Post-myocardial Infarction Tachyarrhythmia:
Drugs or Devices

Abstract: Tachyarrhythmia are common in post myocardial infarction (MI) patients. Control of arrhythmia is important for improving quality of life and survival. Among the post-MI tachyarrhythmia, ventricular tachyarrhythmia and atrial fibrillation influence the survival most.

Drugs for Tachyarrhythmias: Class II agents (β-blockers) such as timolol, propranolol and metoprolol have been shown to reduce overall mortality, sudden death and reinfarction rate in post-MI patients. The greatest mortality benefit is seen in patients with the greatest baseline risk: those with impaired ventricular function or ventricular arrhythmias and those who do not undergo reperfusion. In the presence of sustained or non-sustained ventricular tachyarrhythmia and with a history of resuscitated arrest, class III agents however have been shown to be inferior to Automatic Implantable Cardioverter Defibrillator (AICD).

Aspirin, Clopidogrel, ACEI, Statins, PUFA reduce arrhythmic deaths by reducing the ischemic events.

Tachyarrhythmias: Implantable cardioverter defibrillators (AICDs) reduce mortality compared with medical therapy when used for primary or secondary prevention of sudden cardiac death. Mortality was reduced by 54% versus medical therapy when AICDs were used for primary prevention in patients with non-sustained ventricular tachyarrhythmias, previous MI and left ventricular dysfunction and inducible, nonsuppressible ventricular tachyarrhythmia on electrophysiological testing.

Several large, randomized and controlled trials have demonstrated the effectiveness of cardiac resynchronization therapy (CRT) in post MI patients with heart failure and intra ventricular conduction delays represented by wide QRS during sinus rhythm. Effectiveness of CRT is due to ventricular reverse remodeling resulting in improved symptoms as well as reduction in morbidity and mortality.

Devices (CRT-D) that are capable of achieving cardiac resynchronization as well as functioning like AICD have been found to improve survival and prevent sudden deaths significantly.

Ventricular tachyarrhythmia and AF complicating post MI phase indicate poor prognosis. Anti arrhythmic drugs have limited role in the management of ventricular tachyarrhythmia. Devices like AICD and CRT when indicated improve significantly the quality of life and survival. Post MI patients without LV dysfunction who have AF can be treated with rate limiting drugs alone. Patients with LV dysfunction should be considered for rhythm restoration with either drugs and/or ablation procedures. In resistant cases of post MI tachyarrhythmia a multidisciplinary approach, which can provide pharmacotherapy, revascularization therapy, device and ablation therapy has to be resorted.

INTRODUCTION

Tachyarrhythmia are common in post- myocardial infarction (MI) patients. Control of arrhythmia is important for improving quality of life and survival. Among the post-MI tachyarrhythmias, ventricular tachyarrhythmia and atrial fibrillation influence the survival most. In general, measures to prevent recurrence of coronary events and ventricular remodeling are helpful in reducing these tachyarrhythmia. In addition, anti-arrhythmic therapy has a specific role in the management. This article discusses various options to prevent and treat such arrhythmias based on current guidelines.

POST- MYOCARDIAL INFARCTION VENTRICULAR TACHYARRHYTHMIA
Antiarrhythmic Drugs

Identifying the most suitable antiarrhythmic therapy has been the subject of much research, as available agents differ considerably in their mode of action.1-4

No Role for Class I Agents

Several meta-analyses have been conducted on studies reporting mortality data with the use of various Vaughan-Williams class I antiarrhythmic agents after MI. Results indicate that empiric antiarrhythmic therapy with these agents (e.g. mexiletine, phenytoin, tocainide, flecainide, encainide, procainamide, moricizine) is not beneficial and is probably harmful, despite effective suppression of VPBs.5

Class II Agents Reduce Mortality

Class II agents (β-blockers) such as timolol, propranolol and metoprolol have been shown to reduce overall mortality, sudden death and reinfarction rate in post-MI patients. If started promptly after MI, they also reduce the infarct size and recurrent ischemia. Propranolol and metoprolol were associated with mortality reductions of 26 and 36%, respectively.2,6,7 Early treatment with β-blockers should be started in all patients surviving MI and continued indefinitely unless there are contraindications. Low EF not accompanied by clinical symptoms of heart failure does not represent a contraindication to β-blockers. In fact the greatest mortality benefit is seen in patients with the greatest baseline risk; those with impaired ventricular function or ventricular arrhythmias and those who do not undergo reperfusion.

Although relative contraindications may once have been thought to preclude the use of β-blockers in some patients, evidence now suggests that the benefits of β-blockers in reducing reinfarctions and mortality may actually outweigh the risks, even in patients with mild asthma not currently active, insulin-dependent diabetes mellitus, chronic obstructive pulmonary disease, severe peripheral vascular disease, PR interval greater than 0.24 seconds, and moderate LV failure.

Class III Agents Not Generally Beneficial

Sotalol is effective in preventing recurrent arrhythmia and reducing death from arrhythmia. Its benefits may be related to β-blocking activity of this racemic drug. d-sotalol, the dextrorotatory isomer of sotalol, lacks β-blocking activity and was found to increase mortality.8

Amiodarone reduced the risk of arrhythmic deaths but did not appear to decrease the overall mortality in patients at high risk for cardiac arrhythmias in two large trials.9,10 However, the results of these trials, which were designed to show a significant difference, indicates that amiodarone cannot be recommended for prophylactic use in post-MI patients routinely. In patients with symptomatic non-sustained ventricular tachyarrhythmia without the history of cardiac arrest, amiodarone can be prescribed. In the presence of sustained or non-sustained ventricular tachyarrhythmia, and with a history of resuscitated arrest, class III agents, however, have been shown to be inferior to automatic implantable cardioverter defibrillator (AICD).

Class IV Drugs Do Not Reduce Mortality

A meta-analysis of data from 19,000 patients showed that, in general, treatment with class IV agents (calcium antagonists) does not lower mortality in post-MI patients. In the management of post-MI ventricular tachyarrhythmia these drugs have no role.2,11

NON-ANTIARRHYTHMIC DRUGS FOR VENTRICULAR ARRHYTHMIA PREVENTION
Antiplatelet and Antithrombin Drugs

On the basis of 12 randomized trials in 18,788 patients with prior infarction, the antiplatelet trialists collaboration reported a 25% reduction in the risk of recurrent infarction, stroke, all causes death when daily doses of aspirin between 80 and 325 mg was prescribed for indefinite period of time. These compelling data suggest that all patients recovering from MI should, in the absence of contraindications, continue taking aspirin for an indefinite period. Clopidogrel or ticlopidine may be substituted in patients with true aspirin allergy. Chronic therapy with warfarin after MI presents an alternative to clopidogrel in patients with aspirin allergy.\textsuperscript{2,12,13}

Angiotensin Converting Enzyme Inhibitors and Angiotensin Receptor Blockers

Angiotensin converting enzyme (ACE) inhibitors should be prescribed at discharge for all patients without contraindications after MI. Long-term aldosterone blockade should be prescribed in patients without significant renal dysfunction who are already receiving therapeutic doses of an ACE inhibitor, have an LVEF less than or equal to 0.40, and have either symptomatic heart failure or diabetes. The clinical result is a lessened likelihood for development of CHF, recurrent MI, and death.\textsuperscript{2,14} The angiotensin receptor blockers (ARB), valsartan and candesartan, should be administered over the long-term to post-MI patients with symptomatic heart failure who are intolerant of ACE inhibitors. The choice between an ACE inhibitor and an ARB in patients who are tolerant of ACE inhibitors over the long-term will vary with individual physician and patient preference, as well as cost and anticipated side effect profile. The combination of an ACE inhibitor and an ARB or an ACE inhibitor and an aldosterone antagonist may be considered for the long-term management of post-MI patients with symptomatic heart failure and ejection fraction less than 0.40 and no renal dysfunction.

Aldosterone Antagonist

Aldosterone blockade is another means of inhibiting the renin-angiotensin-aldosterone system that has been applied to patients in the post-STEMI setting. Trials support the long-term use of an aldosterone blocker in post-MI patients with heart failure, an ejection fraction of 0.40 or less, and normal renal function.\textsuperscript{2,15}

HMG CoA-Reductase Inhibitors (Statins)

Large amount of data support the early, intensive treatment of patients with acute coronary syndromes to LDL-C goals substantially less than 100 mg/dL with statin therapy to achieve significant reduction in coronary events and overall mortality. The antiarrhythmic efficacy of statins has been attributed to their pleoptropic actions inclusive of anti-inflammatory and antioxidant actions.\textsuperscript{2}

Polyunsaturated Fatty Acid (PUFA)

Existing evidence suggests that an intake of polyunsaturated fatty acid (PUFA) (n-3) (about 1 g daily), in the form of supplements or, alternatively, by eating at least two large (about 200 g) servings of fatty fish per week helps to prevent sudden cardiac death. At present, there is no reason to encourage (or prescribe) a consumption of much more than 1 to 2 g of PUFA (n-3) per day. The dosage to be recommended in high-risk patients and in the secondary prevention of sudden cardiac death warrants further investigation.\textsuperscript{16}

DEVICES FOR VENTRICULAR ARRHYTHMIA
Automatic Implantable Cardioverter Defibrillator

Automatic implantable cardioverter defibrillators (AICDs) reduce mortality compared with medical therapy when used for primary or secondary prevention of sudden cardiac death. Mortality was reduced by 54% versus medical therapy when AICDs were used for primary prevention in patients with non-sustained ventricular tachyarrhythmias, previous MI and left ventricular dysfunction and inducible, nonsuppressible ventricular tachyarrhythmia on electrophysiological testing.\textsuperscript{1,2,17}

When used as secondary prevention in patients surviving life-threatening ventricular arrhythmias, mortality reductions of 39, 27 and 31% at 1, 2 and 3 years, respectively, were seen versus class III agents. Thus, ICDs should be considered the first-line treatment for such patients. There is no evidence that AICD in the first month after MI, or in conjunction with routine coronary artery bypass grafting surgery reduces mortality in post-MI patients with left ventricular dysfunction. Absolute benefit from AICD is greatest in patients with spontaneous non-sustained ventricular tachyarrhythmia (VT) and inducible sustained VT more severely depressed ejection fraction (< 0.25) or more prolonged QRS complex (>120 ms).

Cardiac Resynchronization Therapy

Several large, randomized and controlled trials have demonstrated the effectiveness of cardiac resynchronization therapy (CRT) in post-MI patients with heart failure and intraventricular conduction delays represented by wide QRS during sinus rhythm. Effectiveness of CRT is due to ventricular reverse remodeling resulting in improved symptoms as well as reduction in morbidity and mortality.

Two trials—the Comparison of medical therapy, pacing, and defibrillation heart failure (COMPANION)\textsuperscript{18} and the cardiac resynchronization in heart failure (CARE-HF)\textsuperscript{19} trials support the hypothesis that long-term CRT decreases all causes of mortality and deaths due to ventricular arrhythmia in post-MI patients with intraventricular conduction delays.

Cardiac Resynchronization with Defibrillator Device

Devices (CRT-D) that are capable of achieving cardiac resynchronization as well as functioning like AICD have been found to improve the survival and prevent sudden deaths significantly. The CRT-D group of COMPANION trial demonstrated 40% reduction in the risk of death or hospitalization compared with optimal medical therapy group.\textsuperscript{18} The recently published SEARCH MI registry designed to enroll MADIT II like patients in Europe confirmed the benefits of AICD and CRT-D devices.\textsuperscript{20} The benefits were of similar magnitude as seen in MADIT II. Unselected clinical population in the SEARCH MI registry validates implantation of such devices in the real world practice. Patients meeting criteria for AICD implantation who have prolonged QRS duration, NYHA class III -IV symptoms should be considered for CRT-D therapy.

Wearable Automatic Defibrillator

The wearable automatic defibrillator is a vest like device worn under the clothing that continuously monitors heart rhythm and automatically delivers an electric shock when VF is detected. This device is worn continuously, except when the wearer is bathing. The wearable automatic defibrillator has been approved in the United States by the FDA for cardiac patients with a transient high-risk for VF such as those awaiting cardiac transplantation, those at very high-risk after a recent MI or an invasive cardiac procedure, or those requiring temporary removal of an infected implanted defibrillator.\textsuperscript{1,2}
Device Safety and Reliability

Generally, a recall is issued when the potential for risk associated with a device is identified. The recent recalls and advisories regarding ICD and CRT devices have raised many important issues for both physicians and their patients. As life-saving devices, ICDs should have the highest standards of reliability. Despite careful design and manufacturing, ICD and CRT devices have finite rates of component failures, as do all electronic devices. Device performance standards; regulatory oversight; information dissemination; and responsibilities of manufacturers, physicians, and regulatory agencies need critical evaluation to reduce the probability of such events in the future.21

Cost Effectiveness of Devices

Devices are expensive, costing Rs. 4-10 lakhs and hence are not affordable to significant number of our patients who need them. Several cost effectiveness analyses of AICD devices in the west have supported the notion that device therapies fall within the boundaries of what is considered as cost effective therapy.

Because the benefits, risks, and costs of devices are of more than minimal concern, the rational approach for the physician is to be mostly selective with the use of limited resources. The AICD should be used in patients who fit the profile of those enrolled in the trials and are at highest risk for sudden cardiac death without substantial co-morbid conditions. Optimal medical treatment is required in these patients. The results of CABG Patch22 and DINAMIT23 indicate that AICD therapy should not be used in patients with CAD and LV dysfunction after recent bypass surgery or in patients presenting with acute MI.

Risk Stratification

Identification of a patient who is at the highest risk for ventricular tachyarrhythmia and sudden death after MI increases the cost effectiveness of device therapy. At present, there is no system for accurately identifying such patients. Those with low EF, ventricular arrhythmia and recurrent ischemia are known to be at greatest risk. 24 hours Holter monitoring, QT dispersion, autonomic assessment and electrophysiological testing have not been found to be predictive when used alone, but are more sensitive and specific when used in combination.1,2

T wave Alternans

T-wave alternans (TWA) has recently gained attention as an effective tool to identify patients at both high and low risk for SCA.24 The TWA test measures beat-to-beat microvolt variations in the shape, amplitude, or timing of the T wave. It is a noninvasive, test that can be performed in a physician’s office with modifications to currently available exercise testing equipment. It has been shown to predict inducibility of ventricular arrhythmia in patients with prior episodes of sustained VT and has recently attracted interest as a risk-stratification tool. The test has a high negative predictive value, that is, a negative test result identifies a patient at very low risk of fatal SCA. Thus TWA may help physicians decide whether ICD therapy is appropriate for a particular patient. In general clinicians should continue to consider prophylactic ICD therapy for patients with LVEF ≤ 30%, provided they had an MI at least 40 days previously and are expected to survive for at least 1 year.

REVASCULARIZATION FOR VENTRICULAR ARRHYTHMIA

Retrospective studies have examined the effectiveness of revascularization in improving the survival and quality of life for post-MI patients who had sustained VT or who have been resuscitated from VF. In general revascularization alone does not prevent the occurrence of ventricular arrhythmias and sudden cardiac arrest (SCA).25
HYBRID THERAPY FOR VENTRICULAR ARRHYTHMIA

In addition to lifestyle modification, drugs to prevent future coronary events and promote positive remodeling it may be required to consider adjunctive revascularization procedures either by surgery or percutaneous methods and ventricular geometry restoration by surgical methods. In those patients who require frequent AICD therapies adjunctive catheter based radio frequency ablation of reentrant circuits due to myocardial scar has to be considered.1,2

POST-MI ATRIAL FIBRILLATION

Although atrial fibrillation (AF) is a common complication of ischemic heart disease, most of the studies of the management of AF have included patients with AF from other causes. The evidence base for the treatment of post-MI patients with AF is diluted by the inclusion of patients with other diseases.

DRUGS TO MAINTAIN SINUS RHYTHM

Both amiodarone and sotalol are effective in maintaining sinus rhythm. Evidence is limited due to the lack of specific reporting of post-MI sub-groups within trials. A pre-specified sub analyses of post-MI patients revealed no significant difference in the efficacy between these two agents for post-MI. Class IC drugs should not be used in post-MI patients, use of disopyramide, quinidine and procainamide should be limited and prescribed on individual basis.26

DRUGS TO CONTROL VENTRICULAR RATE

Rate control is the recommended strategy for the management of patients with well-tolerated AF. In randomized control trials of patients with well tolerated AF, rate control was superior to rhythm control in terms of morbidity and avoidance of hospitalization. There was no difference between the two strategies in the incidence of thromboembolism, congestive heart failure or mortality.27

Although there have been only few long-term studies, a meta-analysis has demonstrated that beta-blocker, calcium channel blocker (verapamil or diltiazem), digoxin and amiodarone are all capable of controlling ventricular rate in post-MI AF. There is no evidence, however, to show superiority of any individual drug over another. The choice of agents usually depends on clinical factors. In certain patients a combination of drugs may be required.28

RHYTHM CONTROL VERSUS HEART RATE CONTROL

In well-tolerated post-MI AF, as mentioned above there is no significant difference between these two strategies, as long as judicious anticoagulations to prevent thromboembolism in persuade in both the strategies and a close watch is maintained to identify occurrence of proarrhythmias.29

In patients with low EF, attempt should be made to maintain sinus rhythm.

NON-ANTIARRHYTHMIC DRUGS FOR ATRIAL FIBRILLATION

Angiotensin Converting Enzyme Inhibitors

Recent accumulating evidence suggests that suppression of the renin-angiotensin-aldosterone system has beneficial effects in the prevention of atrial tachyarrhythmias.1 Meta-analysis of the effect of ACE inhibitors or ARBs have reported relative risk reduction of around 40% for the incidence of AF in CHF patients, compared with non-significant reduction of 27% in post-MI patient.30
Aldosterone Antagonists

Two recent clinical trials established that the addition of aldosterone antagonists to standard CHF neurohormonal inhibitor therapy reduces sudden death mortality in patients with severe CHF or myocardial infarction with left ventricular dysfunction. The potential mechanisms involved in antiarrhythmic benefits of AB in CHF might be related to attenuation of structural and/or electrical remodeling by antagonizing deleterious effects of aldosterone excess. Alternatively, direct actions of aldosterone receptor antagonists on ion channels independent of and unrelated to their effects at mineralocorticoid receptors also might be involved in arrhythmia prevention.29

DEVICES FOR ATRIAL FIBRILLATION

Atrioventricular node ablation and permanent pacing improves heart rate control, ejection fraction, symptomatic and functional status and quality of life in patients with AF whose ventricular rate is uncontrolled and are on medical therapy. In those patients with low EF biventricular pacing by CRT has been shown to be superior to right ventricular pacing.29

HYBRID THERAPY FOR ATRIAL FIBRILLATION

In resistant cases of post-MI AF, in addition to antiarrhythmic and non-antiarrhythmic drugs it may be necessary to contemplate either catheter based or surgical based pulmonary vein isolation and to consider devices like CRT with or without AV node ablation.29

CONCLUSION

Ventricular tachyarrhythmia and AF complicating post-MI phase indicate poor prognosis. Antiarrhythmic drugs have limited role in the management of ventricular tachyarrhythmia. Devices like AICD and CRT when indicated improve significantly the quality of life and survival. Post-MI patients without LV dysfunction who have AF can be treated with rate limiting drugs alone. Those patients with LV dysfunction should be considered for rhythm restoration with either drugs and/or ablation procedures. Maintaining adequate anticoagulation however is the corner stone of AF management. In resistant cases of post-MI tachyarrhythmia a multidisciplinary approach which can provide pharmacotherapy, revascularization therapy, device and ablation therapy has to be resorted.

REFERENCES


20. Survey to Evaluate Arrhythmia Rate in So-called High-risk Myocardial Infarction (SEARCH-MI). Presented by Boriani G on behalf of the SEARCH-MI investigators at European Society of Cardiology Congress 2007; September 2, 2007; Vienna, Austria.


MULTIPLE CHOICE QUESTIONS

1. Primary prevention of sudden cardiac death include:
   A. Patients who have LV dysfunction  
   B. Patients who have MI  
   C. Patients who have VT  
   D. Patients who never had syncope or cardiac arrest

2. Secondary prevention of sudden cardiac death include:
   A. Patients who have LV dysfunction  
   B. Patients who have MI  
   C. Patients who have VT  
   D. Patients who have had syncope or cardiac arrest

3. Agent/s useful in the management of ventricular arrhythmia:
   A. Aspirin  
   B. ACE I  
   C. Statins  
   D. All the above

4. Preferred drug for post-MI VT:
   A. Encainide  
   B. Flecainide  
   C. Morcizin  
   D. None of the above

5. AICD for primary prevention of sudden cardiac death can be considered when:
   A. At least 40 days post-MI  
   B. At least 3 months post-MI  
   C. At least 6 months post-MI  
   D. None of the above

6. With CABG, AICD may be considered:
   A. At the time of surgery  
   B. At the time of discharge  
   C. At least 3 months after surgery  
   D. None of the above

7. Following Vaughn Williams group of drugs is contraindicated in the management of post- MI tachyarrhythmia:
   A. Class IC  
   B. Class II  
   C. Class III  
   D. Class IV

8. Cornerstone of post-MI AF therapy:
   A. Rate control  
   B. Rhythm control  
   C. Anticoagulation  
   D. None of the above

9. Candidate for CRT-D:
   A. Asymptomatic, EF 25%  
   B. Symptomatic class II, EF 35%  
   C. Symptomatic class II, EF 35%, wide QRS  
   D. None of the above

10. This oil may prevent post-MI VT:
    A. Ginger oil  
    B. Groundnut oil  
    C. Olive oil  
    D. Fish oil