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ORIGINAL ARTICLE
Exercise Physiology

Low Activities of Daily Living Associated With Increased Cardiovascular Disease Mortality in Japan

— Analysis of Health Records From a Nationwide Claim-Based Database, JROAD-DPC —

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Background: The aim of this study was to clarify the clinical impact of activities of daily living (ADL) using the Japanese Registry of All Cardiac and Vascular Diseases-Diagnosis Procedure Combination (JROAD-DPC) database.

Methods and Results: From April 2012 to March 2014, the JROAD-DPC database included 206,643 patients with acute coronary syndrome (ACS; n=49,784), heart failure (HF; n=136,878), or aortic aneurysm/dissection (Aorta; n=19,981). We divided them into 3 categories with regard to age (low, 20–59 years; middle, 60–79 years; high, ≥80 years) and admission ADL (low, Barthel index [BI] 0–70; middle, BI 75–95; high, BI 100). ACS, HF, and Aorta patients with low ADL had higher in-hospital mortality rates (18.3%, 16.7%, and 33.4%) than those with middle or high ADL (P<0.001, X^2 test). On multivariable analysis, BI on admission was associated with in-hospital mortality of ACS (OR, 0.986 per 1 BI; P<0.001), HF (OR, 0.986 per 1 BI; P<0.001), and Aorta (OR, 0.986 per 1 BI; P<0.001), adjusted for gender, age, body mass index, hypertension, diabetes mellitus, dyslipidemia, and the Charlson comorbidity index. Moreover, patients with low age and low ADL had a higher in-hospital mortality rate than those with high age and high ADL in regard to HF (8.6% vs. 6.0%).

Conclusions: According to JROAD-DPC data, assessment of admission ADL is important in patients with cardiovascular disease.

Key Words: Activities of daily living; Acute coronary syndrome; Aortic disease; Barthel index; Heart failure

Japan is presently categorized as a "super-aged society", that is, a society in which the proportion of the population aged ≥65 years (the population's aging rate) is >21%. Japan's current aging rate is 27% according to data from the 2015 Population Census conducted by the Statistics Bureau, Ministry of Internal Affairs and Communications of Japan.[1] Because cardiovascular disease (CVD) generally increases in a high-aged population, conducting research and surveys on measures to prevent and treat CVD is important in Japan. CVD patients in an aging population are heterogeneous and come from various backgrounds, so they are difficult to categorize, given that older patients generally have poor disease outcomes. In particular, of the various background characteristics, basal activities of daily living (ADL) is a strong prognostic factor.[2–15] In addition, admission ADL is a simple and useful marker with which to evaluate general condition, but there are few nationwide studies using real-world data to assess the clinical impact of ADL on the prognosis of CVD.

The Japanese Registry of All Cardiac and Vascular Diseases (JROAD) was launched in 2004 to assess the clinical activity of each Japanese institution with cardiovascular beds. As previously reported, nearly all teaching hospitals with cardiovascular beds except for stroke participated in the JROAD to meet the Japanese Circulation Society (JCS) requirement that JCS-certified teaching hospitals provide cardiology training to physicians who

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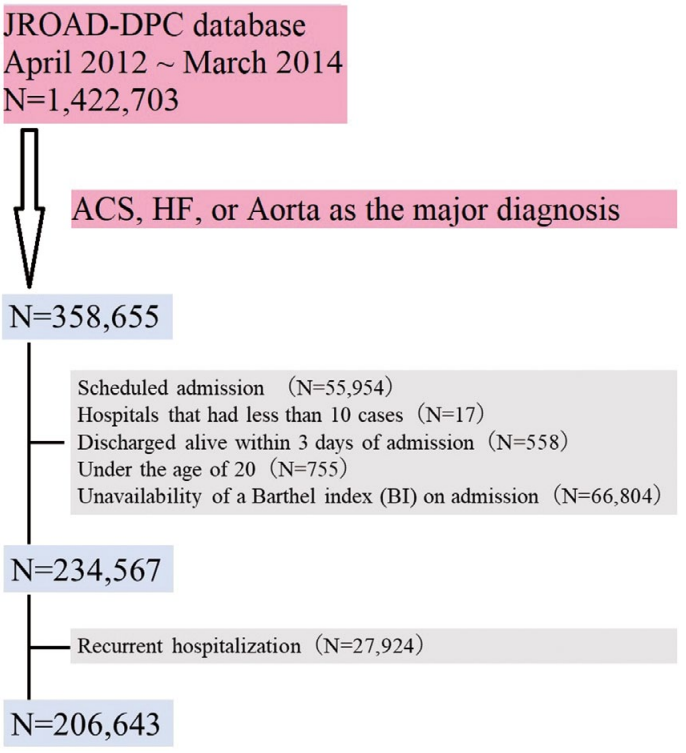

Figure 1. Study flowchart: 206,643 patients with acute coronary syndrome (ACS; n=49,784), heart failure (HF; n=136,878), or aortic aneurysm/dissection (Aorta; n=19,981) met the eligibility criteria and were enrolled in the present study. JROAD-DPC, Japanese Registry of All Cardiac and Vascular Diseases-Diagnosis Procedure Combination.

wish to be JCS board-certified cardiologists and take the JCS board test.[16] Given that Japan has universal health insurance coverage, all patients can obtain standard medical care. In addition, the Japanese Diagnosis Procedure Combination/Per Diem Payment System (DPC/PDPS) listed the lump-sum medical expenses evaluated based on diagnostic and procedural costs beginning in 2002.[17] Using data from the DPC/PDPS, the JROAD was developed as a nationwide claim database (i.e., the JROAD-DPC). The DPC database includes the following individual data: unique hospital identifier; patient age and sex; main diagnosis and comorbidity; drugs and devices; diagnostic and therapeutic procedures; number of days of hospitalization; medical care costs; discharge status; and the admission ADL score evaluated using the Barthel index (BI) on admission.

The aim of this study was therefore to perform a nationwide claim survey using the DPC discharge database and to clarify the clinical impact of admission ADL on the prognosis of patients with CVD in a super-aged society. From the view of a nationwide survey, the differences in ADL by region were also assessed in this study.

Methods

Definition

The JCS publicly advertised the research proposal using the JROAD and the JROAD-DPC. The present study was adopted as the 2016 research proposal (approval number: 2016-12-02). Of the 1,506 hospitals that responded to the JROAD, 739 agreed to participate in the DPC discharge database study. Software was developed to identify patients in the annual de-identified discharge database who were hospitalized because of CVD except for stroke. This identification was based on the International Classification of Diseases (ICD)-10 diagnosis codes related to acute coronary syndrome (ACS): I20.0, I21.0, I21.1, I21.2, I21.3, I21.4, and I21.9); heart failure (HF): I50.0, I50.1, and I50.9; and aortic aneurysm or dissection (Aorta): I71.0, I71.1, I71.2, I71.3, I71.4, I71.5, I71.6, I71.8, and I71.9. Major diagnosis of ACS, HF, and Aorta was defined as being listed as the main diagnosis; as the primary diagnosis for admission; or as having the most medical care costs in the DPC data. If a patient had multiple ICD-10 diagnosis codes with ACS, HF, or Aorta as the major diagnoses, the diagnosis priority order was defined as Aorta, ACS, and then HF. Hospitalization records between 1 April 2012 and 31 March 2014, were collected, but patients with scheduled admission or age <20 years were excluded from the analysis. To rule out mild cases, we excluded hospitals that had <10 cases and patients who were discharged alive ≤3 days after admission. This was consistent with a previous study by the Center for Medicare and Medicaid Service, which maintained anonymous data excluding small case volume.[18] We also referred to the National Database of Health Insurance Claims and Specific Health Checkups of Japan publication rule, which excludes small case volume data, to avoid the identification of individuals.[19] We also excluded patients whose BI on admission was unavailable, and those with recurrent hospitalization between 1 April 2012 and 31 March 2014. The following data were extracted from the database: unique hospital identifier; patient age and sex; main diagnosis; comorbidity at admission; number of days of hospitalization; medical care costs during hospitalization; discharge status; and basal ADL score. Comorbidities were determined primarily from the

Table 1. Clinical Subject Characteristics

	ACS (n=49,784)	HF (n=136,878)	Aorta (n=19,981)	P-value
Male	72.3	51.5	61.0	<0.001
Age (years)	71 (61~80)*,‡,§	81 (72~87)*,†,§	75 (65~83)*,†,‡	<0.001
BMI (kg/m^2)	23.4 (21.1~25.8)*,‡,§	21.9 (19.4~24.8)*,†,§	22.5 (20.0~25.0)*,†,‡	<0.001
HTN	81.6	84.3	72.1	<0.001
DM	31.0	29.5	13.0	<0.001
DLP	72.1	32.4	23.5	<0.001
BI on admission	10 (0~100)*,‡,§	50 (5~100)*,†,§	0 (0~100)*,†,‡	<0.001
BI on discharge	100 (100~100)*,‡,§	100 (55~100)*,†,§	100 (70~100)*,†,‡	<0.001
Charlson comorbidity index	2 (1~3)*,‡,§	2 (1~3)*,†,§	1 (1~2)*,†,‡	<0.001
In-hospital mortality	13.7	11.9	26.2	<0.001
7-day mortality	10.1	4.5	21	<0.001
30-day mortality	12.7	8.9	24.3	<0.001
Ln(medical care costs) (yen)	14.3±0.9*,‡,§	13.6±0.8*,†,§	14.1±1.4*,†,‡	<0.001
Ln(hospitalization days)	2.5±0.9*,‡,§	2.9±0.8*,†,§	2.5±1.3*,†,‡	<0.001

Data given as mean±SD, median (IQR) or % . *P<0.05 †vs. ACS, ‡vs. HF, and §vs. Aorta. ACS: BMI (n=43,226), BI on discharge (n=43,174), and Ln(medical care costs) (n=49,451). HF: BMI (n=121,489), BI on discharge (n=121,047), and Ln(medical care costs) (n=136,156). Aorta: BMI (n=16,081), BI on discharge (n=14,975), and Ln(medical care costs) (n=19,883). ACS, acute coronary syndrome; Aorta, aortic aneurysm/dissection; BI, Barthel index; BMI, body mass index; DLP, dyslipidemia; DM, diabetes mellitus; HF, heart failure; HTN, hypertension.

ICD-10 codes but were also checked against the medication on admission or discharge to determine if these were compatible with the code data. The Charlson comorbidity index[20] was also calculated using ICD-10 coding algorithms.[21] We divided the patients into 3 categories according to age: low, 20–59 years; middle, 60–79 years; and high, ≥80 years. We also divided them into 3 tertiles according to population density: low population density; middle population density; and high population density. The population density was determined using the address of their hospital according to the 2010 Population Census conducted by the Statistics Bureau, Ministry of Internal Affairs and Communications of Japan.[22]

BI

The BI consists of 10 items with varying weights that score ADL: bathing and grooming are scored 0 or 5; and feeding, dressing, controlling the bladder, controlling the bowels, getting onto and off the toilet, and ascending and descending stairs are scored 0, 5, or 10. Items regarding moving from a wheelchair to a bed and walking on a level surface are scored 0, 5, 10, or 15. The total BI is a cumulative score of the 10 items, with a maximum score of 100 corresponding to complete independence, and a minimum score of 0 corresponding to total dependence.[23,24] In the present study, the admission ADL score was evaluated using the BI on admission at each hospital. The patients were also divided into 3 categories according to BI on admission: low ADL, admission BI 0–70; middle ADL, admission BI 75–95; and high ADL, admission BI 100. A BI of 75 (<75) was used as the cut-off score for the low ADL group according to a previous report.[24]

Ethics Statement

This research plan was designed by the authors and approved by the Institutional Review Board of the National Cerebral and Cardiovascular Center, which waived the requirement for individual informed consent according to the "opt-out" principle. In addition, the present study protocol was approved by the Institutional Review Board of Saiseikai Yokohamashi Nanbu Hospital (approval number: 2017-D03; UMIN-CTR ID: UMIN000032690). Each hospital anonymized the patient identities using code change equations produced by each hospital in the original DPC data, which was sent to the Ministry of Health, Labor, and Welfare. Each hospital notified patients through homepages or posters in the hospitals that their information was being collected for this study. Patients could opt out of the database if they wished.

Statistical Analysis

Continuous variables are expressed as mean±SD for parameters with normal distribution and as median (IQR) for parameters with skewed distribution. Differences between 2 groups were tested using Student's t-test for variables with normal distribution. The Mann-Whitney test was used for variables with skewed distribution, and the chi-squared test or Fisher's exact test was used as appropriate for categorical variables. Differences in continuous variables between 3 or more groups were tested using 1-way analysis of variance (ANOVA), followed by post-hoc comparisons (Tukey's honestly significant difference test when equal variance was assumed, and the Games-Howell test when equal variance was not assumed). The primary outcomes were in-hospital mortality, 30-day mortality, and 7-day mortality. The secondary outcomes were the number of days of hospitalization and the medical care costs during hospitalization. The number of days of hospitalization and the medical care costs during hospitalization (Japanese yen) were evaluated using the natural logarithm (Ln). To investigate the impact of ADL on outcome, we conducted multivariable logistic and linear regression analyses using the forced inclusion model including gender, age, body mass index (BMI), coronary risk factors, and the Charlson comorbidity index. All the statistical tests were 2-tailed, and P<0.05 was considered statistically significant. All the statistical analyses were conducted using IBM SPSS version 24.0.

Table 2. Outcome of CVD According to ADL, Age, and Population Density

Outcomes	High ADL (n=14,039)	Middle ADL (n=1,304)	Low ADL (n=28,142)	P-value	20~59 years (n=10,708)	60~79 years (n=26,243)
A) ACS						
In-hospital mortality	3.9	4.5	18.3	<0.001	5.1	10.5
7-day mortality	2.3	2.3	13.7	<0.001	3.9	7.5
30-day mortality	3.4	3.1	17.0	<0.001	4.8	9.5
Ln(medical care costs) (yen)	14.4±0.6*,‡,§	14.3±0.7*,†	14.3±1.0*,†	<0.001	14.4±0.7*,§	14.4±0.8*,§
Ln(hospitalization days)	2.6±0.6*,‡,§	2.7±0.7*,†,§	2.5±1.0*,†,‡	<0.001	2.5±0.7*,‡,§	2.6±0.8*,†,§
	(n=40,556)	**(n=12,222)**	**(n=84,100)**		**(n=9,940)**	**(n=50,130)**
B) HF						
In-hospital mortality	4.2	4.9	16.7	<0.001	4.5	7.9
7-day mortality	1.2	0.9	6.7	<0.001	2.2	3.1
30-day mortality	3.7	2.9	12.7	<0.001	3.5	5.7
Ln(medical care costs) (yen)	13.6±0.7*,‡,§	13.6±0.7*,†,§	13.6±0.8*,†,‡	<0.001	13.7±0.8*,§	13.7±0.8*,§
Ln(hospitalization days)	2.8±0.7*,‡,§	2.9±0.7*,†	2.9±0.9*,†	<0.001	2.8±0.7*,‡,§	2.9±0.8*,†,§
	(n=5,342)	**(n=682)**	**(n=13,957)**		**(n=2,822)**	**(n=9,794)**
C) Aorta						
In-hospital mortality	9.2	11.6	33.4	<0.001	13.1	19.8
7-day mortality	6.0	6.6	27.4	<0.001	10.2	15.8
30-day mortality	8.1	8.5	31.3	<0.001	12.4	18.2
Ln(medical care costs) (yen)	14.3±1.2*,‡,§	14.0±1.2*,†	14.0±1.4*,†	<0.001	14.6±1.2*,‡,§	14.3±1.3*,†,§
Ln(hospitalization days)	2.9±0.9*,§	2.9±0.9*,§	2.4±1.4*,†,‡	<0.001	2.9±1.0*,‡,§	2.7±1.2*,†,§

Outcomes	≥80 years (n=12,833)	P-value	High population density (n=18,847)	Middle population density (n=17,859)	Low population density (n=13,078)	P-value
A) ACS						
In-hospital mortality	27.6	<0.001	11.7	13.2	17.5	<0.001
7-day mortality	20.6	<0.001	7.9	9.5	14	<0.001
30-day mortality	25.6	<0.001	10.5	12.1	16.5	<0.001
Ln(medical care costs) (yen)	14.0±1.1*,†,‡	<0.001	14.4±0.8*,‡,§	14.3±0.8*,†,§	14.2±1.0*,†,‡	<0.001
Ln(hospitalization days)	2.4±1.2*,†,‡	<0.001	2.5±0.8*,§	2.5±0.9*,§	2.5±1.0*,†,‡	<0.001
	(n=76,808)		**(n=52,508)**	**(n=48,736)**	**(n=35,634)**	
B) HF						
In-hospital mortality	15.5	<0.001	10.5	11.7	14.4	<0.001
7-day mortality	5.8	<0.001	3.5	4.6	6	<0.001
30-day mortality	11.6	<0.001	7.6	8.8	10.8	<0.001
Ln(medical care costs) (yen)	13.6±0.8*,†,‡	<0.001	13.7±0.8*,‡,§	13.6±0.8*,†,§	13.6±0.8*,†,‡	<0.001
Ln(hospitalization days)	2.9±0.7*,†,‡	<0.001	2.9±0.8*,‡	2.8±0.8*,†,§	2.9±0.9*,‡	<0.001
	(n=7,365)		**(n=8,010)**	**(n=7,212)**	**(n=4,759)**	
C) Aorta						
In-hospital mortality	39.6	<0.001	23.7	25.2	31.9	<0.001
7-day mortality	32	<0.001	18.3	20	26.8	<0.001
30-day mortality	37.1	<0.001	21.7	23.4	30.1	<0.001
Ln(medical care costs) (yen)	13.6±1.4*,†,‡	<0.001	14.2±1.3*,‡,§	14.1±1.4*,†,§	13.8±1.4*,†,‡	<0.001
Ln(hospitalization days)	2.2±1.4*,†,‡	<0.001	2.6±1.2*,§	2.6±1.3*,§	2.4±1.4*,†,‡	<0.001

Data given as % or mean±SD. *P<0.05 †vs. high ADL/20~59 years/high population density, ‡vs. middle ADL/60~79 years/middle population density, and §vs. low ADL/≥80 years/low population density. AADL, activities of daily living; CVD, cardiovascular disease. Other abbreviations as in Table 1.

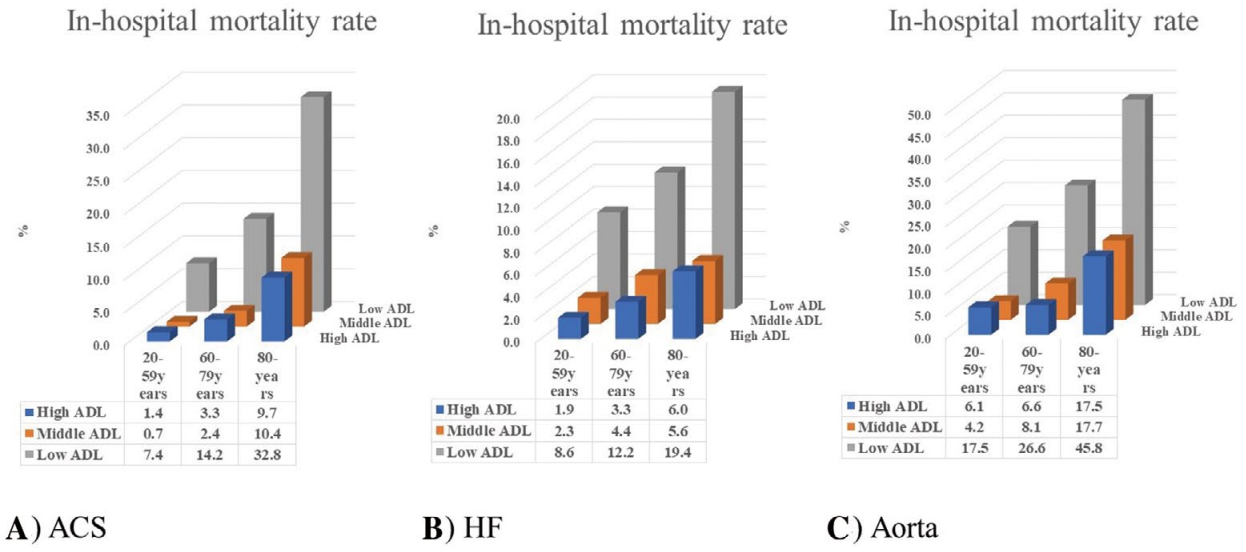

Figure 2. In-hospital mortality rate according to age and activities of daily living (ADL) in patients with (**A**) acute coronary syndrome (ACS); (**B**) heart failure (HF); and (**C**) aortic aneurysm/dissection (Aorta).

Table 3. Multivariable Indicators of CVD Outcome

Variables	In-hospital mortality			7-day mortality		
	OR	95% CI	P-value	OR	95% CI	P-value
A) ACS						
Male	0.997	0.907~1.095	0.946	1.027	0.921~1.144	0.633
Age (per year)	1.043	1.039~1.047	<0.001	1.039	1.034~1.044	<0.001
BMI (per 1 kg/m^2)	1.019	1.008~1.029	0.001	1.017	1.004~1.030	0.009
HTN	0.121	0.111~0.132	<0.001	0.162	0.145~0.181	<0.001
DM	0.979	0.877~1.091	0.697	0.987	0.861~1.131	0.847
DLP	0.115	0.104~0.128	<0.001	0.114	0.099~0.131	<0.001
BI on admission (per 1 BI)	0.986	0.985~0.988	<0.001	0.984	0.983~0.986	<0.001
Charlson comorbidity index (per 1)	1.008	0.971~1.046	0.667	0.795	0.758~0.834	<0.001
B) HF						
Male	0.801	0.766~0.837	<0.001	0.761	0.708~0.818	<0.001
Age (per year)	1.025	1.023~1.028	<0.001	1.016	1.012~1.020	<0.001
BMI (per 1 kg/m^2)	0.956	0.951~0.961	<0.001	0.983	0.974~0.991	<0.001
HTN	0.127	0.121~0.132	<0.001	0.156	0.145~0.168	<0.001
DM	0.832	0.786~0.879	<0.001	0.770	0.697~0.850	<0.001
DLP	0.633	0.597~0.671	<0.001	0.680	0.612~0.756	<0.001
BI on admission (per 1 BI)	0.986	0.985~0.986	<0.001	0.979	0.977~0.980	<0.001
Charlson comorbidity index (per 1)	1.118	1.100~1.135	<0.001	0.952	0.925~0.979	<0.001
C) Aorta						
Male	1.018	0.918~1.129	0.736	1.140	1.013~1.282	0.029
Age (per year)	1.037	1.032~1.042	<0.001	1.036	1.030~1.041	<0.001
BMI (per 1 kg/m^2)	1.014	1.002~1.027	0.020	1.023	1.009~1.037	0.001
HTN	0.097	0.088~0.108	<0.001	0.105	0.094~0.119	<0.001
DM	0.600	0.500~0.718	<0.001	0.578	0.458~0.730	<0.001
DLP	0.520	0.446~0.606	<0.001	0.547	0.452~0.663	<0.001
BI on admission (per 1 BI)	0.986	0.985~0.987	<0.001	0.984	0.983~0.986	<0.001
Charlson comorbidity index (per 1)	0.942	0.897~0.990	0.018	0.769	0.721~0.819	<0.001

Abbreviations as in Table 1.

(**Table 3** continued the next page.)

Results

Baseline Characteristics

Of 1,422,703 patients in the JROAD-DPC database from 1 April 2012 to 31 March 2014, 358,655 patients had major diagnoses of ACS, HF, or Aorta. Of 358,655 patients, 206,643 patients with ACS (n=49,784), HF (n=136,878), and Aorta (n=19,981) met the eligibility criteria and were enrolled in this study (**Figure 1**). **Table 1** lists the baseline characteristics of the patients with ACS, HF, and Aorta. The in-hospital mortality rate was higher in the patients with Aorta (26.2%) than in those with ACS (13.7%) or HF (11.9%; P<0.001). Although the 7-day mortality rate was markedly higher in the patients with ACS (10.1%) than in those with HF (4.5%), the in-hospital mortality rates (ACS, 13.7%; HF, 11.9%) had no apparent numerical differences between the 2 groups. In addition, the BI on admission was higher in the HF group than in the ACS or Aorta groups (P<0.001), indicating the difference in the severity of these diseases in the acute phase. As noted in **Table 1**, although the HF patients had ae lower risk of mortality than the ACS or Aorta groups in the acute phase, the HF patients were older and had been hospitalized longer than the ACS or Aorta patients (P<0.001, respectively), leading to an increase in the mortality rate in the subacute phase.

Impact of BI on Admission

The older group had a higher in-hospital mortality rate, 7-day mortality rate, and 30-day mortality rate than the younger group with these 3 diseases (**Table 2A–C**). Possibly as a result, regarding ACS and Aorta, there were fewer days of hospitalization in the older group, resulting in lower medical care costs (**Table 2A,C**). Regarding HF, however, the number of days of hospitalization and the medical care costs had no apparent numercial differences between the age groups (**Table 2B**).

Likewise, with respect to ADL, the lower ADL group had a higher in-hospital mortality rate (ACS, 18.3%; HF, 16.7%; and Aorta, 33.4%), 7-day mortality rate (ACS, 13.7%; HF, 6.7%; and Aorta, 27.4%), and 30-day mortality rate (ACS, 17.0%; HF, 12.7%; and Aorta, 31.3%) than the high ADL group with these 3 diseases (**Table 2A–C**). Regarding HF, however, the number of days of hospitalization and the medical care costs had no apparent numercial differences between the ADL groups (**Table 2B**).

When the patients were divided into 9 groups according to age (low age group, middle age group, and high age group) and ADL (low ADL group, middle ADL group, and high ADL group), the in-hospital mortality rate of the high age group with middle or high ADL had no apparent numercial differences to that of the low age group with low ADL regarding ACS and Aorta (**Figure 2A,C**). Regarding

30-day mortality			Ln(medical care costs)			Ln(hospitalization days)		
OR	95% CI	P-value	β	95% CI	P-value	β	95% CI	P-value
0.987	0.896~1.088	0.795	−0.097	−0.113~−0.082	<0.001	0.022	0.006~0.038	0.008
1.042	1.038~1.047	<0.001	−0.002	−0.002~−0.001	<0.001	0.002	0.001~0.003	<0.001
1.021	1.010~1.032	<0.001	0.002	0.000~0.004	0.023	−0.006	−0.008~−0.004	<0.001
0.130	0.118~0.143	<0.001	0.222	0.201~0.243	<0.001	0.427	0.406~0.449	<0.001
1.008	0.899~1.130	0.891	0.072	0.056~0.088	<0.001	0.031	0.015~0.047	<0.001
0.120	0.108~0.134	<0.001	0.195	0.177~0.212	<0.001	0.138	0.120~0.157	<0.001
0.986	0.984~0.987	<0.001	−0.001	−0.001~−0.001	<0.001	−0.001	−0.001~0.000	<0.001
0.934	0.898~0.971	0.001	0.055	0.048~0.062	<0.001	0.099	0.092~0.106	<0.001
0.798	0.758~0.839	<0.001	0.007	−0.002~0.015	0.130	0.064	0.055~0.072	<0.001
1.024	1.021~1.026	<0.001	−0.006	−0.007~−0.006	<0.001	0.000	0.000~0.001	0.258
0.968	0.962~0.974	<0.001	−0.003	−0.004~−0.003	<0.001	−0.003	−0.004~−0.002	<0.001
0.143	0.136~0.151	<0.001	0.101	0.088~0.113	<0.001	0.192	0.179~0.204	<0.001
0.821	0.769~0.876	<0.001	0.065	0.054~0.075	<0.001	0.034	0.024~0.044	<0.001
0.638	0.595~0.684	<0.001	0.075	0.066~0.084	<0.001	0.001	−0.008~0.010	0.806
0.984	0.983~0.984	<0.001	−0.002	−0.002~−0.002	<0.001	−0.001	−0.001~−0.001	<0.001
1.055	1.036~1.075	<0.001	0.033	0.030~0.037	<0.001	0.041	0.037~0.044	<0.001
1.096	0.984~1.221	0.094	0.084	0.045~0.122	<0.001	0.006	−0.025~0.038	0.701
1.036	1.031~1.041	<0.001	−0.019	−0.021~−0.017	<0.001	−0.008	−0.010~−0.007	<0.001
1.023	1.010~1.036	<0.001	0.008	0.003~0.013	0.001	−0.001	−0.005~0.003	0.681
0.100	0.089~0.111	<0.001	0.516	0.469~0.563	<0.001	0.903	0.865~0.942	<0.001
0.614	0.505~0.747	<0.001	0.330	0.276~0.384	<0.001	0.142	0.098~0.187	<0.001
0.522	0.442~0.615	<0.001	−0.167	−0.209~−0.124	<0.001	0.008	−0.027~0.043	0.652
0.985	0.984~0.986	<0.001	−0.002	−0.002~−0.001	<0.001	0.001	0.000~0.001	<0.001
0.858	0.813~0.905	<0.001	0.056	0.038~0.074	<0.001	0.097	0.082~0.111	<0.001

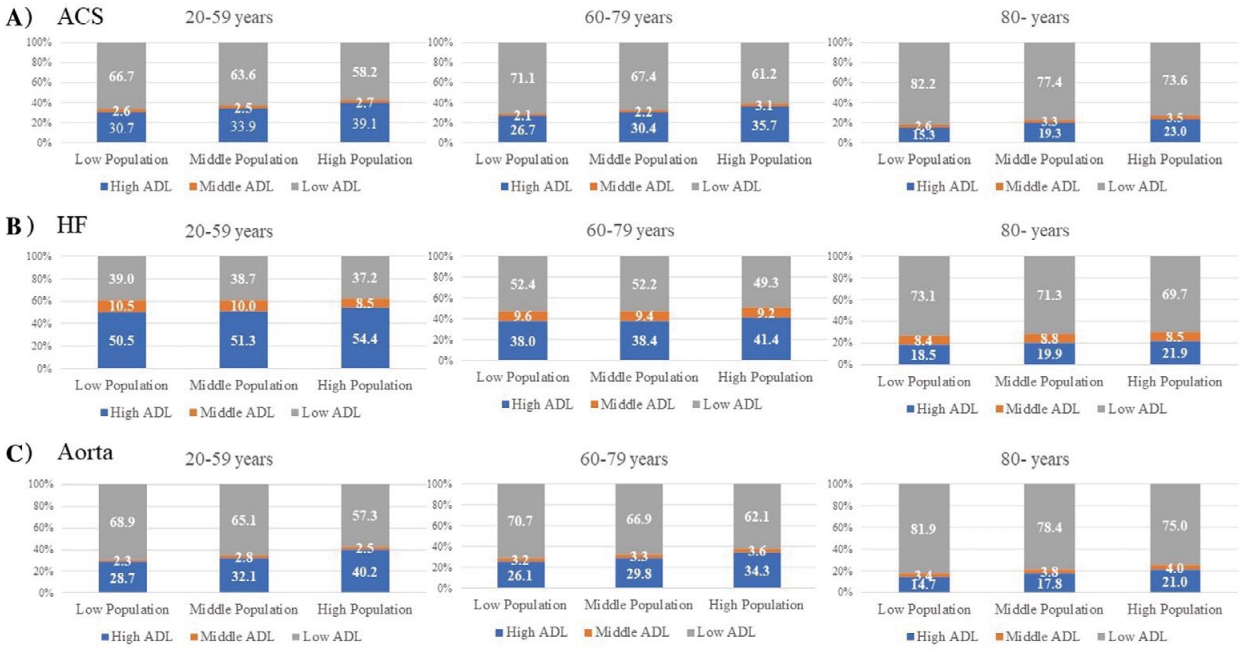

Figure 3. Activities of daily living (ADL) level vs. population density in patients with (**A**) acute coronary syndrome (ACS), (**B**) heart failure (HF) and (**C**) aortic aneurysm/dissection (Aorta). The proportion of patients with low ADL in each age group was higher in the low population density group than in the high population density group, for the 3 cardiovascular diseases (all P<0.01).

HF, however, the in-hospital mortality rate of the high age group with middle or high ADL was significantly lower than that of the low age group with low ADL (high age group with middle ADL, 5.6%; high age group with high ADL, 6.0%; low age group with low ADL, 8.6%; **Figure 2B**).

On multivariable logistic and linear regression analyses using the forced inclusion model, BI on admission was associated with in-hospital mortality, 7-day mortality, 30-day mortality, Ln(number of days of hospitalization), and Ln(medical care costs) (all P<0.001) for ACS, HF, and Aorta when adjusted for male gender, age, BMI, hypertension (HTN), diabetes mellitus (DM), dyslipidemia (DLP), and the Charlson comorbidity index. High BI on admission was associated with a low risk of mortality and low medical care costs for the 3 diseases (**Table 3**).

Differences in ADL by Region

In addition to age and ADL, the low population density group had a higher in-hospital mortality rate, 7-day mortality rate, and 30-day mortality rate than the high population density group for ACS, HF, and Aorta (**Table 2A–C**). Finally, to assess the differences in ADL in the CVD patients by region, the proportion of patients in the low ADL group in each age group was assessed according to population density (low population density group, middle population density group, and high population density group). Surprisingly, the proportion of patients with low ADL in each age group was higher in the low population density group, not in the high population density group, for the 3 CVD (all P<0.01; **Figure 3**).

Discussion

The main findings of the present study were as follows: (1) the patients with HF were older and were hospitalized longer than those with ACS or Aorta; (2) there were no apparent numerical decreases in the number of days of hospitalization or in the medical care costs between the age and ADL groups for HF; (3) ADL by age group had an impact on in-hospital mortality rate, especially in patients with HF; (4) ADL was associated with the mortality rate and medical care costs of CVD; and (5) the proportion of patients with low ADL in each age group was higher in the low population density group for the 3 CVD. To the best of our knowledge, the present study is the first to investigate the clinical impact of ADL on CVD using real-world large-scale data from a nationwide claim-based database.

First, in the present study the HF patients were older and were hospitalized for longer than those with ACS or Aorta. From the perspective of 7-day mortality and BI on admission, the HF patients were at lower risk than those with ACS or Aorta. Given, however, that the HF patients were older and that the longer hospitalization leads to an increase in the mortality rate in the subacute phase, the in-hospital mortality rate in the HF patients was not significantly different from that in the ACS group (11.9% vs. 13.7%). In addition, although 7-day mortality rates were high in the high age group (ACS, 20.6%; Aorta, 32.0%) and in the low ADL group (ACS, 13.7%; Aorta, 27.4%), resulting in fewer days of hospitalization and lower medical care costs for ACS or Aorta, the 7-day mortality rate was not substantially high even in the high age group (5.8%) and the low ADL group (6.7%) for HF. Hence, there were no apparent numerical decreases in the number

of days of hospitalization or the medical care costs between the age and ADL groups for HF. In the present study low ADL was also found to have a strong impact beyond the age groups, especially in patients with HF from the perspective of ADL by age group. This indicates that the ADL level affected various complications during the subacute phase, especially in the patients with HF. This is consistent with a previous report demonstrating a clinical impact of ADL on outcome in HF patients in a limited area with a relatively small group.[25] Furthermore, low ADL was associated with mortality rate and medical care costs for ACS, Aorta, and HF when adjusted for male gender, age, BMI, HTN, DM, DLP, and Charlson comorbidity index. This study has therefore clarified the clinical impact of ADL on CVD using real-world large-scale data from a nationwide claim-based database.

Physical activity is an important factor in total and CVD mortality in the general population.[26] In addition, because the CVD patients with low ADL had poor outcome in the present study, it is important to evaluate ADL levels at admission. Although BI, which is commonly used in the field of stroke,[27,28] is a simple method to evaluate ADL at admission, only a few studies have investigated its usefulness in CVD.[3,8,14] In contrast to gait speed or the measurement of muscle strength, BI can be easily evaluated at admission in all patients including those who die in the acute phase. Previous reports from the Spanish National Heart Failure Registry (Registro Nacional de Insuficencia Cardiaca, RICA), which is a nationwide cohort-based prospective multicenter registry of 4,200 patients at 52 centers from March 2008 until April 2015, investigated BI's usefulness in patients with HF.[8,14,29] RICA, however was not a large-scale data study, and the RICA reports involved only a few thousand elderly (≥75 years) patients, although the RICA inclusion criteria included patients >50 years.

Interestingly, in the present study, for ACS, Aorta, and HF, the proportion of patients with low ADL in each age group was higher in the low population density group compared with the high population density group. We posit 2 possible reasons for this result. One is inequalities in access to health care in certain population density groups. In the low population density group, it may take a long time to be admitted to a hospital after the onset of symptoms, resulting in low ADL caused by disease progression. The other is reduced baseline ADL due to insufficient exercise in smaller cities in present-day Japan. According to the Japan National Health and Nutrition Survey of 15,763 men and 18,479 women, men and women in larger cities took more steps compared with those in smaller cities in Japan.[30] Social intervention may be required to improve baseline ADL, especially in smaller cities.

Study Limitations

This study had several limitations. First, the DPC system focused on JCS-certified hospitals; although these institutions accounted for approximately 30% of all hospital beds in Japan, the applicability of the present findings to non-certified hospitals is unclear. Second, because the DPC system is not based on medical records, the precise definition of the major diagnosis and comorbidities is somewhat difficult. Third, the JROAD-DPC targets JCS-certified teaching hospitals in the DPC system. Therefore, generalization of the results of the JROAD-DPC is limited for small clinics or non-specialist hospitals. Fourth, the definition of in-hospital mortality in the JROAD-DPC did not include death in another hospital after discharge from a participating hospital.

Conclusions

According to JROAD-DPC data, assessment of admission ADL is important in patients with CVD in a super-aged society.

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