Advance Publication

Circulation Journal
doi:10.1253/circj.CJ-24-0697

ORIGINAL ARTICLE

Nationwide Trends in Idiopathic Pericarditis Management and Outcomes in Japan

— A Nationwide JROAD-DPC Analysis —

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Background: Idiopathic pericarditis generally has a favorable prognosis, but contemporary data on treatment patterns and outcomes remain limited.

Methods and Results: Using a nationwide Japanese database, we analyzed 8,020 pericarditis patients hospitalized between April 2016 and March 2021, and identified 3,963 (49%) patients with idiopathic pericarditis after excluding those with infectious, autoimmune or other causes. During the study period, the median age increased from 62 to 68 years ($P_{trend}<0.001$), and prescription rates of non-steroidal anti-inflammatory drugs (NSAIDs) and colchicine, and the simultaneous administration of NSAIDs and colchicine increased over time (from 65.9 to 72.6% [P=0.049], from 17.4 to 44.3% [P<0.001], and from 8.0 to 22.7% [P<0.001], respectively). The mean incidence of in-hospital death and rehospitalization for recurrence was 1.4% and 5.7%, respectively; neither changed over time. The mean length of hospitalization increased from 8 to 10 days and the cost of hospitalization increased from JPY 417,000 to JPY 525,000. Multivariable analysis showed that age and steroid use were significant predictors of in-hospital death, whereas cardiac tamponade was not (adjusted odds ratio 1.32; 95% confidence interval 0.56–3.14).

Conclusions: Among hospitalized patients with idiopathic pericarditis, prescription rates of medications recommended by European Society of Cardiology guidelines have increased, although the concurrent use of NSAIDs and colchicine remains uncommon; there have been no changes in the incidence of in-hospital death. Prospective studies, including outpatients, are needed to clarify the prognosis and recurrence rate of idiopathic pericarditis.

Key Words: Health outcomes research; Hospitalization; Idiopathic; Pericarditis; Trend

Pericarditis is an inflammation of the pericardium with various causes and symptoms, including pleuritic chest pain, pericardial friction rub, electrocardiogram changes, and pericardial effusion.[1] Although idiopathic, autoimmune, and post-cardiac injury pericarditis generally have a good prognosis,[2,3] bacterial, tuberculous, and malignant pericarditis are associated with worse outcomes.[4–7] Idiopathic pericarditis is the most common type of pericarditis[8,9] and typically has a favorable prognosis, although complications in specific subgroups necessitate careful evaluation. Notably, age has been identified as a predictor of in-hospital death in pericarditis, with older patients often facing a higher risk.[10] Despite growing evidence of the impact of aging on cardiovascular conditions,[11–13] no nationwide data specifically address pericarditis management in Japan, leaving outcomes and temporal trends largely unknown. Furthermore, several issues must be addressed regarding the clinical management of pericar-

Received September 3, 2024; revised manuscript received February 10, 2025; accepted February 17, 2025; J-STAGE Advance Publication released online March 30, 2025 Time for primary review: 28 days

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The Guest Editor for this article was Dr. Yoshihiro Fukumoto.

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ISSN-1346-9843

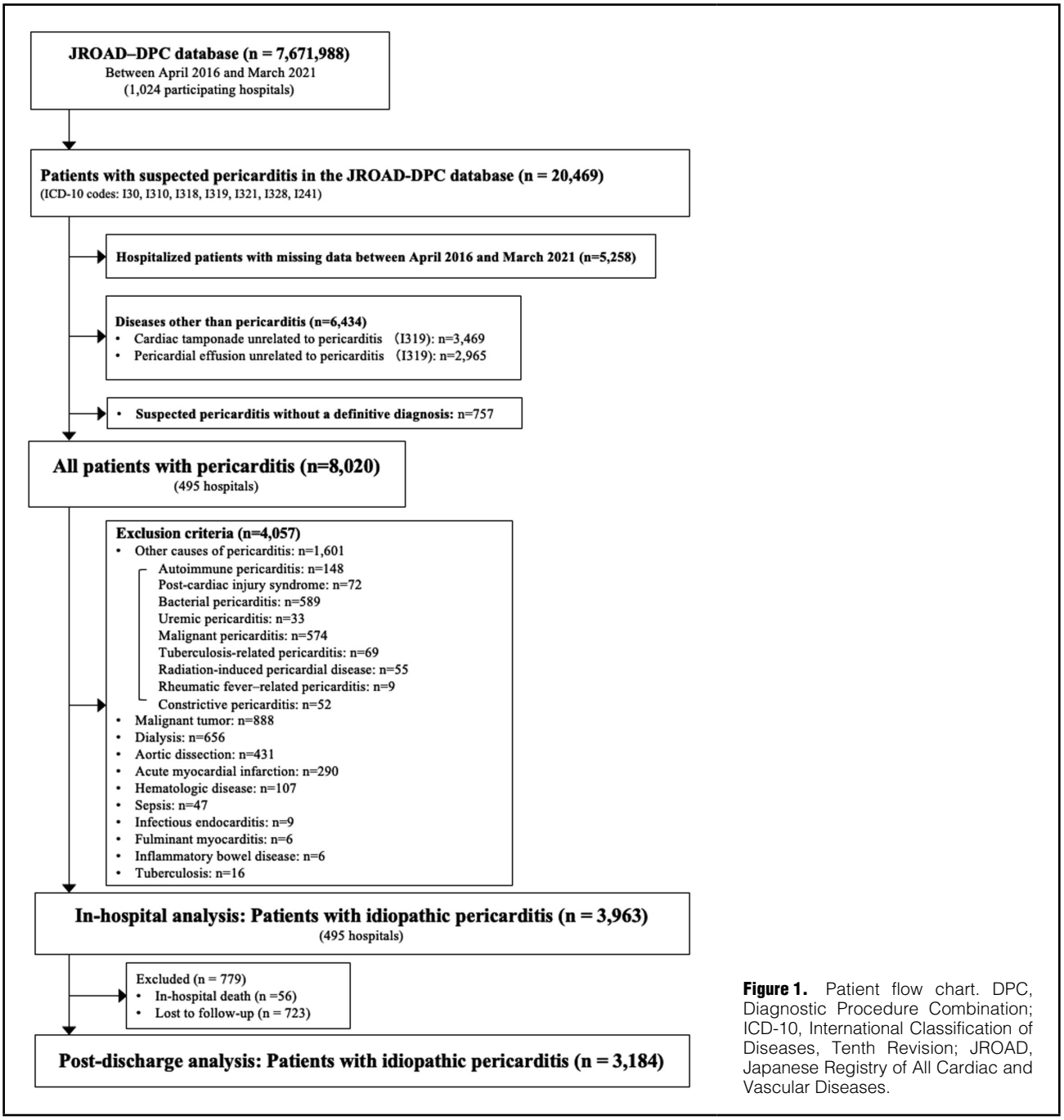

Figure 1. Patient flow chart. DPC, Diagnostic Procedure Combination; ICD-10, International Classification of Diseases, Tenth Revision; JROAD, Japanese Registry of All Cardiac and Vascular Diseases.

ditis in Japan. In the Japanese population, the safety and effectiveness of long-term, high-dose non-steroidal anti-inflammatory drugs (NSAIDs) are uncertain, and colchicine, which is the first-line treatment recommended by the European Society of Cardiology (ESC) guidelines,[1] is not reimbursed in Japan.

Accordingly, the aims of this study were to characterize the clinical features and treatments of idiopathic pericarditis, examine associated outcomes, and track temporal changes in practice within the Japanese Registry of All Cardiac and Vascular Diseases (JROAD)–Diagnosis Procedure Combination (DPC) database.

Methods

Data Source

This analysis used the JROAD-DPC dataset, which has been described previously.[14–16] Briefly, JROAD, established by the Japanese Circulation Society in 2004, provides comprehensive real-world nationwide data from annual surveys on cardiovascular disease hospitalizations. These data include information about resources (e.g., hospital beds and the number of certified cardiologists or surgeons), patient hospitalization numbers, and mortality rates. The aim of JROAD is to assess the clinical performance of teaching hospitals in Japan and provide relevant feedback.

Table 1. Trends Over Time in the Clinical Demographics of the Studied Population in the In-Hospital Analysis

	All (n=3,963)	2016 (n=800)	2017 (n=811)	2018 (n=805)	2019 (n=843)	2020 (n=704)	P_{trend}
Age (years)	64.0 [45.0–76.0]	62.0 [42.0–74.0]	63.0 [45.0–75.0]	62.0 [45.0–75.0]	65.0 [45.0–77.0]	68.0 [51.0–79.0]	<0.001
Male sex	2,893 (73.0)	602 (75.3)	588 (72.5)	591 (73.4)	608 (72.1)	504 (71.6)	0.13
BMI (kg/m^2)	22.8 [20.5–25.2]	22.4 [20.3–24.8]	22.9 [20.6–25.1]	22.9 [20.7–25.1]	22.8 [20.6–25.5]	22.9 [20.2–25.4]	0.040
CCI score	1.0 [0.0–2.0]	1.0 [0.0–2.0]	1.0 [0.0–2.0]	1.0 [0.0–1.0]	1.0 [0.0–2.0]	1.0 [0.0–2.0]	0.046
Recurrent pericarditis	222 (5.6)	30 (3.8)	50 (6.2)	41 (5.1)	50 (5.9)	51 (7.2)	0.011
Hypertension	1,216 (30.7)	218 (27.3)	239 (29.5)	238 (29.6)	278 (33.0)	243 (34.5)	<0.001
Dyslipidemia	702 (17.7)	131 (16.4)	129 (15.9)	136 (16.9)	169 (20.1)	137 (19.5)	0.016
Diabetes	571 (14.4)	111 (13.9)	116 (14.3)	105 (13.0)	122 (14.5)	117 (16.6)	0.18
Atrial fibrillation	570 (14.4)	104 (13.0)	98 (12.1)	112 (13.9)	120 (14.2)	136 (19.3)	<0.001
Ischemic heart disease	596 (15.0)	122 (15.3)	115 (14.2)	130 (16.2)	118 (14.0)	111 (15.8)	0.87
Examinations							
Tumor marker tests	987 (24.9)	163 (20.4)	208 (25.7)	212 (26.3)	215 (25.5)	189 (26.9)	0.009
CT	2,885 (72.8)	553 (69.1)	575 (70.9)	575 (71.4)	635 (75.3)	547 (77.7)	<0.001
CCTA	1,111 (28.0)	214 (26.8)	231 (28.5)	215 (26.7)	224 (26.6)	227 (32.2)	0.10
Coronary angiography	765 (19.3)	154 (19.3)	146 (18.0)	172 (21.4)	169 (20.1)	124 (17.6)	0.86
Medications							
All NSAIDs	2,753 (69.5)	527 (65.9)	579 (71.4)	557 (69.2)	579 (68.7)	511 (72.6)	0.049
Aspirin	1,039 (26.2)	182 (22.8)	214 (26.4)	207 (25.7)	234 (27.8)	202 (28.7)	0.008
Other NSAIDs	1,714 (43.3)	345 (43.1)	365 (45.0)	350 (43.5)	345 (40.9)	309 (43.9)	0.60
Colchicine	1,163 (29.3)	139 (17.4)	197 (24.3)	230 (28.6)	285 (33.8)	312 (44.3)	<0.001
Steroid	535 (13.5)	100 (12.5)	115 (14.2)	108 (13.4)	99 (11.7)	113 (16.1)	0.29
Combination therapy[A]							
All NSAIDs+colchicine	941 (23.7)	110 (13.8)	168 (20.7)	184 (22.9)	225 (26.7)	254 (36.1)	<0.001
Aspirin+colchicine	382 (9.6)	48 (6.0)	68 (8.4)	74 (9.2)	86 (10.2)	106 (15.1)	<0.001
Other NSAIDs+colchicine	559 (14.1)	62 (7.8)	100 (12.3)	110 (13.7)	139 (16.5)	148 (21.0)	<0.001
Simultaneous administration of NSAID and colchicine	596 (15.0)	64 (8.0)	116 (14.3)	109 (13.5)	147 (17.4)	160 (22.7)	<0.001
Triple therapy[B]							
All NSAIDs+colchicine+steroid	160 (4.0)	13 (1.6)	40 (4.9)	19 (2.4)	34 (4.0)	54 (7.7)	<0.001
Aspirin+colchicine+steroid	62 (1.6)	5 (0.6)	19 (2.3)	4 (0.5)	12 (1.4)	22 (3.1)	0.007
Other NSAIDs+colchicine+steroid	98 (2.5)	8 (1.0)	21 (2.6)	15 (1.9)	22 (2.6)	32 (4.5)	<0.001

Unless indicated otherwise, data are given as the median [interquartile range] or n (%). [A]Combination therapy is defined as the concomitant use of non-steroidal anti-inflammatory drugs (NSAIDs) and colchicine. [B]Triple therapy is defined as the concomitant use of NSAIDs, colchicine, and steroids. BMI, body mass index; CCI, Charlson comorbidity index; CCTA, coronary computed tomography angiography; CT, computed tomography.

Participation in JROAD is mandatory for all cardiovascular teaching hospitals, because the database is crucial for physician certification and hospital accreditation by the Japanese Circulation Society. The JROAD-DPC is a nationwide claim-based database that integrates JROAD data with the DPC System. This system encompasses details on patient demographics (age and sex), admission type (emergency or planned), primary diagnosis, comorbidities, complications, examinations, procedures, treatments, length of hospitalization, hospitalization costs, and discharge status. Each hospital anonymizes patient identifiers using specific code-change equations applied to the original DPC data before submission to the Ministry of Health, Labour and Welfare of Japan. Physicians are obliged to refer to medical records to accurately register diagnoses in Japanese, thus enhancing diagnostic accuracy. Since 2016, it has been possible to extract diagnoses from this database using both the International Classification of Diseases, 10th revision (ICD-10) codes and detailed physician input.

Study Population

We used JROAD-DPC data from April 2016 to March 2021, because the JROAD database altered its data collection methods in April 2016. Patients aged ≥20 years with suspected pericarditis were extracted using the following ICD-10 codes: I30, I310, I318, I319, I321, I328, and I241. Because ICD-10 code I319 includes diagnoses of diseases other than pericarditis that are associated with pericardial effusion or cardiac tamponade, we used physicians' records to exclude these patients. These records have been used in the previous JROAD studies to enhance the reliability of diagnoses.[17,18] In addition, cases of pericarditis with potential causes other than idiopathic pericarditis (e.g., post-pericardial injury syndrome, bacterial pericarditis, uremic pericarditis, malignant pericarditis, autoimmune pericar-

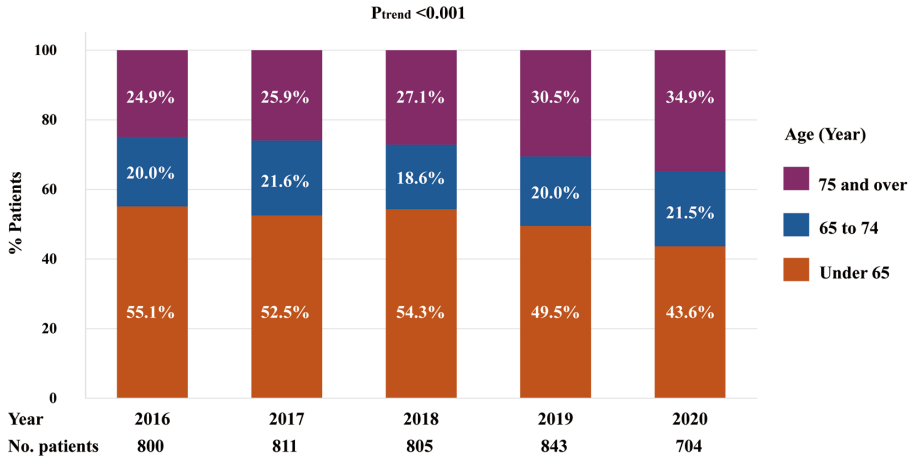

Figure 2. Annual changes in the proportion of age categories from April 2016 to March 2020. Ages were divided into 3 groups: <65 years, 65–74, and ≥75 years. From 2016 to 2020, the proportion of patients aged <65 years decreased from 55.1% to 43.6%, that of patients aged 65–74 years remained stable (from 20.0% to 21.5%), and that of patients aged ≥75 years increased from 24.9% to 34.9% (P_{trend}<0.001).

ditis, rheumatic fever pericarditis, radiation-induced pericardial disease, acute myocardial infarction, aortic dissection, myocarditis, infectious endocarditis, hematologic diseases, inflammatory bowel disease, hemodialysis, sepsis, and tuberculosis) were excluded on the basis of ICD-10 codes and the diagnoses that were entered by physicians. We classified viral pericarditis as idiopathic pericarditis, with reference to previous reports.[2,3,19] Details of the ICD-10 codes and diagnoses used in this study are presented in **Supplementary Table 1**. To conduct a temporal analysis, we excluded facilities that did not continuously participate in JROAD from April 2016 to March 2021.

Outcomes Measures

The primary outcome was in-hospital death; secondary outcomes were cardiac tamponade, length of hospitalization, and hospitalization cost. The outcome of the post-discharge analysis was the number of rehospitalizations due to recurrent pericarditis for 1 year. With reference to a previous study that assessed rehospitalization using JROAD-DPC data,[14] we created a dataset to evaluate readmission to the same hospital within 1 year by matching the hospitalization records of each patient. We examined changes in patient characteristics, treatment patterns, and outcomes over the fiscal year.

Statistical Analysis

Baseline clinical characteristics, medications, and procedures are described using numbers and percentages for categorical variables or the median and interquartile range (IQR) for continuous variables. Ages were divided into 3 groups: <65, 65–74, and ≥75 years. We analyzed temporal changes in patient characteristics, tests, treatments, and outcomes using the Cochran–Armitage trend test for categorical variables and the Jonckheere–Terpstra trend test for continuous variables. Each 1-year study period was defined from April of a given year to March of the following year (i.e., 2016: April 2016–March 2017; 2017: April 2017–March 2018, etc.). In-hospital death and cardiac tamponade were each dichotomized on the basis of their presence or absence. Hospitalization length and cost were each dichotomized at their respective medians into short vs. long hospitalization length and low vs. high hospitalization cost, respectively. Univariate and multivariable mixed-effects logistic regression analyses, with institution as a random intercept, were performed to examine the factors associated with in-hospital death. Prognostic factors for acute pericarditis including idiopathic pericarditis reported in previous reports and extractable from the JROAD-DPC database, such as age, sex, anticoagulant use, NSAID use, steroid use, cardiac tamponade, and Charlson comorbidity index (CCI), were analyzed in univariate analysis[1,2,10,20–22] (**Supplementary Table 2**). After univariate logistic regression analysis, multivariable analysis was performed using factors with P<0.05 in univariate analysis. Two-tailed P<0.05 was considered statistically significant. Analyses were performed using Stata 16 (StataCorp, College Station, TX, USA).

Ethics Statement

This study was designed in accordance with the Declaration of Helsinki and was approved by the Institutional Review Board of the National Cerebral and Cardiovascular Center (R22013-2). The requirement for written consent from each patient was waived due to the observational nature of the study.

Results

Figure 1 shows a flowchart of this study. Among 8,020 cases of pericarditis in the JROAD-DPC databases, 3,963 cases of idiopathic pericarditis were included in the present study.

Table 1 presents clinical characteristics, examination results, and medications. The median age was 64.0 years (IQR 45.0–76.0 years), and 73.0% of patients were male. The median age increased from 2016 to 2020 (P_{trend}<0.001). During the study period, the percentage of patients aged <65 years decreased, whereas the percentage of patients

Table 2. Trends Over Time of Outcomes in the In-Hospital Analysis

	All (n=3,963)	2016 (n=800)	2017 (n=811)	2018 (n=805)	2019 (n=843)	2020 (n=704)	P_{trend}
In hospital-deaths	56 (1.4)	10 (1.3)	7 (0.9)	11 (1.4)	15 (1.8)	13 (1.9)	0.12
Cardiac tamponade	203 (5.1)	34 (4.3)	42 (5.2)	34 (4.2)	50 (5.9)	43 (6.1)	0.08
Length of hospitalization (days)	9.0 [5–14]	8.0 [5.0–14.0]	8.0 [5.0–14.0]	9.0 [5.0–16.0]	8.0 [5.0–14.0]	10.0 [6.0–15.0]	<0.001
Cost of hospitalization (×10³ JPY)	448 [297–710]	417 [275–661]	419 [283–657]	456 [294–714]	442 [301–688]	525 [359–802]	<0.001

Unless indicated otherwise, data are given as the median [interquartile range] or n (%).

Table 3. Baseline Characteristics, Medications, and Outcomes of Surviving Patients or Patients With In-Hospital Death

	Surviving patients (n=3,907)	Patients who died in hospital (n=56)	P value
Age (years)	64.0 [45.0–76.0]	80.5 [70.0–88.0]	<0.001
Male sex	2,857 (73.1)	36 (64.3)	0.14
BMI (kg/m²)	22.8 [20.5–25.2]	21.6 [17.9–24.2]	0.007
CCI score	1.0 [0.0–2.0]	1.0 [1.0–3.0]	<0.001
Recurrent pericarditis	216 (5.5)	6 (10.7)	0.094
Hypertension	1,198 (30.7)	18 (32.1)	0.81
Dyslipidemia	698 (17.9)	4 (7.1)	0.037
Diabetes	556 (14.2)	15 (26.8)	0.008
Atrial fibrillation	556 (14.2)	14 (25.0)	0.023
Ischemic heart disease	592 (15.2)	4 (7.1)	0.096
Medications			
All NSAIDs	2,726 (69.8)	27 (48.2)	<0.001
Aspirin	1,026 (26.3)	13 (23.2)	0.61
Other NSAIDs	1,700 (43.5)	14 (25.0)	0.005
Colchicine	1,151 (29.5)	12 (21.4)	0.19
Steroid	520 (13.3)	15 (26.8)	0.003
Combination therapy[A]			
All NSAIDs+colchicine	931 (23.8)	10 (17.9)	0.30
Aspirin+colchicine	377 (9.6)	5 (8.9)	0.86
Other NSAIDs+colchicine	554 (14.2)	5 (8.9)	0.26
Simultaneous administration of NSAID and colchicine	591 (15.1)	5 (8.9)	0.20
Triple therapy[B]			
All NSAIDs+colchicine+steroid	158 (4.0)	2 (3.6)	0.86
Aspirin+colchicine+steroid	62 (1.6)	0 (0.0)	0.34
Other NSAIDs+colchicine+steroid	96 (2.5)	2 (3.6)	0.59
In-hospital outcome			
Cardiac tamponade	196 (5.0)	7 (12.5)	0.012
Hospitalization length (days)	9.0 [5.0–14.0]	10.0 [4.0–25.0]	0.33
Cost of hospitalization (×10³ JPY)	445 [297–703]	756 [298–1,500]	0.001

Unless indicated otherwise, data are given as the median [interquartile range] or n (%). [A]Combination therapy is defined as the concomitant use of NSAIDs and colchicine. [B]Triple therapy is defined as the concomitant use of NSAIDs, colchicine, and steroids. Abbreviations as in Table 1.

aged 65–74 and ≥75 years increased (P_{trend}<0.001; **Figure 2**). From 2019 to 2020, patients aged ≥65 years accounted for more than half of all individuals with pericarditis. There were no significant changes over time in sex distribution. The prevalence of hypertension and atrial fibrillation increased significantly during the study period (P_{trend}<0.001 for both). The prevalence of dyslipidemia also increased significantly, but to a lesser extent (P_{trend}=0.016). Overall, tumor marker tests were performed in 24.9% of patients and computed tomography was performed in 72.8%. From 2016 to 2020, there was an increase in the percentage of patients who underwent tumor marker tests (P_{trend}=0.009) or computed tomography increased (P_{trend}<0.001). Over the study period, NSAID use increased by 72.6% (P_{trend}=0.049), colchicine use increased by 44.3% (P_{trend}<0.001), combination therapy with NSAIDs and colchicine increased by 36.1% (P_{trend}<0.001), and the simultaneous administration of an NSAID and colchicine increased by 22.7% (P_{trend}<0.001).

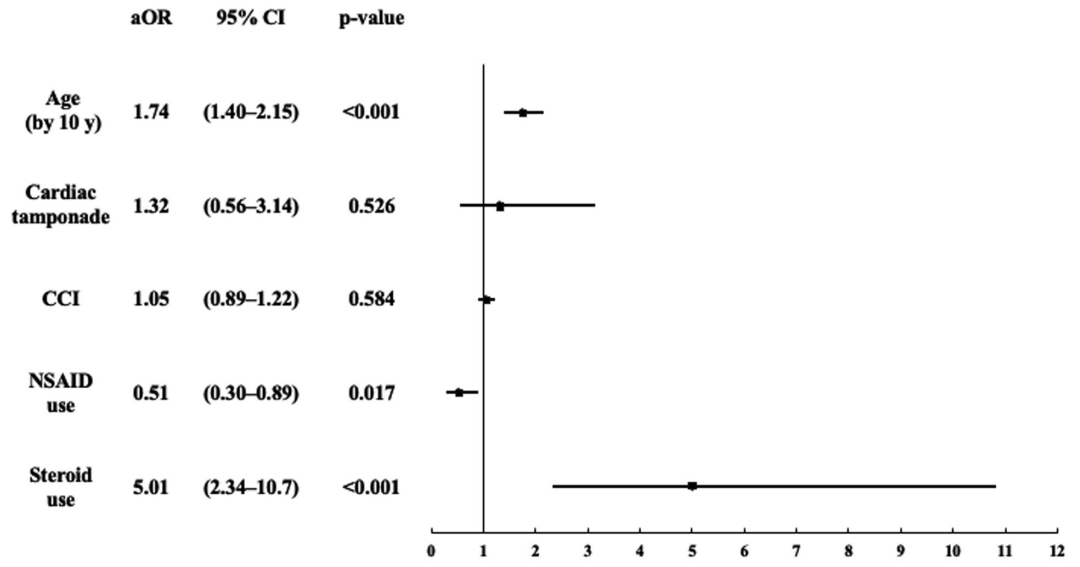

Figure 3. Multivariable mixed-effects logistic regression analysis, adjusted for factors with P<0.05 in univariate analysis, including age, cardiac tamponade, Charlson comorbidity index (CCI), non-steroidal anti-inflammatory drug (NSAID) use, and steroid use. Advanced age and steroid use were statistically significant risk factors for in-hospital death. aOR, adjusted odds ratio; CI, confidence interval.

Table 2 presents details of in-hospital outcomes. The overall incidence of in-hospital death was 1.4%, and that of cardiac tamponade was 5.1%. There was no significant change in the incidence of either from 2016 to 2020. The median hospitalization length was 9 days (IQR 5–14 days), with a median cost of JPY 448,000 (IQR JPY 297,000–710,000). There was a notable increase from 2016 to 2020 in both median hospitalization length and cost (P_{trend}<0.001 for both).

Table 3 presents a comparison of surviving patients or patients who died in hospital. There were several significant differences between surviving patients and those who died in hospital; those who died were older, had a higher CCI, a lower rate of NSAID use, a higher rate of steroid use, and a higher incidence of cardiac tamponade. Those who experienced cardiac tamponade were significantly older, had a significantly higher CCI, significantly lower rate of NSAID use, and significantly higher rates of steroid and triple combination therapy use than those without cardiac tamponade (**Supplementary Table 3**). There were also significant differences between the long and short hospitalization lengths groups, with the former being older, with a higher CCI, a higher incidence of cardiac tamponade, and higher rates of receiving colchicine, steroids, combination therapy, and triple therapy (**Supplementary Table 4**). The group with high hospitalization costs was significantly older and had a significantly lower proportion of men, higher CCI, a higher incidence of in-hospital death and cardiac tamponade, longer hospitalization length, and higher rates of receiving colchicine, steroids, combination therapy, and triple therapy compared with group with low hospitalization costs (**Supplementary Table 5**).

Univariate logistic regression analysis revealed that age, cardiac tamponade, CCI, NSAID use, and steroid use were significant predictive factors for in-hospital death (**Supplementary Table 2**). Multivariable mixed-effects logistic regression analyses, adjusted for factors with P<0.05 in univariate analysis, showed that age and steroid use were statistically significant factors for in-hospital death, whereas cardiac tamponade and CCI were not. In addition, NSAID use had a favorable effect on in-hospital death (**Figure 3**).

After excluding 56 patients (1.4%) who died in hospital and 723 (18.2%) who were lost to follow-up, the post-discharge analysis included 3,184 patients. Compared with patients who were followed-up, those lost to follow-up had a significantly lower CCI, lower rates of NSAID and colchicine use, and shorter hospitalization length (**Supplementary Table 6**). Trends in medication use were consistent between the post-discharge and in-hospital analyses (**Supplementary Table 7**). The overall rehospitalization rate due to recurrent pericarditis within 1 year was 5.7%. The median time to recurrence was 80 days (IQR 32–188 days). There were no significant temporal changes in the rates of rehospitalizations due to recurrent pericarditis (**Supplementary Table 8**). The rehospitalization rate for recurrent pericarditis after discharge was significantly higher among patients who received colchicine than among those who did not (**Supplementary Table 9**).

Discussion

This is the first nationwide survey of idiopathic pericarditis in Japan. The major findings of this study are that: (1) the median age of hospitalized patients with idiopathic pericarditis increased over time; (2) although prescription rates of NSAIDs, aspirin, and colchicine for pericarditis increased over time, as did the use of combination therapy with NSAIDs and colchicine, only 15.0% of patients throughout the study period received NSAIDs and colchicine simultaneously, as recommended by the ESC guidelines; (3) there

were no significant temporal changes in the in-hospital mortality rate, with a mean of 1.4% for the entire survey period; and (4) multivariable analysis showed that age and steroid use were significant predictors of in-hospital death, whereas the presence of cardiac tamponade was not.

Epidemiological studies on pericarditis have predominantly focused on acute pericarditis, and research specifically addressing idiopathic pericarditis is limited, even in Western countries. Regarding the outcomes of acute pericarditis, nationwide data analyses reported in-hospital mortality rates of 1.0–1.1% for acute pericarditis, specifically 1.1% in 1,361 Finnish patients (2000–2009)[10] and 1.0% in 21,540 US patients (2016–2017).[23] Only one small Japanese single-center study has analyzed the outcomes of patients with idiopathic pericarditis, and it reported an in-hospital mortality rate of 1.8%.[9] Consistent with that study, we found that the mean in-hospital mortality rate throughout the study period was 1.4%. In the present study, age and steroid use were identified as independent risk factors for in-hospital mortality. In contrast, NSAID use was found to have a favorable impact on in-hospital mortality (**Figure 3**). A large study of in-hospital mortality in patients with acute pericarditis, including idiopathic pericarditis, was reported by Kytö et al. in 2014 using the DPC database.[10] In that study, the risk factors associated with in-hospital mortality were sepsis and age. There have been no reports of steroid use showing an association with in-hospital mortality, but there are several reports that steroid use contributed to an increased recurrence rate.[1,2,24] Because in-hospital mortality rates for acute pericarditis, including idiopathic pericarditis, remain low,[10,23] further prospective studies in large populations are needed. Regarding temporal changes in in-hospital deaths (**Table 2**), we found that the overall rate of in-hospital death between 2016 and 2020 remained unchanged. However, a previous study from the US reported that in-hospital mortality decreased from 2003 to 2012.[25] Moreover, another study that included only patients aged ≥65 years reported that the in-hospital mortality rate decreased significantly from 4.9% (95% confidence interval 4.4–5.5%) in 1999 to 2.8% (95% confidence interval 2.4–3.2%) in 2012 ($P_{trend}<0.001$).[26] This discrepancy in temporal changes in in-hospital mortality rates between the present study and studies from the US may be explained by 3 factors: (1) the proportion of elderly patients hospitalized for pericarditis increased in Japan but remained unchanged in the US; (2) despite an increase in the percentage of patients in the present study who received colchicine (up to 36.1% in 2020), this rate is still too low to have beneficial effects on mortality; and (3) colchicine may have been preferentially administered to patients with more severe underlying disease as add-on therapy to aspirin or other NSAIDs.

Idiopathic pericarditis may be a marker of occult cancer. In one study, 1,550 of 13,759 patients with pericarditis subsequently developed cancer, primarily lymphoma, leukemia, and lung, kidney, and bladder cancer, during a median follow-up period of 6.4 years, indicating indirect standardized incidence ratios of 1.5 for cancer incidence.[27] Another study of 322 patients with moderate or severe pericardial effusion found that cancer was the underlying cause in 13% of cases.[28] Cancer may have been the reason for some of the deaths in the present study. It is crucial that the current state of pericarditis management in Japan, where the population is steadily aging, is evaluated.

Current Status of Pericarditis Treatment in Japan

A recent report from an Italian institution analyzed 471 pericarditis patients and found that 83.4% were prescribed NSAIDs and 70.0% were prescribed colchicine.[29] In the present study, NSAIDs and colchicine prescription rates increased over time but were lower than those in the aforementioned report, with maxima of 69.5% and 29.3%, respectively. Japanese physicians may have limited treatment options for pericarditis due to limited research on this condition in Japan, the lack of relevant Japanese guidelines, and significant social constraints, such as the absence of insurance approval for the use of colchicine to treat pericarditis. Securing insurance approval is necessary to optimize the treatment of pericarditis.

Hospitalization Length, Hospitalization Cost, and Loss to Follow-up

The baseline characteristics of patients in the long hospitalization length and high hospitalization costs groups were similar: both groups had a higher proportion of older patients, fewer men, higher CCI scores, an increased use of colchicine, steroids, combination therapy, and triple therapy, and more cases of cardiac tamponade than the short hospitalization length and low hospitalization costs groups, respectively, (**Supplementary Tables 4**,**5**). These findings suggest that older patients with multiple comorbidities or severe pericarditis complicated by cardiac tamponade may experience prolonged hospitalization. Conversely, the findings that hospitalization length and cost were higher in patients receiving colchicine or combination therapies, which may be expected to improve outcomes, could indicate that these medications were added in more severe cases, such as in patients who were unresponsive to NSAIDs. However, due to the lack of clinical data in the JROAD-DPC database, we cannot determine the severity of each patient's condition or the circumstances under which medications were administered. Compared with patients who were not lost to follow-up, those lost to follow-up had a lower CCI, lower rates of pharmacological therapy, shorter hospitalization length, and lower hospitalization costs, indicating that milder cases of pericarditis may not have been followed up, which could have affected the results (**Supplementary Table 6**).

Rate of Rehospitalization for Pericarditis Recurrence

The outcome of the post-discharge analysis was the rate of rehospitalization for recurrent pericarditis. Because the JROAD-DPC database only includes inpatient data, recurrences managed on an outpatient basis cannot be confirmed. The 1-year readmission rate for pericarditis recurrence was 5.7%. This rate showed no significant temporal changes. The only previous studies on pericarditis rehospitalization in Japan, which were conducted by our group, reported that the 1-year readmission rate of idiopathic pericarditis was 5.9%,[9] which is slightly higher than that in the present study. Previous reports suggested that combination therapy with NSAIDs and colchicine reduces recurrence, and this combination is a Class 1 treatment recommendation in the ESC guidelines.[1,2] Surprisingly, the present study found a higher rate of colchicine use among patients who required rehospitalization for recurrence than among those who did not (**Supplementary Table 9**). One possible explanation for this finding is that colchicine may have been used for more severe cases that were refractory to NSAIDs. However, the JROAD-DPC database lacks clinical data,

preventing the assessment of patient severity or the reasons for medication administration. Therefore, prospective studies that collect such data are needed.

Study Limitations

This study has several limitations. First, despite using the JROAD-DPC database, the study population was too small to permit a direct comparison with national demographics. However, this study analyzed 3,963 pericarditis patients, the largest sample in Japan to date. Second, the JROAD-DPC data include only inpatients, not outpatients. Therefore, rates of hospitalization for recurrent pericarditis may be underestimated, because milder cases are often managed on an outpatient basis, which may result in a higher average age and disease severity among hospitalized patients. The number of hospitalizations for minor recurrences may have decreased as a result of the growing use of medications recommended in the ESC guidelines.[1] Thus, the in-hospital mortality rate in the present study may have been higher than that in the overall population of individuals with idiopathic pericarditis (including both outpatients and inpatients). Moreover, the JROAD-DPC database only contains data on patients with recurrent idiopathic pericarditis who require hospitalization and who have been admitted to the same hospital as during their first admission. Therefore, it is important to note that this study does not comprehensively cover all cases of pericarditis in Japan; rather, it focuses on the characteristics, treatments, complications, and in-hospital deaths of hospitalized patients. Third, the JROAD-DPC database lacks laboratory, physiological, imaging, and hemodynamic data, as well as specific causes of death, thus preventing a detailed analysis of in-hospital deaths. Fourth, although ICD-10 codes were used to reliably identify heart failure and acute myocardial infarction in the JROAD database,[30] the accuracy of pericarditis diagnoses was not verified. To address this, detailed physicians' records[17,18] were used to exclude patients with suspected pericarditis (n=757) and those without pericarditis who were diagnosed with the ICD-10 code I319 (n=6,434). Finally, the COVID-19 pandemic may have affected the outcomes in 2020.

Conclusions

In Japan, the use of ESC guideline-recommended medications for pericarditis remains uncommon, and in-hospital mortality rates have not changed in recent years. The ongoing accumulation of evidence from Japan is necessary to confirm the safety and efficacy of pericarditis treatments in the Japanese population.

Acknowledgments

The authors appreciate the contributions of all the investigators, clinical research coordinators, and data managers involved in the JROAD-DPC study.

Sources of Funding

H.A. received a research grant from the Naohiko Miyata–Asahi Intecc Foundation for Medical Technology and Research. T.N. received a research grant from the Intramural Research Fund for Cardiovascular Disease of the National Cerebral and Cardiovascular Center (23-B-7).

Disclosures

Y.K. has received research support from Kowa, Nipro, and Abbott, and honoraria from Nipro, Abbott, Kowa, Amgen, Sanofi, Astellas, Takeda, and Daiichi-Sankyo. K. Tsujita has received research support and honoraria from Bayer. F.O., Y.T., K. Tsujita, and T.N. are members of *Circulation Journal*'s Editorial Team. The other authors have no relationships relevant to the contents of this paper.

IRB Information

This study was approved by the Institutional Review Board of the National Cerebral and Cardiovascular Center (Reference no. R22013-2).

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Supplementary Files

Please find supplementary file(s);
https://doi.org/10.1253/circj.CJ-24-0697