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ORIGINAL ARTICLE
Epidemiology

Characteristics and Outcomes of Super-Elderly Patients (Aged ≥90 Years) Hospitalized for Heart Failure

— Analysis of a Nationwide Inpatient Database —

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Background: Although the aged population is increasing in developed countries, clinical evidence on super-elderly heart failure (HF) patients is scarce. This study determined the characteristics and outcomes of Japanese hospitalized super-elderly HF patients (aged ≥90 years) using a nationwide inpatient database.

Methods and Results: A comprehensive analysis was performed of 447,818 HF patients in the Diagnosis Procedure Combination database who were hospitalized and discharged between January 2010 and March 2018. Among the study population, 243,028 patients (54.3%) were aged ≥80 years and 64,628 patients (14.4%) were aged ≥90 years. The percentage of elderly patients increased over time. Elderly patients were more likely to be female and had a higher New York Heart Association functional class at admission. Invasive and advanced procedures were rarely performed, whereas infectious complications were more common in patients with older age. Length of hospital stay and in-hospital mortality increased with age. Multivariable logistic regression analysis fitted with a generalized estimating equation showed higher in-hospital mortality in patients aged ≥80 and ≥90 years (odds ratios 1.99 and 3.23, respectively) compared with those aged <80 years.

Conclusions: The number of hospitalized super-elderly HF patients has increased, and these patients are associated with worse clinical outcomes. The results of this study may be useful in establishing an optimal management strategy for super-elderly HF patients in the era of HF pandemic.

Key Words: Elderly; Epidemiology; Heart failure; Super-elderly; Outcomes

An aging society and the associated increases in cardiovascular diseases are common healthcare concerns in developed countries.[1,2] Because aging is associated with heart failure (HF),[3–5] the number of elderly patients with HF has increased in developed countries. Most previous studies on elderly HF patients defined "elderly" patients as those ≥80 years of age.[6–8] However, the number of patients aged >90 years is also increasing in super-aging societies, and clinical evidence for super-elderly patients is important. Although earlier studies already showed that the percentage of elderly HF patients was increasing[9] and older age was associated with adverse clinical outcomes in patients with HF,[6–8,10,11] clinical data on the prevalence of super-elderly HF patients and the clinical outcomes of super-elderly HF patients are scarce. In this study we explored the outcomes of elderly patients hospitalized for worsened HF, particularly super-elderly patients aged ≥90 years, using a nationwide inpatient database. Considering the rapid increase in the proportion of the aged population in developed countries, the critical epidemiological condition so called "HF pandemic" is approaching; thus, presenting real-world data on super-elderly HF patients is critical at this time.

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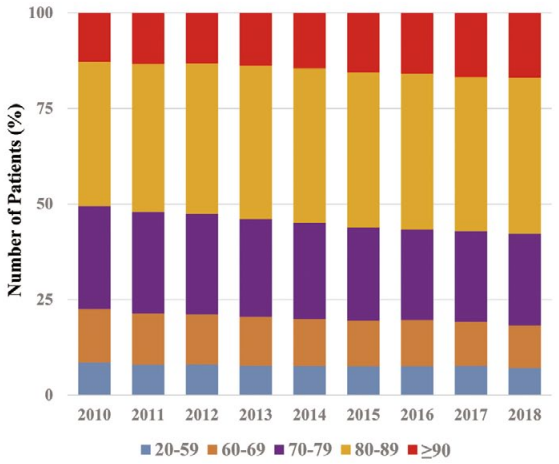
(A) Trends in the Age Distribution of Patients Hospitalized for Heart Failure



(B) Serial Changes in the Number of Patients in Each Age Category

	2010	2011	2012	2013	2014	2015	2016	2017	2018	Overall
20-59 Years	2,377	4,952	5,384	5,129	5,458	5,851	3,279	2,035	400	34,865
60-69 Years	3,837	8,317	8,791	8,516	8,746	9,246	5,262	3,068	636	56,419
70-79 Years	7,420	16,591	17,654	16,976	18,021	18,908	10,288	6,293	1,355	113,506
80-89 Years	10,418	24,054	26,386	26,555	28,868	31,458	17,654	10,691	2,316	178,400
≥ 90 Years	3,522	8,335	8,857	9,202	10,340	12,068	6,893	4,453	958	64,628
Overall	27,574	62,249	67,072	66,378	71,433	77,531	43,376	26,540	5,665	447,818

Figure 1. (**A**) Trends in the age distribution of patients hospitalized for heart failure and (**B**) serial changes in the number of patients in each age category.

Methods

Study Design and Data Source

The Diagnosis Procedure Combination (DPC) database is a nationwide inpatient database in Japan.[12,13] Briefly, the DPC database includes administrative claims and clinical data for approximately 7 million hospitalized patients per year from approximately 1,000 participating hospitals. The main diagnosis, comorbidities at admission, and complications during hospitalization are recorded using the International Classification of Disease and Related Health Problems 10th Revision (ICD-10) codes. In this study, we reviewed data for 466,921 patients aged ≥20 years with New York Heart Association (NYHA) Class ≥II, admitted and discharged between January 2010 and March 2018 with the main discharge diagnosis of HF defined by ICD-10 codes I50.0, I50.1, and I50.9. Patients with a length of hospital stay ≤2 days (n=15,270) and those who underwent major procedures under general anesthesia (n=3,833) were excluded from the study. Thus, the final number of patients analyzed in this study was 447,818.

Ethical Considerations

This study was approved by the Institutional Review Board of the University of Tokyo [3501-(3)]. This study was conducted in accordance with the Declaration of Helsinki. Because of the anonymous nature of the database, the requirement for informed consent was waived.

Statistical Analysis

Categorical and continuous data are presented as numbers with percentages and as the median with interquartile range (IQR). Categorical and continuous variables were compared using Chi-squared tests and 1-way analysis of variance (ANOVA). The association of age category with in-hospital mortality was evaluated using a multivariable logistic regression analysis with adjustment for other covariates, while also adjusting for within-hospital clustering using a generalized estimating equation.[14] Subgroup analyses were conducted according to sex and geographic region. For analysis on geographic region, the study population was divided into 7 regions, namely the Northern, Central, Kanto, Tokyo, Kinki, Chugoku-Shikoku, and Kyushu regions, according to 47 prefectures in Japan. Two-sided

Table 1. Characteristics of the Study Population

	Age (years)			P-value
	<80 (n=204,790)	80–89 (n=178,400)	≥90 (n=64,628)	
Age (years)	71 [13]	84 [5]	92 [4]	<0.001
Age group (years)				
20–59	34,865 (17.0)	–	–	
60–69	56,419 (27.5)	–	–	
70–79	113,506 (55.4)	–	–	
80–89	–	178,400 (100.0)	–	
≥90	–	–	64,628 (100.0)	
Male sex	135,663 (66.2)	82,908 (46.5)	19,621 (30.4)	<0.001
BMI[A] (kg/m^2)	23.2 [5.7]	21.5 [4.9]	20.4 [4.7]	<0.001
Hypertension	139,459 (68.1)	119,622 (67.1)	41,994 (65.0)	<0.001
Diabetes mellitus	81,184 (39.6)	49,046 (27.5)	10,789 (16.7)	<0.001
Chronic renal failure	29,633 (14.5)	27,051 (15.2)	8,819 (13.6)	<0.001
Chronic liver disease	10,103 (4.9)	6,070 (3.4)	1,344 (2.1)	<0.001
Chronic respiratory disease	22,129 (10.8)	21,970 (12.3)	6,642 (10.3)	<0.001
Atrial fibrillation	77,727 (38.0)	74,370 (41.7)	23,590 (36.5)	<0.001
Myocardial infarction	6,168 (3.0)	4,731 (2.7)	1,618 (2.5)	<0.001
Shock	4,418 (2.2)	3,235 (1.8)	1,112 (1.7)	<0.001
VT/VF	13,908 (6.8)	5,424 (3.0)	957 (1.5)	<0.001
NYHA functional class				<0.001
Class II	63,002 (30.8)	50,883 (28.5)	15,930 (24.6)	
Class III	77,383 (37.8)	69,353 (38.9)	24,703 (38.2)	
Class IV	64,405 (31.4)	58,164 (32.6)	23,995 (37.1)	
Educational institute	164,285 (80.2)	141,991 (79.6)	51,257 (79.3)	<0.001
Medications within 2 days after admission				
Orally administered				
β-blocker	78,959 (38.6)	54,843 (30.7)	14,584 (22.6)	<0.001
RAS inhibitor	83,754 (40.9)	63,220 (35.4)	19,384 (30.0)	<0.001
ACEI	38,071 (18.6)	25,622 (14.4)	8,019 (12.4)	<0.001
ARB	47,403 (23.1)	38,804 (21.8)	11,659 (18.0)	<0.001
MCR antagonist	71,847 (35.1)	55,015 (30.8)	18,753 (29.0)	<0.001
Intravenously administered				
Inotropic agent	40,501 (19.8)	28,807 (16.1)	8,928 (13.8)	<0.001
Nitrate	46,936 (22.9)	34,723 (19.5)	11,906 (18.4)	<0.001
Furosemide	132,567 (64.7)	124,149 (69.6)	47,956 (74.2)	<0.001

Unless indicated otherwise, data are given as the median [interquartile range] or n (%). [A]There were missing values for BMI (n=39,590). ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker; BMI, body mass index; MCR, mineralocorticoid receptor; NYHA, New York Heart Association; RAS, renin-angiotensin system; VT/VF, ventricular tachycardia/ventricular fibrillation.

P<0.05 was considered significant. Statistical analyses were performed using SPSS version 25 (IBM Corp., Armonk, NY, USA) and STATA (StataCorp, College Station, TX, USA).

Results

Trend of Age Distribution

The percentage of HF patients aged ≥80 and ≥90 years increased from 50.6% and 12.8%, respectively, in 2010 to 57.8% and 16.9%, respectively, in 2018 (**Figure 1**).

Characteristics of the Study Population

The characteristics of the study population are summarized in **Table 1**. In total, 243,028 patients (54.3%) were aged ≥80 years and 64,628 patients (14.4%) were aged ≥90 years. Elderly patients were more likely to be female. Body mass index was lower in elderly patients. There were significant differences in prevalence of comorbidities, such as hypertension, diabetes, and chronic renal dysfunction among age categories. The percentage of patients categorized as NYHA Class IV at admission increased with age. Information on medications administered within 2 days after admission was also collected. Furosemide was more frequently used in patients aged ≥80 and ≥90 years than in those aged <80 years. Conversely, other medications used for the treatment of HF were less frequently administered in patients aged ≥80 and ≥90 years.

Procedures and Outcomes During Hospitalization

Table 2 summarizes the procedures and outcomes for the study population. Invasive and advanced procedures, including implantable cardioverter defibrillator, cardiac resynchronization therapy, respiratory support, intubation, hemodialysis, intra-aortic balloon pumping, extracorporeal membrane oxygenation, and the use of inotropes, were

Table 2. Procedures and Outcomes for the Study Population

	Age (years)			P-value
	<80 (n=204,790)	80–89 (n=178,400)	≥90 (n=64,628)	
Procedures				
ICD	706 (0.3)	113 (0.1)	2 (0.0)	<0.001
CRT	3,610 (1.8)	927 (0.5)	40 (0.1)	<0.001
Respiratory support	37,555 (18.3)	26,010 (14.6)	7,089 (11.0)	<0.001
Intubation	7,764 (3.8)	4,008 (2.2)	592 (0.9)	<0.001
Hemodialysis	8,298 (4.1)	2,844 (1.6)	243 (0.4)	<0.001
IABP	2,295 (1.1)	799 (0.4)	81 (0.1)	<0.001
ECMO	361 (0.2)	84 (0.0)	5 (0.0)	<0.001
Inotropic use	80,687 (39.4)	66,397 (37.2)	22,625 (35.0)	<0.001
Outcomes				
Pneumonia	3,966 (1.9)	5,645 (3.2)	2,637 (4.1)	<0.001
Urinary tract infection	1,407 (0.7)	2,530 (1.4)	1,346 (2.1)	<0.001
Sepsis	994 (0.5)	1,077 (0.6)	440 (0.7)	<0.001
Deep vein thrombus	596 (0.3)	460 (0.3)	145 (0.2)	0.009
Pulmonary embolism	163 (0.1)	163 (0.1)	35 (0.1)	0.017
LOS (days)	16 [15]	18 [17]	18 [18]	<0.001
In-hospital death	8,056 (3.9)	14,280 (8.0)	8,486 (13.1)	<0.001
Discharge disposition (excluding patients who died in hospital)				<0.001
Home	180,482 (91.7)	134,215 (81.8)	39,043 (69.5)	
Nursing home	2,217 (1.1)	9,469 (5.8)	8,000 (14.2)	
Other hospital	13,305 (6.8)	19,703 (12.0)	8,722 (15.5)	
Other or unknown	730 (0.4)	733 (0.4)	377 (0.7)	

Unless indicated otherwise, data are given as the median [interquartile range] or n (%). CRT, cardiac resynchronization therapy; ECMO, extracorporeal membrane oxygenation; ICD, implantable cardioverter defibrillator; IABP, intra-aortic balloon pump; LOS, length of hospital stay.

rarely performed in patients aged ≥80 and ≥90 years. Infectious complications were frequently observed in patients aged ≥80 and ≥90 years. Patients with older age had a longer length of hospital stay and higher in-hospital mortality. Discharge disposition is also listed in **Table 2**. Most patients aged <80 years were discharged to their homes. Conversely, elderly patients were more likely to be transferred to nursing homes.

Effect of Age Category on In-Hospital Mortality

The multivariable logistic regression analysis fitted with a generalized estimating equation for in-hospital mortality showed that in-hospital mortality was higher in patients aged 80–89 and those aged ≥90 years than in those aged <80 years (**Table 3**).

Subgroup Analyses

The results of the subgroup analyses are shown in **Figure 2**. The proportion of elderly patients was higher among women than men (P<0.001; **Figure 2A**). The age distribution of HF patients differed among geographic regions (P<0.001; **Figure 2B**).

Discussion

The increase in the proportion of super-elderly patients with HF is associated with the rapid increase in the aging society. The percentage of the population aged ≥75 years in Japan increased from 8.6% in 2010 to 14.2% in 2018. It is estimated that there are approximately 1 million HF patients in Japan, and the number of patients with HF is predicted to increase and reach 1.3 million by 2030 in association with an aging society.[15] Therefore, further increases in super-elderly patients hospitalized for HF are expected.

Similar trends have been observed in other countries. The mean (±SD) age of HF patients in The Swedish Heart Failure Registry was 76±12 years, and 37% of patients were aged ≥80 years.[16] Similarly, the National Heart Failure Audit for England and Wales 2008–09 showed that median age of patients hospitalized for HF was 78 years, with more than half the patients aged ≥75 years.[17] Therefore, an increase in elderly patients with HF is a critical issue not only in Japan, but also in most developed countries.

The findings of this study have clinical implications. Despite the rapid increase in the aged population in developed countries, limited information is available regarding the outcomes of super-elderly HF patients. The present study is the first to focus on super-elderly (age ≥90 years) HF patients using a nationwide large-scale database. Most previous studies defined "elderly" HF patients as those aged ≥80 years.[6–8] However, considering that the median age of the present study population was 81 years, and that more than half the patients were aged ≥80 years, they could not be considered as specific subsets. In real-world clinical practice, HF patients aged ≥90 years are not rare; thus, revealing the presentations and outcomes of HF patients aged ≥90 years provides important information in the era of a super-aging society.

Subgroup analysis revealed that elderly patients were more likely to be female, and this finding is in accordance with findings from previous studies.[7,8,11] Further, there was a significant geographic difference in the age distribution

Table 3. Results of the Multivariable Logistic Regression Fitted With a Generalized Estimating Equation for In-Hospital Mortality

	OR	95% CI	P-value
Age (years)			
<80	Ref.		
80–89	1.99	1.92–2.05	<0.001
≥90	3.23	3.09–3.38	<0.001
Sex			
Female	Ref.		
Male	1.10	1.07–1.13	<0.001
BMI (kg/m^2)	0.94	0.94–0.95	<0.001
Hypertension	0.51	0.49–0.53	<0.001
Diabetes	1.03	1.00–1.06	0.027
Chronic renal failure	1.65	1.59–1.71	<0.001
Chronic liver disease	1.41	1.33–1.50	<0.001
Chronic respiratory disease	0.99	0.95–1.03	0.525
Atrial fibrillation	0.91	0.89–0.94	<0.001
Myocardial infarction	1.50	1.40–1.61	<0.001
Shock	3.24	2.93–3.59	<0.001
VT/VF	1.83	1.72–1.94	<0.001
NYHA functional class			
Class II	Ref.		
Class III	1.77	1.67–1.87	<0.001
Class IV	3.89	3.62–4.18	<0.001
Educational institute	0.81	0.78–0.85	<0.001
Drugs administered within 2 days			
β-blocker	0.92	0.90–0.95	<0.001
RAS inhibitor	0.62	0.59–0.64	<0.001
MCR antagonist	0.81	0.79–0.84	<0.001
Intravenous inotropic agent	2.27	2.18–2.37	<0.001
Intravenous nitrate	0.63	0.60–0.66	<0.001
Intravenous furosemide	1.12	1.08–1.16	<0.001

CI, confidence interval; OR, odds ratio. Other abbreviations as in Table 1.

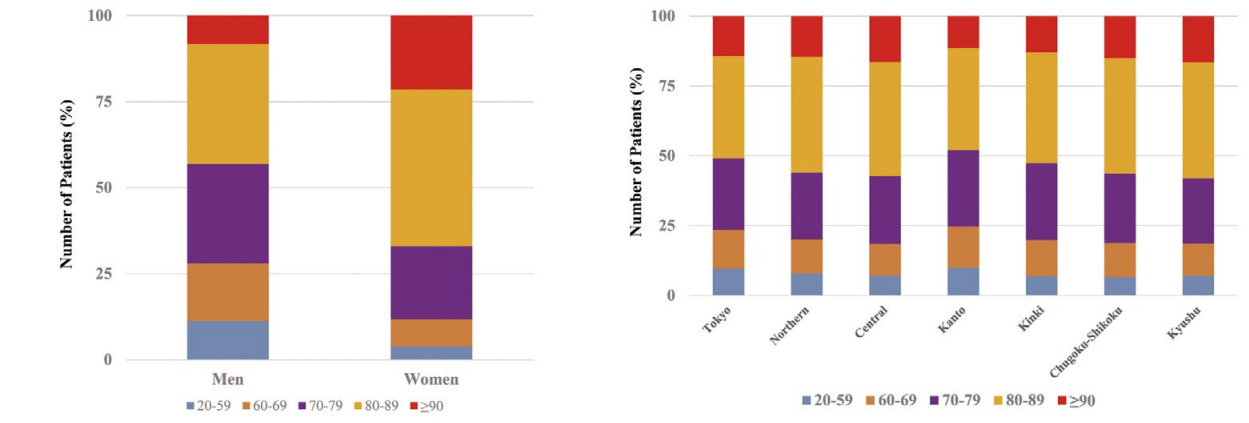


Figure 2. Subgroup analysis of age distribution (**A**) between the sexes and (**B**) among geographic regions of Japan.

of HF patients. Geographic differences in the age of patients with HF among countries has been reported previously,[18] and the results of the present study showed that there can also be a domestic regional difference in the age distribution of patients with HF.

Elderly patients had longer length of hospital stay than patients aged <80 years. However, the difference in length of hospital stay among the 3 groups was clinically not so large. It is assumed that the increase in elderly patients would contribute to longer hospital stays and result in an HF pandemic in acute care hospitals. However, based on the results of the present study, we cannot simply associate the longer hospital stay of HF patients with increased numbers of elderly HF patients. The length of hospital stay of patients with HF is longer in Japan than in other countries, and it is recognized as an important issue of the clinical setting in Japan.[19,20] Conversely, the 30-day HF readmission rate is known to be lower in Japan (5%) than in the US (25%).[21] There appears to be a trade-off between a longer hospital stay and hospital readmission. Both long hospital stays and repeated readmissions can be a significant burden for older patients. Well-balanced in-hospital management is particularly required for patients of older age.

In accordance with previous studies,[6–8,10,11] in-hospital mortality in the present study was higher for patients of older age. Medications other than furosemide were less frequently used in patients of older age. Further, invasive procedures were less frequently performed in elderly HF patients. Avoiding intensive medical treatment and invasive procedures in elderly patients is sometimes reasonable. In addition, the latest guidelines indicate that several promising treatments are not indicated for patients with limited life expectancy.[22,23] Therefore, we often hesitate to introduce invasive therapeutic options for patients of older age and with comorbidities in the real-world clinical setting. However, optimal indications for therapeutic options, including advanced procedures, in super-elderly patients need to be established because this subset of patients is expected to increase further. Given that infectious complications were more frequently observed in patients of older age, the importance of comprehensive management should also be noted. Simultaneously, palliative care is important for patients of older age.[24,25] Although clinical evidence of palliative care for hospitalized HF patients is not yet established,[26,27] Sidebottom et al reported that inpatient consultation by a palliative care team provided significant improvements in all patient-reported outcomes, including quality of life, for patients hospitalized for acute HF.[26] Further, Rogers et al reported that an interdisciplinary palliative care intervention was associated with greater benefits in quality of life, anxiety, depression, and spiritual well-being than usual care alone in patients with advanced HF.[28] We do believe that palliative care, including advance care planning, is required for patients of older age and with limited therapeutic options.

Regarding discharge disposition, more than 90% of patients aged <80 years were discharged to their homes, compared with <70% of patients aged ≥90 years; 14% of patients aged ≥90 years were transferred to nursing homes. These results suggest that social support and regional medical networks would be also important for elderly patients with HF.[29] A multidisciplinary team approach is particularly required for super-elderly patients who have multiple comorbidities and complicated backgrounds.

This study has several limitations. Although we performed multivariable analysis using a generalized estimating equation, there could be residual bias. The validity of the diagnoses and procedures in the database we used has been reported to be high.[30] However, recorded diagnoses are generally considered less well validated because of the nature of administrative data and retrospective studies. The DPC database lacked information on several factors that were potentially associated with outcomes, including blood pressure, HF etiology, and left ventricular ejection fraction.

Conclusions

Analysis of a nationwide database showed that the number of elderly patients hospitalized for HF, particularly super-elderly patients aged ≥90 years, was increasing and that in-hospital mortality was higher for these patients. An evidence-based approach for super-elderly HF patients should be established in the era of HF pandemic.

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Disclosures

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IRB Information

This study was approved by the Institutional Review Board of The University of Tokyo [3501-(3)].

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