Risk stratification of patients with prior myocardial infarction and advanced left ventricular dysfunction by gated myocardial perfusion SPECT imaging

Itsuro Morishima, MD, Takahito Sone, MD, Hideyuki Tsuboi, MD, Hiroaki Mukawa, MD, Michitaka Uesugi, MD, Shuji Morikawa, MD, Kensuke Takagi, MD, Toru Niwa, MD, Yasuhiro Morita, MD, Ryuichiro Murakami, MD, Yasushi Numaguchi, MD, Toyoaki Murohara, MD, and Kenji Okumura, MD

Background. The Multicenter Automatic Defibrillator Implantation Trial II (MADIT-II) has shown that the prophylactic implantable cardiac defibrillator improves the survival rate of patients with prior myocardial infarction and advanced left ventricular (LV) dysfunction. However, a more accurate noninvasive predictor should be found to identify subgroups at high risk, one that would allow implantable cardiac defibrillator therapy to be directed specifically to the patients who would benefit most.

Methods and Results. To elucidate whether technetium 99m tetrofosmin electrocardiogram-gated single photon emission computed tomography (SPECT) imaging at rest can determine the risk of arrhythmic death, 106 patients who met the MADIT-II criteria (LV ejection fraction < 0.3, myocardial infarction >1 month earlier, and no sustained ventricular tachyarrhythmia) were recruited from a pool of 4628 consecutive patients who had undergone resting Tc-99m tetrofosmin SPECT imaging. By use of the endpoints of lethal arrhythmic events, which included documentation of sustained ventricular tachycardia, ventricular fibrillation, or diagnosis of sudden cardiac death, we performed follow-up for a mean of 30 months. Lethal arrhythmic events occurred in 14 patients. Patients with lethal arrhythmic events had a lower LV ejection fraction, greater LV end-systolic and end-diastolic volume indices, and a greater perfusion defect volume than the remaining patients. By receiver operating characteristic curve analysis, myocardial defect volume was the strongest predictor for the development of lethal arrhythmic events.

Conclusion. Our results confirm that perfusion defect volume by Tc-99m tetrofosmin scintigraphy is the most pivotal predictor of the future occurrence of lethal arrhythmic events and of sudden cardiac death. Tc-99m tetrofosmin SPECT images may assist in identifying subsets of patients with a greater likelihood of arrhythmic death among patients with LV dysfunction. (J Nucl Cardiol 2008;15:631-7.)

Key Words: Ventricular tachyarrhythmia • myocardial perfusion single photon emission computed tomography imaging • defect volume • MADIT-II

Both the Multicenter Automatic Defibrillator Implantation Trial II (MADIT-II) and the Sudden Cardiac Death in Heart Failure Trial (SCD-HeFT) have established a survival benefit for implantable cardiac defibrillator (ICD) prophylaxis in patients with left ventricular (LV) dysfunction. As a result, prophylactic ICD therapy is recommended for patients with prior myocardial infarction (MI) and an LV ejection fraction of 0.30 or less. However, the absolute risk reduction in these 2 large studies was not large: SCD-HeFT found a 7.2% reduction at 5 years of follow-up, and MADIT-II showed a 5.6% reduction over a mean follow-up of 20 months, indicating that approximately 14 to 18 ICDs must be implanted to save 1 life. In addition, such criteria for
ICD therapy will lead to a marked rise in ICD implantation and their utility is uncertain from the view of cost-effectiveness. This modest benefit must be balanced against the risk of ICD-related adverse events and the impact of an ICD on quality of life. In general, sudden cardiac death was observed frequently in patients with increasing severity of heart failure, but its occurrence is generally unpredictable and its onset seems random. The proportion of sudden deaths among all deaths is higher in patients with mild heart failure than in those with advanced-stage cardiac failure, suggesting that factors other than the severity of heart failure must contribute to sudden cardiac death. Ordinarily, sudden cardiac death is caused by the onset of a rapid monomorphic ventricular tachycardia (VT) that results in ventricular fibrillation. Because scar tissue resulting from MI is linked to the VT reentry circuit, it is expected that the evaluation of scar tissue may become a useful predictor of sudden cardiac death in the chronic stage of MI. Therefore we tested the hypothesis that scar tissue, as evaluated by perfusion scintigraphy, can aid in the prediction of lethal arrhythmic events. In this study we performed a retrospective analysis of patients who were recruited in accordance with MADIT-II criteria from a pool of consecutive patients who underwent technetium 99m tetrofosmin myocardial perfusion single photon emission computed tomography (SPECT) during a period of 6 years. We analyzed the patients who had lethal arrhythmic events or in whom sudden cardiac death occurred, who should have received ICD therapy for mortality reduction, in comparison to the remaining patients to more accurately stratify individuals according to their risk of lethal arrhythmic events.

METHODS

Patient Population

Of 4628 consecutive patients who underwent Tc-99m tetrofosmin myocardial perfusion SPECT at rest at Ogaki Municipal Hospital, Ogaki, Japan, between January 1999 and December 2004, 106 patients who met the MADIT-II criteria were admitted to the study. The criteria for inclusion were as follows: (1) an LV ejection fraction determined by quantitative gated SPECT (QGS) of 0.3 or less, (2) an MI that had occurred more than 1 month earlier, (3) no revascularization therapy within the preceding 3 months, (4) New York Heart Association (NYHA) functional class of III or less, and (5) no previous history of sustained VT or ventricular fibrillation. The local medical ethics committee approved the study, which was also carried out in accordance with the Declaration of Helsinki.

Gated Myocardial Perfusion Imaging

Of the patients, 90 underwent stress imaging as a routine follow-up assessment of ischemia after coronary revascularization therapies (n = 52) or as an evaluation of ischemia contribution to their LV systolic dysfunction (n = 38). The other 16 patients underwent only rest examination to evaluate infarct size and LV volume. The LV volumes, LV ejection fraction, and perfusion defect volumes were calculated by use of the QGS/quantitative perfusion SPECT (QPS) program. The patients were injected with 925 MBq Tc-99m tetrofosmin while at rest. The SPECT images were acquired with a dual-headed angular rotating gamma camera system (Vertex; ADAC Laboratories, Milpitas, Calif.) equipped with a low-energy general-purpose collimator. The SPECT image acquisition parameters were as follows: 180 (30 steps, 6 per step), 128 × 128 matrix, and 20% main window centered at a photopeak energy of Tc-99m (140 keV). We used 16 individual electrocardiogram (ECG)–gated frames per cardiac cycle (50 seconds per step) during each projection. The images were reconstructed by use of filtered backprojection with Butterworth filtering (cutoff, 0.32 cycles per pixel; order, 10). The LV volumes and LV ejection fraction were measured by the QGS program, and the images were analyzed by the QPS program to determine the defect volume, which reflects the infarct size as well as the lung-heart uptake ratio, an indirect index of pulmonary congestion.

Signal-Averaged ECG

Ventricular late potential (LP) was analyzed by a signal-averaged ECG system (model VCM3000; Fukuda Denshi, Tokyo, Japan). The analysis was based on the quantitative time-domain measurements of the filtered vector magnitude of the orthogonal Frank X, Y, and Z leads. The QRS complexes (200 beats) were amplified, digitized, averaged, and filtered with a high-pass filter (40 Hz). Three parameters were assessed via a computer algorithm: (1) the filtered QRS duration (f-QRS), (2) the root-mean-square voltage of the terminal at 40 milliseconds of the filtered QRS (RMS40), and (3) the duration of signals at less than 40 µV in the terminal-filtered QRS (LAS40). LP was considered to be present when at least 2 of the 3 following criteria were met: (1) f-QRS greater than 130 milliseconds, (2) RMS40 less than 15, and (3) LAS40 greater than 40.

Follow-Up and Endpoints

The patients’ clinical courses were followed up retrospectively until June 2005, by which time all patients had completed the minimal follow-up period of 6 months since the date on which the myocardial perfusion images were obtained. Data were obtained primarily from hospital charts and were supplemented by the patient’s general physician as well as by a telephone interview with the patient or with one of his or her immediate relatives. No patient was lost to follow-up. The primary endpoints were lethal arrhythmic events, which included documentation of sustained VT, ventricular fibrillation, or diagnosis of sudden cardiac death.