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 difference of real-world treatment selection and mortality between AMI-complicated KD and AMI due to typical atherosclerosis (AMI-non KD) is unknown.

Method

The aim of the present study was to reveal the current treatment strategy and prognosis of AMI-complicated KD compared with AMI due to typical atherosclerosis using data from 2012 to 2019 of a nationwide claim database, the Japanese Registry of All Cardiac and Vascular Diseases - Diagnosis Procedure Combination.

Results

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

Conclusions

Compared with AMI-non KD, AMI-complicated KD underwent non-PCI strategy such as bypass surgery or thrombolysis, required intensive therapy with mechanical supports, and presented similar in-hospital mortality. When AMI-complicated KD underwent PCI, stentless PCI using balloon angioplasty or rotablator was more performed compared with AMI-non KD.

Introduction

Kawasaki disease (KD) was first reported from Japan in 1967 as an acute febrile syndrome that develops multi-systemic 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 disease such as angina pectoris (AP), 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), such as 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 current Japan Circulation Society (JCS) guidelines 2020 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 was reported that the survival rate of AMI due to coronary lesions caused by KD is poor, the difference of mortality between AMI-complicated KD and non-KD was 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.

Results

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 from Japan in 1967 and diagnosed while patients were infants or young children, patients over 60 years old were excluded from the present study. A total of 70,300 AMI patients between 0–60 years old were finally analyzed. Among these patients, 70,227 (99.9%) did not have the history of KD (AMI-non KD), and only 73 (0.1%) patients had the history of KD (AMI-KD). In the present study, we compared the difference of the treatment and prognosis between AMI-non KD and AMI-KD.

Table 1 shows the characteristics of the AMI-KD (n = 73) and AMI-non KD patients (n = 70,227). Compared with the AMI-non KD patients, the AMI-KD patients were younger, included fewer males, and had lower body weight, body mass index (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. Impressively, more AMI-KD patients were in Killip class 3 or 4 than the AMI-non KD patients, despite the fact that the AMI-KD patients were younger.

Table 1
Clinical Characteristics

	AMI patients total (n = 70300)	AMI-non KD patients (n = 70227)	AMI-KD patients (n = 73)	P value
Demographic data				
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 (%)	62763 (89.3)	62708 (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	45522 (64.8)	45499 (64.8)	23 (31.5)	< 0.001
Diabetes mellitus	20614 (29.3)	20609 (29.3)	5 (6.8)	< 0.001
Dyslipidemia	48456 (68.9)	48430 (69.0)	26 (35.6)	< 0.001
Hyperuricemia	3508 (5.0)	3506 (5.0)	2 (2.7)	0.377
Killip classification ≥ 3, n (%)	10893 (16.1)	10875 (16.1)	18 (26.5)	0.020
Cardiac arrest, n (%)	1636 (2.3)	1633 (2.3)	3 (4.1)	0.312
Heart failure, n (%)	620 (0.9)	620 (0.9)	0 (0)	0.420

Table 2 shows treatments during hospitalization and patient prognosis. There was a difference in the percentage of patients who received each revascularization therapy between the AMI-non KD and the AMI-KD patients. PCI was more often selected in the AMI-non KD patients, whereas coronary artery bypass grafting (CABG) was more often selected in the AMI-KD patients. In addition, stentless PCIs using percutaneous old balloon angioplasty (POBA) or rotablator were more often performed in the AMI-KD patients. Moreover, thrombolytic therapy such as intracoronary thrombolysis (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, the AMI-KD patients more often needed mechanical supports such as intra-aortic balloon pump (IABP), percutaneous cardiopulmonary support (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 the AMI-non KD and the AMI-KD patients, clopidogrel was less frequently administered in the AMI-non KD patients. In addition, the use of angiotensin converting enzyme inhibitor (ACE-I)/angiotensin II receptor blocker (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 middle-term prognosis, death in 24 hours, 7 days, 30 days after admission and during hospitalization were similar between the AMI-non KD and the AMI-KD patients. In addition, the length of hospital stay was longer in the AMI-KD patients, despite almost the same cost of hospitalization.

Table 2
Treatment during hospitalization and outcome

	AMI patients total (n = 70300)	AMI-non KD patients (n = 70227)	AMI-KD patients (n = 73)	P value
Revascularization				
Percutaneous coronary intervention, n (%)	59298 (84.3)	59259 (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	54287 (77.2)	54271 (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
Monteplase, 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 (%)	10674 (15.2)	10632 (15.1)	42 (57.5)	< 0.001

Impella, intravascular microaxial left ventricular assist device; ACE-I, angiotensin converting enzyme inhibitor; ARB, angiotensin II receptor blocker

1$ = 110 yen

	AMI patients total (n = 70300)	AMI-non KD patients (n = 70227)	AMI-KD patients (n = 73)	P value
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 (%)	59204 (84.2)	59144 (84.2)	60 (82.2)	0.635
Aspirin	57970 (82.5)	57915 (82.5)	55 (75.3)	0.110
Clopidogrel	27228 (38.7)	27214 (38.8)	14 (19.2)	< 0.001
Cilostazol	593 (0.8)	592 (0.8)	1 (1.4)	0.623
ACE-I/ARB, n (%)	45750 (65.1)	45750 (65.1)	31 (42.5)	< 0.001
β-blocker, n (%)	14400 (20.5)	14378 (20.5)	22 (30.1)	0.041
αβ-blocker, n (%)	27663 (39.3)	27640 (39.4)	23 (31.5)	0.170
Statins, n (%)	54538 (77.6)	54506 (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 (%)				
Within 24 hours after admission	1871 (2.7)	1869 (2.7)	2 (2.7)	0.967
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, yen	1785600 (1396036–2368386)	1785585 (1396116–2368060)	1825058 (1372401–3074610)	0.229
$	16232.73 (12691.23-21530.78)	16232.59 (12691.96-21527.89)	16591.44 (12476.37–27951.00)	0.229

Impella, intravascular microaxial left ventricular assist device; ACE-I, angiotensin converting enzyme inhibitor; ARB, angiotensin II receptor blocker

1$ = 110 yen

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 hours, 7 days, 30 days after admission and in-hospital death. Even after adjusted for CABG, these results did not substantially change.

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

	Univariate			Model I			Model II		
	OR	95% CI	P value	OR	95% CI	P value	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	2.459	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 hours 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						

OR, odds ratio; CI, confidence interval

Model I: adjusted for age, sex and institution code.

Model II: adjusted for age, sex, institution code and coronary artery bypass grafting.

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 hours and 7 days after admission, whereas not associated with death in 30 days after admission and in-hospital death.

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

	Univariate			Model I		
	OR	95% CI	P value	OR	95% CI	P value
Treatment						
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						
In-hospital cardiopulmonary resuscitation	4.667	2.273–9.583	< 0.001	4.739	2.270–9.626	< 0.001
Death within 24 hours after admission	7.344	1.764–30.564	0.006	8.881	2.103–37.512	0.003
Death within 24 hours after admission	4.095	1.259–13.315	0.019	4.608	1.408–15.080	0.012
Death within 24 hours after admission	2.648	0.815–8.607	0.105			
In-hospital death	2.430	0.748–7.897	0.140			
OR, odds ratio; CI, confidence interval						
Model I: adjusted for age, sex and institution code.						

Discussion

The major findings of the this study using the JROAD database were as follows: 1) revascularization therapy through CABG, rather than PCI, was more often performed in the AMI-KD patients than the AMI-non KD patients, 2) ICT and intravenous coronary thrombolysis were more often performed in the AMI-KD patients, 3) intensive mechanical therapy

using IABP, PCPS or respirator was more often needed in the AMI-KD patients, 4) more AMI-KD patients progressed to severe general condition that needed in-hospital CPR, but their in-hospital and 30-day mortality did not differ from that of the AMI-non KD patients, 5) on the other hand, KD was associated with stentless PCI such as POBA without stent and rotablator without stent, in-hospital CPR, death in 24 hours and 7 days after admission among the AMI patients who underwent PCI.

With regard to revascularization therapy, primary PCI is recommended in the early phase of ST-segment elevation myocardial infarction (STEMI) in the JCS guidelines 2018 (class I, evidence level A) [7]. AS primary PCI has improved the prognosis of STEMI, its performance rate has progressively increased, even in geriatric patients[8]. The safety of early discharge after primary PCI in low risk patients was also reported [9]. Although primary PCI is also recommended for STEMI complicated with KD (class I, evidence level C) in the JCS guidelines 2020 [6], there is not enough evidence whether primary PCI should be performed in children with coronary aneurysms complicating KD. Several studies showed that PCI for KD resulted in lower efficacy compared with CABG because PCI more often needed repeat-revascularization therapy and less often improved ischemia proportion [10 11]. In addition, KD patients tended to have coronary chronic total occlusion lesions [12] and multi-vessel lesions [13]. The present study showed that the AMI-KD patients tend to undergo CABG rather than PCI compared with the AMI-non KD patients, although primary PCI is recommended in AMI-KD patients. The JCS guidelines 2020 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) [6]. In addition, ICT should be considered if systemic thrombolysis is insufficient for revascularization (class I, evidence level C) [6]. Actually, the current study revealed that systemic thrombolysis and ICT were more frequently selected for the AMI-KD patients compared with the AMI-non KD patients.

Regarding PCI procedure for AMI-KD, several studies reported that stent implantation showed sufficient coronary antegrade flow [14 15], but the long-term results are unknown. Other studies reported that new coronary aneurysms, stent fracture and malapposition occurred after stent implantation in KD patients [16 17]. Therefore, the JCS guidelines 2020 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 for AMI-KD compared with AMI-non KD. On the other hand, the 2nd generation drug eluting stent was useful for hemodialysis patients who tended to have severe calcification coronary lesions [18]. Because KD-complicated coronary arteries also progress to severe calcification with aging, stentless PCI using POBA-alone is maybe not effective such calcification lesions. Atherectomy by rotablator is a suitable procedure for calcification lesions [19], and the procedural success rate for ACS lesions was similar to stable AP lesions [20]. The JCS guidelines 2020 recommend using rotational atherectomy device when elective PCI is performed for stable angina and silent myocardial ischemia of KD (class IIa, evidence level C). Although the effectiveness of rotablator for AMI-KD is unknown, a higher rate of the AMI-KD patients (n = 2, 2.7%) underwent PCI using rotablator than the AMI-non KD patients in the present study.

With regard to the prognosis, the present study showed that the more AMI-KD patients needed intensive therapy using IABP and PCPS. Recently, the effectiveness of additional IABP support for AMI patients requiring PCPS was reported [21]. In the present study, a higher percentage of the AMI-KD patients were classified as Killip 3or 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 was more often occurred in the AMI-KD patients compared with the AMI-non KD patients. Although in-hospital and short/middle-term mortality was almost the same in the AMI-KD and the AMI-non KD patients in the present study, AMI-KD should be considered as a life-threatening disease, because the AMI-KD patients were younger than AMI-non KD.

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

revascularization therapy than CABG for AMI-KD. The efficacy of primary PCI for STEMI is well established; however most of STEMI cases were due to atherosclerosis, such as plaque rupture, erosion and calcified nodule [22]. On the other hand, KD patients develop AMI due to a newly developed thrombus at a coronary stenosis site at the inlet or outlet of an aneurysm [23]. These culprit lesions of AMI-KD are different from typical atherosclerotic culprit lesions of STEMI, therefore primary PCI for AMI-KD probably might be less efficient than for AMI-non KD, leading to a possible increase in short-term mortality.

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 must have been 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 only covers less than 66% of cardiovascular hospitals in Japan. While the JROAD database showed that the number of ACS patients who had the past history of KD during January 2012 – December 2018 was 618, the JROAD-DPC database stated that there were 106 ACS patients with KD during April 2012 – January 2019. This result indicated that there was selection bias in our study. However, the JROAD-DPC database had covered 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, there were some missing data (i.e. height, weight, BMI and cost of hospitalization).

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 strategy such as CABG, ICT and intravenous coronary thrombolysis, and required intensive therapy using IABP, PCPS or respirator, whereas presented similar in-hospital mortality. These findings provide new insights into the treatment strategy for AMI-complicated KD.

Methods

Data source

This survey used data of the JROAD-DPC, a nationwide claim database, which was launched in 2004 by the JCS and 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 several 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.

Study Population

The JROAD-DPC database includes 8,008,221 health records registered between April 2012 and January 2019. We assessed 7,997,963 hearth records which could be determined patients age. In the DPC system, diagnoses at admission are made by attending physicians and categorized into 6 groups: (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, based on the International Classification of

Diseases (ICD-10) diagnosis codes. In the present study, we identified the patients who were diagnosed with ACS or KD (M303) in (1) main diagnosis and/or (2) admission-precipitating diagnosis and/or (3) most resource-consuming diagnosis. ACS were diagnosed if the patients were categorized as or 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.

Data collection

Patient characteristics including age, sex, height, weight, BMI, Brinkman index and comorbidities at the time of admission were extracted from the claim database. Comorbidities were determined using ICD-10 codes. Invasive treatments during hospitalization, such as PCI, CABG, ICT, were also extracted from the claim database. Thrombolytic therapy agents were also extracted. In addition, PCI procedure such as POBA, stent and rotablator, and usage of mechanical supports, such as IABP, PCPS, Impella (intravascular microaxial left ventricular assist device), respirator and dialysis were also extracted the claim database. The medications at discharge including anticoagulants, antiplatelets, ACE-I, ARB, β-blocker, αβ-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.

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 (OR) and 95% confidence interval (95%CI). 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, Armonk, NY, USA).

Declarations

Ethics statement

This research plan was approved by the institutional review board of Fukushima Medical University (approval number: 2021-062) and the National Cerebral and Cardiovascular Center (approval number: 2020-01). The requirement for informed consent was waived because of the anonymized nature of the data. Each hospital anonymized the patient IDs using code-change equations made 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 Guideline for Medical and Health Research Involving Human Subjects.

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Data Availability

The data that support the findings of this study are available from JCS, but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are however available from the authors upon reasonable request and with permission of JCS.

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Figures

Figure 1

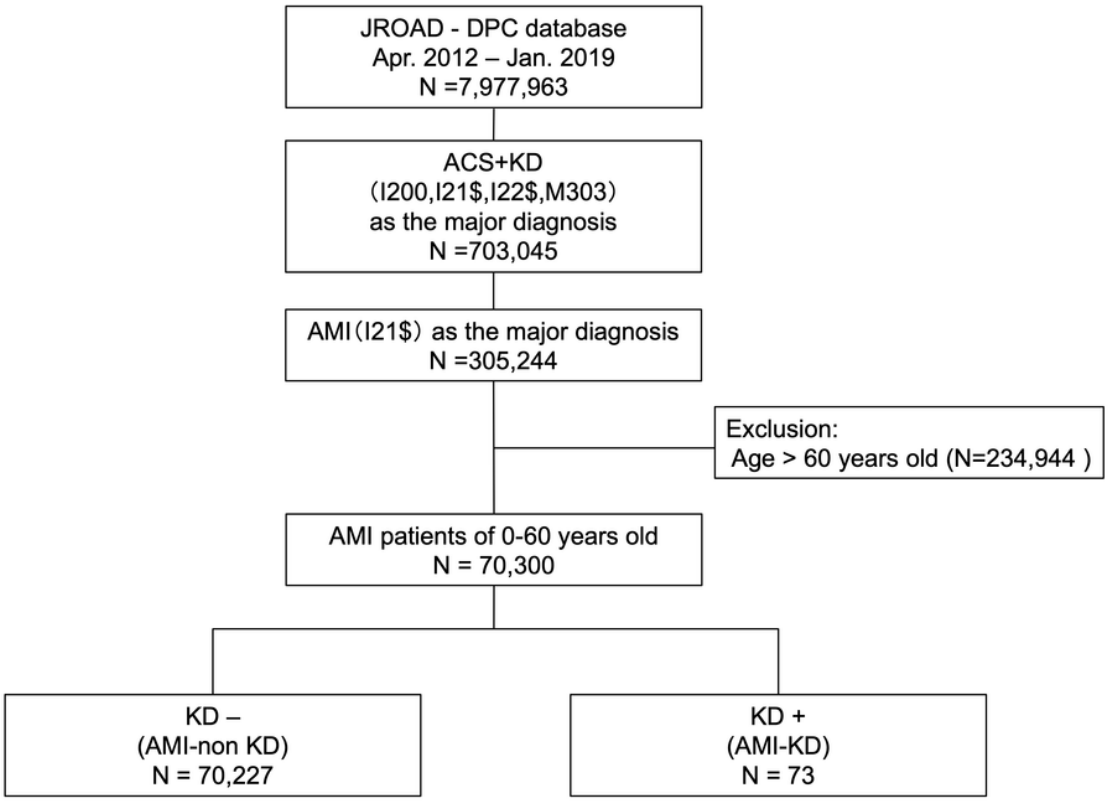

Figure 1

The flow diagram of the present study

A total of 7,977,963 patients were enrolled Japanese Registry of All Cardiac and Vascular Diseases - Diagnosis Procedure Combination (JROAD-DPC) data between April 2012 and January 2019. The 703,045 patients were identified if the patients were diagnosed with acute coronary syndrome (ACS) or Kawasaki disease (KD) as (1) main diagnosis, (2) admission-precipitating diagnosis and (3) most resource-consuming diagnosis. In these population, the 305,244 patients were diagnosed with acute myocardial infarction (AMI). The over 60 years old patient (N = 234,944) were excluded from in

the present study. Total 70,300 AMI patients between 0 - 60 years old were finally analyzed. The 70,227 (99.9%) patients didn't have the history of KD (AMI-non KD), and the 73 (0.1%) patients were diagnosed with KD (AMI-KD).