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EDITORIAL

Measures to Prevent Sudden Cardiac Death Early after Acute Myocardial Infarction

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ABSTRACT

Of all patients having an acute myocardial infarction (AMI), 25-35% will die of sudden cardiac death (SCD) due to ventricular fibrillation (VF) before seeking medical attention. For those who reach the hospital, prognosis is considerably better and has improved over the years. Reperfusion therapy, which is superior with primary percutaneous coronary intervention (PCI) versus thrombolysis, has made the difference. There is currently overwhelming evidence in favor of an expanded role and use of primary PCI in an attempt to reduce the risk of SCD early and late after an AMI. In-hospital SCD due to acute (<48 hours) ventricular tachyarrhythmias is manageable, with either preventive measures or electrical cardioversion; these arrhythmias do not portend an adverse late outcome. **Secondary prevention** of SCD in the early post-AMI period is accomplished via an implantable cardioverter defibrillator (ICD) for sustained ventricular arrhythmias emerging >48 hours after an AMI, not due to reversible or correctable causes. However, the major challenge remains that of **primary prevention** of SCD between the 48-hour period and the first 40 days post-AMI for patients who have low left ventricular ejection fraction (LVEF) and are not candidates for an ICD according to current guidelines. Two ICD trials (DINAMIT and IRIS) have shown no benefit of ICD in this early period. Two recent documents may provide direction as to how to bridge this early gap. The first relates to the "appropriate use criteria for ICDs and cardiac resynchronization therapy (CRT)", and the second is an "expert consensus statement on the use of ICD therapy in patients who are not included or not well represented in clinical trials".

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KEY WORDS: *acute myocardial infarction; sudden cardiac death; ventricular tachyarrhythmias; implantable cardioverter defibrillator; early post-MI period; electrophysiology study*

ABBREVIATIONS
ACC = American College of Cardiology
ACLS = advanced cardiac life support
AHA = American Heart Association
AMI = acute myocardial infarction
CRT = cardiac resynchronization therapy
EP = electrophysiology
ESC = European Society of Cardiology
ICD = implantable cardioverter defibrillator
LOE = level of evidence
LV = left ventricular
LVEF = left ventricular ejection fraction
MR = mortality rate
PCI = percutaneous coronary intervention
SCD = sudden cardiac death
VF = ventricular fibrillation
VT = ventricular tachycardia

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Ventricular arrhythmias are common during the early hours after acute myocardial infarction (AMI).[1,2] The mechanisms for these arrhythmias are multifactorial and include ongoing ischemia, hemodynamic and electrolyte abnormalities, reentry, and enhanced automaticity. Of all patients having an AMI, 25-35% will die of ventricular fibrillation (VF) before seeking medical attention. For those who reach the hospital, prognosis is considerably better and has improved over the years.

The long-term prognostic significance of early (<48 hours) VF or sustained ventricular tachycardia (VT) in patients with AMI remains dubious. In patients with AMI, early VF/VT may identify those at increased risk for 30-day mortality (22% vs 5%) as compared to those without VF/ VT. *Angiotensin converting enzyme (ACE) inhibitors/*

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angiotensin receptor blockers (ARBs) may reduce the 30-day mortality in these patients.[1] Other studies have confirmed that *beta-blocker* therapy, given in the first 24 hours after AMI in patients with early sustained VF/VT, was associated with reduced early mortality without worsening heart failure

Over the years, in-hospital mortality rate (MR) of AMI fell from 11.2% in 1990 to 9.4% in 1999. Most of the decline among patients with AMI is a consequence of ***reperfusion therapy*** via fibrinolysis or primary percutaneous coronary intervention (PCI), with primary PCI being superior to fibrinolysis.[3-5] Analysis by the National Registry of MI indicated that in-hospital MR was 5.7% among those receiving reperfusion therapy, as compared with 14.8% among those who were eligible for but did not receive such therapy.[4] In a meta-analysis [23 studies of primary PCI (3872 patients) and fibrinolytic therapy (3867 patients)],[3] MR at 4-6 weeks after treatment was significantly lower among those who underwent primary PCI (7% vs 9%).

Treatment of in-hospital sustained ventricular arrhythmias is usually easy and effective by applying immediate defibrillation or cardioversion for VF or pulseless sustained VT, respectively, and antiarrhythmic drug therapy according with the 2010 ACLS guidelines for sustained VT with a pulse.[6] The prophylactic use of lidocaine is not recommended. *Prevention* of in-hospital sudden cardiac death (SCD) due to VT/VF is directed toward correction of electrolyte and acid/base abnormalities, optimization of myocardial perfusion, eradication of ongoing ischemia, and treatment of associated complications such as heart failure or shock. Premature ventricular contractions (PVCs), nonsustained VT not associated with hemodynamic compromise, and accelerated idioventricular rhythms (AIVRs) that emerge after reperfusion are not indicative of increased SCD risk and do not require specific therapy in the acute phase of AMI.[1]

Thus, inhospital SCD due to ventricular tachyarrhythmias is manageable. The major mechanism of early death in patients who die the day of or the day following primary angioplasty (day 0 or 1) for AMI is usually pump failure (83%) and not ventricular tachyarrhythmias. Similarly, the major mechanism of death in patients who die within 30 days after primary angioplasty for AMI is still pump failure (61%),[7] and may be the reason why the implantable cardioverter defibrillator (ICD) has not been shown to be effective in reducing MR. However, there is still a good percentage of patients afflicted by SCD during this early period.

Decreased left ventricular (LV) function is a strong predictor of mortality. Although current guidelines recommend prophylactic ICD implantation after AMI and a depressed LV ejection fraction (LVEF) for 1 month, the prognoses of these patients may be better than those observed in randomized trials of ICDs (1-year mortality 6.8-19%), particularly because reperfusion treatment has improved, and the use of life-saving drugs is higher.[1] According to a prospective, observational study, assessing 1-year mortality in patients with depressed LVEFs after primary PCI, among patients who were alive >30 days after primary PCI but remained with low (<30%) LVEFs, overall 1-year mortality was as low as 5.8% compared with earlier times when primary PCI was not available.[8] However, still SCD remained the most common cause of death (40%). Patients who died more often had multivessel disease and a higher incidence of recurrent myocardial infarction within 1 year. Thus, there is still an important role for ICD therapy in these patients.

Current guidelines (**ACC/AHA guidelines 2013 / ESC guidelines 2012**) indicate:[1,2]

- ICD therapy is indicated before discharge for **secondary prevention** in patients who develop sustained VT/VF >48 hours after AMI, provided the arrhythmia is not due to transient or reversible ischemia, reinfarction, or metabolic abnormalities. (Class I, *LOE: B*)
- For other at-risk patients, particularly those with significantly reduced LVEF, candidacy for ICD therapy for primary prevention of SCD should be reassessed at 40 days after discharge
- For **primary prevention**, patients with an initially reduced LVEF who are possible candidates for ICD therapy should undergo reevaluation of LVEF ≥40 days after discharge. (Class I, *LOE: B*)
- The utility of a wearable cardioverter-defibrillator in high-risk patients during the first 4-6 weeks after AMI is under investigation
- Evaluation of the need for a primary preventive ICD implantation may, in some cases, be postponed until 3 months after revascularization procedures, to allow adequate time for recovery of LV function.

In general, patients who undergo coronary revascularization after AMI have a significantly lower rate of SCD than do patients who do not undergo revascularization.[9]

Secondary prevention of SCD in the early post-AMI period is accomplished via an implantable cardioverter defibrillator (ICD) for sustained ventricular arrhythmias emerging >48 hours after an AMI, not due to reversible or correctable causes.

However, the major challenge remains that of **primary prevention** of SCD between the 48-hour period and the first 40 days post-AMI for patients who have low LVEF and are not candidates for an ICD according to current guidelines. These guidelines rely on the results from mainly 2 studies:[10,11]

- The **DINAMIT** study[10] assessed ICD use in 674 patients within 4-40 days after AMI who were receiving optimal medical therapy, had LVEF ≤35% (mean 28%) and markers of autonomic dysfunction (low heart rate variability-HRV). Although low LVEF and low HRV identify patients with increased mortality risk, the trial did not identify any benefits from the use of ICD.
- The **IRIS** study showed similar results.[11] The study included 900 high-risk patients within 1 month of an AMI with LVEF <40% (mean LVEF 35%). Although the ICD

group had a significant decrease in arrhythmic MR, this was offset by an increase in nonarrhythmic death, similar to DINAMIT.

However, one should note that only 27% of patients were treated with primary PCI in the DINAMIT trial; a larger percentage of patients received primary PCI (72%) in the IRIS study. Despite the recommendations of the guidelines to avoid an ICD during the first 30-40 days post-AMI, the mortality risk remains high. According with the VALIANT trial results, mortality is highest early after an AMI, especially during the first one month and particularly for those with LVEF <30%.[12]

An electrophysiology (EP)-guided approach with targeted ICD implantation was proposed by an Australian study for patients after AMI treated with primary PCI. Early ICD implantation was limited to patients with inducible VT.[13] The conclusion of this study was that use of LVEF assessment and EP study for risk stratification soon after primary PCI for AMI, with ICD implantation limited to those with inducible VT, produces a uniformly low mortality on follow-up, including those patients with low LVEF. N.B.: in contrast to prior studies in patients with recent AMI, in which a minority of patients had PCI, this study had 95% of patients revascularized with primary PCI.

There is currently overwhelming evidence in favor of an **expanded role and use of primary PCI** in an attempt to reduce the risk of SCD early and late after AMI. Indeed, although LVEF is a predictor of increased risk for SCD, there is a low incidence of SCD in post-AMI survivors in the primary PCI era.[3-5,7-9,14]

In order to bridge the gap of the first 40 days after AMI for patients with low LVEF, the EPHESUS trial established the benefit of an aldosterone antagonist, eplerenone, added to optimal medical therapy in eligible patients; results indicated that earlier initiation of eplerenone (<7 days) significantly reduced the rates of all-cause mortality, SCD, and cardiovascular mortality/hospitalization.[15]

To further cover the gap of guideline direction regarding bridging for these 40 days after STEMI for patients with low LVEF, two documents have recently been published to guide us through this period of high risk:

According with the ACCF/HRS/AHA/ASE/HFSA/SCAI/SCCT/SCMR 2013 appropriate use criteria for ICDs and CRT, in patients with recent AMI (≤40 days) and low LVEF (≤40%), who develop nonsustained VT >4 days post-AMI, whether revascularized or not, an EP study may be used to guide therapy. Those with inducible VT receive an ICD early post-AMI without having to wait for those 40 days (Heart Rhythm 2013; 10. http://dx.doi.org/10.1016/j.hrthm.2013.01.008).[16] For those amenable to revascularization, the EP study should be performed after the revascularization procedure.

According to another very recent document "in patients who, within 40 days of an AMI, require ***nonelective permanent pacing,*** who also would meet primary prevention criteria for implantation of an ICD, and recovery of LV function is uncertain or not expected, implantation of an ICD with appropriately selected pacing capabilities *is recommended"* (HRS/ACC/AHA Expert Consensus Statement on the Use of Implantable Cardioverter-Defibrillator Therapy in Patients Who Are Not Included or Not Well Represented in Clinical Trials).[17] Also, "In patients who, within 40 days of an AMI, present with ***syncope*** that is thought to be due to ventricular tachyarrhythmia (by clinical history, documented nonsustained VT, or EP study), implantation of an ICD *can be useful".*

Similarly, according with the same document, "in patients within 90 days of revascularization who require *nonelective permanent pacing*, who would also meet primary prevention criteria for implantation of an ICD, and in whom recovery of LV function is uncertain or not expected, implantation of an ICD with appropriately selected pacing capabilities *is recommended".* Also, "in patients who within 90 days of revascularization present with *syncope* that is thought to be due to ventricular tachyarrhythmia (by clinical history or documented nonsustained VT, or EP study), implantation of an ICD *can be useful".*[17]

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