factors" are fewer in number than the original variables and useful in subsequent statistical analysis (i.e., predictive regression models). This analytical method has been widely used in the social sciences and also used an approach to analyzing multiple biomarkers in cardiovascular research.<sup>11–13</sup> By classifying hospital survey items into clinically meaningful factors, exploratory factor analysis can help elucidate the presence of collinearity and identify significant hospital factors.

In the present study, we aimed to identify factors of hospital practice items using exploratory factor analysis and to apply each of the factors to traditional statistical modelling for the prediction of the 7-day, 30-day, and inhospital mortality among patients with HF in Japan.

#### Methods

## Study Design and Hospital and Patient Database

This research was a retrospective, nationwide, observational cohort study. The detailed methods of JROAD and JROAD-DPC were published in our previous study.<sup>8</sup> The JROAD study was launched in 2004 to assess the clinical

activity of each Japanese institution's cardiovascular beds. DPC used data from the Japanese Diagnosis Procedure Combination/Per Diem Payment System (DPC/PDPS), which includes the following individual data: patient age and sex, main diagnosis and comorbidities, drugs and devices, diagnostic and therapeutic procedures, length of stay, and discharge status. The JROAD-DPC database is the combination of JROAD and DPC-based claim data. In brief, all Japanese Circulation Society (JCS)-certified teaching hospitals with cardiovascular beds, except for those with stroke beds, participated in the JROAD. A JCScertified teaching hospital is a facility of a standard that can provide the curriculum necessary for a JCS board-certified cardiologist, and with sufficient numbers of cases and a medical education environment. A total of 1,612 hospitals agreed to participate in the JROAD-DPC database study. Hospitals with  $\leq 10$  patients hospitalized with HF per year were excluded. Thus 1,160 hospitals with 224,594 patient records were used to determine the clustering of hospital survey items (Figure A). The records of patients admitted to hospital with acute HF based on the International Classification of Diseases-10 diagnosis codes related to HF (HF: I50.0; congestive HF, I50.1; left ventricular failure; I50.9; HF, unspecified) were identified and extracted. This method of extracting the coding was the same as used in our previous JROAD-DPC study.8

#### Patients

The following data were extracted from the database: unique hospital identifier, patient's age and sex, diagnoses, comorbidities at admission, in-hospital use of medications, New York Heart Association (NYHA) classification on admission, and discharge status. NYHA classification on admission, collected from the DPC, was determined by the attending physician in each case. Comorbidities were determined primarily from the International Classification of Diseases-10 codes, but they were also checked against the medications and procedures each patient received/ underwent to determine if these were consistent with the code data. A total of 224,594 hospitalization records were collected between April 1, 2012, and March 31, 2014, from 1,160 hospitals. After exclusion of 477 hospitals that did not agree to provide DPC data, 683 hospitals with 198,861 DPC data records were used for exploratory factor analysis to identify clusters associated with the prognosis of HF (Figure B).

## Hospital Practice Factors Identified by Exploratory Factor Analysis

The hospital survey items related to practice volume and structural indicators used for exploratory factor analysis are listed in Supplementary Table 1. First, we collected "hospital survey items" from the JROAD survey. We utilized the term "items", or "hospital survey items" such as the numbers of elective percutaneous coronary intervention (PCI), listed in Supplementary Table 1. We performed exploratory factor analysis using these items, and the new groups, which we defined as "factors" or "hospital practice factors", emerged. We interpreted each "factor" and named it based on the results of items with larger factor loading scores, because the magnitude of factor loading represents the contribution to the factor. We chose the maximum number of factors by gradually increasing the number of factors that could be interpreted, and we named the factors representative items with stronger factor loading in each

Table 2. Baseline Characteristics of Hospi   Participating in JROAD-DPC	tals (n=683)
	Median, [IQR]
Overall	
No. of beds	400, [300, 558]
No. of admissions for HF	158, [101, 234]
Acute decompensated HF	44, [10, 117]
No. of patients with chronic HF	42, [10, 98]
In-hospital deaths of HF patients	12, [6, 19]
Cardiology department	
No. of beds	35, [30, 45]
No. of cardiologists	6, [4, 9]
No. of board-certified cardiologists	4, [3, 6]
No. of hospitalized patients in cardiology department	809, [518, 1,203]
CCU, n (%)	574 (84.0%)
Cardiac catheterization laboratory, n (%)	668 (97.8%)
PCI procedures	655 (95.9%)
Cardiovascular surgery department	406 (59.4%)
No. of beds	5, [0, 15]
No. of cardiovascular surgeons	2, [0, 4]
No. of hospitalized patients	74, [0, 217]
Pediatric cardiology department	151 (22.1%)
No. of beds	0, [0, 0]
No. of pediatric cardiologists	0, [0, 0]
No. of hospitalized patients	0, [0, 0]
Cardiac rehabilitation	334 (48.9%)
Cardiac rehabilitation (new enrollment cases)	0, [0, 195]
Total no. of cardiac rehabilitation patients	0, [0, 2,503]

CCU, coronary care unit; HF, heart failure; PCI, percutaneous coronary intervention.

factor. Factor loading is a value indicating the influence of factors on variables, "items" in this case, which means factors or items are correlated according to the magnitude of the value of factor loading. In other words, if the factor loading score is larger, the correlation between factors and items is stronger. The conventional exploratory factor analysis approach is based on changing strong factor loadings, for example, those in excess of 0.40.

We performed exploratory factor analysis using oblique rotation with the quartimin method after replacement with logarithmic normal distribution and then grouped 90 hospital survey items of practice volume and structural indicators into several factors. We performed exploratory factor analysis and grouped 90 items from the JROAD survey after excluding 8 items that had a strong confounding relationship with endpoint and adjusted variables in this study, 3 items related to hospital case volume of HF, 3 items related to the endpoint of this study, and 2 items related to DPC cording number.

#### **Ethics Statement**

This study was conducted according to the principles of the Declaration of Helsinki. JROAD and JROAD-DPC are secondary analyses of a nationwide survey conducted by the JCS. The research plan was designed by the authors and approved by the institutional review boards of the National Cerebral and Cardiovascular Center (NCVC) and Kyushu University, which waived the requirement

Table 3. Annual Volumes of Hospitals Par JROAD-DPC	rticipating in
	Median, [IQR]
Transthoracic echocardiography	3,103, [2,001, 4,965]
Transesophageal echocardiography	21, [5, 70]
Coronary angiography	333, [181, 594]
Ventriculography	60, [10, 205]
Intravascular ultrasound	132, [52, 252]
Myocardial biopsy	1, [0, 6]
Electrophysiologic study	5, [0, 19]
Catheterization for CHD (diagnosis)	0, [0, 3]
Emergency PCI	50, [23, 88]
Elective PCI	125, [60, 212]
Plain old balloon angioplasty (per lesion)	14, [3, 37]
Plain old balloon angioplasty (per patient)	15, [5, 31]
Bare metal stents (per lesion)	25, [6, 56]
Bare metal stents (per patient)	25, [9, 54]
Drug-eluting stents (per lesion)	124, [39, 240]
Drug-eluting stents (per patients)	108, [47, 201]
Rotablational atherectomy (per lesion)	0, [0, 6]
Rotablational atherectomy (per patient)	0, [0, 6]
Emergency PCI for AMI	38, [18, 66]
Percutaneous transluminal angiography (per patient)	21, [7, 57]
Catheterization for CHD (intervention)	0, [0, 0]
Intra-aortic balloon pumping	11, [4, 28]
Percutaneous cardiopulmonary support	2, [0, 7]
Left ventricular assist device	0, [0, 0]
Pacemaker implantation	26, [14, 41]
Pacemaker implantation (exchange)	11, [6, 20]
ICD implantation	0, [0, 5]
ICD implantation (exchange)	0, [0, 1]
Catheter ablation	3, [0, 42]
CRT	0, [0, 0]
CRT defibrillator implantation	0, [0, 4]
Cardiac surgery	8, [0, 83]
CABG (on-pump)	0, [0, 12]
CABG (off-pump)	0, [0, 11]
Surgery (valvuloplasty)	0, [0, 9]
Surgery (valve replacement)	1, [0, 23]
Surgery of thoracic aortic dissection	0, [0, 8]
Surgery of thoracic aortic aneurysm	0, [0, 8]
Surgery (abdominal aorta+peripheral artery)	7, [0, 54]
Thoracic endovascular aortic repair	0, [0, 2]
Abdominal aortic stent-grafting	0, [0, 10]
Surgery of CHD	0, [0, 1]

AMI, acute myocardial infarction; CABG, coronary artery bypass grafting; CHD, congenital heart disease; CRT, cardiac resynchronization therapy; ICD, implantable cardioverter defibrillator; PCI, percutaneous coronary intervention.

for individual informed consent based on the "opt-out" principle applied. Each hospital anonymized patients' ID using code-change equations applied to the original DPC data, which was sent to the Ministry of Health, Labour and Welfare, and NCVC managed the database. NCVC notified patients that their information was being collected by this study through homepages or posters in each hospital.

Patients could choose to have their information excluded (opt-out).

### Statistical Analysis

All normally distributed continuous variables are presented as mean±SD and the unpaired t-test was used to compare groups. All non-normal distributed continuous variables are presented as median and quartiles (median, [interquartile range: IQR]) and the Wilcoxon signed-rank test was used to compare groups. Non-continuous and categorical variables are presented as percentages and compared using the chi-square test or Fisher's exact test. A P-value <0.05 was considered statistically significant. The analyses were performed using SAS<sup>®</sup>9.4 (SAS Institute Inc., Cary, NC, USA) and JMP<sup>®</sup>13 (SAS Institute Inc.).

We categorized hospitals into quartiles based on the factor score: quartile 1 (very low), quartile 2 (low), quartile 3 (high), and quartile 4 (very high). Each factor level was modelled in quartiles with odds ratios (ORs) referring to the relative risk between Q1 and Q4. To determine the

Table 4. Factor Loading of Items of Practice Volume and Structural Indicators After Exploratory Factor Analysis Using Oblique   Rotation and Quartimin Method							
	Factor						
	1	2	3	4	5		
1. Interventional cardiology							
Elective PCI	0.928	0.059	-0.035	-0.056	0.026		
Emergency PCI	0.916	0.102	-0.014	-0.029	-0.008		
Emergency PCI for AMI	0.906	0.084	-0.004	-0.038	-0.018		
Drug-eluting stents (per patient)	0.884	0.033	0.020	-0.139	0.026		
Coronary angiography	0.880	0.042	-0.005	-0.004	0.023		
Intravascular ultrasound	0.850	0.047	0.014	-0.018	-0.036		
Drug-eluting stents (per lesion)	0.796	-0.054	0.009	-0.082	-0.040		
Bare metal stents (per patient)	0.775	0.048	0.070	-0.094	0.059		
No. of AMI	0.771	0.150	-0.040	0.021	0.022		
Plain old balloon angioplasty (per patient)	0.741	0.074	0.016	-0.098	0.047		
Bare metal stents (per lesion)	0.735	-0.021	0.067	-0.075	-0.007		
Pacemaker implantation	0.695	0.165	-0.022	0.124	0.013		
Plain old balloon angioplasty (per lesion)	0.682	0.013	0.015	-0.085	0.002		
Intra-aortic balloon pumping	0.639	0.321	-0.024	0.053	0.030		
Ventriculography	0.601	-0.019	0.095	0.001	-0.051		
No. of hospitalized patients in cardiology department	0.557	0.063	-0.087	0.166	0.103		
Percutaneous transluminal angiography (per patient)	0.537	0.238	-0.056	-0.049	0.079		
Coronary computed tomography angiography	0.507	0.146	-0.016	-0.011	0.133		
Aortography	0.487	0.015	0.084	0.023	0.024		
Inferior vena cava filter placement	0.468	0.106	0.066	0.110	0.007		
Transthoracic echocardiography	0.449	0.167	0.057	0.190	0.122		
No. of admissions to CCU	0.448	0.231	0.053	0.023	0.025		
Pacemaker implantation (exchange)	0.419	0.229	0.017	0.203	0.005		
2. Cardiovascular surgery	L						
No. of hospitalized patients (cardiovascular surgery)	0.112	0.902	0.042	-0.139	0.023		
Surgery (valve replacement)	0.059	0.894	0.004	0.057	0.052		
Cardiac surgery	0.064	0.892	0.046	0.002	0.054		
No. of beds in cardiovascular surgery department	0.097	0.873	0.054	-0.116	0.035		
Surgery (abdominal aorta+peripheral artery)	0.098	0.854	0.021	-0.088	0.034		
Average length of hospital stay (cardiovascular surgery), days	0.145	0.835	0.006	-0.208	0.017		
CABG (on-pump)	0.068	0.834	-0.011	-0.018	0.075		
CABG (off-pump)	0.031	0.794	-0.012	0.094	0.049		
No. of cardiovascular surgeons	0.048	0.791	0.154	0.050	0.055		
Surgery (valvuloplasty)	0.009	0.783	0.057	0.120	0.085		
Surgery of thoracic aortic dissection	0.010	0.771	0.052	0.114	0.092		
Surgery of thoracic aortic aneurysm	-0.003	0.755	0.071	0.155	0.109		
Abdominal aortic stent-grafting	-0.005	0.650	0.108	0.126	0.088		
Rotablational atherectomy (per patient)	0.112	0.585	-0.063	0.166	0.105		
Rotablational atherectomy (per lesion)	0.149	0.555	-0.051	0.160	0.052		
Thoracic endovascular aortic repair	-0.071	0.538	0.115	0.253	0.106		
Percutaneous cardiopulmonary support	0.281	0.460	0.039	0.122	0.049		

(Table 4 continued the next page.)

	Factor					
	1	2	3	4	5	
3. Pediatric cardiology						
No. of hospitalized patients (pediatric cardiology)	0.022	-0.026	0.998	-0.051	-0.012	
No. of pediatric cardiologists	-0.001	-0.030	0.973	-0.019	-0.005	
No. of beds in pediatric cardiology department	0.015	-0.035	0.939	-0.056	-0.001	
Average length of hospital stay (pediatric cardiology), days	0.049	-0.024	0.864	-0.127	-0.009	
Catheterization for CHD (intervention)	-0.013	-0.006	0.657	0.092	0.063	
Catheterization for CHD (diagnosis)	0.090	0.097	0.618	0.167	0.044	
Surgery of CHD	-0.048	0.326	0.592	0.093	0.052	
4. Electrophysiology				-		
ICD implantation (exchange)	-0.064	0.312	0.137	0.574	0.060	
ICD implantation	-0.036	0.484	0.039	0.558	0.051	
CRT defibrillator implantation	-0.050	0.479	0.027	0.524	0.087	
Signal-averaged ECG	0.022	0.166	0.109	0.500	0.000	
Catheter ablation	0.122	0.350	0.004	0.492	0.052	
No. of cardiologists	0.293	0.154	0.139	0.453	0.107	
CRT	-0.049	0.336	0.088	0.436	0.065	
5. Cardiac rehabilitation						
Total no. of cardiac rehabilitation patients	-0.063	0.091	-0.036	-0.125	1.008	
Cardiac rehabilitation (new enrollment cases)	-0.051	0.107	-0.044	-0.104	1.004	
Dispersibility	23.68	25.42	12.94	16.64	11.42	
Contribution ratio	26.31	28.24	14.38	18.49	12.69	
Cumulative contribution ratio	26.31	54.55	68.93	87.42	100.12	

ECG, electrocardiography. Other abbreviations as in Tables 1,2.

association between the factors and 7-day, 30-day, and in-hospital mortality rates in patients hospitalized for HF, we used a univariate analysis and multivariable logistic regression model. We chose hospital HF case volume, including acute decompensated HF (ADHF) and chronic HF (CHF), as fixed effects, and age, sex, Charlson comorbidity index, NYHA class for HF as patient effects and factors chosen by exploratory factor analysis. To confirm the results, we performed 2 sensitivity analyses using a representative example from each factor with a large factor loading and using another group that excluded the patients without oral medications for HF.

## **Results**

## Baseline Characteristics of the Study Patients (Table 1)

We studied 198,861 HF patients (53% male) with an age of 77.8 $\pm$ 12.9 (mean $\pm$ SD) years. The NYHA functional class was I in 7.9%, II in 28.0%, III in 33.4%, and IV in 30.7% of patients. Among them, 51% of HF patients had hypertension, 26% had diabetes mellitus, 31% had CAD, and 5.7% had cardiomyopathy (**Table 1**). In terms of medications at discharge, 48% of the patients took renin-angiotensin system (RAS) inhibitors, 47% took  $\beta$ -blockers, 48% took loop diuretics, and 35% took spironolactone.

# Baseline Characteristics of the Study Hospitals (Tables 2,3)

Patients were hospitalized in 683 JROAD-DPC-participating hospitals, in which a median of 158 [101, 234] patients are admitted annually for HF. A coronary care unit (CCU) was equipped in 84% of the hospitals; 59% of the hospitals had a cardiovascular surgery department, 22% had a pediatric cardiology department, 98% had a cardiac catheterization laboratory, and 49% had a cardiac rehabilitation program (**Table 2**).

The annual volume of the therapeutic practices is shown in **Table 3**. The numbers of patients who underwent emergency and elective PCI were 50 [23, 88] and 125 [60, 212] (median [IQR]), respectively. Implantation of a cardioverter defibrillator was performed in 0 [0, 5] cases. The number of new enrollments in the cardiac rehabilitation program was 0 [0, 195].

## Hospital Practice Factors Determined by Exploratory Factor Analysis

Table 4 shows the exploratory factor analysis results for hospitals with the highest contribution to the factors by factor loading. There was a reduction in variable numbers from the original 90 variables to 5 composite factors: (1) "Interventional cardiology" factor with strong loadings of items such as coronary intervention and angiography, (2) "Cardiovascular surgery" factor with positive loadings of items such as number of patients hospitalized for cardiovascular surgery, (3) "Pediatric cardiology" factor comprising items such as number of hospitalized pediatric patients, (4) "Electrophysiology" factor comprising items such as implantation of defibrillator and catheter ablation, and (5) "Cardiac rehabilitation" factor comprising the volume of cardiac rehabilitation patients. The combination of these 5 factors explained approximately 100% of the variance in the original data: factor 1, 26.3%; factor 2, 28.2%; factor 3, 14.4%; factor 4, 18.5%; and factor 5, 16.7%. There were only modest correlations between each factor (Supplementary Table 2), because we interpreted the correlation to be strong if the values were  $\geq 0.7$ .

Table 5. OR and 95% CI of Mortality Rates in Patients With HF According to Hospital Practice Factors								
			7-day m	7-day mortality 30-day mortality		In-hospital	mortality	
Quartile	Hospitals (n)	Patients (n)	Multiv	Multivariate Multivariate Mult		Multivariate		riate
	()	(,	OR (95% CI)	P for trend	OR (95% CI)	P for trend	OR (95% CI)	P for trend
Factor 1: Interve	ntional cardiol	ogy						
Q1	170	27,449	Ref.	<0.0001	Ref.	<0.0001	Ref.	0.0158
Q2	171	41,614	0.988 (0.901–1.082)		1.020 (0.954–1.091)		0.979 (0.923–1.038)	
Q3	171	54,719	1.192 (1.072–1.326)		1.105 (1.022–1.195)		0.998 (0.932–1.069)	
Q4	171	75,079	1.322 (1.174–1.488)		1.167 (1.070–1.272)		1.037 (0.962–1.118)	
Factor 2: Cardio	vascular surge	ery						
Q1	170	36,094	Ref.	0.4016	Ref.	0.4071	Ref.	0.2506
Q2	171	37,484	0.868 (0.802–0.939)		0.917 (0.866–0.972)		0.916 (0.871–0.964)	
Q3	171	55,178	0.947 (0.869–1.031)		1.008 (0.947–1.074)		1.041 (0.985–1.100)	
Q4	171	70,105	0.907 (0.815–1.009)		0.986 (0.912–1.065)		0.989 (0.924–1.059)	
Factor 3: Pediatr	ic cardiology							
Q1	170	34,042	Ref.	<0.0001	Ref.	<0.0001	Ref.	<0.0001
Q2	171	38,881	0.882 (0.817–0.952)		0.900 (0.851–0.953)		0.879 (0.836–0.924)	
Q3	171	54,357	0.660 (0.609–0.715)		0.732 (0.690–0.777)		0.757 (0.718–0.798)	
Q4	171	71,581	0.586 (0.529–0.648)		0.677 (0.628–0.729)		0.684 (0.641–0.731)	
Factor 4: Electro	physiology							
Q1	170	60,005	Ref.	<0.0001	Ref.	<0.0001	Ref.	<0.0001
Q2	171	47,375	0.953 (0.888–1.022)		1.004 (0.954–1.057)		0.998 (0.954–1.044)	
Q3	171	40,486	0.829 (0.769–0.894)		0.878 (0.831–0.928)		0.914 (0.871–0.960)	
Q4	171	50,995	0.844 (0.786–0.906)		0.876 (0.832–0.923)		0.895 (0.855–0.937)	
Factor 5: Cardia	c rehabilitation	1						
Q1	170	52,569	Ref.	<0.0001	Ref.	<0.0001	Ref.	<0.0001
Q2	171	30,485	0.798 (0.728–0.874)		0.862 (0.805–0.923)		0.898 (0.846–0.953)	
Q3	171	50,825	0.813 (0.759–0.871)		0.879 (0.835–0.924)		0.927 (0.887–0.970)	
Q4	171	64,982	0.707 (0.661–0.756)		0.832 (0.792–0.873)		0.872 (0.835–0.910)	

ORs and 95% CIs of mortality rates in patients with heart failure (HF) among 4 groups defined by factor analysis. The 5 factor clusters: "Interventional cardiology", "Cardiovascular surgery", "Pediatric cardiology", "Electrophysiology" and "Cardiac rehabilitation". Quartiles, based on the factor score: quartile 1 (Q1: very low), quartile 2 (Q2: low), quartile 3 (Q3: high), quartile 4 (Q4: very high). Multivariate, adjusted for age, sex, Charlson comorbidity index, NYHA class for HF, hospital case volume of HF and 5 factor clusters. CI, confidence intervals; NYHA, New York Heart Association; OR, odds ratios.

### Association Between Hospital Practice Factors and Mortality

The 7-day, 30-day, and in-hospital mortality were 4.0%, 8.0%, and 10.8%, respectively (**Table 2**). The association among the 5 hospital practice factors clustered using the exploratory factor analysis was assessed by logistic regression analysis (**Table 5**).

The "Pediatric cardiology", "Electrophysiology", and "Cardiac rehabilitation" factors were associated with lower 7-day, 30-day, and in-hospital mortality in HF patients. In contrast, the "Interventional cardiology" factor was associated with higher 7-day and 30-day mortality. The "Cardiovascular surgery" factor did not show any significant association with mortality.

## **Sensitivity Analysis**

In order to confirm these results, we performed a sensitivity analysis using representative examples with large factor loadings for each factor (**Table 6**). "Elective PCI" was selected as a representative example from the "Interventional cardiology" factor and "ICD [implantable cardioverter defibrillator] implantation" was selected from the "Electrophysiology" factor. The presence or absence of a department of cardiovascular surgery, a department of pediatric cardiology, and cardiac rehabilitation program were used for the analysis, because 41%, 78% and 51% of hospitals did not have a department of cardiovascular surgery, department of pediatric cardiology and cardiac rehabilitation programs, respectively. Therefore, the ORs

Table 6. OR and 95% CI of Mortality Rates in Patients With HF Defined by Representative Survey Items									
		<b>-</b>	7-day mortality		30-day m	ortality	In-hospital	mortality	
Quartile	Hospitals (n)	Patients (n)	Multiva	ariate	Multiva	Multivariate		riate	
	()	(1)	OR (95% CI)	P for trend	OR (95% CI)	P for trend	OR (95% CI)	P for trend	
Elective PCI									
Q1	168	31,041	Ref.	0.5197	Ref.	0.3745	Ref.	0.0114	
Q2	172	42,875	1.034 (0.956–1.117)		1.016 (0.959–1.075)		1.009 (0.960–1.061)		
Q3	169	53,010	0.994 (0.914–1.080)		0.977 (0.919–1.039)		0.946 (0.896–0.998)		
Q4	174	71,935	1.042 (0.954–1.139)		0.983 (0.921–1.049)		0.946 (0.893–1.002)		
Cardiac surgery									
No	302	65,194	Ref.	<0.0001	Ref.	<0.0001	Ref.	<0.0001	
Yes	381	133,667	1.143 (1.680–1.223)		1.151 (1.095–1.210)		1.120 (1.072–1.171)		
Pediatric cardiol	ogy								
No	572	160,663	Ref.	0.0907	Ref.	0.0005	Ref.	0.0006	
Yes	111	38,198	0.937 (0.875–1.004)		0.913 (0.868–0.960)		0.924 (0.884–0.965)		
ICD implantation									
No	426	98,640	Ref.	<0.0001	Ref.	<0.0001	Ref.	<0.0001	
Yes	257	100,221	0.844 (0.787–0.905)		0.853 (0.810–0.898)		0.857 (0.819–0.897)		
Cardiac rehabilit	ation								
No	345	85,486	Ref.	<0.0001	Ref.	<0.0001	Ref.	<0.0001	
Yes	338	113,375	0.811 (0.771–0.854)		0.906 (0.872–0.941)		0.935 (0.905–0.967)		

ORs and 95% CIs of mortality rates in patients with HF among 4 groups defined by representative survey items of 5 factor clusters for sensitivity analysis. We selected "elective PCI" from "Interventional cardiology", "performing cardiac surgery (cardiac surgery; yes)" from "Cardiovascular surgery", "presence of department of pediatric cardiology (pediatric cardiology; yes)" from "Pediatric cardiology", "performing ICD implantation (ICD implantation; yes)" from "Electrophysiology", and "presence of program of cardiac rehabilitation (cardiac rehabilitation; yes)" from "Cardiac surgery (article cardiology)", "performing ICD implantation (ICD implantation, yes)" from "Electrophysiology", and "presence of program of cardiac rehabilitation (cardiac rehabilitation; yes)" from "Cardiac rehabilitation", Quartiles, based on the factor score: quartile 1 (Q1: very low), quartile 2 (Q2: low), quartile 3 (Q3: high), quartile 4 (Q4: very high) for the analysis of "elective PCI". Multivariate, adjusted for age, sex, Charlson comorbidity index, NYHA class for HF, Hospital case volume of HF. Abbreviations as in Tables 2,3,5.

were estimated according to the presence of these items, instead of each factor. The presence of a department of pediatric cardiology, performing ICD implantation and the presence of a program of cardiac rehabilitation were associated with lower mortality. In contrast, "Performing cardiac surgery" was associated with higher mortality. "Elective PCI" was associated with lower in-hospital mortality; however, the reason why the number of elective PCIs was a hospital factor affecting the short-term mortality of HF could not be explained. These sensitivity analyses demonstrated a similar tendency to the results of the factor analysis, so we confirmed this model.

Finally, we performed another sensitivity analysis using patient subgroups that were prescribed  $\geq 1$  medications among RAS inhibitors,  $\beta$ -blockers, mineralocorticoid receptor antagonists and loop diuretics during hospitalization or at discharge (**Table 7**). The baseline characteristics of this subgroup were shown in **Supplementary Table 3**, and the results of multivariate logistic regression analyses revealed factors 2, 3, 4 and 5 showed the same tendency, and factor 1 did not show any significant difference, which was consistent with our main analysis.

### Discussion

In the present study, we demonstrated that the clustering of 90 survey items of hospital performance sampled using the JROAD database was feasible using exploratory factor analysis. This approach could be useful to explore the interaction between different hospital practice factors and the mortality of HF patients. The present analysis found that hospital practice factors such as "Pediatric cardiology", "Electrophysiology", and "Cardiac rehabilitation" were associated with lower mortality in hospitalized HF patients, whereas "Interventional cardiology" factor was associated with higher mortality.

Numerous previous studies have demonstrated the prognostic impact of various demographic, clinical, and biochemical markers in patients with HF.<sup>2-6</sup> In terms of hospital features, the relationship between hospital case volume and outcomes in patients with HF has been shown.<sup>79</sup> However, it is unlikely that a single marker of hospital performance, such as hospital case volume, could completely reflect the characteristics of hospital care systems.<sup>14-17</sup> Thus, our statistical analysis approach could increase our understanding of real hospital practice factors and predict outcomes of patients with HF.

## Assessment of Hospital Practice by Exploratory Factor Analysis

Hospital practice factors involved in HF management are complicated, and statistical assessment of hospital factors is problematic because it involves multiple practices. Exploratory factor analysis may be useful to assess the

Table 7. OR and 95% CI of Mortality Rates in HF Patients With ≥1 Medications for HF in Sensitivity Analysis								
		<b>.</b>	7-day m	ortality	30-day mortality		In-Hospital	mortality
Quartile	Hospitals (n)	Patients (n)	Multiv	Multivariate		riate	Multiva	riate
	(,	(,	OR (95% CI)	P for trend	OR (95% CI)	P for trend	OR (95% CI)	P for trend
Factor 1: Interve	ntional cardiol	ogy						
Q1	170	24,783	Ref.	0.1447	Ref.	0.1603	Ref.	0.2756
Q2	171	38,155	1.014 (0.900–1.142)		1.036 (0.960–1.119)		0.980 (0.919–1.045)	
Q3	171	50,265	1.041 (0.904–1.200)		1.041 (0.952–1.138)		0.934 (0.866–1.006)	
Q4	171	70,001	1.139 (0.975–1.331)		1.072 (0.972–1.183)		0.949 (0.873–1.030)	
Factor 2: Cardio	vascular surge	ry						
Q1	170	32,862	Ref.	0.7047	Ref.	0.0944	Ref.	0.0658
Q2	171	34,229	0.885 (0.798–0.981)		0.933 (0.873–0.997)		0.927 (0.877–0.981)	
Q3	171	50,522	0.944 (0.843–1.057)		1.012 (0.941–1.087)		1.051 (0.989–1.117)	
Q4	171	65,591	1.057 (0.920–1.215)		1.061 (0.971–1.158)		1.039 (0.965–1.119)	
Factor 3: Pediati	ric cardiology							
Q1	170	30,623	Ref.	<0.0001	Ref.	<0.0001	Ref.	<0.0001
Q2	171	35,466	0.901 (0.813–0.997)		0.911 (0.853–0.973)		0.886 (0.838–0.936)	
Q3	171	50,221	0.761 (0.683–0.849)		0.788 (0.736–0.845)		0.806 (0.760–0.854)	
Q4	171	66,894	0.676 (0.589–0.776)		0.737 (0.676–0.803)		0.733 (0.682–0.788)	
Factor 4: Electro	physiology							
Q1	170	55,263	Ref.	0.2131	Ref.	0.0029	Ref.	0.0045
Q2	171	43,592	1.030 (0.938–1.131)		1.040 (0.981–1.103)		1.021 (0.971–1.073)	
Q3	171	36,965	0.920 (0.832–1.017)		0.928 (0.871–0.988)		0.957 (0.907–1.009)	
Q4	171	47,384	0.938 (0.854–1.032)		0.927 (0.873–0.983)		0.939 (0.893–0.988)	
Factor 5: Cardia	c rehabilitation	I						
Q1	170	48,267	Ref.	0.0002	Ref.	0.0069	Ref.	0.0270
Q2	171	27,808	0.986 (0.874–1.112)		0.951 (0.880–1.028)		0.965 (0.904–1.031)	
Q3	171	46,916	0.942 (0.859–1.033)		0.952 (0.898–1.009)		0.988 (0.940–1.038)	
Q4	171	60,213	0.839 (0.766–0.919)		0.929 (0.878–0.983)		0.952 (0.908–0.999)	

ORs and 95% CIs of mortality rates in HF patients with ≥1 medications for HF in sensitivity analysis among 4 groups. The 5 factor clusters: "Interventional cardiology", "Cardiovascular surgery", "Pediatric cardiology", "Electrophysiology" and "Cardiac rehabilitation". Quartiles, based on the factor score: quartile 1 (Q1: very low), quartile 2 (Q2: low), quartile 3 (Q3: high), quartile 4 (Q4: very high). Multivariate, adjusted for age, sex, Charlson comorbidity index, NYHA class for HF, hospital case volume of HF and 5 factor clusters. Abbreviations as in Tables 2,5.

contributory role of the various factors involved in the management of HF patients. This multivariable statistical technique is a standard approach for investigations when multiple, highly correlated variables are involved.

Exploratory factor analyses are widely used in the social sciences,<sup>18,19</sup> and has been applied to the analysis of multiple biomarkers in studies of cardiovascular medicine.<sup>11–13</sup> Tziakas et al used an exploratory factor analysis approach and reported that markers reflecting anti-inflammatory mechanisms were better prognostic markers in patients with an acute coronary syndrome.<sup>11</sup> Manhenke et al demonstrated that the clustering of 37 circulation biomarkers using exploratory factor analysis was useful to explore the biological interactions between different biomarkers in

cardiovascular disease.<sup>12</sup> Egnot et al demonstrated that high inflammatory and coagulation markers were better associated with femoral atherosclerosis using exploratory factor analysis.<sup>13</sup>

The present study is the first to identify the factors of multiple hospital survey items in the management of HF, and their prognostic ability. Importantly, we have shown that this approach can also be applied to structural indicators.

#### **Composition of Factor Clusters**

The purpose of our study was to determine the institutional characteristics that define the short-term prognosis of HF. We categorized 90 survey items of hospital performance

into 5 factors comprising "Interventional cardiology", "Cardiovascular surgery", "Pediatric cardiology", "Electrophysiology" and "Cardiac rehabilitation". Factor analysis is a method of finding new factors by detecting the strength of the relationship of factor loadings from multiple collinear items. Using this approach, we can aggregate a number of factors that are highly multicollinear and have strong entanglement with each other, which is called "reducing the dimensions". The factor name was determined by referring to the factor loadings obtained from factor analysis. As a quality indicator for HF has not yet been established, this method selected objectively rather than arbitrarily. In the sensitivity analysis, the representative item of each factor was selected by referring to the factor loading quantity, and a similar tendency as this study was shown.

The model extracted by exploratory factor analysis was clinically feasible and could represent a reasonably strong model. This study was not able to explain the composition of the factor clusters and underlying conditions; however, our findings confirmed several relationship patterns in HF care.

#### Prognostic Information

Hospital practice factors such as "Pediatric cardiology," "Electrophysiology," and "Cardiac rehabilitation" were associated with lower mortality in hospitalized HF patients. The "Pediatric cardiology" factor was associated with better prognosis for HF. However, we should interpret the results carefully because the number of hospitals that had pediatric cardiology departments was 22% of the total and 99% of interventions belonged to quartile 4. Therefore, we consider the direct prognostic influence of this factor may be limited. The higher "Pediatric cardiology" activity may have been related to the number of hospital beds (quartile 1; 292 $\pm$ 102 vs. quartile 4; 639 $\pm$ 259) and the number of cardiologists (quartile 1; 4.2 $\pm$ 1.9 vs. quartile 4; 15.2 $\pm$ 13.0), because pediatric cardiologists are highly specialized.

It showed the higher factor score of "Electrophysiology" was associated with better early outcomes in HF. A large number of HF patients are complicated with atrial fibrillation (AF),<sup>20,21</sup> and HF patients with AF have a poor prognosis.<sup>22,23</sup> Many reports have shown that a single non-medication HF treatment improved prognosis in the chronic phase of HF, such as ICD,<sup>24</sup> cardiac resynchronization therapy (CRT),<sup>25,26</sup> or catheter ablation.<sup>27,28</sup> AF and ventricular tachycardia are common arrhythmias in HF patients, so their management is essential for better outcomes. Higher device implantation activity, such as implantation of pacemaker, ICD and CRT, and catheter ablation, is reasonable to improve the management of HF and reduce cardiovascular deaths. In this study, we created a new complex variable called "Electrophysiology" for existing variables in the JROAD-DPC database using exploratory factor analysis; the high hospital activity of the total "Electrophysiology" factor improved early outcomes in HF. It is important to recognize that the results were not only influenced by the treatment itself and our analysis did not conclude that the patients who underwent device implantation and catheter ablation had better outcomes.

Higher "Cardiac rehabilitation" scores were associated with lower early mortality in HF. "Cardiac rehabilitation" has been shown to improve the prognosis in HF by ExTraMATCH (Exercise Training MetaAnalysis of Trials in patients with Chronic Heart failure)<sup>29</sup> and HF-ACTION (Heart Failure: A Controlled Trial Investigating Outcomes of exercise training).<sup>30</sup> Long-term cardiac rehabilitation improves exercise tolerance and quality of life by reducing inflammatory cytokines, angiotensin II, and B-type natriuretic peptide, and by normalizing autonomic derangement and neurohumoral activation, thereby reducing the rate of hospitalization for HF and improving the prognosis in HF.<sup>31</sup> Moreover, rehabilitation during the early phase of hospitalization improves the rates of disuse syndrome, which decrease cardiac function, by improving general condition and muscular strength.<sup>32</sup> No randomized clinical trial has shown that cardiac rehabilitation improves inhospital mortality in HF; however, the present findings suggest that cardiac rehabilitation activity is related to better early outcomes in HF patients.

In contrast, hospital practice factors such as "Interventional cardiology" were associated with higher mortality in hospitalized HF patients. One study reported that the introduction of a CCU reduced mortality rates even though the number of hospitalized cases and their severity increased.33 The severity of hospitalized HF patients might rise with the higher score of "Interventional cardiology", because as the quartile of factor 1 went up, the rate of presence of a CCU also tended to increase (Q1 60%, Q2 83%, Q3 95%, Q4 98%). Other items associated with emergency hospitalization, such as emergency PCI, has the larger factor loading score in factor 1. Therefore, factor 1 may be related with higher mortality. On the other hand, there is another fact that some of the hospitals performing many coronary interventions are not always equipped with cardiac rehabilitation and electrophysiological procedures, which may result in the outcome of HF patients regardless of the involvement of ischemic heart disease. For example, 35% of high-volume centers for cardiac intervention (Q4 of factor 1) are not equipped for cardiac rehabilitation.

The "Cardiovascular surgery" factor was not associated with short-term outcomes in HF, possible because there were not many patients who needed cardiac surgery such as urgent CABG and valve replacement in the acute phase of hospitalization. Most highly invasive cardiac surgeries are performed during the stable phase of HF.

#### Study Limitations

The findings of the present study should be interpreted in light of certain limitations. First, the purpose of this study was not to promote a single set of hospital factors as a superior "package" for individual patient prognosis, but to extend our understanding of the interdependence of hospital practices by the prognostic information of the clustered hospital factors. Therefore, the clinical implications of these findings should be considered with caution. Second, we hypothesized that patient outcomes are determined by hospital factors. However, hospital performance factors other than hospital case volume that could improve the in-hospital mortality in HF have not been examined. Statistical models combining hospital practice factors and conventional patient factors in the JROAD-DPC database might provide superior prognostic information. Third, medical information, including hemodynamics, clinical conditions, the severity of HF at admission and long-term prognosis, was not investigated in this study. Therefore, the information on patients' factors was limited and it was also difficult to evaluate the achievement of guideline-based therapies for HF. Medication using  $\beta$ -blockers and RAS inhibitors prescription at discharge in this dataset was relatively low as reported.8 The average age of patients in

this study was 77.8 years, which was similar to other large registries in Japan in the past; in ATTEND (n=4,842, 2007-2011) it was 73 years, in WET-HF (n=2,551, 2011-2015) it was 75 years, and in REALITY-AHF (n=1,682, 2014–2015) it was 78 years.<sup>34</sup> Because the ratios of patients with ejection fraction (EF) >40 were 47%, 59%, and 63%, respectively, we assumed the percentage of patients with HF with preserved EF (HFpEF) was probably also high in the patients of this study. Therefore, we speculate a high percentage of HFpEF patients may explain the low prescription rate of RAS inhibitors and  $\beta$ -blockers. Fourth, although we used the same criteria as in a previous report<sup>10</sup> for creating the dataset, the reliability and certainty of HF diagnosis from International Classification of Diseases-10 codes need to be clarified in the future. Finally, exploratory factor analyses were applied to only a limited number of facilities included in the JROAD-DPC. We cannot apply our findings to other non-certified hospitals. Larger prospective trials are required to further explore the utility of exploratory factor analysis for this application.

#### Conclusions

Clustering of multiple hospital factors using exploratory factor analysis was feasible and could be useful for exploring the interactions among different hospital practices in HF care. Hospital practice factors, including various cardiovascular care factors, were associated with mortality of HF patients. Hospital practice factors related to pediatric cardiology, electrophysiology, and cardiac rehabilitation may be associated with lower mortality rates in hospitalized HF patients.

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#### **Supplementary Files**

Please find supplementary file(s); http://dx.doi.org/10.1253/circj.CJ-19-0759