Acute myocardial infarction caused by Kawasaki disease requires more intensive therapy: Insights from the Japanese registry of All Cardiac and Vascular Diseases—Diagnosis Procedure combination

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Abstract

Background: Kawasaki disease (KD) induces coronary arteritis, which causes subsequent coronary aneurysms, and contributes to acute myocardial infarction (AMI). However, the differences regarding real-world treatment selection and mortality between AMI-complicated KD and AMI due to typical atherosclerosis (AMI-non KD) are unknown.

Aim: The aim of the present study was to examine the current treatment strategy and prognosis of AMI-complicated KD compared with AMI due to typical atherosclerosis.

Method: We used data from 2012 to 2019 from a nationwide claim database, the Japanese Registry of All Cardiac and Vascular Diseases—Diagnosis Procedure Combination.

Results: Compared to the AMI-non KD patients (n = 70,227), the AMI-complicated KD patients (n = 73): (1) underwent percutaneous coronary intervention (PCI) less often and more coronary artery bypass grafting, intracoronary thrombolysis or intravenous coronary thrombolysis more often; (2) underwent stentless PCI using old balloon angioplasty or rotablator, when they underwent PCI; and (3) needed in-hospital cardiopulmonary resuscitation and intensive mechanical therapy such as intra-aortic balloon pump, percutaneous cardiopulmonary support or a respirator. Both the AMI-non KD and AMI-complicated KD patients had similar in-hospital mortality rates.

Conclusions: Compared with AMI-non KD patients, AMI-complicated KD patients underwent non-PCI strategies such as bypass surgery or thrombolysis, and required intensive therapy with mechanical supports more often, but presented similar in-hospital mortality. When the AMI-complicated KD patients underwent PCI, stentless PCI using balloon angioplasty or rotablator was performed more often compared with the AMI-non KD patients.
1 | INTRODUCTION

Kawasaki disease (KD) was first reported in Japan in 1967 as an acute febrile syndrome that leads to the development of multisystemic vasculitis. KD is a leading cause of acquired heart disease in infants and young children, and rarely develops in adults.1 KD-induced coronary arteritis causes subsequent coronary aneurysms, intimal proliferation and atherosclerotic changes, and contributes to cardiovascular diseases such as angina pectoris (AP) and acute myocardial infarction (AMI), as well as sudden cardiac death.2 In addition, childhood KD complicated with coronary aneurysms can cause adult onset of acute coronary syndrome (ACS), including unstable AP and AMI.3 The prevalence of ACS caused by KD is speculated to be about 5%–10% in young adult cases.4

The survival rate of AMI due to coronary lesions caused by KD is poor,5 so suitable management is important. When AMI complicated with KD occurs, immediate reperfusion therapy is a major treatment strategy, which is quite similar to treatment for atherosclerosis-related AMI in adulthood. Therefore, the 2020 Japan Circulation Society (JCS) guidelines recommend primary percutaneous coronary intervention (PCI) in the early phase of AMI-complicated KD (class I, evidence level C). If primary PCI is difficult to perform, intravenous systemic thrombolytic therapy is recommended (class I, evidence level C).6 However, the real-world treatment for AMI-complicated KD is unknown. In addition, although it has been reported that the survival rate of AMI due to coronary lesions caused by KD is poor, the difference in mortality between AMI-complicated KD and non-KD is unknown because the morbidity of AMI-complicated KD is very low. To resolve this limitation, we used a well-validated nationwide cardiovascular hospitalization database; the Japanese Registry of All Cardiac and Vascular Diseases—Diagnosis Procedure Combination (JROAD-DPC).

The aims of this study were to investigate the clinical treatment selection and short-middle term prognosis of AMI complicated with KD, as well as to compare the results with those of AMI not complicated with KD.

2 | METHODS

2.1 | Data source

This survey used data from the JROAD-DPC, a nationwide claim database, which was launched in 2004 by the JCS that provides primary data from an annual survey. All teaching hospitals with cardiovascular beds are registered with the JROAD because its participation is mandatory for physicians to become board-certified cardiologists in Japan. However, the JROAD database does 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 and contains patient demographics and disease-specific data for each patient. The JROAD-DPC database was created by combining the JROAD data derived from a JCS national survey in 2012 and the DPC database. The validity of the DPC database is generally high, especially that of primary diagnoses and procedure records.

2.2 | Study population

The JROAD-DPC database includes 8,008,221 health records registered between April 2012 and January 2019. We assessed the 7,997,963 records in which the age of the patient could be determined. In the DPC system, diagnoses at admission are made by attending physicians and categorized into six groups according to 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 after admission. In the present study, we identified the patients who were diagnosed with ACS or KD (M303) in (1) main diagnosis, (2) admission-precipitating diagnosis and/or (3) most resource-consuming diagnosis. ACS was diagnosed if the patients were categorized with unstable AP (I200), AMI (I21.0, I21.1, I21.2, I21.3, I21.4, and I21.9), or recurrent AMI (I22.8 and I22.9). In addition, we identified the patients who had KD as present or past illness, if the patients were categorized as KD (M303) in (1) main diagnosis, (2) admission-precipitating diagnosis, (3) most resource-consuming diagnosis, (4) second most resource-consuming diagnosis, or (5) comorbidities present on admission.

2.3 | Flow diagram

Figure 1 shows the flow diagram of the present study. A total of 305,244 patients were diagnosed with AMI as (1) main diagnosis, (2) admission-precipitating diagnosis or (3) most resource-consuming diagnosis. Because KD was first reported in Japan in 1967 and patients were diagnosed when they were infants or young children, patients over 60 years old were excluded from the present study. Finally, a total of 70,300 AMI patients between 0 and 60 years old were analyzed. Among these AMI patients, 70,227 (99.9%) did not have KD (AMI-non KD), and only 73 (0.1%) patients had KD as present or past illness (AMI-KD). In the present study, we compared the differences in treatment and prognosis between AMI-non KD and AMI-KD patients.
2.4 | Data collection

Patient characteristics at the time of admission, including age, sex, height, weight, body mass index (BMI), Brinkman index, and comorbidities, were extracted from the claim database. Comorbidities were determined using ICD-10 codes. Invasive treatments during hospitalization, such as PCI, coronary artery bypass grafting (CABG), and intracoronary thrombolysis (ICT), were also extracted from the claim database. Thrombolytic therapy agents were also extracted. In addition, PCI procedures such as percutaneous old balloon angioplasty (POBA), stent and rotablator, and the usage of mechanical support, such as intra-aortic balloon pump (IABP), percutaneous cardiopulmonary support (PCPS), Impella (intravascular microaxial left ventricular assist device), respirator and dialysis, were also extracted from the claim database. Medications that were still being taken at discharge including anticoagulants, antiplatelets, angiotensin converting enzyme inhibitor (ACE-I), angiotensin II receptor blocker (ARB), β-blocker, α-blocker and statin were extracted from the claim database. The JROAD-DPC database includes mortality data during hospitalization and after discharge; therefore, short-time mortality data were extracted in the present study.

2.5 | Statistical analysis

Categorical variables are expressed as numbers and percentages, and continuous variables are presented as the median (interquartile range). Changes of categorical variables and continuous variables were evaluated using the Chi-square test and Mann–Whitney U test, respectively. Bivariate study analysis was performed by simple logistic regression with calculation of the odds ratio and 95% confidence interval. Multivariate analysis was performed using multiple logistic regression analysis. The threshold for significance was \( p < 0.05 \). All statistical analyses were conducted using SPSS version 25.0 (SPSS).

3 | RESULTS

Table 1 shows the characteristics of the AMI-non KD (n = 70,227) and AMI-KD patients (n = 73). Compared with the AMI-non KD patients, the AMI-KD patients were younger, included fewer males, and had a lower body weight, BMI and Brickman index. In addition, the AMI-KD patients had a lower incidence of coronary risk factors, such as hypertension, diabetes mellitus and dyslipidemia, than the AMI-non KD patients. Of note, more AMI-KD patients were in Killip class 3 or 4 than the AMI-non KD patients, even though the AMI-KD patients were younger.

Table 2 shows treatments during hospitalization and patient prognosis. The percentage of patients who received each revascularization therapy was different between the AMI-non KD and the AMI-KD patients. PCI was selected more often in the AMI-non KD patients, whereas CABG was selected more often in the
### TABLE 1 Clinical characteristics

| Demographic data | Total AMI patients (n = 70,300) | AMI-non KD patients (n = 70,227) | AMI-KD patients (n = 73) | p value |
|------------------|-------------------------------|---------------------------------|-------------------------|---------|
| Age, years       | 53.0 (47.0–57.0)              | 53.0 (47.0–57.0)                | 35.0 (23.0–41.0)         | <0.001  |
| Male sex, n (%)  | 62,763 (89.3)                 | 62,708 (89.3)                  | 55 (75.3)               | <0.001  |
| Height, cm       | 169.0 (164.0–173.0)           | 169.0 (164.0–173.0)            | 166 (156.5–172.5)        | 0.170   |
| Weight, kg       | 72.2 (64.1–81.6)              | 72.2 (64.1–81.6)               | 62.7 (55.0–74.0)         | <0.001  |
| Body mass index, kg/m² | 25.4 (23.0–28.2)  | 25.4 (23.0–28.2)               | 23.9 (19.4–26.1)         | <0.001  |
| Brinkman index   | 520.0 (50.0–840.0)            | 520.0 (55.5–840.0)             | 0 (0–440.0)              | <0.001  |
| Comorbidities, n (%) |                  |                                 |                         |         |
| Hypertension     | 45,522 (64.8)                | 45,499 (64.8)                  | 23 (31.5)               | <0.001  |
| Diabetes mellitus| 20,614 (29.3)                | 20,609 (29.3)                  | 5 (6.8)                 | <0.001  |
| Dyslipidemia     | 48,456 (68.9)                | 48,430 (69.0)                  | 26 (35.6)               | <0.001  |
| Hyperuricemia    | 3508 (5.0)                   | 3506 (5.0)                     | 2 (2.7)                 | 0.377   |
| Killip classification ≥3, n (%) | 10,893 (16.1)  | 10,875 (16.1)                  | 18 (26.5)               | 0.020   |
| Cardiac arrest, n (%) | 1636 (2.3)                  | 1633 (2.3)                     | 3 (4.1)                 | 0.312   |

Abbreviations: AMI, acute myocardial infarction; KD, Kawasaki disease.

Ami-KD patients. In addition, stentless PCIs using POBA or rotablator were performed more often in the AMI-KD patients. Moreover, thrombolytic therapy such as ICT and intravenous coronary thrombolysis with urokinase or monteplase was more often performed in the AMI-KD patients. Compared with the AMI-non KD patients, more the AMI-KD patients needed mechanical support, such as IABP, PCPS and respirator. Medications at discharge were also different. More patients with AMI-KD were treated with anticoagulant therapy using warfarin. Although aspirin was similarly administered in both the AMI-non KD and AMI-KD patients, clopidogrel was less frequently administered in the AMI-KD patients. In addition, the use of ACE-I/ARB and statin was lower in the AMI-KD patients. Of note, in-hospital cardiopulmonary resuscitation (CPR) incidence was higher in the AMI-KD patients. On the other hand, regarding short and medium-term prognosis, death in 24 h, 7 days, and 30 days after admission were similar between the AMI-KD and AMI-non KD patients. In addition, the length of hospital stay was longer in the AMI-KD patients, despite almost the same the medical costs.

Table 3 presents the impact of KD on therapies and prognosis assessed by simple and multivariate regression analysis (n = 70,300). In the multivariate regression analysis adjusted for age, sex, and institution code, KD was significantly associated with lower frequency of PCI and higher frequency of CABG, ICT, intravenous coronary thrombolysis with urokinase or monteplase, mechanical supports by IABP, PCPS or respirator, and in-hospital CPR. In contrast, presence of KD was not associated with death in 24 h, 7 days, 30 days after admission, and in-hospital death. Even after being adjusted for CABG, these results did not substantially change.

Table 4 shows the impact of KD among the AMI patients who underwent PCI (n = 59,298). Focusing on PCI procedure, KD was associated with POBA without stent, rotablator and rotablator without stent, as well as with in-hospital CPR, death in 24 h and 7 days after admission, whereas it was not associated with death in 30 days after admission and in-hospital death.

### 4 DISCUSSION

The major findings of this study using the JROAD database were as follows: (1) revascularization therapy through CABG, rather than PCI, was performed more often in AMI-KD patients than AMI-non KD patients; (2) ICT and intravenous coronary thrombolysis were performed more often in the AMI-KD patients; (3) intensive mechanical therapy using IABP, PCPS or respirator was more often needed in the AMI-KD patients; (4) there were more AMI-KD patients who required in-hospital CPR due to the severity of their conditions, but their in-hospital and 30-day mortality did not differ from that of the AMI-non KD patients; and (5) among the patients who underwent PCI, KD was associated with stentless PCI, such as POBA without stent and rotablator without stent, in-hospital CPR, death in 24 h and 7 days after admission.

Previous studies using JROAD-DPC data reported a ratio of male to female AMI patients of about 7 to 3.7,8 On the other hand, our study population was 89.3% male. In contrast to these other studies investigating AMI patients of all ages, our study investigated AMI patients between 0 and 60 years old because KD was first reported in Japan in 1967 and diagnosed while patients were infants or young...
| Treatment during hospitalization and outcome | AMI patients (n = 70,300) | AMI-non KD patients (n = 70,227) | AMI-KD patients (n = 73) | p value |
|---------------------------------------------|---------------------------|----------------------------------|--------------------------|---------|
| Revascularization                           |                           |                                  |                          |         |
| Percutaneous coronary intervention, n (%)   | 59,298 (84.3)             | 59,259 (84.4)                    | 39 (53.4)                | <0.001  |
| Percutaneous old balloon angioplasty        | 8882 (12.6)               | 8859 (12.6)                      | 23 (31.5)                | <0.001  |
| Percutaneous old balloon angioplasty without stent | 4563 (6.5)               | 4542 (6.5)                      | 21 (28.8)                | <0.001  |
| Stent                                       | 54,287 (77.2)             | 54,271 (77.3)                    | 16 (21.9)                | <0.001  |
| Rotablator                                  | 233 (0.3)                 | 231 (0.3)                       | 2 (2.7)                  | <0.001  |
| Rotablator without stent                    | 113 (0.2)                 | 111 (0.2)                       | 2 (2.7)                  | <0.001  |
| Coronary artery bypass grafting, n (%)      | 1293 (1.8)                | 1279 (1.8)                      | 14 (19.2)                | <0.001  |
| Intracoronary thrombolysis, n (%)           | 110 (0.2)                 | 108 (0.2)                       | 2 (2.7)                  | <0.001  |
| Alteplase, n (%)                            | 74 (0.1)                  | 74 (0.1)                        | 0 (0)                    | 0.781   |
| Urokinase, n (%)                            | 686 (1.0)                 | 682 (1.0)                       | 4 (5.5)                  | <0.001  |
| Monteleplase, n (%)                         | 485 (0.7)                 | 480 (0.7)                       | 5 (6.8)                  | <0.001  |
| Mechanical support                          |                           |                                  |                          |         |
| Intra-aortic balloon pump, n (%)            | 9489 (13.5)               | 9465 (13.5)                     | 24 (32.9)                | <0.001  |
| Percutaneous cardiopulmonary support, n (%) | 2274 (3.2)                | 2267 (3.2)                      | 7 (9.6)                  | 0.002   |
| Impella, n (%)                              | 18 (0.0)                  | 18 (0.0)                        | 0 (0)                    | 0.891   |
| Respirator, n (%)                           | 5887 (8.4)                | 5872 (8.4)                      | 15 (20.5)                | <0.001  |
| Dialysis, n (%)                             | 1070 (1.5)                | 1070 (1.5)                      | 0 (0)                    | 0.288   |
| Medication at discharge                     |                           |                                  |                          |         |
| Anticoagulants, n (%)                       | 10,674 (15.2)             | 10,632 (15.1)                   | 42 (57.5)                | <0.001  |
| Warfarin                                    | 4006 (5.7)                | 3969 (5.7)                      | 37 (50.7)                | <0.001  |
| Dabigatran                                  | 251 (0.4)                 | 251 (0.4)                       | 0 (0)                    | 0.609   |
| Xa inhibitor                                | 1326 (1.9)                | 1323 (1.9)                      | 3 (4.1)                  | 0.162   |
| Antiplatelet agents, n (%)                  | 59,204 (84.2)             | 59,144 (84.2)                   | 60 (82.2)                | 0.635   |
| Aspirin                                     | 57,970 (82.5)             | 57,915 (82.5)                   | 55 (75.3)                | 0.110   |
| Clopidogrel                                 | 27,228 (38.7)             | 27,214 (38.8)                   | 14 (19.2)                | <0.001  |
| Cilostazol                                  | 593 (0.8)                 | 592 (0.8)                       | 1 (1.4)                  | 0.623   |
| ACE-I/ARB, n (%)                            | 45,750 (65.1)             | 45,750 (65.1)                   | 31 (42.5)                | <0.001  |
| β-blocker, n (%)                            | 14,400 (20.5)             | 14,378 (20.5)                   | 22 (30.1)                | 0.041   |
| αβ-blocker, n (%)                           | 27,663 (39.3)             | 27,640 (39.4)                   | 23 (31.5)                | 0.170   |
| Statins, n (%)                              | 54,538 (77.6)             | 54,506 (77.6)                   | 32 (43.8)                | <0.001  |
| Outcome                                     |                           |                                  |                          |         |
| In-hospital cardiopulmonary resuscitation, n (%) | 5769 (8.2)               | 5757 (8.2)                      | 12 (16.4)                | 0.010   |
| Death, n (%)                                | 1871 (2.7)                | 1869 (2.7)                      | 2 (2.7)                  | 0.967   |
| Within 24 h after admission                 |                           |                                  |                          |         |

(Continues)
children. The other previous studies using Japanese databases reported the percentage of males to be about 90% in young AMI patients,\textsuperscript{9,10} which is consistent with our data. With regard to antiplatelets and anticoagulants, dual antiplatelet therapy with aspirin and a P2Y12 inhibitor (such as clopidogrel or prasugrel) is standard for AMI patients undergoing PCI. On the contrary, a previous study of KD patients with giant coronary aneurysm showed that the combination therapy with aspirin and warfarin suppressed the incidence of AMI compared with the therapy with aspirin alone.\textsuperscript{11} Therefore, the 2020 JCS guidelines recommended the usage of warfarin, but not P2Y12 inhibitor, in combination with low-dose aspirin for patients with past history of AMI (Class IIa, level C).\textsuperscript{6} Consistent with the recommendation, our data showed that warfarin was more frequently administered at discharge in the AMI-KD patients.

With regard to revascularization therapy, primary PCI is recommended in the early phase of ST-segment elevation myocardial infarction (STEMI) in the 2018 JCS guidelines (class I, evidence level A).\textsuperscript{12} As primary PCI has improved the prognosis of STEMI, performance rate of primary PCI in these patients has progressively increased.

### TABLE 2 (Continued)

|                         | Total AMI patients (n = 70,300) | AMI-non KD patients (n = 70,227) | AMI-KD patients (n = 73) | p value |
|-------------------------|---------------------------------|---------------------------------|--------------------------|---------|
| Within 7 days after admission | 2799 (4.0)                      | 2796 (4.0)                      | 3 (4.1)                  | 0.955   |
| Within 30 days after admission | 3534 (5.0)                      | 3531 (5.0)                      | 3 (4.1)                  | 0.720   |
| In-hospital             | 3731 (5.3)                      | 3728 (5.3)                      | 3 (4.1)                  | 0.648   |
| Length of hospital stay, days | 12.0 (9.0–16.0)                | 12.0 (9.0–16.0)                | 16.0 (10.0–21.0)         | 0.002   |
| Cost of hospitalization, Japanese yen | 1,785,600 (1,396,036–2,368,386) | 1,785,585 (1,396,116–2,368,060) | 1,825,058 (1,372,401–3,074,610) | 0.229 |
| Cost of hospitalization, US dollars | 16,232.73 (12,691.23–21,530.78) | 16,232.59 (12,691.96–21,527.89) | 16,591.44 (12,476.37–27,951.00) | 0.229 |

Note: Impella, intravascular microaxial left ventricular assist device; $1 = ¥110.
Abbreviations: ACE-I, angiotensin converting enzyme inhibitor; AMI, acute myocardial infarction; ARB, angiotensin II receptor blocker; KD, Kawasaki disease.

### TABLE 3 Logistic regression analysis: Impact of Kawasaki disease (n = 70,300)

|                         | Univariate OR 95% CI p value | Model I OR 95% CI p value | Model II OR 95% CI p value |
|-------------------------|------------------------------|----------------------------|---------------------------|
| Treatment               |                              |                            |                           |
| Percutaneous coronary intervention | 0.212 0.134–0.336 <0.001 | 0.409 0.252–0.663 <0.001 | N.A. N.A. N.A. |
| Coronary artery bypass grafting | 12.792 7.124–22.967 <0.001 | 20.424 11.106–37.561 <0.001 | N.A. N.A. N.A. |
| Intracoronary thrombolysis | 18.289 4.430–75.504 <0.001 | 9.111 1.967–42.188 0.005 | 7.989 1.689–37.788 0.009 |
| Urokinase               | 5.911 2.151–16.243 <0.001 | 2.958 1.042–8.397 0.042 | 3.027 1.061–8.630 0.038 |
| Monteplase              | 10.684 4.290–26.612 <0.001 | 7.304 2.811–18.980 <0.001 | 7.223 2.761–18.893 <0.001 |
| Intra-aortic balloon pump | 3.144 1.929–5.126 <0.001 | 4.032 2.459–6.611 <0.001 | 4.245 1.402–4.314 0.002 |
| Percutaneous cardiopulmonary support | 3.179 1.457–6.937 0.004 | 3.053 1.386–6.725 0.006 | 2.465 1.110–5.472 0.027 |
| Respirator              | 2.834 1.606–5.004 <0.001 | 3.705 2.085–6.584 <0.001 | 1.973 1.031–3.777 0.040 |
| Outcome                 |                              |                            |                           |
| In-hospital cardiopulmonary resuscitation | 2.203 1.186–4.093 0.012 | 2.391 1.281–4.464 0.006 | 2.129 1.136–3.989 0.018 |
| Death within 24 h after admission | 1.030 0.253–4.203 0.967 |                              |                           |
| Death within 7 days after admission | 1.034 0.325–3.285 0.955 |                              |                           |
| Death within 30 days after admission | 0.810 0.255–2.572 0.720 |                              |                           |
| In-hospital death        | 0.764 0.241–2.429 0.649 |                              |                           |

Note: Model I: adjusted for age, sex and institution code. Model II: adjusted for age, sex, institution code, and coronary artery bypass grafting.
Abbreviations: CI, confidence interval; OR, odds ratio.
increased, even in geriatric patients. The safety of early discharge after primary PCI in low risk patients has also been reported. Although primary PCI is also recommended for STEMI complicated with KD (class I, evidence level C) in the 2020 JCS guidelines, there is not enough evidence regarding whether primary PCI should be performed in children with coronary aneurysms complicating KD. Several studies have shown that PCI for KD resulted in lower efficacy compared with CABG, because PCI needed repeat-revascularization therapy more often and improved ischemia proportion less often. In addition, KD patients tended to have coronary chronic total occlusion lesions and multi-vessel lesions. The present study showed that AMI-KD patients tended to require CABG rather than PCI, compared with the AMI-non KD patients, although primary PCI is recommended in AMI-KD patients. The 2020 JCS guidelines also recommend systemic thrombolysis with intravenous infusion of urokinase or t-PA for AMI-KD when PCI is difficult to perform (class I, evidence level C). In addition, ICT should be considered if systemic thrombolysis is insufficient for revascularization (class I, evidence level C). The current study revealed that systemic thrombolysis and ICT were more frequently selected for AMI-KD patients compared with AMI-non KD patients.

Regarding PCI procedure for AMI-KD, several studies have reported that stent implantation showed sufficient coronary antegrade flow, but the long-term results are unknown. Other studies have reported that new coronary aneurysms, stent fractures, and malapposition occurred after stent implantation in KD patients. Therefore, the 2020 JCS guidelines do not reveal the class of recommendation and level of evidence for stent implantation. The present study also showed that primary stentless PCI was more frequently performed in AMI-KD patients compared with AMI-non KD patients. The culprit lesion of AMI-KD patients often contains the dilatation lesion, aneurysms, and the negative remodeling of vessels at the distal position of dilatation lesion. The anatomical complexity of coronary arteries may make it difficult to select appropriate stent size and length, which is the reason for lower prevalence of stent usage. On the other hand, the 2nd generation drug eluting stent was useful for hemodialysis patients who tended to have severely calcified coronary lesions. Because KD-complicated coronary arteries also progress to severe calcification with aging, stentless PCI using POBA-alone may not be effective for these calcified lesions. Atherectomy by rotablator is a suitable procedure for calcification lesions, and the procedural success rate for ACS lesions was similar to stable AP lesions. The 2020 JCS guidelines recommend using a rotational atherectomy device when elective PCI is performed for stable angina and silent myocardial ischemia of KD (class IIa, evidence level C) because coronary artery calcification is often observed at the stenosis in KD patients. Although the effectiveness of rotablator for AMI-KD is unknown, a higher rate of the AMI-KD patients (n = 2, 2.7%) in the present study underwent PCI using rotablator than the AMI-non KD patients.

With regard to prognosis, the present study showed that more AMI-KD patients needed intensive therapy using IABP and PCPS.

### Table 4: Logistic regression analysis: Impact of Kawasaki disease among patients who underwent percutaneous coronary intervention (n = 59,298)

| Treatment                              | Univariate OR (95% CI) | p value | Model I OR (95% CI) | p value |
|----------------------------------------|------------------------|---------|---------------------|---------|
| Percutaneous old balloon angioplasty   | 8.178 (4.319–15.486)   | <0.001  | 6.182 (3.249–11.764)| <0.001  |
| Percutaneous old balloon angioplasty without stent | 14.055 (7.483–26.397) | <0.001  | 8.691 (4.569–16.534)| <0.001  |
| Stent                                  | 0.064 (0.034–0.121)    | <0.001  | 0.099 (0.052–0.189) | <0.001  |
| Rotablator                             | 13.813 (3.310–57.645)  | <0.001  | 23.740 (5.511–102.256)| <0.001  |
| Rotablator without stent               | 28.804 (6.859–120.965) | <0.001  | 39.677 (8.928–176.321)| <0.001  |
| Intra-aortic balloon pump              | 4.231 (2.235–8.012)    | <0.001  | 4.619 (2.434–8.766) | <0.001  |
| Percutaneous cardiopulmonary support   | 5.349 (2.239–12.781)   | <0.001  | 5.056 (2.104–12.149)| <0.001  |
| Respirator                             | 2.810 (1.240–6.370)    | 0.013   | 3.267 (1.436–7.429) | 0.005   |

Outcome

| Outcome                               | Univariate OR (95% CI) | p value | Model I OR (95% CI) | p value |
|---------------------------------------|------------------------|---------|---------------------|---------|
| In-hospital cardiopulmonary resuscitation | 4.667 (2.273–9.583)   | <0.001  | 4.739 (2.270–9.626)| <0.001  |
| Death within 24 h after admission     | 7.344 (1.764–30.564)   | 0.006   | 8.881 (2.103–37.512)| 0.003   |
| Death within 7 days after admission   | 4.095 (1.259–13.315)   | 0.019   | 4.608 (1.408–15.080)| 0.012   |
| Death within 30 days after admission  | 2.648 (0.815–8.607)    | 0.105   |                     |         |
| In-hospital death                     | 2.430 (0.748–7.897)    | 0.140   |                     |         |

Note: Model I: adjusted for age, sex and institution code.
Abbreviations: CI, confidence interval; OR, odds ratio.
Recently, the effectiveness of additional IABP support for AMI patients requiring PCPS was reported. In the present study, a higher percentage of the AMI-KD patients were classified as Killip 3 or 4 than the AMI-non KD patients (26.5% vs. 16.1%). Moreover, the present study showed that in-hospital CPR was more often performed in the AMI-KD patients, which may mean that in-hospital cardiac arrest occurred more often in the AMI-KD patients compared with the AMI-non KD patients.

Of note, regarding the prognosis of AMI patients who underwent PCI, the present study showed that short-term mortality was higher in the patients with AMI-KD than with AMI-non KD. This result did not mean that PCI was less suitable for revascularization therapy than CABG for AMI-KD. The efficacy of primary PCI for STEMI is well established; however, most STEMI cases were due to atherosclerosis, such as plaque rupture, erosion, and calcified nodules. On the other hand, KD patients developed AMI due to a newly developed thrombus at a coronary stenosis site at the inlet or outlet of an aneurysm. These culprit lesions of AMI-KD are different from typical atherosclerotic culprit lesions of STEMI; therefore, primary PCI for AMI-KD is likely to be less efficient than for AMI-non KD, leading to a possible increase in short-term mortality.

4.1 Study strengths and limitations

Although this study used a validated nationwide registry to compare AMI-KD with AMI-non KD, there were several limitations. First, although the DPC data were confirmed by physicians and are highly reliable, some of the data are based on medical claims and may contain certain errors. Moreover, the JROAD-DPC database covers less than 66% of cardiovascular hospitals in Japan. While the JROAD database between January 2012 and December 2018 showed that the number of ACS patients who had a history of KD was 618, the database between January 2012 and December 2018 showed that less than 66% of cardiovascular hospitals in Japan. While the JROAD database covers about 83% of acute care hospitals in Japan by 2018, so the validity of the dataset is generally high. Second, the JROAD-DPC data did not encompass detailed clinical data, such as data of coronary angiography. Therefore, the number of coronary artery lesions and severity of stenosis, which reflect the selection of revascularization therapy and the usage of mechanical support devices, were unknown. Third, of 70,300 AMI patients, only 73 (0.1%) patients had a history of KD, and this low occurrence may create biases and skewed data. Fourth, there were missing data for some patients (i.e., height, weight, BMI, and cost of hospitalization).

5 CONCLUSIONS

The present study using the JROAD-DPC database revealed that, compared with patients with AMI-non KD, more AMI-KD patients underwent non-PCI strategies such as CABG, ICT, and intravenous coronary thrombolysis, and required intensive therapy using IABP, PCPS, or a respirator, but presented similar in-hospital mortality. When KD patients underwent PCI, stentless PCI using balloon angioplasty or rotablator was performed more often in those with AMI-complicated KD than in those with AMI-non KD. These findings provide new insights into the treatment strategy for AMI-complicated KD.

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CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

The data underlying this article were provided by Japanese Circulation Society. Data will be shared on request to the corresponding author with permission of Japanese Circulation Society.

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