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Long-Term prognostic value of infarct transmurality determined by contrast-enhanced cardiac magnetic resonance after ST-segment elevation myocardial infarction

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의 학 과

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ST분절 상승 심근 경색증후 조영 증강 심장 자기 공명으로 측정한 전층 경색의 장기 예후 예측의 유용성

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배경: ST 분절 상승 심근 경색(STEMI) 환자에서 조영 증강 심장 자기 공명(CE-CMR)에 의해 평가된 최대 경색 경벽의 장기 예후 중요성은 아직 연구된 바가 없다. 이 연구의 목적은 미세혈관 폐쇄(MVO) 및 심근내출혈(IMH)과 같은 STEMI 환자의 다른 CE-CMR 예측인자에 비해 최대 경색 경벽성이 추가적인 장기 예후 가치가 있는지 확인하는 것이다.

방법과 결과: 이 연구에서는 심근 손상의 확립된 매개변수와 최대 경색 경벽성을 평가하기 위해 STEMI 후 CE-CMR 검사를 받은 112 명의 환자를 분석하였다. 모든 원인으로 인한 사망, 비치명적 재경색 및 새로운 심부전 입원을 포함하는 주요 심장 부작용(MACE)의 발생을 일차 종료

점으로 정하고 분석하였다.

MACE는 중앙값 7.9년(IQR, 5.8~9.2년)의 추적 기간 동안 10명의 환자에서 발생했다(사망 2명, 치명적이지 않은 심근 경색증 3명, 심부전 입원 5명). MACE가 있는 환자는 MACE가 없는 환자에 비해 경벽 경색, 경색 크기 > 5.4%, MVO 및 IMH의 비율이 유의하게 더 높았다. 단계적 다변수 Cox 회귀 분석에서 경색의 75% 이상으로 정의된 경색의 경벽 범위는 MVO 및 IMH에 대한 보정 후 MACE의 강력한 예측 인자였다[위험비 8.7, 95% 신뢰 구간(CI) 1.1-71; P= 0.043].

결론: 관상동맥 재개통술을 시행 받은 STEMI 환자에서 경색 후 CE-CMR 기반 최대 경색 경벽성은 강력하고 독립적인 장기 예후 인자이다. 따라서 MVO 및 IMH와 같은 CE-CMR 매개변수에 최대 경색 횡단성을 추가하면 STEMI에서 장기적인 부작용의 위험이 높은 환자를 식별할 수 있다.

Abstract

Long-Term prognostic value of infarct transmurality determined by contrast-enhanced cardiac magnetic resonance after ST-segment elevation myocardial infarction

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Background- The long-term prognostic significance of maximal infarct transmurality evaluated by contrast-enhanced cardiac magnetic resonance (CE-CMR) in ST-segment elevation myocardial infarction (STEMI) patients has yet to be determined. This study aimed to see if maximal infarct transmurality has any additional long-term prognostic value over other CE-CMR predictors in STEMI patients, such as microvascular obstruction (MVO) and intramyocardial hemorrhage (IMH).

Methods and Results- The study included 112 consecutive patients who underwent CE-CMR after STEMI to assess established parameters of myocardial injury as well as the maximal infarct transmurality. The primary clinical endpoint was the occurrence of major adverse cardiac events (MACE), which included all-cause death, non-fatal reinfarction, and new heart failure hospitalization.

The MACE occurred in 10 patients over a median follow-up of 7.9 years (IQR, 5.8

to 9.2 years) (2 deaths, 3 nonfatal MI, and 5 heart failure hospitalization). Patients with MACE had significantly higher rates of transmural infarction, infarct size > 5.4 percent, MVO, and IMH compared to patients without the MACE. In stepwise multivariable Cox regression analysis, the transmural extent of infarction defined as 75 percent or more of infarct transmurality was a strong predictor of the MACE after correction for MVO and IMH [hazard ratio 8.7, 95% confidence intervals (CIs) 1.1–71; P= 0.043].

Conclusions- In revascularized STEMI patients, post-infarction CE-CMR-based maximal infarct transmurality is a strong independent long-term prognosticator. Adding maximal infarct transmurality to CE-CMR parameters like MVO and IMH could thus identify patients at high risk of long-term adverse outcomes in STEMI.

Key words: ST-segment elevation myocardial infarction; contrast-enhanced cardiac magnetic resonance; infarct transmurality; long-term prognosticator

Introduction

Over the last several decades, advances in percutaneous coronary intervention (PCI) and medical treatment have resulted in a dramatic improvement in the outcome of patients with ST-elevation myocardial infarction (STEMI). In around half of the patients with ST-elevation myocardial infarction, despite the effective opening of the culprit artery by the primary percutaneous coronary intervention (PPCI), myocardial tissue perfusion does not improve completely (STEMI)[1, 2]. Even after surviving an acute infarction, an increasing percentage of patients are at long-term risk of sudden cardiac death or heart failure[3]. As a result, early risk stratification is recommended for all patients, and the best way to estimate prognosis following STEMI is still being researched[4].

Contrast-enhanced cardiac magnetic resonance (CE-CMR) imaging is well suited to determining structural and functional changes following STEMI because it provides great tissue characterization without exposing the patient to radiation. Several CE-CMR parameters have been shown to have prognostic significance in post-infarction patients in previous research. These include morphological changes (infarct size, area at risk [AAR], myocardial salvage index [MSI]), microvascular injury such as microvascular obstruction (MVO) and/or intramyocardial hemorrhage (IMH), and functional impairment (left ventricular ejection fraction [LVEF], myocardial strain)[5–15]. Previous CE-CMR studies in STEMI patients, on the other hand, were limited by a lack of long-term follow-up and the use of soft clinical end-points. As a result, long-term follow-up data and hard clinical end-points are hard to come by.

The transmurality of myocardial infarction can be accurately assessed using CE-

CMR[16], and the transmurality predicts improvement in contractile function[10]. However, the long-term prognostic value of transmurality has not been examined in over two decades, as far as we know.

This study aimed to see if maximal infarct transmurality has any additional long-term prognostic value in STEMI patients over other CE-CMR predictors such as microvascular obstruction (MVO) and intramyocardial hemorrhage (IMH).

Methods

Subjects

A total of 515 consecutive patients with STEMI who underwent primary percutaneous coronary intervention (PCI) between November 2010 and July 2014 were enrolled in this study. Patients were included if they were older than 18 years and had undergone primary PCI within 12 hours after symptom onset. Patients who refused to consent to undergo CE-CMR imaging or who had contraindications for CE-CMR imaging were eventually excluded; 112 patients were finally included. The Chosun University Hospital Research Ethics Committee approved the current study protocol (approval CHOSUN 2014-12-001).

Definition of STEMI

STEMI was defined as at least 1 mm ST-segment elevation in two or more standard leads, at least 2 mm in two or more nearby precordial leads, or suspected new-onset left bundle branch block.

Percutaneous coronary intervention

Before the intervention, all patients were given a dual oral antiplatelet medication (300 mg aspirin, 600 mg clopidogrel), followed by maintenance dosages of aspirin (100–200 mg daily) and clopidogrel (75 mg daily). Standard interventional techniques were used for coronary angiography and stent implantation. Glycoprotein IIb/IIIa receptor antagonists were given intravenously as needed.

The primary clinical endpoint

The primary clinical endpoint [major adverse cardiac events (MACE)] was defined as a composite of all-cause death, non-fatal reinfarction, and the occurrence of new heart failure hospitalization following hospital discharge for the index event. Each patient only contributed once to the MACE endpoint (death>reinfarction>congestive heart failure) to avoid double-counting of patients who had multiple events.

CE-CMR imaging protocol and analysis

The CE-CMR process and imaging techniques have been described in detail elsewhere[17–20], and are discussed here. Myocardial infarction and cardiac function were assessed using a comprehensive CE-CMR study. A 1.5-T MR scanner (Avanto, Siemens Medical Solutions, Erlangen, Germany) and a 3.0-T MR scanner (Magnetom Skyra, Siemens Medical Solutions, Erlangen, Germany) with dedicated cardiac surface coils were used for the examinations.

T2- and T1-weighted images were acquired as a stack of contiguous 8-mm-thick images in the cardiac short-axis view. Cine images were obtained by a fast gradient-echo sequence (steady-state free precession) in the short-axis, 2-chamber, and 4-chamber views. Short-axis images of the LV were acquired from the apex to the base to contain the entire LV volume, with the slice thickness fixed at 8 mm without gaps. Following scouting and cine imaging, stress perfusion imaging was performed. Adenosine (140 $\mu g \cdot kg^{-1} \cdot min^{-1}$) was administered for 6 minutes. Following that, a dose of 0.2 mmol/kg gadolinium-diethylene triamine pentaacetic acid (Magnevist, Bayer Schering Pharma, Berlin, Germany) was administered intravenously at a rate of 3 mL/s followed by a 20-

mL saline flush for 4 minutes under adenosine infusion. Delayed hyperenhancement and the amount of microvascular obstruction (MVO) were accessed 5 min and 15 minutes after contrast administration in 10-12 contiguous 8-mm-thick slices with no gap. The field-of-view and image matrix were 224 × 340 mm (230 × 350 mm in 3T MR) and 256 × 146 (256 × 156 in 3T MR), respectively.

All of the cardiac MR image parameters were determined at our MRI core laboratory. The LV end-diastolic volume (LVEDV), LV end-systolic volume (LVESV), and LVEF were measured. By multiplying the myocardial volume by the myocardial density (1.05 g/mL), the myocardial mass was calculated. LV mass was indexed to the body surface area. The LV infarct size and volume were calculated using delayed enhancement. The volume and the extent of MVO, defined as a late hypo-enhanced zone within the infarcted myocardium on the delayed enhancement image, were determined in the same way as the infarct volume. The myocardial AAR was defined as myocardium with signal intensity greater than two standard deviations (SDs) above the mean signal intensity of a distant normal myocardium and expressed as a percentage of LV myocardial volume. The following formula was used to determine the myocardial salvage index: myocardial salvage index = (AAR − infarct size) × 100 / AAR. By dividing the greatest hyper-enhanced thickness by the whole myocardial thickness in each segment, we calculated infarct transmurality for all segments. The transmural extent of infarction was defined as 75 percent or more of infarct transmurality[21]. A region of the hypointense core within the infarcted area with a reduction of T2-signal intensities below 20ms was designated as an IMH.

Statistical analysis

All values are expressed as means ± standard deviations (SDs), medians (interquartile ranges [IQRs]), or numbers (percentages). The chi-square (statistic) analysis was used to compare baseline characteristics between groups for non-continuous variables.

The Kaplan–Meier method was used to calculate and visualize MACE-free survival. The potential independent association between transmural infarction/infarct size/MVO/IMH/LVEF and MACE-free survival was investigated using multivariable Cox regression models. A receiver operating characteristic (ROC) curve analysis was used to categorize continuous CE-CMR variables (infarct size and LVEF) as above or below the cutoff values for predicting MACE in this model. All of the tests were two-tailed, with a significance threshold of 0.05. Statistical analysis was performed with SPSS 28.0.0.0 (IBM, Armonk, NY, USA) and MedCalc Version 20.019 (MedCalc Software Ltd, Acacialaan, Ostend, Belgium).

Results

Baseline characteristics of the cohort

Table 1 summarizes the baseline clinical and CMR parameters. The average age of the patients was 59.0 years, and 85.7 percent of them were men. More than a sixth of the patients had diabetes, and more than two-thirds were smokers. A Killip class II to IV symptom was experienced by more than half of the patients, with the majority having an anterior or inferior STEMI.

The median interval between STEMI and CMR was 41 days (IQR, 31–52 days). Mean LVEF was 49.8%, maximal mean infarct transmurality was 66%, and mean infarct size was 6.88% of LV. MVO was detected in 26 of 112 patients (23.2%), and in these subjects, the mean MVO extent was 1.1% of LV. IMH was found in 30 of the 112 patients studied (26.8 %).

Clinical follow-up

The median duration of follow-up was 7.9 years (IQR, 5.8 to 9.2 years; total range 1.1 to 10.8 years). The primary endpoint occurred in 10 patients (8.9%). Two patients experienced death (1.8%). Five patients (4.5%) were admitted to the hospital with decompensated heart failure. Three patients (2.7%) had a nonfatal myocardial infarction during follow-up, and 22 patients (19.6%) had coronary revascularization.

Clinical outcomes and cutoff values of continuous CE-CMR variables (infarct

size, area at risk, myocardial salvage index, and LVEF)

The ROC curve analysis indicated a cutoff value of 5.4% for infarct size, with 90.0% sensitivity (95% CI: 55.5–99.7) and 46.1% specificity (95% CI: 36.2–56.2) (area under the ROC curve [AUC] = 0.656, *P = 0.043*), 13.3% for the area at risk, with 70.0% sensitivity (95% CI: 34.8–93.3) and 46.1% specificity (95% CI: 36.2–56.2) (area under the ROC curve [AUC] = 0.503, *P = 0.973*), 0.55% for myocardial salvage index, with 70.0% sensitivity (95% CI: 34.8–93.3) and 59.8% specificity (95% CI: 49.6–69.4) (area under the ROC curve [AUC] = 0.645, *P = 0.095*), and 50% for EF, with 70.0% sensitivity (95% CI: 34.8–93.3) and 57.8% specificity (95% CI: 47.7–67.6) (area under the ROC curve [AUC] = 0.620, *P = 0.236*) as the best cutoff for predicting the primary endpoint.

Infarct-related CE-CMR variables according to the primary outcome

Fig. 1 shows representative CE-CMR images of reperfused STEMI patients. The MACE group had greater rates of transmural infarction (90% vs. 42%, P = 0.004), infarct size > 5.4 percent (90% vs. 54%, P = 0.028), MVO (60% vs. 20%, P = 0.004), and IMH (60% vs. 24%, P = 0.013) than the non-MACE group. LV dysfunction (EF less than 50%) was more common in the MACE group than in the non-MACE group, but the difference was statistically insignificant (70% vs. 42%, P = 0.091).

Survival analyses

According to the Kaplan-Meier curve analyses, patients with transmural infarction,

infarct size > 5.4 % of LV, MVO, and IMH had a higher risk of experiencing the primary endpoint (Fig. 2). Although patients with an EF of less than 50% were more likely than those with an EF of 50% to experience the primary endpoint, there was no statistically significant difference between the two groups.

Univariate Cox regression analysis for the primary endpoint

The occurrence of the primary outcome was strongly linked to transmural infarction (hazard ratio 11.4, 95% CI 1.4–89.9; P= 0.021), MVO (hazard ratio 5.1, 95% CI 1.4–18.1; P= 0.012), and IMH (hazard ratio 4.3, 95% CI 1.2–15.2; P= 0.024). Infarct size > 5.4 % of LV, area at risk > 13.3%, myocardial salvage index of less than 0.55%, and an EF of less than 50% were not significantly associated with the primary outcome (Table 2).

Multivariate Cox regression analysis for the primary endpoint

The significant univariate variables (transmural infarction, MVO, and IMH) were included in the multivariate logistic regression analysis. After adjusting for the other factors, the variable shown to be an independent risk factor for the primary outcome was transmural infarction (Table 2).

Incremental prognostic value of all of the transmural infarction, MVO, and IMH

Even though transmural infarction was the only independent predictor of the primary

outcome, we performed survival analysis to compare groups of triple-positive (transmural infarction with all of the presence of MVO and IMH) and non-triple-positive patients. It exhibited an additional prognostic value of all of the transmural infarction, MVO, and IMH (triple combination) for the primary endpoint (Fig. 3). In addition, among patients with transmural infarction, we separated the group into subgroups with triple-positive and non-triple-positive; the rate of long-term primary outcome was greater in the triple-positive subgroup than in the non-triple-positive subgroup (Fig. 4).

Discussion

The following are the key conclusions of our investigation: (i) After adjusting for other important CE-CMR factors (MVO and IMH), maximal transmural infarction detected by CE-CMR was a strong independent predictor of long-term MACE (all-cause death, non-fatal reinfarction, and the occurrence of new heart failure hospitalization) after STEMI; (ii) transmural infarction was more closely connected with long-term MACE than infarct size; and (iii) when transmural infarction, MVO, and IMH were used together, they provided additive prognostic information. As a result, using CE-CMR imaging to estimate infarct transmurality, MVO, and IMH may help with long-term risk classification and management for STEMI patients. To further elucidate these concepts, larger clinical investigations are required.

Long-term risk stratification following STEMI is still critical, even in the era of primary PCI. Pedersen et al.[3] found that death surpassed 7% within the first month after STEMI in a large cohort of STEMI patients treated with primary PCI. After that, mortality gradually reduced, though it remained high. The myocardial function should be determined in all patients with acute STEMI, as recommended by current guidelines[4].

Because of its unique ability to offer a thorough assessment of LV structure and function as well as quantitative multiparametric characterization of infarcted myocardium, CE-CMR has the potential to become the imaging modality of choice for investigating patients after STEMI. As a result, CMR is widely used to determine LV function, infarct size, transmurality, and microvascular injury following myocardial infarction[22–24]. However, previous CE-CMR investigations in STEMI patients have

been restricted by a lack of long-term follow-up and the use of soft clinical end-points. As a result, information on long-term follow-up and hard clinical end-points are scarce. MVO is related to severe microvascular damage[25]. Nagao et al. showed that MVO is related to a lower myocardial perfusion index, and late enhancement with or without MVO is an important predictor of perfusion status after reperfusion therapy[25]. During a median of 2.7 years, Ahn et al.[15] found that patients with a transmural necrotic segment count of more than 5 had a greater risk of MACE (cardiac mortality, recurrent MI, and heart failure hospitalization). Symons et al.[13] showed that MVO was a strong independent prognosticator of the composite of all-cause mortality and HF hospitalization after a median follow-up of 5.5 years in multicenter registry research that included more than 800 STEMI patients evaluated by CE-CMR following infarction. IMH was an independent prognostic CE-CMR predictor of MACE (all-cause death, non-fatal reinfarction, and the development of new heart failure) in revascularized STEMI patients at 12 months, according to Reinstadler et al.[5]. Our analysis now provides significant evidence that CE-CMR-derived infarct transmurality, MVO, and IMH are linked with MACE at long-term follow-up, in line with these and other publications[5–15]. Surprisingly, individuals with transmural infarction had an 11-fold higher risk of death, reinfarction, or being hospitalized for heart failure than those who did not have a transmural infarction. In addition, stepwise inclusion of the relevant dichotomized CE-CMR factors in the multivariate analysis revealed that transmural infarction had the best predictive power for predicting the long-term primary outcome, outperforming MVO and IMH.

Stone et al.[26] demonstrated that infarct size, as measured by CMR or technetium-

99m sestamibi SPECT within 1 month of primary PCI, was strongly associated with all-cause mortality and hospitalization for heart failure within 1 year in a meta-analysis of 10 studies involving over 2,600 STEMI patients. However, we discovered that infarct size was not an independent predictor of clinical outcomes, which is consistent with previous studies [13, 27–30]. There is a plausible explanation for why infarct size was not an independent predictor of clinical outcomes, even though infarct transmurality was a strong independent predictor and had a weak but significant positive correlation with infarct size ($r = 0.59$, $P < 0.0001$, data not shown). It could imply that the depth of the infarction (transmurality), rather than the overall infarct size, has a bigger impact on the long-term prognosis. As a result, infarct size appears to be underpowered in terms of predicting MACE. However, the exact pathophysiological mechanisms that relate transmurality (rather than infarct size) to poorer outcomes are unknown.

The perfusion territory of the occluded artery determines the spatial extent of the "at-risk" region after coronary artery occlusion. Necrosis begins in the subendocardium and develops in a wave-front toward the epicardium with increasing occlusion duration within the at-risk zone[31]. CE-CMR can accurately assess the transmurality of myocardial infarction[16], and the transmurality predicts improvement in contractile function[10]. However, as far as we know, the long-term prognostic utility of transmurality has not been investigated in over two decades. As a result, this is the first study to look at the long-term prognostic usefulness of myocardial infarction transmural extent measured by CE-CMR following STEMI.

Even though MVO and IMH were not independent predictors of long-term MACE following transmural infarction adjudication, the combination of MVO, IMH, and

transmural infarction had the greater predictive potential for long-term clinical outcomes. Furthermore, the triple-positive (transmural infarction with MVO and IMH) cohort showed a greater rate of long-term primary outcome than the non-triple-positive category among patients with transmural infarction. As a result of these findings, transmural infarction, MVO, and IMH may have incremental prognostic significance; patients who test positive for all three should be treated more aggressively.

Study limitations

Our study had a small sample size and was conducted in a single center. The number of observed occurrences was modest while being comparable to other studies[5, 13]. Moreover, this study refers to the retrospective analysis. As a result, the findings and conclusions are susceptible to the limitations that come with this type of research.

In comparison to other research, the time it took to get CE-CMR images was quite long (median 41days vs. 3-7 days)[5, 13, 25]. In addition, the T2-weighted image of the myocardium is an unstable image. Therefore, 40 days after MI onset may be late to determine edema. Furthermore, this may be an inappropriate time to evaluate an area at risk or salvage area for acute reperfused MI. In the same context, MVO immediately after onset may also disappear after 40 days; this may underestimate MVO. Nonetheless, in individuals with transmural infarction and non-transmural infarction, the period between infarction and CE-CMR was identical, reducing the possibility of bias.

T2* is optimal for the presence of hemorrhagic infarction; T2-weighted is less sensitive. This is a possible explanation for the outstanding prognostic value of the maximal infarct

transmurality over IMH.

Patients having contraindications to CE-CMR (e.g., unstable hemodynamics or renal insufficiency with creatinine clearance <30 ml/min) could not be included in the trial, hence this patient group is not represented in the study population.

Conclusion

At long-term follow-up, post-infarction CE-CMR-based maximal transmurality is a robust independent prognosticator in reperfused STEMI patients over and above established CE-CMR markers (MVO and IMH). As a result, adding a transmurality to MVO and IMH assessment can identify patients with the highest risk of long-term adverse outcomes in STEMI.

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Fig. 1

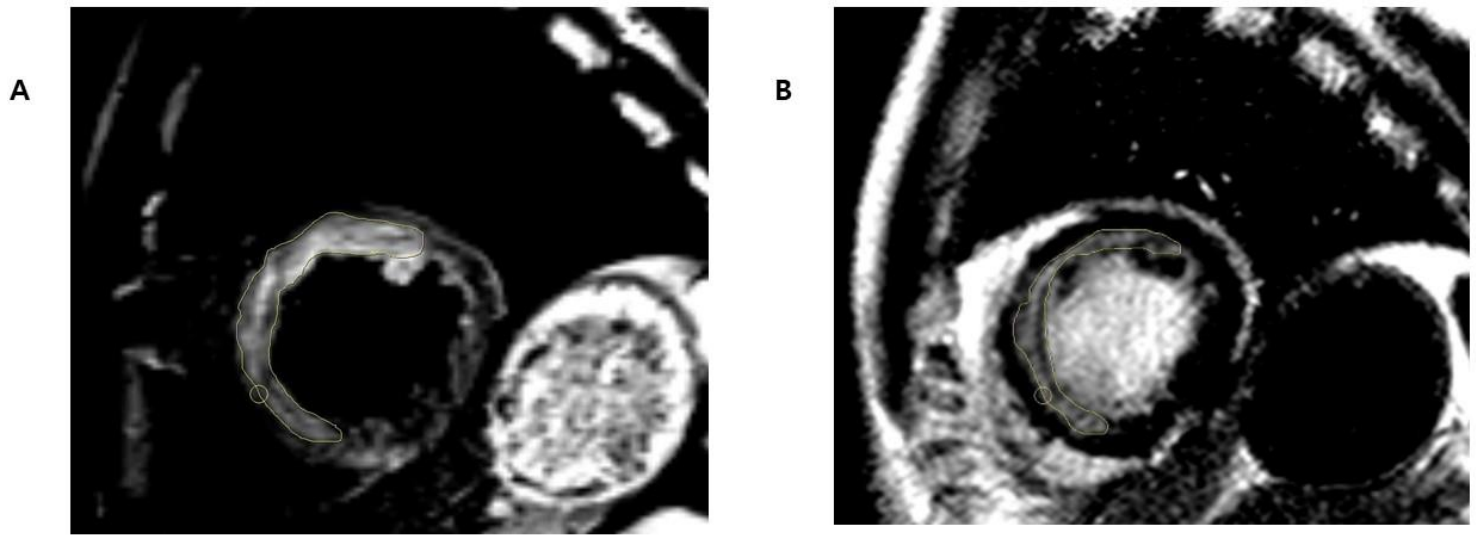

Figure 1. Short-axis contrast-enhanced magnetic resonance images. T2-weighted short-axis image showing edema **(A)** and the corresponding delayed enhancement (85% of transmurality) and microvascular obstruction (MVO) **(B)**.

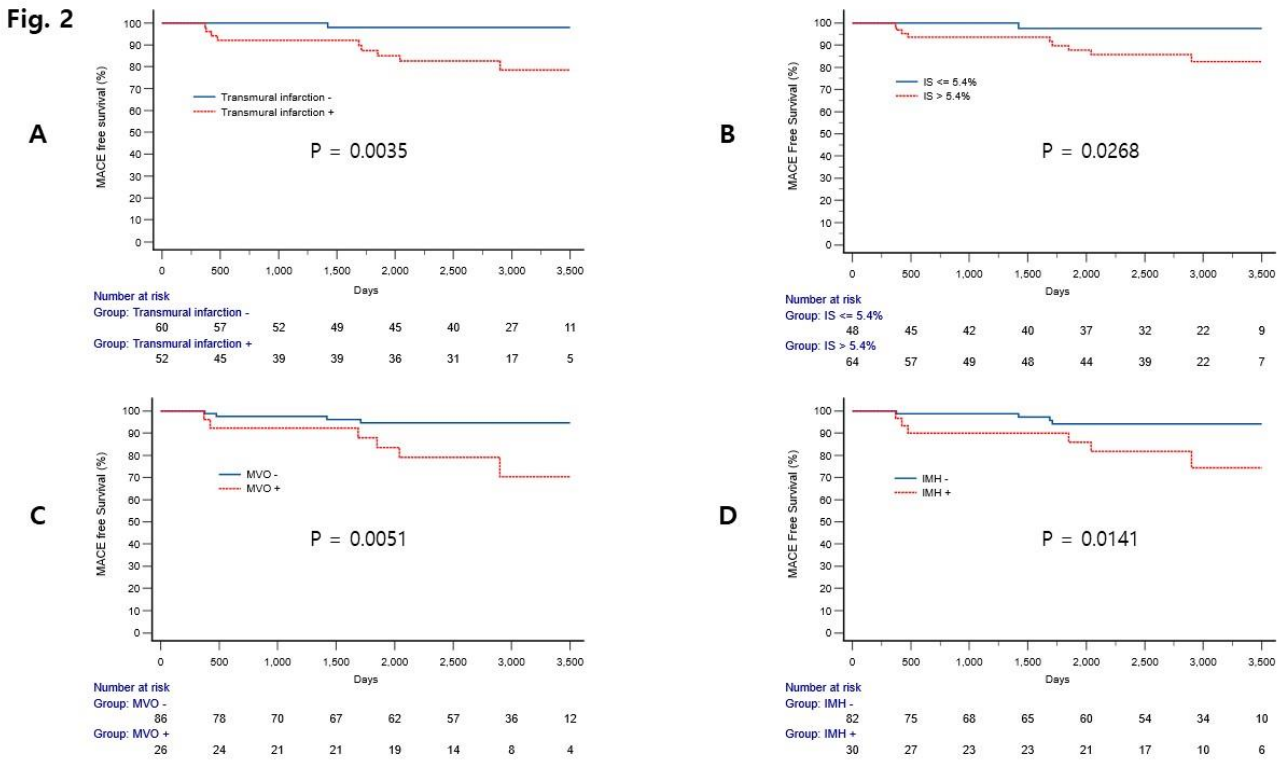

Figure 2. MACE Free Survival for the Primary Endpoint. Kaplan-Meier curves show the time-to-first event for the primary composite endpoint according to the transmural infarction **(A)**, the cutoffs of infarct size (IS) **(B)**, microvascular obstruction (MVO) **(C)**, and intramyocardial hemorrhage (IMH) **(D)**.

Fig. 3

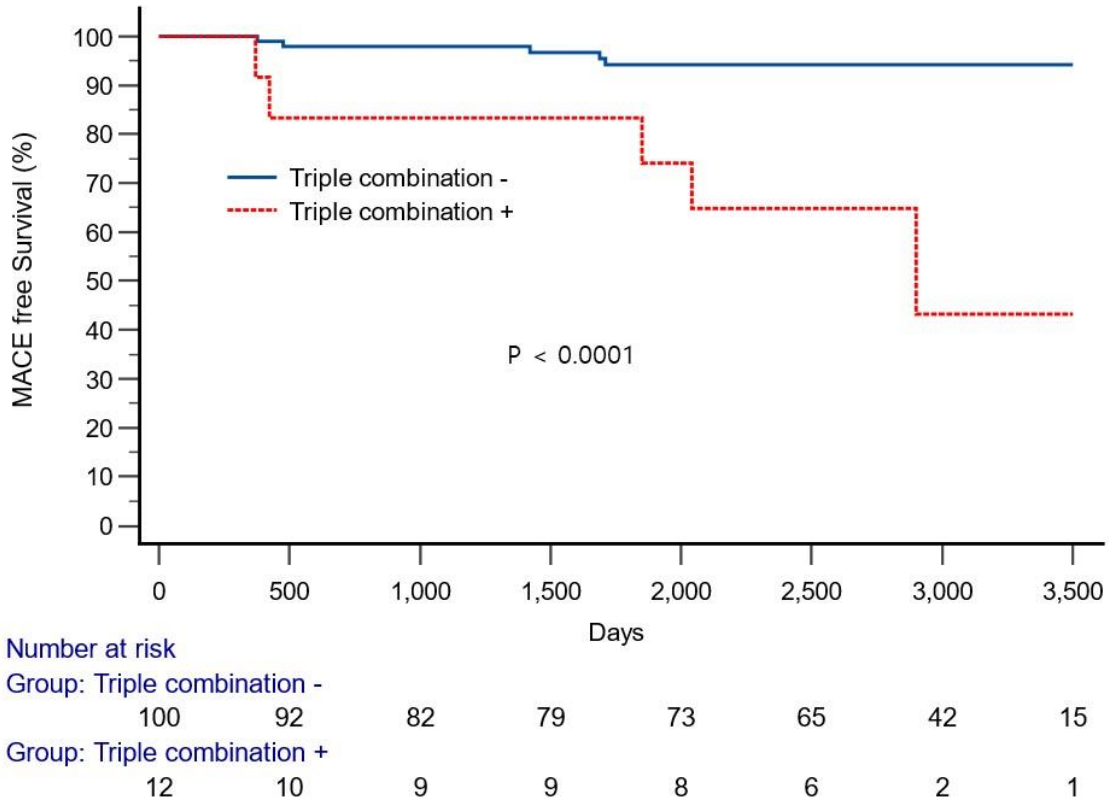

Figure 3. Impact of Outcome Predictor Combination on Long-Term Prognosis. The Kaplan-Meier curve depicts the time to the first event for the primary composite endpoint when transmural infarction, microvascular obstruction (MVO), and intramyocardial hemorrhage (IMH) are combined.

Fig. 4

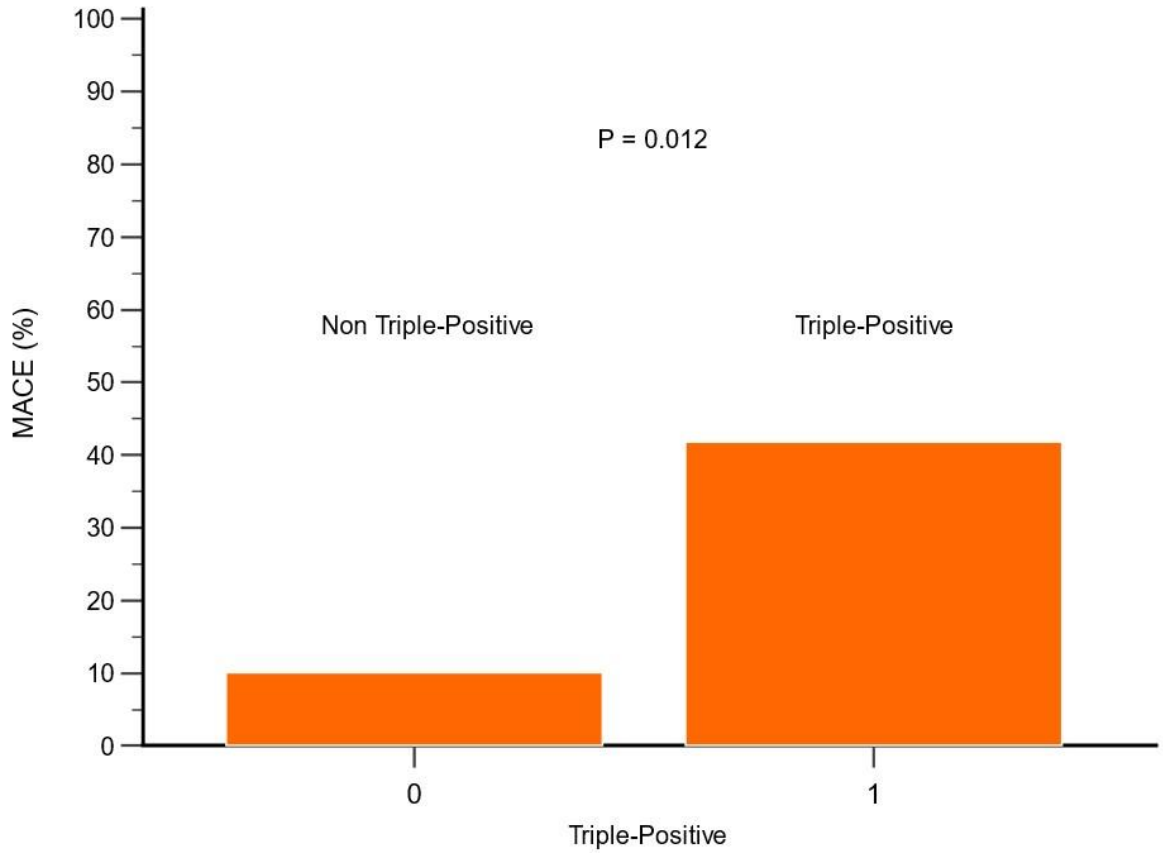

Figure 4. Primary Endpoint Event Rate. Event rate (%) of the primary endpoint according to predictor combination of transmural infarction, microvascular obstruction (MVO), and intramyocardial hemorrhage (IMH)

Table 1. Baseline characteristics

Characteristic	*Total (n=112)*	*Without MACE (n=102)*	*MACE (n=10)*	*P value*
Clinical characteristics				
Age (years)	59.0±10.4	58.6±10.1	62.9±12.8	0.217
Male sex (%)	85.7	86.3	80.0	0.588
Hypertension (%)	41.1	59.8	50.0	0.548
Diabetes mellitus (%)	17.9	17.6	20.0	0.853
Dyslipidemia (%)	11.6	11.8	10.0	0.868
Smokers (%)*	72.3	72.5	70.0	0.863
Prior PCI (%)	5.4	4.9	10.0	0.494
Killip class ≥2 (%)	51.8	51.0	60.0	0.586
Anterior infarction (%)	42.9	43.1	40.0	0.848
SBP at admission (mmHg)	126.1±24.3	125.2±24.8	135.0±17.2	0.225
Initial heart rate(beat/min)	73.5±17.1	73.4±17.4	75.0±13.5	0.388
Door-to-balloon time (min)	79.5±21.3	79.6±22.2	78.3±7.8	0.854
Symptom-to-balloon time (min)	264.9±166.7	260.0±165.7	314.9±178.6	0.322
TIMI risk score	3.5±2.3	3.5±2.3	3.8±2.0	0.669
Peak CK-MB (ng/dL)	222.1±123.5	217.7±124.1	267.0±112.5	0.230
Peak hs-cTnT (ng/mL)	6.39±3.78	6.10±3.59	9.30±4.67	0.010
Creatinine (mg/dL)	1.00±0.19	1.00±0.19	1.00±0.19	0.963

Peak hsCRP (mg/dL)	3.32±4.43	3.02±4.04	6.45±6.82	0.018
Angiographic data				
Culprit artery				
LAD (%)	42.9	43.1	40.0	0.848
LCx (%)	14.3	15.7	0.0	0.176
RCA (%)	42.9	41.2	60.0	0.251
Multivessel disease (%)	56.3	57.8	40.0	0.278
Baseline TIMI flow grade 0-1 (%)	79.5	78.4	90.0	0.387
Final TIMI flow grade 3 (%)	92.0	92.2	90.0	0.811
Angiographic no-reflow (%)	2.7	2.0	10.0	0.133
Thrombus aspiration (%)	23.2	24.5	10.0	0.300
Bare-metal stents (%)	24.1	23.5	30.0	0.648
Stent diameter at culprit artery, mm	3.13±0.59	3.11±0.60	3.35±0.46	0.216
Stent length at culprit artery, mm	31.5±18.0	30.8±17.5	38.1±22.6	0.224
Glycoprotein IIb/IIIa inhibitor (%)	57.1	58.8	40.0	0.251
CE-CMR imaging data				
LVEDV (mL)	140.1±32.9	139.5±33.1	145.6±31.6	0.581
LVESV (mL)	70.4±28.8	69.8±29.3	76.4±22.9	0.494
LV mass index (g/m^2)	89.1±16.2	88.5±15.7	97.5±19.9	0.092
LV ejection fraction (%)	49.8±9.8	50.1±9.9	46.8±9.0	0.313
Infarct size, % of LV	6.88±5.5	6.69±5.5	8.76±4.7	0.255

Area at risk, % of LV	17.4±11.1	17.4±11.2	17.0±11.1	0.896
Myocardial salvage index (%)	0.58±0.26	0.60±0.26	0.46±0.27	0.114
Frequency of IMH (%)	26.8	23.5	60.0	0.013
Frequency of MVO (%)	23.2	19.6	60.0	0.004
MVO area, % of LV**	0.24±0.55	0.21±0.53	0.58±0.62	0.041
Number of segments with transmural infarction	1.45±1.73	1.34±1.73	2.60±1.35	0.028
Maximal infarct transmurality (%)	66.0±29.0	63.9±29.3	87.7±11.9	<0.001
Frequency of transmural extent of infarction (%)	46.4	42.2	90.0	0.004

* Active smokers and ex-smokers who quit smoking less than a year before enrolling are both considered smokers.

** In patients with MVO.

PCI denotes percutaneous coronary intervention; SBP, systolic blood pressure; CK, creatine kinase; hs-cTnT, high-sensitivity cardiac troponin T; hsCRP, high sensitivity C-reactive protein; LAD, left anterior descending coronary artery; LCX, left circumflex coronary artery; RCA, right coronary artery; TIMI, thrombolysis in myocardial infarction; CE-CMR, Contrast-enhanced cardiac magnetic resonance; LV, left ventricle; LVEDV, left ventricular end-diastolic volume; LVESV, left ventricular end-systolic volume; MVO, microvascular obstruction.

Table 2. Univariate and multivariate Cox regression analyses determine the significant and independent CE-CMR predictors for the long-term MACE

Factor	Univariate OR (95% CI), *P*-value	Multivariate OR (95% CI), *P*-value
Transmural infarction	11.4 (1.44–89.9), 0.021	8.69 (1.07–70.7), 0.043
Infarct size (>5.4%)	2.45 (0.63–9.48), 0.194	
MVO	5.09 (1.43–18.1), 0.012	1.97 (0.43–8.97), 0.382
IMH	4.28 (1.21–15.2), 0.024	2.45 (0.55–11.0), 0.240
Area at riak (>13.3%)	1.95 (0.50–7.54), 0.333	
Myocardial salvage index (≤0.55%)	3.31 (0.86–12.8), 0.083	
Low LVEF (≤50%)	2.90 (0.75–11.2), 0.123	

The reference group was as follows: Infarct transmurality <75%, Infarct size (≤5.4%), no MVO, no IMH, area at risk (≤13.3%), myocardial salvage index (>0.55%), preserved LVEF (>50%). Each level of infarct size, area at risk, myocardial salvage index, and LVEF were cut-off values for the long-term MACE by ROC analysis.

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