Determinants of Improvement of Mid-term Ejection Fraction in Patients with Acute Myocardial Infarction

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Summary
Persistent severe left ventricular (LV) systolic dysfunction after acute myocardial infarction (AMI) is associated with increased morbidity and mortality, whereas mid-term recovery of LV systolic function after AMI is associated with better long-term outcomes. The purpose of this study was to investigate the determinants of mid-term improvement of LV ejection fraction (EF) in AMI patients. We included 210 AMI patients who had modified Simpson EF both at the index admission and mid-term follow up. The difference of EF between the index admission and mid-term follow-up was calculated in all study patients. The EF improvement group was defined as mid-term ≥ 10% EF increase compared with the index admission EF. Of 210 AMI patients, 46 (21.9%) were allocated to the EF improvement group and 164 (78.1%) to the non-EF improvement group. Brain natriuretic peptide (BNP) at the timing of admission was significantly greater in the EF improvement group (735.8 ± 1077.6 pg/mL) than in the non-EF improvement group (239.0 ± 419.8 pg/mL) (P < 0.001). Multivariate logistic regression analysis revealed that log_{10} BNP at the timing of admission (OR 3.36, 95% CI 1.69-6.66, P < 0.001) and left main trunk-left anterior descending artery (LM-LAD) as the infarct-related artery (OR 3.34, 95% CI 1.59-7.02, P = 0.001) were significantly associated with EF improvement. In conclusion, elevated BNP at the timing of admission and LM-LAD as the infarct-related artery were significantly associated with mid-term LVEF recovery. Our results support aggressive acute treatment for those severe AMI, because the possibility of mid-term LVEF recovery is greater compared with other AMI.

Key words: Modified Simpson methods

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Acute myocardial infarction (AMI) is the major cause of chronic heart failure and is associated with morbidity and mortality. Although AMI worsens both systolic and diastolic left ventricular function, ejection fraction (EF) assessed by echocardiography is a simple and strong predictor of poor clinical outcomes after AMI. Because depressed EF caused by AMI would be modified by various factors, including successful primary percutaneous coronary intervention (PCI), EF in chronic phase of AMI may be a more important predictor of clinical outcomes compared with EF in acute phase of AMI. Furthermore, mid-term recovery of EF after AMI was associated with a better long-term clinical outcome. Therefore, it is important to find determinants of improvement of EF from initial clinical characteristics in AMI patients. The purpose of this study was to investigate determinants of mid-term improvement of EF in AMI patients.

Methods

Study patients: We reviewed data of AMI patients from hospital records in our medical center from January 2016 to December 2017, during which most AMI patients underwent echocardiography both at the index admission and mid-term (5-14 months from hospital discharge) follow-up. The Teichholz method was routinely used for EF measurement in our echo laboratory, but modified Simpson method was added for AMI patients if possible. Echocardiography was performed by experienced echosonographers. We included consecutive AMI patients who had EF and excluded AMI patients who did not have EF using modified Simpson method both at the index admission and mid-term follow-up during January 2016 to December 2017. We also excluded AMI patients who had another AMI before the mid-term follow-up. Moreover, we calculated the EF difference between the index admission and mid-term follow-up and defined the EF improvement group as mid-term ≥ 10% EF increase compared
with the index admission EF. We adopted ≥ 10% as the cut-off value of EF improvement, because ≥ 10% EF increase was used as the indicator of EF improvement in several studies of AMI or aortic stenosis. All study population was divided into the EF improvement group and the non-EF improvement group (< 10% EF increase or EF decrease compared with the index admission). This study was approved by the institutional review board, and written informed consent was waived because of the retrospective study design.

**Definition:** The diagnosis of AMI required the following criteria: symptoms consistent with AMI; elevated cardiac enzymes, including Troponin T, Troponin I, and/or creatinine kinase (at least two-fold increase from the normal upper limit); and ST-segment elevation or depression in electrocardiograms compatible with AMI. Diagnostic ST elevation was defined as a new ST elevation at the J point in at least two contiguous leads of 2 mm (0.2 mV), and others were defined as not an ST elevation. Hypertension was defined as a medical treatment for hypertension and/or a history of hypertension before admission. Dyslipidemia was defined as total cholesterol levels ≥ 220 mg/dL or low-density lipoprotein cholesterol levels ≥ 140 mg/dL or medical treatment for dyslipidemia or a history of dyslipidemia. Diabetes mellitus was defined as hemoglobin A1c levels ≥ 6.5% (as NGSP value) or medical treatment for diabetes mellitus or a history of diabetes mellitus. We also calculate the estimated glomerular filtration rate (eGFR) from the serum creatinine levels, age, weight, and gender using the following formula:

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eGFR = 194 \times \text{Cr}^{-1.094} \times \text{age}^{-0.287} \times 0.739\]

(female). Delayed reperfusion was defined as the time from symptom onset to reperfusion > 24 hours. Left ventricular wall motion was evaluated in the echocardiography to divide left ventricular 17 sections and score motion of each section. The scores of 1, 2, 3, and 4 are given to normal or hyperkinetic, hypokinetic, akinetic, and dyskinetic or aneurysmal segments, respectively. The LVWMI was calculated as the mean score of the total visualized scores.

**Statistical analysis:** Data are shown as mean ± SD or percentage. Categorical variables are presented as numbers (percentage) and were compared using Pearson’s \(t^2\) test. The Kolmogorov-Smirnov test was conducted to determine if the continuous variables were normally distributed. Normally distributed continuous variables were compared between the groups using the unpaired Student’s \(t\) test. Otherwise, continuous variables were compared using the Mann-Whitney \(U\) test. Univariate and multivariate logistic regression analyses were conducted to identify the determinants of mid-term EF improvement. In this model, the EF improvement group was used as the dependent variable. The multivariate logistic regression model included covariates found to have a significant association with the EF improvement group in univariate analysis (defined as \(P < 0.05\)). Brain natriuretic peptide (BNP) was log-transformed to obtain a normal distribution for the multivariate logistic regression analysis. The odds ratio (OR) and the 95% confidence interval (CI) were also calculated. A \(P\) value < 0.05 was considered statistically significant. We analyzed all data by SPSS ver. 24 for Windows (SPSS, Inc., Chicago, Illinois).

**Results**

A total of 550 AMI patients were admitted to our hospital from January 2016 to December 2017. Of the 550 AMI patients, 103 were excluded because EF using modified Simpson method was not available during the index admission. Five patients were excluded because of another AMI before the routine mid-term follow-up. Furthermore, 232 patients were excluded because EF using modified Simpson method was not available at the timing of the routine mid-term follow-up. The final study population was 210 patients, which was divided into the EF improvement group \((n = 46)\) and the non-EF improvement group \((n = 164)\) (Figure).

The comparison of patient characteristics between the two groups is shown in Table I. BNP at the timing of admission was significantly greater in the EF improvement group \((735.8 ± 1077.6\, \text{pg/mL})\) than in the non-EF improvement group \((239.0 ± 419.8\, \text{pg/mL})\) \((P < 0.001)\). Simpson EF on admission was significantly lower in the EF improvement group \((39.9% ± 12.2\%)\) than in the non-EF improvement group \((56.6% ± 10.8\%)\) \((P < 0.001)\). Beta-blocker prescription at hospital discharge was significantly lower in the EF improvement group \((89.1\%)\) than in the non-EF improvement group \((97.0\%)\) \((P = 0.04)\). The prevalence of delayed reperfusion was significantly higher in the EF improvement group \((55.6\%)\) than in the non-EF improvement group \((35.6\%)\) \((P = 0.02)\). The LVWMI difference between the index admission and mid-term follow-up was greater in the EF improvement group \((7.3 ± 8.9)\) than in the non-EF improvement group \((1.1 ± 4.2)\) \((P < 0.001)\). The comparison of angiographic lesion characteristic between the two groups is shown in Table II. The prevalence of left main trunk-left anterior descending artery as the infarct-related artery was significantly greater in the EF improvement group than in the non-EF improvement group \((P = 0.016)\). Four patients had final TIMI ≤ 2 flow in the EF improvement group. Three of those four patients had initial TIMI 0 flow, which was improved to TIMI 2 flow by PCI. One of those patients had delayed NSTEMI showing initial TIMI 0 flow. We did not revascularize the culprit of NSTEMI in the index admission because of the LMT dissection caused by a diagnostic catheter. Therefore, the patient’s final TIMI flow remained TIMI 0 flow.

Table III presents univariate and multivariate logistic regression analyses to identify the determinants of the EF improvement group. Log$_{10}$BNP (OR 3.31, 95% CI 1.50-
6.03, \( P = 0.002 \) and left main trunk-left anterior descending artery (LM-LAD) as the infarct-related artery (OR 4.94, 95% CI 1.95-12.52, \( P = 0.001 \)) were significantly associated with the EF improvement group in multivariate analysis.

**Discussion**

We included 210 AMI patients who measured EF by modified Simpson method both at the index admission and at the mid-term follow-up. Of the 201 AMI patients, 46 achieved \( \geq 10\% \) EF increase between the index admission and mid-term follow-up. Multivariate logistic regression analysis revealed that \( \log_{10} \text{BNP} \) was significantly associated with \( \geq 10\% \) EF increase, which suggests that BNP is not only a biomarker predicting poor clinical outcomes but also a biomarker predicting the chance for recovery. Furthermore, LM-LAD as the infarct-related artery was also significantly associated with \( \geq 10\% \) EF increase, indicating that the chance of EF recovery may be greater in anterior AMI than in non-anterior AMI.

In the present study, BNP at the timing of admission was an independent determinant of mid-term EF recovery. Although several groups reported the predictors of LV systolic function recovery, there were a few studies including BNP as covariates. Brooks et al. investigated the predictors of LV recovery after the 90-day follow-up in patients presenting with AMI and LV dysfunction, in which max BNP was not different among the 90-day EF \( \leq 35\% \), 90-day EF 36%-49\%, and 90-day EF \( \geq 50\% \). However, max BNP in the 90-day EF \( \geq 50\% \) group was the highest among the groups without reaching statistical significance, which may be compatible with our results. Oh et al. also investigated the predictors of mid-term LV recovery in patients presenting with AMI and LV dysfunction and reported that N-terminal pro BNP was greater in patients without EF recovery than in patients with EF recovery, which produced the opposite result of our study. Although we measured BNP at the timing of admission, Oh et al. might measure N-terminal pro BNP at a later timing, such as before discharge. Therefore, the timing of BNP measurement is important when BNP is considered to be a marker of mid-term EF recovery in AMI patients.

We should discuss why BNP at the timing of admission was significantly associated with mid-term EF recovery. Since elevated BNP levels reflect fluid retention, baseline LVEF might be suppressed by fluid retention in patients with elevated BNP levels, which results in the underestimation of baseline LVEF. Because patients with elevated BNP had received appropriate acute care, including primary PCI, cardiac rehabilitation, and introduction of optimal medical therapy, fluid retention might be resolved at the timing of follow-up echocardiography. Furthermore, since BNP itself acts as a vasodilator and antagonizes the vasoconstrictor effects of the renin-angiotensin-aldosterone system, endogenous BNP itself might modify EF like nesiritide or carperitide. In the present study, LM-LAD as the infarct-related artery was an independent determinant of mid-term EF recovery. Ottervanger et al. also reported that long-term recovery of LVEF after AMI was observed in anterior infarct location, which supports our results. On the other hand, Oh et al. reported that non-LAD culprit lesion was a predictor of EF recovery in AMI patients, which was the opposite result of our study. That disagreement may come from the difference in the EF recovery definitions. In their definition, the EF recovery group must have both baseline LVEF < 45\% and follow-up LVEF \( \geq 45\% \).
Table I. The Comparison of Patient Clinical Characteristic Between the EF Improvement Group and the Non-EF Improvement Group

|                                      | All (n = 210) | EF improvement group (n = 46) | Non-EF improvement group (n = 164) | P value |
|--------------------------------------|--------------|------------------------------|-----------------------------------|---------|
| Age, year                            | 68.1 ± 13.0  | 69.6 ± 14.4                  | 67.7 ± 12.5                       | 0.12    |
| Male sex, n (%)                      | 162 (77.1)   | 35 (76.1)                    | 127 (77.4)                        | 0.85    |
| Body mass index, kg/m² (n)           | 24.4 ± 3.7 (n = 208) | 23.9 ± 3.1 (n = 46) | 24.5 ± 3.9 (n = 162) | 0.24    |
| Hypertension, n (%)                  | 164/206 (79.6)| 38 (82.6)                   | 126 (78.8)                        | 0.57    |
| Diabetes mellitus, n (%)             | 95/206 (46.1)| 25 (55.6)                    | 70 (43.5)                         | 0.15    |
| Dyslipidemia, n (%)                  | 120/203 (59.1)| 25 (55.6)                   | 95 (60.1)                         | 0.58    |
| Current smoker, n (%)                | 74/206 (35.9)| 12 (27.3)                    | 62 (38.3)                         | 0.18    |
| Hemodialysis, n (%)                  | 9 (4.3)      | 3 (6.5)                      | 6 (3.7)                           | 0.31    |
| STEMI, n (%)                         | 125 (59.5)   | 27 (58.7)                    | 98 (59.8)                         | 0.90    |
| History of previous myocardial infarction, n (%) | 25 (11.9) | 2 (4.3)                      | 23 (14.0)                         | 0.73    |
| History of previous CABG, n (%)      | 4 (1.9)      | 0 (0)                        | 4 (2.4)                           | 0.37    |
| History of previous PCI, n (%)       | 33 (15.7)    | 6 (13.0)                     | 27 (16.5)                         | 0.57    |
| Killip classification                 |              |                              |                                   | 0.62    |
| 1 or 2                               | 172 (81.9)   | 33 (71.7)                    | 139 (84.8)                        |         |
| 3                                    | 16 (7.6)     | 7 (15.2)                     | 9 (5.5)                           |         |
| 4                                    | 22 (10.5)    | 6 (13.0)                     | 16 (9.8)                          |         |
| Cardiac arrest on out of hospital, n (%) | 7 (3.3)     | 2 (4.3)                      | 5 (3.0)                           | 0.48    |
| Serum creatinine, mg/dL              | 1.33 ± 2.00  | 1.5 ± 2.1                    | 1.2 ± 2.0                         | 0.21    |
| eGFR, mL/minute/1.73 m²              | 71.8 ± 29.1  | 68.5 ± 36.1                  | 72.7 ± 30.9                       | 0.17    |
| Peak CK, mg/dL                       | 1547.7 ± 2023.9 | 1238.1 ± 1458.7 | 1634.6 ± 2151.8                    | 0.39    |
| Peak CK-MB, mg/dL                    | 146.5 ± 197.4 | 109.3 ± 150.1               | 156.9 ± 208.0                     | 0.43    |
| Brain natriuretic peptide (BNP) at admission, pg/mL | 348.0 ± 656.0 (n = 205) | 735.8 ± 1077.6 (n = 45) | 239.0 ± 419.8 (n = 160) | <0.001 |
| log10BNP, pg/mL                      | 2.1 ± 0.7 (n = 205) | 2.5 ± 0.7 (n = 45) | 1.9 ± 0.6 (n = 160) | <0.001 |
| Medical therapy at the timing of hospital discharge |              |                              |                                   |         |
| ACE inhibitors or ARB, n (%)         | 185 (88.1)   | 43 (93.5)                    | 142 (86.6)                        | 0.20    |
| Beta-blockers, n (%)                 | 200 (95.2)   | 41 (89.1)                    | 159 (97.0)                        | 0.04    |
| Diuretics, n (%)                     | 59 (28.1)    | 18 (39.1)                    | 41 (25.0)                         | 0.06    |
| Calcium channel blocker, n (%)       | 41 (19.5)    | 10 (21.7)                    | 31 (18.9)                         | 0.67    |
| Aspirin, n (%)                       | 207 (98.6)   | 45 (97.8)                    | 162 (98.8)                        | 0.53    |
| Thienopyridine, n (%)                | 201 (95.7)   | 43 (93.5)                    | 158 (96.3)                        | 0.31    |
| Dual antiplatelet therapy, n (%)     | 200 (95.2)   | 43 (93.5)                    | 157 (95.7)                        | 0.38    |
| Statin, n (%)                        | 208 (99.0)   | 45 (97.8)                    | 163 (99.4)                        | 0.33    |
| Oral antidiabetic, n (%)             | 66 (31.4)    | 13 (28.3)                    | 53 (32.3)                         | 0.60    |
| Insulin, n (%)                       | 11 (5.2)     | 2 (4.3)                      | 9 (5.5)                           | 0.55    |
| Findings in echocardiogram           |              |                              |                                   |         |
| Simpson EF on admission (%)          | 54.7 ± 13.3  | 39.9 ± 12.2                  | 56.6 ± 10.8                       | 0.00    |
| Simpson EF on discharge (%)          | 55.5 ± 11.2  | 57.0 ± 11.7                  | 55.0 ± 11.0                       | 0.28    |
| Moderate to severe aortic stenosis, n (%) | 4 (1.9) | 0 (0)                       | 4 (2.4)                           | 0.37    |
| Moderate to severe aortic regurgitation, n (%) | 5 (2.4) | 2 (4.3)                      | 3 (1.8)                           | 0.30    |
| Moderate to severe mitral regurgitation, n (%) | 12 (5.7) | 3 (6.5)                      | 9 (5.5)                           | 0.51    |
| Difference of LVWMI                  | 2.4 ± 6.1    | 7.3 ± 8.9                    | 1.1 ± 4.2                         | <0.001  |
| Delayed reperfusion, n (%)           | 82/205 (40.0)| 25 (55.6)                    | 57 (35.6)                         | 0.02    |
| Door to balloon time, minutes (%)    | 75.9 ± 39.0 (n = 110) | 91.2 ± 45.1 (n = 20) | 72.5 ± 36.9 (n = 90)               | 0.03    |
| Index echocardiography day from admission, days | 5.3 ± 3.8 | 7.0 ± 5.0                    | 4.8 ± 3.2                         | 0.01    |

LVWMI indicates left ventricular wall motion index.

Thus, if a patient’s baseline LVEF and follow-up LVEF were 20% and 40%, respectively, he or she would be categorized to the non-EF recovery group. On the other hand, if a patient’s baseline LVEF and follow-up LVEF were 44% and 46%, respectively, he or she would be categorized to the EF recovery group. Since LVEF is generally lower in anterior AMI (LM-LAD as the infarct-related artery) than non-anterior AMI, anterior AMI whose baseline EF was low might be categorized to the non-EF recovery group even if significant EF recovery was observed in their study. Moreover, such depressed LVEF in anterior AMI may be the main cause of EF recovery in anterior AMI compared with non-anterior AMI. Baseline LVEF in patients with non-anterior AMI might be preserved even if there was a segmental asynergy. The difference between mid-term LVEF and baseline LVEF would be minimum if the baseline LVEF was preserved.

Clinical implications of the present study should be noted. In general, AMI patients with elevated BNP would be categorized to Killip class ≥ 3, which has greater morbidity and mortality compared with Killip class ≤ 2. Anterior AMI patients also have greater morbidity and mortality compared with non-anterior AMI. Our results support aggressive acute treatment for those severe AMI patients, because mid-term LVEF may recover, which would be associated with long-term better outcomes.
and cardiac rehabilitation for better clinical outcomes. Ultimately, our study would not answer which therapy was important for LVEF recovery, because PCI to the culprit lesion was performed in more than 95% of the study patients, beta-blockers were prescribed to more than 95% of the study patients at the timing of discharge, and ACE inhibitors/angiotensin receptor blockers were also prescribed to more than 85% of the study patients at the timing of discharge. However, it would be important to recognize elevated BNP and anterior AMI as the markers of midterm LVEF recovery and manage those high-risk patients adequately with primary PCI, optimal medical therapy, and cardiac rehabilitation for better clinical outcomes.

Study limitations: Since this study was a single-center, retrospective observational study, there is a risk of selection bias. In the measurement of LVEF, modified Simpson method was used for the present study. Although modified Simpson method can evaluate LVEF more accurately than Teichholz method, the accuracy would be less in LVEF measured by the modified Simpson method compared with LVEF measured by cardiac magnetic resonance imaging. In most cases, baseline LVEF was measured just before discharge in the index admission. Thus, baseline LVEF might be already improved following acute care, including primary PCI, which may underestimate the LVEF.

Table II. The Comparison of Angiographic Lesion and Procedural Characteristic Between the EF-Improvement Group and the Non-EF Improvement Group

|                                | All (n = 210) | EF improvement group (n = 46) | Non-EF improvement group (n = 164) | P value |
|--------------------------------|--------------|-------------------------------|-----------------------------------|---------|
| **Infarct-related artery**     |              |                               |                                   |         |
| Left main trunk-left anterior descending artery, n (%) | 115 (54.8)   | 35 (76.1)                     | 80 (48.8)                         | 0.016   |
| Left circumflex artery, n (%)  | 28 (13.3)    | 4 (8.7)                       | 24 (14.6)                         |         |
| Right coronary artery, n (%)   | 58 (27.6)    | 5 (10.9)                      | 53 (32.3)                         |         |
| Graft of CABG, n (%)           | 1 (0.5)      | 2 (4.3)                       | 1 (0.6)                           |         |
| Not determined, n (%)          | 8 (3.8)      | 6 (3.7)                       |                                   |         |
| Infarct-related artery part    |              |                               |                                   | 0.01    |
| Left main trunk, n (%)         | 7 (3.3)      | 2 (4.3)                       | 5 (3.1)                           |         |
| Proximal left anterior descending artery, n (%) | 78 (37.1) | 21 (45.7) | 57 (34.8) |         |
| Middle left anterior descending artery, n (%) | 30 (14.3) | 12 (26.1) | 18 (11.0) |         |
| Distal left anterior descending artery, n (%) | 0 | 0 | 0 |         |
| Proximal left circumflex artery, n (%) | 13 (6.2) | 1 (2.2) | 12 (7.3) |         |
| Distal left circumflex artery, n (%) | 15 (7.1) | 3 (6.5) | 12 (7.3) |         |
| Proximal right coronary artery, n (%) | 21 (10) | 1 (2.2) | 20 (12.2) |         |
| Middle right coronary artery, n (%) | 16 (7.6) | 3 (6.5) | 13 (7.9) |         |
| Distal right coronary artery, n (%) | 21 (10) | 1 (2.2) | 20 (12.2) |         |
| **Number of narrowed coronary arteries** |             |                               |                                   | 0.948   |
| 1                              | 83 (39.5)    | 17 (37.0)                     | 66 (40.2)                         |         |
| 2                              | 67 (31.9)    | 15 (32.6)                     | 52 (31.7)                         |         |
| 3                              | 57 (27.1)    | 13 (28.3)                     | 44 (26.8)                         |         |
| No organic stenosis (vasospasm)| 3 (1.4)      | 1 (2.2)                       | 2 (1.2)                           |         |
| **Initial TIMI flow grade**    |              |                               |                                   | 0.419   |
| 0                              | 90 (42.9)    | 18 (39.1)                     | 72 (43.9)                         |         |
| 1                              | 20 (9.5)     | 2 (4.3)                       | 18 (11.0)                         |         |
| 2                              | 27 (12.9)    | 7 (15.2)                      | 20 (12.2)                         |         |
| 3                              | 73 (34.6)    | 19 (41.3)                     | 54 (32.9)                         |         |
| **Final TIMI flow grade**      |              |                               |                                   | 0.533   |
| 0                              | 2 (1.0)      | 1 (2.2)                       | 1 (0.6)                           |         |
| 1                              | 0 (0)        | 0 (0)                         | 0 (0)                             |         |
| 2                              | 11 (5.2)     | 3 (6.5)                       | 8 (4.9)                           |         |
| 3                              | 197 (93.8)   | 42 (91.3)                     | 155 (94.5)                        |         |
| **Therapy to culprit lesion**  |              |                               |                                   | 0.301   |
| PCI, n (%)                     | 205 (97.6)   | 44 (95.7)                     | 161 (98.2)                        |         |
| CABG, n (%)                    | 0 (0)        | 0 (0)                         | 0 (0)                             |         |
| Medication, n (%)              | 5 (2.4)      | 2 (4.3)                       | 3 (1.8)                           |         |
| **Type of deployed stents during PCI** |        |                               |                                   | 0.241   |
| Bare-metal stent, n (%)        | 0 (0)        | 0 (0)                         | 0 (0)                             |         |
| Drug-eluting stent, n (%)      | 189/205 (92.2) | 39 (88.6) | 150 (93.2) |         |
| Percutaneous old balloon angioplasty, n (%) | 16/205 (7.8) | 5 (11.4) | 11 (6.8) |         |
| Thrombectomy, n (%)            | 23 (11.0)    | 6 (13.0)                      | 17 (10.4)                         | 0.607   |
| Left main trunk stenosis > 50%, n (%) | 24 (11.4) | 6 (13.0) | 18 (11.0) | 0.697   |
| Temporary pacemaker support, n (%) | 13 (6.2) | 2 (4.3) | 11 (6.7) | 0.428   |
| Intra-aortic balloon pump support, n (%) | 21 (10.0) | 7 (15.2) | 14 (8.5) | 0.146   |
| Percutaneous cardiopulmonary support device, n (%) | 3 (1.4) | 0 (0) | 3 (1.8) | 0.474   |
### Table III. Univariate and Multivariate Logistic Regression Analyses to Identify the Determinants of Mid-term EF Improvement

| Variable                                                                 | Univariate logistic regression analysis | Multivariate logistic regression analysis |
|--------------------------------------------------------------------------|----------------------------------------|-----------------------------------------|
|                                                                         | OR   | 95% CI       | P value | OR   | 95% CI       | P value |
| Age                                                                     | 1.01 | 0.99-1.04    | 0.38    |      |              |         |
| Male sex                                                                | 1.08 | 0.50-2.33    | 0.85    |      |              |         |
| Body mass index                                                          | 0.95 | 0.88-1.04    | 0.29    |      |              |         |
| Hypertension                                                            | 0.78 | 0.33-1.83    | 0.57    |      |              |         |
| Diabetes mellitus                                                        | 1.63 | 0.84-3.16    | 0.15    |      |              |         |
| Dyslipidemia                                                             | 0.83 | 0.43-1.62    | 0.58    |      |              |         |
| Current smoker                                                           | 0.61 | 0.29-1.26    | 0.18    |      |              |         |
| Hemodialysis                                                             | 1.84 | 0.44-7.65    | 0.40    |      |              |         |
| STEMI                                                                   | 1.05 | 0.54-2.03    | 0.897   |      |              |         |
| History of previous myocardial infarction                               | 0.28 | 0.63-1.23    | 0.091   |      |              |         |
| History of previous CABG                                                 |      |              |         |      |              |         |
| Killip classification 1 or 2                                            | 0.44 | 0.20-0.94    | 0.04    | 0.59 | 0.21-1.69    | 0.33    |
| Cardiac arrest on out of hospital                                       | 1.45 | 0.27-7.71    | 0.67    |      |              |         |
| Serum creatinine                                                        | 1.04 | 0.90-1.21    | 0.61    |      |              |         |
| eGFR                                                                    | 0.99 | 0.99-1.01    | 0.44    |      |              |         |
| Peak CPK                                                                | 1.00 | 1.00-1.00    | 0.24    |      |              |         |
| Peak CK-MB                                                              | 0.99 | 0.99-1.00    | 0.15    |      |              |         |
| Brain natriuretic peptide                                               | 1.00 | 1.00-1.00    | 0.00    |      |              |         |
| log10BNP                                                                | 4.17 | 2.30-7.50    | 0.00    | 3.01 | 1.50-6.03    | 0.002   |
| ACE inhibitors or ARB                                                   | 2.22 | 0.63-7.78    | 0.21    |      |              |         |
| Beta-blockers                                                           | 0.26 | 0.71-0.93    | 0.04    | 0.58 | 0.12-2.92    | 0.51    |
| Diuretics                                                              | 1.93 | 0.97-3.84    | 0.06    |      |              |         |
| Calcium channel blocker                                                 | 1.19 | 0.53-2.66    | 0.67    |      |              |         |
| Aspirin                                                                 | 0.56 | 0.05-6.27    | 0.63    |      |              |         |
| Thienopyridine                                                          | 0.54 | 0.13-2.28    | 0.40    |      |              |         |
| DAPT                                                                    | 0.64 | 0.16-2.58    | 0.53    |      |              |         |
| Statin                                                                  | 0.28 | 0.17-4.50    | 0.37    |      |              |         |
| Insulin                                                                 | 0.78 | 0.16-3.76    | 0.76    |      |              |         |
| Oral antidiabetic                                                        | 0.83 | 0.40-1.70    | 0.60    |      |              |         |
| Simpson EF on admission                                                  | 0.89 | 0.86-0.92    | 0.00    |      |              |         |
| Simpson EF on discharge                                                 | 1.02 | 0.99-1.05    | 0.31    |      |              |         |
| Moderate to severe aortic stenosis                                       |      |              |         |      |              |         |
| Moderate to severe aortic regurgitation                                  | 2.44 | 0.40-15.06   | 0.34    |      |              |         |
| Moderate to severe mitral regurgitation                                  | 1.20 | 0.31-4.63    | 0.79    |      |              |         |
| Time from symptom onset to reperfusion > 24 hours                       | 2.26 | 1.16-4.42    | 0.02    | 2.26 | 0.93-5.51    | 0.07    |
| Door to balloon time                                                     | 1.01 | 1.00-1.02    | 0.06    |      |              |         |
| Index echocardiography day from admission                               | 1.14 | 1.05-1.24    | 0.01    | 1.09 | 0.99-1.20    | 0.08    |
| Infarct-related artery                                                   |      |              |         |      |              |         |
| Left main trunk-Left anterior descending artery                          | 3.34 | 1.59-7.02    | 0.001   | 4.93 | 1.95-12.50   | 0.001   |
| Number of narrowed coronary arteries                                    |      |              |         |      |              |         |
| 2 (versus 1)                                                            | 1.12 | 0.51-2.45    | 0.78    |      |              |         |
| 3 (versus 1)                                                            | 1.15 | 0.51-2.60    | 0.74    |      |              |         |
| No organic stenosis (versus 1)                                           | 1.94 | 0.17-22.70   | 0.60    |      |              |         |
| Initial TIMI flow grade                                                 |      |              |         |      |              |         |
| 3                                                                       | 1.43 | 0.73-2.81    | 0.29    |      |              |         |
| Final TIMI flow grade                                                   |      |              |         |      |              |         |
| 3                                                                       | 0.61 | 0.18-2.08    | 0.43    |      |              |         |
| Therapy to culprit lesion                                               |      |              |         |      |              |         |
| PCI                                                                     | 0.41 | 0.07-2.53    | 0.34    |      |              |         |
| CABG                                                                    |      |              |         |      |              |         |
| Medication                                                              |      |              |         |      |              |         |
| Type of deployed stents during PCI                                      |      |              |         |      |              |         |
| Drug-eluting stent                                                      | 0.57 | 0.19-1.74    | 0.33    |      |              |         |
| Thrombectomy                                                            | 1.33 | 0.49-3.60    | 0.57    |      |              |         |
| Left main trunk stenosis > 50%                                           | 1.22 | 0.45-3.27    | 0.70    |      |              |         |
| Temporary pacemaker                                                     | 0.63 | 0.14-2.96    | 0.56    |      |              |         |
| Intra-aortic balloon pump                                               | 1.92 | 0.73-5.09    | 0.19    |      |              |         |
| Percutaneous cardiopulmonary support device                             |      |              |         |      |              |         |
difference between baseline and mid-term follow-up. Moreover, delayed reperfusion was frequently observed in the EF improvement group, which was inconsistent with the result in previous study.\(^8\) That inconsistency may be attributed to the difference in the definitions of baseline EF. Since the previous study measured the baseline EF within 24 hours from admission,\(^8\) their results might reflect the effect of primary PCI more significantly compared with our results. Furthermore, there were four patients with final TIMI ≤ 2 flow in the EF improvement group. Although the mechanism of EF improvement with insufficient revascularization was not clear, the timing of index echocardiography might be affected. If the index echocardiography was performed several days after PCI, the positive effect of PCI might be attenuated. We calculated the difference of LVWMI as a marker of improvement of segmental asynery. However, since LVWMI is a semi-quantitative index, the accuracy might be less in LVWMI compared with that in strain and strain-rate imaging.\(^3,33\) Finally, we should mention the survivor bias. Because our study included patients who were successfully discharged from the index admission and came to follow-up clinics, the most severe patients who died during the index admission were excluded like early studies that compared initial EF with follow-up EF.\(^8,23,24,25,34\)

Conclusions

Elevated BNP at the timing of admission and LM-LAD as the infarct-related artery were significantly associated with mid-term LVEF recovery. Our results support aggressive acute treatment for those severe AMI patients, because the possibility of mid-term LVEF recovery is greater compared with other AMI patients.

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Disclosure

Conflicts of interest: Dr. Sakakura has received speaking honoraria from Abbott Vascular, Boston Scientific, Medtronic Cardiovascular, Terumo, OrbisNeich, Japan Life-line, and NIPRO. He has served as a proctor for Rotablator for Boston Scientific and has served as a consultant for Abbott Vascular and Boston Scientific. Prof. Fujita served as a consultant for Mehergen Group Holdings, Inc.

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