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The Prognostic Value of the Left Ventricular Ejection Fraction Is Dependent upon the Severity of Mitral Regurgitation in Patients with Acute Myocardial Infarction

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The prognostic value of the left ventricle ejection fraction (LVEF) after acute myocardial infarction (AMI) has been questioned even though it is an accurate marker of left ventricle (LV) systolic dysfunction. This study aimed to examine the prognostic impact of LVEF in patients with AMI with or without high-grade mitral regurgitation (MR). A total of 15,097 patients with AMI who received echocardiography were registered in the Korean Acute Myocardial Infarction Registry (KAMIR) between January 2005 and July 2011. Patients with low-grade MR (grades 0-2) and high-grade MR (grades 3-4) were divided into the following two sub-groups according to LVEF: LVEF ≤ 40% (n = 2,422 and 197, respectively) and LVEF > 40% (n = 12,252 and 226, respectively). The primary endpoints were major adverse cardiac events (MACE), cardiac death, and all-cause death during the first year after registration. Independent predictors of mortality in the multivariate analysis in AMI patients with low-grade MR were age ≥ 75 yr, Killip class ≥ III, N-terminal pro-B-type natriuretic peptide > 4,000 pg/mL, high-sensitivity C-reactive protein ≥ 2.59 mg/L, LVEF ≤ 40%, estimated glomerular filtration rate (eGFR), and percutaneous coronary intervention (PCI). However, PCI was an independent predictor in AMI patients with high-grade MR. No differences in primary endpoints between AMI patients with high-grade MR (grades 3-4) and EF ≤ 40% or EF > 40% were noted. MR is a predictor of a poor outcome regardless of ejection fraction. LVEF is an inadequate method to evaluate contractile function of the ischemic heart in the face of significant MR.

Keywords: Mitral Regurgitation; Acute Myocardial Infarction; Left Ventricular Ejection Fraction

INTRODUCTION

Mitral regurgitation (MR) is a frequent complication and a powerful predictor of long-term cardiovascular mortality after acute myocardial infarction (AMI) (1-5). Although left ventricular (LV) ejection fraction (EF) is a determinant of poor prognosis and an accurate marker of LV systolic dysfunction, the prognostic value of LVEF after MI has been questioned (6). In patients with chronic MR, LVEF underestimates the degree of LV systolic dysfunction because of volume overload. LVEF is also highly influenced not only by LV contractility but also by LV geometry, loading condition, and MR severity (7, 8). In patients with AMI, low LVEF can be the result of reduced contractile function due to extensive myocardial damage, LV dilatation, or myocardial stunning (9).

The role of LVEF as a prognostic factor in AMI patients with significant MR has been poorly addressed (10, 11). Furthermore, the prognostic value of LVEF in AMI patients with severe MR has not been previously reported. This study aimed to examine the prognostic significance of LVEF in the long-term outcome of AMI patients with or without severe MR in the clinical setting.

MATERIALS AND METHODS

Study population

The Korean Acute Myocardial Infarction Registry (KAMIR) is a Korean, prospective, open, observational, multicenter, on-line registry of AMI data with support from the Korean Society of Cardiology that was initiated in November 2005. The 50 partici-

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pating hospitals are capable of performing primary percutaneous coronary intervention (PCI). Details of the KAMIR have been published previously (2, 12, 13). A total of 15,097 patients with AMI who received echocardiography were registered in the KAMIR between January 2005 and July 2011. Patients with low-grade MR (grade 0-2) were divided into two groups according to LVEF, namely, LVEF ≤ 40% (n = 2,426) or EF > 40% (n = 12,252). Patients with high-grade MR (grade 3-4) were similarly divided into two groups (EF ≤ 40% [n = 197] or EF > 40% [n = 226]).

The endpoints of the study were major adverse cardiac events (MACE), cardiac death, and all-cause death during the year following registration. MACEs were defined as the composite of all-cause death, MI, and repeated PCI or coronary artery bypass grafting (CABG) during 12 months of clinical follow-up.

The follow-ups in the outpatient clinic occurred immediately after hospital discharge, one month post-discharge, and at intervals of less than 6 months thereafter. Information on events and mortality was obtained from hospital records and phone calls.

The diagnosis of non-ST elevation myocardial infarction (NSTEMI) and ST elevation myocardial infarction (STEMI) was based on the definitions from the American College of Cardiology/American Heart Association (ACC/AHA guidelines) (14, 15).

Coronary angiogram

Coronary angiograms were performed using standard techniques. Significant coronary artery disease (CAD) was defined as ≥ 70% stenosis of an epicardial coronary artery. The extent of CAD was characterized by one-, two-, or three-vessel disease or left main disease (14, 15). Percutaneous coronary intervention (PCI) was performed according to the physician's discretion. Coronary blood flow in the infarct-related artery before and after stent implantation was graded according to the classification used in the Thrombolysis in Myocardial Infarction trials.

Echocardiography

All index transthoracic echocardiographs were recorded during routine clinical practice according to the current guidelines (16). Two-dimensional M-mode echocardiography and Doppler ultrasound examinations were performed within 3 days of the PCI.

In each patient, LVEF was measured using bidimensional echocardiography from two- and four-chamber apical views by the modified Simpson's method (17). The wall motion score index was derived according to a 17 segment model (18). For each segment, wall motion was scored from 1 (normal) to 4 (dyskinesia). The presence and degree of MR were measured using the proximal isovelocity surface area (PISA) method and a validated nomogram for semi-quantitative estimation (19). MR was classified into four degrees of severity (I: mild, II: mild to moderate, III: moderate, IV: severe).

Statistical analysis

Data are expressed as the means ± SD for continuous variables and absolute numbers (proportions) for categorical variables. All comparisons between baseline variables were performed by the Pearson chi-square test for categorical variables and the *t*-test for continuous variables.

Cox proportional hazards regression was used to estimate the relative mortality risk at 1 yr. We controlled for all available variables considered potentially relevant in all regression analysis of low-grade MR (grade 0-2) and high-grade MR (grade 3-4): age, gender, Killip class, Q wave on electrocardiography (ECG), Ischemic heart disease history (IHD), diabetes mellitus (DM), N-terminal pro-B type natriuretic peptide (NT-proBNP), glucose level, high-sensitivity C-reactive protein (Hs-CRP), LVEF, estimated glomerular filtration rate (eGFR), and PCI. Best cutoff values of continuous variables were assessed by the receiver operating curve. All statistical tests were 2-sided, and a P value < 0.05 was considered statistically significant. Statistical analysis was performed using SPSS 18.0 for Windows (SPSS, Inc., Chicago, IL, USA). Survival analysis was performed using the Kaplan-Meier method with log-rank tests to compare survival between groups.

Ethics statement

The institutional review board of all participating institutions approved the study protocol. The approval number of Chonnam National University Hospital was 05-49. Written informed consent was obtained from all participating patients.

RESULTS

Baseline clinical characteristics and laboratory findings

The baseline clinical characteristics are presented in Table 1. Among the patients with low-grade MR (grade 0-2), the patients in the LVEF ≤ 40% group were older, were more likely to be women, had decreased body mass indexes (BMIs) and blood pressures, had higher heart rates and Killip classes and were more likely to have histories of hypertension, DM, and IHD compared with the patients in the LVEF > 40% group. Patients with reduced LVEF were more likely to present STEMI, Q waves, and atrial fibrillation/flutter on electrocardiography. However, among the patients with high-grade MR (grade 3-4), the patients in the LVEF ≤ 40% group were more likely to be men, have higher heart rates, have histories of DM and IHD, and present Q waves on ECG compared with the patients in the LVEF > 40% group. Regardless of MR grade, the LVEF ≤ 40% group had higher glucose, Hs-CRP, and NT-proBNP levels compared with the LVEF > 40% group (Table 2).

Coronary angiogram

In AMI patients with low-grade MR (grade 0-2), the LVEF ≤ 40%

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Table 1. Clinical characteristics of patients

Clinical characteristics	MR Grades 0-2 EF ≤ 40% (n = 2,422)	MR Grades 0-2 EF > 40% (n = 12,252)	MR Grades 0-2 *P* value	MR Grades 3-4 EF ≤ 40% (n = 197)	MR Grades 3-4 EF > 40% (n = 226)	MR Grades 3-4 *P* value
Age (mean ± SD) (yr)	67.0 ± 12.2	63.4 ± 12.5	< 0.001	71.1 ± 11.7	72.6 ± 10.6	0.164
Men (%)	1,695 (70.1)	8,906 (72.6)	0.006	106 (54.1)	97 (42.9)	0.022
Body mass index, median (IQR)	23 (21-25.4)	24 (22-26)	< 0.001	23 (21-24)	23 (21-25)	0.791
Heart rate (beats/min)	83 (72-99.5)	74 (64-84)	< 0.001	90 (72-107)	78 (64-91)	< 0.001
Blood pressure (mmHg)						
Systolic	121 (110-140)	130 (110-150)	< 0.001	120 (100-146)	128 (105-140)	0.518
Diastolic	80 (69-90)	80 (70-90)	< 0.001	71 (60-87)	77 (63.5-89.5)	0.626
Killip class ≥ III	673 (28.7)	1,003 (8.5)	< 0.001	91 (46.4)	87 (38.7)	0.094
Risk factor (%)						
Hypertension	1,209 (50.2)	5,818 (47.8)	0.018	103 (53.1)	130 (61.3)	0.693
Diabetes mellitus	829 (34.2)	3,078 (25.3)	< 0.001	93 (47.2)	70 (31.4)	< 0.001
Currently smoking	1,169 (48.9)	6,552 (54.0)	< 0.001	74 (38.1)	67 (30.0)	0.081
Dyslipidemia*	224 (9.3)	1,407 (11.6)	0.001	27 (13.9)	37 (16.4)	0.459
Ischemic heart disease history	500 (20.8)	1,688 (13.9)	< 0.001	62 (31.5)	45 (20.4)	0.009
STEMI	1,535 (63.4)	6,927 (56.5)	< 0.001	77 (39.1)	81 (36.0)	0.546
NSTEMI	887 (36.6)	5,325 (43.5)	< 0.001	120 (60.9)	144 (64.0)	0.540
Q wave	473 (19.6)	1,547 (12.6)	< 0.001	43 (22.5)	19 (8.7)	< 0.001
Atrial fibrillation/ flutter	130 (5.4)	389 (3.2)	< 0.001	23 (11.8)	22 (10.0)	0.546

Data are expressed as the mean ± SD or number (%), or median (IQR) as appropriate. *Defined as patients who were previously diagnosed by a physician and/or patients receiving lipid-lowering drugs. NSTEMI, non-ST elevation myocardial infarction; STEMI, ST elevation myocardial infarction; MR, mitral regurgitation; EF, ejection fraction.

Table 2. Laboratory findings and echocardiographic parameters

Variables	MR Grades 0-2 EF ≤ 40% (n = 2,422)	MR Grades 0-2 EF > 40% (n = 12,252)	MR Grades 0-2 *P* value	MR Grades 3-4 EF ≤ 40% (n = 197)	MR Grades 3-4 EF > 40% (n = 226)	MR Grades 3-4 *P* value
Peak CK-MB (U/L)	162.7 ± 332.3	118.1 ± 223.1	< 0.001	121.8 ± 310.8	98.4 ± 146.8	0.314
Glucose (mg/dL)	188.2 ± 92.3	164.1 ± 75.6	< 0.001	205.6 ± 100.1	179.7 ± 90.2	0.006
Glomerular filtration rate (mL/min/1.73 m^2)	59.9 ± 37.3	73.6 ± 40.3	< 0.001	49.9 ± 26.2	53.6 ± 28.1	0.183
Total cholesterol (mg/dL)	178.1 ± 45.7	183.8 ± 43.4	< 0.001	169.6 ± 50.1	174.0 ± 49.8	0.370
Triglycerides (mg/dL)	113.4 ± 73.8	132.9 ± 111.2	< 0.001	101.4 ± 56.9	107.7 ± 57.3	0.273
High-density lipoprotein cholesterol (mg/dL)	44.3 ± 15.3	44.9 ± 21.4	0.221	43.4 ± 14.5	43.7 ± 13.6	0.845
Low-density lipoprotein cholesterol (mg/dL)	114.2 ± 42.8	117.1 ± 39.6	0.003	109.6 ± 46.3	110.2 ± 40.2	0.904
High-sensitivity C-reactive protein (mg/dL)	12.8 ± 41.4	7.28 ± 35.8	< 0.001	19.3 ± 86.4	12.7 ± 45.1	0.035
NT-pro BNP (pg/mL)	5,472.8 ± 9,110.1	1,626.0 ± 443.6	< 0.001	8,984.9 ± 10,105.8	6,116.4 ± 9,101.3	0.009
Echocardiographic parameters						
Left ventricular ejection fraction (%)	33.4 ± 6.25	56.0 ± 8.8	< 0.001	31.4 ± 6.7	51.9 ± 7.7	< 0.001
Regional wall motion score	25.3 ± 12.6	18.5 ± 9.3	< 0.001	28.4 ± 13.8	21.3 ± 10.3	< 0.001
Left ventricular end-diastolic dimension (mm)	52.9 ± 9.30	48.4 ± 8.0	< 0.001	56.1 ± 9.8	50.1 ± 8.3	< 0.001
Left end-systolic dimension (mm)	42.1 ± 9.2	33.3 ± 7.2	< 0.001	43.3 ± 12.3	36.2 ± 8.2	< 0.001

Data are expressed as the mean ± SD. MR, mitral regurgitation; EF, ejection fraction; CK-MB, creatine kinase myocardial band; NT-pro BNP, N-terminal pro-B-type natriuretic peptide.

group had more severe coronary angiogram findings than the LVEF > 40% group (Table 3). However, in patients with high-grade MR (grade 3-4), the LVEF ≤ 40% group had no significantly different coronary angiographic findings, except for left anterior coronary artery disease, compared with the LVEF > 40% group. PCI was performed in a significantly lower number of patients in the high grade MR group as compared to the low grade MR group. However, based on LVEF, there was no significant difference between the number of PCI performed on patients in the high grade MR group (Table 3).

Independent predictors of mortality

The independent predictors of cardiac death in the multivariate analysis in AMI patients with low-grade MR were age ≥ 75 yr, Killip class ≥ III, IHD history, NT-proBN*P* > 4,000 pg/mL, Hs-CRP ≥ 2.59 mg/L, eGFR, PCI, and LVEF ≤ 40% (Table 4). However, PCI was an independent predictor in patients with AMI with high-grade MR (Table 5). Primary endpoints in the MR grade 0-2 group based on Kaplan-Meier analysis were significantly different according to EF (EF ≤ 40% vs. EF > 40%, total death, 330/2,422 vs. 373/12,252, *P* < 0.001; MACEs, 489/2,422 vs. 1,091/12,252, *P* < 0.001; cardiac death, 281/2,422 vs. 254/12,252,

Table 3. Coronary angiography findings

Variables	MR Grades 0-2 EF ≤ 40% (n = 2,422)	MR Grades 0-2 EF > 40% (n = 12,252)	MR Grades 0-2 *P* value	MR Grades 3-4 EF ≤ 40% (n = 197)	MR Grades 3-4 EF > 40% (n = 226)	MR Grades 3-4 *P* value
Coronary angiographic findings, n (%)	2,236/2,422 (92.3)	11,942/12,252 (97.4)	< 0.001	168/197 (85.2)	199/ 226 (88.0)	0.563
Number of vessels with significant stenotic lesions			< 0.001			0.958
0	44/2,236 (2.0)	489/11,942 (4.1)		6/168 (3.6)	6/199 (2.6)	
1	1,370/2,236 (61.3)	7,439/11,942 (62.3)		91/168 (54.0)	114/199 (57.4)	
2	446/2,236 (19.9)	2,531/11,942 (21.2)		37/168 (22.1)	41/199 (21.0)	
3	259/2,236 (11.6)	1,158/11,942 (9.7)		24/168 (14.2)	29/199 (14.6)	
LMA involvement	117/ 2,236 (5.2)	331/ 11,942 (2.8)		10/ 168 (6.1)	9/ 199 (4.4)	
Infarct-related artery						
Left anterior descending coronary artery	1,737/2,236 (77.6)	6,448/11,942 (54.0)	< 0.001	94/168 (56.4)	80/199 (40.4)	0.003
Left circumflex coronary artery	499/ 2,236 (22.3)	3,295/11,942 (27.6)	< 0.001	43/168 (26.1)	77/199 (38.9)	0.013
Right coronary artery	606/ 2,236 (27.1)	5,087/11,942 (42.6)	< 0.001	74/168 (44.2)	112/199 (56.5)	0.026
LMA	117/ 2,236 (5.2)	331/11,942 (2.8)	< 0.001	10/168 (6.1)	9/199 (4.4)	0.083
ACC/AHA lesion type			< 0.001			0.616
A	84/2,236 (3.8)	394/11,942 (3.3)		6/168 (3.4)	5/199 (2.3)	
B1	330/2,236 (14.8)	2,161/11,942 (18.1)		31/168 (18.5)	27/199 (13.8)	
B2	595/2,236 (26.6)	4,119/11,942 (34.5)		41/168 (24.5)	49/199 (24.9)	
C	1,225/2,236 (54.8)	5,268/11,942 (44.1)		90/168 (53.6)	118/199 (59.0)	
Initial TIMI flow grade 0	1,113/2,236 (49.8)	5,230/11,942 (43.8)	< 0.001	79/168 (47.4)	93/199 (46.9)	1.000
Final TIMI flow grade 3	1,994/2,236 (89.2)	11,321/11,942 (94.8)	< 0.001	147/168 (87.5)	187/199 (94.0)	0.072
PCI	2,117/2,422 (87.4)	11,291/12,252 (92.1)	< 0.001	136/197 (69.0)	170/226 (75.2)	0.229
Number of stents	1.56 ± 0.87	1.53 ± 0.83	0.180	1.65 ± 0.98	1.61 ± 0.94	0.730
Total stent length (mm)	24.86 ± 7.23	24.01 ± 7.0	< 0.001	24.4 ± 6.8	24.8 ± 6.3	0.657
Thrombolytic therapy	88/2,422 (3.6)	656/12,252 (5.3)	0.007	3/197 (1.5)	5/226 (2.2)	0.347
CABG	17/2,422 (0.7)	34/12,252 (0.2)	0.001	2/197 (1.0)	4/226 (1.8)	0.690

Data are expressed as the number of patients (%). MR, mitral regurgitation; EF, ejection fraction; ACC/AHA, American College of Cardiology/American Heart Association; TIMI, Thrombolysis In Myocardial Infarction; CABG, coronary artery bypass graft; LMA, left main coronary artery; PCI, percutaneous coronary intervention.

Table 4. Cox regression analysis of cardiac death by 1 yr in the mitral regurgitation grades 0-2 groups of acute myocardial infarction patients

Variables	Univariate HR	95% CI Lower	95% CI Upper	*P* value	Multivariate HR	95% CI Lower	95% CI Upper	*P* value
Age ≥ 75	3.214	2.743	3.765	< 0.001	1.527	1.191	1.957	0.001
Gender (Male)	0.532	0.453	0.625	< 0.001	1.148	0.895	1.473	0.276
Killip ≥ III	5.645	4.797	6.643	< 0.001	1.833	1.405	2.39	< 0.001
Qwave	1.307	1.06	1.611	0.012	1.021	0.76	1.372	0.891
Ischemic heart disease	1.876	1.56	2.256	< 0.001	1.308	0.997	1.716	0.052
Diabetes mellitus	1.877	1.597	2.206	< 0.001	0.954	0.733	1.241	0.725
NT-proBNP > 4,000 (pg/mL)	8.134	6.628	9.982	< 0.001	1.807	1.349	2.42	< 0.001
Glucose ≥ 160 (mg/dL)	2.008	1.71	2.358	< 0.001	1.173	0.915	1.505	0.208
Hs-CRP ≥ 2.59 (mg/dL)	3.063	2.553	3.675	< 0.001	1.668	1.31	2.125	< 0.001
LVEF ≤ 40%	8.223	5.81	11.637	< 0.001	3.802	2.174	6.65	< 0.001
LVEF ≤ 40%*log (time)	1.177	1.07	1.295	0.001	1.204	1.046	1.386	0.010
eGFR (mL/min/1.73 m^2)	0.969	0.967	0.972	< 0.001	0.98	0.975	0.985	< 0.001
PCI	0.216	0.182	0.257	< 0.001	0.368	0.283	0.479	< 0.001

CK-MB was excluded because it was not primary variable and had interaction with time. *LVEF ≤ 40% had time dependent hazard ratio (HR = 9.452 on 30 day, 10.504 on 180 day, 10.951 on 365 day). LVEF, Left ventricular ejection fraction; eGFR, estimated glomerular filtration rate; PCI, percutaneous coronary intervention;CK-MB, creatine kinase myocardial band; Hs-CRP, high-sensitivity C-reactive protein; NT-proBNP, N-terminal pro-B-type natriuretic peptide.

$P < 0.001$ by the log-rank test). However, primary endpoints among AMI patients with MR grade 3-4 was not different according to EF (EF ≤ 40% vs. EF > 40%, total death, 42/197 vs. 37/226, $P = 0.216$; MACEs, 55/197 vs. 49/226, $P = 0.357$; cardiac death, 37/197 vs. 31/226, $P = 0.216$ by the log-rank test) (Fig. 1). Fig. 1 reveals that patients with grades 3-4 MR and preserved EF exhibit a poor prognosis given the advanced age of this patient population compared with groups with low-grade MR (Table 1).

DISCUSSION

The present study showed that in the presence of high-grade MR, LVEF is not an independent predictor of mortality. LVEF is the most widely used variable to represent LV systolic function

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Table 5. Cox regression analysis of cardiac death by 1 yr in the mitral regurgitation grades 3-4 groups of acute myocardial infarction patients

Variables	Univariate HR	95% CI		*P* value	Multivariate HR	95% CI		*P* value
		Lower	Upper			Lower	Upper	
Age ≥ 75	1.880	1.168	3.026	0.009	1.867	0.886	3.934	0.101
Gender (Male)	0.601	0.370	0.976	0.040	1.149	0.574	2.302	0.694
Killip ≥ III	1.697	1.053	2.735	0.030	1.036	0.498	2.153	0.925
Q wave	0.820	0.407	1.653	0.580	1.093	0.449	2.660	0.845
Ischemic heart disease	1.732	1.062	2.824	0.028	1.087	0.514	2.297	0.827
Diabetes mellitus	0.913	0.562	1.483	0.713	1.026	0.465	2.262	0.949
NT-proBNP > 4,000 (pg/mL)	2.234	1.232	4.050	0.008	1.165	0.558	2.432	0.684
Glucose ≥ 160 (mg/dL)	1.893	1.161	3.087	0.011	0.936	0.429	2.042	0.869
Hs-CRP ≥ 2.59 (mg/dL)	2.285	1.250	4.175	0.007	1.616	0.768	3.400	0.206
LVEF ≤ 40%	1.341	0.841	2.138	0.217	0.836	0.400	1.747	0.633
CK-MB (U/L)	0.999	0.997	1.001	0.296	0.997	0.992	1.001	0.170
PCI	0.310	0.195	0.494	< 0.001	0.381	0.192	0.755	0.006

eGFR was excluded because it was not primary variable and had interaction with time. LVEF, Left ventricular ejection fraction; eGFR, estimated glomerular filtration rate; PCI, percutaneous coronary intervention; CK-MB, creatine kinase myocardial band; NT-pro BNP, N-terminal pro-B type natriuretic; Hs-CRP, high-sensitivity C-reactive protein.

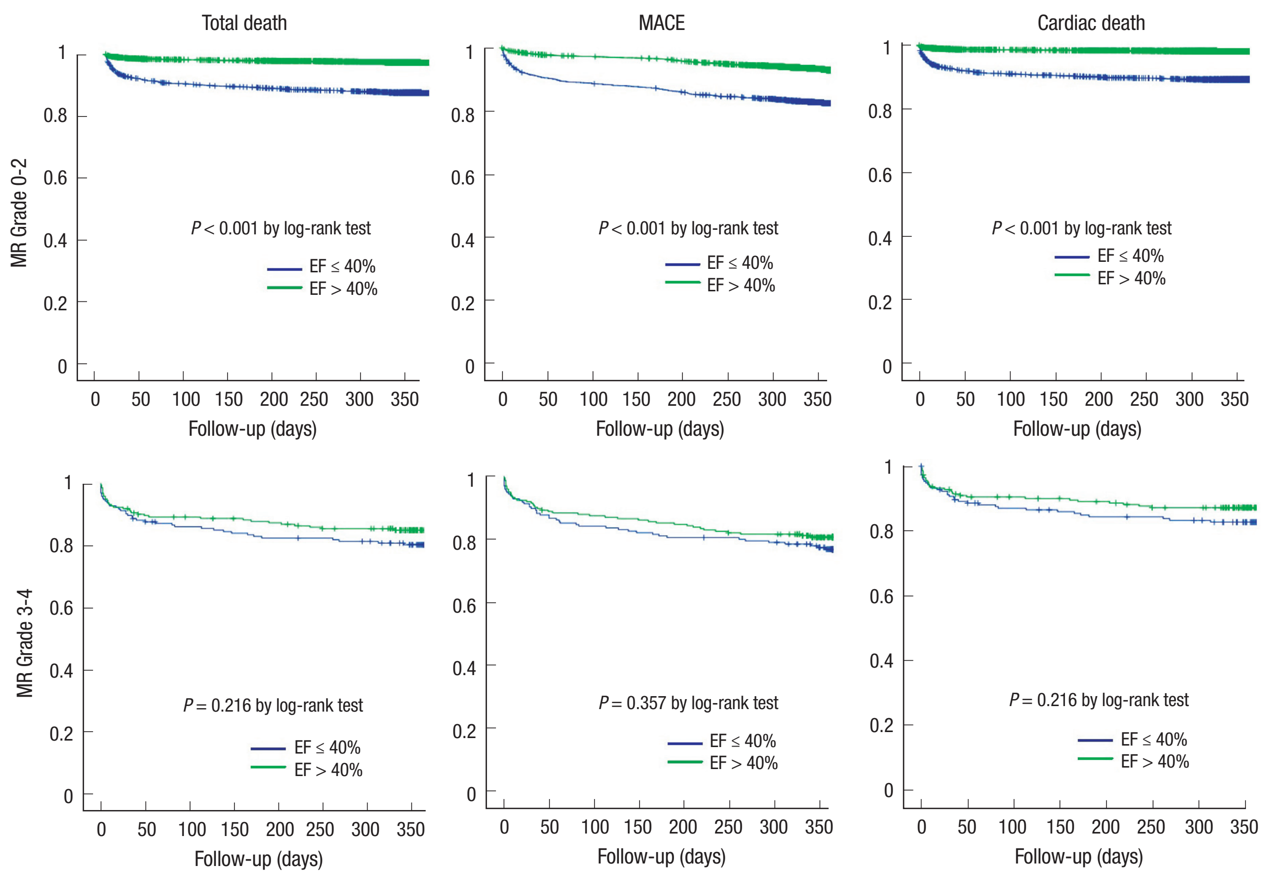

Fig. 1. Kaplan-Meier analysis of all-cause mortality, major adverse cardiac event (MACE), and cardiac death in the mitral regurgitation grades 0-2 (upper panel) and grades 3-4 (lower panel) groups of acute myocardial infarction patients. Primary endpoints were significant in the groups with mild mitral regurgitation (MR) according to ejection fraction (EF) (≤ 40% and > 40%). However, the groups with severe MR did not exhibit significant differences in all-cause mortality based on EF (≤ 40% and > 40%).

in patients with AMI. Furthermore, low LVEF was associated with high one-year mortality after AMI in patients without high-grade MR in the present study. Because the majority (97%) of the patients with AMI did not have high-grade MR. However, the prognostic value of LVEF after AMI has been questioned in several studies that could not confirm LVEF as a prognostic factor in AMI patients. Left ventricular end-diastolic volume (LVEDV) and left ventricular end-systolic volume (LVESV) were described as more meaningful prognostic factors than LVEF because a low EF might be attributed to extensive myocardial damage, LV dilatation, or a hibernating or stunned myocardium (6, 9). The present study suggests that ischemic high grade MR could be one reason for this result because LVEDV and LVESV could be increased by volume overload disease, such as ischemic MR. A previous study reported that the presence of MR was associated with an increased likelihood of adverse outcomes but not LV EF in patients with AMI with MR (11).

Ischemic MR could be caused by global LV remodeling with spherical LV enlargement or local inferior wall remodeling with predominantly posterior leaflet restriction. In case of non-ischemic MR, an increase in preload and/or a decrease in afterload will result in a falsely higher EF because the EF is load-sensitive (20). However, some have argued that the 'low impedance leak' effect might exclusively apply to acute severe MR and that the afterload is likely increased when the LV is dilated. Furthermore, the decline in EF following MVR could result from chordal transection. Whitlow et al. (21) have shown that the EF is essentially unchanged at 12 months among patients experiencing significant reductions in MR and 'reverse' remodeling using edge-to-edge clip devices without the confounding effects of CABG, sternotomy, or chordal transection.

Alternatively, a portion of the LV dysfunction in AMI patient results from afterload excess; this finding could explain why reduced LVEF has no impact on survival in patients with severe MR. Accordingly, contractile function might be better than the EF suggests because the LV is managing afterload excess.

The LVEF is derived from the LV volume. Although heart rate and fiber shortening both affect LVEF, it is influenced to a far greater extent by LVEDV given that changes in stroke volume tend to be considerably smaller than changes in LVEDV (22). In the AMI setting, LVEDV is not yet fully dilated by acute severe MR. In addition, ischemic MR might have a transiently severe grade.

LVEF is a determinant of the degree of functional ischemic mitral regurgitation in patients with systolic left ventricular dysfunction (4). However, there is only a weak correlation between LVEF and MR severity (7, 8). Recently, several small population studies have examined the role of assessing LV systolic function in addition to LVEF in ischemic MR (23, 24).

PCI was performed in a significantly lower number of patients in the group of LVEF < 40% with low grade MR as compared to the group of LVEF > 40% with low grade MR. That could contribute the difference of survival in low grade MR not high grade MR. Furthermore, PCI was an independent predictor of lower cardiac death in high grade MR (Table 4). Reperfusion therapy for patients in AMI with severe MR could be beneficial for survival.

This study was a retrospective study. There are no detailed descriptions of MR volume or effective regurgitant orifice area (ERO) due to a lack of central readings of the echocardiograms in the core laboratory. Furthermore, the etiologies of MR and the presence of non-ischemic MR were not distinguished. Long-term follow-up echocardiography data were limited. The number of patients with severe MR was considerably lower than that in the other group. Nevertheless, this study demonstrated the prognostic impact of LVEF according to the presence of severe MR in a large, real-world population.

In conclusion, MR is a predictor of poor outcome regardless of ejection infarction. LVEF is an inadequate method to evaluate contractile function of the ischemic heart in the face of high grade MR. Other new parameters for assessing LV systolic function beyond LVEF are needed in patients with significant ischemic MR.

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DISCLOSURE

The authors have no conflicts of interest to disclose.

AUTHOR CONTRIBUTION

Conception and coordination of the study: Cho JS, Jeong MH. Acquisition of data: all authors. Data review: Cho JS, Jeong MH. Statistical analysis: Cho JS, Her SH. Manuscript preparation: Cho JS, Jeong MH. Manuscript approval: all authors.

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