

MASTER Trial Top-line Results Presented at American Heart Association Meeting

Microvolt T-Wave Alternans found to be predictive of total

mortality but not of ICD discharge

Dr. Theodore Chow today will present the results of the MASTER trial sponsored by Medtronic, Inc. The MASTER trial analyzed the results from 575 patients with left ventricular ejection fraction less than or equal to 30%. All of the patients underwent Microvolt T-Wave Alternans (MTWA) testing with Cambridge Heart's HearTwave II system, and all received an implantable cardioverter defibrillator (ICD). At a press conference this morning, Dr. Chow presented the top-line results: while the ICD discharge rate, the primary endpoint, was lower in the MTWA negative group than in the non-negative group, this difference did not achieve statistical significance. However, MTWA was found to be predictive of total mortality (total mortality was 13% in the MTWA non-negative group and 6% in the MTWA negative group, hazard ratio = 2.04, $p = 0.02$).

A large series of studies have shown MTWA to be highly predictive of sudden cardiac death and cardiac arrest in patients who have not received ICDs, but it is not as predictive of the surrogate endpoint of ICD discharge in patients who already have ICDs. For example, the ALPHA trial, published in the November 2007 issue of the Journal of the American College of Cardiology, prospectively studied 446 patients with non-ischemic cardiomyopathy who had not received ICDs at enrollment. ALPHA found MTWA was highly predictive of sudden cardiac death and life-threatening arrhythmias. Similarly, the Bloomfield study involved 549 patients with left ventricular function on an ischemic or non-ischemic basis, an overwhelming majority of whom had not received ICDs. Bloomfield showed MTWA was a highly accurate predictor of mortality and non-fatal sustained ventricular arrhythmias. These results were published in the same journal in 2006.

Armondas et al conducted a meta-analysis of prospective studies, which comprised 1,811 patients, predominantly without implanted ICDs. These results similarly concluded MTWA was a very powerful predictor of arrhythmic risk. These data were published appeared in 2005 in the journal Nature Clinical Practice Cardiovascular Medicine.

"ICD discharge may be a poor surrogate endpoint for sudden cardiac death. Ellenbogen et al found in their 2006 study in Circulation that fewer than 50% of even 'appropriate' ICD shocks terminated an arrhythmia which would have been lethal if left untreated. ICD shocks for non-life threatening arrhythmias from a statistical perspective constitute noise when ICD shocks are used as a surrogate for sudden cardiac death in a clinical trial," stated Dr. Richard Cohen, Founder and Director of Cambridge Heart. "The fact MTWA was found to be predictive of mortality in the MASTER trial supports the notion that MTWA is predictive of actual risk."

