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ORIGINAL ARTICLE

Temporal Trends in the Practice Pattern for Sleep-Disordered Breathing in Patients With Cardiovascular Diseases in Japan

— Insights From the Japanese Registry of All Cardiac and Vascular Diseases – Diagnosis Procedure Combination —

Ryohei Takeishi, MD; Akiomi Yoshihisa, MD, PhD; Yu Hotsuki, MD; Fumiya Anzai, MD, PhD; Yu Sato, MD; Yoko Sumita; Michikazu Nakai, PhD; Tomofumi Misaka, MD, PhD; Yasuchika Takeishi, MD, PhD

Background: After the publication of the Japanese Circulation Society guideline of sleep-disordered breathing (SDB) in 2010, with new evidence and changes to the health insurance system, trends in the practice pattern for SDB in patients with cardiovascular disease (CVD) might have changed.

Methods and Results: This study evaluated the temporal changes in the practice pattern for SDB by using a nationwide claim database, the Japanese Registry of All Cardiac and Vascular Diseases – Diagnosis Procedure Combination (JROAD-DPC), from 2012 to 2019. The main findings were: (1) the number of CVD patients diagnosed with SDB increased (especially those with atrial fibrillation [AF] and heart failure [HF]); (2) the number of diagnostic tests for SDB performed during hospitalization increased for AF patients (from 1.3% in 2012 to 1.8% in 2019), whereas it decreased for other CVD patients; (3) the number of patients diagnosed with SDB increased in each type of CVD, except for patients with acute myocardial infarction (AMI); (4) continuous positive airway pressure (CPAP) treatment increased for AF patients (from 15.2% to 17.5%); (5) CPAP treatment decreased for patients with angina pectoris (AP) and AMI, and any treatment decreased for HF patients (from 46.1% to 39.7%); and (6) SDB was treated more often in HF patients than in AF, AP, and AMI patients (41.7% vs. 17.2%, 19.1% and 20.4%, respectively).

Conclusions: The practice pattern for SDB in CVD patients has changed from 2012 to 2019.

Key Words: Atrial fibrillation; Continuous positive airway pressure; Coronary artery disease; Health insurance system; Heart failure

Sleep-disordered breathing (SDB) is a major health problem worldwide, and it is related to a high risk of cardiovascular disease (CVD), including sudden death, atrial fibrillation (AF), stroke, and coronary artery disease (CAD), leading to heart failure (HF).[1–9] SDB is highly prevalent[10–14] and is associated with an elevated risk of serious cardiovascular outcomes.[2,3,5] In consideration of high concurrent risk of CVD with SDB, the Japanese Circulation Society (JCS) has published the "Guidelines for Diagnosis and Treatment of Sleep-Disordered Breathing in Cardiovascular Medicine (the 2010 JCS guidelines)", and appropriate screening, management and treatment of SDB in patients with CVD have been recommended.[15]

With regard to treatment for SDB, continuous positive airway pressure (CPAP) is the gold standard therapy for obstructive sleep apnea (OSA). CPAP is strongly recommended for patients with an apnea hypopnea index (AHI) ≥30, patients with an AHI ≥15 who have prior CVD history, and/or CVD risks or clinical symptoms due to SDB (class I, evidence level B).[15] However, after the 2010 JCS guidelines were published, a recent randomized controlled trial (RCT) focusing on treatment using CPAP, published in 2016, failed to demonstrate a beneficial prognostic impact on the primary or secondary setting of CVD.[16–20] In addition, adaptive servo-ventilation (ASV) is globally used to treat central sleep apnea (CSA) in HF patients,[21] and was originally used to manage congestive HF in Japan. Due to the evidence from the treatment of sleep-disordered breathing with predominant central sleep apnea by adaptive servo ventilation in patients with heart failure (SERVE-HF)

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Department of Cardiovascular Medicine, Fukushima Medical University, Fukushima (R.T., A.Y., Y.H., F.A., Y. Sato, T.M., Y.T.); Department of Clinical Laboratory Sciences, Fukushima Medical University School of Health Science, Fukushima (A.Y.); and Department of Medical and Health Information Management, National Cerebral and Cardiovascular Center, Suita (Y. Sumita, M.N.), Japan

Mailing address: Akiomi Yoshihisa, MD, PhD, Department of Cardiovascular Medicine, Fukushima Medical University, 1 Hikarigaoka, Fukushima 960-1295, Japan. E-mail: yoshihis@fmu.ac.jp

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trial published in 2015, the recommendations for ASV treatment for patients with CSA and congestive HF were changed and updated in 2015–2016.[22,23] Moreover, in the revision of the health insurance system of Japan in 2016, insurance coverage for ASV was updated. ASV has only been approved for symptomatic HF patients (NYHA class III or IV) with Cheyne-Stokes respiration and a confirmed AHI ≥20 by polysomnography (PSG) or with an AHI ≥15 even after undergoing CPAP. Additionally, it has been reported that careful consideration should be given when treating ASV in HF patients with an ejection fraction (EF) of ≤45%.[24]

Therefore, after the publication of the 2010 JCS guidelines,[15] because of changes in evidence from recent studies[16–20,22,23] and changes in the health insurance system, trends in the practice pattern for SDB in patients with CVD in Japan might change over time. Additionally, because of limited access to the diagnostic devices described above and an estimated high prevalence of SDB, at present, the majority of subjects with SDB may be undiagnosed and undertreated. Therefore, the aim of the present study was to evaluate the epidemiology and temporal changes in the practice pattern for SDB from 2012 to 2019 using a nationwide claim database in Japan.

Methods

Data Source

This survey used data from the Japanese Registry of All Cardiac and Vascular Diseases – Diagnosis Procedure Combination (JROAD-DPC), a nationwide claim database, as previously reported.[25–27] However, the JROAD database did not include individual patient data. The DPC system is a case-mix patient classification system launched by the Ministry of Health, Labor, and Welfare of Japan in 2002. It contains patient demographics and disease-specific data for each patient. Based on the DPC database, the JROAD-DPC database was created by combining JROAD data derived from a JCS national survey in 2012. The validity of the DPC database is generally high, especially for primary diagnoses and procedure records.[28]

Study Population

The JROAD-DPC database included a total of 9,825,635 health records between April 2012 and March 2020. In the DPC system, the diagnoses are made by the attending physicians, and are categorized into 6 groups based on the International Classification of Diseases (ICD-10) diagnosis codes; (1) main diagnosis; (2) admission-precipitating diagnosis; (3) most resource-consuming diagnosis; (4) second most resource-consuming diagnosis; (5) comorbidities present on admission; and (6) complications arising from SDB after admission. Because the patients with SDB are known to be at increased risk for several adverse clinical outcomes, such as CVD, in the present study, we identified the patients aged ≥20 years who were hospitalized with: (1) main diagnosis; (2) admission-precipitating diagnosis; and/or (3) most resource-consuming diagnosis of AF (ICD-10 codes: I48.0, I48.1, I48.2, I48.3, I48.4, I48.9), angina pectoris (AP) (I20.0, I20.1, I20.8, I20.9), acute myocardial infarction (AMI) (I21.0, I21.1, I21.3, I21.4, I21.9), HF (I11.0, I13.0, I50.0, I50.1, I50.9) , supraventricular arrhythmia (I47.0, I47.1. I47.2, I47.9), ventricular fibrillation (I49.0), cardiac arrest with successful resuscitation (I46.0, I46.1, I46.9), pulmonary hypertension (I27.0, I27.2), subarachnoid hemorrhage (I60.0, I60.1, I60.2, I60.3, I60.4, I60.5, I60.6, I60.7, I60.8, I60.9), intracerebral hemorrhage (I61.0, I61.1, I61.2, I61.3, I61.4, I61.5, I61.6, I61.8, I61.9), and cerebral infarction (I63.0, I63.1, I63.2, I63.3, I63.4, I63.5, I63.6, I63.8, I63.9). The total number of health records included in the present study was 5,037,339.

Data Collection

Patient characteristics, including age, sex, initial diagnosis, and comorbidities at the time of admission, were extracted from the claim data. The comorbidities were determined using ICD-10 codes. With respect to SDB, diagnostic tests and treatments, such as polygraphy, PSG, CPAP, home oxygen therapy (HOT), and respirators including ASV or Bi-level positive airway pressure (Bi-PAP) were also extracted using the claim data. The health insurance claims related to SDB diagnostic tests are stored in "Test (code D)", and treatments are stored in "Operation (Code C)". The definition of the classification code are as follows: polygraphy (D237-1), PSG (D237-2, D237-3), CPAP (C107-2, C165-0), and HOT (C103-0). Because the claim data between 2012 and 2015 cannot distinguish ASV from home mechanical ventilation (e.g., Bi-PAP), we categorized it as a respirator, and it was defined as any one of the following classification codes: C107-0, C107-2, and C165-0.

Statistical Analysis

Categorical variables are expressed as numbers and percentages, and continuous variables are presented as the median (interquartile range). We evaluated patient characteristics, and changes of proportions of SDB diagnosis, treatment and test options over time. The Cochran-Armitage test was used for the categorical variables, and the Jonckheere-Terpstra trend test was used for the continuous variables to identify trends. The threshold for significance was $P<0.05$. All statistical analyses were conducted using Statistical Package for Social Sciences version 27.0 (IBM, Armonk, NY, USA) or EZR version 1.52 (Saitama Medical Center, Jichi Medical University, Saitama, Japan), which is a graphical user interface for R (The R Foundation for Statistical Computing, Vienna, Austria).[29]

Ethics Statement

The requirement for informed consent was waived because of the anonymized nature of the data. Each hospital anonymized the patient data using the code-change equations created by each hospital and sent them to the Ministry of Health, Labor and Welfare. All participants were notified through homepages or posters at each hospital of their participation in the study, and it was explained that they were free to opt-out of participation at any time. Our study complies with the Declaration of Helsinki and the Japanese Ethical Guidelines for Medical and Health Research Involving Human Subjects.

Results

Table 1 shows the characteristics of hospitalized patients with SDB between 2012 and 2019. A total of 46,162 patients were identified using the ICD-10 code "G47.3" who were hospitalized with any of the following: (1) main diagnosis; (2) admission-precipitating diagnosis; (3) most resource-consuming diagnosis; (4) second most resource-consuming diagnosis; (5) comorbidities present on admission; and (6) complications arising from SDB after

Table 1. Baseline Characteristics of Patients With SDB (n=46,162)

	Total (n=46,162)	2012 (n=3,547)	2013 (n=4,052)	2014 (n=4,424)	2015 (n=5,276)	2016 (n=7,004)	2017 (n=7,107)	2018 (n=7,313)	2019 (n=7,439)	P value
Demographic data										
Age (years)	67 [57, 76]	66 [57, 76]	67 [57, 76]	67 [57, 76]	67 [57, 76]	67 [56, 76]	67 [57, 76]	68 [58, 77]	68 [57, 77]	0.473
Male sex (n, %)	37,045 (80.2)	2,872 (81.0)	3,226 (79.6)	3,520 (79.6)	4,215 (79.9)	5,676 (81.0)	5,750 (80.9)	5,891 (80.6)	5,895 (79.2)	0.673
BMI (kg/m^2)	26.4 [23.4, 30.3]	26.2 [23.3, 30.1]	26.3 [23.3, 30.3]	26.3 [23.3, 30.2]	26.4 [23.4, 30.2]	26.5 [23.4, 30.5]	26.7 [23.6, 30.7]	26.3 [23.4, 30.2]	26.4 [23.4, 30.4]	0.404
Past history, n (%)										
HT	27,875 (60.4)	1,998 (56.3)	2,282 (56.3)	2,432 (55.0)	2,893 (54.8)	4,517 (64.5)	4,475 (63.0)	4,587 (62.7)	4,691 (63.1)	<0.001*
DM	16,585 (35.9)	1,270 (35.8)	1,338 (33.0)	1,518 (34.3)	1,771 (33.6)	2,638 (37.8)	2,688 (37.8)	2,700 (36.9)	2,672 (35.9)	<0.001*
DLp	17,108 (37.0)	1,308 (36.9)	1,392 (34.4)	1,519 (34.3)	1,755 (33.3)	2,895 (41.3)	3,021 (42.5)	3,059 (41.8)	3,159 (42.5)	<0.001*
CVA	6,490 (14.0)	203 (5.7)	244 (6.0)	262 (5.9)	821 (15.6)	1,209 (17.3)	1,240 (17.4)	1,267 (17.3)	1,244 (16.7)	<0.001*
PAD	2,245 (4.9)	173 (4.9)	160 (3.9)	203 (4.6)	214 (4.1)	324 (4.6)	341 (4.8)	409 (5.6)	421 (5.7)	<0.001*
CKD	5,549 (12.0)	349 (9.8)	431 (10.6)	462 (10.4)	578 (11.0)	926 (13.2)	879 (12.4)	933 (12.8)	991 (13.3)	<0.001*
HF	23,348 (50.6)	1,874 (52.8)	2,190 (54.0)	2,334 (52.8)	2,483 (47.1)	3,503 (50.0)	3,553 (50.0)	3,555 (48.6)	3,856 (51.8)	<0.001*
AF	14,254 (30.9)	822 (23.2)	1,059 (26.1)	1,194 (27.0)	1,455 (27.6)	2,223 (31.7)	2,315 (32.6)	2,520 (34.5)	2,666 (35.8)	<0.001*
Diagnostic test, n (%)										
Polygraphy or PSG	14,325 (31.0)	1,486 (41.9)	1,758 (43.4)	1,710 (38.7)	1,851 (35.1)	2,069 (29.5)	1,836 (25.8)	1,852 (25.3)	1,763 (23.7)	<0.001*
Polygraphy	11,877 (25.7)	1,184 (33.4)	1,396 (34.5)	1,386 (31.3)	1,481 (28.1)	1,736 (24.8)	1,580 (22.2)	1,580 (21.6)	1,534 (20.6)	<0.001*
PSG	2,998 (6.5)	358 (10.1)	429 (10.6)	392 (8.9)	444 (8.4)	433 (6.2)	322 (4.5)	347 (4.7)	273 (3.7)	<0.001*
Polygraphy and PSG	550 (1.2)	56 (1.6)	67 (1.7)	68 (1.5)	74 (1.4)	100 (1.4)	66 (0.9)	75 (1.0)	44 (0.6)	<0.001*
Treatment										
CPAP (n, %)	10,116 (21.9)	729 (20.6)	845 (20.9)	1,052 (23.8)	1,216 (23.0)	1,556 (22.2)	1,573 (22.1)	1,567 (21.4)	1,578 (21.2)	0.553*
Respirator (n, %)	2,735 (5.9)	329 (9.3)	357 (8.8)	251 (5.7)	181 (3.4)	443 (6.3)	392 (5.5)	368 (5.0)	414 (5.6)	<0.001*
HOT (n, %)	1,959 (4.2)	145 (4.1)	201 (5.1)	198 (4.5)	178 (3.4)	312 (4.5)	327 (4.6)	277 (3.8)	321 (4.3)	0.491*
Hospitalization length (days)	11 [4, 21]	12 [4, 21]	12 [4, 21]	11 [4, 20]	11 [4, 21]	12 [4, 21]	11 [4, 21]	10 [4, 21]	10 [4, 20]	<0.001**

Values are shown as the mean [IQR]. *Changes to categorical variables were evaluated by using the Cochran-Armitage test for trend. **Changes to continuous variables were evaluated by using the Jonckheere-Terpstra test for trend. AF, atrial fibrillation; BMI, body mass index; CKD, chronic kidney disease; CPAP, continuous positive airway pressure; CVA, cerebrovascular accident; DLp, dyslipidemia; DM, diabetes mellitus; HF, heart failure; HOT, home oxygen therapy; HT, hypertension; PAD, peripheral artery disease; PSG, polysomnography; SDB, sleep-disordered breathing.

admission. The total number of hospitalizations increased yearly, and this was used to calculate the proportions. The median age was 67 years, 80.2% were men, and the median body mass index was 26.4 kg/m^2. Patients with hypertension and HF accounted for 60.4% and 50.6% of all subjects respectively. Impressively, the number of diagnosed cases of SDB in the DPC database increased overtime (from 3,547 in 2012 to 7,439 in 2019), as did the proportion of patients with CVD (from 5.7% in 2012 to 16.7% in 2019) and AF (from 23.2% in 2012 to 34.5% in 2019). Along with decreased hospitalization length (from 12 days in 2012 to 10 days in 2019), the proportion of diagnostic tests (polygraphy, PSG) performed during hospitalization significantly decreased (from 41.9% in 2012 to 23.7% in 2019). In contrast, CPAP treatment based on DPC data only at hospital discharge remained almost unchanged during the study period (20.6% in 2012 and 21.2% in 2019).

The temporal trends in the prevalence and practice patterns for SDB in each CVD patient (AF, AP, AMI and HF) are presented in **Table 2** and **Figure**. Each CVD category was calculated from population denominators, and shows the increasing trend through the observational

period. In patients with AF (**Table 2A** and **Figure A**, n=424,106), diagnosed cases of SDB increased (from 1.3% in 2012 to 1.8% in 2019), and CPAP treatment among patients with both AF and SDB (n=6,796) increased (from 15.2% in 2012 to 17.5% in 2019). An increased number of catheter ablations (from 27,221 in 2012 to 79,902 in 2019) may account for the incrase. In patients with AP (**Table 2B** and **Figure B**, n=1,723,751), the proportion of SDB diagnostic tests decreased (from 0.7% in 2012 to 0.4% in 2019), and CPAP treatment among patients with both AP and SDB (n=12,445) also decreased (from 22.1% in 2012 to 16.3% in 2019). In patients with AMI (**Table 2C** and **Figure C**, n=365,572) with shortened hospitalization lengths of stay (from 14 days in 2012 to 12 days in 2019), the proportion of SDB diagnostic tests conducted decreased (from 3.0% in 2012 to 1.9% in 2019), In addition, CPAP treatment among patients with both AMI and SDB (n=3,539) also decreased (from 21.4% in 2012 to 17.8% in 2019). In

Table 2. (A) Patients With AF (n=424,106), (B) Patients With Angina Pectoris (n=1,723,751), (C) Patients With Acute Myocardial Infarction (n=365,572), (D) Patients With HF (n=1,170,872)

(A)	Total (n=424,106)	2012 (n=27,221)	2013 (n=34,782)	2014 (n=41,040)	2015 (n=47,207)	2016 (n=55,826)	2017 (n=63,851)	2018 (n=74,277)	2019 (n=79,902)	P value
SDB based on DPC (n, %)	6,796 (1.6)	348 (1.3)	496 (1.4)	556 (1.4)	667 (1.4)	974 (1.7)	1,051 (1.6)	1,292 (1.7)	1,412 (1.8)	<0.001*
SDB treated using CPAP (n, % of SDB patients)	1,170 (17.2)	53 (15.2)	80 (16.1)	105 (18.9)	115 (17.2)	177 (18.2)	185 (17.6)	208 (16.1)	247 (17.5)	<0.001*
SDB with diagnostic tests	1,953 (0.5)	159 (0.6)	207 (0.6)	236 (0.6)	225 (0.5)	310 (0.6)	250 (0.4)	304 (0.4)	262 (0.3)	<0.001*
Non-SDB with diagnostic tests	7,889 (1.9)	427 (1.6)	614 (1.8)	1,064 (2.6)	870 (1.8)	1,069 (1.9)	845 (1.3)	1,374 (1.8)	1,626 (2.0)	0.546*
SDB without diagnostic tests	4,843 (1.1)	189 (0.7)	289 (0.8)	320 (0.8)	442 (0.9)	664 (1.2)	801 (1.3)	988 (1.3)	1,150 (1.4)	<0.001*
Diagnostic tests (Polygraphy or PSG; n, %)	9,842 (2.3)	586 (2.2)	821 (2.4)	1,300 (3.2)	1,095 (2.3)	1,379 (2.5)	1,095 (1.7)	1,678 (2.3)	1,888 (2.4)	<0.001*
Polygraphy	9,111 (2.1)	535 (2.0)	692 (2.0)	1,189 (2.9)	961 (2.0)	1,280 (2.3)	1,043 (1.6)	1,591 (2.1)	1,820 (2.3)	0.275*
PSG	808 (0.2)	54 (0.2)	135 (0.4)	121 (0.3)	142 (0.3)	112 (0.2)	61 (0.1)	100 (0.1)	83 (0.1)	<0.001*
Polygraphy and PSG	77 (0.0)	3 (0.0)	6 (0.0)	10 (0.0)	8 (0.0)	13 (0.0)	9 (0.0)	13 (0.0)	15 (0.0)	0.912*
CPAP (n, %)	1,634 (0.4)	70 (0.3)	102 (0.3)	143 (0.3)	157 (0.3)	252 (0.5)	258 (0.4)	314 (0.4)	338 (0.4)	<0.001*
Hospitalization length (days)		6 [4, 10]	6 [4, 9]	5 [4, 9]	5 [4, 8]	5 [4, 8]	5 [4, 7]	5 [4, 7]	4 [4, 6]	<0.001**

(B)	Total (n=1,723,751)	2012 (n=27,221)	2013 (n=34,782)	2014 (n=41,040)	2015 (n=47,207)	2016 (n=55,826)	2017 (n=63,851)	2018 (n=74,277)	2019 (n=79,902)	P value
SDB based on DPC (n, %)	12,445 (0.7)	1,203 (0.7)	1,215 (0.7)	1,462 (0.7)	1,490 (0.7)	1,826 (0.8)	1,786 (0.8)	1,787 (0.8)	1,676 (0.8)	<0.001*
SDB treated using CPAP (n, % of SDB patients)	2,376 (19.1)	266 (22.1)	258 (21.2)	320 (21.9)	297 (19.9)	343 (18.8)	328 (18.4)	291 (16.3)	273 (16.3)	0.009*
SDB with diagnostic tests	2,169 (0.1)	310 (0.2)	338 (0.2)	352 (0.2)	340 (0.2)	265 (0.1)	186 (0.1)	198 (0.1)	180 (0.1)	<0.001*
Non-SDB with diagnostic tests	5,700 (0.3)	868 (0.5)	922 (0.5)	868 (0.4)	643 (0.3)	616 (0.3)	495 (0.2)	675 (0.3)	613 (0.3)	<0.001*
SDB without diagnostic tests	10,276 (0.6)	893 (0.5)	877 (0.5)	1,110 (0.5)	1,150 (0.5)	1,561 (0.7)	1,600 (0.7)	1,589 (0.7)	1,496 (0.7)	<0.001*
Diagnostic tests (Polygraphy or PSG; n, %)	7,878 (0.5)	1,178 (0.7)	1,260 (0.7)	1,229 (0.6)	983 (0.5)	881 (0.4)	681 (0.3)	873 (0.4)	793 (0.4)	<0.001*
Polygraphy	7,022 (0.4)	1,062 (0.6)	1,125 (0.6)	1,064 (0.5)	841 (0.4)	797 (0.3)	605 (0.3)	799 (0.3)	729 (0.4)	<0.001*
PSG	931 (0.1)	126 (0.1)	150 (0.1)	171 (0.1)	154 (0.1)	95 (0.0)	79 (0.0)	86 (0.0)	70 (0.0)	<0.001*
Polygraphy and PSG	84 (0.0)	10 (0.0)	15 (0.0)	15 (0.0)	12 (0.0)	11 (0.0)	3 (0.0)	12 (0.0)	6 (0.0)	0.007*
CPAP (n, %)	3,230 (0.2)	346 (0.2)	341 (0.2)	460 (0.2)	419 (0.2)	465 (0.2)	423 (0.2)	405 (0.2)	371 (0.2)	0.004*
Hospitalization length (days)		3 [3, 5]	3 [3, 5]	3 [3, 5]	3 [3, 4]	3 [3, 4]	3 [3, 4]	3 [3, 4]	3 [3, 4]	<0.001**

(**Table 2** continued the next page.)

(C)	Total (n=365,572)	2012 (n=35,817)	2013 (n=37,598)	2014 (n=42,416)	2015 (n=45,294)	2016 (n=49,481)	2017 (n=49,937)	2018 (n=51,856)	2019 (n=53,173)	P value
SDB based on DPC (n, %)	3,539 (1.0)	359 (1.0)	360 (1.0)	406 (1.0)	430 (0.9)	497 (1.0)	480 (1.0)	512 (1.0)	495 (0.9)	0.641*
SDB treated using CPAP (n, % of SDB patients)	725 (20.4)	77 (21.4)	88 (24.4)	100 (24.6)	97 (22.6)	97 (19.5)	91 (19.0)	87 (17.8)	88 (17.8)	<0.001*
SDB with diagnostic tests	1,879 (0.5)	250 (0.7)	239 (0.6)	256 (0.6)	235 (0.5)	254 (0.5)	226 (0.5)	218 (0.4)	201 (0.4)	<0.001*
Non-SDB with diagnostic tests	7,198 (2.0)	830 (2.3)	1,026 (2.7)	1,022 (2.4)	937 (2.1)	977 (2.0)	746 (1.5)	845 (1.6)	815 (1.5)	<0.001*
SDB without diagnostic tests	1,660 (0.5)	109 (0.3)	121 (0.3)	150 (0.4)	195 (0.4)	243 (0.5)	254 (0.5)	294 (0.6)	294 (0.6)	<0.001*
Diagnostic tests (Polygraphy or PSG; n, %)	9,077 (2.5)	1,080 (3.0)	1,265 (3.4)	1,278 (3.0)	1,172 (2.6)	1,231 (2.5)	972 (1.9)	1,063 (2.0)	1,016 (1.9)	<0.001*
Polygraphy	8,089 (2.2)	956 (2.7)	1,153 (3.1)	1,146 (2.7)	1,041 (2.3)	1,072 (2.2)	838 (1.7)	963 (1.9)	920 (2.2)	<0.001*
PSG	1,142 (0.3)	152 (0.4)	143 (0.4)	149 (0.4)	142 (0.3)	170 (0.3)	153 (0.3)	121 (0.2)	112 (0.2)	<0.001*
Polygraphy and PSG	154 (0.0)	28 (0.1)	31 (0.1)	17 (0.0)	11 (0.0)	11 (0.0)	19 (0.0)	21 (0.0)	16 (0.0)	<0.001*
CPAP (n, %)	1,101 (0.3)	101 (0.3)	119 (0.3)	137 (0.3)	132 (0.3)	166 (0.3)	153 (0.3)	142 (0.3)	151 (0.3)	0.443*
Hospitalization length (days)		14 [8, 20]	13 [8, 19]	13 [8, 19]	13 [8, 19]	13 [8, 18]	13 [8, 18]	12 [8, 18]	12 [8, 17]	<0.001**

(D)	Total (n=1,170,872)	2012 (n=108,607)	2013 (n=116,020)	2014 (n=131,672)	2015 (n=141,989)	2016 (n=157,922)	2017 (n=167,062)	2018 (n=172,395)	2019 (n=175,215)	P value
SDB based on DPC (n, %)	17,935 (1.5)	1,533 (1.4)	1,796 (1.5)	1,865 (1.4)	1,961 (1.4)	2,706 (1.7)	2,705 (1.6)	2,629 (1.5)	2,740 (1.6)	<0.001*
SDB with either treatment (CPAP, respirator, HOT; n, %)	7,485 (41.7)	707 (46.1)	814 (45.3)	832 (44.6)	867 (44.2)	1,096 (40.5)	1,056 (39.0)	1,024 (39.0)	1,089 (39.7)	<0.001*
SDB with diagnostic tests	6,759 (0.6)	773 (0.7)	900 (0.8)	831 (0.6)	743 (0.5)	942 (0.6)	876 (0.5)	868 (0.5)	826 (0.5)	<0.001*
Non-SDB with diagnostic tests	18,314 (1.6)	2,139 (2.0)	2,500 (2.2)	2,519 (1.9)	2,360 (1.7)	2,182 (1.4)	1,889 (1.1)	2,256 (1.3)	2,469 (1.4)	<0.001*
SDB without diagnostic tests	11,216 (1.0)	800 (0.7)	896 (0.8)	1,034 (0.8)	1,218 (0.9)	1,764 (1.1)	1,829 (1.1)	1,761 (1.0)	1,914 (1.1)	<0.001*
Diagnostic tests (Polygraphy or PSG; n, %)	25,033 (2.1)	2,872 (2.6)	3,400 (2.9)	3,350 (2.5)	3,103 (2.2)	3,124 (2.0)	2,765 (1.7)	3,124 (1.8)	3,295 (1.9)	<0.001*
Polygraphy	22,032 (1.9)	2,450 (2.3)	2,942 (2.5)	2,883 (2.2)	2,639 (1.9)	2,747 (1.5)	2,479 (1.5)	2,847 (1.7)	3,045 (1.7)	<0.001*
PSG	3,685 (0.3)	501 (0.5)	561 (0.5)	557 (0.4)	540 (0.4)	475 (0.3)	351 (0.2)	374 (0.2)	326 (0.2)	<0.001*
Polygraphy and PSG	684 (0.0)	79 (0.1)	103 (0.1)	90 (0.1)	76 (0.1)	98 (0.1)	65 (0.0)	97 (0.1)	76 (0.0)	<0.001*
CPAP (n, %)	10,627 (0.9)	413 (0.4)	520 (0.4)	730 (0.6)	916 (0.6)	2,085 (1.3)	2,098 (1.3)	1,905 (1.1)	1,960 (1.1)	<0.001*
Respirator (n, %)	21,935 (1.9)	2,117 (1.9)	2,820 (2.4)	3,332 (2.5)	2,543 (1.8)	2,995 (1.9)	2,895 (1.7)	2,611 (1.5)	2,622 (1.5)	<0.001*
HOT (n, %)	30,667 (2.6)	3,177 (2.9)	3,364 (2.9)	3,665 (2.8)	3,726 (2.6)	4,185 (2.7)	4,325 (2.6)	4,117 (2.4)	4,108 (2.6)	<0.001*
Hospitalization length (days)		17 [11, 28]	17 [11, 28]	17 [11, 27]	17 [11, 27]	17 [11, 27]	17 [11, 27]	16 [10, 26]	16 [10, 27]	<0.001**

Values are shown as the mean [IQR]. *Changes to categorical variables were evaluated by using the Cochran-Armitage test for trend. **Changes to continuous variables were evaluated by using the Jonckheere-Terpstra test for trend. DPC, Diagnosis Procedure Combination. Other abbreviations as in Table 1.

patients with HF (**Table 2D** and **Figure D**, n=1,170,872), although the number of diagnosed cases of SDB increased (from 1.4% in 2012 to 1.6% in 2019), and there were shortened hospitalization lengths of stay (from 17 days in 2012 to 16 days in 2019), the proportion of diagnostic tests performed during hospitalization decreased (from 2.6% in 2012 to 1.9% in 2019), and the percentage of SDB patients treated using CPAP, respirator or HOT among patients with both HF and SDB (n=17,935) tended to decrease from 2012 to 2019, especially in 2016 (from 46.1% in 2012

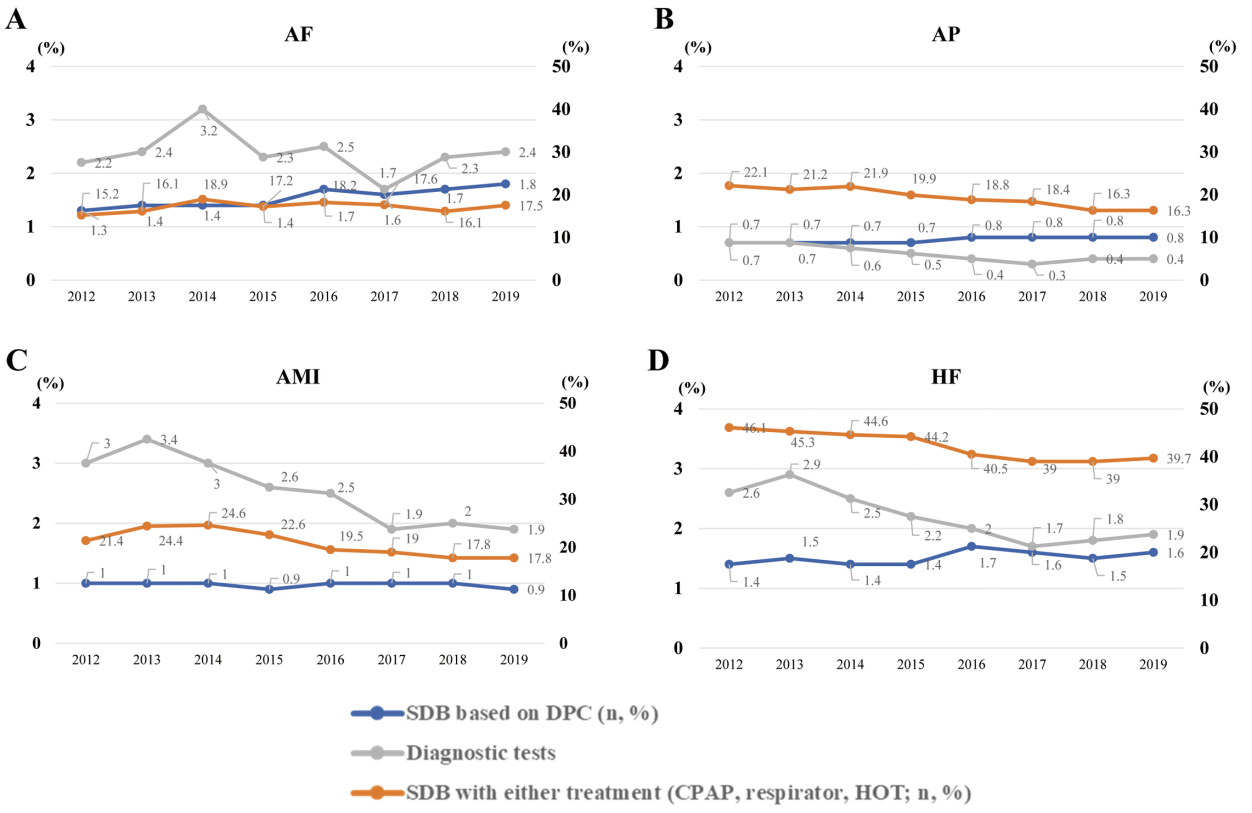

Figure. Temporal trends in the prevalence and practice patterns for sleep disordered breathing (SDB) in each patient with cardiovascular disease. (**A**) The blue line represents the percentage of diagnosed SDB patients based on DPC (n=6,796). The gray line represents the diagnostic tests performed for SDB during hospitalization (n=9,842) among patients who were hospitalized with: (1) main diagnosis; (2) admission-precipitating diagnosis; and/or (3) most resource-consuming diagnosis of AF (n=424,106). The orange line represents the percentage of SDB patients using CPAP (n=1,170) among patients with both AF and SDB (n=6,796). (**B**) The blue line represents the percentage of diagnosed SDB patients based on DPC (n=12,445). The gray line represents the performed diagnostic tests for SDB during hospitalization (n=7,878) among patients who were hospitalized with: (1) main diagnosis; (2) admission-precipitating diagnosis; and/or (3) most resource-consuming diagnosis of AP (n=1,723,751). The orange line represents the percentage of SDB patients using CPAP (n=2,376) among patients with both AP and SDB (n=12,445). (**C**) The blue line represents the percentage of diagnosed SDB patients based on DPC (n=3,539). The gray line represents the performed diagnostic tests for SDB during hospitalization (n=9,077) among patients who were hospitalized with: (1) main diagnosis; (2) admission-precipitating diagnosis; and/or (3) most resource-consuming diagnosis of AMI (n=365,572). The orange line represents the percentage of SDB patients using CPAP (n=725) among patients with both AMI and SDB (n=3,539). (**D**) The blue line represents the percentage of diagnosed SDB patients based on DPC (n=17,935). The gray line represents the performed diagnostic tests for SDB during hospitalization (n=25,033) among patients who were hospitalized with: (1) main diagnosis; (2) admission-precipitating diagnosis; and/or (3) most resource-consuming diagnosis of HF (n=1,170,872). The orange line represents the percentage of SDB patients using either CPAP, respirator or HOT (n=7,485) among patients with both HF and SDB (n=17,935). AF, atrial fibrillation; AMI, acute myocardial infarction; AP, angina pectoris; CPAP, continuous positive airway pressure; DPC, Diagnosis Procedure Combination; HF, heart failure; HOT, home oxygen therapy.

to 39.7% in 2019). However, SDB was treated more often in HF patients than in AF, AP and AMI patients (41.7% vs. 17.2%, 19.1% and 20.4%, respectively).

Discussion

Although we could not investigate the diagnosis and treatment of SDB status before admission or after hospital discharge, and therefore diagnosis and treatment of SDB might be underestimated, the main findings of the present study from the JROAD database were as follows: (1) the number of CVD patients diagnosed with SDB has increased (especially in patients with AF and HF); (2) with a decreasing length of hospitalization stay and revised evidence or changes in the health insurance system, the proportion of performed diagnostic tests (polygraphy, PSG) during hospitalization showed a decreasing trend in each category of CVD patient, except for those with AF; (3) in contrast, the rate of patients with past and newly diagnosed SDB was increased in all CVD groups, except for the AMI group; (4) CPAP treatment tended to increase in AF patients over time; (5) in contrast, CPAP treatment tended to decrease in patients with AP and/or AMI, and either treatment with CPAP, respirator and HOT tended to decrease in HF patients; and (6) SDB in HF patients was treated more often than SDB in AF, AP and AMI patients (41.7% vs. 17.2%, 19.1% and 20.4%, respectively).

With regard to patients with AF, the prevalence of SDB

is ~50%,[15] and SDB is associated with the occurrence of AF[30] and the recurrence of AF after electrical cardioversion or catheter ablation.[31] CPAP is associated with a significantly decreased recurrence rate of AF, even after electrical cardioversion or catheter ablation.[32,33] In addition, patients are less likely to progress to more permanent forms of AF and have significantly reduced occurrence of paroxysmal AF.[34] Recent meta-analysis has revealed that OSA treated with CPAP after AF intervention has a reduced AF risk.[35] Thus, the 2016 European Society of Cardiology Guidelines for the management of AF recommends to consider SDB screening in AF patients who have risk factors and to optimize SDB treatment for improving AF treatment results (class IIa, evidence level B).[36] In consideration of the above situations for AF patients in the present study, with an increasing number of admissions for catheter ablation and spread of comprehensive management including SDB, even with shortened hospitalization lengths of stay, diagnosed SDB and CPAP treatment have been widespread in AF patients.

With regard to patients who have CAD, the prevalence of SDB is 38–65%,[2] and the prevalence of acute coronary syndrome is 57%, and SDB is associated with higher cardiovascular events and/or mortality.[15,37] However, several RCTs published in 2016 failed to demonstrate improvement of CVD outcomes in patients with CAD.[16] Possible explanations for the lack of improvement regarding CVD were assumed to be due to the exclusion of study subjects who suffered from extreme sleepiness or severe SDB, a relatively short mean follow up, poor CPAP compliance, diagnosis determined by a portable sleep monitor, and/or other factors.[16] In contrast, a favorable trend with adequate nightly CPAP duration (>4 h/night) was reported in another study, which involved patients with newly revascularized CAD and moderate-to-severe OSA.[17] In the present study and in consideration of the above situations, with shortened hospitalization lengths of stay for patients with AP or AMI, SDB diagnostic tests and CPAP treatment tended to decrease in patients with both AP and AMI.

Regarding HF, prevalence of OSA was 47% in acute decompensated HF patients, 20% in chronic HF patients with reduced EF, and 23% in chronic HF patients with preserved EF, whereas CSA was 31% in acute decompensated HF patients, 33% in chronic HF patients with reduced EF, and 24% in chronic HF patients with preserved EF, and both OSA and CSA are associated with an adverse prognosis in HF patients.[1,2] However, evidence of treatment for both OSA and CSA in HF patients have not been established. CPAP for OSA in patients with HF ameliorates EF, and possibly improves cardiovascular prognosis.[38] In contrast, treatment of CSA in HF patients improves not only LV systolic[39–42] and diastolic function,[43] but also pulmonary,[44] renal,[45,46] and vascular function;[43,47] and thus it also potentially improves prognosis in HF patients with reduced or preserved EF.[4,39–45,48–52] However, the SERVE-HF trial using ASV, which was published in 2015, failed to demonstrate that treatment of CSA improves the prognosis of HF patients with CSA.[22] Due to the evidence from this trial, the recommendations of ASV treatment for patients with CSA and congestive HF have been updated, and ASV has been suggested to not be used in patients who have HF with an EF ≤45% and who have predominantly CSA (class III, evidence level A).[22,23] However, in patients with HF and a preserved EF, there are some trials reporting favorable outcomes.[43,53] In addition, several studies in Japan have reported that ASV decreases the incidence of cardiac events in patients with HF with or without SDB.[54,55] Based on these reports, ASV use is recommended for relieving symptoms of congestion in patients with HF receiving optimized treatment for HF in Japan (class IIa, evidence level B).[56] Therefore, JCS 2017/JHFS Guidelines on Diagnosis and Treatment of Acute and Chronic Heart Failure recommends CPAP use for patients with symptomatic OSA and HF (class I, evidence level A), and for patients with reduced EF and moderate or severe OSA to improve cardiac function (class IIa, evidence level A).[56] However, evidence for using CPAP to improve prognosis in patients with HF and moderate or severe OSA has not been reported yet (class IIb, evidence level C). Another therapeutic option, HOT, showed a favorable outcome in stable HF patients with CSA and Cheyne-Stokes respiration, including improvement of LV function.[57,58] However, a recent RCT failed to demonstrate the improvement of cardiac function in HF patients with SDB.[59] Although the routine use of HOT in HF patients with SDB remains controversial, it is recommended in Japan for symptomatic HF patients (NYHA class III or IV) with Cheyne-Stokes respiration and an AHI ≥20 confirmed by PSG (class IIa, evidence level B).[56] Unfortunately, in the present study, the purpose of using a respirator (including ASV or Bi-PAP) for treating SDB or congestion could not be determined from the JROAD-DPC data. In consideration of the above situations, in the present study, although diagnosed SDB has increased, diagnostic testing and treatment of SDB (using either CPAP, ASV, Bi-PAP, and HOT) during hospitalization tended to decrease between 2012 (especially in 2016) and 2019.

Study Strengths and Limitations

The current study has several limitations. First, although DPC data must be confirmed by a physician and are highly reliable, some of the data are based on medical claims, and these data may contain certain errors (i.e., diagnosis and treatment of SDB). Because the current analysis was based on DPC data, which were only evaluated during hospitalization and at hospital discharge, we could not evaluate diagnosis or treatment of SDB in the outpatient setting. We could not investigate the diagnosis and treatment of SDB status before admission or after hospital discharge. In particular, data showing a relatively low proportion of CPAP, HOT, and/or respirator use at discharge should be viewed cautiously. Second, because the JROAD-DPC database consisted of data from only cardiovascular departments, we could not collect data from other departments (e.g., internal medicine, respiratory department, sleep medicine, otolaryngology); therefore, the diagnosis and treatment of SDB might be underestimated. In contrast, because we could not fully distinguish each patient in the JROAD-DPC database, the results could have possibly been overestimated because patients could have been counted more than once. Third, because not all the cardiovascular hospitals in Japan participate in the JROAD-DPC, there might be a possibility of potential selection bias; however, this system covered ~83% of acute care hospitals in Japan by 2018, so the validity of the dataset is generally high. Fourth, the prevalence of ASV/HOT use was high in Japan compared with that in the United States, so these results might not be generalizable to other countries. Fifth, because JROAD data before the publication of the 2010

JCS guidelines[15] were lacking, changes in SDB practice patterns before and after the publication of the 2010 JCS guidelines could not be rigorously examined. Finally, the JROAD-DPC database does not contain detailed clinical data, and the use of a respirator (including ASV) or HOT for treating SDB or not could not be determined from this dataset.

Conclusions

A nationwide claim database, JROAD-DPC, suggested the possibility of a growing interest in SDB practice; for example, the prevalence of SDB management in patients with AF and HF, and impaired management of SDB in patients with AP and AMI, based on recent evidence and changes in the health insurance system.

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IRB Information

This research plan was approved by the institutional review board of Fukushima Medical University (approval number: 2021-061) and the National Cerebral and Cardiovascular Center (approval number: 2020-01).

Data Availability

The deidentified participant data will not be shared.

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