

Original
Article

Characteristics and In-Hospital Outcomes of Patients Who Underwent Coronary Artery Bypass Grafting during Hospitalization for ST-Segment Elevation or Non-ST-Segment Elevation Myocardial Infarction

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Purpose: Little is known about the outcomes of patients with ST-segment elevation myocardial infarction (STEMI) or non-ST-segment elevation myocardial infarction (NSTEMI) who undergo coronary artery bypass grafting (CABG) in the current percutaneous coronary intervention (PCI) era.

Methods: We analyzed 25120 acute myocardial infarction (AMI) patients hospitalized between January 2011 and December 2016. In-hospital outcomes were compared between patients who underwent CABG during hospitalization and those who did not undergo CABG in the STEMI group (n = 19428) and NSTEMI group (n = 5692).

Results: Overall, CABG was performed in 2.3% of patients, while 90.0% of registered patients underwent primary PCI. In both the STEMI and NSTEMI groups, patients who underwent CABG were more likely to have heart failure, cardiogenic shock, diabetes, left main trunk lesion, and multivessel disease than those who did not undergo CABG. In multivariable analysis, CABG was associated with lower all-cause mortality in both the STEMI group (adjusted odds ratio [OR] = 0.43, 95% confidence interval [CI] 0.26–0.72) and NSTEMI group (adjusted OR = 0.34, 95% CI 0.14–0.84).

Conclusion: AMI patients undergoing CABG were more likely to have high-risk characteristics than those who did not undergo CABG. However, after adjusting for baseline differences, CABG was associated with lower in-hospital mortality in both the STEMI and NSTEMI groups.

Keywords: acute myocardial infarction, nationwide registry, coronary artery bypass grafting, clinical outcomes

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Received: January 24, 2023; Accepted: June 11, 2023

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Introduction

Myocardial revascularization is the cornerstone of acute myocardial infarction (AMI) treatment. With the development of percutaneous coronary intervention (PCI), primary PCI became a first-line therapy for patients with AMI.^{1,2)} In parallel, decreased use of coronary artery bypass grafting (CABG) in patients with AMI has been reported.³⁾ Nevertheless, CABG is still considered an important treatment option for patients with AMI, especially in the presence of complex multivessel coronary artery disease or coronary lesions not amenable to PCI. In addition, patients with multivessel disease might undergo CABG during hospitalization for AMI when surgical revascularization is suitable for non-culprit lesions that remain after primary PCI.

AMI has been classified into ST-segment elevation myocardial infarction (STEMI) and non-ST-segment elevation myocardial infarction (NSTEMI) based on electrocardiography findings. Previous studies have demonstrated differences in patient background, management, and prognosis between patients with STEMI and NSTEMI.^{4,5)} However, contemporary data about utilization, patient characteristics, and clinical course after CABG during hospitalization for STEMI and NSTEMI from multicenter studies are limited. In this study, we aimed to investigate in-hospital outcomes of patients undergoing CABG after STEMI or NSTEMI using a large, contemporary, nationwide AMI registry.

Materials and Methods

Study population

The Japan AMI registry (JAMIR) retrospectively collected clinical data from 10 representative regional AMI registry groups or institutions in Japan.^{5–9)} A total of 46242 consecutive patients with spontaneous, universal classification type 1 AMI between January 2011 and December 2016 were retrospectively registered.¹⁰⁾ Criteria for AMI from the WHO Monitoring of Trends and Determinants in Cardiovascular Disease (MONICA) were also used when troponin levels were difficult to assess.¹¹⁾ The JAMIR excluded patients with AMI associated with PCI or CABG and those admitted to the hospital ≥ 24 h after onset. STEMI was diagnosed when ST elevation ≥ 1 mm was observed in at least two contiguous leads at any location on the index or qualifying electrocardiogram, when new left bundle branch block was presumed or when new Q waves were observed. In the

absence of ST-segment elevation, patients meeting the diagnostic criteria for myocardial infarction (MI) were considered to have NSTEMI. In the JAMIR, treatment strategy, including utilization of CABG, was discussed with the attending doctor and heart team at each institution. The primary outcome of the present study was in-hospital mortality, which was defined as death from any cause. The secondary outcome was in-hospital cardiac mortality, which was defined as death from cardiovascular cause. Because of the observational nature of this registry, informed consent was not obtained. However, details about the study were posted on a website (opt-out) to inform the subjects of the content and timeline of the study to ensure that they had the opportunity to refuse inclusion in this registry. The study was conducted in accordance with the tenets of the Declaration of Helsinki. The institutional review boards of all participating centers approved the study (Institutional Review Board Number: M26-140-7).

Statistical analysis

Baseline continuous variables are presented as mean with standard deviation or median with interquartile range, depending on the distribution of the variable. Categorical variables are presented as percentages. The t-test and the Mann–Whitney U test were used to compare continuous variables. The χ^2 test was used to compare dichotomous variables. Multiple logistic regression was used to evaluate variables that were significantly associated with in-hospital mortality. All tests were two-sided, and the level of significance was set at 0.05. All statistical analyses were performed using JMP version 16 (SAS Institute, Cary, NC, USA).

Results

Patient characteristics

Of 46242 patients in the JAMIR, the study excluded 21122 patients without information regarding CABG during hospitalization ($n = 18068$) or ST-segment elevation ($n = 3054$). Ultimately, 25120 patients were included in the analysis (**Fig. 1**). In the study population, 19428 patients had STEMI and 5692 patients had NSTEMI. CABG was performed in 2.3% ($n = 567$) of the overall cohort, 1.6% ($n = 302$) of the STEMI group, and 4.7% ($n = 265$) of the NSTEMI group. Primary PCI was performed in 90.0% of the overall cohort, 92.6% of the STEMI group, and 81.4% of the NSTEMI group.

Table 1 shows the comparison of the baseline characteristics of patients by CABG status in the STEMI and

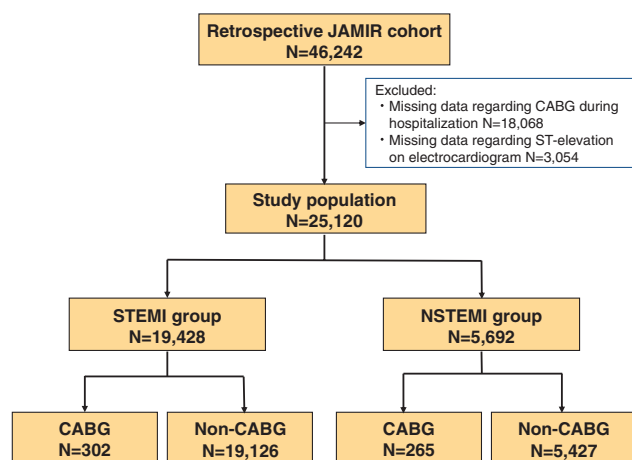


Fig. 1 Study flow chart. CABG: coronary artery bypass grafting; JAMIR: Japan acute myocardial infarction registry; NSTEMI: non-ST-segment elevation myocardial infarction; STEMI: ST-segment elevation myocardial infarction

NSTEMI groups. In the STEMI group, patients who underwent CABG were more likely to have diabetes (43.5% vs. 33.9%), heart failure on admission (26.2% vs. 15.2%), cardiogenic shock (22.2% vs. 9.5%), anterior AMI (80.4% vs. 60.4%), left main trunk (LMT) lesion (5.3% vs. 1.6%), and multivessel disease (78.9% vs. 41.8%) than those who did not undergo CABG. Primary PCI was less frequently performed in patients who underwent CABG than those who did not undergo CABG (42.8% vs. 93.4%). Mechanical circulatory support was used more frequently in patients who underwent CABG (86.6% vs. 23.2%).

In the NSTEMI group, patients who underwent CABG were more likely to have diabetes (50.0% vs. 36.6%), heart failure on admission (26.8% vs. 14.0%), cardiogenic shock (14.3% vs. 8.6%), anterior AMI (71.3% vs. 53.4%), LMT lesion (11.2% vs. 3.4%), and multivessel disease (86.8% vs. 47.1%) than those who did not undergo CABG. Primary PCI was less frequently performed in patients undergoing CABG than those not undergoing CABG (21.2% vs. 84.3%). Mechanical circulatory support was used more frequently in patients undergoing CABG (80.9% vs. 18.2%).

In-hospital outcomes in the STEMI and NSTEMI groups by CABG status

Figure 2A shows in-hospital outcomes in the STEMI group by CABG status. All-cause mortality was significantly higher among patients who underwent CABG than those who did not undergo CABG (15.9% vs. 7.3%, $P < 0.001$). Cardiac mortality was comparable between

the two groups (7.0% vs. 5.3%, $P = 0.21$). **Figure 2B** shows in-hospital outcomes in the NSTEMI group by CABG status. There were no significant differences in all-cause mortality (7.2% vs. 8.2%, $P = 0.56$) and cardiac mortality (4.2% vs. 5.6%, $P = 0.32$) between patients who underwent CABG and those who did not undergo CABG.

Multivariate analysis of in-hospital mortality in the STEMI and NSTEMI groups

We performed multivariate analysis to adjust differences in patient characteristics between patients undergoing CABG and those not undergoing CABG. Factors associated with in-hospital mortality are shown in **Table 2** for the STEMI group and in **Table 3** for the NSTEMI group. After adjustment with logistic regression analysis, CABG was associated with lower in-hospital mortality in both the STEMI group (adjusted odds ratio [OR] = 0.43, 95% confidence interval [CI] 0.26–0.72, $P = 0.001$) and NSTEMI group (adjusted OR = 0.34, 95% CI 0.14–0.84, $P = 0.02$).

Discussion

The major findings of this study are as follows. 1) In a nationwide multicenter registry in Japan, 90% of patients with AMI underwent primary PCI, while CABG was rarely performed during hospitalization, especially in patients with STEMI (1.6% in the STEMI group and 4.7% in the NSTEMI group). 2) In both the STEMI and NSTEMI groups, patients who underwent CABG were more likely to have high-risk characteristics such as heart failure or cardiogenic shock on admission, left main culprit lesion, multivessel disease, and frequent use of mechanical circulatory support. 3) In-hospital mortality was significantly higher in patients who underwent CABG than those who did not undergo CABG in the STEMI group, but not in the NSTEMI group. 4) After adjustment for patient characteristics with multivariate analysis, CABG was associated with a lower incidence of in-hospital mortality in both the STEMI and NSTEMI groups.

Current guidelines indicate that CABG plays a different role in the acute phase of STEMI versus NSTEMI.^{1,2)} In patients with STEMI, primary PCI is recommended to achieve prompt revascularization; CABG is indicated in the limited setting of cardiogenic shock, unsuccessful or complicated primary PCI, or mechanical complications. By contrast, NSTEMI guidelines recommend PCI or CABG depending on the patient's clinical status and comorbidities as well as lesion complexity. Previous studies have reported a lower rate of CABG for STEMI

Table 1 Comparison of patient characteristics between CABG and Non-CABG subjects in the STEMI and NSTEMI group

	STEMI group			NSTEMI group		
	CABG	Non-CABG	P value	CABG	Non-CABG	P value
	n = 302	n = 19126		n = 265	n = 5427	
Age, y	69.0 ± 11.4	68.1 ± 13.3	0.26	69.5 ± 11.2	70.0 ± 13.1	0.52
Female, %	24.8	23.6	0.62	20.0	24.3	0.11
Heart failure (Killip class II or III), %	26.2	15.2	<0.001	26.8	14.0	<0.001
Cardiogenic shock (Killip class IV), %	22.2	9.5	<0.001	14.3	8.6	0.001
Hypertension, %	66.7	68.6	0.67	70.4	72.0	0.72
Diabetes, %	43.5	33.9	0.04	50.0	36.6	0.004
Dyslipidemia, %	43.5	52.1	0.08	47.4	53.8	0.17
Current smoking, %	41.1	46.1	0.09	45.9	41.3	0.16
Peak CK, IU/L	1911 (837, 3720)	1969 (872, 3743)	0.97	754 (342, 1689)	703 (324, 1548)	0.32
Multivessel disease, %	78.9	41.8	<0.001	86.8	47.1	<0.001
Anterior AMI, %	80.4	60.4	<0.001	71.3	53.4	<0.001
LMT lesion, %	5.3	1.6	<0.001	11.2	3.4	<0.001
Primary PCI, %	42.8	93.4	<0.001	21.2	84.3	<0.001
Use of mechanical circulatory support, %	86.6	23.2	<0.001	80.9	18.2	<0.001
IABP, %	85.8	22.5	<0.001	78.9	17.5	<0.001
V-A ECMO, %	12.6	3.8	<0.001	7.5	4.7	0.08

AMI: acute myocardial infarction; CABG: coronary artery bypass grafting; CK: creatine kinase; ECMO: extracorporeal membrane oxygenation; IABP: intra-aortic balloon pumping; LMT: left main trunk; NSTEMI: non-ST-segment elevation myocardial infarction; PCI: percutaneous coronary intervention; STEMI: ST-segment elevation myocardial infarction; V-A: veno-arterial

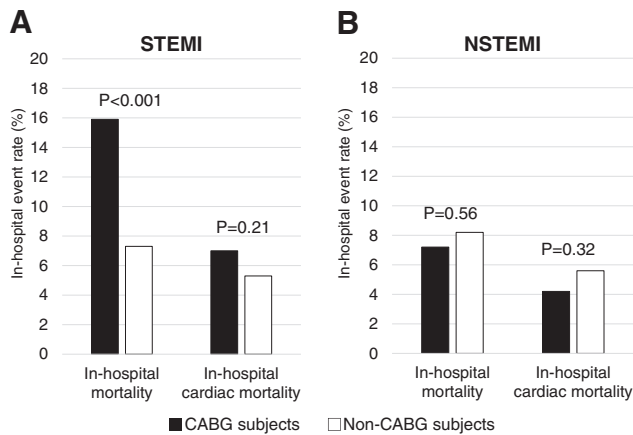


Fig. 2 In-hospital outcomes by CABG status. ST-segment elevation (STEMI) group (A). Non-ST-segment elevation (NSTEMI) group (B). CABG: coronary artery bypass grafting; STEMI: ST-segment elevation myocardial infarction; NSTEMI: non-ST-segment elevation myocardial infarction

Table 2 Independent determinants of in-hospital death in the STEMI group

	OR	95% CI	P value
Undergoing CABG	0.43	0.26–0.72	0.001
Age ≥75 years	1.86	1.53–2.26	<0.001
Female	1.21	0.97–1.50	0.09
Killip class ≥ II	3.64	2.94–4.51	<0.001
Multivessel disease	1.02	0.84–1.23	0.87
Anterior AMI	1.22	0.97–1.54	0.08
LMT lesion	2.00	1.33–3.01	<0.001
Primary PCI	0.58	0.42–0.81	0.001
Use of mechanical circulatory support	6.80	5.33–8.66	<0.001

AMI: acute myocardial infarction; CABG: coronary artery bypass grafting; CI: confidence interval; LMT: left main trunk; OR: odds ratio; PCI: percutaneous coronary intervention; STEMI: ST-segment elevation myocardial infarction

(5%–8%) than for NSTEMI (7%–13%)^{3,12–14}. Similarly, this study demonstrated less frequent use of CABG for STEMI versus NSTEMI. The difference in CABG utilization might be related to the different indications for CABG in clinical practice between STEMI and NSTEMI.

Prior studies reported that early mortality in patients with AMI undergoing CABG ranges from 3% to 25% depending on patient characteristics and clinical status.^{3,13,15–18} Available evidence suggests that patients with NSTEMI have favorable outcomes after CABG. In a pooled analysis of randomized trials comparing CABG and PCI in patients with non-ST-segment elevation acute coronary syndrome, CABG was associated with lower 5-year mortality than PCI with drug-eluting stents.¹⁹

Table 3 Independent determinants of in-hospital death in the NSTEMI group

	OR	95% CI	P value
Undergoing CABG	0.34	0.14–0.84	0.02
Age ≥75 years	1.84	1.22–2.78	0.004
Female	0.94	0.58–1.51	0.79
Killip class ≥ II	6.11	3.70–10.08	<0.001
Multivessel disease	0.83	0.55–1.27	0.40
Anterior AMI	1.18	0.74–1.91	0.49
LMT lesion	0.80	0.39–1.64	0.54
Primary PCI	1.24	0.60–2.53	0.56
Use of mechanical circulatory support	7.24	4.27–12.29	<0.001

AMI: acute myocardial infarction; CABG: coronary artery bypass grafting; CI: confidence interval; LMT: left main trunk; NSTEMI: non-ST-segment elevation myocardial infarction; OR: odds ratio; PCI: percutaneous coronary intervention

A population-based analysis reported a lower rate of major cardiovascular events with CABG versus PCI in patients with acute coronary syndrome and diabetes.²⁰ In the present analysis, NSTEMI was associated with comparable unadjusted mortality in patients who underwent CABG and those who did not undergo CABG, despite high-risk characteristics in the CABG group. Our findings further support the idea that CABG is an important option for the management of patients with NSTEMI.

In contrast to NSTEMI, there are conflicting results on the outcomes of CABG for STEMI. Previous observational studies demonstrated increased mortality associated with CABG performed early after STEMI.^{15,18} A multi-center registry in Germany showed that the in-hospital mortality rate in STEMI patients who underwent CABG was 12.6%, which was worse than the mortality rate in patients who underwent CABG for NSTEMI (7.6%) or unstable angina (4.2%).¹⁵ On the other hand, several studies showed that CABG was associated with acceptable outcomes in patients with STEMI. In a nationwide AMI registry enrolling patients between 2007 and 2014 in the United States (n = 241244), the observed mortality rate for CABG in STEMI patients was comparable to the rate in patients not treated with CABG (5.4% vs. 5.1%, P = 0.15).²¹ In our unadjusted analysis, CABG was associated with higher in-hospital mortality in the STEMI group but not in the NSTEMI group. Worse in-hospital outcomes after CABG in the STEMI group could be explained by the relatively higher prevalence of adverse clinical characteristics such as cardiogenic shock, use of mechanical circulatory support, and primary PCI before surgery in the STEMI group than in

the NSTEMI group.^{15,22,23)} Of note, logistic regression analysis (**Tables 2 and 3**) demonstrated that CABG was associated with a lower incidence of in-hospital mortality after adjustment for patient characteristics in both groups. These results suggest that higher unadjusted in-hospital mortality after CABG in the STEMI group can be mostly attributed to the high-risk patient background. While primary PCI is an important revascularization, especially in patients with STEMI, CABG per se might confer a favorable effect on mortality in both STEMI and NSTEMI patients with suitable backgrounds. Given that previous studies have shown that CABG might be potentially beneficial in high-risk patients such as those with cardiogenic shock,^{24,25)} unsuccessful PCI,^{26,27)} and mechanical complications,^{28–30)} the outcomes of AMI patients would probably be much worse in the absence of CABG as a treatment option.

Limitations

The results of this study should be interpreted in the context of limitations. First, this study was observational and the decision to perform CABG was not randomized. Although we performed multivariate analysis to reduce bias, confounding factors including the performance evaluation of CABG cannot be fully eliminated. Second, the current study could not collect data regarding reasons for the use of CABG. The clinical outcomes of AMI patients undergoing CABG would be different according to the reason for the use of CABG such as salvage CABG after failed PCI or CABG for residual disease after successful primary PCI. The efficacy and safety of CABG in different clinical settings remain to be elucidated. Third, there was insufficient information about the timing of CABG (duration between myocardial infarction and CABG) and surgical details such as which grafts were used or whether CABG was on-pump or not. Fourth, information about antiplatelet therapy during hospitalization, which could affect clinical outcomes, especially bleeding events, was unavailable. Finally, long-term outcomes were not available in our study. Additional contemporary studies with long-term follow-up are required to fully characterize the safety and efficacy of CABG during hospitalization for AMI.

Conclusion

Analysis of the nationwide, multicenter JAMIR database showed that patients who underwent CABG after AMI were more likely to have high-risk characteristics than those who did not undergo CABG. However, CABG was associated with lower in-hospital mortality in both

the STEMI and NSTEMI groups after adjustment for baseline patient characteristics. CABG seems to be an important component of the treatment strategy in selected patients with AMI even in the primary PCI era. Further investigations are needed to clarify the benefit of CABG on long-term outcomes in patients with AMI.

Acknowledgments

This work was supported in part by the First Incentive Payment for Medical Technology and Research from the Naohiko Miyata-Asahi Intecc Foundation for Medical Technology.

We wish to thank all the investigators, clinical research coordinators, and data managers involved in the JAMIR study for their contributions. The JAMIR study group consists of the following institutions and members:

Sapporo ACS Network: Takashi Takenaka (Hokkaido Medical Center) and Daisuke Hotta (Hokkaido Cardiovascular Hospital); Iwate ACS Registry: Tomonori Itoh (Iwate Medical University School of Medicine); Yamagata AMI Registry: Tetsu Watanabe (Yamagata University School of Medicine); Miyagi AMI Registry Study: Kiyotaka Hao (Tohoku University); Jichi Medical University: Kazuomi Kario; Tokyo CCU Network Scientific Committee: Ken Nagao (Nihon University Hospital), Naoki Sato (Nippon Medical School Musashi-Kosugi Hospital), Atsuo Namiki (Kanto Rosai Hospital), Hiroshi Suzuki (Showa University Fujigaoka Hospital), and Makoto Suzuki (Sakakibara Heart Institute); Yokohama Cardiovascular Workshop: Masami Kosuge (Yokohama City University Medical Center); Mie ACS Registry: Masaaki Ito (Mie University) and Takashi Tanigawa (Matsusaka Chuo Hospital); NCVC AMI Registry: Yasuhide Asaumi (National Cerebral and Cardiovascular Center); Kumamoto Acute Coronary Events Study: Kenichi Tsujita (Kumamoto University); and JAMIR Data Center: Yoshihiro Miyamoto (National Cerebral and Cardiovascular Center).

Disclosure Statement

There are no financial or other relationships that could lead to a conflict of interest.

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