incidence of a reperfusion injury was markedly reduced in the carperitide group (25.9% reduction; p=0.019). In terms of outcomes, carpertide-treated patients had a 73.3% reduction in risk of cardiac death or re-hospitalization for heart failure (HR=0.267; 95% CI [0.089-0.800]; p=0.011).

The nicorandil study randomized 545 patients, 276 to nicorandil and 269 to placebo. Patients were followed for an average of 2.5 years. Nicorandil did not demonstrate an effect on CK AUC, LVEF, or reperfusion injury, although it had a modest decrease in cardiac death and heart failure outcomes (HR=0.779; 95% CI [0.307-1.973]; p=0.597). Nicorandil oral therapy fared better. A subsequent analysis of nicorandil oral administration the chronic phase had positive effects on LVEF (p=0.034) and inhibited new lesions in non-culprit coronary arteries (p=0.010).

"These results will change the strategy of the acute phase treatment of heart attack", predicted Dr. Kitakaze. Larger prospective randomized trials are needed to confirm these promising results.

The Alternans Before Cardioverter Defibrillator (ABCD) Trial

The Alternans Before Cardioverter Defibrillator (ABCD) Trial sought to determine if this non-invasive test could help predict the risk of sudden cardiac death (SCD) and thereby direct the therapy of implanted cardiac defibrillators (ICD) as good as, or better than current methods. Electrophysiology study (EP) is the prevailing method and involves threading a catheter through a patient's veins into the heart to induce an arrhythmia with an electric shock. This invasive technique requires a high degree of skill, which limits its availability, and exposes the patient to a certain degree of procedural risk. The Microvolt T-Wave Alternans (MTWA) Test™, however, involves only the topical placement of electrocardiogram sensors on the chest.

"The ABCD trial is the first to use MTWA to guide implantation of defibrillators," said David Rosenbaum, MD, Professor of Medicine at Case Western Reserve University in Cleveland and lead author on the study.

The trial was initiated in May 2001 and enrolled 566 patients with ischemic cardiomyopathy from 43 centers in the United States, Germany and Israel. Participants were 18 years of age and older, had no prior arrhythmias and left ventricle injection fractions (LVEF) ≤40. Patients were placed into one of two groups according to initial test results. If either the EPS or MTWA test was positive, patients received an ICD; if both tests were negative, an ICD was optional but encouraged. Seventy percent of this later group chose to receive the defibrillator; 88% of the total population therefore received ICDs. The median follow-up time was 1.9 years with events adjudicated by an independent committee who were blinded to the screening methodology.

At one year, both EPS and MTWA strategies had similar positive and negative predictive values. The event rates for patients that had an indication for an ICD according to both tests were higher (12.6%) than those with negative predictor values (2.3%; p=0.017). Negative predictive values of both methods combined was better than that of either method alone.

"Another finding of the ABCD trial…is that risk stratification can improve the therapeutic efficacy of ICD implantation to a far greater extent than increases in risk. And, of course the appropriate level of acceptable risk must be individualized to specific patients," said Dr. Rosenbaum. For example, 95% of patients who have an indication for ICD implantation by LVEF alone do not experience an event (representing therapeutic

inefficiency), whereas only 65% of patients with an indication for a device by MTWA are event free. The therapeutic risk of each of these indicators (untreated patients who experience an event) increases only from 0% to 1.5%.

Finally, the predictive values of these tests appear to depend on timing. The EP study was not predictive until nine months or more and remained predictive for two years, whereas the MTWA test was predictive as early as 6 months, but lost its predictive value after 12 months. These findings suggest that periodic screening, combined with more than one risk test may be appropriate.

Myoblast Autologous Grafting in Ischemic Cardiomyopathy (MAGIC) Trial

The Myoblast Autologous Grafting in Ischemic Cardiomyopathy (MAGIC) Trial examined the safety and efficacy of autologous skeletal myoblast cell therapy for improving local or global cardiac contractility in patients with ischemic heart failure. This is the first multi-center, randomized, double blind and placebo controlled trial of skeletal myoblast implantation and one that is designed with the power sufficient to determine whether autologous grafting is a viable solution for ischemic cardiomyopathy.

Patients were randomized to three parallel groups: 33 patients received a low dose of smooth muscle cells (SMC; 400 ± 100 x 10^6 cells), 33 patients received a high dose of SMC (800 ± 100 x 10^6 cells), and 34 patients received placebo consisting of suspension medium alone. All but eight patients had concomitant coronary artery bypass grafting (CABG) in non-cell transplanted segments. According to lead investigator Philippe Menasché, MD, Hôpital Bichat, Paris, it is important to note that "in almost all cases, cells were placed where the heart muscle was not previously revascularized."

The study failed to reach its primary endpoint of improving the contractility of the heart (left ventricle ejection fraction, or LVEF, as measured by echocardiography). The pre-specified secondary endpoint of decreasing left ventricular dilation, however, reached statistical significance at six months. In the placebo or low dose group there was no change, but there was a major decrease in dilation in the high dose group (p=0.006). In half of the patients, LVEF was measured by radionuclide angiography, and in this cohort of patients the increase in ejection fraction was statistically significant (3%) in the high dose group (p=0.04).

Due to concerns that skeletal myoblasts may be proarrythmogenic, as they fail to integrate electro-mechanically to the surrounding myocardium, defibrillators were implanted in all patients prior to hospital discharge. These devices were used to determine time to first ventricular arrhythmia, which was deemed not significantly different between the three groups at 6 months.

"I can tell you that now half of the patients have completed one year of the study and there is still no difference in ventricular arrhythmias between the groups," commented Dr. Menasché, when emphasizing the safety of the procedure.

"While there was absence of significant improvement of regional and or global contractility measured by echocardiography, there is possible evidence for reversal of adverse remodeling," concluded Dr. Menasché. He also emphasized that long-term follow up results are often more important than interim results and the discovery of long-term benefit may lie ahead.