**Cardiac Magnetic Resonance**

# Infarct Morphology Identifies Patients With Substrate for Sustained Ventricular Tachycardia

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| **OBJECTIVES** | We sought to evaluate whether infarct size characterization by cardiac magnetic resonance imaging (MRI) is a better predictor of inducible ventricular tachycardia (VT) than left ventricular ejection fraction (LVEF). |
| **BACKGROUND** | Inducibility of VT at electrophysiologic study (EPS) and low LVEF can identify patients with a substrate for VT. Magnetic resonance imaging has been shown to identify, with high precision, areas of myocardial infarction and may therefore be a better tool to evaluate for a substrate for VT. |
| **METHODS** | We studied 48 patients with known coronary artery disease who were referred for EPS using cine and gadolinium-enhanced MRI. Wall motion and infarct characteristics were determined blindly and compared among patients with no inducible ventricular arrhythmias (n = 21), those with inducible monomorphic VT (MVT, n = 18), and those with either inducible polymorphic VT or ventricular fibrillation (n = 9). |
| **RESULTS** | Patients with MVT had larger infarcts than patients who did not have inducible arrhythmias (mass: $49 \pm 5$ g [SE] vs. $28 \pm 5$ g, $p < 0.005$; surface area: $172 \pm 15$ cm$^2$ vs. $93 \pm 14$ cm$^2$, $p < 0.0005$). Patients with polymorphic VT/fibrillation had intermediate values (mass: $36 \pm 7$ g; surface area: $115 \pm 22$ cm$^2$). Ejection fraction was inversely related to infarct mass and surface area, with $R^2$ values ranging from 0.21 to 0.27. Logistic regression and receiver-operating characteristic analysis demonstrated that infarct mass and surface area were better predictors of inducibility of MVT than LVEF. |
| **CONCLUSIONS** | Infarct surface area and mass, as measured by cardiac MRI, are better identifiers of patients who have a substrate for MVT than LVEF. Further evaluation of infarct size characterization by cardiac MRI as a predictor of sudden cardiac death is warranted.   (J Am Coll Cardiol 2005;45:1104–8) © 2005 by the American College of Cardiology Foundation |

Sudden cardiac death in patients with coronary artery disease (CAD) is predominantly caused by ventricular tachycardia (VT)/ventricular fibrillation (VF). Patients with a low left ventricular ejection fraction (LVEF) and inducible VT during electrophysiologic study (EPS) are at risk of sudden death and may benefit from implantable cardioverter-defibrillator (ICD) therapy (1–3). Low LVEF and VT inducibility identify a substrate for VT. Ventricular tachycardia occurs more commonly in the setting of larger infarcts (4–7), and LVEF is inversely related to infarct size (8–11). Furthermore, EPS directly establishes the presence of a substrate by the actual induction of VT. To date, there is only indirect information relating infarct size or morphology to the presence of a substrate for VT in humans. Contrast-enhanced magnetic resonance imaging (ceMRI) with a gadolinium-based contrast agent has been shown to identify, with high precision, areas of myocardial infarction in both animals (12,13) and humans (14–16). We hypoth-esized that infarct size and/or morphology detected by ceMRI is a better predictor of EPS inducibility of VT than LVEF.

## METHODS

Forty-eight patients with CAD referred for EPS to assess for inducibility of VT were enrolled in accordance with the policies of the Institutional Review Board. Patients underwent MRI scanning within $32 \pm 6$ days of EPS. Patients were placed supine in a 1.5-T Magnetom Sonata scanner (Siemens, Medical Solutions, Malvern, Pennsylvania); fiberoptic electrocardiographic (ECG) leads were placed for scanner gating and a phased-array receiver coil was placed on the chest for imaging. All images were acquired using 10- to 15-s breath-holds. Short-axis slices were acquired from the base to apex, making sure to include the entire left ventricle using methods previously described (16,17). A gadolinium-based contrast agent (0.1 to 0.2 mmol/kg, Magnevist, Berlex Pharmaceuticals, Wayne, New Jersey) was administered intravenously, and images were obtained as described previously (15).

Image data sets were scored by reviewers blinded to the EPS results. All images were reviewed off-line and arranged from base to apex using National Institutes of Health

Abbreviations and Acronyms
CAD   = coronary artery disease
ceMRI = contrast-enhanced magnetic resonance imaging
EPS   = electrophysiologic study
LVEF  = left ventricular ejection fraction
MRI   = magnetic resonance imaging
MVT   = monomorphic ventricular tachycardia
PVT   = polymorphic ventricular tachycardia
ROC   = receiver-operating characteristic
VF    = ventricular fibrillation
VT    = ventricular tachycardia

(NIH) Image Software. The presence of a ventricular aneurysm and segmental wall motion abnormalities was noted. Endocardial and epicardial borders of the myocardium were manually planimetered on the short-axis cine images for each patient. Volumes were derived by summation of the pixel areas, followed by multiplication of in-plane resolution and the effective slice thickness. The LVEF was computed as:

$$\frac{\text{end-diastolic volume} - \text{end-systolic volume}}{\text{end-diastolic volume}}$$

Left ventricular mass was determined by subtracting endocardial volume from epicardial volume at end diastole and multiplying by a density of 1.05 g/ml [18]. Infarct morphology was evaluated using the ceMRI images. The presence of myocardial infarction, its location, and the degree of transmurality were agreed upon by two observers. To measure infarct mass and surface area, the infarct region was outlined according to whether the image intensity was $\geq 2$ SD that of a remote region in the same slice. From the contours, a pixel value was computed for the area and surface of each individual infarct territory. Based on the pixel values, the image resolution and slice thickness, and an assumed density of 1.05 g/ml, the pixel values were converted into actual cardiac masses and surface areas. Infarct surface area and infarct mass (absolute and percent left ventricular mass) were calculated. The surface area to volume ratio was calculated as an index of complex infarct morphology.

Electrophysiologic study was performed using standard techniques. Programmed ventricular stimulation was performed using up to three extrastimuli at two right ventricular sites during two drive-cycle lengths. Study end points were either induction of sustained VT or completion of the study protocol. Results were classified as: 1) inducible, sustained monomorphic VT (MVT); 2) inducible polymorphic VT (PVT, >15 complexes), VF, or ventricular flutter; or 3) no inducible VT/VF. Induction of MVT is highly reproducible [19,20] and typically identifies the presence of a fixed substrate for reentry [20]. In contrast, induction of PVT/VF may be nonspecific due to aggressive stimulation; these arrhythmias can be induced in patients with normal hearts and normal QT intervals [21–24]. Yet, PVT/VF is commonly induced in survivors of cardiac arrest [22,25].

Thus, in order to evaluate the utility of infarct characteristics identified by MRI to identify patients with a substrate for VT, the main analysis of this report focuses on patients with inducible MVT versus those without inducible VT/VF.

Data are presented as the mean value $\pm$ SE. Linear and logistic regression analysis, analysis of variance, contingency analysis, and the *t* test or Fisher exact test were used as appropriate. The receiver-operating characteristic (ROC) curves were generated and compared for prediction of inducibility according to the method described by Metz [26]. A p value <0.05 was regarded as statistically significant.

## RESULTS

Clinical and MRI characteristics of the study population are summarized in Table 1. Sustained MVT was induced with one (n = 1), two (n = 10), or three (n = 7) extrastimuli in 18 patients (cycle length 270 $\pm$ 11 ms), whereas PVT/VF was induced with three extrastimuli in all nine subjects. The three patients without evidence of hyperenhancement on ceMRI had LVEFs of 44% to 62%; all had CAD by angiography and had EPS for near syncope or risk stratification for nonsustained VT. Infarct mass, absolute (49 $\pm$ 5 g vs. 28 $\pm$ 5 g, p < 0.005) and as percent left ventricular mass (26 $\pm$ 3% vs. 14 $\pm$ 3%, p < 0.004), and surface area (172 $\pm$ 15 cm$^2$ vs. 93 $\pm$ 14 cm$^2$, p < 0.0005) were larger in patients with inducible MVT than in those without inducible VT/VF. The LVEF was lower in patients with inducible MVT versus those without inducible ventricular arrhythmias, but this difference was not statistically significant (28 $\pm$ 2% vs. 35 $\pm$ 3%, p < 0.08). In general, values for the MRI findings in patients with PVT/VF were intermediate between those noted in patients with inducible MVT and patients without inducible ventricular arrhythmias; there were no significant differences between the patients with inducible PVT/VF and those without VT/VF. Significant differences between the patients with PVT/VF and the patients with inducible MVT were noted only for infarct surface area (p < 0.04) and the number of disconnected areas of infarction (p < 0.02). When patients taking amiodarone were excluded from the analysis, the qualitative findings remained unchanged.

Figure 1 shows the relationship between infarct size parameters and LVEF. Although infarct size correlates negatively with LVEF, the strength of the correlation is weak, with $R^2$ values from 0.21 to 0.27. Of note, the distribution of patients with inducible MVT tends to cluster above the regression line, whereas those without inducible VT/VF tend to cluster below the line, consistent with the notion that LVEF may "overstate" infarct size in patients without inducible MVT, and vice versa.

Logistic regression revealed that infarct surface area and infarct mass were significant predictors of inducible VT, whereas LVEF was not. The logistic regression models revealed chi-square and p values of 6.6 and <0.01 for infarct surface area, 0.3 and <0.6 for LVEF, 5.2 and <0.02 for infarct