Journal of the American College of Cardiology
© 2012 by the American College of Cardiology Foundation
Published by Elsevier Inc.

Vol. 59, No. 8, 2012
ISSN 0735-1097/$36.00
doi:10.1016/j.jacc.2011.10.890

CME

Prognostic Value of Myocardial Contrast Delayed Enhancement With 64-Slice Multidetector Computed Tomography After Acute Myocardial Infarction

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CME Editor Disclosure: *JACC* CME Editor Ajit Raisinghani, MD, FACC, reports that he has no financial relationships or interests to disclose.

Author Disclosures: All authors have reported that they have no relationships relevant to the contents of this paper to disclose.

Medium of Participation: Print (article only); online (article and quiz)

CME Term of Approval:

Issue date: February 21, 2012
Expiration date: February 20, 2013

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Manuscript received July 5, 2011; revised manuscript received October 11, 2011, accepted October 17, 2011.

Prognostic Value of Myocardial Contrast Delayed Enhancement With 64-Slice Multidetector Computed Tomography After Acute Myocardial Infarction

Objectives This study evaluated the clinical value of myocardial contrast delayed enhancement (DE) with multidetector computed tomography (MDCT) for predicting clinical outcome after acute myocardial infarction (AMI).

Background Although some studies have described the use of MDCT for assessment of myocardial viability after AMI, clinical experience remains limited.

Methods In 102 patients with first AMI, 64-slice MDCT without iodine reinjection was performed immediately following successful percutaneous coronary intervention (PCI). We measured the size of myocardial contrast DE on MDCT and compared it with clinical outcome. Primary composite cardiac events were cardiac death or hospitalization for worsening heart failure.

Results Among the 102 patients (24 ± 10 months follow-up), 19 patients experienced primary composite cardiac events (cardiac death, n = 7; heart failure, n = 12). Kaplan-Meier analysis showed higher risk of cardiac events for patients in the third tertile of myocardial contrast DE size (≥36 g) than for those in the other 2 tertiles ($p < 0.0001$). Multivariable Cox proportional hazards regression analysis indicated that myocardial contrast DE size (adjusted hazard ratio [HR] for tertile 3 vs. 1: 16.1, 95% confidence interval [CI]: 1.45 to 72.4, $p = 0.022$; HR for tertile 3 vs. 2: 5.06, 95% CI: 1.25 to 22.7, $p = 0.039$) was a significant independent predictor for cardiac events after adjustment for Thrombolysis In Myocardial Infarction risk score, left ventricular ejection fraction, total defect score on single-photon emission CT with technetium tetrofosmin, and transmural extent of myocardial contrast DE on MDCT.

Conclusions Myocardial contrast DE size on MDCT immediately after primary PCI may provide promising information for predicting clinical outcome in patients with AMI. (J Am Coll Cardiol 2012;59:730–8) © 2012 by the American College of Cardiology Foundation

Primary percutaneous coronary intervention (PCI) has improved the prognosis of patients with acute myocardial infarction (AMI) (1); however, left ventricular (LV) remodeling occurs in an appreciable proportion of patients with AMI, despite patency of and epicardial blood flow in the infarct-related artery after primary PCI. LV remodeling following AMI is a major predictor of morbidity and mortality for overt congestive heart failure and life-threatening arrhythmias (2). LV remodeling is predicted by the extent of transmurality and infarct size after AMI (3). Late gadolinium enhanced cardiac magnetic resonance imaging (MRI) is the current clinical standard for the assessment of LV infarct size (4) and the prediction of functional recovery and prognosis after AMI (5).

The recent advent of multidetector computed tomography (MDCT) has enabled the detection of AMI (6), whereas myocardial delayed enhancement (DE) on MDCT demonstrates accurate measurement of infarct size in AMI, analogous to hyperenhancement contrast-enhanced cardiac MRI in animals (7) and humans (8). A preliminary study recently showed that transmural contrast enhancement on MDCT without iodine reinjection immediately after coronary angiography for AMI correlated with nonviable myocardium (9). We also demonstrated that myocardial contrast DE patterns might be reliably useful in predicting functional recovery of the post-ischemic myocardium and LV remodeling in patients with AMI (10). Although some studies have described the use of MDCT for assessment of myocardial viability after AMI, clinical experience remains limited (11). Furthermore, whether the extent of myocardial contrast DE adds prognostic information above that of angiographic and LV functional parameters or traditional clinical risk stratification, such as the Thrombolysis In Myocardial Infarction (TIMI) risk score (12), is unclear. This study was designed to evaluate the clinical value of myocardial contrast DE with MDCT for predicting clinical outcome after AMI.

Methods

Study population. We initially assessed a prospective, consecutive series of 110 patients with first AMI for inclusion into the study from September 2006 to December 2007. AMI was defined as: 1) chest pain >30 min in duration with presentation within 12 h after onset of symptoms; 2) ST-segment elevation >0.1 mV within 2 contiguous electrocardiograph leads; and 3) elevated creatine kinase-myocardial band (CK-MB) isoenzymes within 12 h of chest pain. All patients underwent detailed assessment of medical history and a physical examination at the index hospitalization. TIMI risk score was calculated for all patients (12). Exclusion criteria were a history of previous MI or heart failure and renal insufficiency (creatinine >1.5 mg/dl). Cardiogenic shock caused death in 2 patients, 1 patient died from noncardiac death due to cancer, 3 patients refused to give their informed consent, and 2 patients were lost to follow-up. The remaining 102 patients represent the population of this study. Written informed consent was

Abbreviations and Acronyms

^{99m}Tc = technetium
AMI = acute myocardial infarction
BNP = B-type natriuretic peptide
CAG = coronary angiography
CI = confidence interval
CK-MB = creatine kinase-myocardial band
DE = delayed enhancement
ECG = electrocardiography
EDV = end-diastolic volume
ESV = end-systolic volume
HR = hazard ratio
LV = left ventricular
LVEF = left ventricular ejection fraction
MDCT = multidetector computed tomography
MRI = magnetic resonance imaging
PCI = percutaneous coronary intervention
SI = signal intensity
SPECT = single-photon emission computed tomography
TDS = total defect scores
TIMI = Thrombolysis In Myocardial Infarction

obtained from all patients, and the study protocol was approved by our institutional review board.

Coronary angiography and PCI procedure. Experienced interventional cardiologists performed coronary angiography (CAG) through the femoral approach with 6-F catheters. The culprit coronary artery was defined on the basis of electrocardiography (ECG) and CAG results. All patients underwent PCI with both aspirin and a loading dose of 300 mg clopidogrel. Glycoprotein IIb/IIIa receptor antagonist was not available for administration in Japan at the time of the study. The contrast agent used was iopamidol 370 mg I/ml (Schering AG, Berlin, Germany). Post-procedural optimal coronary flow was defined as TIMI flow grade ≥3, and incomplete reperfusion or lack of procedural success was defined as TIMI flow grade 0 to 2 (13). Myocardial blush grade was defined according to a previous method (14). Good collateral flow was defined as grade 2 or 3 (15). Time to reperfusion was defined as the period from time of onset of symptoms to time of reperfusion. All patients underwent 64-slice MDCT with no additional contrast medium administered immediately following the final angiogram of the primary PCI procedure. Total contrast volume and time from last coronary injection to initiation of the CT scan were measured. All patients underwent follow-up CAG 6 months after the initial procedure.

64-slice MDCT scanning procedure. Scanning was performed with a 64 × 0.5 mm slice collimation CT scanner (Aquilion 64, Toshiba Medical Systems Corporation, Otawara, Japan) with a gantry rotation speed of 400 ms/rotation. Scanning was performed using a tube energy of 120 kV and effective tube current of 250 mA at a table feed of 6.4 mm/gantry rotation with beam pitch of 0.2 and a radiation dose of 7.0 ± 1.0 mSv. Acquisition of CT data and an ECG trace were automatically started during a 7- to 9-s breath-hold.

Reconstruction and analysis of 64-slice MDCT images. Analysis of the scans was performed on a ZIOSTATION workstation (ZIOSOFT Inc., Tokyo, Japan). The original axial CT images and multiplanar reformations were used for analysis of the myocardium. The images used for interpretation and for quantitative analysis were reconstructed at a slice thickness of 1 mm and an increment of 1 mm in the diastolic phase (75%) of the R–R interval. When the images were blurred by motion artifacts due to high heart rate (>90 beats/min), systolic reconstructions were performed. Images were analyzed using a 17-segment model (16). Extent of hyperenhancement was judged as transmural if ≥75% of the LV wall thickness in each segment of the axial, short-axis, and long-axis multiplanar images was visually involved and subendocardial if <75%. Infarct area was defined as a hyperenhancement with signal intensity (SI) higher than 2 SD above the mean SI of remote normal myocardium (17). Infarct size was calculated on the basis of graphics displayed by SI histogram thresholding using a step-based algorithm to detect voxels within the defined SI range in the 3 dimensions and to define clusters of voxels that meet the hyperenhancement definition. Using this method, the dedicated software determined the mean SI of the hyperenhancement in HU and calculated total myocardial contrast DE size in grams (Fig. 1). The MDCT images were analyzed by 2 independent observers to calculate interobserver and intraobserver agreements in a random subset of 30 patients.

Radionuclide imaging. ECG-gated myocardial single-photon emission computed tomography (SPECT) with technetium (^{99m}Tc) tetrofosmin was performed at 1 week after admission. Imaging was performed at rest in the supine position 1 h after intravenous injection of 740 MBq ^{99m}Tc-tetrofosmin as the radiotracer using a double-detector SPECT system (PICKER PRISM 2000 XP, Shimadzu Corporation, Kyoto, Japan) equipped with a low-energy, high-resolution collimator. The radiation dose from a resting ^{99m}Tc-tetrofosmin study averages 6.7 mSv (18). Data from 72 projections were obtained with a 64 × 64 matrix over 360° and were acquired for 40 s for each projection. Total acquisition time was approximately 24 min. Images were gated at 16 frames per cardiac cycle with an R-wave trigger, and calculation of standard parameters similar to left ventricular ejection fraction (LVEF), LV end-diastolic volume (EDV), and LV end-systolic volume (ESV) were provided with commercially available software (19). SPECT images of the LV were divided into 17 segments (16), and each segment was visually scored according to 4 grades (0 = normal uptake, 1 = mildly decreased uptake, 2 = moderately decreased uptake, 3 = severely decreased uptake). Total defect scores (TDS) were calculated by summation.

Biochemical analysis. Serum CK-MB levels were analyzed by enzymatic means, and plasma B-type natriuretic peptide (BNP) concentrations were measured with a specific immunoradiometric commercial assay using a commercial kit (Shionogi Inc., Osaka, Japan). Blood samples for plasma BNP were obtained from all patients on hospital day 28 after admission.

Clinical endpoints. For the present analysis, the primary composite cardiac events were defined as cardiac death or hospitalization for worsening heart failure. Cardiac death was defined as death due to myocardial infarction, congestive heart failure, or documented sudden cardiac death. The diagnosis of congestive heart failure was made on the basis of the criteria in the Framingham Heart Study (20). Hospitaliza-

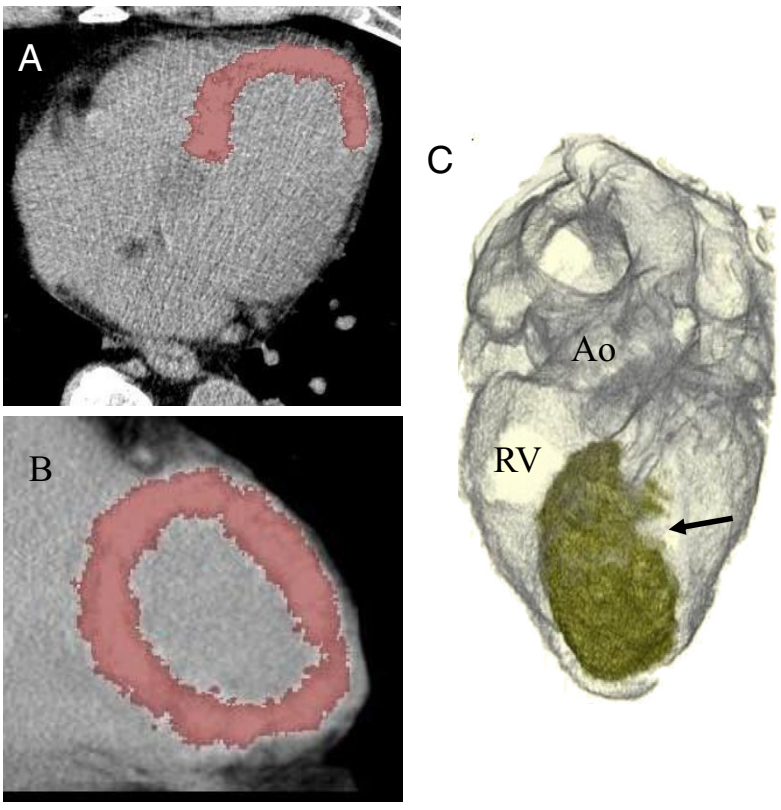

Figure 1 **Contrast DE Size Assessment by MDCT**

Multidetector computed tomography (MDCT) images show the infarct area **(red region)** defined as a hyperenhancement with a signal intensity (SI) higher than 2 SD above the mean SI of remote normal myocardium on **(A)** axial and **(B)** short-axis multiplanar reconstructions. **(C)** Infarct size was calculated using a step-based algorithm to detect voxels within the defined SI range in the 3 dimensions and to define clusters of voxels that meet the hyperenhancement definition **(green region)**. The myocardial contrast delayed enhancement (DE) size in this patient was 63.4 g **(black arrow)**. Ao = ascending aorta; RV = right ventricle.

tion for worsening heart failure was defined as evidence of pulmonary congestion on a chest radiograph and treatment with intravenous diuretic therapy during hospitalization. When ≥2 events occurred simultaneously, the most severe event was chosen (death > heart failure). After hospital discharge, all patients were followed up every month at our hospital's outpatient clinic up to a mean follow-up period of 24 ± 10 months (range 2 weeks to 34 months). Cardiac events were documented by clinical visits and standardized follow-up phone calls to the patients or their families, followed by review of medical records. The diagnosis of cardiac events was adjudicated by independent cardiologists who were blinded to the findings of CAG and CT imaging.

Statistical analysis. All data are expressed as the mean ± SD or as median (interquartile range) for non-normally distributed data. Comparisons of categorical variables between groups were performed by the chi-square test or Fisher exact test. Comparisons of continuous variables were analyzed by unpaired *t* test or Mann-Whitney *U* test according to the data distribution. Paired comparisons among three groups were analyzed by 1-way analysis of variance with the ad hoc multiple comparison method (Tukey-Kramer). Event-free survival curves for cardiac events were constructed by the Kaplan-Meier method, and statistical differences between curves were assessed by log-rank test. Multivariable Cox proportional hazards models were developed to calculate hazard ratio (HR), 95% confidence interval (CI), and Wald chi-square test value. Linear regression analyses were performed with Pearson's correlation coefficients. Interobserver and intraobserver variance was calculated as mean difference ± SD. All probability values were considered significant when <0.05.

Results

Patient characteristics. Baseline clinical characteristics of the patients are summarized in Table 1. The median time delay between last injection of contrast medium and MDCT scanning was 14 ± 2.5 min (range 8 to 18 min). Mean heart rate during scanning was 78 ± 17 beats/min (range 41 to 102 beats/min). Iodine volume injected during PCI was 196 ± 23 ml (range 158 to 244 ml). The myocardial contrast DE region of infarcted myocardium

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Table 1 Clinical Characteristics of the Study Population According to the Cardiac Events

Characteristic	All Patients (N = 102)	Events (+) (n = 19)	Events (−) (n = 83)	p Value
Age (yrs)	63 ± 10	62 ± 12	63 ± 10	0.615
Male	86 (84)	17 (89)	69 (83)	0.493
Hypertension	42 (41)	9 (47)	33 (40)	0.543
Dyslipidemia	68 (67)	14 (73)	54 (65)	0.472
Diabetes	34 (33)	6 (32)	28 (34)	0.857
Smoking	62 (61)	13 (68)	49 (59)	0.449
Time to reperfusion (h)	4.5 ± 3.0	5.4 ± 3.1	4.3 ± 2.9	0.144
Infarct location (anterior/inferior/lateral)	56/32/14	15/2/2	41/30/12	0.053
Infarct-related artery (%)				0.053
LAD	56 (57)	15 (80)	41 (49)	
RCA	32 (31)	2 (10)	30 (36)	
LCX	14 (12)	2 (10)	12 (14)	
Medications after admission				
Beta-blocker	58 (57)	14 (74)	44 (53)	0.101
ACE inhibitor/ARB	91 (89)	18 (95)	73 (88)	0.201
Calcium-channel blocker	32 (31)	3 (16)	29 (34)	0.169
Statin	90 (88)	18 (95)	72 (87)	0.456
Diuretic	34 (33)	12 (63)	22 (27)	0.006

Values are mean ± SD, n (%), or n.

ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blocker; LAD = left anterior descending; LCX = left circumflex; RCA = right coronary artery.

(189 ± 38 HU) showed significantly higher SI than did the remote myocardium (76 ± 12 HU) and LV cavity (99 ± 19 HU; $p < 0.0001$). Interobserver and intraobserver measurements of myocardial contrast DE size on MDCT were closely correlated ($r = 0.98$, $p < 0.0001$; and $r = 0.99$, $p < 0.0001$, respectively), and mean differences in myocardial contrast DE size were small (0.09 ± 0.99 g and −1.60 ± 0.71 g, respectively). All patients underwent stent implantation in the infarct-related artery (Online Fig. 1). There were 4 patients with binary restenosis (>50% stenosis) of the culprit coronary arteries at 6-month follow-up CAG.

Biomarker, angiographic, MDCT, and SPECT findings according to the cardiac events. There were no differences in the incidence of post-TIMI flow grade 3, post-myocardial blush grade 3, and recovery of ST-segment resolution between the two groups (Table 2). Peak serum CK-MB, plasma BNP levels, mean infarct size, extent of LV segments with transmurality, LVEDV, LVESV, and

Table 2 Biochemical Markers, CT, and Technetium-99m SPECT Findings According to the Cardiac Events

	All Patients (N = 102)	Events (+) (n = 19)	Events (−) (n = 83)	p Value
Peak CK-MB (IU/ml)	233 (97–437)	648 (437–765)	153 (87–311)	<0.001
BNP on day 28 (pg/ml)	101 (32–245)	277 (141–520)	73 (25–184)	<0.001
TIMI risk score	3.54 ± 2.06	4.68 ± 1.73	3.28 ± 2.05	0.007
ST-segment resolution (%)	65 ± 28	46 ± 9	68 ± 29	0.155
Angiographic characteristics (%)				
Post-TIMI flow grade 3	92 (90)	15 (79)	77 (93)	0.082
Post-myocardial blush grade 3	46 (45)	7 (37)	39 (46)	0.187
Good collateral flow	14 (13)	2 (11)	12 (14)	0.239
CT measurements				
Myocardial contrast DE size (g)	21.0 (7.31–40.9)	60.0 (35.7–63.0)	13.7 (4.75–30.9)	<0.001
Transmural extent (n)	2 (0–6)	7 (2–10)	1 (0–4)	<0.001
SPECT measurements				
LVEF (%)	49.4 ± 11.9	43.8 ± 8.5	50.7 ± 12.3	0.024
LVEDV (ml)	97.6 ± 35.4	113.0 ± 33.5	93.9 ± 34.9	0.025
LVESV (ml)	52.3 ± 28.3	66.1 ± 26.2	49.2 ± 27.9	0.018
Total defect score	15.6 ± 11.1	25.1 ± 9.7	13.3 ± 10.1	<0.001

Values are median (interquartile range [25% to 75%]), mean ± SD, or n (%).

BNP = B-type natriuretic peptide; CK-MB = creatine kinase-myocardial band; CT = computed tomography; DE = delayed enhancement; LVEDV = left ventricular end-diastolic volume; LVEF = left ventricular ejection fraction; LVESV = left ventricular end-systolic volume; SPECT = single-photon emission tomography; TIMI = Thrombolysis In Myocardial Infarction.

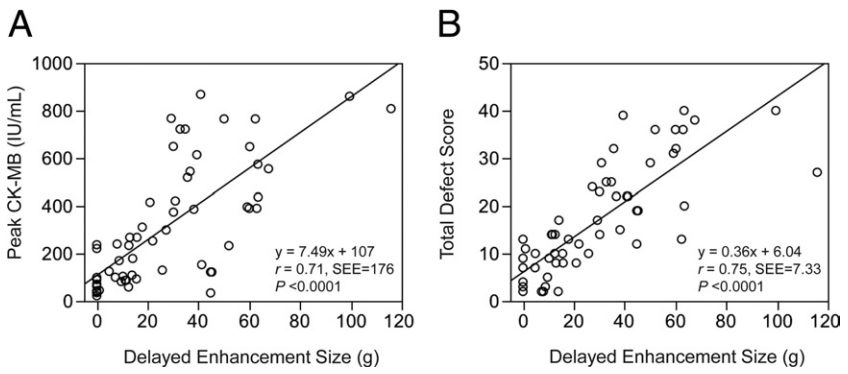

Figure 2 **Relation Between Contrast DE Size and Peak CK-MB Levels, TDS**

(A) Relation between delayed enhancement size and peak CK-MB levels (y = 7.49x + 107, r = 0.71, SEE = 176, p < 0.0001). **(B)** Relation between delayed enhancement size and total defect score (y = 0.36x + 6.04, r = 0.75, SEE = 7.33, p < 0.0001). CK-MB = creatine kinase-myocardial band; SEE = standard error of estimate; TDS = total defect scores; other abbreviations as in Figure 1.

TDS were significantly higher in patients with cardiac events than in patients without cardiac events, whereas mean LVEF was significantly lower in patients with cardiac events than in patients without cardiac events. There was a significant positive correlation between myocardial contrast DE size and peak CK-MB level (r = 0.71, p < 0.0001) and TDS (r = 0.75, p < 0.0001) (Fig. 2).

Prognostic value of myocardial contrast DE size on MDCT. Among the 102 patients, 19 patients (18.6%) had cardiac events during follow-up. Cardiac death occurred in 7 patients (6.9%), and 12 patients (11.8%) were hospitalized during follow-up because of worsening heart failure. Among the 7 cardiac deaths, 2 patients died from documented sudden cardiac death due to ventricular fibrillation, and the remaining 5 patients died from refractory heart failure. We performed a tertile analysis of DE size on MDCT and related it to cardiac event–free survival rate. On the basis of cutoff points of tertiles of DE size, the study population was divided into 3 groups: tertile 1 (n = 34), <11 g; tertile 2 (n = 34), ≥11 to <36 g; and tertile 3 (n = 34), ≥36 g. Kaplan-Meier analysis showed a higher risk of cardiac events for patients within tertile 3 than for those within the other 2 tertiles (p < 0.0001) (Fig. 3).

Univariate analysis (Table 3) indicated that TIMI risk score, LVEF, TDS, tertile of myocardial contrast DE size, and the number of LV segments showing transmural extent were significantly associated with cardiac events. Cox proportional hazards regression analysis indicated that myocardial contrast DE size (adjusted HR for tertile 3 vs. 1: 16.1, 95% CI: 1.45 to 72.4, p = 0.022; HR for tertile 3 vs. 2: 5.06, 95% CI: 1.25 to 22.7, p = 0.039) was a significant independent predictor for cardiac events after adjustment for TIMI risk score, LVEF, TDS, and the number of LV segments showing transmural extent (Table 4). A list of all patients with their cardiac events and associated TIMI risk score, LVEF, TDS, tertile of myocardial contrast DE size, and transmural extent of contrast DE are shown in Online Table 1. All patients with cardiac events had transmural infarction.

Discussion

The major important findings of the present study are as follows. First, myocardial contrast DE size was the most powerful independent predictor for cardiac events after AMI, and second, the AMI patients with larger myocardial contrast DE size were at much higher risk of cardiac events during follow-up periods. Thus, in the setting of traditional prognostic markers, determination of myocardial contrast DE size on MDCT images immediately after primary PCI may provide promising information for predicting clinical outcome in patients with AMI. Although some reports have addressed viability imaging by MDCT, this is the first report, to our knowledge, to assess its prognostic value.

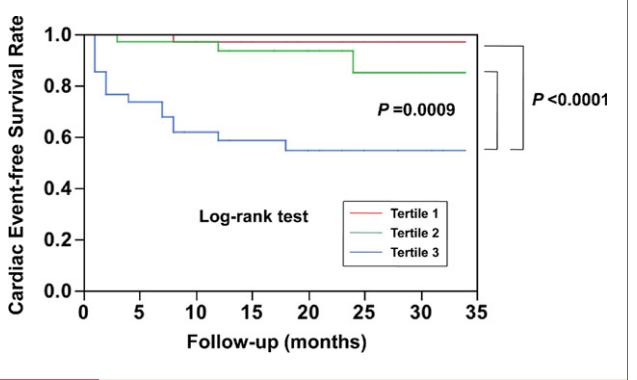

Figure 3 **Kaplan-Meier Curves for Incidence of Cardiac Events Defined by Contrast DE Size**

Kaplan-Meier curves for the incidence of cardiac events defined by tertiles of myocardial contrast delayed enhancement (DE) size. The three tertiles are based on cutoff points of delayed enhancement size. Tertile 1 (n = 34), <11 g; Tertile 2 (n = 34), ≥11 to <36 g; Tertile 3 (n = 34), ≥36 g. Tertile 1 vs. 3: p < 0.0001, Tertile 2 vs. 3: p = 0.0009 log-rank test.

Table 3 Univariate Analyses for Prediction of Cardiac Events

Factor	Hazard Ratio	95% Confidence Interval	Wald Chi-Square	p Value
TIMI risk score	1.31	1.06–1.60	6.43	0.011
Post-TIMI flow grade	0.26	0.11–1.15	4.43	0.097
SPECT measurements				
LVEF (%)	0.95	0.91–0.99	4.93	0.026
LVEDV (ml)	1.01	0.99–1.03	4.25	0.106
LVESV (ml)	1.02	0.99–1.04	4.62	0.076
Total defect score	1.08	1.04–1.12	15.60	<0.001
Extent of myocardial contrast DE size*				
Tertile 3 vs. 1	18.70	2.46–61.1	8.28	<0.001
Tertile 3 vs. 2	6.17	1.78–21.2	8.04	<0.001
Transmural extent (n)	1.22	1.10–1.35	14.10	<0.001

*Median (interquartile range [25% to 75%]): Tertile 1, 0.00 (0.00–7.49) g; Tertile 2, 21.0 (13.9–30.1) g; Tertile 3, 50.1 (40.5–62.4) g.
Abbreviations as in Table 2.

Myocardial infarct size on MDCT. Previous studies demonstrated that contrast-enhanced MDCT can identify infarcted myocardium using an intravenous contrast injection in occlusion/reperfusion animal models (7) and that 64-slice CT without iodine reinjection immediately after coronary angiography for AMI was a promising method of assessing very early viability when dobutamine echocardiography and delayed contrast-enhanced MRI were considered the reference methods (9). In addition, our previous study showing that transmural contrast DE on MDCT revealed larger infarct size and LV remodeling in the chronic phase, followed by a greater incidence of hospitalization for worsening heart failure, and indicated the clinical usefulness of myocardial contrast DE patterns (10). The highly concentrated iodinated contrast agent injected during PCI and the slow wash-in and wash-out from the damaged myocytes provide myocardial infarction enhancement without additional contrast. In the present study, myocardial DE on MDCT could be acquired with short time delay between the last injection of contrast medium and MDCT scanning because the MDCT room is next to the catheterization laboratory in our institution. This time frame is unlikely to be achieved in some hospitals. However, myocardial contrast DE could be identified as late as 40 min after contrast injection (7). Therefore, if MDCT equipment is close to the catheterization laboratory, this reliable procedure can be clinically implemented in medical center hospitals.

Evaluation of infarct size and morphology with DE-MRI has been well validated and is currently considered the clinical gold standard for viability assessment (21,22). Because of its high contrast-to-noise ratio and lack of ionizing radiation, DE-MRI is a highly attractive modality for myocardial viability imaging. The spatial resolution of MRI is quite high (1.5 to 2 mm). Although a certain partial volume effect may contribute to an overestimation of infarct size by DE-MRI, gadolinium accumulation in the interstitium in viable myocardium and concomitant edema may be seen as predominant factors (23). The excellent agreement between the area of delayed contrast enhancement on late-phase CT and DE-MRI is reported in various studies, indicating the robustness of CT for viability imaging in AMI (7,8). In addition, with its high isotropic resolution, MDCT has the potential to greatly decrease partial volume effects and accurately characterizes tissue compositions and dynamic remodeling processes, as has been demonstrated recently for the peri-infarct zone (24). In the present study, the relation between DE size and total defect score evaluated by ^{99m}Tc-tetrofosmin demonstrated quite scattered individual measurements. Some patients without DE had slightly reduced uptake of ^{99m}Tc-tetrofosmin in the infarct territories. It might be postulated that myocardial damage such as edema in cases of small infarction size is too little to enhance the myocardium. In addition, localized attenuation by overlying soft tissue or partial volume effect may create artifacts that mimic true perfusion abnormalities.

Myocardial contrast DE size as a marker of long-term clinical outcome. Most importantly in the present study, the patients with larger myocardial contrast DE size had a greater incidence of cardiac events and worse long-term prognosis than those with smaller DE size. Because we could measure

Table 4 Multivariable Cox Proportional Hazards Model for Prediction of Cardiac Events

Factor	Hazard Ratio	95% Confidence Interval	Wald Chi-Square	p Value
Extent of myocardial contrast DE size*				
Tertile 3 vs. 1	16.10	1.45–72.4	4.49	0.022
Tertile 3 vs. 2	5.06	1.25–22.7	4.26	0.039

Data were adjusted for the following variables related with cardiac events ($p < 0.05$): TIMI risk score, LVEF, total defect score, and transmural extent in Table 3. *Median (interquartile range [25% to 75%]): Tertile 1, 0.00 (0.00 to 7.49) g; Tertile 2, 21.0 (13.9 to 30.1) g; Tertile 3: 50.1 (40.5 to 62.4) g.
Abbreviations as in Table 2.

infarct size on MDCT just after primary PCI, our results suggested that myocardial contrast DE size could be an early predictive marker for future cardiac events. The number of LV segments with transmural DE (infarct size) has been shown to be a major factor for the prediction of remodeling (3), and moreover, infarct size is a prognostic predictor after AMI (25). Infarct size, anterior infarct location, perfusion status, and congestive heart failure on admission are reported to be major predictors of LV remodeling (2). In the present study, patients with larger myocardial contrast DE size had higher levels of peak CK-MB and plasma BNP, which are useful biomarkers of LV remodeling and poor clinical outcome. The 18.6% cardiac event rate of this study may appear to be slightly high compared with that of a previous study (26). The reason for this event rate may be because the patients included in the present study had higher TIMI risk scores. It is possible to show the correlation between myocardial DE size on MDCT and clinical outcome, and furthermore, it is potentially feasible to implement such a procedure clinically. Only 57% of our study population was treated with a beta-blocker after admission, which is very low in comparison with the U.S. population with AMI. It has been reported that even for patients with myocardial ischemia, calcium antagonists are preferred over beta-blockers for the treatment of angina, maybe from fear of coronary spasm, the rate of which is reported to be higher in Japanese than in Westerners (27).

Clinical implications. Contrast-enhanced MRI is well established for the assessment of myocardial viability without ionizing radiation and nephrotoxic contrast material. However, the facts that MDCT can be performed with short examination times and that it is generally available and easily performed are considered important advantages in comparison with contrast-enhanced MRI. Furthermore, myocardial contrast DE size may be a very early predictive marker for future clinical cardiac events and may add incremental prognostic value over that of classical parameters such as LVEF and TIMI risk score. Further large studies to confirm these findings in clinical examinations are needed.

Study limitations. First, radiation dose levels were high. If only end-diastolic images were used for data analysis, the use of an ECG-pulsing technique or prospective ECG triggering could have provided a significant dose reduction (28). Post-infarction DE has been successfully performed at low kV settings (80 kV), drastically reducing radiation dose and improving contrast visualization at the same time (9). Dual-energy scanning would definitely allow better assessment and eventually reduce the radiation dose (29). Second, the sample size was relatively small. The prognosis of our patients receiving primary PCI was good, and multivariate testing was limited due to the small number of endpoints. Therefore, the ability to predict cardiac events could be limited. Third, the definition of hyperenhancement was not standardized, so there was a limitation due to the use of a global classification, in particular for patients with both transmural and subendocardial hyperenhancement. We applied previously published signal density threshold algorithms to define the infarct region. However, specific optimal cutoff values for normal and infarct cores are unknown and are likely dependent on study quality. Finally, areas of microvascular obstruction could not be detected exactly with MDCT using direct acquisition of the late phase in the present study. AMI is associated with myocardial edema (23), and therefore, this might also influence the extent of myocardial contrast DE in the present study. It is possible that the prognostic value of the extent of DE on MDCT is a reflection not only of the extent of necrosis but also, at least in part, of the area at risk.

Conclusions

This study demonstrates that myocardial contrast DE size on MDCT images obtained immediately after primary PCI may provide promising information for predicting clinical outcome in patients with AMI.

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Key Words: acute myocardial infarction ■ multidetector computed tomography ■ myocardial contrast delayed enhancement ■ prognosis.

APPENDIX

For clinical characteristics of patients with cardiac events and an example of a transmural anteroseptal acute myocardial infarction, please see the online version of this article.