

# ArrhythmiaNEWS

From the Al-Sabah Arrhythmia Institute at St. Luke's-Roosevelt Hospital Center

*Arrhythmia News* is a physician bulletin providing arrhythmia updates and information on services at **St. Luke's-Roosevelt Hospital Center** which may benefit your practice and your patients.

## 8TH ANNUAL New Frontiers in Heart Failure Therapy

*Integrating Devices and  
Pharmacotherapy*

Saturday, January 26, 2008

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## Is T-Wave Alternans Testing a Useful Risk Stratification Tool for ICD Therapy?

With the application of ICD therapy for the primary prevention of sudden cardiac death over a large population of patients with left ventricular dysfunction, methods to better sub-stratify patients into high and low risk groups are necessary. T-wave alternans (TWA) testing predicts vulnerability for the development of ventricular arrhythmias and has emerged as a potential tool for risk stratification.

Microvolt TWA uses a computer algorithm and specialized recording equipment to collect and process information on the beat to beat variation in T-wave amplitude that occurs at a given heart rate. The heart rate is usually increased either invasively with atrial based pac-

ing or non-invasively by means of exercise testing. For a given patient TWA occurs consistently at a given heart rate so that the heart rate must be increased, typically above 105 beats per minute to perform the test. Results are typically described as positive, indeterminate or negative. Patients with indeterminate results are typically grouped with T-wave positive patients as "non-negative" as they have been shown to make up a group at an equally high risk for the development of ventricular arrhythmias. Reasons to classify tests as indeterminate include the presence of atrial fibrillation, inability to reach a heart rate of 105 bpm or frequent atrial or ventricular ectopy.

Initial data from observation or retrospective studies suggested that TWA could effectively identify (1) high-risk patients likely to derive significant benefit with an ICD as well as (2) extremely low risk patients in whom ICD implantation would not be associated with clinical benefit. However, data from recent large multicenter trials have called into question the value of TWA testing when applied to large intermediate to low risk populations. In this summary, we review data from these recent trials.

## Clinical Trial Results

The **ABCD** (1) trial compared TWA testing with programmed ventricular stimulation in a population of 556 patients similar to those enrolled in the **MUSTT** trial (prior MI, LVEF  $\leq$  40% and NSVT). All patients underwent electrophysiologic testing and TWA testing; patients with either a positive TWA test or inducible ventricular

arrhythmia underwent insertion of an ICD. Over a follow-up of 1.9 years, these two tests were equivalent in terms of predicting clinical events at 1 yr (programmed stimulation (11%) and TWA (9%). The negative predictive value (95% for both) were equivalent as well. However, the best discriminative results were obtained when the results of **both** tests were available.

The **ALPHA** study (2) evaluated patients with non-ischemic cardiomyopathy (LVEF  $\leq$  40%) and class II or III heart failure. Over 3,513 pts were screened to enroll 446 pts who were followed for 18-24 months after undergoing exercise TWA testing. A composite endpoint of cardiac death and life threatening ventricular arrhythmia was reached in 6.5% of patients with a "non-negative" TWA test versus 1.6% of patients with a negative TWA test at 1 year. The authors concluded that TWA testing can identify a large group of patients with an excellent prognosis who are unlikely to benefit from an ICD. Overall, a positive predictive value of 9% and a negative predictive value of 97% were seen at 18 months. However, the study was limited by a very low (4.2%) 1-year, all cause mortality.

Gold et al. (3) prospectively applied exercise TWA testing to 490 patients enrolled in the **SCDHeFT** trial. The SCDHeft trial enrolled patients with both non-ischemic and ischemic cardiomyopathy (LVEF  $\leq$  35%) and class II or III heart failure. In this sub study, a primary endpoint of sudden cardiac death, sustained VT/VF or appropriate ICD therapy at a mean follow-up of 35

months was not different between TWA+ and TWA- patients. It was also not different between TWA “non-negative” and TWA- patients. A secondary endpoint of total mortality also showed no difference between the two groups.

The **MASTER 1** <sup>(4)</sup> trial, recently presented at this past November’s American Heart Association meeting, applied exercise TWA testing to 650 patients who met **MADIT II** enrollment criteria (prior MI and LVEF ≤ 30%). A primary endpoint of life threatening ventricular tachyarrhythmia events occurred in 10% of TWA negative and 13% of TWA “non-negative” patients. While total mortality was lower in the TWA negative group, the difference was due entirely to a decrease in non-arrhythmic mortality, raising the possibility that TWA testing identifies a sicker patient population rather than a group prone to cardiac arrhythmias.

**In summary, microvolt TWA appears to have only limited clinical utility.** It cannot be applied to patients with atrial fibrillation or flutter, those with frequent ambient atrial or ventricular ectopy, and those with chronotropic incompetence; in addition, it may have poor predictive value in the setting of underlying bundle branch block. In two recent large prospective primary prevention trials involving enrollment criteria similar to the **MADIT II** and

**SCD-HeFT** trials, TWA **failed** to identify patients at an increased risk for sudden death.

Whether strategies that combine TWA with other risk stratification schemes, such as autonomic testing, signal average electrocardiography and ejection fraction <sup>(5)</sup> are capable of identifying a population within the group of patients currently eligible for primary prophylaxis who are sufficiently low risk to allow them to forego ICD implantation await further studies. For the present time we are left with depressed ejection fraction (LV ≤ 35%) and a history of clinical NYHA class II and III heart failure to make clinical decisions on the eligibility of our patients to undergo ICD implantation for the primary prevention of sudden cardiac death.

#### References:

1. Costantini O, Rosenbaum DS, Hohnloser SH, et al. *The Alternans Before Cardioverter Defibrillator (ABCD) Trial: A noninvasive strategy for primary prevention of sudden cardiac death using T-wave alternans*. *Circulation* 114 (22): 2426, November 28, 2006.
2. Salerno-Uriarte JA, De Ferrari GM, Klersy C, et al. *Prognostic value of T-wave alternans in patients with heart failure due to nonischemic cardiomyopathy. Results of the ALPHA study*. *J Am Coll Cardiol* 2007; 50: 1896-904

3. Gold MR, Ensley D, Chilson D, et al. *T-wave alternans SCD HeFT study: Primary endpoint analysis*. *Circulation* 2006; 114: II 428-II 429 (abstract)

4. Murphy SA. *Microvolt T wave alternans testing for risk stratification of post MI patients (MASTER 1 trial)*. *Circulation* 2007 (abstract; late breaking clinical trials)

5. Exner DV, Kavanagh KM, Slawnych MP, et al. *Noninvasive risk assessment early after a myocardial infarction. The Refine study*. *J Am Coll Cardiol* 2007; 50: 2275-84.

### The Al-Sabah Arrhythmia Institute at St. Luke’s-Roosevelt Hospital Center

Jonathan Steinberg, MD; Director  
Suneet Mittal, MD; Director, EP Lab  
Aysha Arshad, MD  
Mark Preminger, MD  
Tina Sichrovsky, MD  
Walter Pierce, MD  
Private Office: (212) 492-5550  
Hospital Office: (212) 523-4007  
Ridgewood, NJ: (201) 251-9080  
Staten Island: (718) 981-0396  
Middletown, NY: (845) 373-7400  
Goshen, NY: (845) 373-7400  
FAX: (212) 523-3915

Useful Risk Stratification Tool for ICD Therapy?

This issue: Is T-Wave Alternans Testing a

## ArrhythmiaNEWS

New Physician on Staff  
Mark Preminger, MD has  
joined the staff of the  
Al-Sabah Arrhythmia Institute  
at St. Luke’s-Roosevelt

St. Luke’s-Roosevelt Hospital Center  
1111 Amsterdam Avenue at 114th St.  
New York, NY 10025

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