

The table below summarizes the results of four major clinical trials of MTWA. Combined, these trials enrolled over 2,800 subjects including patients with left ventricular dysfunction (Bloomfield, Chow, ALPHA) as well as those with preserved EF (Ikeda).

	LV Dysfunction (Current Primary Prevention Population)			Preserved EF
	Bloomfield et al [1]	Chow et al [2]	ALPHA [3]	Ikeda et al [4]
<i>Year</i>	2006	2006	2007	2006
<i>Population</i>	Ischemic/Non-ischemic LVEF ≤ 40%	Ischemic LVEF ≤ 35%	Non-ischemic Class II/III HF LVEF ≤ 40%	Ischemic Post-MI LVEF ≥ 40%
<i>N</i>	549	768	446	1041
<i>Primary Endpoint</i>	All-cause mortality or non-fatal sustained ventricular arrhythmias	All-cause mortality	Cardiac death and life-threatening arrhythmias	Sudden cardiac death and life-threatening arrhythmic events
<i>Testing Modality</i>	Bicycle or treadmill exercise	Treadmill exercise	Bicycle or treadmill exercise	Bicycle or treadmill exercise
<i>Follow-up time</i>	20 ± 6 months	18 ± 10 months	Up to 18 months	32 ± 14 months
<i>MTWA Results</i>	66% Non-negative	67% Non-negative	65% Non-negative	18% Positive
<i>MTWA Hazard Ratio</i>	6.53 (2.35 - 18.11) p < 0.001	2.24 (1.34 - 3.75) p = 0.002	4.01 (1.41 - 11.41) p = 0.002	19.7 (5.5 - 70.4) p < 0.0001
<i>Negative Predictive Value</i>	97.5% (2-year)	Not reported	98.7% (1-year)	99.6%
<i>Conclusions</i>	“Among patients with heart disease and LVEF ≤ 0.40, MTWA can identify not only a high-risk group, but also a low-risk group unlikely to benefit from ICD prophylaxis.”	“Microvolt T-wave alternans is a strong and independent predictor of all-cause and arrhythmic mortality in patients with ischemic cardiomyopathy.”	“Among NYHA functional class II/III nonischemic cardiomyopathy patients, an abnormal TWA test is associated with a 4-fold higher risk of cardiac death and life-threatening arrhythmias.”	“In patients with preserved cardiac function, the incidence of indeterminate results of microvolt TWA is low, and a positive test result is associated with arrhythmic events.”

A

B

C

D

E

- A** The Bloomfield, Chow and ALPHA studies address patients with LV dysfunction (EF \leq 35 or 40%), most of whom are currently indicated for ICD placement via current primary prevention guidelines. The Ikeda study addresses the post-MI population with preserved EF (\geq 40%), a population which falls outside of current ICD indications.
- B** The Ikeda study is the largest MTWA study published to date; the ALPHA study is the largest MTWA study in the non-ischemic population.
- C** In patients with LV dysfunction, indeterminate tests are often grouped with positive tests to form an MTWA “non-negative” or “abnormal” group. The rationale for this stems from data showing that indeterminate tests due to certain physiologic causes (e.g., ectopy, inability to raise heart rate) are associated with a level of risk equivalent to that of a positive test [5, 6].

In the low EF population, results consistently show that two-thirds of patients test non-negative for MTWA. The positivity rate is lower in the preserved EF group, a population in which the risk for SCD is much lower.
- D** In each of these studies, the reported hazard ratio indicates that patients with a “non-negative” MTWA test are at significantly increased risk for an event compared to those with a negative test result.
- E** The negative predictive value of MTWA is consistently high, indicating that patients with a negative test result are at very low risk of an event in the next 12-18 months.

1. Bloomfield, D.M., et al., *Microvolt T-wave alternans and the risk of death or sustained ventricular arrhythmias in patients with left ventricular dysfunction*. J Am Coll Cardiol, 2006. **47**(2): p. 456-63.
2. Chow, T., et al., *Prognostic utility of microvolt T-wave alternans in risk stratification of patients with ischemic cardiomyopathy*. J Am Coll Cardiol, 2006. **47**(9): p. 1820-7.
3. Salerno-Uriarte, J.A., 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**(19): p. 1896-1904.
4. Ikeda, T., et al., *Predictive value of microvolt T-wave alternans for sudden cardiac death in patients with preserved cardiac function after acute myocardial infarction: results of a collaborative cohort study*. J Am Coll Cardiol, 2006. **48**(11): p. 2268-74.
5. Kaufman, E.S., et al., *"Indeterminate" microvolt T-wave alternans tests predict high risk of death or sustained ventricular arrhythmias in patients with left ventricular dysfunction*. J Am Coll Cardiol, 2006. **48**(7): p. 1399-404.
6. Chan, P.S., et al., *Prognostic implication of redefining indeterminate microvolt T-wave alternans studies as abnormal or normal*. Am Heart J, 2007. **153**(4): p. 523-9.



100 Ames Pond Drive
 Tewksbury, MA 01876
 PH: 888-226-9283
 FAX: 978-654-4501

For more information, please contact:
 Lahn Fendelander
 VP, Clinical Affairs
lahnf@cambridgeheart.com