**T-Wave Alternans: Not Ready for Prime Time**

**BY BRUCE JANCIN**

Snowmass, Colo. — The value of T-wave alternans testing as a risk stratification tool for selecting implantable cardioverter defibrillator candidates has been cast into serious doubt by the disappointing results of two recent large clinical trials.

"You're being told that ventricular fibrillation is not an episode that you can have and then go about your business; it's almost like a death sentence," said Dr. Gold, professor of medicine and director of adult cardiology at the Medical University of South Carolina, Charleston.

The hypothesis underlying TWA testing is that it non-invasively identifies patients having an electrophysiologic substrate for reentrant ventricular tachyarrhythmias. If true, that would allow more selective placement of cost-ly ICDs than is currently possible. Many patients who receive an ICD for primary prevention solely on the basis of the current criterion of a left ventricular ejection fraction below 35% will never use the device during their lifetime.

However, the results of the recent Microvolt T-Wave Alternans Testing for Risk Stratification of Post-MI Patients (MASTER 1) and Alternans Before Cardiodefibrillator (ABCD) trials raise a question as to whether the test really identifies a population that is at risk and therefore an increased risk for all-cause mortality rather than specifically for the arrhythmic sudden cardiac deaths (SCDs) that ICDs are designed to prevent.

In other words, TWA testing might not provide incremental value over clinical markers of increased mortality risk, such as comorbidities, advanced age, and lower left ventricular ejection fraction (EF), the cardiologist said at the conference, cosponsored by the American College of Cardiology.

Even in those who do get an appropriate ICD shock, it doesn't mean what it used to. "It used to be we'd pat the patient on the back and say, Congratulations, you just had your life saved. Go on about your business." In fact, that's not true any-thing, increasing, despite all the things we're doing. ICDs were supposed to be the cure for this problem," noted Dr. Gold.

Preliminary 2007 national data indicate that while the total number of cardiovascular deaths continues to decline, the proportion of cardiovascular mortality due to sudden death has climbed to 70%.

Sudden deaths "appear to be, if anything, increasing, despite all the things that we're doing. ICDs were supposed to be the cure for this problem," noted Dr. Gold, professor of medicine and director of adult cardiology at the Medical University of South Carolina, Charleston.

The problem with using ICDs for pri-mary prevention of sudden cardiac death (SCD) is that these expensive devices are being placed in the wrong people. "70%-80% of SCDs occur in people who do not meet standard indications for an ICD, and of those who do get ICDs, about 70% aren't going to use them in the first 4 or 5 years," the cardiologist said at the conference, cosponsored by the American College of Cardiology.

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The difficulty in using ICDs for sec-ondary prevention, he noted, is that so few individuals survive a first out-of-hospital cardiac arrest. In Chicago, New York, and Boston, the rate hovers around 1%.

"The basis of the strategy of ICDs for pri-mary prevention is what Dr. Gold calls the rule of 80s: the concept that 80% of SCDs are brought on by ventricular tachycardia degenerating into ventricular fibril-la tion, 80% occur in men, 80% have coronary artery disease with prior MI, and 80% are associ-ated with heart fail-ure with left ven-tricular systolic dysfunction. That was true 20 years ago, but it's no longer the case today because of the remarkable advances in the treatment of acute MI.

For example, a recent analysis of 714 consecutive SCDs in the population-based Oregon Sudden Unexplained Death Study showed only one in six subjects had under-gone assessment of left ventricular ejection fraction (EF). In other words, there's no prior suspicion of ventricular fibrillation in 83% of patients with SCD. Moreover, 70% of those with an EF measurement had a value greater than 35%, so they didn't meet current criteria for pro-phyllactic ICD placement (J. Am. Coll. Cardiol. 2006;47:1161-6).

Roughly half of Oregon SCDs with a known EF had a normal value. Only 53% in that subgroup were men, and only 50% with a normal EF had known coronary artery disease. So much for the rule of 80s.

Similarly, a history of heart failure was present in only 12% of 492 consecutive patients with out-of-hospital SCD in the Maastricht, Netherlands, area (Eur Heart J. 2003;24:1204-9). Fifty-four percent of the Dutch patients had SCD as their first manifestation of any cardiac disease. Of those with a prior MI, the average time from MI to sudden arrest was 9.7 years, in contrast to the standard teaching that the highest-risk period is the first year post MI.

The paradox is that the patients who are dying suddenly largely have preserved EF. The bottom line is there aren't a lot of patients with very low EFs anymore because we treat MI so well. "It's that huge pool of patients with only mild reductions in EF that are dying suddenly," he said.

Dr. Gold stressed that the key to making a bigger impact on SCD is improved non-invasive risk stratification for ICD place-ment. However, he noted, "there were no prior indications for the oncoming T-wave alternans measurement to make the latest disappointment." (See story above.)