Review Article

Risk Stratification for Sudden Cardiac Death after Acute Myocardial Infarction

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Abstract

Many patients who survive an acute myocardial infarction (AMI) remain at risk of recurrent cardiac events and sudden cardiac death after discharge, despite optimal medical treatment. Assessment of the degree of left ventricular dysfunction and residual myocardial ischaemia is useful to identify the patients at greatest risk. In addition, there is increasing evidence that a number of other cardiovascular tests can be used to detect autonomic dysfunction and myocardial substrate abnormalities postAMI that increase the risk of life-threatening ventricular arrhythmias. These investigations include ECG-based tests (signal averaged ECG and T-wave alternans), Holter-based recordings (heart rate variability and heart rate turbulence) and imaging techniques (echocardiography and cardiac magnetic resonance), as well as invasive electrophysiological testing. This article reviews the current evidence for the use of these additional cardiac investigations among survivors of AMI to aid in their risk stratification for malignant ventricular arrhythmias and sudden cardiac death.

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Introduction

In today's modern era of evidence-based medicine and interventional cardiology, most patients who suffer an acute myocardial infarction (AMI) are started on medication with proven prognostic benefit [e.g. β-blockers, angiotensin converting enzyme (ACE)-inhibitors and statins] and undergo coronary angiography with revascularisation as dictated by their presentation and symptoms. Despite these measures, evidence suggests that risk stratification of AMI survivors is still suboptimal with some patients remaining at high risk of recurrent cardiac events and sudden death after leaving hospital.[1,2] A wide variety of patient- and cardiac-related factors can also influence mortality rates, as shown in Table 1.[3] Left ventricular ejection fraction (LVEF) remains one of the most important predictors of an adverse outcome among AMI survivors and therefore is an essential parameter to assess before the patient leaves hospital. A number of studies have provided convincing data for the use of echocardiography and nuclear imaging to determine left ventricular dysfunction and residual myocardial ischaemia postAMI, allowing for earlier, more aggressive treatment in patients with abnormal findings.[3-5] In addition, since the occurrence of malignant ventricular arrhythmias, in the form of ventricular tachycardia (VT) or ventricular fibrillation (VF), is one of the leading causes of sudden death among AMI survivors after discharge,[6] cardiovascular investigations which can identify the myocardial substrate abnormalities that give rise to these arrhythmias can be used to refine risk.

The focus of this article is to review the current evidence for the use of cardiovascular investigations which may have a role to play in identifying those patients at greatest risk for ventricular arrhythmias and sudden cardiac death. Specifically, this review pertains to the primary prevention of sudden cardiac death among AMI survivors who may benefit from the prophylactic insertion of an implantable cardioverter defibrillator (ICD).

Importance of Risk Stratification

Identification of AMI survivors who are at greatest risk of developing VT/VF will allow for closer monitoring following discharge and earlier implementation of treatment such as ICD insertion to lower the risk of sudden cardiac death. A number of large, randomised, multicentre trials have conclusively demonstrated that ICDs reduce all cause mortality in patients with depressed left ventricular function

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when implanted late after an AMI.[7-11] The benefit appears to be less marked if the ICD is inserted early after the acute event.[12,13] Since the ICD is an expensive technology with associated risks of its own (such as risks of the initial implant, on-going risk of infection and risk of inappropriate shocks), the device should only be considered in the subset of patients deemed to be at greatest risk for sudden cardiac death. Current American and European guidelines recommend a central role for LVEF in determining which patients should be considered for ICD implantation (Table 2), in line with the use of this parameter (LVEF <30% to 40%) as an inclusion criteria in most of the large primary prevention ICD trials to date. In addition, some of the guidelines also recommend the use of invasive electrophysiological study to guide patient selection, based predominantly on data from the Multicenter Automatic Defibrillator Implantation Trial (MADIT)[7] and Multicenter UnSustained Tachycardia Trial (MUSTT).[9]

Unfortunately, there is considerable risk heterogeneity even among patients with low LVEF. Consequently, patients with a solely depressed LVEF and no other risk factors for sudden cardiac death may have a relatively lower mortality risk compared to those with multiple risk factors.[14] There is thus a need for improved methods of risk stratifying which patients are at greatest risk for sudden cardiac death after an AMI.

Assessment of Left Ventricular Function

The degree of left ventricular dysfunction is an important and widely used parameter to risk stratify patients postAMI, since mortality and re-infarction rates have been shown to be inversely related to LVEF in several large studies.[3,4,15] However, assessment of LVEF in isolation after AMI can be misleading due to the presence of myocardial stunning and potential for improvement with appropriate medication and revascularisation. Left ventricular end-systolic volume (LVESV) or left ventricular end-diastolic volume (LVEDV) may be more meaningful predictors of prognosis than LVEF. White et al[16] found that LVESV was a major determinant of survival after AMI in a group of 605 patients and was superior to LVEF in patients with depressed LVEF <50%. Other echocardiographic parameters, such as wall motion score index and assessment of diastolic function, can also be used to provide prognostic information postAMI.[4] Recent advances in imaging technology have allowed for the prognostic role of newer echocardiographic techniques, which can discriminate between active and passive myocardial contraction, to be assessed.[4,17] These include measurements of strain (a reflection of tissue deformation) and strain rate (tissue deformation per time period) using speckle-tracking imaging or tissue Doppler imaging.

Although significant left ventricular dysfunction following AMI can provide the myocardial substrate for the development of ventricular arrhythmias, assessment of LVEF alone is probably insufficient in determining arrhythmic risk among AMI survivors.[14] Since the risk of sudden cardiac death is determined by a variety of factors, as highlighted in Table 1, it is likely that a variety of investigations providing information on different aspects of cardiovascular pathophysiology postAMI are required for clinicians to accurately risk stratify patients.

The 12-lead ECG

A number of parameters on the conventional 12-lead ECG have been demonstrated to give important prognostic information in patients following an AMI. These include the presence of bundle branch block, QRS duration, left ventricular hypertrophy (LVH) and QT dispersion.[3,18,19] Many of these parameters are likely to represent more advanced degrees of ventricular dysfunction following an AMI, which itself is a cause for increased mortality, rather than a specific increase in risk for VT/VF. For example, the MUSTT investigators found that left bundle branch block and non-specific intraventricular conduction delay (IVCD) were associated with increased total mortality risk, although there was no significant link between bundle branch block and inducible monomorphic VT.[20] In the PainFree RX II trial, QRS duration did not predict the delivery of appropriate therapies for VT/VF in 431 patients with coronary artery disease who received an ICD for either primary or secondary

Table 1. Patient- and Cardiac-related Factors that are Independently Predictive of Increased Mortality Following Acute Myocardial Infarction

Patient characteristics	• Age
	• Female gender
	• Prior myocardial infarction
	• Smoking
	• Diabetes
	• Hypertension
	• History of cerebrovascular disease
	• Depression
Cardiac parameters	• Left ventricular ejection fraction
	• Presence of congestive heart failure
	• Presence of mitral regurgitation
	• Infarct size
	• Infarct location (anterior and right ventricular infarcts are worse)
	• Coronary artery anatomy (left main stem and multi-vessel disease are worse)
	• Atrial fibrillation
	• Presence of bundle branch block
	• High-grade atrioventricular block

prevention.[21] In addition, parameters such as QT dispersion vary widely between individuals and there is considerable overlap in QT dispersion values between healthy subjects and cardiac patients as well as between cardiac patients with and without ventricular arrhythmias.[18] As such, the use individual ECG parameters in deciding which patients postAMI should receive an ICD is limited.

The presence of a fragmented QRS complex (fQRS) on the routine 12-lead ECG has recently been described as a marker of abnormal ventricular depolarisation and demonstrated to be a predictor of mortality and sudden cardiac death.[22] Fragmented QRS complexes include various RSR' patterns, with or without QRS duration <120 ms and probably represents conduction delay caused by myocardial scar in patients with ischaemic heart disease. fQRS is a simple, inexpensive and easily accessible ECG sign that may be of value in determining the risk for sudden cardiac death and guiding prophylactic ICD insertion in AMI survivors. However, a greater understanding of the significance and relevance of this non-specific finding is required before it can routinely be adopted into clinical practice.

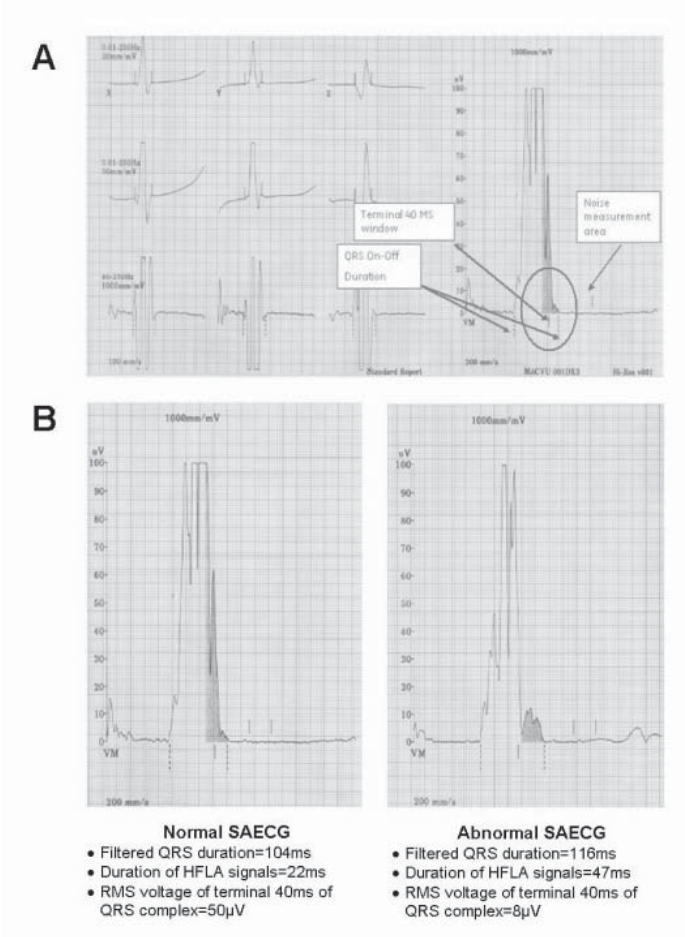

Fig. 1. Sample signal averaged ECG (SAECG) traces.
A. Measurements taken from SAECG obtained from averaging 253 beats. B. Examples of a normal and abnormal SAECG. A SAECG is considered to be abnormal when at least 2 of the following 3 parameters are present: duration of filtered QRS complex >114 ms, duration of high frequency low amplitude (HFLA) potentials of the terminal portion of the filtered QRS complex >38 ms and root mean square (RMS) of the terminal 40 ms of the filtered QRS complex <20 μV. Note the increased duration of the HFLA potentials and reduced RMS voltage of the terminal 40 ms of the QRS complex in the abnormal case.

Signal-averaged Electrocardiography

The signal-averaged electrocardiogram (SAECG) compares and averages consecutive QRS complexes (usually around 300) to produce a filtered QRS complex that provides information on the presence of ventricular late potentials (VLPs). An example of a normal and abnormal SAECG is shown in Figure 1, with the generally accepted cut-off values. VLPs represent slowed conduction through a diseased myocardium, which may serve as a substrate for subsequent ventricular arrhythmias, and have been documented in 25% to 50% of patients soon after an AMI.[23] A number of studies conducted in the pre-thrombolysis and thrombolysis eras demonstrated that the SAECG can be predictive of arrhythmic events and sudden cardiac death in patients following AMI.[23-26] Kuchar et al[25] prospectively assessed 165 patients following an AMI and showed that the pre-discharge SAECG was highly predictive of arrhythmic events after a median follow-up of 11 months. Similarly, Steinberg et al[26] found that the SAECG in 182 consecutive patients postAMI was an independent predictor of sudden cardiac death during a 14-month follow-up. However, although the negative predictive value (NPV) of SAECG is high (>95%), the positive predictive accuracy is much lower, thus decreasing its usefulness as a single variable to identify high-risk patients.[25,26] The CABG Patch Trial was an important negative study in which SAECG appeared to be unhelpful in identifying a high-risk group of patients.[27] In this study, 900 patients with LVEF <36% and abnormalities on SAECG were randomly assigned to receive a prophylactic ICD at the time of coronary artery bypass surgery or to a control group. The investigators found no significant difference in survival between the 2 groups during an average follow-up of 32 ± 16 months. One explanation for this negative finding is that patients recruited in this study (on the basis of LVEF and SAECG abnormalities) were at lower risk of ventricular arrhythmias compared with those recruited in earlier primary prevention studies, such as MADIT, in which subjects had similar degrees of LV dysfunction (≤35%) and ventricular arrhythmias at electrophysiological testing or documented asymptomatic non-sustained VT.[7]

With the increasing use of primary percutaneous coronary intervention (PCI) in the treatment of AMI, the prognostic value of the SAECG has become less clear. Bauer et al[28] performed SAECGs in 968 patients following AMI, 91% of whom underwent PCI, and found that the presence of VLPs was not significantly associated with cardiac death

or a serious arrhythmic event during a median follow-up of 34 months. Ikeda et al[29] also found that VLPs had no significant prognostic role in predicting the primary outcome of death or resuscitated cardiac arrest when measured in 627 patients postAMI (82% underwent PCI), although the follow-up was short (3 to 6 months) in this study.

The value of the SAECG in risk stratification postAMI may be increased when it is used in combination with other tests to further refine risk in patients already deemed to be at higher risk, such as those with decreased LVEF. Gomes et al[30] demonstrated that the combination of an abnormal SAECG and LVEF <30% in 1268 patients with coronary artery disease and non-sustained VT identified a particularly high-risk subset of patients which represented 21% of the total population. In this group, 36% and 44% succumbed to arrhythmic and cardiac death, respectively. Other investigators have demonstrated some value of combining the SAECG with Holter analysis or nuclear imaging to improve risk prediction.[26,31,32]

Holter Analysis

Detection of Ventricular Arrhythmias

Early studies on the use of ambulatory ECG-recordings (24-hr Holter monitoring) in the risk stratification of patients postAMI reported that the detection of ventricular arrhythmias, most often non-sustained VT or frequent premature ventricular complexes (PVCs), is predictive of serious arrhythmic events and death.[33-36] A more recent study conducted in the modern era of interventional cardiology demonstrated that non-sustained VT remained an independent predictor of sudden cardiac death in 2130 patients following AMI after adjusting for age, diabetes and LVEF and was especially useful in patients with LVEF >35%.[37] However, the sole use of conventional 24-hr Holter monitoring for prediction of ventricular arrhythmias is significantly limited by its low sensitivity and specificity. Recent advances in Holter-based technology have made it possible for additional parameters to be obtained from ambulatory ECG-recordings which appear to be useful in identifying the high risk patient postAMI. These parameters, such as heart rate variability and heart rate turbulence, represent changes in cardiac autonomic tone which occur following AMI. There is strong evidence linking changes in the autonomic nervous system with sudden cardiac death-increased sympathetic activity favours the development of cardiac arrhythmias, while increased vagal tone appears to be protective.[38-42]

Heart Rate Variability

Heart rate variability (HRV) can be assessed using various methods by measuring ECG recordings over a short (2 to 30 min) or longer (24 h) periods. HRV decreases early after AMI and begins to increase towards normal within 6 to 12 weeks.[41,43] Measurements of HRV can be expressed as the standard deviation of all normal RR intervals (SDNN) using time-domain analysis or by the power or amplitude of the oscillations of RR intervals over specific frequency cycles, using frequency-domain analysis. An example of a normal and abnormal 24-hr HRV time domain-analysis is shown in Figure 2. Evidence suggests that decreased HRV is associated with increased ventricular arrhythmias and mortality.[36,42] In the Multicenter Postinfarction Study (MPS), involving 808 AMI survivors, Kleiger et al[39] reported that patients with SDNN of <50 ms obtained from pre-discharge 24-hr Holter recording had increased 1-year mortality (independently of LV function) compared with patients with SDNN between 50 and 100 ms and those with SDNN >100 ms. However, HRV is also influenced by other variables such as age, gender and certain medication (e.g. thrombolysis, antiarrhythmic drugs, β-blockers and ACE inhibitors)[36,44-46] and varies according to sinus node function.[18] This, and the fact that HRV cannot be evaluated in patients with atrial fibrillation or frequent arrhythmias, has limited its use as a sole determinant of increased risk in the postAMI patient. More recent studies using additional software have shown that other indices of HRV, such as deceleration capacity, may be stronger predictors of mortality following AMI than traditional measures of HRV or even LVEF.[47,48]

Heart Rate Turbulence

Heart rate turbulence (HRT) is a more recently described parameter measured from Holter analysis that appears

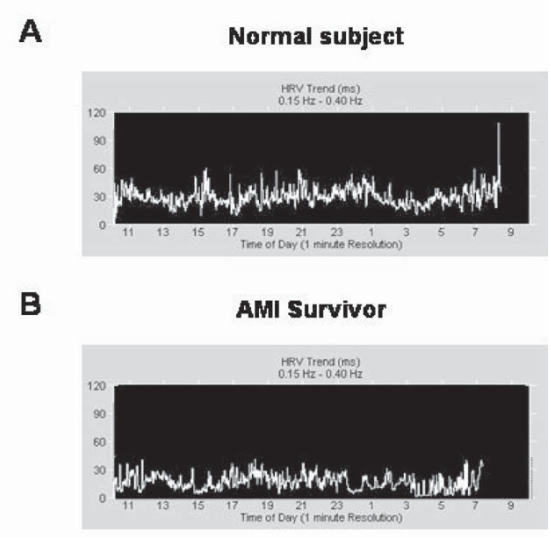

Fig. 2. Sample traces of heart rate variability (HRV) trends over a 24-hr period from continuous Holter recording in a normal subject (A) and in a patient following acute myocardial infarction, AMI (B).
The standard deviation of all normal RR intervals (SDNN) assessed using time-domain analysis measured 204 ms and 41 ms for subjects A and B, respectively. A SDNN<50 ms is considered abnormal and indicative of a worse prognosis.

to have a useful role in risk stratification.[49,50] HRT is a measure of fluctuations in sinus rhythm (SR) cycle length following a single PVC. In normal and low-risk patients, there is a characteristic acceleration followed by a subsequent deceleration in SR cycle length after a PVC – this pattern is not present in high-risk patients. Several large-scale retrospective and prospective studies have provided strong evidence that HRT is a powerful independent predictor of risk following AMI.[37, 49,51,52] The REFINE study (Noninvasive Risk Assessment Early After a Myocardial Infarction) investigators performed a number of autonomic function tests, including measurements of HRT, in 322 patients with LVEF <50% postAMI and demonstrated that these tests could reliably identify those at high risk of serious cardiac events.[52] Interestingly, they found that the time at which the tests were performed postAMI was important – performing the tests at 10 to 14 weeks, but not 2 to 4 weeks, postMI was predictive of mortality and sudden cardiac death. Another recent prospective study involving 2343 survivors of AMI found that the combination of HRT and deceleration capacity could be used together to identify a high-risk group equivalent in size and mortality to patients with LVEF<30%.[53] In contrast, in a retrospective analysis of 884 patients enrolled in the MADIT II study, HRT parameters were not found to be predictive of outcome, after adjustment for confounding covariates.[54] However, HRT parameters in this study were obtained from 10 minute ECG recordings, which may have limited the ability to derive accurate HRT data.

Other Measurements from Holter Analysis

The value of other Holter-based parameters in risk prediction has also been assessed and some of the initial results appear promising. These include measurements of Holter-derived T-wave variability and QT dynamics, both of which are markers of repolarisation abnormalities.[55,56]

T-Wave Alternans

Electrical alternans of the T-wave (i.e. alternating amplitude from beat to beat) on the ECG is thought to be due to dispersion of repolarisation and has been demonstrated to be associated with life-threatening ventricular arrhythmias. Recent advances in technology have allowed for the assessment T-wave alternans during exercise (microvolt T-wave alternans, MTWA) using fast Fourier transform spectral analysis or during ambulatory Holter-based recordings (modified moving average analysis).[57,58] A number of studies have shown that measurements of T-wave alternans may be predictive of arrhythmic events and mortality in patients with ischaemic heart disease.[59-61] Rosenbaum et al. first showed that MTWA detected during atrial pacing (over a range 95 to 150 beats/min) was an independent predictor of inducible sustained VT.[62] Since then, MTWA has been demonstrated by other investigators to be a powerful predictor of life-threatening arrhythmias and sudden cardiac death in patients postAMI, both with and without depressed LV function.[29,63-65] MTWA appears to be a better risk predictor when compared with SAECG[66, 67] and may be even more powerful when combined with LVEF and invasive electrophysiological testing.[68] In a recent prospective multicentre study involving 575 patients, Chow et al[69] found that MTWA testing in patients with ischaemic heart disease and LVEF<30% who already qualified for an ICD did not predict subsequent ventricular arrhythmic events, although MTWA non-negative patients (i.e. positive and indeterminate MTWA results) had significantly higher mortality compared with MTWA negative patients. The

Table 2. American and European Guidelines for ICD Insertion for Primary Prevention of Sudden Cardiac Death in Patients with Prior Myocardial Infarction.

Guidelines	Patients for which ICD is recommended	Class of recommendation (Level of evidence)
2002 ACC/AHA/NASPE guidelines for implantation of cardiac pacemakers and anti-arrhythmia devices	LVEF ≤30%, NYHA II, III LVEF 30-40%, NSVT, +ve EP study	IIa (B) IIb (B)
2004 ACC/AHA guidelines for the management of patients with STEMI	LVEF ≤30%, NYHA II, III LVEF 30-40%, NSVT, +ve EP study	IIa (B) I (B)
2005 ESC guidelines for the diagnosis and treatment of chronic heart failure	LVEF ≤30%, NYHA II, III LVEF 30-35%, NYHA II, III	I (A) I (A)
2005 ACC/AHA guidelines for the diagnosis and management of chronic heart failure in the adult	LVEF ≤30%, NYHA II, III LVEF 30-35%, NYHA II, III LVEF ≤30%, NYHA I	I (B) IIa (B) IIa (B)

The above guidelines relate to the primary prevention of sudden cardiac death in patients with prior myocardial infarction; recommendations for ICD insertion in patients with non-ischaemic cardiomyopathy or for secondary prevention are not covered in this table.

AHA: American Heart Association; ACC: American College of Cardiology; NASPE: North American Society of Pacing and Electrophysiology; ESC: European Society of Cardiology; LVEF: left ventricular ejection fraction; NSVT: non-sustained ventricular tachycardia; NYHA: New York Heart Association functional class; STEMI: ST-elevation myocardial infarction

Table 3. Summary of the Advantages and Disadvantages/ Limitations of the Current Methods Available for Arrhythmic Risk Prediction in Patients PostAMI

Risk stratification method	Relevant studies referenced in this review	Advantages	Disadvantages/ limitations	Comments
Echocardiography	• Greenberg et al, 1984[15] • White et al, 1987[16] • Mollema et al, 2007[17] • Buxton et al. 2007[14]	• Available in almost all hospitals • Routinely performed in patients postAMI • Provides additional information (e.g. valvular function) • Cut-off values for ICD insertion stated in guidelines	• LVEF is an indicator of increased mortality, rather than SCD- therefore there are limitations to its use in guiding ICD insertion • Majority of patients who die suddenly have LVEF >40% • LVEF may improve with time (with medication or revascularisation)	• Assessment of LVEF remains essential in risk stratification, in line with current guidelines • Can be used to initially select which patients to perform further risk stratification on
12-lead ECG	• Malik et al, 2000[19] • Lanza 2007[18] • Zimetbaum et al, 2004[20] • Buxton et al, 2005[21] • Das et al, 2007[22]	• Cheap, quick and easy to perform • Can be obtained serially at each follow-up visit to reassess risk • Large databases can be generated and analysed retrospectively/ prospectively	• Many abnormal parameters are markers of increased mortality, rather than specifically SCD • Low positive predictive and negative predictive accuracies • Subject to inter-observer variability (unless automated software is used) • Considerable overlap in some parameters between healthy subjects and patients	• Remains a standard investigation in patients with CAD • Low positive and negative predictive accuracies for SCD limit its use in risk stratification
Signal averaged ECG	• Grimm et al, 1988[23] • Hartikainen et al, 1996[24] • Kuchar et al, 1986 [25] • Steinberg et al, 1992[26] • Bigger et al, 1997[27] • Bauer et al, 2005[28]	• Easy and quick to perform • High negative predictive accuracy • Can be used in patients with AF	• Low positive predictive accuracy • Numerous negative studies, especially in current era of interventional cardiology • Better at predicting risk of VT than VF • Normal standards for patients with bundle branch block or paced rhythm have not been established	• Improved risk stratification when used in combination with other tests • Probably more useful in identifying low risk patients
Standard 24hr Holter	• Bigger et al, 1984[33] • Kostis et al, 1987[34] • Maggioni et al, 1993[35] • Farrell et al, 1991[36] • Makikallio et al, 2005[37]	• Provides information on other arrhythmias postAMI (e.g. AF, heart block) • Standard test, easy to perform • Can be used in patients in AF or paced rhythms	• Low sensitivity and specificity	• Most promising use is in combination with other parameters (e.g. HRV and HRT) obtained from Holter recordings

AF: atrial fibrillation; AMI: acute myocardial infarction; CAD: coronary artery disease; ICD: implantable cardioverter defibrillator; HRT: heart rate turbulence; HRV: heart rate variability; LVEF: left ventricular ejection fraction; PVC: premature ventricular complex; SCD: sudden cardiac death; SR: sinus rhythm; VT/VF: ventricular tachycardia/ fibrillation

Table 3. Contd.

Risk stratification method	Relevant studies referenced in this review	Advantages	Disadvantages/limitations	Comments
Heart rate variability	• Farrell et al, 1991[36] • La Rovere et al, 1998[42] • Kleiger et al, 1987[39] • Bauer et al, 2006[48]	• Can be automatically recorded with standard Holter (using additional software) • Short (2-30mins) and longer (24hrs) measurements are possible	• Cannot be reliably assessed in patients with AF or frequent PVCs • Influenced by a number of factors (e.g. age, gender medication) • May be affected by functional state of sinus node • Short-term measurements in risk prediction have not been well tested • No concensus on which parameters of HRV or method of assessment is best	• A consensus opinion on which parameters of HRV to record and which method of assessing HRV is required
Heart rate turbulence	• Schmidt et al, 1999[49] • Ghuran et al, 2002[51] • Makikallio et al, 2005[37] • Exner et al, 2007[52] • Bauer et al, 2009[53] • Berkowitsch et al, 2004[54]	• Value in risk prediction supported by several recent large-scale prospective studies • Provides prognostic information in patients with normal and impaired LVEF	• Optimal time postAMI to perform the test has not been established • Can only be performed in patients in SR with a significant number of PVCs	• A promising test for risk prediction that can be used with other Holter-based measurements • More information is required on when is the optimal time to perform the test
T wave alternans	• Ikeda et al, 2002[29] • Verrier et al, 2003[59] • Bloomfield et al, 2004[64] • Ikeda et al, 2006 • Stein et al, 2008[60] • Chow et al, 2008[69] • Slawnwych et al, 2009[61] • Constantini et al, 2009[70]	• Easy to perform in postAMI patient • Can use existing equipment or modification of equipment • High negative predictive accuracy	• Can only be used in patients in SR • “Clean” ECG trace required (difficult to obtain during exercise) • Indeterminate result if target heart rate not achieved during exercise • Low positive predictive accuracy	• Useful in risk stratifying patients with impaired and preserved LVEF • Useful role in determining which patients are unlikely to benefit from ICD insertion • Improved risk stratification when used in combination with other tests
Invasive electrophysiological study	• Wellens et al 1997[71] • Peterson et al 1997[72] • Bourke et al, 1995[73] • Roy et al, 1985[74] • Huikuir et al, 2009[77]	• Can be performed in patients with atrial arrhythmias and paced rhythm • Easily measured end-point	• Invasive • Relatively costly • Requires specialised equipment and trained staff to perform • Varying protocol between different electrophysiologists • Conflicting data on its value in the literature	• In view of the invasive nature of the test, its most likely use is in combination with other non-invasive tests to help refine risk in high-risk patients
Cardiac magnetic resonance	• Yan et al, 2006[78] • Schmidt et al, 2007[79] • Roes et al, 2009[80]	• Provides additional anatomical information (e.g. accurate assessment of LV function)	• Relatively more costly than other non-invasive tests • Requires hospital to have a MRI scanner • Relatively longer to analyse results • Cannot be performed in patients with ICDs	• Good potential for use in this field • Only imaging technique to date to provide information on arrhythmic risk • Larger, prospective studies are required

value of MTWA in risk stratification may actually be in deciding which patients are least likely to benefit from ICD insertion, as suggested by the ABCD (Alternans Before Cardioverter Defibillator) trial.[70] This prospective, multi-centre study was the first to use MTWA to guide prophylactic ICD insertion. The investigators demonstrated that MTWA achieved one-year positive and negative predictive values of 9% and 95%, respectively and that its use in risk stratification was comparable to invasive electrophysiological study at 1 year and complementary when applied in combination.

Invasive Electrophysiological Study

The idea of performing programmed ventricular stimulation or electrophysiological (EP) testing in AMI survivors is to investigate the ability of the diseased myocardium to sustain re-entrant ventricular arrhythmias, which can degenerate into VF and cause sudden death. Early studies on the use of EP testing to risk stratify patients postAMI reported conflicting data with nearly half of all studies finding that the inducibility of sustained VT was unhelpful in predicting later mortality or arrhythmic events.[71,72] The apparent confusion in the literature is probably related to differences in patient population, stimulation protocols and time intervals between AMI and EP testing. For example, Bourke et al[73] performed EP testing in 502 patients 11 ± 4 days after AMI using a protocol containing 4 extrastimuli from the right ventricular apex only and demonstrated that the induction of sustained monomorphic VT with a cycle length >230 ms was an indicator of electrical instability and a poorer prognosis. In contrast, Roy et al[74] performed EP testing in 150 survivors of AMI 12 ± 2 days following the acute event using a protocol consisting of up to 3 extrastimuli from the right ventricular apex and right ventricular outflow tract. During a mean follow-up of 10 ± 5 months, they found no significant difference in outcome between patients with and without inducible ventricular arrhythmias during EP testing.

Despite the invasive nature of EP testing and the requirement for specialist equipment and personnel, it is still recommended in some of the current guidelines on the selection of candidates with ischaemic heart disease and reduced LVEF for prophylactic ICD insertion (Table 2). These recommendations are predominantly based on data from the MADIT and MUSTT studies. The future role of EP testing in risk prediction may lie in its combined use with other non-invasive tests, such as MTWA and HRV, to further refine the selection of potential ICD recipients.[70,75-77]

Role of Cardiac Magnetic Resonance

In recent years, the use of cardiac MRI in assessing myocardial scar burden among AMI survivors and predicting mortality and arrhythmic events has been explored. Yan et al[78] were the first to demonstrate that quantification of the peri-infarct zone by contrast-enhanced cardiac magnetic resonance (CMR) is an independent predictor of mortality following AMI. A number of other investigators have since demonstrated that tissue heterogeneity in the peri-infarct zone, as detected by contrast-enhanced CMR, is likely to signify a pro-arrhythmic substrate and is one of the strongest predictors of ventricular arrhythmias and appropriate ICD therapies.[79,80] These pioneering studies have opened up the field to additional imaging based methods for arrhythmic risk stratification of AMI-survivors and pave the way for larger, prospective, multicentre studies using these techniques.

Conclusions

A wide variety of factors affect the prognosis of AMI survivors. Assessment of the degree of left ventricular dysfunction, with or without invasive EP testing, remains the key investigation in determining which patients should be offered an ICD, as recommended by current international guidelines. Although not yet reflected in current guidelines, a number of non-invasive cardiovascular investigations can provide additional information which may prove useful to clinicians in deciding which patients are at greatest risk of developing malignant ventricular arrhythmias following AMI. Many studies to date have provided evidence in support of a role for each of these tests individually or in combination in the risk stratification of AMI survivors. The pros and cons of each of these tests and relevant studies referred to in this review are summarised in Table 3. A number of unanswered questions remain, such as when is the best time to perform the tests, how often should the tests be repeated and which criteria should be taken to signify an abnormal result. Future prospective, multicentre studies are required to correlate use of these tests or combination of tests with outcome before they can be universally adopted and their use reflected in guidelines. With improvements in technology and more patients surviving AMI, it is likely to be only a matter of time before additional cardiovascular investigations are routinely used in the risk stratification of patients postAMI for sudden cardiac death. However, until such data is available, clinicians should follow current recommendations in deciding which patients postAMI should be offered an ICD.

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