Outcomes of Patients With Acute Myocardial Infarction Who Recovered From Severe In-hospital Complications

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Acute myocardial infarction (AMI) would sometimes raise severe in-hospital complications such as cardiopulmonary arrest, shock, stroke, atrioventricular block, and respiratory failure. The purpose of this retrospective study was to compare the clinical outcomes of AMI patients who recovered from severe in-hospital complications with those who did not have in-hospital complications. We included 494 AMI patients, and divided those into the in-hospital complications group (n = 166) and noncomplications group (n = 328). The primary end point was the major adverse cardiovascular events (MACE) defined as the composite of all cause death, nonfatal myocardial infarction (MI), and readmission for heart failure within 1 year after the hospital discharge. A total of 50 postdischarge MACE were observed during the study period. MACE was more frequently observed in the in-hospital complications group (14.5%) than in the noncomplications group (7.9%) (p = 0.023). The presence of in-hospital complications was significantly associated with the MACE (Odds Ratio 1.889, 95% Confidence Interval 1.077 to 3.313, p = 0.026) after controlling age, gender, ST-elevation MI, and culprit of AMI. In conclusion, the MACE was significantly frequent in AMI patients who recovered from severe in-hospital complications and discharged to home, as compared with those who did not have in-hospital complications. AMI patients who recovered from complications could be recognized as a high risk group, and should be carefully managed after discharge to prevent cardiovascular events. **(Am J Cardiol 2020;135:24−31)**

Despite the advances in multidisciplinary treatment for acute myocardial infarction (AMI), patients with AMI may have severe in-hospital complications such as cardiopulmonary arrest (CPA), shock, stroke, atrioventricular block, and respiratory failure.[1,2] The in-hospital outcomes of AMI patients who had those complications were usually categorized as the following 3 types: (1) in-hospital death due to those complications, (2) transfer to other hospitals because of severe damage, and (3) discharge to home. Of those 3 types, "discharge to home" would be the best in-hospital outcomes. However, it is unknown whether we should pay special attention to AMI patients who recovered from severe complications and discharged to home, because the prognosis of those patients were not fully understood. The purpose of this study was to compare the clinical outcomes of AMI patients who recovered from severe in-hospital complications and discharged to home with those who did not have in-hospital complications.

Methods

We conducted a single center retrospective study. We reviewed AMI patients treated at our institution between October 2016 and December 2018. In the present study, AMI was defined according to the universal definition.[3] The inclusion criteria were (1) AMI patients during the above study period, and (2) patients who discharged to home. The exclusion criteria were (1) second or more than second AMI during the study period, (2) patients who were managed by other departments such as cardiovascular surgery, general surgery, and hematology, (3) patients who had in-hospital death, (4) patients who were transferred to other hospitals, (5) patients without follow-up information. The final study population was divided according to the presence of severe in-hospital complications, which was defined as CPA, shock, stroke, atrioventricular block, and respiratory failure.[1,2,4] The patients who had severe in-hospital complications and discharged to home were defined as the in-hospital complications group. The patients who did not have severe in-hospital complications were defined as the noncomplications group.

The primary end point was the major adverse cardiovascular events (MACE) defined as the composite of all cause death, nonfatal MI, and readmission for heart failure within 1-year after the hospital discharge. Information regarding the above clinical outcomes were acquired from hospital records. The day of discharge was defined as the index day (day 1). The study patients were followed until meeting the MACE or until the study end date (365 days after discharge). This study was approved by the institutional review board of Saitama Medical Center, Jichi Medical University (S19-154), and written informed consent was waived because of the retrospective study design.

Hypertension was defined as systolic blood pressure >140 mm Hg, diastolic blood pressure >90 mm Hg, or

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medical treatment for hypertension.[4] Diabetes mellitus was defined as hemoglobin A1c >6.5% or treatment for diabetes mellitus.[4] We also calculated estimated glomerular filtration rate (eGFR) using serum creatinine (Cr), age, weight, and gender according to the following formula: eGFR = 194 × Cr−1.094 × age−0.287 (male), or eGFR= 194 × Cr−1.094 × age−0.287 × 0.739 (female).[5] Shock was defined as systolic blood pressure <90 mm Hg, vasopressors required to maintain blood pressure, or attempted cardiopulmonary resuscitation.[4] Stroke was an acute episode of focal or global neurological dysfunction caused by brain, spinal cord, or retinal vascular injury as a result of hemorrhage or infarction.[1,2,4] High-grade atrioventricular block was defined as third degree atrioventricular block, insertion of temporary transvenous pacemaker system, and permanent pacemaker implantation.[1,2,4] Respiratory failure was defined as arterial pO_2 on room air less than 60 mm Hg and use of mechanical ventilation irrespective of causes of respiratory failure.[1,2,4] Major bleeding was defined as a drop of ≥2 g/dl in hemoglobin level or administration of ≥2 units of packed red blood cells.[6] In echocardiography, ejection fraction (EF) was measured using a modified Simpson method. The Teichholz method was adopted only when a modified Simpson method was not available. Right ventricular infarction was defined as ST-segment elevation in V4R (≥1 mm) or abnormal right ventricular wall motion on echocardiography, accompanying clinical symptoms such as hypotension.[4] Global Registry of Acute Coronary Events risk score and TIMI risk score for each patient were compared between the 2 groups (TIMI risk score was calculated only for the ST-segment elevation MI [STEMI] patients).[7,8]

Data are expressed as mean ± standard deviation or percentage. Categorical variables are presented as n (%) and were compared using the chi squared test (or Fisher's exact test for small samples). Normally distributed continuous variables were compared with Student's *t* test. Otherwise, continuous variables were compared with a Mann−Whitney U test. Event free survival curves were constructed using the Kaplan−Meier method, and statistical differences between curves were assessed by the log-lank test. p value < 0.05 was considered statistically significant. We also performed a multivariate Cox regression analysis to investigate the association between in-hospital complications and MACE after controlling known clinical confounders such as age, sex, STEMI, and left anterior descending artery as a culprit.[9−12] Hazard ratios and the 95% confidence intervals (CI) were calculated. All analyses were performed using statistical software, SPSS 25/ Windows (SPSS, Chicago Illinois).

Results

Between October 2016 and December 2018, a total of 653 patients were diagnosed as AMI, and 159 patients were excluded according to the exclusion criteria. Finally, 494 patients were included as the final study population, and were divided into the in-hospital complications group (n = 166) and noncomplications group (n = 328) (Figure 1).

The clinical characteristics between the 2 groups are shown in Table 1. Shock on admission, CPA on admission, peak-CK, peak-CKMB, and brain natriuretic peptide (BNP) at admission were higher in the in-hospital complications group than in the noncomplications group. Optimal medical therapy at discharge including aspirin, thienopyridine, statins, ACE- inhibitor or ARB, and beta-blocker were equally prescribed in the 2 groups. The lesion and procedural characteristics between the 2 groups are shown in Table 2. The site of infarction was not significantly different between the 2 groups. The clinical outcomes between the 2 groups are shown in Table 3. MACE were more frequently observed in the in-hospital complications group (14.5%) than in the noncomplications group (7.9%) (p = 0.0023).

Figure 2 shows Kaplan-Meier curves for MACE between the 2 groups. The median follow-up duration was 284 days. A total of 50 MACE were observed during the follow-up duration. The multivariate Cox regression analysis was performed in Table 4. The in-hospital complications group was significantly associated with MACE (odds ratio 1.889, 95% CI 1.077 to 3.313, p = 0.026) after controlling age, gender, STEMI (vs NSTEMI), and left anterior descending artery as a culprit (vs other vessels).

Discussion

The present study included 494 AMI patients who discharged to home, and divided those into the in-hospital complications group (n = 166) and the noncomplications group (n = 328) according to the presence of in-hospital severe complications. The MACE was more frequently observed in the in-hospital complications group than in the noncomplications group (p = 0.023). Furthermore, the presence of in-hospital complications was significantly associated with MACE (Odds Ratio 1.889, 95% CI 1.077 to 3.313, p = 0.026) after controlling known clinical risk factors.

We should discuss why MACE were more frequently observed in the in-hospital complications group than in the noncomplications group. Although the MACE was defined as the composite of all cause death, nonfatal MI, and readmission for heart failure in the present study, only readmission for heart failure was more frequently observed in the in-hospital complications group than in the noncomplications group. Thus, the main reason for the difference of MACE would be derived from the readmission for heart failure. Although we focused on patients who could directly discharge to home, left ventricular (LV) EF before discharge was significantly lower in the in-hospital complications group than in the noncomplications group. Furthermore, BNP levels at admission were significantly higher in the in-hospital complications group than in the noncomplications group. In general, survival rates were better in patients with preserved LVEF than in patients with low LVEF, and low LVEF was a powerful predictor of cardiovascular outcome in heart failure patients.[13,14] Also, BNP is useful in confirming the presence of heart failure as well as assessing the prognosis of patients with heart failure.[15,16] Therefore, patients in the in-hospital complications group had a greater risk for heart failure at discharge.

In contrast, we should mention why all-cause death was not different between the 2 groups. We defined severe in-hospital complications as the composite of CPA, shock, stroke, atrioventricular block, and respiratory failure. CPA

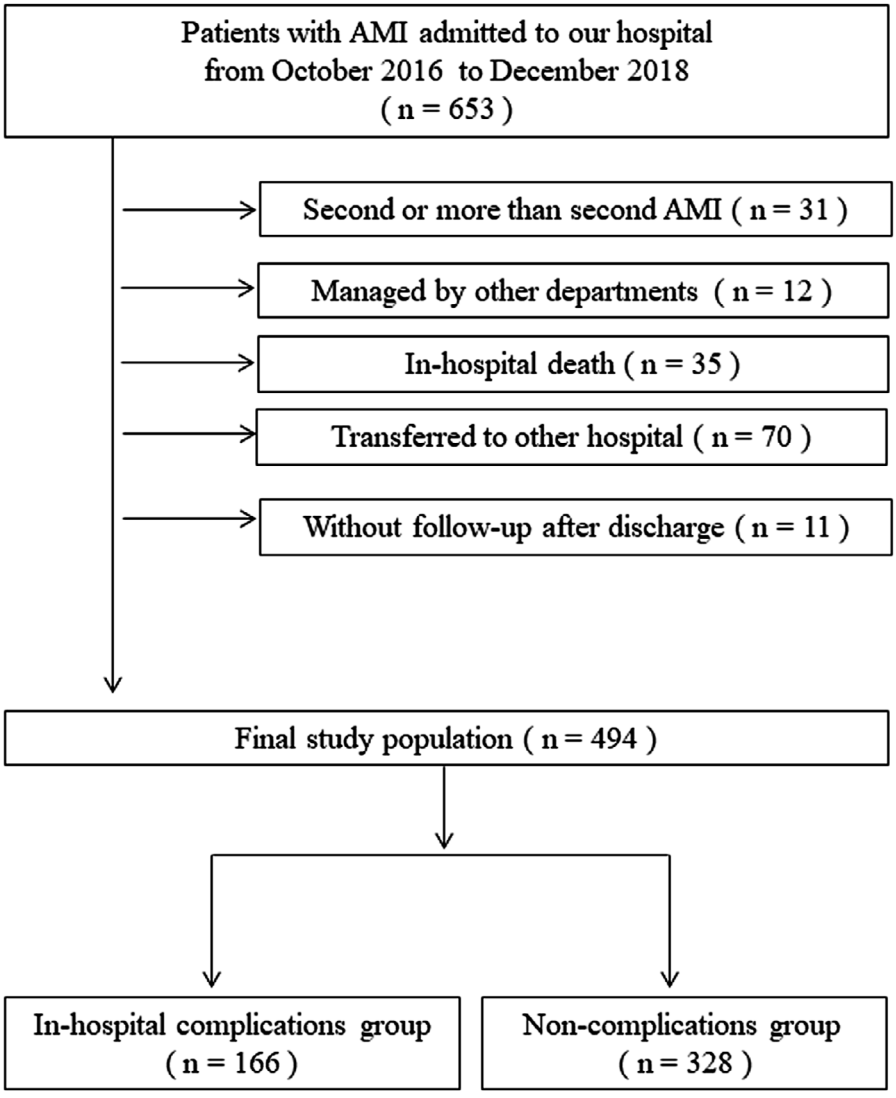

Figure 1. Study flow chart. Abbreviation: AMI = acute myocardial infarction.

and shock are common causes of death in the patients with AMI, and the morbidity and mortality were still high, in spite of the advancement of the treatment.[17-21] And then, stroke, atrioventricular block and respiratory failure is also related to undesirable clinical outcomes.[22-24] Considering these previous studies, it is reasonable to expect the greater mortality in the in-hospital complications group, which was not shown in the present study. The possible reasons would be the short observational period (1 year) or the small number of study patients, which would yield beta errors. Since the patients who could directory discharge to home is known to have better activities of daily living,[25] patients in the in-hospital complications group might not have a greater risk for death.

The clinical implications of the present study should be noted. The AMI patients who recovered from severe in-hospital complications and directly discharge to home would have a greater risk of cardiovascular events, especially heart failure. Those patients have not been recognized as a high risk group in the real-world clinical practice. It may be a first step for better clinical outcomes to recognize those patients as a high risk group. A careful follow up by cardiologists after discharge may be important for those patients to prevent readmission for heart failure, which was not assessed in the present study. Future studies to assess the effect of a careful follow-up are warranted.

The present study has the following limitations. First, since this is a single-center, retrospective study, there may be patient selection bias. Second, although we had information regarding the optimal medical therapy at discharge, we could not gather information regarding the optimal medical therapy during the follow-up period. Therefore, optimal medical therapy might be discontinued during the follow-up period, which might affect the clinical outcomes. Third, since there were no similar studies, we could not conduct a power analysis to define appropriate sample size. Our sample size might be too small to detect true differences (possibility of beta error).[26] Finally, although we constructed a multivariate Cox regression analysis to confirm the association between the MACE and the in-hospital complications

Table 1
Comparison of clinical characteristics between the in-hospital complications group and noncomplications group

Variable	All (n = 494)	In-hospital Complications Group (n = 166)	Non-complications Group (n = 328)	p value
Age (years)	69 ± 13	71 ± 13	68 ± 13	0.019
Men	381 (77.1%)	124 (74.7%)	257 (78.4%)	0.361
Body Mass Index, (kg/m^2)	24.1 ± 3.6 (n = 492)	23.9 ± 3.7 (n = 166)	24.3 ± 3.5 (n = 326)	0.128
ST elevated myocardial infarction	266 (53.8%)	100 (60.2%)	166 (50.6%)	0.043
Hypertension	400 / 490 (81.6%)	134 / 164 (81.7%)	266 / 326 (81.6%)	0.976
Diabetes mellitus	208 / 489 (42.5%)	69 / 164 (42.1%)	139 / 325 (42.8)	0.883
Dyslipidemia	286 / 482 (59.3%)	87 / 160 (54.4%)	199 /322 (61.8%)	0.118
Current smoker	155 / 488 (31.8%)	52 / 165 (31.5%)	103 / 323 (31.9%)	0.933
Creatinine on admission, (mg/dl)	1.63 ± 2.3	2.07 ± 2.72	1.41 + 2.10	< 0.001
Estimated glomerular filtration rate, (ml/min/1.73m^2)	63 ± 30	53 ± 30	68 ± 29	< 0.001
Hemodialysis on admission	45 (9.1%)	23 (13.9%)	22 (6.7%)	0.009
History of previous myocardial infarction	60 (12.1%)	18 (10.8%)	42 (12.8%)	0.528
History of previous percutaneous coronary intervention	92 (18.6%)	22 (13.3%)	70 (21.3%)	0.029
History of previous Coronary artery bypass graft surgery	18 (3.6%)	5 (3.0%)	13 (4.0%)	0.594
History of admission for heart failure	20 (4.0%)	11 (6.6%)	9 (2.7%)	0.039
Killip class (1 or 2, 3, or 4)				
1 or 2	400 (81.0%)	80 (48.2%)	320 (97.6%)	< 0.001
3 or 4	94 (18.8%)	86 (51.8%)	8 (2.4%)	
Shock on admission	34 (6.9%)	26 (15.7%)	8 (2.4%)	< 0.001
Cardio-pulmonary arrest on admission	12 (2.4%)	12 (7.2%)	(0%)	< 0.001
Admission within 24 h from onset of symptoms	369 (74.7%)	133 (80.1%)	236 (72.0%)	0.049
Systolic blood pressure on admission, (mm Hg)	144 ± 31	140 ± 35	146 ± 28	0.024
Diastolic blood pressure on admission, (mm Hg)	84 ± 20 (n = 491)	83 ± 23 (n = 164)	84 ± 18 (n = 327)	0.629
Heart rate on admission, (bpm)	82 ± 22	90 ± 27	78 ± 17	< 0.001
Left ventricular ejection fraction before discharge	53 ± 14 (n = 490)	45 ± 14 (n = 163)	57 ± 12 (n = 327)	< 0.001
Intra-aortic balloon pumping	31 (6.3%)	22 (13.3%)	9 (2.7%)	< 0.001
Veno-arterial extracorporeal membrane oxygenation	4 (0.8%)	4 (2.4%)	0 (0%)	0.005
Peak creatine kinase, (mU/ml)	1335 ± 1743	1763 ± 2144	1118 ± 1457	0.001
Peak Creatine kinase-muscle/brain, (mU/ml)	126 ± 170 (n = 492)	153 ± 194 (n = 165)	113 ± 155 (n = 327)	0.002
Brain natriuretic peptide at admission, (pg/ml)	398 ± 651 (n = 473)	714 ± 791 (n = 157)	241 ± 501 (n = 316)	< 0.001
Medication at admission				
Aspirin	130 / 479 (27.1%)	35 / 159 (22.0%)	95 / 320 (29.7%)	0.075
Thienopyridine	84 / 479 (17.5%)	24 / 159 (15.1%)	60 / 320 (18.8%)	0.322
Statin	161 / 477 (33.8%)	53 / 159 (33.3%)	108 / 318 (34.0%)	0.891
Angiotensin-converting enzyme - inhibitor or Angiotensin II receptor blocker	174 / 476 (36.6%)	64 / 159 (40.3%)	110 / 317 (34.7%)	0.236
Beta-blocker	107 / 476 (22.5%)	39 / 159 (24.5%)	68 / 317 (21.5%)	0.448
Calcium channel blocker	175 / 476 (36.8%)	73 / 159 (45.9%)	102 / 317 (32.2%)	0.003
Diuretics	61 / 478 (12.8%)	30 / 159 (18.9%)	31 / 319 (9.7%)	0.005
Oral antidiabetic drug	120 / 478 (25.1%)	40 / 159 (25.2%)	80 / 319 (25.1%)	0.985
Insulin	31 / 478 (6.5%)	13 / 159 (8.2%)	18 / 319 (5.6%)	0.289
Medication at discharge				
Aspirin	484 (98.0%)	164 (98.8%)	320 (97.6%)	0.507
Thienopyridine	468 (94.7%)	160 (96.4%)	308 (93.9%)	0.243
Statin	488 (98.8%)	165 (99.4%)	323 (98.5%)	0.669
Angiotensin-converting enzyme - inhibitor or Angiotensin II receptor blocker	453 (91.7%)	149 (89.8%)	304 (92.7%)	0.266
Beta blocker	468 (94.7%)	157 (94.6%)	311 (94.8%)	0.911
Severe in-hospital complications				
Cardiopulmonary arrest	14 (2.8%)	14 (8.4%)	0 (0%)	<0.001
Shock	51 (10.3%)	51 (10.3%)	0 (0%)	<0.001
Stroke	0 (0%)	0 (0%)	0 (0%)	
Atrioventricular block	7 (1.4%)	7 (4.2%)	0 (0%)	<0.001
Respiratory failure	142 (28.7%)	142 (85.5%)	0 (0%)	<0.001
Major bleeding (in-hospital)	45 (9.1%)	32 (19.3%)	13 (4.0%)	<0.001
Length of hospital stay (days)	7.9 ± 9.9	11.6 ± 14.0	6.09 ± 6.1	< 0.001

(*continued*)

Table 1 (***Continued***)

Variable	All (n = 494)	In-hospital Complications Group (n = 166)	Non-complications Group (n = 328)	p value
Length of coronary care unit stay (days)	1.5 ± 1.7 (n = 489)	2.60 ± 2.3 (n = 164)	1.0 ± 0.9 (n = 325)	< 0.001
Global Registry of Acute Coronary Events score	133 ± 35	156 ± 34	121 ± 29	< 0.001
Thrombolysis in myocardial infarction risk score	5.4 ± 2.4 (n = 255)	6.3 ± 2.6 (n = 97)	4.9 ± 2.1 (n = 158)	< 0.001

Data are expressed as the mean ± SD or number (percentage). The Person's chi-square test was used for categorical variables. Normally distributed continuous variables were compared by student *t* test and Mann-Whitney U test was performed for abnormally distributed continuous variables.

Dyslipidemia was defined as total cholesterol >220 mg/dl, low-density lipoprotein cholesterol >140 mg/dl, or treatment for hyperlipidemia.

Table 2
Comparison of lesion and procedural characteristics between the in-hospital complications group and noncomplications group

Variable	All (n = 494)	In-hospital Complications Group (n = 166)	Non-complications Group (n = 328)	p Value
Site of a myocardial infarct wall				
Anterior	247 (50.0%)	91 (54.8%)	156 (47.6%)	0.309
Inferior	142 (28.7%)	39 (23.5%)	103 (31.4%)	
Posterior	78 (15.3%)	27 (16.3%)	51 (15.5%)	
Not determined	27 (5.5%)	9 (5.4%)	18 (5.5%)	
Number of narrowed coronary arteries				
Single	213 (43.1%)	62 (37.3%)	151 (46.0%)	0.230
Double	165 (33.4%)	62 (37.3%)	103 (31.4%)	
Triple	107 (21.7%)	40 (24.1%)	67 (20.4%)	
Not determined	9 (1.8%)	2 (1.2%)	7 (2.1%)	
Treatment for culprit vessel				
Percutaneous coronary intervention	470 (95.1%)	161 (97.0%)	309 (94.2%)	0.237
Medication only	19 (3.8%)	3 (1.8%)	16 (4.9%)	
Coronary artery bypass graft surgery	5 (1.0%)	2 (1.2%)	3 (0.9%)	
First thrombolysis in myocardial infarction flow (0, 1, 2, 3)				
0 or 1	214 (43.3%)	82 (49.4%)	132 (40.2%)	0.052
2 or 3,	280 (56.7%)	84 (50.6%)	196 (59.8%)	
Final thrombolysis in myocardial infarction flow (0, 1, 2, or 3)				
0 or 1 or 2	21 (4.3%)	9 (5.4%)	12 (3.7%)	0.359
3	473 (95.7%)	157 (94.6%)	316 (96.3%)	
Acute myocardial infarction with nonculprit chronic total occlusion	57 (11.5%)	25 (15.1%)	32 (9.8%)	0.081
Use of aspiration catheter	39 (7.9%)	14 (8.4%)	25 (7.6%)	0.752
Final percutaneous coronary intervention procedure				
Percutaneous old balloon angioplasty	24 / 470 (5.1%)	10 /161 (6.2%)	14 / 309 (4.5%)	0.441
Aspiration only	1 / 470 (0.2%)	0 (0%)	1 /309 (0.3%)	
Drug coated balloon	25 / 470 (5.3%)	5 / 161 (3.1%)	20 /309 (6.5%)	
Bare-metal stent	8 / 470 (1.7%)	4 / 161 (2.5%)	4 / 309 (1.3%)	
Drug-eluting stent	409 / 470 (87.0%)	142 / 161 (88.2%)	267 /309 (86.4%)	
Percutaneous old balloon angioplasty + aspiration	2 / 470 (0.4%)	0 (0%)	2 / 309 (0.6%)	
Others	1 / 470 (0.2%)	0 (0%)	1 / 309 (0.3%)	
Access site				
Radial	341 / 470 (72.6%)	99 / 161 (61.5%)	242 / 309 (78.3)	< 0.001
Brachial	12 /470 (2.6%)	5 / 161 (3.1%)	7 / 3109 (2.3%)	
Femoral	117 / 470 (24.9%)	57 / 161 (35.4%)	60 /309 (19.4%)	
Catheter size (Fr)				
6Fr	310 / 470 (66.0%)	99 / 161 (61.5%)	211 / 309 (68.3%)	0.336
7Fr	155 / 470 (33.0%)	60 / 161 (37.3%)	95 / 309 (30.7%)	
8Fr	5 / 470 (1.1%)	2 / 161 (1.2%)	3 / 309 (1.0%)	

Data are expressed as number (percentage). The Person's chi-square test was used for categorical variables.

Table 3
Comparison of clinical outcomes between the in-hospital complications group and noncomplications group

Variable	All (n = 494)	in-hospital complications group (n = 166)	noncomplications group (n = 328)	P
Major adverse cardiac events (All cause death, Nonfatal Myocardial infarction, Readmission for heart failure)	50 (10.1%)	24 (14.5%)	26 (7.9%)	0.023
All cause death	24 (4.9%)	9 (5.4%)	15 (4.6%)	0.679
Cardiac death	9 (1.8%)	4 (2.4%)	5 (1.5%)	0.487
No-fatal Myocardial infarction	30 (6.1%)	10 (6.0%)	20 (6.1%)	0.974
Readmission for heart failure	32 (6.5%)	19 (11.4%)	13 (4.0%)	0.001
Stent thrombosis	5 (1.0%)	2 (1.2%)	3 (0.9%)	0.761
Target vessel revascularization (all)	76 (15.4%)	26 (15.7%)	50 (15.3%)	0.914
Target vessel revascularization (ischemic-driven)	30 (6.1%)	8 (4.8%)	22 (6.7%)	0.402
Target lesion revascularization (all)	45 (9.1%)	18 (10.8%)	27 (8.2%)	0.341
Target lesion revascularization (ischemic driven)	19 (3.9%)	6 (3.6%)	13 (4.0%)	0.844
Unplanned readmission ≤28 days (all)	39 (7.9%)	25 (15.1%)	14 (4.3%)	< 0.001
Unplanned readmission ≤28 days (cardiovascular)	24 (4.9%)	14 (8.4%)	10 (3.0%)	0.009

Data are expressed as the mean ± SD or number (percentage). The Person's chi-square test was used for categorical variables. Normally distributed continuous variables were compared by student *t* test and Mann-Whitney U test was performed for abnormally distributed continuous variables.

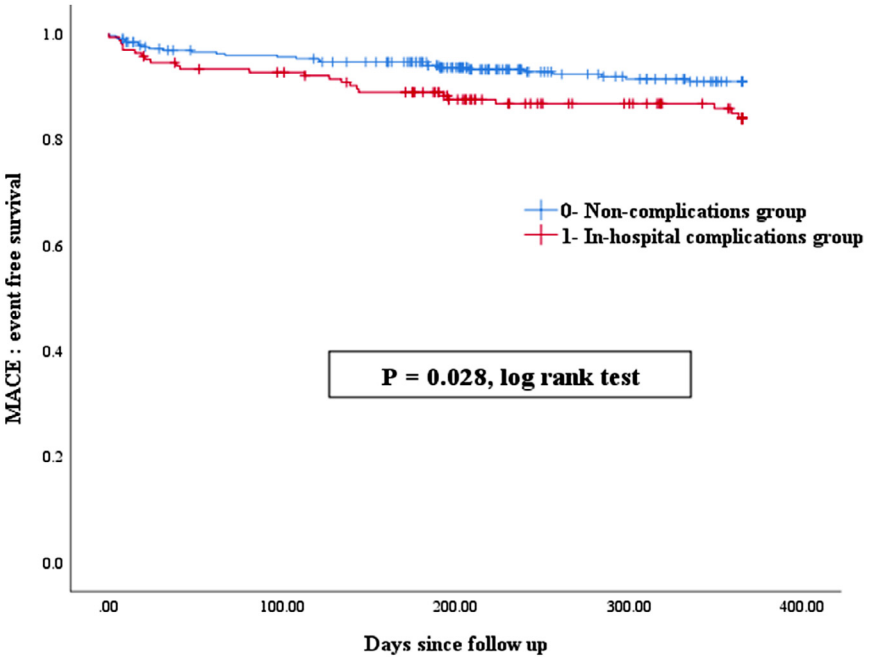

Figure 2. Kaplan-Meier curves for 1-year MACE between the in-hospital complications group and non-complications group. A log rank test was used.

group, the number of confounding factors were limited, because the number of events per variable should be less than 10.[27,28]

In conclusion, the MACE was significantly frequent in AMI patients who recovered from severe in-hospital complications and discharged to home, as compared with those who did not have in-hospital complications. AMI patients who recovered from complications could be recognized as a high risk group, and should be carefully managed by cardiologist after discharge to prevent cardiovascular events.

Author contribution

Shinnosuke Sawano, MD: Conceptualization, Methodology, Validation, Formal analysis, Investigation, Data curation, Writing-Original Draft.

Kenichi Sakakura, MD: Conceptualization, Methodology, Validation, Investigation, Data curation, Writing-Review & Editing, Supervision.

Yousuke Taniguchi, MD: Data curation.

Kei Yamamoto, MD: Data curation.

Takunori Tsukui, MD: Data curation.

Table 4
Multivariate Cox hazard analysis to predict the 1-year MACE

Independent Variables	Dependent Variable: MACE		
	Hazard Ratios	95% confidence Interval	p Value
In-hospital complications group (vs noncomplications group)	1.889	1.077-3.313	0.026
Age (years)	1.025	0.999-1.051	0.064
Men (vs women)	1.146	0.588-2.234	0.689
Left anterior descending artery as a culprit (vs other)	0.795	0.453-1.397	0.425
ST elevated myocardial infarction (vs non-ST elevated myocardial infarction)	0.573	0.322-1.019	0.058

MACE = major adverse cardiac events.

Masaru Seguchi, MD: Data curation.
Hiroyuki Jinnouchi, MD: Data curation.
Hiroshi Wada, MD: Data curation.
Hideo Fujita, MD: Writing-Review & Editing, Supervision, Project administration.

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