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Horizon Scanning Technology Prioritising Summary Update

Microvolt T-wave alternans to determine benefit of ICD therapy

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Enquiries about the content of the report should be directed to:

HealthPACT Secretariat
Department of Health and Ageing
MDP 106
GPO Box 9848
Canberra ACT 2606
AUSTRALIA

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This Horizon scanning prioritising summary was prepared by Linda Mundy and Professor Janet Hiller from the National Horizon Scanning Unit, Adelaide Health Technology Assessment, Discipline of Public Health, School of Population Health and Clinical Practice, Mail Drop 545, University of Adelaide, Adelaide, SA, 5005.

PRIORITISING SUMMARY UPDATE 2008

REGISTER ID:	**000238**
NAME OF TECHNOLOGY:	**MICROVOLT T-WAVE ALTERNANS**
PURPOSE AND TARGET GROUP:	**DETERMINING THE LIKELY BENEFIT OF ICD THERAPY IN THE PREVENTION OF SUDDEN CARDIAC DEATH**

2008 SAFETY AND EFFECTIVENESS ISSUES

Patients undergoing a microvolt T-wave alternans (MTWA) test may be classified as negative, positive or indeterminate. The high negative predictive value of the MTWA test means that it is capable of identifying patients with a low-risk of death, who would be unlikely to benefit from the implantation of a cardioverter defibrillator (ICD). Patients with an abnormal MTWA test would therefore be considered to be good candidates for ICD therapy. However, approximately 20-40 per cent of all MTWA tests are indeterminate. In a large prospective cohort Kaufman et al (2006) evaluated 549 patients who satisfied the inclusion criteria (LVEF[1] ≤40%, aged >18, no atrial fibrillation, NYHA[1] functional class I, II or III, and a stable sinus rhythm) (level II prognostic evidence). Of the 549 enrolled patients, 195 (35.5%) had a negative, 163 (29.7%) a positive and 191 (34.8%) an indeterminate MTWA test result at baseline. The LVEF for the negative, positive and indeterminate patients were 26 ± 9, 23 ± 8, and 27 ± 8 per cent, respectively. The primary endpoint was all-cause mortality or documented non-fatal sustained ventricular arrhythmia (SVA). Patients were followed up for a mean of 20 ± 6 months.

During the follow-up period there were 51 primary outcome events (40 deaths and 11 SVA). The two-year rate for death or a non-fatal SVA was 17.8 per cent in patients with an indeterminate MTWA test, compared to 12.3 and 2.4 per cent in patients with a positive and negative MTWA test, respectively. In addition, during the follow-up period, 69 patients were implanted with an ICD: representing 13 per cent of patients with a negative MTWA test (n=25), 13 per cent of patients with a positive MTWA test (n=21) and 12 per cent of patients with an indeterminate MTWA test (n=23). Of the 11 patients with a non-fatal SVA, all were implanted with an ICD. Two of these patients had a negative MTWA test, five had a positive and four had an indeterminate MTWA test, respectively. The authors concluded that an indeterminate MTWA predicted death or SVA as least as well as a positive MTWA test, and that a negative MTWA test was associated with a very low-risk of death. Therefore it would be appropriate to combine patients with an indeterminate or positive MTWA test into one high-risk group, who would benefit from implantation with an ICD (Kaufman et al 2006).

[1] LVEF = left ventricular eject fraction, NYHA = New York Heart Association, ICD = implantable cardiac defibrillator

A large prospective cohort study, the ALPHA study, evaluated all patients attending Italian heart failure clinics during a three year period (level II prognostic evidence) (Salerno-Uriarte et al 2007). Of 3,513 patients, 446 satisfied the eligibility criteria (LVEF[2] <40%, aged >18 and <80 years, no atrial fibrillation, NYHA[1] functional class II or III, non-ischaemic cardiomyopathy, no implanted pacemaker or ICD[1] and no history of cardiac arrest, syncope or ventricular tachycardia). Patients were evaluated every six months up to 18 months, with some patients followed-up for 24 months. Due to the recent publication by Kaufman et al (2006), patients with a baseline positive or indeterminate MTWA test were grouped together as abnormal.

Of the 446 enrolled patients, 154 (34.6%) had a negative, 200 (44.8%) a positive and 92 (20.6%) an indeterminate MTWA test result at baseline. Therefore a total of 292 (65.5%) of patients were considered to have an abnormal MTWA test. When compared to those patients with a normal MTWA test, the abnormal MTWA patients were significantly older (59.9 ± 12.7 vs 57.4 ± 12.1, p=0.042), a greater proportion of them were in the NYHA class III (57 vs 18, p=0.045), had a poorer quality of life (Minnesota QOL score 22.9 ± 17.1 vs 17.0 ± 13.1, p<0.001) and a lower LVEF (28.6 ± 6.9 vs 31.3 ± 7.3, p<0.001).

Table 1 Results of MTWA tests, abnormal vs normal

Event	Normal MTWA Number Rate* [95% CI]	Abnormal MTWA Number Rate* [95% CI]	HR [95%CI]	p value
Primary end point				
Cardiac death + life threatening arrhythmia	4/154 (2.6%) 1.6 [0.6, 4.4]	29/292 (9.9%) 6.5 [4.5, 9.4]	4.01 [1.41, 11.41]	0.002
Secondary end points				
Total mortality	3/154 (1.9%) 1.2 [0.4, 3.8]	25/292 (8.6%) 5.7 [3.8, 8.4]	4.6 [1.39, 15.25]	0.002
Arrhythmic death + life threatening arrhythmia	2/154 (1.3%) 0.8 [0.2, 3.3]	20/292 (6.8%) 4.5 [2.9, 7.0]	5.53 [1.29, 23.65]	0.004
Hospitalisation	24/154 (16.6%) 9.9 [6.3, 14.7]	61/292 (20.9%) 13.8 [10.6, 17.8]	1.39 [0.86, 2.32]	0.165

MTWA = microvolt T wave alternans test, * Rate = events per 100 person-years, HR = hazard ratio

At time of baseline MTWA testing patients were assessed for eligibility for implantation with a biventricular device, based primarily on their NYHA classification and the presence of a wide QRS interval. A total of 31 patients were considered to be eligible for implantation with a cardiac resynchronisation device (CRT): 17 were implanted with a CRT-pacing device (16 with an abnormal and 1 with a normal MTWA test) and 14 were implanted with a CRT-defibrillator device (12 with an abnormal and 2 with a normal MTWA test).

The results of MTWA testing on the primary and secondary endpoints are summarised in Table 1. Patients with an abnormal MTWA test result were at four

[2] LVEF = left ventricular eject fraction, NYHA = New York Heart Association, ICD = implantable cardiac defibrillator

times the risk of experiencing the primary end-point of cardiac death and life-threatening arrhythmia. Four ventricular tachycardia events were detected by CRT devices implanted, all of which occurred in patients with an abnormal MTWA test. When a sensitivity analysis was performed, removing these four events from the analysis, the resulting hazard ratio was 3.44 (95% CI [1.20, 9.90], $p = 0.008$), representing a significant excess risk in the abnormal MTWA test group.

The negative predictive values of a *normal* MTWA test and positive predictive values of an *abnormal* MTWA test, with respect to the prediction of events at 12 and 18 months are summarised in Table 2. The authors conclude that patients with a normal MTWA test appear to have a good prognosis as demonstrated by the high negative predictive value of the test. It would appear that these patients would *not* benefit from the implantation of a CRT device.

Table 2 Positive and negative predictive values for MTWA testing

Event	NPV [95% CI]		PPV [95% CI]	
	12 months	18 months	12 months	18 months
Primary end point				
Cardiac death + life threatening arrhythmia	98.7% [95.4, 99.8]	97.3% [93.3, 99.3]	6.5% [4.0, 10.0]	9.0% [5.9, 13.0]
Secondary end points				
Total mortality	99.3% [96.4, 100]	98.0% [94.2, 99.6]	4.2% [2.2, 7.3]	7.7% [4.1, 11.5]
Arrhythmic death + life threatening arrhythmia	99.3% [96.4, 100]	98.6% [95.2, 99.8]	4.9% [2.7, 8.1]	7.0% [4.3, 10.7]

NPV = negative predictive value, PPV = positive predictive value

Nieminen et al (2007) conducted a large prospective cohort study in Finland on 1,037 consecutive *low-risk* patients referred for exercise testing and undergoing evaluation for suspected coronary heart disease (level II prognostic evidence). All patients underwent MTWA testing and were followed-up for a mean of 44 ± 7 months. The maximum MTWA value at a heart rate <125 [3]beats per minute was obtained and used to stratify patients at risk of all-cause death, cardiovascular death and sudden cardiac death. The authors tested several MTWA cut-off points before assigning <65 μ volts as a cut-off point for negative patients (n=950) and ≥65 μV for positive patients (n=87). During the follow-up period there were 59 deaths, of which 34 were classified as cardiovascular death and 20 as sudden cardiac death. The cause of death in the remaining four patients was unknown. Although the number of deaths in positive and negative MTWA test patients was not stated, a MTWA >65 μV at baseline was associated with a significant increase in relative risk of 7.4 for sudden cardiac death, 6.0 for cardiovascular mortality, and 3.3 for total mortality. Sensitivity, specificity, negative and positive predictive values are summarised in Table 3.

Table 3 Sensitivity, specificity, positive and negative predictive values for MTWA cut-off 65 μV

[3] The majority of MTWA testing reported in the literature uses a value of ≤110 beats per minute

	Sensitivity	Specificity	PPV	NPV
Sudden cardiac death	35.0	92.1	8.0	98.6
Cardiovascular death	32.4	92.4	12.6	97.6
All-cause death	22.0	92.4	14.9	95.2

NPV = negative predictive value, PPV = positive predictive value

The specificity and negative predictive values of MTWA testing were high (92 and >95%) indicating that the test can identify low-risk patients who do not require intervention in the form of an ICD. However, the sensitivity and positive predictive values were low (<35 and <15%), which indicates those patients who may be classified as high-risk would need to undergo further diagnostic testing to establish a diagnosis and their risk of a cardiac event. The authors suggest that MTWA testing could be used as a screening tool in a general population undergoing clinical exercise testing (Nieminen et al 2007).

Cantillon et al (2007) examined the ability of MTWA testing to stratify patients with left ventricular dysfunction (LVEF ≤35%) into high and low risk groups. Of 650 patients undergoing electrophysiologic evaluation, 308 met the inclusion criteria. Patients not followed-up for at least 12-months were deemed lost to follow-up (n=20). A total of 286 patients were followed-up for a mean of 38 ± 11 months (level II prognostic evidence). MTWA testing determined that 90 patients were negative and a total of 196 had a positive or indeterminate test. A total of 174 patients underwent ICD implantation with similar numbers in the MTWA negative patients (n=49, 54%) and the MTWA non-negative patients (n=125, 64%). At 2-years, nine MTWA negative patients had died compared to 34 MTWA non-negative patients (10% vs 17%, p=0.04). Arrhythmia-free survival was significantly higher in the MTWA negative patients compared to the MTWA non-negative patients (81% vs 66%, p<0.0001). MTWA testing was found to be a strong predictor of the primary end-point of arrhythmia-free survival with a hazard ratio[4] of 2.33 (95% CI [1.44, 3.67], p<0.01). Although these results agree with all previous studies, the authors were concerned about the number of events in the MTWA negative patient group (Cantillon et al 2007).

2008 SUMMARY OF FINDINGS

All studies included for assessment in this update concluded that microvolt T wave alternans testing, after adjustment for confounding factors (LVEF, NYHA classification etc) was useful for the stratification of cardiac patients into low and high risk groups, and as such is able to identify those patients who would benefit most from the implantation of an ICD.

Based on the good quality evidence it would appear that MTWA testing is useful for the stratification of high and low risk cardiac patients. The gold standard cut-off

[4] Hazard ratio for mortality not reported as mortality was not a primary end-point

MTWA value has yet to be established and there may be some doubt as to the suitability of all patients to undergo this test (ie those with a low left ventricular ejection fraction). However, if MTWA testing is found to be effective, it may ensure that only those patients who will benefit from the ICD therapy are implanted.

2008 HEALTHPACT ACTION:

An increasing number of patients with a low ejection fraction are currently being implanted with implantable cardioverter defibrillators in Australia and New Zealand. The assessment of microvolt T-wave alternans has the potential to determine which patients would be successful candidates for implantation and therefore may potentially reduce costs. HealthPACT has therefore recommended that this technology be referred to the MSAC for a full health technology assessment.

2008 NUMBER OF INCLUDED STUDIES

Total number of studies	
Level II prognostic evidence	4

2008 REFERENCES:

Cantillon, D. J., Stein, K. M. et al (2007). 'Predictive value of microvolt T-wave alternans in patients with left ventricular dysfunction', *J Am Coll Cardiol,* 50 (2), 166-173.

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PRIORITISING SUMMARY 2007

REGISTER ID: **000238**

NAME OF TECHNOLOGY: **MICROVOLT T-WAVE ALTERNANS**

PURPOSE AND TARGET GROUP: **DETERMINING THE LIKELY BENEFIT OF ICD THERAPY IN THE PREVENTION OF SUDDEN CARDIAC DEATH**

STAGE OF DEVELOPMENT (IN AUSTRALIA):

- ☐ Yet to emerge
- ☐ Experimental
- ☐ Investigational
- ☒ Nearly established
- ☐ Established
- ☐ Established *but* changed indication or modification of technique
- ☐ Should be taken out of use

AUSTRALIAN THERAPEUTIC GOODS ADMINISTRATION APPROVAL

- ☒ Yes — ARTG number 65760
- ☐ No
- ☐ Not applicable

INTERNATIONAL UTILISATION:

COUNTRY	LEVEL OF USE		
	Trials Underway or Completed	Limited Use	Widely Diffused
United States			✓
Europe		✓	
Australia		✓	

IMPACT SUMMARY:

Recent clinical trials have demonstrated that implantable cardioverter defibrillators (ICDs) improve survival in post myocardial infarction patients with low ejection fraction. In this group of patients however, only a small percentage will experience any benefit from an ICD. Given the high costs and procedural morbidity associated with ICD implantation, a strong emphasis has been placed on risk stratification techniques to determine among eligible patients those that are likely to benefit from ICD implantation. Microvolt T-wave alternans (MTWA) testing, a non-invasive measure strongly related to arrhythmic events, has shown promise as a risk stratification technique amongst patients with low ejection fraction. The current prioritising summary outlines the technique of MTWA testing and investigates its effectiveness and cost implications in the risk stratification of ICD eligible patients.

BACKGROUND

Sudden cardiac death (SCD) resulting from ventricular arrhythmias is a leading cause of mortality in patients with ischemic heart disease and left ventricular dysfunction (Greenberg et al 2004). Although SCD can be prevented through the implantation of an ICD, cardiologists have lacked appropriate diagnostic tools to accurately determine which patients are at high risk of experiencing ventricular arrhythmias. ICDs were first used as a secondary prevention measure in patients with previously documented ventricular arrhythmias. While these patients are at high risk of SCD, they account for only a small percentage of total SCD cases. Most patients with left ventricular dysfunction who die from ventricular arrhythmias do so during their first cardiac arrest (Huikuri et al 2006). Clinical interest has therefore focused on primary prevention strategies in patients yet to experience life-threatening arrhythmic events.

Several recent clinical trials have demonstrated the benefits of ICD implantation in all patients with ischemic or non-ischemic heart disease and left ventricular dysfunction. The Multicenter Automatic Defibrillator Implantation Trial II (MADIT II) compared ICD implantation to conventional therapy in post myocardial infarction patients with a left ventricular ejection fraction of 0.30 or less. Over an average follow-up period of 20 months, the trial reported a 28 per cent relative reduction in mortality rates (or 5.6% absolute reduction) in patients implanted with an ICD in comparison to patients that received conventional therapy (Moss et al 2002). Similarly, the Sudden Cardiac Death in Heart Failure Trial (SCD-HeFT) investigated the effectiveness of ICD implantation in patients with a left ventricular ejection fraction of 0.35 or less and previous heart failure of ischemic or non-ischemic nature. During an average follow-up period of 45.5 months, ICD implantation was associated with a 23 per cent relative reduction in overall mortality rates (Bardy et al 2005). Despite the apparent survival benefits in this patient group, only a small percentage of patients experience any benefit from an ICD. In the MADIT-II trial for example, only 23 per cent of patients in the treatment arm received appropriate ICD pacing or defibrillation during the follow-up period (Singh et al 2005). The majority of patients were implanted with a device that provided no therapy, creating unnecessary costs and morbidity associated with the implantation procedure. In addition to ischemic or non-ischemic heart disease and left ventricular dysfunction, further diagnostic tests are required to better discriminate between patients likely to and unlikely to benefit from ICD implantation.

MTWA testing has emerged as a promising risk stratification tool for determining which patients with low left ventricular ejection fraction should receive an ICD. MTWA refers to beat-to-beat changes in T wave amplitude and morphology, and has been closely linked to susceptibility to ventricular arrhythmias and SCD in a wide variety of patient populations (see for example Hohnloser et al 1998; Ikeda et al 2000; Klingenheben et al 2000). A regular electrocardiogram cannot detect fluctuations in T-waves due to their small size, and thus the test requires specialised recording and

signal processing methods. MTWA is typically recorded during a period of controlled exercise (as the test requires elevation of the heart rate to above 110 beats per minute) and later analysed using spectral decomposition methods. Two measures are obtained from the testing procedure, the magnitude of the T-waves (typically expressed in microvolts) and the alternans ratio, a quantity defined as the number of standard deviations by which the peak signal of the T-wave exceeds background noise. A positive test result is defined as alternans voltage of ≥ 1.9 μV at 0.5 cycles-per-beat and an alternans ratio of ≥ 3. A negative test result is defined as the absence of alternans at 0.5 cycles-per-beat when the heart rate is sustained at > 105 beats per minute for a period of at least one minute. Otherwise, the test is considered to be indeterminate (Klingenheben & Hohnloser 2002).

MTWA can be measured using the commercially available HearTwave® II Cardiac Diagnostic System (Cambridge Heart, Inc., Bedford, MA). The system consists of an LCD screen display, a computer, digital ECG amplifier, a signal input (multi-lead ECG), and a signal processor and analysis module. Data are obtained from electrodes and sensors attached through a lead wire set to a belt-worn patient module. The system is typically used to measure and interpret MTWA during bicycle or treadmill stress tests, but can also be used during pharmacological or echocardiographic stress tests. Following completion of the test, the system generates a printed report.

CLINICAL NEED AND BURDEN OF DISEASE

Individuals at the highest risk of ventricular arrhythmias and SCD are those with a history of myocardial infarction, coronary artery disease, left ventricular dysfunction and cardiomyopathies. Individuals with a family history of SCD or genetic defects such as long QT syndrome are also at a high risk of SCD (Lopshire & Zipes 2006). A recent Australian study investigated the causes of SCD in people less than 35 years of age (Doolan et al 2004). In the cross-sectional study (level IV Aetiology evidence), 10,199 autopsies performed between January 1994 and December 2002 at a major Sydney forensic unit were reviewed. A total of 193 cases were classified as SCDs. The cause of SCD was not established but presumed to be due to a primary arrhythmia in 31 per cent of cases. Coronary artery disease was reported in 24 per cent of cases, hypertrophic cardiomyopathy or unexplained left ventricular hypertrophy in 15 per cent of cases, and myocarditis in 12 per cent of cases.

In 2004-2005, a total of 3,216 ICDs were implanted in patients in Australian public hospitals, the procedure associated with an average length of stay of 5.5 days (AIHW 2006). It is likely however that a much larger patient group would be eligible for ICD implantation and subsequently MTWA testing if MADIT-II inclusion criteria were adopted. In 2004-2005, 10,056 Australians were diagnosed with left ventricular

failure, while a further 47,633 experienced an acute myocardial infarction (AIHW 2006).

DIFFUSION

MTWA testing was first available in the United States in 2002 when the FDA provided 510(k) clearance for the HearTwave™ Alternans Processing System or CH2000 (Cambridge Heart, Inc., Bedford, MA). Since that time, Cambridge Heart, Inc. has received 510(k) clearance from the FDA for the HearTwave® II Cardiac Diagnostic System. The system has been commercially available in the United States since April 2005 and is reimbursed through Medicare for the purposes of risk stratification of SCD. In Australia, the HearTwave® II Cardiac Diagnostic System is marketed through Equipmed Pty Ltd after recent approval from the TGA (ARTG Number 65760). At this stage uptake of the system in Australia has been limited however, this may be due to the lack of reimbursement for MTWA testing through the MBS (personal communication Equipmed Pty Ltd, December 2006).

COMPARATORS

There are a number of comparators to MTWA testing in the risk stratification of patients with ischemic heart disease and left ventricular dysfunction. Other potential techniques of risk stratification include the detection of arrhythmias using a Holter monitor or during an electrophysiological study, the measurement of heart rate variability, QRS duration and baroreceptor sensitivity. Signal-averaged electrocardiography is another risk stratification method that measures beat-averaged conduction rather than beat-to-beat fluctuations. It is therefore conceivable that MTWA could be used in conjunction with a variety of other prognostic tests in order to more efficiently stratify patients for ICD implantation. Among patients with ischemic heart disease and left ventricular dysfunction, the measurement of MTWA is an attractive option given the high negative predictive ability and non-invasive nature of the test.

EFFECTIVENESS AND SAFETY ISSUES

Gehi et al (2005) conducted a meta-analysis into the value of MTWA in predicting future arrhythmic events (level I prognostic evidence). In the analysis, a total of 19 studies published between January 1990 and December 2004 were identified. All studies met the following inclusion criteria: prospective cohort study involving more than 10 human subjects who underwent MTWA testing for the prediction of ventricular arrhythmias or SCD; provided data on MTWA test results and clinical outcomes; provided a clear definition of the criteria used to classify MTWA results as normal or abnormal; and had a follow-up time of 6-months or longer. A total of 2,608 patients across a wide range of populations were analysed in the study, including patients with congestive heart failure (CHF), ischemic CHF, non-ischemic CHF, post

myocardial infarction, athletes and healthy participants. The mean age of participants in the studies ranged between 25 and 64 years, with a mean length of follow-up of 19-months. A negative MTWA test result was reported in 25 to 54 per cent of study subjects.

Using random effects models, Gehi et al (2005) calculated a pooled positive predictive value (PPV) for future arrhythmic events (classified as SCD, cardiac death, ventricular fibrillation, ventricular tachycardia or ICD event) of 19.3 per cent (95% CI, 17.7%-21.0%), a pooled negative predictive value (NPV) of 97.2 per cent (95% CI, 96.5%-97.9%) and a pooled relative risk of 3.77 (95% CI, 2.39-5.95). Sub-group analyses revealed no statistically significant differences in the predictive ability of MTWA testing between ischemic and non-ischemic patients. A significant difference in the PPV of MTWA testing between post myocardial infarction patients and CHF patients was reported however (6.0% vs. 25.5%, $p < 0.0001$). No evidence of publication bias was found during the study ($p = 0.15$).

In a recent multicenter prospective cohort study, Chow et al (2006) investigated whether MTWA testing was an independent predictor of mortality in 768 patients with ischemic cardiomyopathy and left ventricular ejection fraction ≤ 35 per cent (level II prognostic evidence). The mean length of follow-up in the study was 18 ± 10 months. A total of 514 patients (67% of sample) reported a non-negative MTWA test (positive or indeterminate). After adjusting for a variety of prognostic factors (including ICD status), patients with a non-negative MTWA result were found to be at a significantly higher risk of all-cause mortality than those with a negative result (HR = 2.24, 95% CI, 1.34-3.75, $p = 0.002$). The risk of mortality due to arrhythmic events was also found to be significantly higher in patients with a non-negative MTWA result after adjusting for prognostic factors (HR = 2.29, 95% CI, 1.00-5.24, $p = 0.049$).

Bloomfield et al (2006) recently published results of a multicenter prospective cohort study (level II prognostic evidence) involving 587 patients with ischemic heart disease or non-ischemic cardiomyopathy and left ventricular ejection ≤ 40 per cent. The mean length of follow-up in the study was 20 ± 6 months. Of the 549 patients that could be evaluated, 360 (66%) reported a non-negative MTWA test result (positive or indeterminate). A total of 40 deaths and 11 non-fatal sustained ventricular arrhythmias, all of which were appropriate for ICD shocks, were observed during follow-up. The risk for all-cause mortality or ventricular arrhythmias was reported to be significantly higher amongst patients who reported a non-negative MTWA test result in comparison to patients who reported a negative result (HR = 6.5,

95% CI, 2.4-18.1, p <0.0001). Only two deaths and two non-fatal sustained ventricular arrhythmias occurred in patients with a negative MTWA result, giving the test a PPV and NPV of 13.5 and 97.9 per cent respectively.

COST IMPACT

Equipmed has indicated that the cost of the HearTwave® II Cardiac Diagnostic System in Australia is around $30,000 for the basic package, or around $40,000 with treadmill and stress functionality included (personal communication Equipmed Pty Ltd, December 2006). Although the Australian costs of MTWA testing are unknown, in the United States the average cost of an MTWA test ranges from $400 to $650 US dollars (Daccarett et al 2006).

A recent study by Chan et al (2006) investigated the cost-effectiveness of MTWA testing in determining which patients satisfying MADIT-II inclusion criteria should receive an ICD. Three therapeutic strategies were compared in the study: ICD placement in all patients; ICD placement in patients reporting a non-negative MTWA result; and medical management. The authors reported an incremental cost-effectiveness ratio (ICER) of $48,700 per quality adjusted life year (QALY) when comparing a strategy of MTWA risk stratification to standard medical management, suggesting that MTWA testing is costly but potentially cost effective. An ICER of $88,700 per QALY was calculated when comparing a strategy of ICD placement in all patients to ICD placement following MTWA risk stratification, suggesting that a strategy of ICD placement in all patients offers little additional benefits at a high cost.

ETHICAL, CULTURAL OR RELIGIOUS CONSIDERATIONS

No issues were identified/raised in the sources examined.

OTHER ISSUES

MTWA should not be measured in patients who may not be able to tolerate the exercise test, which includes patients with a serious ongoing cardiac dysrhythmia, unstable coronary artery disease, atrial fibrillation, or patients who have experienced a myocardial infarction in the last six days. MTWA testing may also be inaccurate in patients with frequent atrial or ventricular ectopy and patients who cannot attain a heart rate between 90 and 110 beats per minute (Haghjoo et al 2006).

RECOMMENDATION:

A large number of studies have demonstrated the diagnostic effectiveness of MTWA testing in predicting future arrhythmic events across a variety of patient populations. Due to its high negative predictive ability, MTWA testing appears to be a useful method for identifying which patients with ischemic or non-ischemic heart disease

and left ventricular dysfunction are unlikely to receive benefit from ICD therapy. The technique is reported to be safe and convenient, and is currently reimbursed through Medicare in the United States for the purposes of risk stratification of SCD. Given the high rates of mortality associated with SCD and the availability of numerous high quality studies on MTWA testing, HealthPACT recommended that this technology be monitored.

SOURCES OF FURTHER INFORMATION:

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LIST OF STUDIES INCLUDED

Total number of studies	
Level I evidence	1
Level II evidence	2

SEARCH CRITERIA TO BE USED:

Ventricular Dysfunction, Left/*complications/*mortality
Myocardial Infarction/*physiopathology/*therapy
Electrophysiology
Defibrillators, Implantable
Death, Sudden, Cardiac/*etiology